IAN 2026

XLIV Annual Meeting of
Indian Academy of Neurosciences

बीआरआईसी
बायोटेक्नोलॉजी विभाग का संगठन
BRIC
a DBT Organization

National Brain Research Centre
NBRC

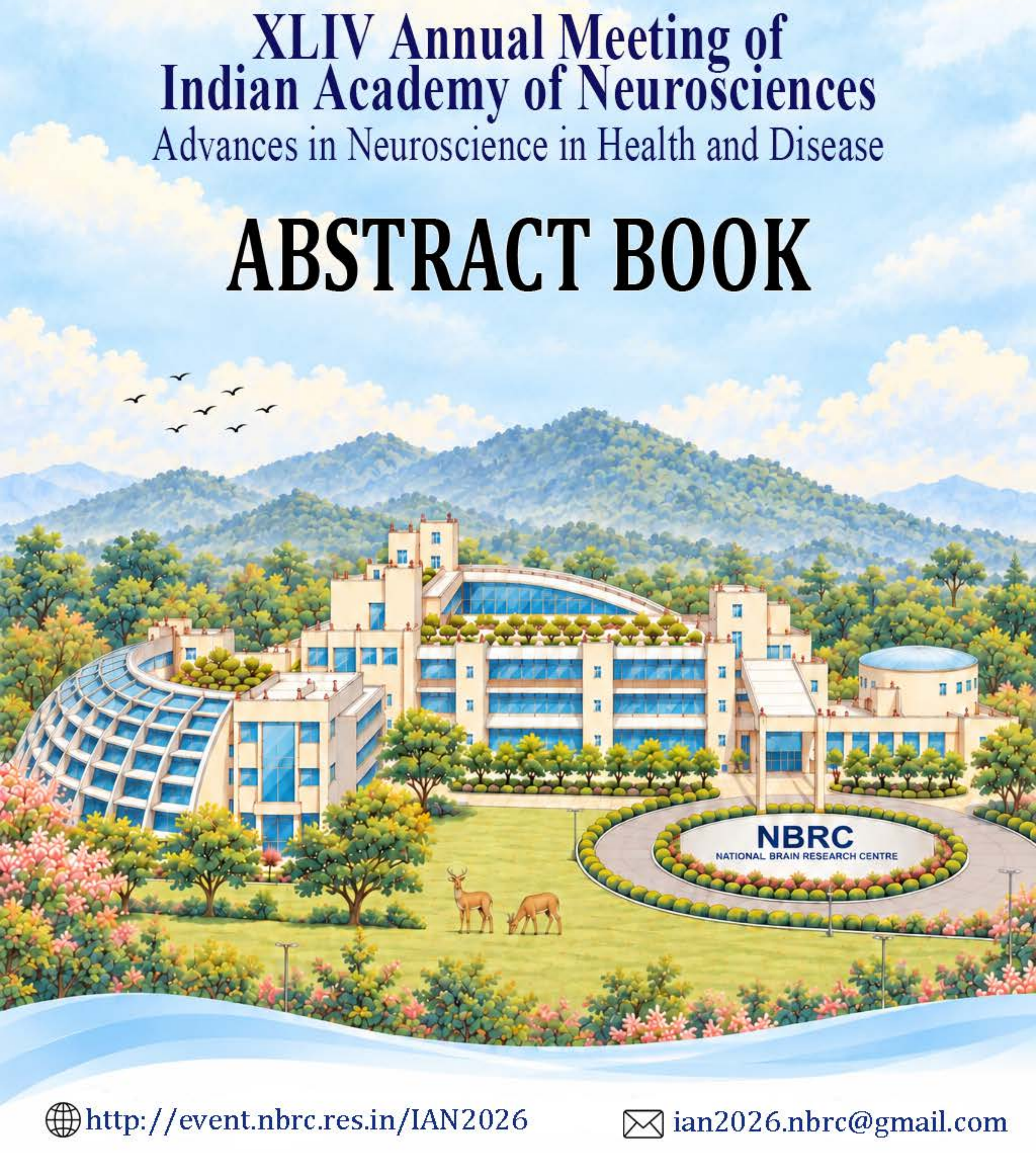
October 6-9, 2026

BRIC-National Brain Research Centre,
Manesar, India

XLIV Annual Meeting of Indian Academy of Neurosciences

Advances in Neuroscience in Health and Disease

ABSTRACT BOOK



http://event.nbrc.res.in/IAN2026

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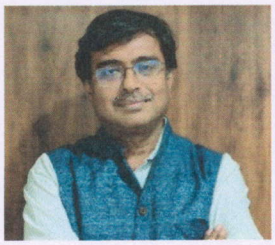
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National Brain Research Centre
राष्ट्रीय मस्तिष्क अनुसंधान केंद्र
एन बी आर सी
NBRC

ब्रिक-राष्ट्रीय मस्तिष्क अनुसंधान केंद्र
BRIC-National Brain Research Centre
(जैव प्रौद्योगिकी अनुसंधान एवं नवाचार परिषद, भारत सरकार)
एन॰ एच॰-08, मानेसर-122052 (हरियाणा), भारत
(An Institute of the Biotechnology Research and Innovation Council, Govt. of India), NH-08, Manesar-122052 (Haryana), INDIA

डॉ. सागर सेनगुप्ता, पीएच.डी.
एफएनएएससी, एफएएससी, एफएनए
निदेशक (अतिरिक्त प्रभार)

Dr. Sagar Sengupta, Ph.D.
FNASc, FASc, FNA
Director (Additional Charge)



Welcome Address for IAN 2026

It gives me immense pleasure to welcome all delegates, distinguished scientists, clinicians, young researchers and students to the **XLIV Annual Meeting of the Indian Academy of Neurosciences (IAN 2026)**, being hosted by the **BRIC-National Brain Research Centre (NBRC), Manesar**, India.

The Annual Meeting of the Indian Academy of Neurosciences has, over the years, evolved into an important national forum for bringing together diverse disciplines engaged in understanding the brain and nervous system. Neuroscience today stands at a remarkable intersection of basic biology, medicine, technology, computation and engineering. Advances in genomics, neuroimaging, artificial intelligence, single-cell and spatial approaches, neurotechnology and systems neuroscience are providing unprecedented opportunities to understand the complexity of the human brain and to translate this knowledge into better approaches for the prevention, diagnosis and treatment of neurological and psychiatric disorders.

The theme and scientific programme of IAN 2026 provide an opportunity to reflect on these exciting developments while fostering dialogue across disciplines. Equally important, such meetings provide a platform for young investigators and students to interact with established researchers, exchange ideas and build collaborations that can shape the future of neuroscience in India.

For BRIC-NBRC, hosting the Annual Meeting of IAN is particularly meaningful. The Centre was established with the vision of advancing brain research in India through excellence in fundamental and translational neuroscience, while nurturing the next generation of neuroscientists. We are therefore delighted to welcome the Indian neuroscience community to our campus and to share in this collective endeavour of advancing our understanding of the brain.

I am confident that the scientific deliberations, discussions and interactions during IAN 2026 will generate new ideas, strengthen existing collaborations and open new avenues for interdisciplinary research. Beyond the formal scientific sessions, I hope the meeting will provide an atmosphere of collegiality, curiosity and intellectual exchange that will remain with all participants long after the meeting concludes.

On behalf of the **BRIC-National Brain Research Centre**, I extend my warm greetings to the office-bearers and members of the **Indian Academy of Neurosciences**, the organising committee, invited speakers and all participants. I wish **IAN 2026** a stimulating and memorable meeting and look forward to welcoming you all to Manesar.

With best wishes for a successful and intellectually enriching IAN 2026.

Sagar Sengupta
Director (Additional Charge)
BRIC-National Brain Research Centre
Manesar (Gurgaon), Haryana, India

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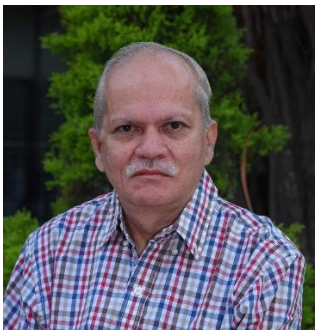
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INDIAN ACADEMY OF NEUROSCIENCES

(Registered Under Societies Registration Act XXI 1860)

Dr Vinay K. Khanna
PhD, FNASc, FIANS, FST, FAEB
President

September 27, 2026



Message

I extend my warm greetings to the members and delegates on the occasion of ***XLIV Annual Meeting of the Indian Academy of Neurosciences*** being hosted by BRIC – National Brain Research Centre, Manesar, India, from October 6 – 9, 2026.

The growing burden of neurological and psychiatric disorders is a cause of serious concern. Despite complexities of the human brain, significant breakthroughs in research both in basic and clinical neurosciences have helped to develop better strategies in the prevention, diagnosis, and treatment of neurological and psychiatric disorders. Translating scientific advances into affordable and accessible healthcare still remain a serious challenge.

The theme of the conference this year - Advances in Neuroscience in Health and Disease, is contemporary and highly relevant. The scientific programme curated for the meeting promises to present the most recent advances and will serve the best delicacies in neuroscience.

I am confident that the deliberations, interactions and exchange of ideas among the neuroscientists, young researchers and students will establish new collaborations and pave the way for shaping the future of neuroscience.

I convey my heartfelt congratulations to the organizing committee and all those who have worked diligently to bring this important scientific gathering to fruition.

With best wishes,

Vinay Kumar Khanna

Former Chief Scientist & Professor AcSIR, Area Coordinator - Systems Toxicology & Health Risk Assessment Group & Food, Drug and Chemical Toxicology Group, CSIR - Indian Institute of Toxicology Research, Vishvigyan Bhavan 31, Mahatma Gandhi Marg, Lucknow - 226 001, Uttar Pradesh, India
Email: neuroscienceacademy@gmail.com; vkkhanna1@rediffmail.com

Local Organizing Committees

Organizing Secretary, IAN-2026 - Pankaj Seth

Co- Organizing Secretary IAN-2026 - Sourav Banerjee

Co- Organizing Secretary IAN-2026 - Dhananjay Huilgol,

Scientific sessions Committee: Soumya Iyengar, M Dhruba Singh, Vidhya Munnamalai, Bhavani Shankar Sahu

Registration and conference website Committee: Anirban Basu, Dhananjay Huilgol, Khushbu Agarwal

Accommodation and Transport Committee: Ahmad Raza Khan, Anindya Ghosh-Roy, Ellora Sen , Arpan Banerjee

Food Committee: Bhavani Shankar Sahu, Sourav Banerjee

Sponsorship Committee: Anirban Basu, Bhavani Shankar Sahu, Dhananjay Huilgol, Pankaj Seth.

Time	Program / Activity
10:00 - 11:00	**Inaugural Function**
10:00	Lighting of the lamp
10:05	Welcome Address- Dr. Pankaj Seth, Organising Secretary
10:15	IAN Secretary's Report-Dr. Suman Jain, General Secretary-IAN
10:25	Introduction of Newly Elected - Dr. Rajat Sandhir, IAN Fellows Dean-IAN
10:35	Address by the IAN President- Dr. Vinay Kumar Khanna, Chief Scientist, IITR, Lucknow & IAN President
10:45	Presidential Address - Dr. Sagar Sengupta, Director, BRIC-NBRC
10:55	Vote of Thanks - Dr. Dhananjay Huilgol, Convener National Anthem

44th Annual Meeting of Indian Academy of Neurosciences

(October 6th – 9th, 2026)

Theme: Advances in Neuroscience in Health and Disease

Scientific Programme IAN-2026

(Host institution: BRIC-National Brain Research Centre, Manesar, India)

Conference Venue: Savoy Suites, Manesar (Gurgaon), Haryana, India

Keynote Talks – 35+10 min; Plenary Talks – 30+5 min;

Symposium talks – 20+4 min; Short Talks – 10+2 min; Oral Session talks - 12+3 min

Day 1 (6th October 2026; Tuesday)

Time	Hall 1	Hall 2
09:30 - 11.00	**Registration and Inauguration (Welcoming new IAN fellows)**	
11:00 – 13:00	**Science Policy and Current funding priorities of funding agencies** **Moderator – TBD** **Coordinator 1: Garima Gupta** Department of Biotechnology, Govt of India, Delhi, India **Coordinator 2: Balachandar Venkatesh** Anusandhan National Research Foundation, Govt of India, India **Coordinator 3: Parthasarathi Ramakrishnan** HRD, Council of Scientific & Industrial Research, Govt of India, India	**Skills of Scientific Communication** **Moderator – TBD** **Panelists –** **Sandhya Koushika, TIFR, Mumbai** **Jonaki Sen, IIT-Kanpur** **Vatsala Thirumalai, NCBS, Bengaluru** https://forms.gle/bv9yMWNEjp8tuqLY6
13:00 – 14:00	**Lunch**	
14:00 – 14:45 **Hall 1**	**Keynote Lecture 1 (Hall 1)** Chairpersons: Pankaj Seth BRIC-NBRC, Vinay K Khanna, Lucknow **Speaker: Vidita A. Vaidya** Tata Institute of Fundamental Research, Mumbai, India **Title:** *Serotonergic psychedelics – from molecules to mood*	

14:45 – 15:20 **Hall 1**	**Plenary Lecture 1 (Hall 1)** Chairpersons: Vidita Vaidya, TIFR, Mumbai, Aurnab Ghose, IISER-Pune **Speaker: Christian Gonzalez-Billault,** Universidad de Chile, Chile **Title:** *Cell biology of the neuron, from development through aging*	
15:20 – 15:30	***Technical Talk 1*** Coordinators: Yogita Adhlakha, Amity NOIDA / Kaushik Sharma, SRHU, Dehradun ***Speaker:*** **Stephan Martin, DSI (Harvard Bioscience)** **Title:** Cardio-Genomic & Neuro-Cardiovascular Interactions in Unrestrained Models	
15:30 – 16:00	**Networking over tea and cookies**	
	Hall 1	**Hall 2**
16:00 – 18:00	**Symposium I** ***Neurodevelopmental & psychiatric disorders*** ***Chairpersons:*** Bhavana Muralidharan BRIC-inStem, Bengaluru M Dhruba Singh, BRIC-NBRC **1. Sabita Mishra** Maulana Azad Medical College, Delhi, India **Title:** *Transmission electron microscopy of the human fetal cochlear nucleus in the prenatal period* **2. Sandipan Ray** Indian Institute of Technology, Hyderabad, India **Title:** *Delineating the underlying mechanism of action of Lithium in modulating behavioral rhythms and metabolism* **3. Lucina Uddin** University of California, Los Angeles, USA **Title:** *Towards a universal taxonomy of functional brain networks*	**Symposium II** ***Dissecting circuits for behaviours*** ***Chairpersons:*** Sourav Banerjee BRIC-NBRC, Manesar Kavita Babu, CNS, IISc, Bengaluru **1. Kausik Si** Stowers Institute for Medical Research, Kansas City, USA **Title:** *Encoding memory in amyloids* **2. Prabahan Chakaraborty** SRM Institute of Science and Technology, Kattankulathur, India **Title:** *Circuit and memory deficits in obesity: rescue by meal scheduling* **3. Nitin Singh Chouhan** Tata Institute of Fundamental Research, Mumbai, India **Title:** *Distinct neurotransmitters mediate state-dependent memory consolidation in Drosophila*

	4. Tanzila Mukhtar University of Kashmir, India **Title:** *α7 nicotinic acetylcholine receptors regulate radial glia fate in the developing human cortex* **5. Short talk***:* **Abhinav** Postgraduate Institute of Medical Education and Research, Chandigarh, India **Title:** *NMDA receptor subtype GluN2B modulates synaptic transmission and plasticity in the neocortex* **6**. **Short talk***:* **Shweta Yalshetti** The Indian Institute of Technology Dharwad, India **Title:** *Stress–Stroke Interactions: investigation of molecular mechanisms underlying the adverse effects of stress on stroke outcomes,*	**4. Hassan Mohd** Indian Institute of Scientific Education and Research-Mohali, India **Title:** *Top-down circuits regulating compulsive eating behaviour* **5. Short talk***:* **Mouli Dutta** Presidency University, Kolkata, India **Title:** *Elucidating the role of Sox2ot in sex-dependent behavioural consequences of early life stress* **6. Short talk***:* **Seetha Khandige** Manipal Academy of Higher education, Manipal, India **Title:** *Dysfunctional anterior default mode network in obsessive-compulsive disorder: an EEG microstate analysis*
18:00 – 19:00 **Hall 1**	**Panel Discussion:** *Diversity and Inclusion in Neuroscience* Moderator: Lucina Uddin, University of California, Los Angeles, USA Panelists: Vidita A. Vaidya, TIFR, Mumbai, Shashi Bala Singh, Delhi, Ellora Sen BRIC-NBRC, Manesar, Christian Gonzalez-Billault Universidad de Chile, Chile, Sabine Kastner, USA, Prasanna Reddy, DIPAS, Delhi.	
19:00 – 20:00 **Hall 1**	**Sabine Kastner,** Princeton University, USA and Editor-in-chief, Journal of Neuroscience. **Chairpersons:** Sourav Banerjee, Manesar, Khushbu Agarwal, BRIC-NBRC, Manesar **Title: TBA**	
20:00 onwards	**Networking Dinner:** ***make new synapses and strengthen the existing ones***	

Day 2 (7th October 2026; Wednesday)

Time	Hall 1	Hall 2
09:00 - 09:45 **Hall 1**	**B.K. Bachhawat Memorial Lifetime Achievement Award Lecture** **Chairpersons:** Vinay K Khanna, Lucknow and Shashi Bala Singh, New Delhi **Speaker: Y.K. Gupta** AIIMS, Kalyani, India **Title: The Neuropharmacology Expedition: Research, Mentorship, and Clinical Impact**	
09:45 - 10:20 **Hall 1**	**Plenary talk 2** **Chairpersons:** Sheffali Gulati, AIIMS, New Delhi, Suman Jain, AIIMS, New Delhi **Speaker: Vatsala Thirumalai** National Centre for Biological Sciences (NCBS-TIFR), Bengaluru, India **Title:** *Neural circuits generating behaviorally relevant predictions and their developmental emergence*	
10:20 - 10:45	**Networking over tea-coffee & snacks**	
10:45 – 1:00	**Symposium III** ***Glia in health and disease*** **Chairperson:** Ishan K. Patro, Jiwaji University, Gwalior Vidhya Munnamalai, BRIC-NBRC, Manesar **1. Binukumar B.K** CSIR-Institute of Genomics and Integrative Biology, New Delhi, India **Title:** *Cdk5-mediated oligodendrocyte activation, neuroinflammation, and mitochondrial dysfunction: a mechanistic link between Type 2 diabetes and Alzheimer's disease*	**Symposium IV** ***AI-ML and BMI for Neuroscience*** **Chairpersons:** Dipanjan Roy, IIT-Jodhpur Ahmad R Khan, BRIC-NBRC, Manesar **1. Brigitte Röder** University of Hamburg, Germany **Title:** *The role of visual experience for the development of recurrent processing in the human brain*

	2. Shubha Tole Tata Institute of Fundamental Research, Mumbai, India **Title:** *Regulation of gliogenesis in the developing cerebral cortex* **3. Bhavana Muralidharan** BRIC-inStem, Bengaluru, India **Title:** *Human brain-enriched extracellular matrix genes regulate progenitor dynamics and cortical folding* **4. *Short talk:* Apoorva** Banaras Hindu University, Varanasi, India **Title:** *West Nile Virus downregulates TRIM71 to inhibit type I interferon response in human microglial cells* **5. *Short talk:* Vanshika Ahuja** Sir Ganga Ram Hospital, Delhi, India **Title:** *Altered stress granules and Paraspeckle dynamics by ALS-associated FUS mutations in neuronal and astrocytic models.*	**2. Kamalesh K Gulia** Sree Chitra Tirunal Institute for Medical Sciences & Technology, Trivandrum, India **Title:** *Prenatal sleep deprivation and altered behaviour in offspring: AI-ML tools to decipher bioacoustics in babies* **3. Sridharan Devarajan** Indian Institute Science, Bengaluru, India **Title:** *Tracking and training attention with a cognitive Brain Machine Interface* **4. Vivek Tiwari** Indian Institute of Scientific Education & Research-Behrampur, India **Title:** *AI-driven functional neuroimaging and lesion network mapping in cognitive states an epilepsy: inflammatory and vascular cascades mediate white matter hyperintensity-induced network desegregation* **5. Sanjeev Nara** Indian Institute of Technology - Mandi, India **Title:** *Neural correlates of aestheic experiences in natural environments: Insights from neuroimaging and Deep Neural Networks* **6. Short talk*:* Madhuvanthi Muliya** Indian Institute of Technology Madras, Chennai, India **Title:** *CADUN: A computational Framework of spatial decision making under uncertainty using utility-driven reinforcement learning* **7. Short talk*:* Manojkumar K.** CSIR-Centre for Cellular and Molecular Biology, Hyderabad, India

		Title: *KiMA: An open-source, web-based suite for multi-modal gait and kinematics analysis in spinal cord injury models*
13:00 - 14:00	**Lunch**	
14:00 – 16:00	**Poster session I - (Hall 3) Poster number 001 – 098**	
16:00 – 16:35 Hall 1	**Plenary Talk 3** **Chairpersons:** *Anirban Basu, BRIC-NBRC, Sunit K Singh, ACBR, New Delhi* **Speaker: Manjari Tripathi** All India Institute of Medical Sciences (AIIMS), New Delhi, India **Title:** *Magnetic source images for maximising precision*	
16:35 – 18:30	**Symposium V** ***Nutrition, Gut and the Brain*** ***Chairpersons:*** S.N Singh, DIPAS, New Delhi Aurnab Ghose, IISER-Pune **1. Arup Acharjee** University of Allahabad, Prayagraj, India **Title:** *From proteomic discovery to functional rescue: FAK1 inhibition restores hippocampal synaptic homeostasis and cognition in hepatic encephalopathy* **2. Gaurav Das** BRIC-National Centre for Cell Sciences, Pune, India **Title:** *Neuronal toll signaling mediates metabolic adaptation to mild dietary oxidative stress in Drosophila* **3. Papia Acharjee** Banaras Hindu University, Varanasi, **Title:** *Hippocampal proteome study identifies emerging role of fetuin a in neuroinflammation in aging brain with minimal hepatic encephalopathy: study in a rat model*	**Symposium VI** ***Neuroscience of Sleep &Consciousness*** ***Chairpersons:*** KP Mishra, DIPAS, New Delhi Sheeba Vasu, JNCASR, Bengaluru **1. Dinesh Pal** University of Michigan, Ann Arbor, USA **Title:** *Serotonergic psychedelics: modulation of sleep and anesthetic-induced unconsciousness* **2. Krishna Melnattur** Ashoka University, Sonipat, India **Title:** Mutations in Drosophila antimicrobial peptides differently affect sleep and plasticity **3. Sheeba Vasu** Jawaharlal Nehru Centre for Advanced Scientific Research, Bengaluru, India **Title:** *How populations derived by laboratory selection for early and late circadian phases have co-evolved divergent sleep architecture*

	4. Suman Jain AIIMS-New Delhi, India ***Title:*** *Combinatorial Strategy of Probiotics and cortical Transcranial magnetic stimulation promote functional recovery in rat model of Parkinson's disease by modulating gut-brain axis* **5.Short talk: Manu Mallahalli** National Institute of Neuroscience, Tokyo, Japan **Title:** *Microbial signals drive neuroinflammation and CNS degeneration via host immune programming* **6. Short talk: Pratik R. Chaudhari** Indian Institute of Technology Madras, Chennai, India **Title:** *Nicotinamide supplementation prevents the emergence of early-life stress driven inflammatory signatures, blood-brain barrier compromise, hippocampal mitochondrial dysfunction and cognitive aging*	**4. Sushil Jha** Jawaharlal Nehru University, New Delhi, India ***Title:*** *Why sleep is essential for effective learning and memory?* **5. Short talk: Pallabi Kisku** BRIC-National Brain Research Centre, Manesar, India **Title:** *Role of sleep-regulated lncRNAs in translation machinery and memory consolidation in the hippocampus* **6. Short Talk: Shubham S Bartwal** National Institute of Pharmaceutical Education and Research (NIPER), Hajipur, Bihar, India **Title:** *Taxifolin as a novel melatonergic chronopharmacological modulator restores sleep, mood, and social behaviour in environmental rhythm disruption*
18:30 – 18:45	**Networking over tea-coffee & snacks**	
18:45 – 20:45	**Oral Session - I** **Neurodegenerative disorders** **Chairpersons:** Nisha Patro, Jiwaji University, Gwalior Sabita Mishra, MAMC, Delhi **Speakers:** **Usha Rajamma (Newly elected IAN Fellow)** Inter-University Centre for Biomedical Research & Super Specialty Hospital, Kottayam, India	**Oral Session - II** **Neurodegeneration & Age-related Disorders** **Chairpersons:** Rajinder Gupta, DIPAS, New Delhi Chinmay Mukhopadhyay, Jawaharlal Nehru University, New Delhi **Speakers:** **Thomas Gregor Isaac (Newly elected IAN Fellow)** Centre for Brain Research, Indian Institute of Science, Bengaluru, India **Title:** *Understanding modifiable risk and resilience factors of Dementia in the Indian context*

	Title: *Mitochondrial DNA on nuclear genome: insight into autism spectrum disorder aetiology*	
	Mehdi Hayat Shahi (Newly elected IAN Fellow) Aligarh Muslim University, Aligarh	**RajniKant Mishra** Banaras Hindu University, Varanasi
	Title: *The Sonic Hedgehog (Shh) cell signaling pathway is a formidable target for brain tumor therapy.*	**Title:** Pax6 affects genes of motor and non-motor functions in brain
	Yogita K. Adlakha Amity University, NOIDA, India	**Suhail Rasool,** Suninflam, Palo Alto, USA
	Title: *Metabolomic profiling reveals dynamic changes in fatty acid metabolism during human neural stem cell fate commitment*	**Title:** *Reversal of Alzheimer's Disease pathology by TB006 antibody targeting Galectin-3*
	Vibha Taneja Sir Gangaram Hospital, New Delhi	**KP Mohanakumar** Inter-University Centre for Biomedical Research & Super Specialty Hospital, Kottayam, India
	Title: *Genetic and epigenetic (microRNA) determinants in ALS: Insights from a North Indian Cohort*	**Title:** *Water Beetle as a Novel Animal Model for Parkinson's Disease*
	Prachi Srivastava Amity University Uttar Pradesh Lucknow Campus, Lucknow	**Surya Pratap Singh** Banaras Hindu University, Varanasi
	Title: *Toxicology approaches reveal potential molecular targets of neurological issues associated with progression of organic and persistent organic pollutant*	**Title:***18β-Glycyrrhetinic acid regulates autophagy dysregulation in the MPTP/p-induced model of Parkinson's disease*
	Madhumita Ghosh Amity University, NOIDA, India	**Abhishek Kumar Singh** Manipal Academy of Higher Education, Manipal
	Title: *Dopamine promotes retinal progenitor cell integration and layer repair in NMDA induced degeneration models*	**Title:** *Senolytic nanocarriers targeting Alzheimer's Disease-Associated senescence and neurodegeneration*

	Pankaj Kumar Indira Gandhi Institute of Medical Sciences, Patna **Title:** *Therapeutic potential of TUDCA in modulating retinal microglial activation, oxidative stress, and neuroinflammation in diabetic retinopathy* **Amrita Pathak** Amity University Noida, India **Title:** *Long distance signalling by Degenerative Signalling Endosomes in Neurodevelopment and disease*	**Mani Chopra** Department of Zoology Panjab University – Chandigarh **Title:** *Prenatal stress mediated gut-brain axis perturbations and associated behavioral deficits: Attenuation by gestational Morin in Wistar rats*
20:45 onwards	**Networking Dinner:** ***make new synapses and strengthen the existing ones***	

Day 3 (8th October 2026; Thursday)

Time	Hall 1	Hall 2
09:00 – 09:45 **Hall 1**	**KT Shetty Oration** **Chairpersons:** Pankaj Seth, BRIC-NBRC, Manesar, Rajat Sandhir, Panjab University, Chandigarh **Speaker: Ravi Manjithaya,** JNCASR, Bengaluru, India **Title:** *Modulation of autophagy in the context of movement disorders*	
09:45 - 10:30 **Hall 1**	**Keynote Lecture 2** **Chairpersons: Shashi Bala Singh, New Delhi and Soumya Iyengar, BRIC-NBRC, Manesar** **Speaker: Nachum Ulanovsky** Weizmann Institute of Science, Rohovat, Israel **Title:** *Neuroscience going wild: Neural coding in social groups of bats and in bats navigating outdoors on a remote oceanic island*	
10:30 – 11:05	**IAN-FAONS Plenary talk 4**	

Hall 1	**Speaker: Goichi Miyoshi** Gunma University Graduate School of Medicine, Japan **Chairpersons:** Dhananjay Huilgol, BRIC-NBRC, Manesar, Usha Panjwani, New Delhi **Title:** *An early postnatal critical period for the development of inhibitory neurons in social circuit regulation*	
11:05 – 11:15	**Technical Talk 2** Coordinators: Prachi Srivastava Amity NOIDA & Kanchan Bisht, SRHU, Dehradun **Speaker: Dr Manik, Thermofisher Scientific** ***Title:*** *Spatial Biology: Upcoming solution from Thermofisher Scientific*	
11:15 – 11:25	**Technical Talk 3** Coordinators: TBA **Speaker: Mr. Shridhar Tiwari, Leica** ***Title:*** *Nanoscale Super-Resolution-TauSTED Xtend: Sharp, Simple, Stunning*	
11:25 – 12:00	**Networking over tea-coffee & snacks**	
12:00 – 13:45	**Symposium VII** ***Physiology & pathophysiology of endocrine systems*** **Chairpersons:** Bhavani Sahu, BRIC-NBRC, Manesar Bhupesh Mehta, NIMHANS, Bengaluru **1. Anita Jagota** University of Hyderabad, Hyderabad, India **Title:** *Clock dynamics in aging and neurodegenerative disorders: therapeutic interventions* **2. Ashok Kumar Datusalia**	**Symposium VIII** ***Neurobiology of reward and addiction*** **Chairpersons:** Sushil Jha, JNU, New Delhi Soumya Iyengar, BRIC-NBRC, Manesar **1. Yoganarasimha Doreswamy** National Institute of Mental Health and Neurosciences, Bengaluru, India **Title:** *Neuromodulatory effects of transcutaneous auricular vagus nerve stimulation (taVNS) in an animal model of endogenous depression* **2. Meenakshi Bawari** Assam University, Silchar, India **Title:** *In silico investigation of phytochemical modulators targeting opioid and dopaminergic receptors:*

	National Institute of Pharmaceutical Education and Research- Raebareli, India **Title:** *Behavioural stratification reveals molecular and structural correlates of stress vulnerability and resilience* **3. B.N. Srikumar** National Institute of Mental Health and Neurosciences, Bengaluru, India **Title:** *The sex-specific interplay between cholinergic signaling and finasteride on depression and cognition* **4. Giriraj Sahu** Indian Institute of Science, Bengaluru, India **Title:** *Interfering peptides targeting the intrinsic inhibitory slow afterhyperpolarization protein complex stabilize neuronal excitability and restrict epileptic seizures.* **5. Short talk: Sushma Dagar,** BRIC-National Brain Research Centre, Manesar, India **Title:** *Obesity-associated metabolic stress impairs dense-core vesicle exocytosis through VAMP2 SUMOylation in neuroendocrine cells*	*implications for reward pathway regulation and addiction therapeutics* **3. Suhel Parvez** Jamia Hamdard, New Delhi, India **Title:** *Integration of peripheral and central immune alteration in neurodegeneration* **4. Gurudutt Pendyala** University of Nebraska Medical Center, Omaha, USA **Title:** *Novel insights from chronic midazolam exposure on neonates and long-term neurodevelopment* **5. Short Talk: Vishal Chhabra** National Institute of Pharmaceutical Education and Research (NIPER), Hajipur, India **Title:** *GLP-1R–HCRTR2 crosstalk in gut dysbiosis drives metabolic and circadian disruption leading to cognitive impairment*
13:45 - 14:30	**Working Lunch**	
14:30 – 16:30	**Poster session II with Tea and Coffee** **Poster number 099 - onward**	
16:30 – 17:05 **Hall 1**	**Plenary Talk 5** **Chairpersons:** Sandhya Koushika, TIFR, Mumbai, Kavita Babu, IISc, Bengaluru	

	Speaker: Manuel Zimmer **EMBO Global Investigator** University of Vienna, Austria **Title:** *Neuronal population dynamics of sensory processing and decision making in C. Elegans*
17:05 – 19:00	**Young Scientist Colloquium-I: Tulsabai Somani Educational Trust Award** (for early career scientists below 40: includes senior graduate students and postdocs) **Chairpersons:** Vijay Paramanik, Indira Gandhi National Tribal University, Amarkantak and Vinod Tiwari, Banaras Hindu University, Varanasi
17:05 – 17:15	**Akshaya R**, Indian Institute of Scientific Education and Research, Trivandrum *Title: Metabolic dysregulations associated with diabetes influence Parkinson's disease pathology in the brain and peripheral tissues of mice*
17:15 – 17:25	**Zeenia Kersi Avari**, Institute for Advanced Training & Research in Interdisciplinary Sciences, Mumbai. *Title: Molecular Heterogeneity in GNE Myopathy: Domain-Specific Mutation Patterns*
17:25 – 17:35	**Utkarsh Prakash Patil**, Rashtrasant Tukadoji Maharaj Nagpur University, Nagpur *Title: CART peptide regulates motivated behaviours via reciprocal nucleus accumbens-ventral tegmental area direct and indirect circuitry*
17:35 – 17:45	**Keerthana Padmanabhan**, National Institute of Mental Health and Neuro Sciences, Bengaluru *Title: Altered structural and synaptic plasticity, neurochemical changes contribute to depression- and anxiety-like behaviour in a rat model of Premenstrual Dysphoric Disorder (PMDD)*
17:45 – 17:55	**Tanwi Trushna**, ICMR National Institute for Research in Environmental Health (ICMR-NIREH), Bhopal *Title: Auditory P300 Responses During High Particulate Exposure Episodes: Pilot Case-Crossover Evidence from Healthy Adults*
17:55 – 18:05	**Harsha P J**, Inter-University Centre for Biomedical Research & Super Specialty Hospital, Kottayam. *Title: Mimosine suppresses ferroptosis nexus linking labile iron, glutathione and lipid peroxidation in experimental animal model of neurodegeneration*
18:05 – 18:15	**Puja Ghosh,** BRIC-Institute for Stem Cell Science and Regenerative Medicine Bengaluru

18:15 – 18:25	*Title: Loss of the chromatin modifier- ISD1 impairs ependymal development and ciliary function leading to ventriculomegaly* **Anjali,** BRIC-National Brain Research Centre, Manesar *Title: Developmental trajectories of Inhibitory Interneurons and Perineuronal Nets in the Human Auditory Cortex*
19:00 – 20:00	**Indian Academy of Neurosciences General Body Meeting**
20:00 onwards	**Cultural Programme and Gala Dinner**

Day 4 (9th October 2026; Friday)

Time	Hall 1
09:00-09:45	**S. S. Parmar Oration** **Chairpersons:** Raj Mehra, Gurgaon, Ashok K Agrawal**,** Lucknow **Speaker: Anindya Ghosh-Roy,** BRIC-National Brain Research Centre, Manesar, India **Title:** *Neuronal Injury Model Reveals Differences in Axon and Dendrite Regeneration*
09:45-10:20	**Plenary Talk 6** **Chairpersons:** Anita Jagota, University of Hyderabad, Hyderabad, Gurudutt Pendyala, University of Nebraska Medical Centre, Nebraska, USA **Speaker: Amita Sehgal** Perelman School of Medicine, University of Pennsylvania, Philadelphia, USA. **Title:** *Metabolic basis of sleep*
10:20 – 11:05	**P.N. Tandon Oration** **Chairpersons:** Ishan Patro, Jiwaji University and Anirban Basu, Manesar **Speaker –Ashish Suri, AIIMS-New Delhi**

	Title: *From Prof. P. N. Tandon's Laboratory to an AI-Enabled Future: Five Decades of Simulation-Based Neurosurgical Skills Training at AIIMS, New Delhi*
11:05 - 11:15	**Technical Talk 4** **Coordinators: TBA** **Speaker: Dr. Titas Mondal, Lab India** ***Title:*** *Thinking outside the flask: 3D cell culture with Clinostar*
11:15 - 11:25	**Technical Talk 5** **Coordinators: TBA** **Speaker: Dr. Paramita Sen** **Title:** *Femtoquest*
11:30 – 13:00	**Young Scientist Colloquium-II: DM Kar Prize** (for early career scientists below 35: includes young graduate students) **Chairpersons:** Surajit Sarkar, Delhi University, Delhi, and Krishan K Soni, PGIMER, Chandigarh
11:35 – 11:45	**Nishad Keethedeth**, Inter University Centre for Biomedical Research & Super Specialty Hospital, Kottayam, Kerala *Title: Mitochondria-Targeted Antioxidants Restore Striatal Dopamine and Protect Nigral Neurons in Parkinson's Disease Model*
11:45 – 11:55	**Komal Bana**, Indian Institute of Technology, Roorkee *Title: Astrocyte-Derived Exosomal Signaling Drives Pathological Neuronal Transcriptional Reprogramming in Alzheimer's Disease*
11:55 – 12:05	**Bhaskar Sharma**, All India Institute of Medical Sciences, New Delhi *Title: Kallikrein–Kinin-Mediated Immune Activation in Age-Associated Choriocapillaris Degeneration*
12:05 – 12:15	**Savitra Ambadas Bothikar**, Rashtrasant Tukadoji Maharaj Nagpur University, Nagpur. *Title: Central amygdala to hypothalamic paraventricular nucleus glutamatergic circuitry regulates anger-induced physiological and behavioural responses* **Karishma Abhishek S**, National Institute of Mental Health and Neuro Sciences, Bengaluru.

12:15 – 12:25	*Title: Chloride Homeostasis at the Crossroads of Excitatory–Inhibitory Imbalance, and Neurobehavioral Comorbidities in Temporal Lobe Epilepsy: Therapeutic Implications* **Dhanshree Sayangrushi Borkar**, National Forensic Sciences University, Gandhinagar.	
12:25 – 12:35	*Title: Molecular Signatures of Nano-neonicotinoid Neurotoxicity: Linking Striatal Gene Expression to Neurobehavioral Dysfunction in Mice* **Mohit Kumar**, BRIC- National Agri-Food and Biomanufacturing Institute, SAS Nagar, Mohali	
12:35 – 12:45	*Title: Sex-Specific Effects of Nutritional Ketosis on Sugar Withdrawal Symptoms, Sugar Craving and Compulsive-like Behavior in C57BL/6 Mice* **Anirudh Satheesan**, BRIC- National Brain Research Centre, Manesar	
12:45 – 12:55	*Title: Acute Japanese encephalitis virus-associated gut dysbiosis and protective effects of short-chain fatty acids on neuroinflammation in neonatal mice*	
13:00 – 14:00	**Lunch**	
14:00 – 15:00	**ALBA-IBRO session: Navigating non-academic careers in neuroscience** Session with panelists organized by Keerthana Iyer, ALBA Network-FENS	
15:00 – 17:00	**Symposium IX** ***Connectomics and adaptive reorganization*** **Chairpersons:** Amrutha Swaminathan, IISER-Trivandrum, Trivandrum. Anindya Ghosh-Roy, BRIC-NBRC, Manesar **1. Anil Annamneedi** Sai University, Chennai, India	**Symposium X** ***Cell and molecular biology of neurons*** **Chairpersons:** Sandhya Koushika, TIFR, Mumbai Akshay Anand, PGIMER, Chandigarh **1. Swananda Marathe** Indian Institute of Technology - Dharwad, India

	Title: *GABAergic dysfunction: The emerging role of the presynaptic organizer Bassoon* **2. Ashesh Kumar Dhawale** Centre for Neuroscience, Indian Institute of Science, Bengaluru, India **Title:** *The role of the basal ganglia in value-guided decisions* **3. Ashutosh Kumar** All India Institute of Medical Sciences- Patna, India **Title:** *Extreme heterogeneity and super-growers: mapping persistent hippocampal neurogenesis in adult humans* **4. Sachin Deshmukh** Shiv Nadar Institution of Eminence, Delhi-NCR, India **Title:** *Task demands shape hippocampal function* **5. Short Talk:** **Anushka Walupante** Savitribai Phule Pune University, Pune, India **Title***: Role of orexin-expressing neurons in cerebellar dentate nucleus in goal-directed reward seeking behavior* **6. Short Talk: Kashish Parnami** Amity University, NOIDA, India	**Title:** *Role of astrocytes in long-lasting adverse behavioural effects of early life stress* **2. Shashank Shekhar** Centre of Bio Medical Research**,** Lucknow, India **Title:** *ATF4 transcription factor sequestration in cytosolic condensates; a novel regulator of chronic ISR signaling in Drosophila and mice brain* **3. Pramod Kumar Avti** Post Graduate Institute of Medical Education and Research, Chandigarh, India **Title:** *Role of Type 2 Diabetes drug as a repurposing agent and ameliorating inflammation in stroke* **4. Vimlesh Kumar** Indian Institute of Scientific Education & Research-Bhopal, India **Title:** *A degeneration checkpoint for G4C2 repeat neurotoxicity.* **5. Short Talk:** **Pooja Shukla** Amity University, NOIDA, India **Title:** *Palmitoylation: the fatty chain driving neurodegeneration* **6. Short Talk: Rituparna Sahu** Indian Institute of Science, Bengaluru, India

	Title: *Progressive alterations in visual cortical activity during retinal degeneration: electrophysiological assessment in genetic and chemically induced mouse models.*	**Title:** *Selective activator of calcium-activated potassium channels, NS-309 act as a novel antiepileptic drug by restricting the hyperexcitability phenomenon in acquired epilepsy.*
17:00 onwards	**Valedictory function and award distributions** **Guest of Honour – Dr. Brahm Deep Sindhu** Director Health Services Haryana State, India **Closing remarks by Dr. Vinay K Khanna, President, IAN**	
	Networking over tea-coffee & snacks **Meeting Closes – Evening is free to explore Delhi NCR**	

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Speaker Abstracts

KEYNOTE 1:

Serotonergic psychedelics – from molecules to mood

Vidita Vaidya
Dept of Biological Sciences, Tata Institute of Fundamental Research, Mumbai, India, Navy Nagar, Colaba, Mumbai 400005

Serotonergic psychedelics have a long history of use in indigenous cultures for religious and healing purposes. The modern scientific era began roughly a century ago with the isolation of mescaline and the subsequent synthesis of compounds such as lysergic acid diethylamide (LSD). These molecules are now experiencing a resurgence of scientific and clinical interest as potential rapid-acting antidepressants and anxiolytics. In my talk I will discuss work from our research group investigating the mechanisms of action of serotonergic psychedelics across multiple scales — from molecular and cellular signaling changes to neural circuits governing mood-related behavior in rodent models. I will discuss the effects of these compounds on mitochondrial function, and the central role of the serotonin 2A ($5\text{-}HT_{2A}$) receptor and specific downstream signaling cascades in mediating the bioenergetic and neuroprotective effects. I will then describe work related to the role of $5\text{-}HT_{2A}$ receptor expressing parvalbumin-positive inhibitory interneurons in the ventral hippocampus that contribute to the rapid anxiolytic actions of the serotonergic psychedelic, DOI. Together, these findings bridge molecular pharmacology and systems neuroscience to illuminate how these compounds can influence brain function and mood-related behavior.

KEYNOTE 2

Neuroscience going wild: Neural coding in social groups of bats and in bats navigating outdoors on a remote oceanic island

Nachum Ulanovsky
Department of Brain Sciences, Weizmann Institute of Science, Rehovot, Israel

Background: We study the neural basis of natural behaviors, in particular navigation and social behaviors – taking a "Natural Neuroscience" approach. In my talk I will discuss three recent studies: (1) Our discovery that in social groups, hippocampal neurons encode rich social signals – including the identities, sex, hierarchy, and affiliation of other individuals, as well as their locations. Thus, the hippocampus forms a social-spatial cognitive map. (2) A coding-transformation that we discovered in the hippocampus of bats flying in a very long 200-meter tunnel – from sparse coding in hippocampal area CA3 to dense coding in area CA1. We showed that this transformation of the neural code, supports both rapid learning of spatial maps in the CA3-CA1 synapses, as well as precise spatial coding in CA1. (3) Neuroscience in the wild: recordings of place cells and head-direction cells in bats navigating outdoors on a remote oceanic island in the Indian Ocean, near Zanzibar. We discovered that head-direction cells can serve as neural compasses for outdoor navigation, and that place cells serve as cognitive maps outdoors. Further, by using simultaneous recordings of >100 neurons, we showed that the neural manifold exhibits much higher dimensionality outdoors than indoors – carrying surprising and important implications for how the brain represents the real world.
Purpose: In my talk I will discuss three recent studies that investigated the brain under more naturalistic settings and behaviors than typically done in classical neuroscience research.
Methods: We used 64-channel wireless-electrophysiology devices (neural loggers) and 16-tetrode microdrives to record the activity of ensembles of neurons in the hippocampus and presubiculum of freely-flying bats – either in socially-interacting groups of bats indoors, or in bats flying in a 200-meter long tunnel, or in bats navigating outdoors on a remote oceanic island in the Indian Ocean, near Zanzibar.
Results: In study 1, we discovered that in social groups, hippocampal neurons encode rich social signals – including the identities, sex, hierarchy, and affiliation of other individuals, as well as their locations. In study 2, we discovered a coding-transformation in the hippocampus of bats flying in a very long 200-meter tunnel – from sparse coding in hippocampal area CA3 to dense coding in area CA1. In study 3, in bats navigating outdoors on a remote island, we discovered that head-direction cells can serve as neural compasses for outdoor navigation, and that place cells serve as cognitive maps outdoors. Further, by using simultaneous recordings of >100 neurons, we showed that the neural manifold exhibits much higher dimensionality outdoors than indoors.
Conclusion: These three studies demonstrate different levels of experimental control vs. ecological validity in our efforts to understand the neural basis of behavior and cognition.
Keywords: Hippocampus, place cells, systems neuroscience, social neuroscience, ecological neuroscience, wireless posterelectrophysiology

PL1

Cell biology of the neuron, from development through aging

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Department of Neuroscience, Faculty of Medicine, Universidad de Chile, Santiago, Chile
Public Health Unit, Institute for Nutrition and Food Technologies (INTA), Universidad de Chile, Santiago, Chile
Geroscience Center for Brain Health and Metabolism (GERO), Santiago, Chile
The Buck Institute for Research on Aging, Novato, CA, USA

Why do we age? The underlying biology tells a subtler story, one in which genetic programs and epigenetic, environmentally responsive circuits contribute in comparable measure to the trajectory of cellular decline. This lecture threads together two lines of evidence from our research, one mechanistic and one populational, that together reshape how we think about preserving brain function across the lifespan.

At the cellular level, we will discuss how reactive oxygen species, long regarded as agents of damage, are, in fact, signaling molecules that instruct neuronal development and, by extension, healthy brain aging. Our work shows that NADPH oxidase 2 (NOX2)-derived hydrogen peroxide locally activates the small GTPase Rac1 at the nascent axon, specifying neuronal polarity and driving axonal elongation. This oxidative signal is coupled to ryanodine receptor–mediated calcium release and to NMDA receptor/glutamate signaling, forming a self-amplifying feed-forward loop that converts transient redox fluctuations into sustained axonal growth, uncovering a previously unrecognized, non-canonical role for NMDARs in early neuronal development. In addition, peroxiredoxin 2 emerges as the gatekeeper of this process, maintaining peroxide within the physiological window required for axon growth; pharmacologically disrupting it or mutating its catalytic cysteines collapses polarization.

Extending this logic that redox and metabolic tone govern brain resilience, we will discuss evidence that a cyclic ketogenic diet restores hippocampal long-term potentiation, dendritic complexity, and memory in aged mice, even when initiated late in life, through β-hydroxybutyrate-driven PKA signaling and cortical proteome remodeling, while concurrently reshaping skeletal muscle fiber composition and neuromuscular junction receptor turnover.

Finally, we will move into human studies. Drawing on the Santiago Longitudinal Study, a birth cohort followed for nearly three decades, we show that early-life obesity accelerates epigenetic aging, telomere attrition, and inflammaging, yielding biological ages older than chronological age (ObAge) by adulthood. Yet a subset of obese individuals, the "obesity resilients" (ObRes), escapes this trajectory, displaying a negative epigenetic age gap, restored IGF signaling and telomere length, and a reversed plasma proteomic signature that maps directly onto the hallmarks of aging.

Together, these findings argue that redox signaling, nutrition, and epigenetic plasticity are not peripheral modifiers of aging but central determinants of it, and that any serious attempt to intervene on the aging brain must reckon with the adaptive, physiological role that stress signals like ROS continue to play across the lifespan.

PL2

Neural circuits generating behaviorally relevant predictions and their developmental emergencies

Shivangi Verma[1], Sarthak Chandra[1], Shraddha Pathak[1], Sriram Narayanan[1] and Vatsala Thirumalai[1]
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Background: One of the principal functions of the brain is to learn from experience and use such learning to guide future actions. This phenomenon requires generating specific predictions regarding sensory inputs, motor actions and rewards and the cerebellum is thought to generate internal models in all these situations.

Purpose: We aimed to understand how predictive computations are represented in neural circuits or how they emerge during development using the larval zebrafish cerebellum as our model circuit.

Methods: We investigated predictive processing in the larval zebrafish cerebellum using a virtual optomotor paradigm combined with calcium imaging, electrophysiology, and behavioral analysis. Head-restrained larvae experienced sequences of visual flow with predictable statistics interspersed with unexpected probe stimuli.

Results: Fish learned sensory regularities, exhibiting shorter swim latencies for expected stimuli and delayed responses following deviations. Functional imaging revealed distinct Purkinje neuron populations tuned to forward or backward optic flow. Backward-tuned Purkinje neurons exhibited graded responses to mismatches between expected and experienced sensory feedback, consistent with prediction error encoding, whereas forward-tuned neurons encoded expected visual flow. Granule cells encoded sensory expectation but lacked mismatch responses, indicating that prediction errors arise downstream of mossy fiber input. To determine how these computations mature, we examined developmental pruning of climbing fiber (CF)-Purkinje neuron synapses during the first two weeks post fertilization. Whole-cell recordings demonstrated a transition from polyinnervation to predominantly mono-innervation, accompanied by increased temporal precision, response salience, and directional selectivity of CF-evoked responses. These changes produced higher-fidelity mismatch signals and stronger modulation of swim latency by sensory prediction.

Conclusion

Together, our results demonstrate that the larval zebrafish cerebellum forms internal models of the sensory environment and that developmental refinement of olivocerebellar connectivity is critical for the emergence of accurate prediction error signaling and predictive sensorimotor behavior.

Keywords: Zebrafish, electrophysiology, behavior, calcium imaging

PL3

Manjari Tripathi

All India Institute of Medical Sciences, New Delhi, India

PL4 (IAN- FAONS Session)

An early postnatal critical period for the development of inhibitory neurons in social circuit regulation

Goichi Miyoshi

Gunma University Graduate School of Medicine, Japan

Background: Autism spectrum disorder (ASD) is a neurodevelopmental condition characterized by impaired social behavior, yet the developmental timing and mechanisms linking early circuit abnormalities to later social impairments remain poorly understood. Although dysfunction of GABAergic inhibitory circuits has long been implicated in ASD, when such dysfunction becomes causal and when intervention is most effective remains unclear.

Purpose: We aimed to identify the developmental critical period during which inhibitory circuit dysfunction leads to ASD-related social impairments and to determine how GABAergic interneuron maturation during this period contributes to the establishment of social behavior.

Methods: We focused on the syndromic ASD gene *FOXG1*, which has also been implicated in idiopathic ASD, and generated mouse models with temporally controlled *FOXG1* dysregulation. Social behavior and inhibitory circuit function were examined across postnatal development. GABAergic tone was further reduced genetically through a *Gad2* mutation or increased by transplantation of GABAergic interneuron precursors into the medial prefrontal cortex (mPFC) either before or after the identified critical period. To investigate the molecular and cellular mechanisms underlying circuit maturation, we further combined these genetic models with single-cell RNA sequencing, *in vivo* calcium imaging, optogenetic circuit manipulation, local field potential recordings, and behavioral analyses.

Results: Both *FOXG1* haploinsufficiency and augmentation produced robust ASD-like social impairments. Developmental analyses identified the second postnatal week as a critical period for determining later social behavior, and augmentation of *FOXG1* restricted to this one-week window was sufficient to reproduce the ASD-related social impairments. During the same period, the *FOXG1* haploinsufficiency ASD model transiently exhibited reduced GABAergic tone in the mPFC. Further reduction of GABAergic tone through *Gad2* mutation exacerbated subsequent social impairments, whereas transplantation of GABAergic interneuron precursors into the mPFC before the critical period ameliorated these impairments. In contrast, transplantation after the critical period was ineffective. Ongoing analyses further indicate that distinct GABAergic interneuron subtypes undergo developmentally coordinated maturation during this period and may differentially contribute to the establishment of functional social circuits.

Conclusion: Our findings identify the second postnatal week as a critical developmental window during which appropriate GABAergic inhibitory circuit function is required for the establishment of later social behavior. We show that maturation of specific interneuron subtypes during this period may organize the developing social circuit and determine vulnerability to ASD-related phenotypes. Defining the molecular and circuit mechanisms governing this developmental process may reveal time- and cell type-specific targets for early intervention in ASD.

PL5 (EMBO Global Speaker)
Neuronal population dynamics of decision making in C. elegans

Jalaja Madhusudhanan[1,2], Anton Parinov[1,2,3], Charles Fieseler[1], Manuel Zimmer[1,4]

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Background: Large-scale neuronal recordings across model organisms reveal that correlates of sensory processing, decision-making, and behavioral output are distributed broadly across the brain. However, the functional role of these distributed signals and their causal involvement in perceptual decision-making remain unclear.

Purpose: To determine how distributed neuronal population dynamics shape behavioral choice and whether neurons encoding decision bias also causally influence decision-making.

Methods: We combined an aversive hyperoxia decision-making paradigm with whole-brain calcium imaging at single-cell resolution in C. elegans. Computational analyses identified neuronal signals and latent brain states predictive of behavioral choice. Single-neuron optogenetic manipulations tested the causal contributions of individual neurons.

Results: Hyperoxic stimuli evoked bimodal escape behavior: approximately 60% of trials produced transient backward crawling, while the remainder elicited sustained forward locomotion. Choice between these strategies was not determined at the sensory neuron level but emerged within neuromodulatory and interneuron circuits. Behavioral choice was best predicted by a latent brain state distributed across many neurons and established tens of seconds before stimulus onset. Individual neurons simultaneously encoded decision bias and motor programs in a multiplexed manner. However, optogenetic manipulations revealed that only a discrete subset of these neurons causally biased choice, identifying potential control points within a broadly correlated neuronal network. These findings link apparently stochastic behavioral choices to a pre-existing, distributed brain state and reveal a dissociation between representational and causal structure: behavioral choice is broadly represented across the brain but controlled through a sparse set of privileged neuron types.

Conclusion: We propose that multiplexed encoding, the dissociation between distributed representations of decision bias and sparse causal control constitutes a general principle of neural computation that may extend to animals with larger brains.

PL6

Metabolic basis of sleep

Bumsik Cho, Fu Li, Amita Sehgal
HHMI, Perelman School of Medicine, University of Pennsylvania, Philadelphia

Background: There is universal agreement that lack of sleep impairs performance, especially cognitive ability, during waking hours and considerable evidence supports adverse effects of sleep loss on other physiological parameters as well. Thus, sleep is important for waking function. However, what happens during sleep to facilitate wake performance and promote health?

Purpose: To determine the function of sleep

Methods: Assays of sleep behavior in Drosophila and mice, measuring hemocyte localization in Drosophila, assaying lipid droplets in the fly brain, measuring endocytosis in the mouse brain

Results: We find that Drosophila neurons pass their oxidative damage to glia in the form of oxidized lipids, in a sleep-dependent fashion. This protects neuronal mitochondria. The lipids are then transferred from neurons to glia and then to blood cells (hemocytes) in a daily cycle. Sleep also promotes clearance of metabolic waste via autophagy and endocytosis through the blood brain barrier (BBB). Similar sleep-regulated endocytosis occurs in the mouse brain

Conclusions: Sleep is required for metabolic homeostasis in the brain. In the Drosophila model, our studies are converging on the idea that sleep helps to maintain the integrity of neuronal mitochondria, at least in part by regulating lipid metabolism and promoting clearance. Data from mice support clearance through the BBB during sleep.

Keywords: Sleep, BBB, clearance, Drosophila, mouse, lipids, mitochondria

SYMPOSIUM I
Neurodevelopmental & Psychiatric Disorders

S001

Title: Transmission Electron Microscopy of the Human fetal cochlear nucleus in prenatal period

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Background: Morphological maturation of human cochlear nucleus (CN), the first relay nuclei of the auditory pathway occurs at 20 weeks of gestation. Transmission electron microscopy studies of CN in lower animals, have provided insights into the ultrastructural features of neurons, synaptogenesis, and myelination, which are important indicators of the functional maturity.

Purpose: Ultrastructural maturation of CN in human during development are still lacking. Hence we proposed to study the ultrastructural features of the developing human CN, with respect to neuronal differentiation, synaptogenesis, and myelination, at different gestational ages.

Methods: Ten fetal brainstem (14- 28 weeks of gestation) were obtained from Lok Nayak hospital after consent and institutional ethical clearance. The samples were dissected and the sections of cochlear nucleus were processed for TEM. The ultrathin sections were photomicrographed (Talos F200S) and studied for identifying the neurons and glia, synaptogenesis and myelination at different gestational ages. The synapses were manually counted and the area was measured using ImageJ software (version 1.52a, NIH, USA).

Results: TEM showed transverse, oblique and longitudinal sections of developing neurons, glial cells, undifferentiated cells, axons, dendrites and blood vessels. At 22 weeks distinct synapses with clear vesicles were observed. The synapses were of asymmetric axo-dendritic type. Few symmetric synapses and perforated synapse were also identified. Initiation of myelination was seen at 14 weeks and thicker myelinations of the processes were observed at 22 weeks of gestation.

Conclusion: In the present study, myelination and synaptogenesis at 22 weeks of gestation suggest that this may be the period of onset of hearing and a reliable marker of functional maturation of the cochlear nucleus.

Key words: Cochlear nucleus, TEM, functional maturation, myelination, synaptogenesis

S002

Delineating the underlying mechanism of action of Lithium in modulating behavioral rhythms and metabolism

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Background: Lithium is a mood stabilizer, which is primarily applied to treat manic and depressive episodes in bipolar disorder. Lithium and circadian rhythms are dynamically and bidirectionally coupled. Lithium stabilizes circadian oscillations, while endogenous rhythms also modulate Lithium's therapeutic efficacy. It is not well known whether Lithium exerts its effect through metabolic modulation.

Purpose: We intend here to investigate the effects of Lithium on rhythmic behavior and metabolism in mice and Drosophila.

Methods: 8–12 weeks old adult male albino mice were treated intraperitoneally with 0.9% NaCl as a control and 300mg/kg body weight of Lithium Carbonate daily for 7 days. At the end of treatment, animals underwent behavioral tests, including the Y-Maze, Radial Arm Maze (RAM), and Novel Object Recognition (NOR), followed by the collection of blood and multiple tissue samples for mass spectrometry-based metabolomics analyses. We also investigated the effects of Lithium in the wild-type and chronic mild unpredictable stress model of Drosophila.

Results: The effect of Lithium on learning, memory, and cognition was observed in mice and Drosophila. The performance indices by mice in the Y maze test were significantly altered post-treatment. In the NOR test, there was a significant difference among groups in discrimination indices, with LC-treated mice spending significantly more time exploring the novel object. In the RAM test, the maximum working memory error was observed in the control group. Metabolomic analyses in mouse tissues and Drosophila revealed lithium-induced alterations in amino acid and carbon metabolism pathways.

Conclusion:Our findings emphasize the convergent role of Lithium treatment as a circadian rhythm and metabolic modulator, by modulating GSK-3/Shaggy-mediated circadian pathways and improving mood-related behaviors, including cognition and memory.

Keywords: Lithium, circadian rhythm, sleep, mood disorders, metabolomics

S003

Towards a Universal Taxonomy of Functional Brain Networks

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Background: While the idea that the human brain is composed of multiple large functional networks has been gaining traction in cognitive and network neuroscience, the field has yet to reach consensus on several key issues regarding terminology. What constitutes a functional brain network? Are there "core" functional networks, and if so, what are their spatial topographies? What naming conventions, if universally adopted, will provide the most utility and facilitate communication amongst researchers? Can a taxonomy of functional brain networks be delineated?

Purpose and Methods: The Workgroup for HArmonized Taxonomy of NETworks (WHATNET) was formed in 2020 as an Organization for Human Brain Mapping–endorsed best practices committee to provide recommendations on points of consensus, identify open questions, and highlight areas of ongoing debate in the service of moving the field toward standardized reporting of network neuroscience results.

Methods and Results: The group has developed a Network Correspondence Toolbox (NCT) to permit researchers to examine and report spatial correspondence between their novel neuroimaging results and multiple widely used functional brain atlases.

Conclusion: The adoption of the NCT will make it easier for researchers to report their findings in a standardized manner, thus aiding reproducibility and facilitating comparisons between studies to produce interdisciplinary insights.

Keywords: network neuroscience, default mode network, salience network, network nomenclature

S004

Title: **α7 nicotinic acetylcholine receptors regulate radial glia fate in the developing human cortex**

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Background: Prenatal nicotine exposure impairs fetal cortical grey matter volume, but the precise cellular mechanisms remain poorly understood.

Purpose: To elucidate the role of nicotinic acetylcholine receptors (nAChRs) in radial glia (RG) during human cortical development.

Methods: NAChR subunit expression was characterized in SOX2+ progenitor cells and neurons. NAChR activation and knockdown were performed in organotypic slices and dissociated cultures to assess effects on RG proliferation and neuronal differentiation. Bulk and single-cell RNA sequencing was used to profile nicotine-induced transcriptional changes across ages and cell types, and YAP1 inhibition was tested for its ability to reverse nicotine-induced phenotypes in outer RG (oRG) cells.

Results: Two nAChR subunits, CHRNA7 and the human-specific CHRFAM7A, were identified, with CHRFAM7A particularly enriched along RG endfeet. nAChR activation increased RG proliferation while decreasing neuronal differentiation, whereas nAChR knockdown reduced RG and increased neurons. Single-cell RNA sequencing revealed that nicotine exposure downregulated key genes in excitatory neurons (ENs), with CHRNA7 or CHRFAM7A selectively modulating these changes, suggesting an evolutionary divergence in regulatory pathways. YAP1 was identified as a critical downstream effector of nAChR signaling, and its inhibition reversed nicotine-induced phenotypic alterations in oRG cells.

Conclusion: These findings identify a nAChR-YAP1 signaling axis that governs progenitor proliferation and neuronal differentiation during human cortical development, with the human-specific CHRFAM7A subunit contributing to an evolutionarily divergent regulatory pathway, together highlighting YAP1 as a central mediator of nicotine-induced neurodevelopmental pathophysiology.

Keywords: Nicotinic acetylcholine receptors, human brain development, radial glia

S005

Neuromodulatory effects of transcutaneous auricular vagus nerve stimulation (taVNS) in an animal model of endogenous depression

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Background: Major Depression Disorder (MDD) is a leading cause of disability worldwide, affecting around 3.8% of the population. Although the first line of treatment for MDD is pharmacological, they become ineffective in 30-40% of patients, resulting in treatment-resistant depression (TRD). Among the non-pharmacological treatments, transcutaneous auricular vagus nerve stimulation (taVNS) appears to be a promising non-invasive neuromodulatory technique to reduce depressive symptoms in TRD patients. However, the underlying mode of action still remains unclear.

Purpose: This study aims to understand the effect of taVNS on behavioral, biochemical and molecular alterations in an animal model of endogenous depression.

Methods: Animal model of endogenous depression was developed by injecting Clomipramine (15 mg/kg body weight), twice daily from postnatal day (PND) 8 to 21. Bilateral taVNS was administered for 30 min/day from PND 70 to 90. All the assessments and quantifications were carried out from day 91 onwards.

Results: Depressed animals exhibited hallmark endophenotypes, viz., behavioral despair and anhedonia; excitation-inhibition imbalance; along with a reduction in receptor expression, neurotrophic factor and neurogenesis. Whereas the depressed animals subjected to three weeks of taVNS, (1) showed significant reduction in behavioral despair and anhedonia, (2) restored altered neurotransmitter levels and receptor expression, and (3) enhanced neuroplasticity and neurogenesis.

Conclusion: Our findings suggest that the taVNS collectively targets the core pathophysiology of endogenous depression at multiple levels and provides a novel insight into the antidepressant mechanisms of taVNS.

Keywords: Endogenous Depression, taVNS, Neuroplasticity, Neurogenesis

ST01

Title: NMDA receptor subtype GluN2B modulates synaptic transmission and plasticity in the neocortex

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Background: Epilepsy is one of the most prominent neurological disorders and frequently associated cognitive impairment and altered synaptic plasticity may contribute to these deficits. NMDA receptors play pivotal role in learning and memory. Long Term Potentiation (LTP) and Long-Term Depression (LTD) are two cellular model for memory and extensively studied in epileptic hippocampus, but very limited studies available on epileptic neocortex.

Purpose: To determine the role of NMDA receptor subtype (GluN2A and GluN2B) in epileptiform neocortex and evaluate its effect on synaptic plasticity (LTD).

Methods: Wistar rat (PD14-25) neocortical slices were used for the experiments. Slices were treated with high potassium zero magnesium Artificial Cerebrospinal Fluid (HK-ACSF) to induce epileptiform activity. Here, we explored the role of NMDA receptor using AP-5, Ro 25-698 (GluN2B antagonist) and TCN-201 (GluN2A antagonist). Synaptic plasticity experiments were assessed via 1 Hz. 900 pulses (LTD) stimulation protocol.

Results: AP-5 completely abolished epileptiform activity, indicating NMDA receptor dependence. Ro 25-6981 predominately reduce epileptiform activity, whereas, TCN-201 produced little or no effect. LTD protocol under epileptiform condition showed significant potentiation in amplitude of fEPSPs. Interestingly Ro 25-698 reduced this potentiation, whereas TCN-201 did not showed any effect on potentiation.

Conclusion: Our data suggests that the GluN2B mediated epileptiform activity, altered synaptic plasticity within the neocortex. This data explains or provides functional insight into the mechanisms that may contributes to cognitive impairments in epilepsy. The GluN2B may acts an attractive therapeutic target.

Key words: GluN2B, epileptiform activity, synaptic plasticity, Ro25-698, and TCN-201

ST02

Title: **Stress–Stroke Interactions: Investigation of molecular mechanisms underlying the adverse effects of stress on stroke outcomes.**

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Background: Ischemic stroke stands as a leading global cause of disability. Neurological recovery relies heavily on immediate endogenous repair mechanisms that work to encapsulate the damaged neural tissue. Following injury, the brain constructs a localized physical barrier known as the glial scar to isolate the infarct zone and protect viable surrounding pathways. Chronic stress clinically correlates with significantly poorer stroke recovery, yet the cellular dynamics that impair this protective response remain poorly characterized.

Purpose: This study investigated how stress and elevated glucocorticoids disrupt the cellular proliferation necessary for proper scar architecture, mapping the resulting impacts on tissue repair and long-term functional recovery.

Methods: Localized ischemic injury was induced in mice using a photothrombotic stroke model combined with a CORT treatment. Astrocytic proliferation and scar morphology within the peri-infarct zone were evaluated using immunohistochemical markers alongside standardized sensorimotor behavioral assessments. Complementary in vitro assays tracked the direct effects of corticosterone (CORT) on astrocyte cell-cycle profiling and regulatory protein expression.

Results: Stress significantly reduced peri-infarct astrocyte proliferation, resulting in malformed glial scars and expanded infarct volumes. Consequently, stressed animals exhibited persistent sensorimotor deficits and delayed functional recovery. Mechanistically, in vitro analyses demonstrated that CORT directly suppresses astrocytic proliferation by driving Cyclin D1 degradation and triggering a distinct G1-phase cell-cycle arrest. Expression mapping verified a significant arrest in cell-cycle progression among CORT-treated astrocytes.

Conclusion: Stress-mediated inhibition of astrocyte proliferation serves as a definitive mechanism linking elevated glucocorticoid signaling to defective brain repair post-stroke. Interventions targeting Cyclin D1 stability or astrocytic cell-cycle checkpoints offer promising therapeutic avenues to optimize scar architecture and enhance functional outcomes.

Keywords: Ischemic Stroke, Stress, Photothrombotic stroke, Astrogliosis, Glial Scar

SYMPOSIUM 2
Dissecting circuits for behaviours

S006
Title: Encoding Memory in Amyloids

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Background.: For over a century, amyloids have been associated with pathology of the nervous system and are thought to be an unintended byproduct of protein mismanagement, an irreversible dead-end for a protein.

Purpose: We wish to understand how a temporally restricted experience produces a persistent change in behavior and how, among the myriad experiences an animal encounters, only some produce persistent change in behavior.

Methods: We use animal behavior, neuronal circuit analysis, high resolution imaging, biochemical assay, and cryoEM-based structural analysis to understand when, where, and how a specific protein participates in memory.

Results: We were thus surprised to find, while seeking to understand how memories withstand time, that certain amyloids stabilize memory. The discovery of functional amyloids in the brain forced us to rethink long standing assumptions on how and why amyloids are formed in the brain. Beyond nervous system, emerging evidence suggests amyloids can encode other forms of cellular memory such as transcriptional memory or signaling memory. Collectively these amyloids have given us access to areas, such as what structural features make an amyloid functional, how cells assemble amyloids in a controlled way, and once formed, how cells remove amyloids when needed.

Conclusion: We anticipate that studying amyloids as part of normal biological processes, not just pathological anomalies, will help us understand several unresolved fundamental questions in this emerging field: e.g. why through evolution do proteins retain the ability to form amyloids if they are inherently toxic? and why is the nervous system so vulnerable to amyloid-based diseases?

S007

Title: Circuit and Memory Deficits in Obesity: Rescue by Meal Scheduling

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Background: Not just what we eat, when we eat also affects metabolism and cognitive performance. This is particularly critical for obese adolescents, although mechanisms are poorly understood and effective treatment strategies are sparse.

Purpose: To identify an efficient clinical approach to correct obesity associated cognitive decline particularly in adolescents and young adults, using a preclinical framework.

Methods: Male and female adolescent C57B6 mice were given longitudinal, ad libitum access to westernized high-fat diet (HFD) for up to 12 weeks. Memory was longitudinally assayed the novel object recognition test, and dendritic plasticity was evaluated in vivo with 2 photon imaging. Circuit manipulation was achieved by chemogenetic viruses, and engram trapping by the Fos2ACre line. Finally, role of glucocorticoid receptor signaling was evaluated using a combination of pharmacology and knock-in mice.

Results: HFD exposure starting at adolescence not only disrupted the feeding-fasting cycle in both males and females, but it also impaired long-term memory. This was coupled with contrasting patterns of in vivo plasticity in cortex and hippocampus. Tamoxifen-labelled engram cells using the ‘trapping’ approach revealed impaired representation of memory, while chemogenetic circuit manipulation revealed functional contributions from both hippocampus and cortex. Furthermore, using pharmacology and knock-in mice, we further report impaired glucocorticoid receptor (GR) phosphorylation in this crucial neural circuit. Remarkably, four weeks of time-restricted access to the same HFD completely reversed memory deficits in both sexes. It also reversed cognitive loss, and corrected cortico-hippocampal plasticity, engram representation and GR phosphorylation deficits.

Conclusion: Together with additional results where we explore other environmental factors disrupting mental health, our findings highlight the detrimental impact of dietary choices on brain health, underlining the efficiency of non-pharmacological interventions like time-restricted feeding as a robust intervention for obesity-related cognitive decline.

Keywords: High-fat diet, Cortex, Hippocampus, Fos-Trap, Time-restricted feeding

S008

Title: Distinct neurotransmitters mediate state-dependent memory consolidation in Drosophila.

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Background: Behavioral plasticity is critical for adaptation, enabling animals to dynamically modulate their behavior in response to acute environmental fluctuations. For instance, while Drosophila typically rely on sleep to consolidate reward memories, they can form appetitive memories without sleep when they are starved. Notably, distinct circuit-based mechanisms mediate memory consolidation in fed and starved flies.

Purpose: In this study, we asked how distinct consolidation pathways are recruited in a state-dependent manner to establish appetitive memories.

Methods : We trained Drosophila in an appetitive conditioning paradigm before placing them on food or agar vials to induce consolidation through distinct memory pathways. We also utilized the UAS-Gal4 system to manipulate neural circuits and gene expression.

Results: We found that VPM3, a pair of neurons located in the ventral paired median (VPM) cluster of the fly brain, mediates memory consolidation in both fed and starved states. VPM3 neurons release octopamine, a neuromodulator that is functionally equivalent to mammalian noradrenaline. Suppressing octopamine biosynthesis in VPM3 neurons impaired long-term memory in fed flies. Moreover, octopamine-mediated modulation of PPL1-γ2α'1 dopaminergic neurons via Octβ2R receptors is essential for long-term memory in fed conditions. Surprisingly, downregulating octopamine signaling did not affect long-term memory in starved flies. Instead, disrupting glutamatergic transmission from VPM3 neurons impaired long-term memory in starved flies. We further established that memory consolidation under starvation relies on glutamatergic modulation of α'β' medial neurons of the mushroom body.

Conclusion: Together, our findings reveal that VPM3 neurons exhibit state-dependent neurotransmitter plasticity that enables memory consolidation through distinct neural pathways.

Keywords: Drosophila, Sleep-dependent memory, sleep-independent memory, octopamine, and dual-transmission.

S009

Top-down circuits regulating compulsive eating behavior

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Background: Obesity is an emerging global health concern. Much of the increase in obesity over recent decades has been attributed to changes in food environments and eating behaviors. Modern obesogenic environments provide easy access to energy-dense, highly palatable foods, promoting overconsumption and weight gain. The interaction between environmental cues and palatable diets can also generate addiction-like and compulsive eating behaviors, which may contribute to the development and persistence of obesity.

Purpose: This study aimed to identify the neural circuit mechanisms underlying binge-eating and compulsive eating behaviors and to determine potential circuit targets for mitigating maladaptive food consumption.

Methods: We used a binge-eating-induced compulsive eating (BiCOM) paradigm in mice to investigate the neural mechanisms underlying compulsive eating. Neural circuit activity and connectivity were examined using circuit-specific manipulations and in vivo imaging. We investigated the role of rostral zona incerta GABAergic (ZIGABA) neurons, their inputs from the medial prefrontal cortex (mPFC), and habenular inputs to the ZI in regulating compulsive eating.

Results: We found that ZIGABA neurons drive compulsive eating. Manipulation of either ZIGABA neurons or their mPFC and habenular inputs bidirectionally modulated compulsive eating behavior. In vivo imaging of mPFC neurons to ZI revealed that the BiCOM paradigm altered mPFC neural dynamics, generating persistent attractor states with sustained selectivity for palatable food. Our findings also identify the habenula as an important input to the ZI, suggesting that habenular–ZI circuitry may contribute to the regulation of compulsive food consumption.

Conclusion: These findings identify key neural circuit mechanisms between prefrontal cortex, habenula and hypothalamus underlying compulsive eating. The mPFC-Habenula-ZI crosstalk with each other regulates compulsive eating and represent potential neural circuit targets for reducing maladaptive overconsumption and developing therapeutic strategies for obesity and related eating disorders.

ST03

Title: Elucidating the Role of Sox2ot in Sex-Dependent Behavioural Consequences of Early Life Stress

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Background: Early life stress during adolescence is intricately entangled with long-term neurobehavioural anomalies and mental illness. Although these disorders occur in both males and females, they show striking sex differences in prevalence, severity, and symptoms. Accumulating evidence points towards pivotal regulatory roles of long non-coding RNAs (lncRNAs) in transcriptional and epigenetic processes. Furthermore, a few lncRNAs have been reported to exert pathophysiology of depression in a sex-specific manner. However, their impact on sex-specific outcomes following early-life stress remains obscure.

Purpose: This study aims to investigate whether brain region-specific lncRNA expression is crucial for sexspecific behavioural alterations resulting from peripubertal stress (PPS), with a close attention to the lncRNA Sox2ot and its overlapping transcription factor Sox2.

Methods: Male and female mice were subjected to a fear-inducing PPS paradigm from P28-P42, and underwent a battery of behavioural assessments in adulthood (P90). Quantitative real-time PCR validation of Sox2ot and Sox2 expression was done in the PFC of both sexes from peripuberty to adulthood.

Results: Adult male mice displayed heightened aggression following PPS exposure, whereas females exhibited compulsive-like behaviour. A drastic upregulation of Sox2ot was observed in the PFC of female mice from peripuberty to adulthood, whilst a trend of downregulation was observed in males, suggesting sex-specific expression. Furthermore, the pluripotency gene Sox2 exhibited a concordant pattern of upregulation in female PFC and decreased expression in PPS-exposed males.

Conclusion: Our findings vindicate that PPS incites aggression in male mice and compulsive-like behaviour in females. We also pinpoint Sox2ot as a prospective candidate mediating sex-specific neurobehavioural responses to early-life stress. The harmonized and sexually dimorphic expression of Sox2ot and Sox2 suggests a potential role for this lncRNA-gene axis in predisposing sex-biased neurobehavioural trajectories following early-life stress.

Keywords: Early life stress, Sex differences, Long non-coding RNAs, Aggression, Compulsive-like behaviour.

ST04

Title: Dysfunctional Anterior Default Mode Network in Obsessive-Compulsive Disorder: an EEG Microstate Analysis

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Background: Obsessive-compulsive disorder (OCD) is a chronic psychiatric disorder characterized by the presence of recurrent and intrusive thoughts, images, or urges (obsessions) that often lead to repetitive behaviors or mental acts (compulsions) performed to reduce distress or anxiety. Although neuroimaging studies have consistently implicated the networks involved in internal cognition in OCD, relatively little is known about the temporal dynamics of these networks.

Purpose: This study aimed to compare resting-state EEG microstate parameters between individuals with OCD and healthy controls across six microstate classes (A–F), with particular emphasis on identifying alterations in temporal characteristics and transitions between large-scale brain networks.

Methods: A cross-sectional analysis was conducted using open-source resting-state EEG recordings from 41 participants, composed of 20 individuals with OCD and 21 healthy controls. EEG data were preprocessed using EEGLAB in MATLAB and six microstate classes were identified using kmeans clustering. Microstate occurrence, duration, coverage, and transition probabilities were computed using the EEGLAB Microstate Toolbox. Group differences were assessed using independent-samples t-tests with statistical significance set at $p<0.05$.

Results: Individuals with OCD demonstrated significantly reduced occurrence and coverage of microstate F compared with healthy controls. In addition, transition probabilities from microstate B to F and from microstate C to F were significantly lower in the OCD group. No significant group differences were observed for the remaining microstate classes or parameters. The findings suggest reduced activity of the brain state represented by microstate F and impaired transitions into this state during resting conditions.

Conclusion: The present study suggests that OCD is associated with alterations in resting-state EEG microstate dynamics involving microstate F, which has been linked to the anterior subdivision of the default mode network (DMN). Unlike previous studies that have implicated the DMN more broadly, these findings narrow the dysfunction specifically to the anterior DMN. EEG microstate analysis therefore provides a promising approach for advancing our understanding of OCD pathophysiology and may contribute to the identification of a possible neurophysiological marker for the disorder.

Keywords: Obsessive-Compulsive Disorder, Electroencephalography, EEG Microstates, Default Mode Network

*Sabine Kastner
Editor-in-chief, Journal of Neuroscience

B.K. Bachhawat Memorial Lifetime Achievement Award Lecture

The Neuropharmacology Expedition: Research, Mentorship, and Clinical Impact

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The journey of a scientist is shaped not only by discoveries but also by mentors, collaborators, and the persistent pursuit of questions that improve human health. My journey in neuropharmacology began in 1978 under the mentorship of Professor K. P. Bhargava, a pioneering pharmacologist at the King George's Medical College, Lucknow. Prof. Bhargava rigorous scientific vision provided the foundation for my subsequent work in neuropharmacology and experimental therapeutics. My early research focused on the neuropharmacology of emesis, specifically the localization and characterization of neurotransmitter receptors controlling vomiting and the mechanisms of cytotoxic drug-induced emesis. Investigations into enkephalinergic, histaminergic, dopaminergic, and serotonergic mechanisms established a critical foundation for understanding the central control of vomiting. This work was later extended by my students and colleagues to evaluate newer antiemetic approaches, including the experimental investigation of ginger (Zingiber officinale) against chemotherapy-induced emesis. My group also developed the PICA model, which was analogous to vomiting in rats. The neuropharmacology program subsequently expanded into other major areas, particularly stroke, epilepsy, and Alzheimer's disease.

At AIIMS, New Delhi, I established a dedicated Neuropharmacology Laboratory to investigate pharmacological agents—both synthetic and herbal—in experimental models of neurological disorders. Development of the middle cerebral artery occlusion model of stroke was used to develop neurotherapeutics from medicinal plants and new chemical entities, while epilepsy studies examined anticonvulsant mechanisms, endogenous neuromodulatory systems, and neuroprotective interventions. Investigations in Alzheimer's disease explored experimental models of cognitive impairment and the pharmacological potential of medicinal plants. These programs were supported by grants from ICMR, CSIR, DST, DBT, INSA, and other organizations.

A crucial dimension of this journey has been translating experimental pharmacology into clinical practice. My work expanded into therapeutic drug monitoring, clinical research, pharmacovigilance, and drug safety. At AIIMS, I contributed to developing the discipline of Clinical Pharmacology and the DM Clinical Pharmacology program, as well as establishing a National Therapeutic Drug Monitoring facility. I also helped strengthen the Pharmacovigilance Programme of India and the National Poisons Information Centre, reinforcing pharmacology's role in ensuring the rational and safe use of medicines. Perhaps the most enduring aspect of this expedition has been mentorship. Scientific progress is sustained when knowledge is transmitted across generations. Over the years, I have mentored postgraduate, doctoral, and young research scientists whose work has spanned emesis, epilepsy, stroke, Alzheimer's disease, neuroprotection, herbal–drug interactions, and clinical pharmacology. This lecture will reflect upon my neuropharmacology journey—from the early exploration of central mechanisms of emesis to experimental models of stroke, epilepsy, and Alzheimer's disease; from laboratory discoveries to clinical pharmacology and medicine safety; and from individual research to the creation of a culture of mentorship and scientific inquiry.

Symposium III

Glia in Health and Disease

S010

Cdk5-Mediated Oligodendrocyte Activation, Neuroinflammation, and Mitochondrial Dysfunction: A Mechanistic Link Between Type 2 Diabetes and Alzheimer's Disease

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Background: Type 2 Diabetes (T2D) is a major risk factor for cognitive decline and Alzheimer's disease (AD), but the molecular mechanisms linking these disorders remain incompletely understood. Emerging evidence suggests that aberrant activation of cyclin-dependent kinase 5 (Cdk5) contributes to neurodegeneration through multiple cellular pathways.

Purpose: To investigate the role of Cdk5 in mediating oligodendrocyte activation, neuroinflammation, myelin degeneration, and mitochondrial dysfunction, and to determine whether Cdk5 represents a mechanistic link between T2D and AD.

Methods: We employed complementary *in vitro* and *in vivo* models, including glucose-treated oligodendrocytes and neurons, and a Type 2 Diabetes (T2D) mouse models (db/db and HFD). Cdk5 activity, cPLA2 phosphorylation, and neuroinflammatory markers were assessed using biochemical and molecular techniques. Global phosphorylation profiling was performed by LC–MS-based phosphoproteomics, gene expression was analyzed by real-time PCR, and protein localization was examined by immunocytochemistry. Mitochondrial function was evaluated using the Seahorse XF Mito Stress Test, while mitophagy was assessed to determine the impact of diabetic stress on mitochondrial quality control. The therapeutic efficacy of pharmacological Cdk5 inhibition was further investigated by evaluating its ability to attenuate neuroinflammation, preserve myelin integrity, restore mitochondrial homeostasis, and enhance mitophagy.

Results: Glucose toxicity induced Cdk5 hyperactivation in oligodendrocytes, resulting in increased cPLA2 phosphorylation, chronic neuroinflammation, and progressive myelin degradation. Hyperactive Cdk5 also impaired mitophagy, leading to mitochondrial dysfunction and neuronal degeneration in cultured neurons and T2D mouse brains. Pharmacological inhibition of Cdk5 significantly reduced neuroinflammation, preserved myelin integrity, restored mitochondrial homeostasis, and enhanced mitophagy, demonstrating its neuroprotective effects.

Conclusion: Our findings identify Cdk5 as a central molecular regulator linking T2D-associated metabolic stress to oligodendrocyte dysfunction, neuroinflammation, myelin degeneration, and mitochondrial impairment. Targeting Cdk5 may represent a promising therapeutic strategy to prevent or slow diabetes-associated neurodegeneration and cognitive decline, thereby reducing the risk of Alzheimer's disease.

Keywords: Cdk5, Type 2 Diabetes, Alzheimer's disease, neuroinflammation, mitochondrial impairment.

S11

Regulation of gliogenesis in the developing mouse hippocampus

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Background: A fundamental feature of the vertebrate central nervous system is that common progenitors produce first neurons and then glia. We explored how cell-intrinsic factors modulate how a progenitor responds to cell-extrinsic cues to achieve this transition the developing neocortex and hippocampus.

Methods: Mice carrying floxed alleles of either Foxg1 or Lhx2 were used together with spatiotemporally restricted Cre drivers, or in utero electroporation of plasmids encoding Cre recombinase at embryonic day E15.5 when neurogenesis is underway. The resulting neurons or glia were examined at postnatal stages (P15- P30) using either cell identity markers (GFAP/ ALDH1L1 for glia, NEUN for neurons). In each case, cells positive for neuronal or glial markers were scored as a percentage of the total GFP electroporated cells. For rescue experiments, plasmids encoding full length constructs of Lhx2 were co-electroporated together with Cre recombinase into Foxg1 floxed embryos.

Results: We found loss of either Foxg1 (unpublished) or Lhx2 (published) in hippocampal neurogenic progenitors at E15.5 causes premature gliogenesis. We tested whether these factors act in the same pathway by overexpressing Lhx2 while simultaneously deleting Foxg1, and vice-versa, using in utero electroporation at E15.5. We found that overexpression of Lhx2 rescues neurogenesis despite the loss of Foxg1. In contrast, overexpression of Foxg1 together with loss of Lhx2 did not rescue neurogenesis. Ongoing experiments are testing whether Notch or Fgf-mediated mechanisms are involved in this pathway in the hippocampus. These results are unpublished.

Conclusion: This finding reveals that two regulators of the neuron-glia cell-fate switch, Foxg1 and Lhx2, interact in the same pathway in the developing hippocampus. This contrasts with previous findings in the neocortex, where loss of Foxg1 causes premature gliogenesis instead of neurogenesis but loss of Lhx2 does not affect neurogenesis. This raises intriguing questions about spatiotemporal regulation of Lhx2 by Foxg1.

S12

Astrocytic glutamate release lowers the threshold for structural plasticity and enhances memory engram encoding

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Background

Astrocytes, the most abundant glial cells, are now recognised as active partners at the synapse rather than passive support cells. Among their functions is the calcium-dependent release of glutamate, positioning them to shape synaptic and structural plasticity, a leading candidate mechanism for memory formation and storage. Long-term plasticity involves trafficking of AMPA receptors to the postsynaptic density, and receptor conductance scales with dendritic spine-head volume, yet the quantitative contribution of astrocytic glutamate to this structural remodelling remains unclear.

Purpose: To determine the nature and extent of astrocytic glutamatergic influence on structural plasticity of dendritic spines, at both the single-spine and population levels, and to test whether astrocytes alter the threshold for plasticity and the encoding of memory engrams.

Methods: We developed biophysical computational models to describe 1) calcium-dependent glutamate exocytosis from astrocytes, resolving IP3-mediated calcium signalling and distinguishing kiss-and-run from full-fusion release modes through the calcium dynamics of distinct synaptotagmins and 2) activity-driven structural plasticity of the postsynaptic spine, linking AMPA-receptor trafficking to spine-head volume. Presynaptic stimulation was simulated across a range of physiologically relevant stimuli, with and without astrocytic projections, for single spines and for a population of synapses at physiological hippocampal coverage.

Results: The presence of astrocytic projections lowered the minimum stimulation frequency required to induce long-term structural plasticity, and potentiated spines grew larger than those without astrocytic input. At the population level, astrocytic signalling increased the mean volume of spines recruited into a memory engram, an effect that persisted even at the fractional synaptic coverage observed in the hippocampus.

Conclusion: Astrocytic glutamate is a quantitatively significant modulator of structural plasticity and engram encoding, lowering the threshold for potentiation and strengthening the spines that store a memory. This framework provides a mechanistic basis for probing how disrupted gliotransmission, such as in amyloid pathology, may alter plasticity under pathological conditions.

Keywords: Astrocytes; gliotransmission

S13

Human brain-enriched extracellular matrix genes regulate progenitor dynamics and cortical folding

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Background and Purpose: Cortical development requires a precisely timed transition of neural stem cells (NSCs) from symmetric proliferative divisions to asymmetric neurogenic divisions, a process tightly controlled by chromatin-modifying enzymes. The histone demethylase LSD1, which catalyzes the removal of H3K4me1/2 and H3K9me1/2 marks, is known to regulate neuronal differentiation; however, the full extent of its regulatory network in human cortical development has remained unclear.

Methods: Using genome-wide LSD1 ChIP sequencing, RNA sequencing, and histone modification profiling in human iPSC-derived NSCs, we identify a broad repressive role for LSD1 in maintaining progenitor identity and enabling the neurogenic transition. Inhibition of LSD1 leads to global increases in active histone marks, including H3K4me1/2 and H3K9me1, and derepression of key downstream pathways, notably Notch signaling genes and a striking cohort of human neural progenitor–enriched extracellular matrix (ECM) and adhesion molecules. Functionally, upregulation of these pathways following LSD1 inhibition impairs neurogenesis. Moreover, overexpression of individual downstream effectors phenocopies this defect, highlighting their contribution to LSD1-mediated lineage progression.

Results and Conclusion: Extending these findings in vivo, we show that overexpression of LSD1-repressed ECM genes in the embryonic mouse cortex at E13.5 induces fold-like structures postnatally. This ectopic folding is accompanied by increased numbers of basal radial glia–like cells expressing PAX6, TBR2, and HOPX, as well as expansion of apical progenitors, suggesting that ECM-mediated changes in tissue stiffness influence progenitor dynamics. We also observe distinct spatiotemporal expression patterns of these ECM genes coinciding with tissue folding, supporting a model in which changes in tissue stiffness contribute to cortical gyrification. Comparative epigenomic analyses further reveal human-specific enhancer signatures marked by H3K4me2 and H3K27ac at these ECM loci, implicating the evolutionary acquisition of regulatory elements that may potentiate cortical expansion. Together, this work uncovers a unified LSD1-dependent regulatory axis that coordinates neurogenic timing with ECM-mediated control of cortical growth. These findings reveal an epigenetic mechanism that couples progenitor differentiation to structural programs underlying human cortical expansion and folding.

ST5

West Nile Virus downregulates TRIM71 to inhibit type I interferon response in human microglial cells

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Background: West Nile virus (WNV) is a neurotropic, positive-sense, single-stranded RNA virus. WNV infection may lead to neurological manifestations such as meningitis and encephalitis. The type I interferon (IFN) response is the first line of host defence against viral infections. Viruses have evolved multiple strategies to suppress the type I IFN response and facilitate immune evasion. Although several tripartite motif-containing proteins (TRIMs) are reported to regulate antiviral immune responses during viral infections, the contribution of TRIM71 to microglial antiviral responses during WNV infection remains poorly understood.

Purpose: This study investigated the role of TRIM71 in regulating type I IFN signalling during WNV infection in human microglial cells.

Methods: Human microglial cells were infected with WNV and subjected to TRIM71 overexpression/CRISPR-Cas9-mediated knockout. Gene and protein expression analyses were performed using quantitative RT-PCR, immunoblotting, ELISA, and immunofluorescence to evaluate type I IFN signalling and interferon-stimulated gene (ISG) expression.

Results: WNV infection promoted proteasome-dependent degradation of TRIM71, resulting in increased nuclear accumulation of AGO2, reduced STING expression, decreased IRF3 phosphorylation, and suppression of the type I IFN response and ISGs. TRIM71 overexpression suppressed AGO2, activated STING-mediated IRF3 signalling, and restored the expression of IFN-α/β and multiple antiviral ISGs. Conversely, TRIM71 knockout recapitulated the key features of WNV infection, evidenced by increased AGO2 levels, reduced STING levels, impaired IRF3 activation, and suppressed IFN-α/β responses. Further, domain-specific analyses demonstrated that both the RING and NHL domains are essential for the antiviral function of TRIM71.

Conclusion: WNV triggers proteasome-mediated degradation of TRIM71, consequently impairing the AGO2/type I IFN and STING/IRF3/type I IFN axis. These findings establish TRIM71 as a key regulator of antiviral innate immunity in human microglial cells and indicate that WNV-induced TRIM71 degradation serves as a viral immune-evasion strategy to inhibit type I IFN responses.

Keywords: West Nile virus, TRIM, microglia, antiviral response, interferons

ST6

Altered Stress Granules and Paraspeckle dynamics by ALS-associated FUS mutations in neuronal and astrocytic models

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Background

Amyotrophic lateral sclerosis (ALS) is neurodegenerative disorder in which mutations in Fused in Sarcoma (FUS) causes mislocalization, RNA metabolic dysfunction and aberrant regulation of ribonucleoprotein (RNP) condensates, including stress granules (SGs) and paraspeckles (PSs). We have identified novel FUS mutations in sporadic ALS patients, making it imperative to investigate the molecular consequences and pathogenic mechanisms associated with these variants.

Purpose: To investigate the effects of ALS-associated FUS mutations on SG and PS dynamics in neuronal and astrocytic cell models.

Methods: Neuronal and astrocytic cells were transfected with wild-type or mutant FUS-GFP constructs. NEAT1_2 expression was analysed by RT-PCR, while SG markers (G3BP1, TIA1) and PS proteins (NONO, SFPQ) were assessed by immunoblotting and immunofluorescence. Cells were exposed to sorbitol, sodium arsenite or astrocyte-conditioned media to evaluate RNP granule dynamics. Astrocytic inflammatory and reactivity markers were also analysed in the astrocytic model.

Results: Mutant FUS showed marked cytoplasmic mislocalization in both cell types. Astrocytes exhibited increased SG and PS markers together with elevated IL-6 expression despite minimal changes in GFAP, S100B and EAAT2, indicating a neuroinflammatory phenotype independent of classical astrogliosis. In contrast, neurons displayed reduced SG and PS components even after osmotic stress or astrocyte-conditioned media. Under arsenite stress, mutant FUS co-localized with G3BP1 in ~50% of SG-positive cells. During recovery, mutant FUS cells exhibited delayed SG disassembly with persistent G3BP1-positive puncta. Concurrently, NONO, but not SFPQ, was selectively recruited into mutant FUS-positive cytoplasmic condensates and remained cytoplasmic for up to 2hours before progressively relocalizing to the nucleus.

Conclusions: ALS-associated FUS mutations induce cell type-specific dysregulation of RNP granules, characterized by enhanced SG/PS engagement in astrocytes but impaired stress responses in neurons. The temporal changes support a dynamic SG–PS crosstalk in which transient NONO sequestration is associated with delayed SG resolution, potential mechanisms underlying FUS-mediated ALS pathogenesis.

Keywords: Amyotrophic Lateral Sclerosis, Fused in Sarcoma, Stress Granules, Paraspeckles

Symposium IV

AI-ML and BMI for Neuroscience

S14

The role of visual experience for the development of recurrent processing in the human brain

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Background: The brain develops in tight interaction with its environment. Non-human animal work has suggested that experience is crucial for the tuning of neural networks particularly at certain time epochs called sensitive periods. To study experience-dependent brain development in humans, we have to make use of natural models such as people who were born blind and recover vision later by sight-restoring surgery. Research in individuals with reversed bilateral congenital cataracts has indicated permanent impairments in low- and high-level visual functions.

Purpose: The present talk summarizes findings from both non-invasive electrophysiological studies and brain imaging studies in humans with reversed congenital cataracts which tested the recovery of recurrent processing.

Methods: The EEG was recorded both during rest and during visual stimulation. In addition, we applied resting state functional magnetic resonance imaging and retinotopic mapping (fMRI).

Results: During repetitive visual stimulation, we found in the steady state visual evoked potentials an attenuation of higher harmonics and a lack of intermodulation frequencies in individuals with reversed congenital cataracts. Moreover, alpha activity was severely attenuated while gamma activity was enhanced. The retinotopic mapping results revealed larger population receptive fields in individuals with reversed congenital cataracts which, unlike in normally sighted controls, did not increase downstream. Connective field modeling indicated a lack of tuning of feedback connectivity in sight restored individuals.

Conclusion: Results from both electrophysiological and brain imaging methods in sight recovery individuals with a history of a transient phase of congenital blindness suggest that the tuning of feedback connectivity and the orchestration of feedforward and feedback processing in the human visual system crucially depends on early visual experience

S15

Prenatal sleep deprivation and altered behaviour in offspring: AI-ML tools to decipher bioacoustics in babies

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Maternal sleep loss during pregnancy alters not only the behavior but also the ultrasonic vocalization patterns in pups as evident from our pre-clinical studies done in rats (1,2). Recent report on humans showed an association of prenatal sleep with neonatal temperament (3). As a translational part, we evaluated changes in cry signal of human neonates born to mother with normal and poor sleep quality during late pregnancy using AI and ML tools. After taking IEC approval from the Institute, pregnant mothers were recruited for this study and their questionnaire based sleep health index was assessed during last trimester. At time of birth, 15 sec continuous cries of babies (1st Cry during normal birth or C-sec babies) and later during vaccination, hunger and spontaneous state were recorded from a local Hospital using H5-Zoom microphones. These signals were processed using librosa and parselmouth platforms to extract 27 acoustic features. After preprocessing, K mean classifier was used for preliminary clustering of cries. Further, hybrid CNN with attention and LSTM network were used for classification of Vaccine and Hunger cries. K mean algorithm clustered two distinct group of cries. These changes in the bioacoustics features between two modes of delivery and effects of sleep loss during pregnancy on development of baby's cries pattern will be discussed for an early detection of anomalies

S16

Tracking and training attention with a cognitive brain-machine interface

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Background

Visual attention allows prioritization of relevant information, but attentional lapses are common and can impair performance. Although attention has been widely studied, mechanisms of recovery from lapses remain poorly understood, and current interventions often rely on medications with possible side effects.

Purpose: This study investigates a non-invasive alternative using closed-loop neurofeedback. A new cognitive brain-machine interface (cBMI) continuously monitors attentional lapses via real-time SSVEP tracking and tests whether training can reduce lapses and produce attention improvements that generalize across spatial locations.

Methods: Twenty-four healthy participants were assigned to either a real-time neurofeedback group (n = 12) or a yoked control group (n = 12). During training, participants viewed two flickering gratings that generated distinct SSVEP signals. cBMI feedback was displayed as a rotating bar whose angle reflected the difference between attended and unattended SSVEP power; a descending bead created urgency by requiring sustained attention to keep it from falling. Training targeted only one hemifield to create attentional competition. Sustained attention was assessed before and after training using a cued continuous performance search task (CPST), which measured target detection performance across both trained and untrained visual hemifields.

Results: Participants receiving actual neurofeedback progressively learned to enhance attention-related neural activity by increasing SSVEP responses at attended locations and suppressing responses at unattended locations, whereas control participants showed no such effect ($p<0.01$). This attentional modulation emerged over successive training blocks, demonstrating improved sustained spatial attention. Behaviorally, neurofeedback participants showed significant gains in sustained attention (d') not only in the trained hemifield but also in the untrained hemifield, indicating transfer of learning across tasks and locations ($p<0.01$). Moreover, greater neural modulation predicted larger behavioral improvements ($r=0.49$, $p<0.05$). EEG decoding further showed enhanced post-training neural discriminability of attended locations, supporting neurofeedback-driven strengthening of attention-related neural representations ($p<0.05$).

Conclusion: SSVEP-based neurofeedback rapidly improved sustained spatial attention, generalized across untrained locations, and linked neural changes to behavioral gains. This cBMI holds potential for clinical translation.

Keywords: Sustained attention, real-time neurofeedback, BMI, neural decoding, CPST

S17

AI-Driven Functional Neuroimaging and Lesion Network Mapping in Cognitive States and Epilepsy: Inflammatory and Vascular Cascades Mediate White Matter Hyperintensity-Induced Network Desegregation

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Background: A substantial subset of cognitively normal older adults accumulates a high burden of periventricular (PVWMH) and deep (DWMH) white matter hyperintensities, surrogate neuroimaging markers of cerebral small-vessel disease, whereas others remain largely resilient.

Purpose: The site-specific microvascular insults drive cognitive decline via distinct multi-scale cascades, translating localized vascular damage into large-scale functional desegregation.

Methods: Utilizing an AI-augmented quantitative framework across an in-house IISER Berhampur aging cohort alongside multi-center longitudinal aging cohorts, we integrated resting- and task-based functional MRI with comprehensive quantification of PVWMH and WMH, its impact on Default Mode Network (DMN) and the Dorsal Attention Network (DAN) mediated via molecular secretions in cerebrospinal fluid (CSF) and plasma to map large network dynamics, hierarchical structural-to-functional transition in aging and epilepsy patients.

Results: Using advanced quantitative AI wrapped framework, it was evident that it is PVWMH, not DWMH, that selectively abolishes the canonical antagonistic relationship between the Default Mode Network (DMN) and the Dorsal Attention Network (DAN), a vital functional network dynamic, essential for flexibly toggling between internally directed mentation and externally focused execution. By eroding this core architecture, PVWMH collapses network segregation beyond normative aging and destabilizes intrinsic neural entropy. DWMHs instead demonstrated a distinct salience-network phenotype, establishing lesion location as the principal determinant of functional reorganization. Crucially, we uncover the neurobiological substrates driving this desegregation. Molecular profiling revealed that PVWMH initiates a cascade of vascular insult and blood-brain barrier (BBB) breakdown, characterized by upregulated markers of vascular remodeling (PDGFRB, VEGFD). The reduction in segregation of DMN-DAN in presence of PVWMH mimics the similar temporal network dynamics as observed in epilepsy patients. The DMN-DAN structural breach precipitates profound neuroinflammation and systemic immune activation. We identify a direct mechanistic link between the inflammatory milieu and large-scale network collapse. Notably, mediation models establish that IL-13 acts as a primary driver of PVWMH-induced DMN-DAN hyper-coupling, accompanied by diffuse myelin and axonal injury.

Conclusion: We propose a unifying, functional and AI-based multi-scale neurobiological framework of small-vessel disease, wherein periventricular vascular injury serves as a central substrate for loss in DMN-DAN networks together with elevated neuroinflammation, BBB permeability that and axonal degeneration.

S18

Sanjeev Nara

Neural Correlates of Aesthetic Experiences in Natural Environments: Insights from Neuroimaging and Deep Neural Networks

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Background: Understanding how the brain gives rise to aesthetic experiences in natural environments remains a central question in neuroaesthetics. Although previous studies have shown that the beauty of natural images emerges during perceptual analysis, the computational processes underlying this phenomenon remain unclear.

Purpose: Our studies examined the computational principles underlying aesthetic perception by combining deep neural network (DNN) modelling with functional magnetic resonance imaging (fMRI) and electroencephalography (EEG).

Methods: We quantified spatial integration in a deep neural network by measuring the deviation between activations for the whole image and its constituent parts. This measure was evaluated against beauty ratings across four studies. A complementary fMRI study tested whether integrative processing in the human visual cortex similarly predicted perceived beauty. We then used EEG to examine the temporal dynamics of these neural representations while varying stimulus presentation time and task demands across two experiments.

Results: The deep neural network measure predicted beauty ratings across all four studies. Integrative processing in the human visual cortex also predicted perceived beauty, identifying spatial integration as a computational principle underlying aesthetic experience. EEG representational similarity analysis showed that neural representations of beauty emerged within 150–200 ms after stimulus onset and remained sustained over time. These neural dynamics were preserved when stimulus presentation was reduced from 1450 ms to 100 ms and when explicit beauty judgments were replaced with an orthogonal task.

Conclusion: The neural correlates of scene beauty were robust across stimulus presentation and task demands. Together, these findings suggest that aesthetic perception relies on spatial integration during perceptual analysis and is reflected in early, sustained neural representations that may support the spontaneous experience of beauty in natural environments.

Keywords: Neuroaesthetic, EEG, fMRI, Deep Neural Networks (DNN)

ST7

CADUN: A Computational Framework of Spatial Decision Making under Uncertainty using Utility-driven Reinforcement Learning

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Background: Spatial navigation in real-world environments requires decisions to be made under uncertainty that arises from changing environment contingencies such as reward availability and partial observability. Adaptive and robust spatial behaviours like rapid adaptation to unexpected feedback are produced by evaluation of spatial outcomes and opportunities defined by the inference of hidden environmental and task-relevant contexts. The decisions are made by computing value or expected reward over space which encapsulates the constraints relevant to the task and the environment.

Purpose: A generalized computational framework for spatial decision making can explain a spectrum of behaviours of spatial navigation in dynamic real-world environments using tasks that simulate varied environmental constraints as well as spatial cognitive deficits.

Methods: A foundational theory of spatial discounting characterizing value propagation over space has been proposed to understand the decision variables employed in spatial navigation. Building on this theory, a computational reinforcement learning model of spatial decision making, Context-Aware Deep Utility Network (CADUN) has been developed that integrates rewarddriven latent state inference encoding contextual memory, with state-action value and uncertainty estimation to compute utility over space.

Results: The model learns representations of expected value and uncertainty in partially observable 2D virtual environments with stochastic reward contingencies. Following failure to receiving reward at an expected goal location, latent representation encodings switch contexts, enabling immediate redirection to alternate reward locations. The resulting utility value profile over the environmentspace reveals how value and uncertainty shape action selection together, reflecting the learned contexts.

Conclusion: A computational framework is presented connecting the development of spatial value profiles, latent-state inference, and decision making over spatial uncertainty. The framework motivates investigation into adaptive navigation behaviour and its potential disruptions in disorders symptomatic of spatial deficits such as Alzheimer's Disease and Parkinson's Disease. Thus, it provides a systems-level understanding, and testable insights into supporting neural mechanisms of spatial navigation.

Keywords: Decision making, spatial navigation, reinforcement learning, context learning and memory

ST8

KiMA: Kinematics Motion Analysis for multi-modal gait analysis in spinal cord injury models

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Background: Accurate quantification of locomotor recovery is essential for evaluating therapeutic outcomes in spinal cord injury (SCI) models. However, commonly used manual scoring systems suffer from observer bias, while commercial automated gait-analysis platforms remain expensive and proprietary. Although markerless pose-estimation tools like DeepLabCut yield precise coordinate data, translating these outputs into biologically meaningful locomotor parameters typically requires custom coding and fragmented software pipelines.

Purpose: To address these computational barriers, we developed KiMA (Kinematics and Multi-modal Analysis), an open-source, web-based suite designed to unify and streamline gait and hindlimb kinematics analysis in rodent models of SCI without requiring local installation or programming expertise.

Methods: KiMA accepts DeepLabCut coordinate outputs within a browser-based application, maintaining crossplatform compatibility and local data privacy. The tool automates coordinate parsing, stick-figure reconstruction, and frame-by-frame movement inspection across workflows tailored for treadmill locomotion, footfall patterns, and CatWalk-style gait tracking.

Results: The platform quantifies comprehensive kinematic and spatial-temporal parameters, including joint angles (metatarsophalangeal, ankle, knee, hip, and pelvic), stride length, stride width, cadence, stance/swing durations, paw-contact events, swing clearance, and locomotor symmetry. For cohort-level interpretation, KiMA provides integrated statistical exploration including group comparisons, correlation analysis, and principal component analysis (PCA) alongside direct export of processed datasets and publication-ready vector figures.

Conclusion: By integrating video reconstruction, feature extraction, and multivariate statistics into a single user-friendly graphical interface, KiMA lowers the technical barrier for markerless motion analysis and enhances sensitivity for detecting subtle functional recovery in SCI research.

Keywords: Spinal cord injury, gait analysis, kinematics, DeepLabCut, locomotor recovery, markerless tracking

POSTER SESSION I

P-SN01

Mapping spontaneous neuronal activity pattern in wild type and autism spectrum disorder mouse models

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Background:Autism Spectrum Disorder (ASD) is a genetically heterogeneous neurodevelopmental condition characterised by deficits in social communication and restricted repetitive behaviours. Although there are hundreds of ASD-associated risk genes, many of these are predominantly involved in pathways regulating synapse development and neuronal excitability. Consistent with this, spontaneous neuronal activity (SNA) which is known for establishing proper functional brain networks is reported to be altered in ASD patients and mutation-based animal and cellular models. However, the mechanisms through which altered spontaneous neuronal activity contribute to behavioural phenotypes of ASD is under explored.

Purpose: We aim to investigate the brain-wide patterns of SNA across different developmental timepoints in multiple mouse models of ASD: Cntnap2 knockout mouse, FMR1 knockout mouse and 16p11.2 deletion mouse.

Methods: Each model was crossed with a reporter line Npas4-Cre;Ai9, which enables permanent tdTomato labelling of only activity-responsive neurons. Brain sections from the resulting pups, maintained under home-cage conditions, were imaged with a confocal microscope and analyzed for NPAS4-dependent tdTomato expression as a measure of basal SNA. Furthermore, we plan to perform RNA sequencing of tdTomato-labelled neurons to investigate the molecular signatures that defines such activity.

Results: Preliminary brain-wide analysis shows regional differences in mean fluorescence intensity between ASD models and wild type controls, suggesting altered neuronal excitability.

Conclusion: This study will provide insight into how ASD-associated genetic alterations disrupt brain-wide SNA and its underlying molecular programs and correlate these changes to the diverse behavioural phenotypes observed in ASD.

Keywords: Autism spectrum disorder (ASD); Spontaneous Neuronal Activity (SNA); Neuronal excitability; Npas4-Cre;Ai9.

P-SN02

Neuropeptide S suppresses pain-related aversion via activation of GABAergic interneurons within anterior cingulate cortex

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Background: Neuropeptide S (NPS) is a 20-amino acid peptide known to regulate various biological functions including pain and pain-related behaviours. NPS receptors are localized in the anterior cingulate cortex (ACC), a key brain region involved in pain processing and known to suppress pain-related anxiety. Although the involvement of the NPS/NPS receptor system in pain-related aversion has been suggested, the underlying mechanisms are still unknown.

Purpose: To investigate the role of the endogenous NPS system in pain-related aversion and mechanism underlying anti-aversive effect of NPS in the ACC.

Methods: Male Wistar rats were evaluated for anti-aversive effect of NPS in formalin-induced conditioned place aversion (F-CPA) using an unbiased place preference paradigm along with measurement of paw licking behaviour. The GABAergic signalling was evaluated using intra-ACC pretreatment of GABA-A receptor antagonist bicuculline. Immunohistochemistry was performed to assess the co-localization of NPS receptors (NPSR) on $GAD67^+$ (marker of GABA) neurons in the ACC. Neuronal activation was assessed by $GAD67^+$/c-Fos co-expression, and extracellular GABA levels in the ACC were measured using microdialysis-HPLC method. Additionally, mRNA expression of GAD67, VGluT2, and NPSR was analysed by RT-qPCR.

Results:NPS significantly attenuated the F-CPA without affecting paw licking nociceptive behaviour**.** The anti-aversive effect of NPS was suppressed by bicuculline pretreatment, while NPS (intra-ACC) increased activation of GABAergic interneurons (GAD67/c-Fos) in the ACC. Intra-ACC administration of NPS or SHA-68 does not affect locomotor activity in rats. NPS infusion into the ACC enhanced the GABA efflux and molecular analysis revealed increased GAD67 and decreased VGLuT2 expression.

Conclusion: We suggest that NPS in the ACC increased GABAergic neurotransmission and attenuated pain induced aversion in rats. These results highlight the NPS/NPSR system as potential therapeutic target for pain related aversion.

Keywords:NPS/ NPS receptor; Anterior cingulate cortex; Pain-induced aversion.

P-SN03

Intra and Inter Domain Hydrophobic Coupling Between S6 Segments Contribute to Voltage-Gated Sodium Channel Gating

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Background: Voltage-gated sodium (Nav) channel genetic variants have been associated with varied pathophysiology, including epilepsy, cardiac arrhythmia, and chronic pain. These variants are commonly classified as gain-of-function (GoF) or loss-of-function (LoF) mutations. Despite extensive structural and functional studies, the biophysical mechanisms underlying altered channel gating caused by disease-causing mutations remain obscure. Because most solved Nav channel structures are in the inactivated state, and do not depict the biophysical transitions between states.

Purpose: This study characterizes the biophysical mechanisms contributing to GoF/LoF mutations of Nav channels by determining the open and closed states of the channels using in silico prediction and functional patch clamp electrophysiology validation.

Methods: Alphafold2 was used to predict the closed and open states of Nav channels to understand the biophysical processes involved in channel gating. Site-directed mutagenesis (SDM) in conjunction with patch-clamp electrophysiology was used to validate the functional implications of mutations in channel gating.

Results: In this study, we identified a set of conserved hydrophobic residues on the S6 helices, forming an outer ring, that are structurally coupled to the intracellular gate in Nav channels. Using SDM and patch-clamp electrophysiology, we demonstrate that the outer ring of hydrophobic residues plays a critical role in channel opening and closing. From these, a mechanistic model was derived that explains how perturbations of this structural network by disease-associated mutations alter channel gating, thereby providing a unifying framework for understanding the molecular basis of Nav channelopathies.

Conclusion: In this study, we identified a novel outer ring of hydrophobic residues on the S6 helices of the pore domain in Nav channels and characterized its interactions with the intracellular gate. Our model provides a mechanistic framework for understanding how these interactions regulate Nav channel gating in physiology and pathophysiology, with implications for the development of targeted therapies.

Keywords: Alphafold2, Patch-Clamp Electrophysiology, MD Simulations, Nav Channels, Gating, Ion Channels.

P-SN04

Bioactive scaffolds and Stem Cell Therapy for Spinal Cord Injury

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Background:Spinal cord injury (SCI) causes permanent motor and sensory deficits due to the limited regenerative capacity of the adult Central Nervous System. While Gene Therapy, Stem Cell Transplantation, and Bio-scaffold based approaches show therapeutic promise, none by itself achieves robust functional recovery, highlighting the need for combinatorial strategies.

Purpose: This study evaluates whether combining Transcription Factor-mediated gene therapy, iPSC-derived motor neuron progenitors (MNPs) transplantation, and a laminin-derived bioactive peptide hydrogel enhances spinal cord repair compared with individual treatment modalities.

Methods: Human iPSC-derived motor neuron progenitors (MNPs) are transplanted into a mouse Spinal Cord contusion injury model together with a custom self-assembling hydrogel designed to provide structural support and promote cell survival and integration. Transcription factor (TF) mediated gene therapy is delivered using retrogradely/anterogradely transported AAVs to activate intrinsic regenerative programs in injured neurons while maintaining translational relevance. Histological and molecular analyses of spinal cord tissue, as well as machine learning based behavioral assessments are performed to evaluate graft survival, tissue integration, axonal regeneration, and functional recovery.

Results: Preliminary *in vivo* studies demonstrate successful integration and retention of the bioactive peptide hydrogel within the injured spinal cord, with no evidence of adverse tissue disruption. The hydrogel supports the retention and integration of co-transplanted MNPs at the injury site. Ongoing analyses are evaluating the effects of hydrogel supported MNP transplantation and TF-mediated gene therapy on corticospinal tract regeneration, graft survival, and motor recovery.

Conclusion: This triple modality approach combines cellular, genetic, and biomaterial-based therapies with translational methods to address key barriers to spinal cord regeneration and may provide a translational framework for next generation SCI treatments.

Keywords: Spinal Cord Injury, Gene Therapy, Motor Neuron Progenitor Cells, Bioscaffolds, Regeneration, Translational.

P-SN05

Maternal Chronic Intermittent Hypoxia Induces Alterations in Hippocampal Architecture and Cognitive Function in Rat Offspring

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Background: Maternal chronic intermittent hypoxia (CIH), a common feature of obstructive sleep apnea during pregnancy, is a prenatal insult that may severely impact fetal brain development. The hippocampus is very sensitive to hypoxic injury. However, the molecular and behavioral effects of maternal CIH on offspring have not been fully elucidated.

Purpose: In this study was intended to examine the impacts of maternal CIH on hippocampus architecture, neuroinflammatory responses, neuronal integrity, and behavioral outcomes in rat offspring.

Methods: Pregnant Wistar rats were subjected to chronic intermittent hypoxia during gestation, while control dams were treated to normoxia. Offspring were tested at postnatal day 5 to 7 for neonatal developing reflexes and at day 28 for adult cognitive behavior using well-established behavioral paradigms. Cresyl violet (CV) staining and immunohistochemistry for neuronal survival (NeuN), astrocyte activation (GFAP) and microglial activation (IBA1) were used to investigate the hippocampal architecture. Micromorphological and immunohistochemical alterations were evaluated.

Results: Maternal CIH adversely affected developmental milestones of the neonates and led to persistent abnormalities in adult cognitive ability. Histological study indicated altered cytoarchitecture of the hippocampus with lower neuronal density relative to normoxic controls. Immunohistochemistry showed reduced NeuN staining, indicative of neuronal loss, and elevated GFAP and IBA1 staining, indicative of astroglial and microglial activation, in the hippocampus. These structural and cellular changes were correlated with the reported behavioral deficits.

Conclusion: Long-lasting changes in hippocampus organization, neuroinflammatory responses and cognitive performance are induced by chronic intermittent hypoxia exposure during the prenatal period in rat offspring. These results give evidence that maternal hypoxia stress alters normal neurodevelopment and may predispose to neurodevelopmental problems.

Keywords: Maternal Hypoxia, Sleep Apnea, Cognition, gliosis, GFAP, Iba1, hippocampus, cholinergic system

P-SN06

Transcriptomic Analysis of Fatty Acid Metabolism Genes in Autism Spectrum Disorder

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Background: Autism spectrum disorder (ASD) is a highly heritable and complex neurodevelopmental condition driven primarily by complex genetic and environmental factors, characterized by impairment in communication, restricted social interests and stereotypical-repetitive behaviour. Fatty acid metabolism plays a significant role during brain development, however how it disrupts prenatal neurodevelopment in ASD remains unknown.

Purpose: This study investigates the specific role of the genes involved in the Fatty Acid metabolism, focusing on how the alterations impact early neurodevelopment in ASD.

Methods: A bioinformatic workflow was used to investigate fatty-acid metabolism genes in ASD. Pathway genes were selected based on their function and literature analyses. Their developmental expression profiles were assessed using the BrainSpan RNA sequencing database. Pathway analysis was performed through specific modules associated with peroxisomal, mitochondrial β-oxidation, and mitochondrial fatty-acid synthesis. Gene-network analyses were performed using GeneMANIA and differential expression was examined in ASD-associated datasets. Integration of genetic, transcriptomic, and metabolomic datasets was done to reveal the role of fatty-acid metabolism in ASD.

Results: Prioritized fatty-acid metabolism genes exhibited sustained expression across prenatal and postnatal neurodevelopment. Functional and network analyses of fatty acid metabolism genes demonstrated enrichment of mitochondrial function, cellular respiration, energy metabolism, and oxidative stress pathways, supporting their potential involvement in ASD-associated neurodevelopmental mechanisms. Mutated genes of ASD such as PTEN and CHD8 showed significant association with fatty acid metabolism genes.

Conclusion: Understanding the developmental timing of these fatty acid genes matters because it pinpoints the exact prenatal windows when metabolic disruptions can permanently alter brain wiring. By establishing a link between lipid metabolism and early neural formation, these findings prove that abnormal fatty acid processing is a core driver and not a by-product for ASD biology which ultimately, validates that these specific genes open the door to using lipid metabolic profiles as early diagnostic biomarkers and targets for timely, personalized therapeutic interventions.

Keywords: Autism, Neurodevelopment, Transcriptomics, Fatty Acid Genes, Metabolism

P-SN07

Neuroinflammatory Mechanisms Mediated by the PGE_2–PGES–EP Axis in TAAInduced Hepatic Encephalopathy in Rat Model.

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Background: Moderate hepatic encephalopathy (MoHE) is a neuropsychiatric condition of chronic liver dysfunction characterized by hyperammonaemia, glutamate-mediated excitotoxicity, neuroinflammation, and cognitive impairment. Prostaglandin-E_2 (PGE_2), Prostaglandin-E Synthase (PGES), and the E-Prostanoid (EP) receptor signaling pathway have emerged as critical regulators of neuroinflammatory responses. The contribution of the PGE_2–PGES–EP axis to hippocampal neuroinflammation during thioacetamide (TAA)-induced MoHE is still unknown.

Purpose: This study aims to elucidate the role of PGE_2–PGES–EP signaling axis in regulating neuroinflammation and cognitive dysfunction, and to further investigate the relationship between altered prostaglandin signaling, inflammatory mediators, and neuronal damage in the hippocampal region.

Methods: Adult male Charles Foster rats (4–5 months) were chronically administered TAA to induce MoHE. The model was validated through liver function tests (sGOT and sGPT), liver H&E, brain Nissl staining and behavioral assessments (NOR and Y-maze). Neuroinflammation was evaluated by Immunofluorescence and Western blotting to quantify the expression of pro-inflammatory (IL-6) and anti-inflammatory cytokines (IL-10). Hippocampal expression of PGES and EP receptors will be quantified using ELISA, Western blotting, Immunohistochemistry.

Results: TAA administration successfully induced MoHE and significantly elevated sGOT and sGPT levels in the brain. TAA-treated rats exhibited impaired spatial memory and cognition in the NOR and Y-maze tests. Hippocampal neuroinflammation was characterized by significantly increased IL-6, whereas reduced IL-10 expression, indicating an enhanced pro-inflammatory cytokine associated with cognitive dysfunction. Altered hippocampal PGES and EP receptor expression is expected to correlate with enhanced neuroinflammation and cognitive impairment.

Conclusion: The study will provide mechanistic insights into the involvement of the PGE_2–PGES–EP signaling axis in the pathogenesis of neuroinflammation during MoHE. Identifying this pathway as a crucial regulator of excitotoxic damage may provide new molecular therapeutic targets aimed at reducing neuroinflammation and maintaining cognitive function in hepatic encephalopathy.

Keywords: Hepatic Encephalopathy, Neuroinflammation, Excitotoxicity, PGE2, EP receptors.

P-SN08

Developmental Expression of ASD-risk Genes associated with Vocal Deficits in the Zebra Finch Song Control System

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Background: Autism spectrum disorder (ASD) is a neurodevelopmental disorder primarily caused by multiple reported genetic variations. Since rodents produce innate vocalizations, they cannot be used to model different aspects of the vocal deficits associated with ASD. In contrast, male zebra finches learn their songs from their fathers early in development and could potentially be used for studying ASD-related vocal behavior.

Purpose: This study focuses on finding expression patterns of ASD-risk genes in brain regions associated with vocalization and vocal learning in zebra finches, across development.

Methods: The transcriptome databases of different song control nuclei were obtained from the GEO database. A protein-protein interaction (PPI) network was constructed to identify hub genes, using Cytoscape. Following enrichment analysis to identify biological pathways, genes associated with synaptic organization and vocal deficits (*SCN2A, NLGN3, NRXN1, GRIN2B, SHANK2, SHANK3, and SYNGAP1*) were chosen for the expression study. Tissue from different song control nuclei was dissected from the brains of male zebra finches across development [between 20dph and adulthood (≥120dph)], followed by RNA isolation and cDNA preparation. Quantitative PCR (qRTPCR) was then used to examine the expression of the genes in these tissues.

Results: Higher numbers of ASD-risk genes were expressed in the song nucleus RA (robust nucleus of the arcopallium) in males and at older age groups, whereas the striatal nucleus Area X has conserved expression of about 532 ASD-risk genes classified into synaptic organization, cell signaling, transcription organization and regulation, metabolism, and translation. Our preliminary data using qRT-PCR further demonstrate the presence of these genes in song control regions.

Conclusion: Our results suggest that a number of ASD-risk genes are present in vocal control regions of zebra finches, which are vocal learners. These findings suggest that zebra finches may be used as a model system to study the mechanisms underlying vocal deficits associated with ASD.

Keywords: ASD, vocal deficits, zebra finches, vocal learners, enrichment analysis, ASD-risk genes

P-SN09

Role of Subplate Neurons in Development of AuditoryCortex in CNTNAP kockout Mouse Model of Autism

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Background: Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by impaired social communication and atypical sensory processing. Mutations in CNTNAP2 are strongly associated with disrupted cortical development and auditory processing deficits. Subplate neurons (SpNs), the earliest-born cortical neurons, play critical roles in neuronal migration, thalamocortical connectivity, microcircuit formation, and maturation of the auditory cortex. However, the contribution of subplate dysfunction to auditory cortical abnormalities in CNTNAP2 knockout mice remains unclear.

Purpose: To investigate the role of subplate neurons in the development and functional maturation of the auditory cortex in CNTNAP2 knockout mice by examining spontaneous neuronal activity, subplate microcircuit organization, and auditory stimulus-evoked responses.

Methods: Spontaneous neuronal activity will be examined during three developmental stages: before hair-cell maturation (P1–P6), before ear-canal opening (P7–P11), and after ear-canal opening (P12–P14). Widefield calcium imaging will be used to characterize spontaneous activity across the auditory cortex, while in vivo two-photon calcium imaging will assess neuronal activity within the auditory cortex and the underlying subplate layer. In vivo electrophysiological recordings will be performed to characterize spontaneous neuronal spiking during these developmental stages. Subplate microcircuit organization will be investigated in acute brain slices by combining glutamate uncaging of subplate neurons with ex vivo two-photon calcium imaging to map functional connectivity within the subplate and across auditory cortical layers. At P60, auditory stimulus-evoked responses will be evaluated using awake in vivo two-photon calcium imaging, and neuronal firing properties will be assessed using in vivo electrophysiological recordings under anesthesia.

Results: Preliminary widefield calcium imaging revealed altered spontaneous neuronal activity in the developing auditory cortex of CNTNAP2 heterozygous mice compared with wild-type littermates. Specifically, heterozygous mice exhibited a higher frequency of spontaneous calcium events, whereas wild-type mice showed a lower event frequency. In contrast, the magnitude of spontaneous calcium events was reduced in heterozygous mice and greater in wild-type controls. These findings indicate that CNTNAP2 deficiency disrupts early spontaneous activity patterns during auditory-cortical development. Ongoing studies will further investigate subplate microcircuit connectivity, neuronal spiking activity, and auditory stimulus-evoked responses to determine how these early functional alterations contribute to abnormal auditory cortical circuit maturation.

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Keywords: Autism, Auditory cortex, Subplate neuron, Spontaneous neuronal activity, Invivo Calcium Imaging

P-SN10

Circadian collapse to neurodegeneration: REV-ERBα/FABP7-mediated blood-brain barrier failure as the causal link between depression and Alzheimer's disease

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Background: Major depressive disorder confers a two-fold elevated risk for Alzheimer's disease (AD), yet the molecular interface transducing psychiatric stress into neurodegenerative cascades remains obscure. Circadian rhythm disruption and blood-brain barrier (BBB) compromise represent convergent pathophysiological hallmarks of both conditions, but a unifying mechanistic node has not been elucidated.

Purpose: To investigate whether stress-induced repression of the circadian nuclear receptor REV-ERBα derepresses FABP7, instigating mitochondrial-BBB dysfunction as a causative bridge from depression to AD, and to validate this axis as a therapeutically actionable target.

Methods: Chronic unpredictable mild stress (CUMS) was administered to amyloid-β-infused Sprague-Dawley rats. Comprehensive assessments encompassed circadian locomotor activity profiling, REV-ERBα/FABP7 expression quantification, high-resolution transmission electron microscopy for mitochondrial ultrastructure, and BBB permeability assays (tight junction immunoblotting, Evans Blue extravasation, fluorescein-dextran tracer flux). Neuroinflammatory cytokines and amyloid pathology were quantified by ELISA and Thioflavin-S histochemistry. Causal validation employed pharmacological REV-ERBα agonism (SR9009), NAD^+/SIRT1 metabolic modulation by P7C3-A20, and *FABP7* siRNA knockdown in both in vivo and in vitro BBB co-culture systems.

Results: CUMS elicited depressive-anxiogenic endophenotypes concomitant with circadian fragmentation and REV-ERBα suppression, which induced FABP7 overexpression and circadian arrhythmicity. This dysregulation initiated a pathogenic triad: (1) cellular bioenergetic failure (depressed oxygen consumption rate, ATP depletion, cristae disintegration, reactive oxygen species overload), (2) BBB dysfunction (occludin/claudin-5 loss, hyperpermeability), and (3) feed-forward neuroinflammatory polarization (elevated IL-1β, TNF-α, IL-6). This synergistically exacerbated Aβ plaque deposition, elevated Aβ40/42 levels, and exacerbated cognitive impairment phenotypes significantly attenuated by SR9009 or NAD^+/SIRT1 intervention. Remarkably, *FABP7* siRNA knockdown fully recapitulated these neuroprotective outcomes, establishing FABP7 as a causal effector.

Conclusion: We identify the REV-ERBα/FABP7 lipid-dysregulation axis as the first unified molecular substrate synchronizing circadian collapse with AD pathogenesis. This study positions FABP7 as a novel, causal, and pharmacologically tractable target for circadian-immune neuroprotection in AD.

Keywords: Alzheimer’s disease, Depression, Circadian rhythm. Blood-brain barrier

P-SN11

GREM1-mediated signaling in developing human brain and Down syndrome

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Background: Down syndrome, caused by trisomy 21, is the most common chromosomal cause of intellectual disability, with no disease-modifying therapies for its neurodevelopmental deficits. This project identifies Gremlin-1 (GREM1), a secreted BMP antagonist, as a novel driver of cortical pathology in Down syndrome, using iPSC-derived cortical organoids and human tissue to map its dysregulation and test rescue strategies. Cortical development requires coordinated progenitor proliferation, differentiation, and circuit formation; trisomy 21 disrupts this process through poorly defined mechanisms, affecting ~1 in 700 births globally and 30,000–35,000 infants yearly in India. Human iPSC-derived organoids now overcome long-standing limitations of mouse and postmortem models. Our lab found GREM1 selectively enriched in deep-layer cortical neurons and significantly upregulated in Down syndrome, a signaling axis never previously linked to Down syndrome pathology or targeted therapeutically.

Purpose: To determine how excess GREM1-mediated BMP antagonism disrupts cortical lamination and deep layer neuron specification in Down syndrome, and whether restoring BMP balance can rescue this deficit, reframing Down syndrome as a targetable signaling disorder.

Methods: We will: (1) map GREM1 expression across postmortem tissue and Down syndrome/isogenic organoids; (2) apply single-nucleus RNA-seq and CellChat ligand-receptor inference to define GREM1-driven signaling disruption; (3) test lentiviral GREM1 knockdown and small-molecule BMP pathway inhibitors to rescue deep-layer neurogenesis and nominate therapeutic candidates.

Results: Preliminary spatial transcriptomic and single-nucleus data confirm GREM1 enrichment in deep-layer neurons and significant upregulation in Down syndrome, localized to EN-L5/6 and upper-layer populations. iPSC lines, organoid protocols, and lentiviral knockdown are already established and validated.

Conclusion: This project will generate the first cell-type-resolved map of GREM1 signaling in human cortical development and Down syndrome, testing a druggable mechanism linking prenatal cortical disruption to lifelong neurological and neurodegenerative vulnerability, and advancing Down syndrome research toward disease-modifying intervention.

Keywords: Down syndrome, cortical development, iPSC-derived cortical organoids, GREM1

P-SN12

Identifying expression patterns of high-confidence ASD risk genes in the zebra finch song control circuitry across development: towards a vocal learning model of ASD

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Background: Although vocal deficits are amongst the core features of autism spectrum disorder (ASD), they cannot be studied in traditional model systems such as rodents, which are not vocal learners. Zebra finches learn their vocalizations during a sensitive period and possess neural circuits for vocal learning which are similar to those in humans. Whereas a number of high-confidence ASD-risk genes have been identified, how they lead to ASD-related vocal deficits is unclear. Given the predominance of gene expression regulators amongst ASD-risk genes, a possible convergence could be linked to dysregulation of genes involved in neuronal development and other ASD-risk genes, potentially contributing to ASD-associated phenotypes.

Purpose: To establish zebra finches as a translationally relevant model system to study ASD-associated vocal deficits by identifying the developmental expression profile of high-confidence ASD risk genes involved in gene expression regulation across the song control circuitry.

Methods: The SFARI database was used to filter out ASD-associated genes with a high confidence score (S1). Based on literature, candidate genes which were strongly associated with ASD were selected for our study. This list was further filtered using g:Profiler and literature for gene expression regulators causing speech and language impairment. Song control regions from male zebra finches were isolated across development [between 20dph, and adulthood (≥120dph)]. The Trizol method was used to isolate RNA, followed by cDNA synthesis and qRT-PCR.

Results: The high-confidence ASD risk genes ADNP, ARID1B, ANKRD11, AUTS2, CHD2, and DYRK1A were selected; they have not been examined previously in zebra finches. Preliminary findings from qRT-PCR expression profiling demonstrate that these genes are present in various song control regions.

Conclusion: This study is intended to generate a developmental expression profile of high-confidence ASD-risk genes to establish zebra finches as a translationally relevant model to study and direct therapeutics targeting vocal communication deficits in ASD.

Keywords: ASD, vocal deficits, zebra finches, vocal learners, , song control system, ASD-risk genes

P-SN13

Temporal Dynamics of Social Isolation-Induced Behavioural Changes and Their Differential Adrenergic Regulation in Adult Zebrafish

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Background: Social isolation (SI) is a significant psychosocial stressor associated with significant alterations in behavioural disturbances. However, the temporal progression of these behavioural disturbances and the neurochemical mechanisms underlying these changes remain incompletely understood.

Purpose: This study aimed to characterize the temporal progression and reversibility of SI-induced behavioural alterations in adult zebrafish (Danio rerio) and to determine the differential contribution of α1- and β-adrenergic receptor signalling in modulating these behavioural changes.

Methods: Adult zebrafish were subjected to isolation for 30 days, with behavioural assessments conducted at five-day intervals to evaluate locomotor activity, anxiety-like behaviour, social interaction, and risk-taking behaviour. Following isolation, animals underwent 20 days of resocialization to examine behavioural recovery. Isolated zebrafish were also treated with prazosin, an α1-adrenergic receptor antagonist, and propranolol, a β-adrenergic receptor antagonist, and their behavioural responses were evaluated.

Results: SI produced progressive and time-dependent alterations in locomotor activity, anxiety-like behaviour, social behaviour, and risk-taking behaviour, with the most profound changes observed around Day 20, followed by a gradual return towards control levels by Day 30. Resocialization restored most behavioural parameters to control levels, although reduced immobility persisted. Prazosin reversed SI-induced alterations in locomotor activity, anxiety-like behaviour, social behaviour, and risk-taking behaviour, but showed no effects on immobility. In contrast, propranolol selectively normalized changes in locomotion and significantly restored immobility, while having no effect on other behavioural parameters.

Conclusion: These findings show that SI induces dynamic but partially reversible behavioural changes in adult zebrafish. The different behavioural responses of α1- and β-adrenergic receptor antagonists indicate that stress-induced behavioural alterations are regulated in a receptor-specific manner, with distinct adrenergic mechanisms contributing to different behavioural domains.

Keywords: Social isolation, zebrafish behaviour, resocialization, adrenergic signalling.

P-SN14

Investigating the role of SST interneurons on olfactory working memory following early life adversity in mice

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Background: Olfactory working memory (OWM) enables the transient storage and retrieval of odour information to guide odour directed behaviour. Early life stress (ELS) induces long-lasting alterations in brain development and cognitive function, but its effects on OWM and the underlying neural mechanisms remain poorly understood. Somatostatin (SST)-expressing interneurons are important for working memory, while SST interneurons in the olfactory bulb (OB) regulate the activity of principal neurons involved in odour processing. However, if ELS-induced alterations in OB-SST interneurons directly contribute to OWM deficits remain unknown. This led us to examine the impact of ELS on OB-SST interneurons and its subsequent effects on OWM in mice.

Purpose: This study intended to investigate the effect of ELS on OWM; examined the subsequent involvement of OB-SST interneurons through optogenetic modulation, and evaluated whether environmental enrichment could rescue ELS-induced OWM deficits.

Methods: ELS was induced through early weaning at postnatal day14. OWM was assessed using an olfactory matching paradigm under freely moving conditions. c-FOS expression in SST+ interneurons across OB layers was carried out using immunohistochemistryThe rescue of impaired OWM was carried out by rearing the stressed mice under enrichment cage, where, they were provided with somatosensory enrichment, enhanced social interaction and aerobic exercises. All the parameters were analysed using Graph pad prism 8 and python.

Results: ELS mice exhibited impaired OWM, achieving approximately 55–60% accuracy at a 4-s ISI compared with approximately 82% in normally weaned controls. ELS mice also showed prolonged olfactory matching times, indicating impaired task acquisition. Reduced c-FOS expression in the OB suggested diminished neural recruitment during the task. Optogenetic inhibition of SST interneurons during the ISI, led to a reduction in OM accuracy suggesting a role of OB-SST interneurons in OWM. Environmental enrichment partially rescued ELS-induced deficits in OWM accuracy and OB c-FOS activity.

Conclusion: ELS impairs OWM and is associated with reduced activation of SST-expressing interneurons in the OB. Our findings suggest that OB-SST interneurons contribute to OWM and that their dysfunction may underlie cognitive deficits induced by ELS. Environmental enrichment can partially restore these behavioural and neural deficits.

Keywords: Olfactory working memory, Somatostatin interneurons, Olfactory bulb, Early life stress, Environmental enrichment.

P-SN15

Context-dependent neurotransmission drives alternate memory consolidation pathways

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Background: Sleep serves as a vital physiological process, playing a key role in maintaining homeostasis and enabling cognitive functions like memory consolidation. However, sleep is a highly plastic behaviour that adapts to changing environmental conditions.

Interestingly, Drosophila melanogaster can alternate between distinct memory consolidation pathways depending on the availability of food. Memory formation in well-fed flies requires sleep post training (sleep-dependent pathway), whereas starvation-induced memory is not contingent on sleep (sleep-independent pathway). This adaptive plasticity allows flies to forage for food while also consolidating food-related memories.

Purpose: While distinct neural circuits in the mushroom body (the learning centre of the fruit fly) mediate sleep-dependent and sleep-independent memory consolidation, how these alternate consolidation pathways are recruited is not well understood.

Methods: While distinct neural circuits in the mushroom body (the learning centre of the fruit fly) mediate sleep-dependent and sleep-independent memory consolidation, how these alternate consolidation pathways are recruited is not well understood.

Results: Our findings indicate that a pair of multi-transmitter neurons, ventral paired medial 3 (VPM3), mediate both sleep-dependent and sleep-independent consolidation through context-dependent neurotransmission. VPM3 secretes both Octopamine and Glutamate. We demonstrate that Octopamine release from VPM3 facilitates sleep-dependent memory consolidation in fed flies by integrating sweet taste through Octβ2R receptors. While Glutamate release from VPM3 is essential for consolidating sleep-independent memories under starved settings.

Conclusion: Hence, our findings demonstrate the role of multi-transmitter neurons in mediating memory consolidation via context-dependent release of neurotransmitters.

Keywords: Memory consolidation, multi-transmitter neurons, context-dependent neurotransmission, octopamine, appetitive olfactory memory, behavioral plasticity

P-SN16

Behavioral and Prefrontal Cortical Correlates of Emotional Attention in Major Depressive Disorder: A Functional Near-Infrared Spectroscopy St

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Background: Major depressive disorder (MDD) is one of the most common mood disorders. MDD is characterized by impaired emotional processing and cognitive dysfunction, particularly deficits in attention. A negative attentional bias is considered a key neurocognitive feature of depression. Although attentional bias has been widely investigated using behavioral paradigms, its underlying prefrontal hemodynamic correlates remain poorly understood. Functional near-infrared spectroscopy (fNIRS) offers a non-invasive approach to assess cortical activity and may help identify objective neurophysiological markers of cognitive dysfunction in MDD.

Purpose: To compare behavioral performance and task-related prefrontal cortical activation during an emotional Dot Probe Task (DPT) between patients with MDD and healthy controls using fNIRS.

Methods: This cross-sectional study enrolled 100 participants (50 patients with MDD and 50 healthy controls matched for age and sex). Participants completed a DPT while PFC activity was recorded using a fNIRS-system. Behavioral parameters (reaction time and attentional bias indices) and Task-related oxygenated hemoglobin (HbO) responses were compared between the two groups using independent t-test.

Results: Compared with healthy controls, patients with MDD showed significantly reduced positive attentional bias (−40.0±39.3 vs. 26.5±45.7 ms; $p<0.001$) and greater negative attentional bias (32.1±36.6 vs. −11.2±30.7 ms; $p<0.001$). Reaction times were significantly slower during positive incongruent ($p=0.042$), negative congruent ($p<0.001$), and negative incongruent ($p=0.009$) trials. GLM analysis of HbO responses revealed reduced activation in the left medial PFC during the negative congruent condition ($p=0.011$) and increased activation in the right medial PFC during the negative incongruent condition ($p=0.029$).

Conclusion: Patients with MDD demonstrate impaired emotional attentional processing, characterized by reduced attention to positive stimuli, enhanced attention to negative stimuli, and slower responses during emotionally salient conditions. fNIRS revealed altered medial PFC activation suggests disruption of neural mechanisms underlying attentional bias. Combining behavioural assessment with fNIRS may provide objective neurophysiological markers of cognitive dysfunction in MDD.

Keywords: Major Depressive Disorder; Functional Near-Infrared Spectroscopy; Dot Probe Task; Attentional Bias; Prefrontal Cortex; Cognitive Dysfunction

P-SN17

Beyond Conventional DTI: Characterizing White Matter Microstructural Alterations in Major Depressive Disorder Using Axial and Radial Tortuosity

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Background: Multimodal MRI and postmortem brain studies have provided evidence for structural and microstructural alterations in Major Depressive Disorder conditions (MDD). However, existing findings show lack of sensitivity and consistency. Non-conventional Diffusion tensor imaging (DTI) metrics such as axial tortuosity (AT) and radial tortuosity (RT) provide insights regarding geometric complexity of tissue and may serve as a more sensitive and specific marker of microstructural alterations.

Purpose: To investigate the microstructural brain alterations in MDD using conventional and nonconventional DTI parameters.

Methods: The data for this study was obtained from OpenNeuro database "Ketamine mechanism of action study" (Evans et.al, 2026; OpenNeuro ds005917). The study consisted of 47 participants aged 18-65 years, 27 MDD , and 20 healthy subjects. Diffusion-weighted images were pre-processed using the FMRIB Software Library (FSL) followed by tensor fitting to generate Axial Diffusivity (AD), Fractional Anisotropy (FA), Mean Diffusivity (MD) and Radial Diffusivity (RD), AT and RT maps. Tract-Based Spatial Statistics (TBSS) was employed to identify white matter alterations, followed by atlas-based localization and receiver operating characteristic (ROC) analysis.

Results: Subjects with MDD exhibited significantly reduced AT, FA and RT along with increased AD, MD, and RD values in comparison with healthy controls (all $p < 0.01$). Atlas localization identified prominent involvement of the superior longitudinal fasciculus, anterior thalamic radiation, inferior fronto-occipital fasciculus, and corticospinal tract. All diffusion metrics demonstrated strong discriminatory performance in ROC analysis with AT yielding the highest accuracy at AUC = 0.915, outperforming conventional DTI metrics.

Conclusion: MDD is associated with potential disruption in white matter tracts, axonal integrity, and myelin organization as reflected by the computed DTI metrics. The higher AUC values of AT and RT in the ROC analysis suggest their potential as a more sensitive and efficient marker for characterizing microstructural alterations in MDD.

Keywords: Major Depressive Disorder, Axial tortuosity, Radial Tortuosity, Diffusion Tensor Imaging, White matter microstructure.

P-SN18

Jagged1-Notch1 signaling mediated astrocyte-neuron communication in stress response and antidepressant activity

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Background: Major depressive disorder (MDD) is a common neuropsychiatric disorder in which astrocyte dysfunction and impaired neuron–glia communication are increasingly recognized as key contributors. Our previous work showed that astrocyte-specific deletion of Jagged1 induces anxiety- and depression-like behaviors, suggesting an essential role for astrocytic Jagged1 in mood regulation.

Purpose: To investigate whether astrocytic Jagged1 regulates mood through astrocyte-to-neuron Notch1 signaling and to determine its involvement in the therapeutic actions of antidepressants.

Methods: Primary astrocytes were treated with norepinephrine to examine Jagged1 regulation. Astrocyte-specific inducible Jagged1 conditional knockout (GFAP-CreERT2) mice were used to assess behavioral effects. Hippocampal Jagged1 expression and neuronal Notch signaling were evaluated following chronic antidepressant treatment.

Results: Norepinephrine significantly increased Jagged1 expression in primary astrocytes. Chronic fluoxetine and desipramine treatment similarly upregulated hippocampal Jagged1, whereas chronic unpredictable multiple stress (CUMS) reduced its expression. Astrocyte specific Jagged1 deletion produced robust anxiety- and depression-like behaviors. In addition, chronic antidepressant treatment activated neuronal Notch signaling, suggesting that astrocyte-derived Jagged1 mediates astrocyte-to-neuron communication.

Conclusion: Astrocytic Jagged1–Notch signaling is a critical regulator of mood-related behavior and a potential mediator of antidepressant action. These findings identify the astrocytic Jagged1–neuronal Notch axis as a promising therapeutic target for developing novel antidepressant therapies.

Keywords: Jagged1, Notch1, CMUS, Norepinephrine, Antidepressants.

P-SN19

Effect of PD linked pathogenic *LRRK2* I1371V mutation in Human Microglia

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Background: Parkinson's disease (PD) is a severe neurodegenerative condition marked by a specific loss of dopaminergic (DA) neurons in the midbrain region's substantia nigra. One of the most common causes is pathogenic mutations in the *LRRK2* gene. Microglia, the brain's resident immune cells, show high expression of LRRK2. Microglia play a dual role in PD. While they are essential for clearing pathogens and protein debris, under disease conditions, the activation of microglia becomes a chronic self-perpetuating cycle of neuroinflammation and disease progression.

Purpose: The pathogenic GTPase domain mutation LRKK2 I1371V is more frequently found in Indian and East-Asian populations. The I1371V variant significantly impact on the development and functionality of Astrocytes and Dopaminergic (DA) neurons. Thus we aimed to study the effect of this mutation on key microglial functions.

Methods: Human microglial cell line C20 was used in this study. The cells were transfected with pDEST51-LRRK2-WT, LRRK2-IV and Empty Vector plasmids. These cells were then used to study functional properties like phagocytosis, endocytosis, secretion as well as programmed cell death and neuroinflammatory pathways in the presence of kinase inhibitor GW5074.

Results: Significant functional impairments in LRRK2-IV C20 cells including motility, membrane anisotropy and surface protein expression, which are partially recovered when treated with kinase inhibitor GW5074.

Conclusion: The *LRRK2* mutation I1371V leads to pathogenic effects in microglial cell functions and activities, with kinase inhibition a definite avenue for continued research.

Keywords:Parkinson's Disease, Microglia, Neurodegenerative Diseases, Neuroinflammation

P-SN20

Microglia Derived Extracellular Vesicles Carry Differentially Expressed Protein Signatures In Dementia Cohort Compared To Control

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Background: Microglia respond to subtle changes in their cellular niche, maintain the homeostasis by phagocytosis and are also involved in synaptic pruning and cell to cell communication via receptor mediated interactions or secretory vesicles. These secretory or extracellular vehicles (EVs) are reported to carry cytokines, chemokines and factors that result in neuroinflammation in disorders like Parkinson's, Alzheimer's, Frontotemporal Dementia, Multiple Sclerosis, and related conditions.

Purpose: Exosomes have been reported to propagate pathological peptides like Amyloid beta (Aβ) and tau-5, Alpha synuclein (α-syn), and other misfolded or mutated proteins that are evident and part of microglial exosome cargo. Thus, our study focuses on investigating the biomarker potential of extracellular vesicles (EVs) in dementia and other neuropathies.

Methods: To achieve our objective, in-vitro models and mammalian samples were investigated for the proteomic profile of exosomes. Control and diseased blood samples from 50 to 70 age group were collected and microglia specific exosomes were isolated which were subsequently processed for LCMS/MS based discovery proteomic analysis.

Results: Mass Spectrometry analysis resulted in 259 significant proteins to be differentially expressed, out of which top 50 upregulated and down regulated genes were analysed, in which proteins like GRID2, INPPB, NLRP1, IMPA1, ARHGEF12, SYCP2, SOX4 and HSP70 were highly upregulated suggesting neuroinflammation. Whereas proteins like PkD2, TAF2, ROCK2, SCN2A, CARD14, were downregulated in dementia patients as compared to control.

Conclusion: Study shows significant changes in protein expression compared to control that highlights the scope to identify key biomarker proteins in case of dementia and related disorders. Gene ontology of the resulting proteins also shows that apoptotic pathways might be highly affected in case of dementia. upregulation of proteins like NLRP1, SOX4, and IMPA along with HSP70, also suggest the neuroinflammatory pathways being activated that may lead to neuroinflammation causing dementia.

Keywords: Microglia, Exosomes, Neuroinflammation, Dementia

P-SN21

Regulation of ferroportin in Lipopolysaccharide-induced microglial cells

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Background: Recent reports reveal iron accumulation in microglia present in inflammatory foci contributing to neuroinflammation. The cellular mechanism of iron accumulation in inflammatory microglia is not understood so far.

Purpose: Iron release in all mammalian cells is controlled by membrane protein ferroportin (Fpn). Lipopolysaccharide (LPS) decreases Fpn mRNA by transcriptional mechanism in systemic macrophages (Drakesmith et al, 2015; Marques et al, 2025). Inflammation also induces release of the peptide hormone hepcidin from hepatocytes to promote Fpn proteasomal degradation in macrophages (Nemeth et al, 2004). This study was undertaken to explore the regulation of Fpn and whether that may explain elevated iron level detected in inflammatory microglia present in neuroinflammatory foci. LPS-induced microglial cells are considered to understand the regulation of Fpn and cellular iron accumulation.

Methods: Gene expression and protein level were detected by qRT-PCR and Western blot, respectively. Fpn promoter activity was detected by dual-luciferase reporter assay. Microglial inflammatory response was detected by pro-inflammatory cytokine level and IBA1 immunocytochemistry. Intracellular iron pool was detected by Calcein-AM assay. The study was performed using mouse BV-2 and human CHME3 microglial cells.

Results: LPS treatment decreased Fpn and increased intracellular iron levels in microglia. Simultaneously, microglial activation marker (IBA1) and pro-inflammatory cytokines were also increased. Fpn level was affected at mRNA level and by protein degradation. LPS-induced silencing of Fpn transcription is mediated by its enhancer region. Further, Fpn protein degradation is promoted by hepcidin as the binding mutant of FpnFlag remained unaltered by LPS. Simultaneously, hepcidin mRNA expression was increased in LPS-treated microglial cells. The decrease in Fpn resulted in an increase in the intracellular iron pool.

Conclusion: Results reveal a dual mechanism of decrease in iron export component ferroportin in LPS-induced microglial cells. Considering Fpn as the unique iron exporter in microglia, these results suggest a potential mechanism of iron accumulation in inflammatory microglia.

Keywords: Microglia, Inflammation, LPS, Ferroportin, Iron accumulation

P-SN22

Differential Spatial Propagation of Gliosis Correlates with Cholinergic Microarchitecture Following Stereotactic Amyloid Beta Injection in the Rat Hippocampus and Striatum

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Background: Selective regional vulnerability is a hallmark of Alzheimer's disease (AD), where the hippocampus is severely affected while other brain regions such as the striatum remain comparatively resistant. Although amyloid beta (Aβ)-induced gliosis and cholinergic dysfunction have been extensively reported, the structural basis underlying differential inflammatory propagation between distinct brain regions remains poorly understood.

Purpose: The present study investigated region-specific astrocytic and microglial responses following stereotactic Aβ1–42 injection in the hippocampus and striatum and evaluated whether these inflammatory patterns correlate with cholinergic microarchitecture.

Methods: Aggregated Aβ1–42 was stereotactically injected into the hippocampus and striatum of adult Wistar rats. Immunohistochemistry for glial fibrillary acidic protein (GFAP), ionized calcium-binding adaptor molecule-1 (Iba1), and choline acetyltransferase (ChAT) was performed to evaluate astrocytic activation, microglial organization, and cholinergic architecture respectively. Spatial propagation distance and cholinergic varicosity morphology were quantitatively analyzed.

Results: The hippocampus demonstrated extensive astrocytic and microglial propagation following Aβ exposure compared with the striatum. GFAP-positive astrocytes in the hippocampus showed organized spreading within the dentate gyrus, particularly along the granule cell layer and molecular layer, extending approximately 15–20 μm beyond the injection site. In contrast, astrocytic spread in the striatum remained localized to approximately 5 μm surrounding the injection core. Iba1 immunohistochemistry revealed clustered phagocytic microglial organization in the hippocampus, whereas the striatum exhibited comparatively restricted inflammatory activation. ChAT immunohistochemistry demonstrated marked regional variation in cholinergic varicosity morphology, with larger varicosities observed in the hippocampus (~7 μm) compared with compact varicosities in the striatum (~2 μm).

Conclusion: The findings demonstrate region-specific inflammatory propagation following stereotactic Aβ administration and suggest that intrinsic cholinergic microarchitecture may contribute to selective neuroinflammatory vulnerability in the rat brain.

Keywords: Amyloid beta, Alzheimer's disease, gliosis, GFAP, Iba1, ChAT, hippocampus, striatum, cholinergic system, neuroinflammation

P-SN23

Elucidating the Impact of SARS-CoV-2 on Neurodevelopment Using Human Brain Organoids

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Background: The COVID-19 pandemic, caused by SARS-CoV-2, has been associated with neurological complications, along with respiratory illness, with nearly 50% of patients developing neurological post-acute sequelae (neuro-PASC). *In utero* exposure to SARS-CoV-2 increases susceptibility to neurodevelopmental disorders (NDD) in offspring as the developing fetal brain is highly vulnerable to maternal immune activation, placental dysfunction, direct vertical transmission, which can lead to disrupted neural circuit formation and long-term neurodevelopmental consequences.

Purpose: In this study, we aim to investigate the potential mechanisms by which SARS-CoV-2 impacts fetal neurodevelopment.

Methods: We employed a physiologically relevant model system of microglia containing human brain organoids (Mi-HBOs) via co-culturing HPSCs with iPSCs to study the virus-induced neurodevelopmental alterations. Mi-HBOs at D60 were used for viral infections at MOI = 1 and MOI = 2 and harvested at 72 hpi for biochemical and molecular analyses.

Results: Mi-HBOs recapitulate key features of early human neurodevelopment through organized tissue architecture, stage-specific gene expression, and the presence of relevant neuronal and glial populations. Cortex-like organization was confirmed by the expression of layer-specific markers including PAX6, BRN2, CUX1, RORβ, SATB2, and CTIP2, while $IBA1^{+}$ microglia confirmed the incorporation of immune components within the model. Live infection with SARS-CoV-2 Omicron BA.1 was successfully established, validating Mi-HBOs for investigating virus-induced neurodevelopmental alterations. SARS-CoV-2 infection produced MOI-dependent dysregulation of NDD-associated genes, with SYNGAP, RELN, ARID1B, CTIP2, FMR1, and NPY broadly suppressed at MOI = 1. At MOI = 2, several of these changes were attenuated or reversed, suggesting a potential compensatory transcriptional response to increased viral burden. However, NPY remained persistently suppressed, highlighting selective disruption of NPY-associated neuromodulatory signaling.

Conclusion: These results demonstrate a SARS-CoV-2 caused disruption in cortical specification during early brain development. The irreversible suppression of NPY across different doses, points to an inhibitory signalling vulnerability during early brain development. Moreover, Mi-HBOs offer a microglia-competent interface to elucidate inflammatory and developmental consequences of viral exposure to the brain.

Keywords: SARS-CoV-2, COVID-19, Brain Organoids, Neuro-PASC, Neurodevelopmental Disorders

P-SN24

Phospho-STAT3 Dependent Transcriptional Regulation of Myelin Basic Protein is Disrupted Under Hypoxia in Human Fetal Neural Stem Cells Derived PreMyelinating Oligodendrocytes

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Background: White matter injury (WMI) is the most common brain lesion in preterm infants and primarily results from hypoxic–ischemic injury. It preferentially affects vulnerable premyelinating oligodendrocytes (pre-OLs) during the critical developmental window of 23–32 weeks postconceptional age, resulting in maturation arrest and hypomyelination. However, the molecular mechanisms underlying hypoxia-induced impairment of oligodendrocyte differentiation remain poorly understood.

Purpose: This study aimed to identify signaling pathways disrupted by hypoxia in human fetal neural stem cell-derived pre-OLs and determine their role in oligodendrocyte maturation and myelin basic protein (MBP) expression.

Methods: Transcriptomic analysis was performed to identify pathways altered during hypoxia-induced pre-OL maturation arrest. IL-6/STAT3 signaling was validated by assessing IL-6 expression, STAT3 phosphorylation, and PIAS3 expression. Oligodendrocyte maturation was evaluated by morphology, MBP-positive cells, and MBP transcription. STAT3 regulation of the MBP promoter was investigated using in silico promoter analysis, molecular dynamics simulations, dual-luciferase assays, site-directed mutagenesis, and chromatin immunoprecipitation (ChIP). In vivo validation was performed using the Rice–Vannucci neonatal hypoxic–ischemic model in P6 rats, with P-STAT3 evaluated at P8.

Results: Hypoxia selectively suppressed the JAK-STAT pathway, accompanied by reduced IL-6 expression and STAT3 phosphorylation and increased PIAS3 expression. Hypoxia impaired oligodendrocyte differentiation and reduced MBP expression. Multiple STAT3-binding sites were identified in the MBP promoter, and functional assays demonstrated that STAT3 directly regulates MBP promoter activity. Two sites showed the strongest regulatory effects, while ChIP confirmed STAT3 binding at selected MBP promoter sites. Importantly, p-STAT3 expression was also reduced in P8 rats following hypoxic–ischemic injury compared with sham controls.

Conclusion: These findings identify STAT3 as a direct transcriptional regulator of MBP and demonstrate that hypoxia-induced suppression of the IL-6/STAT3 axis contributes to pre-OL maturation arrest. The IL-6/STAT3 pathway may represent a potential therapeutic target for hypoxia-associated WMI and impaired developmental myelination.

Keywords: Human fetal neural stem cells, pre-OLs, hypoxia, phosphorylated STAT3

P-SN25

Regulation of Astrocytic TIMP-1 and Therapeutic potential of a TIMP-1-Derived Peptide in Alzheimer's Disease

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Background: Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by the accumulation of extracellular amyloid-β (Aβ) plaques and intracellular tau neurofibrillary tangles. Tissue inhibitor of metalloproteinase-1 (TIMP-1), a neuroprotective cytokine secreted by astrocytes in response to Aβ, is reported to be dysregulated during AD pathogenesis. However, the molecular mechanisms underlying the regulation of TIMP-1 expression and its neuroprotective effects remain incompletely understood.

Purpose: This study was designed to investigate the molecular mechanism regulating TIMP-1 expression and to evaluate the neuroprotective effects of a nine-amino-acid TIMP-1-derived peptide corresponding to its CD63-binding domain in *in vitro* and *in vivo* models of AD.

Methods: For *in vitro* studies, primary mouse cortical astrocytes were treated with oligomeric Aβ1-42 for different time periods in the presence or absence of pharmacological inhibitors of specific signaling pathways. Primary mouse cortical neurons were treated with the TIMP-1 peptide, with or without Aβ1-42, for 16 h, followed by assessment of neuronal survival and apoptotic signaling. For *in vivo* studies, C57BL/6 and 5xFAD mice (n = 5 per group; 5–6 months old; 25–30 g) received intracerebroventricular administration of the TIMP-1 peptide by stereotactic surgery. Following treatment, a battery of behavioral tests was performed to assess learning and memory. At the end of the treatment period, brains were collected for biochemical and molecular analyses.

Results: Aβ1-42 treatment increased TIMP-1 transcript and protein expression in primary astrocytes, with maximal increases observed at 3 and 6 h, respectively. Pharmacological inhibition of ERK signaling with U0126 significantly attenuated Aβ-induced TIMP-1 expression, indicating that ERK signaling contributes to the regulation of TIMP-1 in astrocytes. In primary neurons, the TIMP-1 peptide restored Aβ-induced Akt inactivation and significantly reduced neuronal apoptosis. Furthermore, intracerebroventricular administration of the TIMP-1 peptide significantly improved cognitive and memory deficits in 5xFAD mice.

Conclusion: Our findings demonstrate that Aβ-induced TIMP-1 expression in astrocytes is regulated, at least in part, through the ERK signaling pathway. Moreover, the TIMP-1-derived peptide exerts significant neuroprotective effects *in vitro* and improves cognitive deficits in an AD mouse model. These findings identify the TIMP-1 peptide as a potential therapeutic candidate for AD.

P-SN26

Neuroprotective Effects of Low-Intensity Focused Ultrasound in Early Traumatic Brain Injury via the Orexin-A/NF-κB/NLRP3 Signaling Pathway in Rats

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Background: Traumatic brain injury (TBI) is a major risk to human health, with high rates of disability and death. To mitigate the effects of TBI on individuals and society, more effective treatment options must be investigated. Ultrasound, an emerging neuromodulation technology, is utilized to treat several neurological illnesses, however the neuroprotective mechanism of low-intensity focused ultrasound (LIFUS) in TBI remains unknown.

Purpose: The purpose of this study was to look into the protective effects and probable mechanisms of LIFUS in TBI.

Methods: The free-fall method was used to generate a rat model of TBI. After generating the TBI model, the hypothalamus region was exposed to LIFUS radiation, and an orexin receptor 1 (OXR1) antagonist (SB334867) was administered intraperitoneally. Three days later, a neurobehavioral test, Nissl staining, hematoxylin and eosin staining of brain tissue, and brain water content were all conducted. LIFUS's neuroprotective mechanisms were evaluated using Western blotting, quantitative real-time polymerase chain reaction, immunofluorescence staining, and immunohistochemistry staining.

Results: LIFUS treatment alleviated tissue damage, neurological impairments, and cerebral edema. LIFUS can boost OX-A and OXR1 expression, inhibit NF-κB and NLRP3 activation, and reduce pro-inflammatory factors after TBI. However, SB334867 can counteract this effect.

Conclusions: This data demonstrates that LIFUS may serve a neuroprotective effect by boosting OX-A release from the hypothalamus and suppressing the inflammatory response after TBI via the OX-A/NF-κB/NLRP3 pathway.

Keywords: Traumatic brain injury, Orexin-A, NF-Kb, NLRP3 Signaling Pathway, SB334867

P-SN27

A Framework for 3D Reconstruction of Brain Regions from Whole-Brain Histology

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Background: The human fetal brain undergoes rapid development with structural and cytoarchitectural changes during gestation. Serial histology sections provide the gold standard for cytoarchitectural studies, but are limited to 2D analysis. 3D reconstruction of these serial 2D sections can bridge micro-to-macro-level analysis, from the cell to the volume. Furthermore, integrating 3D-reconstructed histology data with corresponding in-skull magnetic resonance imaging facilitates comparisons across ages.

Purpose: This study presents a methodology for generating anatomically consistent 3D reconstructions of brain regions from whole-brain histology integrated with MRI reference data. Using the fetal human hippocampal formation (HCF) as an example, we demonstrate how reconstructed datasets can be used for quantitative morphological analysis and visualization across gestational ages.

Methods: In-skull MRI volumes were first brought into the common reference coordinate space using ultrasound-based landmark-based alignment. Serial histological sections were digitized at 0.5 μm/pixel, reconstructed into 3D volumes at 60 μm resolution, and registered to the corresponding MRI volume to preserve anatomical correspondence. Hippocampal formation annotations were generated on selected high-resolution sections at a sampling rate of one in three sections and propagated to intermediate sections using optical-flow interpolation. The resulting segmentations were integrated to generate 3D models for quantitative analyses, including volume, spatial orientation, centreline, and shape variation assessments.

Results: This framework generated an anatomically consistent 3D reconstruction that preserved the complex morphology of the human HCF. The resulting 3D models enabled visualization of the developmental changes and quantitative comparison across gestational ages. Analyses revealed age-related differences in hippocampal morphology, orientation, and shape, which were not readily evident from the histological sections

Conclusion: This framework provides a robust method for converting a whole-brain histology dataset into quantitative 3D models. This approach allows for comparisons of developing brain regions and has wide applications in developmental neuroscience.

Keywords: 3D Reconstruction, Histology, Morphometric analysis

P-SN28

An AI Pipeline for Human Brain Mapping of Astrocyte Morphological Distribution in Immunohistochemistry Whole-Slide Images

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Background: Astrocytes exhibit substantial morphological heterogeneity in human brain tissue. Characterizing how diverse astrocyte morphologies are distributed within tissue sections is important for understanding cellular heterogeneity and tissue-level organization. However, quantitative methods for characterizing and spatially mapping astrocyte morphological diversity within human brain whole-slide images remain limited.

Purpose: We developed an AI-based pipeline that automatically detects and segments GFAP-positive astrocytes, extracts quantitative morphological features, and groups cells with similar morphological characteristics. The framework maps these morphology-defined astrocyte groups onto whole-slide images for spatial analysis.

Methods: An optimized DAB-based GFAP immunohistochemistry protocol was applied to 20 μm postmortem human brain sections, which were whole-slide scanned at 0.5 μm/pixel and tiled into 512 × 512 patches. A YOLOv8s detector was trained on 3,999 training, 445 validation, and 1,112 test tiles to automatically localize GFAP-positive cells. Detected cells were subsequently used to generate segmentation masks through automated image processing. These masks were used to train a SimCLR-pretrained ResNet18-UNet model for pixel-level segmentation, enabling accurate delineation of cellular morphology. The resulting segmented cell polygons were quantified using area, circularity, solidity, extent, aspect ratio, and shape complexity. Standardized morphological features were clustered using K-means into three morphology groups and mapped onto whole-slide images for spatial visualization.

Results: On held-out data, the detector achieved 77.58% precision, 75.03% recall, and 76.28% F1-score. Comparable performance on an external dataset. demonstrated cross-source generalization. Morphological features extracted from the segmented cells enabled clustering. Spatial mapping visualized the distribution of these morphology groups across whole human brain sections.

Conclusion: This AI-driven framework enables large-scale characterization and spatial mapping of astrocyte morphologies, providing a foundation for studying astrocyte organization across whole human brain sections.

Keywords: GFAP astrocytes; whole-slide imaging; image segmentation; immunohistochemistry; YOLOv8; morphological clustering.

P-SN29

Spectral morphometry of the developing fetal cortex: anisotropic gyrification along intrinsic developmental axes

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Background: Mammalian cerebral cortices, with their highly gyrified pial surfaces, are among the most complex structures in nature, reflecting the interplay of morphological, functional and developmental processes across multiple scales. Quantifying cortical shape across development remains challenging because the gyrification index lacks specificity and directionality, while local mappings lack a natural, geometry-informed coordinate system defined on the pial surface and transferable across cortices.

Purpose: To develop an intrinsic geometric framework for characterizing cortical morphology and to determine how directional cortical folding evolves during fetal development.

Methods: We applied a spectral geometric framework to pial surfaces from fetal brains spanning 13–35 gestational weeks. Cortical surfaces were decomposed using eigenmodes of the Laplace-Beltrami operator to derive three scale- and direction-independent dipolar coordinate fields. A spectrally aligned, squeezed hemisphere was constructed for each specimen by deforming an ideal hemisphere along three orthogonal axes to match Euclidean distances between extrema of the cortical dipolar modes. Directional gyrification indices were then defined by comparing wavelengths associated with each coordinate in the cortex and in this reference geometry.

Results: Each cortical surface exhibited two exact and one approximate dipolar coordinate fields aligned with standard developmental axes, with wavelengths decreasing from rostro-caudal to dorsal-ventral to medio-lateral. The resulting coordinates provided a compact intrinsic description of cortical geometry throughout development and defined a gyrification-sensitive measure of cortical size that increased steadily with gestation, remained uniform across hemispheres and was unaffected by acceleration of cortical folding around 27 weeks. Directional gyrification indices revealed that cortical folding is fundamentally anisotropic, with a pronounced rostro–caudal bias emerging around 27 gestational weeks.

Conclusion: Cortical folding is not an isotropic phenomenon but is structured along intrinsic developmental axes of the cortex itself. The proposed spectral coordinate system provides a natural, transferable and geometry-informed framework for quantifying cortical shape, enabling direct comparisons across developmental stages and potentially across individuals and species.

Keywords: Laplace–Beltrami eigenmodes, fetal development, spectral geometry, cortical morphology, directional gyrification, intrinsic developmental axes

P-SN30

A novel physics-based methodology for automated brain anatomical segmentation utilizing cell spatial distribution alone.

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Background: Identifying brain structures requires deep anatomical, histopathological, and biochemical expertise, particularly during early developmental stages of a human brain when regions are constantly forming and shifting. Fundamentally, the brain's macroscopic structure directly reflects the spatial arrangement of its cells, which is driven by neural connectivity. For the expert neuroanatomist, assessing basic cell density is insufficient for characterizing tissue. The true analytical challenge requires decoding complex spatial heterogeneity, distinguishing between evenly spaced, random, or highly clustered cellular distributions to extract complex anatomical information.

Purpose: This study aims to determine whether complex spatial patterns of cortical cell positioning encode latent anatomical information. To investigate this, we introduce a modular, principled methodology to extract these patterns for the automated segmentation of the early-developing human brain.

Methods: This AI-free pipeline maps anatomical structures using pure spatial coordinates, thus requiring no training data or hyperparameter tuning, and precluding hallucinations. Stained images (Nissl/IHC/H&E) are converted into (x,y) point clouds. Neighbourhoods are defined by circles overlaid on cartesian grids, with KNN-defined radii. A physics-inspired multipoles method then extracts features at each grid point. Following PCA dimensionality reduction, a second KNN step defines the number of neighboring cells before Louvain clustering generates the final map.

Results: The pipeline achieved optimal results on high-quality Nissl stains, clearly delineating anatomical regions. Crucially, the multipoles method captured complex features, identifying discrete cortical layers undetectable in original images or manual annotations. This precisely mapped structural boundaries, enabling continuous tracking of cortical thickness from early fetal brain formation through later development.

Conclusion: By bypassing AI, our physics-based approach reveals discrete cortical layers hidden in standard histology. This transparent, unbiased and modular approach accurately tracks cortical thickness throughout human foetal development. A primary future challenge entails testing this pipeline across diverse age groups and brain regions to establish generalized robustness.

Keywords: Fetal Brain Development, Physics-Based Multipoles, Cellular Spatial Heterogeneity, Automated Segmentation, Cortical Layers, Point Cloud Analysis

P-SN31

Lactobacillus paracasei ameliorates chronic-constriction injury precipitated neuropathic pain via modulating gut-brain function in rats

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Background: Neuropathic pain affects ~7–10% of the global population and remains a major clinical challenge due to limited therapeutic options. Emerging literature indicates the importance of gut microbiota in neuroinflammation and pain management via modulating the gut-brain axis.

Purpose: To investigate the therapeutic potential of *Lactobacillus paracasei* (MCC4488) in a chronic constriction injury (CCI)-induced sciatic neuropathic rat model.

Methods: Adult Sprague-Dawley rats underwent unilateral sciatic nerve CCI surgery to develop neuropathic pain. *L. paracasei* treatment (1×10 9 CFU/mL) was given for 21 days. The post-surgical pain responses were assessed by von Frey filaments, hot plate, open-field test, rotarod, and walking track analyses. The levels of cytokines, oxidative stress markers, and short-chain fatty acids (SCFAs), and neuronal-glial responses and gut histology were performed using biochemical assays, ELISA, immunocytochemistry, H&E staining, and NMR spectroscopy.

Results: Rats subjected to CCI surgery exhibited profound mechanical allodynia, thermal hyperalgesia, locomotor deficits, and sciatic nerve dysfunction. *L. paracasei* treatment significantly attenuated these CCI-generated pain indices. *L. paracasei* also reduced lipid peroxidation and restored glutathione and catalase activity. We also observed reduced expression of C-reactive protein and Ki67 in the sciatic nerve, and GFAP and c-Fos in somatosensory cortex. Histological analyses of sciatic nerve and colon revealed restoration of nerve architecture and colonic mucosal integrity in probiotic-recipient group. Additionally, *L. paracasei* enhanced SCFAs production (mainly Lactate) in fecal samples.

Conclusion: *L. paracasei* MCC4488 effectively ameliorated CCI-induced neuropathic pain by reducing neuroinflammation, improving antioxidant mechanism, restoring gut integrity, and modulating gut-brain axis mediators. These findings suggest that *L. paracasei* may represent a promising probiotic-based therapeutic strategy for the management of neuropathic pain.

Key Words: Neuropathic pain, Chronic Constriction Injury, *Lactobacillus paracasei*, Gut-brain axis.

P-SN32

A Novel Withanolide Directly Binds Tubulin to Promote Microtubule Assembly and Attenuates Dopaminergic Neurodegeneration in Experimental Parkinson's Disease

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Background: Parkinson's disease (PD) is characterized by progressive degeneration of dopaminergic neurons, with microtubule destabilization emerging as an early pathogenic event that disrupts axonal transport and promotes α-synuclein pathology. Therapeutic agents that directly stabilize microtubules may therefore offer disease-modifying benefits.

Purpose: This study investigated the neuroprotective efficacy of a novel withanolide and elucidated its mechanism of action by examining its direct interaction with tubulin, ability to promote microtubule assembly, and modulation of the PI3K/AKT/GSK-3β signaling pathway.

Methods: Molecular docking, molecular dynamics simulations, turbidimetric tubulin polymerization assays, and dissociation constant analyses were performed to characterize tubulin binding. Neuroprotective efficacy was evaluated in rotenone-treated SH-SY5Y cells and a rotenone-induced mouse model of PD using behavioral assessments, immunofluorescence, biochemical analyses, and immunoblotting to examine microtubule integrity, dopaminergic neuronal survival, oxidative stress, apoptosis, and associated signaling pathways.

Results: The novel withanolide exhibited stable binding to the α/β-tubulin heterodimer and significantly enhanced tubulin polymerization, demonstrating direct microtubule-stabilizing activity. Treatment restored microtubule integrity, improved motor performance, preserved tyrosine hydroxylase-positive neurons, reduced oxidative stress and apoptosis, and attenuated pathological αsynuclein accumulation. Furthermore, the compound activated PI3K/AKT signaling, promoted inhibitory phosphorylation of GSK-3β, and restored acetylated α-tubulin levels, indicating coordinated regulation of cytoskeletal stability and neuronal survival.

Conclusion: These findings identify a novel withanolide as a direct tubulin-binding, microtubulestabilizing agent that confers neuroprotection through coordinated regulation of cytoskeletal integrity and PI3K/AKT/GSK-3β signaling. This study highlights microtubule stabilization as a promising disease-modifying therapeutic strategy for Parkinson's disease.

Keywords: Parkinson's disease; novel withanolide; tubulin; microtubule stabilization; PI3K/AKT/GSK-3β; neuroprotection.

P-SN33

Marine bacterium *Stutzerimonas stutzeri* mitigates Parkinson's disease pathology in *Caenorhabditis elegans* via ferroptosis modulation

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Background: Parkinson's disease (PD) is a rapidly escalating neurodegenerative disorder marked by dopaminergic neurodegeneration, α-synuclein aggregation, and motor and non-motor impairments. Current therapies largely provide symptomatic relief and fail to prevent disease progression, underscoring the need for novel disease-modifying strategies. The marine biome has emerged as an unexplored reservoir of bioactive metabolites with neuroprotective potential, yet their therapeutic relevance in PD remains incompletely explored.

Purpose: This study was intended to evaluate the neuroprotective effects of *Stutzerimonas stutzeri*, a marine bacterium isolated from the Gulf of Mannar, in *Caenorhabditis elegans* models of Parkinson's disease.

Methods: *C. elegans* PD models were subjected to dietary administration of *S. stutzeri*. Following treatment, neuroprotective efficacy was evaluated by assessing dopaminergic neuronal loss, αsynuclein expression levels, and motor and sensory phenotypes. Furthermore, mechanistic analyses were conducted to investigate the modulation of ferroptosis by measuring iron homeostasis, lipid peroxidation levels, and *ftn-1* expression.

Results: Dietary administration of *S. stutzeri* successfully rescued dopaminergic neuronal loss, significantly mitigated α-synuclein expression, and improved both motor and sensory phenotypes in the *Caenorhabditis elegans* PD models. Mechanistic evaluations revealed a marked suppression of ferroptosis, which was evidenced by the restoration of iron homeostasis, attenuation of lipid peroxidation, and the recovery of *ftn-1* expression.

Conclusion: *S. stutzeri* serves as a previously unrecognized marine-derived therapeutic prospect for PD intervention. The findings highlight ferroptosis modulation as a tractable therapeutic axis in neurodegeneration, suggesting potential avenues for future disease-modifying treatments.

Keywords: Parkinson's disease, *Stutzerimonas stutzeri*, *Caenorhabditis elegans*, Ferroptosis, Neuroprotection

P-SN34

A Comprehensive Longitudinal Multimodal Brain Data Repository for Neuropsychiatric Disorder Research

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Severe psychiatric and neurodegenerative disorders impose an immense burden on patients, families, and healthcare systems worldwide. Early diagnosis remains challenging due to the complex, heterogeneous nature of these conditions and their underlying biology. CALM-Brain is a large-scale longitudinal data resource addressing this gap, built on one of the most comprehensive neuropsychiatric cohorts assembled in India, through a collaboration between NIMHANS and NCBS.

The cohort includes patients with schizophrenia, bipolar disorder, obsessive-compulsive disorder, dementia, and addiction, alongside their unaffected first-degree relatives and healthy controls. Participants undergo repeated assessments over time, combining detailed clinical and neuropsychological evaluation with multimodal brain data, structural and functional MRI, EEG, functional near-infrared spectroscopy, eye tracking, and life-event history, enabling longitudinal tracking of disease trajectory rather than single-timepoint diagnosis. For a subset of participants, whole-exome sequencing data is also available, enabling investigation from the level of genetics through to brain imaging and clinical presentation

The current curated release includes 2,282 subjects from 942 families (ages 16–92; 56% male, 44% female). Structural MRI spans 918 sessions across 821 subjects, including repeated longitudinal scans. Data are preprocessed (including de-identification, cortical segmentation, and volumetric measures) and organized in BIDS format.
Qualified researchers can register to search and browse available data. A Docker image replicating the server environment is also planned, pre-loaded with open sample data, ready-to-use tutorials, and demonstration analyses,allowing new users to get familiar with the dataset and tools ahead of requesting access.

P-SN35

Mind the Gap: Investigating the Role of Innexins in Sleep Regulation in Drosophila melanogaster

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Background: Sleep is a highly conserved behavioural state regulated by complex interactions between neuronal and glial networks. Innexins, a family of channel-forming proteins in invertebrates, which are analogous to vertebrate connexins, mediate intercellular communication through gap junctions and hemichannels and can modulate circuits. Despite their importance in cellular communication, the role of Innexins in sleep regulation remains poorly understood.

Purpose: My study aims to investigate the contribution of specific Innexins to sleep regulation in Drosophila melanogaster. To investigate the role of Innexins in sleep regulation, CRISPR-mediated knockout of selected Innexins was performed in specific neuronal and glial populations of the Drosophila melanogaster brain. Behavioural sleep assays were conducted to assess the effects of these manipulations on sleep parameters. In parallel, immunohistochemical analyses were performed to examine the expression patterns of selected Innexins in the adult brain.

Results: Preliminary analyses indicate that perturbing the expression of specific Innexins in neuronal and glial populations alters sleep parameters in Drosophila. These findings suggest that Innexin-mediated signalling in these populations may contribute to sleep regulation. Ongoing experiments aim to characterize the cellular and behavioural consequences of Innexin manipulation. These findings suggest that Innexin-mediated signalling in neurons and glia may regulate sleep in Drosophila melanogaster.

Conclusions: This work provides a framework for understanding how intercellular communication via Innexins influences sleep circuit function and the regulation of behavioural states.

P-SN36

Role of Complement factors in Sleep

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Background: Animal behaviour is regulated by complex interactions between genetic, molecular, and environmental factors. While complement cascade proteins are well known for their roles in innate immunity, emerging evidence suggests that they also contribute to normal brain function and behaviour. However, their involvement in regulating neurodevelopment and behaviour remains poorly understood.

Purpose: This study aimed to investigate the role of a key complement factor in regulating circadian gene expression, sleep behaviour, and light-dependent responses using a zebrafish model.

Methods: RNA sequencing data from a zebrafish complement mutant were analysed to identify differentially expressed genes. Larval behavioural assays, including sleep analysis and the light-dark transition (LDT) assay, were performed to assess behavioural phenotypes. Quantitative real-time PCR (qRT-PCR) was used to validate changes in gene expression. Immunohistochemical assays were performed to investigate structural and functional changes in the nervous system, and the key pathways involved.

Results: Unbiased transcriptomic analysis revealed differential expression of multiple genes involved in circadian rhythms and light perception in complement-deficient larvae, a finding validated by qPCR. Behavioural analysis showed that homozygous mutants exhibited reduced sleep compared with wild-type siblings. Although the total number of sleep bouts remained unchanged, individual sleep bouts were significantly shorter. Mutants also displayed light-dependent behavioural phenotypes suggestive of altered light sensitivity.

Conclusion: These findings reveal a role for a key complement factor in regulating sleep and light perception. The study provides new insights into the interplay between immune signalling, circadian regulation, and sensory processing, highlighting complement factors as potential modulators of behavioural and neural function.

Keywords: Zebrafish, Complement factors, sleep; light perception

P-SN37

Stroke Mimicking as Parakinesia Brachitis Oscitans- "Clock that triggers Limb Elevation"

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Background: The arm moves automatically right when a yawn starts The shoulder usually pulls backward and inward (abduction and internal rotation), the elbow bends, and the fingers straighten, It most often appears after any type of stroke, indicating that some deep extrapyramidal nerve connections remain alive and active even if voluntary control is lost. The rare phenomenon of abnormal involuntary movement of paralyzed upper limb in association with yawning following stroke was termed as parakinesia brachitis oscitans by Walusinski et al.

Purpose: To prognosticate Parakinesia Brachitis Oscitans presence as positive indicator of recovery following Stroke, highlight pathophysiology of Parakinesia brachitis oscitans following stroke.

Methods: 66-year-old female without comorbidities, presented with chief complaints of sudden left sided limb weakness, with choreiform movements of left upper and left lower limb(Predominant), with parakinesias (another action), in form of twisting , elevating left upper limb while walking , yawning, adjusting her clothes to suppress these involuntary movements CNS examination revealed- Power of 5/5 in both upper limb, 4/5 in left lower limb at hip , knee , ankle, with deep tendon reflexes diminished(1+), cerebellar examination suggestive of impaired tandem walking. MRI brain done outside showed acute infarct in right Putamen , right posterior limb of internal capsule.

Results: Patient followed in our Neurology OPD after 1 month where Parakinesia Brachitis oscitans phenomenon was persistent but frequency had come down once in 4 or 5 days. Power of limbs had improved significantly with medications and Physiotherapy

Conclusion: These involuntary, patterned movements reported by Yung-Tsan Wu et al. (Taiwan – 2013) in 52 year old male where territory of stroke was in Right Putamen coincide with our case , however it was male predominant case report, with PBO disappearing in 1 month post stroke Its presence can serve as a clinical sign of potential motor recovery.

P-SN38

From Acute Injury to Chronic Dysfunction: Resting-State fMRI Signatures of Traumatic Brain Injury

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Background: Mild traumatic brain injury (mTBI) is believed to cause widespread disruptions in the organization of large-scale brain networks, resulting in altered interregional communication and persistent cognitive and functional deficits.

Purpose: Static function connectivity (sFC) derived from the time-averaged correlation of the resting-state fMRI BOLD signal of the brain regions, was used to characterise network level pathology in mTBI during the acute phase (within 15 days post injury) and follow-up (>4 months), in comparison to healthy controls.

Methods: Seventeen healthy volunteers (age 36.17±8.31, 9 male and 8 female) and 106 acute (age 35.59±12.4, 18 female and 88 male) and 48 chronic patients (age 34.33±12.34, 6 female and 42 male) were included in this study. CONN : functional connectivity toolbox (https://www.conn-toolbox.org), was used to perform ROI-to-ROI connectivity analysis (132 Harvard-Oxford brain atlas ROIs covering the entire brain as well as 32 networks ROIs depicting intrinsic brain networks) between the groups using appropriate GLM models.

Result: The TBI patients showed reduction in attention, memory and executive functions. ROI-to-ROI analysis revealed predominant hypoconnectivity in TBI as compared to controls. In the acute phase selective hyperconnectivity between regions of the salience and dorsal attention, fronto parietal and motor networks, as well as between the language processing centres of the brain was also obtained. Chronic TBI showed reduced connectivity in language and temporal regions.

Conclusion: In acute TBI, increased connectivity between salience-frontoparietal-language-motor regions suggests early compensatory reorganisation. Acute TBI brains show over-engagement of these networks as a compensatory response to injury, attempting to maintain cognitive and sensorimotor functions. In chronic TBI, hypoconnectivity is seen in language and temporal networks, indicating impaired language comprehension and semantic processing, and this condition reflects failure of long-term compensation, with persistent disconnection in language and associative networks. Shift from hyper-to hypoconnectivity, indicates the dynamic evolution of functional brain networks after TBI. These findings support a model in which early compensatory hyperconnectivity transitions into chronic disconnection, reduced flexibility and impaired cognitive functions.

Keywords: Longitudinal traumatic brain injury, Large scale networks, Static functional connectivity.

P-SN39

Retinoic acid receptor Transcription Factors: Role & Molecular mechanisms in CNS axon regeneration

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Background: The sharp decline in the regenerative capacity of the mammalian central nervous system (CNS) during maturation is partly driven by the progressive silencing of embryonic pro-growth transcriptional networks. Reactivating these intrinsic developmental programs in adulthood represents a critical strategy for neurorepair yet the full set of Transcription Factors required for repair remains largely unknown.

Purpose: This study identified and characterized the regenerative potential of Retinoic Acid Receptors (RARs), a vital subfamily of Nuclear Receptor Transcription Factors, to drive neuronal plasticity and CNS axon regeneration following injury.

Methods: *In vitro* growth assessments were conducted using Neuro2a cells to evaluate the growth phenotypes following targeted overexpression of specific RARs, both individually and in combination. *In vivo* translation involved a general CNS injury model and a severe thoracic spinal cord injury model to assess therapeutic potential. To delineate the precise molecular mechanisms underpinning regeneration, the study utilized single-nucleus RNA sequencing (snRNA-seq) combined with CUT&RUN genomic mapping. Direct transcription factor binding was correlated with transcriptomic shifts to map specific gene regulatory networks underlying successful regeneration.

Results: *In vitro*, targeted overexpression of specific RARs significantly enhanced neurite outgrowth in Neuro2a cells compared to controls. *In vivo*, RAR overexpression coupled with CNS injury induced robust compensatory neuronal sprouting in the pyramidotomy injury model. In the thoracic spinal cord injury model, RAR treatment drove a significant increase in the number of regenerative axons traversing the injury site compared to controls. In both *in vivo* models, combinatorial delivery yielded the most pronounced regenerative response. Multi-omic analyses via snRNA-seq of the motor cortex revealed distinct transcriptomic remodelling, isolating the specific pro-growth pathways and cellular subpopulations activated by the RAR treatment. Concurrently, CUT&RUN profiling successfully mapped the direct downstream genomic binding sites of these overexpressed factors, identifying the specific gene regulatory networks responsible for the observed regenerative phenotypes.

Conclusion: Together, integrated structural and multi-omic analyses establish RARs as critical regulators of CNS regeneration. These findings provide a solid foundation for developing targeted gene therapies for severe CNS injuries.

Keywords: Retinoic Acid Receptors, Axon regeneration, Spinal cord injury, CNS plasticity, Neurorepair, snRNA-seq, CUT&RUN.

P-SN40

Therapeutic Evaluation of a Mutant Huntingtin-Specific RNA Aptamer in a *Drosophila* Model of Huntington's Disease

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Background: Huntington's disease (HD) is a hereditary, advancing neurodegenerative condition caused by expansion of CAG trinucleotide repeats in exon 1 of the *huntingtin* gene. This genetic mutation produces a mutant huntingtin protein that undergoes aggregation, leading to oxidative stress, mitochondrial dysfunction, proteostasis impairment, neuronal degeneration and behavioural deficits. Currently available treatments for HD are largely symptomatic and do not target the underlying disease pathology. RNA aptamers are short nucleic acid molecules that bind targets with high specificity. Using Systematic Evolution of Ligands by Exponential Enrichment (SELEX), RNA aptamers that selectively bind mutant huntingtin were previously identified in our laboratory. Among these, aptamer 2.3.42 showed high affinity and specificity for mutant huntingtin and was found to inhibit aggregation, reduce oxidative stress, improve proteostasis and enhance cell survival in yeast and mammalian HD models.

Purpose: The present study aims to evaluate the therapeutic potential of aptamer 2.3.42 in *Drosophila melanogaster* and determine whether its protective effects can be extended to an *in vivo* HD model.

Methods: A transgenic UAS-aptamer fly line was generated using phiC31-mediated integration and crossed with the GMR-GAL4: UAS-htt Ex1-pQ93 HD model line. The resulting progeny were subjected to behavioural analyses, including phototaxis, climbing and lifespan assays, to evaluate the effects of aptamer expression. Retinal degeneration was further examined using stereomicroscopy, nail imprinting and FE-SEM analysis.

Results: Aptamer 2.3.42 significantly improved locomotor and behavioural performance in the *Drosophila* HD model. Aptamer expression reduced HD-associated neurodegenerative phenotypes. The loss of eye pigmentation observed in HD flies was markedly improved following aptamer expression. Overall, aptamer 2.3.42 rescued multiple behavioural and morphological impairments induced by mutant huntingtin expression.

Conclusion: This study investigated the *in vivo* efficacy of a mutant huntingtin-specific RNA aptamer as an aggregation-targeting therapeutic strategy for HD. The findings will provide insights into its potential for further preclinical development and evaluation in higher animal models.

Keywords: RNA aptamer; Huntington's disease; *Drosophila melanogaster*; protein aggregation; *in vivo* validation

P-SN41

Effect of noopept, a dipeptide on SOD1 and FUS based cell-model of Amyotrophic Lateral Sclerosis.

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Background: ALS-associated mutations in SOD1 and FUS drive key disease mechanisms, including protein misfolding, oxidative stress, mitochondrial dysfunction, and impaired RNA metabolism. Till date, there is no cure for ALS. Noopept, a dipeptide known to cross blood-brain barrier, has a neuroprotective role in neurodegenerative diseases including Alzheimer's disease, Parkinson Disease. However, role of noopept in ALS remains unexplored.

Purpose: To check the potential role of noopept as therapeutics in ALS-associated SOD1 and FUS mutation.

Methods: Effect of noopept was examined in NSC-34 motor neuron cells expressing wild-type(WT) and mutant $SOD1^{(L84F/G85R)}$ and $FUS^{(WT/P525L/D490Gfs).}$ Cytotoxicity, protein aggregation, neurite outgrowth, mitochondrial dynamics, and transcriptomic changes were assessed using LDH assays, western blotting, Sholl's analysis, Mitotracker labeling, and microarray analysis. Effect of noopept was also examined in the FUS model in the presence of exogenous stress.

Result: In the SOD1-based ALS cell model noopept showed cytoprotective and anti-aggregating effects. Microarray results have shown significant upregulation of gene associated with axonal guidance, retionic acid signalling, neurite outgrowth. Enhanced neuronal differentiation was observed following noopept treatment, with retinoic acid used as a control. Additionally, improved mitochondrial dynamics were observed, with upregulation of OPA1 and DRP1, key proteins involved in mitochondrial fusion and fission processes.

In FUS-based ALS model under sodium arsenite induced stress, mutant FUS showed enhanced TIA-1 colocalization in stressed cells compared to untreated controls, but noopept treatment did not significantly reduce this colocalization. Expression of mutant FUS led to ~10% decrease in mitochondrial footprint at axonal terminii, suggesting a possible impairment of mitochondrial trafficking.

Conclusion: Noopept may be a potent nootropic which exhibits neuroprotective effect and can be exploited to develop effective therapies for ALS.

Keywords: Amyotrophic Lateral Sclerosis, Noopept, SOD1 (L84F/G85R) and FUS (P525L/D490Gfs) Mutation, Microarray, Neurite growth, mitochondrial dynamics, Neuroprotection.

P-SN42

A Huntingtin-Derived Helical Peptide as a Therapeutic Strategy for Huntington's disease

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Background: Huntington's disease is characterized by progressive neurodegeneration associated with mutant huntingtin (mHTT) aggregation and transmission, leading to neuronal dysfunction and loss. The accumulation of mHTT disrupts cellular proteostasis, mitochondrial function, and trafficking, causing oxidative stress. Most therapies target mHTT expression or clearance, but direct inhibition of protein aggregation is still limited.

Purpose: The N-terminalα-helical region of wild-type huntingtin stabilises aggregation-prone proteins and suppresses their aggregation, indicating that a huntingtin-derived helical peptide could directly modulate mHTT aggregation and cellular protein homeostasis. This study evaluated the neuroprotective potential of the helical peptide in yeast, mammalian cells and Drosophila eye HD models expressing mHTT. In yeast and cell models of HD, intercellular transfer and modulation of mutant huntingtin aggregate spread were investigated.

Methods: In the yeast HD model, researchers evaluated the extracellular release of the helical peptide and treated mHTT-expressing cells with helical peptide lysates to assess aggregation, cell viability and oxidative stress. In the HD cell model used Neuro2a cells co-expressing the helical peptide and mHTT to examine peptide uptake, co-localisation and modulation of aggregation. In the Drosophila HD eye model, co-expression of a helical peptide and mHTT enabled assessment of neurodegeneration and provided a comprehensive evaluation of the therapeutic potential.

Results: In yeast cells expressing mHTT, the huntingtin-derived helical peptide increased soluble mHTT by 46%, reduced aggregation by 15%, improved cell viability by 50% and decreased oxidative stress by 49%. Ongoing studies in cell and Drosophila eye HD models are evaluating peptide uptake, aggregate modulation and neuroprotective effects.

Conclusion: The huntingtin-derived helical peptide may limit mutant huntingtin aggregation and propagation, modulate proteostasis and represent a promising therapeutic strategy for HD.

Keywords: Protein aggregation; Proteostasis; Intercellular propagation; Neurodegeneration; Mutant huntingtin

P-SN43

Role of the retromer component VPS35 as a critical regulator of mitochondrial dynamics in Parkinson's disease.

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Background: Mitochondrial dysfunction, including disrupted mitochondrial dynamics, is a hallmark of neurodegenerative disorders, including Parkinson's disease (PD). A PD-associated VPS35 mutant has been reported to cause mitochondrial defects and impair mitophagy. Still, the role of this retromer in the trafficking of mitochondrial fusion (MFN1/2, OPA1) and fission (dynamin-related protein 1 (DRP1), proteins is not clear.

Purpose: Although VPS35 has emerged as a critical regulator of endosomal trafficking, the molecular mechanisms linking VPS35 to the mitochondrial fission machinery remain incompletely understood. Here, we investigated the role of VPS35 in coordinating mitochondrial protein trafficking.

Methods: To investigate the role of VPS35 in coordinating mitochondrial protein trafficking, we employed VPS35 siRNA-mediated silencing, fluorescence microscopy, Co-Immunoprecipitation, Western blotting, and computational docking tools.

Results: We have shown that VPS35 siRNA-induced mitochondrial fragmentation is DRP-1-dependent and VPS35 is required for the retrieval of DRP-1 from mitochondria following fission events. Loss of VPS35 leads to mitochondrial retention of DRP1, resulting in excessive fission and mitochondrial fragmentation

Conclusion: Our research findings establish a mechanistic link between retromer dysfunction and aberrant mitochondrial dynamics and reveal a potential therapeutic target for diseases associated with VPS35 deficiency.

Keywords: Parkinson's disease, VPS35, Mitochondria, Neurodegeneration

P-SN44

Neuroprotective Effects of a Sulfonic Acid Analogue Through Modulation of Oxidative Stress, α-Synuclein Pathology, and NRF2 Signalling in Rotenone-Induced Models of Parkinson's Disease

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Background: Parkinson's disease (PD) is a progressive neurodegenerative disorder involving nigrostriatal dopaminergic degeneration, oxidative stress, mitochondrial dysfunction, impaired protein homeostasis, and pathological α-synuclein aggregation. Current therapies mainly provide symptomatic relief without preventing disease progression. Sulfonic acid analogue, with multifunctional neuroprotective and anti-aggregation properties, represents a potential disease-modifying candidate, but its efficacy and mechanisms in experimental PD remain unclear.

Purpose: This study aimed to evaluate the neuroprotective effects of sulfonic acid analogue in rotenone-induced models of Parkinson's disease and investigate the molecular mechanisms underlying its therapeutic actions.

Methods: A translational approach employing Caenorhabditis elegans and Swiss albino mice was used. Behavioural assessments were performed to evaluate dopamine-dependent and motor functions. Lipid peroxidation and oxidative stress was assessed by estimating malondialdehyde, reduced glutathione, and catalase. Dopaminergic integrity and molecular mechanisms were investigated using immunohistochemistry and Western blot analysis of dopaminergic, α-synuclein, antioxidant, autophagy, and apoptotic markers.

Results: Sulfonic acid analogue demonstrated a favourable safety profile in C. elegans(LC_{50}= 1647.02 μM) and significantly restored dopamine-dependent behavioural responses following rotenone exposure. In Swiss albino mice, sulfonic acid analogue significantly attenuated rotenone-induced motor dysfunction, reduced lipid peroxidation, and restored endogenous antioxidant defences. Molecular analyses revealed activation of the NRF2/NQO1/HO-1 antioxidant pathway, suppression of α-synuclein and phosphorylated α-synuclein accumulation, normalization of p62 expression, restoration of BCL-2 levels, and preservation of TH-positive dopaminergic neurons within the substantia nigra. Among the tested doses, 100 mg/kg consistently produced the most pronounced neuroprotective effects across behavioural, biochemical, molecular, and immunohistochemical outcomes.

Conclusion: Sulfonic acid analogue effectively mitigated rotenone-induced Parkinsonian neurodegeneration by restoring antioxidant signalling, reducing pathological protein aggregation, improving proteostasis, limiting apoptotic signalling, and preserving dopaminergic neuronal integrity. These findings provide mechanistic evidence supporting sulfonic acid analogue as a promising multi-target therapeutic candidate for further preclinical and translational investigation in Parkinson's disease.

Keywords: Parkinson's disease; Sulfonic acid Analogue; Oxidative Stress; NRF2 signalling; α-Synuclein; Neuroprotection; Rotenone

P-SN45

Expression of Sortilin in Adult Human Inferior Colliculus

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Background: Age-related hearing loss (ARHL) is a leading cause of disability. This decline in function could be central or peripheral. The inferior colliculus (IC) is a key nucleus in the central auditory pathway, and is responsible for spatiotemporal localisation and it undergoes age-related degeneration. The excitatory and inhibitory neurons in IC are maintained by neurotrophins. Sortilin (vacuolar protein sorting 10 (Vps10p) domain protein family) acts as a receptor of the cell and traffics different proteins within the cell. Sortilin's role in neurotrophin signalling and neuronal death is well established in other brain regions

Purpose: This study was intended to investigate the expression of sortilin in the human IC–a critical hub involved in age-related hearing loss, which remains largely unexplored in the literature.

Methods: Human midbrain samples containing the IC were collected from the mortuary during routine autopsies after obtaining prior approval from the Institute Ethics Committee and informed consent from the legal representatives of the deceased. The samples were fixed by immersion in chilled 4% paraformaldehyde (0.1M PB, pH 7.4). After fixation, the samples were cryoprotected, mounted and sectioned on cryotome to obtain 50 µm thick, transverse sections. These sections were stained with cresyl violet, and the expression of sortilin was determined by immunohistochemistry.

Results: The CV-stained sections showed three subdivisions of the IC- central, dorsal and lateral. All three expressed sortilin in the cytoplasm of most neurons and some glial cells.

Conclusion: The expression of neurotrophin receptors could be exploited to prevent senescence in the central auditory pathway.

Keywords: Age-related hearing loss; Inferior colliculus; sortilin; neurotrophins; cytoplasmic expression.

P-SN46

Redox Dysregulation as a Putative Driver of Cell-Specific Mitochondrial Remodeling in Hepatic Encephalopathy

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Background: Hepatic encephalopathy (HE) is a neuropsychiatric disorder associated with liver dysfunction and impaired cerebral function. It is characterized by hyperammonemia, oxidative stress, neuroinflammation, and mitochondrial dysfunction. Although mitochondrial abnormalities are well established in HE, emerging evidence suggests that redox imbalance may differentially remodel mitochondrial structure and function across distinct brain cell populations.

Purpose: This study aims to investigate whether persistent redox dysregulation drives cell-specific mitochondrial remodeling in MoHE and to identify divergent mitochondrial responses that may underlie selective cellular vulnerability.

Methods: Young male Charles Foster rats weighing 150–180g were used, and HE was induced by intraperitoneal thioacetamide administration. Model characterization was validated by serum biochemical parameters, behavioral tests, ammonia estimation, and histopathological analysis of brain and liver tissues. Oxidative stress in the cerebral cortex was assessed by measuring ROS, lipid peroxidation, antioxidant enzyme activities, and glutathione homeostasis. Mitochondrial dynamics will be examined by analyzing fusion proteins (MFN1, MFN2, OPA1) and fission proteins (DRP1, FIS1) and by assessing mitochondrial morphology, biogenesis, and mitophagy. Cell-specific mitochondrial changes will be explored using immunofluorescence-based co-localization analysis.

Results: HE caused marked hepatic and neuronal injury, evidenced by elevated liver injury markers, hyperammonemia, oxidative stress, hepatic necrosis, and reduced neuronal density. Although cell-specific mitochondrial dysfunction has not been directly assessed, existing literature suggests that oxidative stress and hyperammonemia can disrupt mitochondrial homeostasis in HE. These findings support the possibility that sustained redox imbalance may compromise mitochondrial quality control across vulnerable brain cell populations during HE.

Conclusion: Although oxidative stress in HE is well established, the brain is a heterogeneous structure in which distinct cell populations respond differently to injury. This study proposes that redox dysregulation may induce heterogeneous mitochondrial remodeling across vulnerable neural cell types rather than a uniform mitochondrial response throughout the brain.

Keywords: Hepatic encephalopathy; Oxidative stress; Mitochondrial dynamics; Cell-specific remodeling

P-SN47

SHROOM1 restricts proliferation through cytoskeleton regulation during cochlear development.

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Background: Cochlear development, which is essential for auditory function, involves complex coordination of signaling pathways, cell proliferation, and cytoskeletal organization. Unfortunately, cell proliferation ceases at E13.5, making regeneration difficult to achieve after damage, which can lead to hearing loss. Studies have shown that the BMP signaling pathway is required for cell differentiation and cytoskeletal remodeling. Interestingly, loss of BMP signaling also induced proliferation. However, the downstream effector linking BMP signaling, cytoskeletal organization, and cell-cycle regulation remains poorly understood.

Purpose: This study aimed to characterize the role of BMP-regulated gene Shroom1 in cochlear development.

Methods: Transcriptomic analysis of embryonic cochlea treated with a BMP inhibitor identifies Shroom1, a previously uncharacterized cytoskeletal gene, as a potential downstream target of BMP signaling. Whole-mount cochlear explants were cultured in vitro for drug treatments, while Shroom1 overexpression and shRNA-mediated knockdown were performed by electroporation. Shroom1 knockout and overexpression explants were used to validate loss- and gain-of-function effects. Actin organization and cell proliferation were assessed by immunostaining and BrdU incorporation. Statistical analyses were performed using Student's t-test, with $P < 0.05$ considered significant.

Results: Overexpression of Shroom1 increased actin content, confirming its role as a cytoskeletal regulator. To transiently perturb SHROOM1 function, we tested Shroom1 shRNAs in the cochlea, which reduced actin levels. Surprisingly, Shroom1-OE decreased Ki67+ proliferating cells. Shroom1 KO mouse models also showed an increase in proliferation through BrdU uptake; thus, the actin cytoskeleton has an underappreciated role in restricting cell cycle regulation. These data are similar to the results from wildtype cochlea that were treated with Latrunculin A, which also increased BrdU uptake.

Conclusion: Together, these findings show an exciting link between actin and cell cycle re-entry for regenerative purposes. Furthermore, SHROOM1 is an excellent sensory-specific candidate regulator of progenitor cell maintenance.

Key Words: SHROOM1, cochlea, BMP, actin, cytoskeleton, proliferation.

P-SN48

Role of Fibroblast growth factor signaling and F-actin cytoskeleton in dendrite regeneration in *C. elegans*

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Background: Past research has provided significant insight into the mechanisms of axonal regeneration after nerve damage, yet how dendrites regenerate remains unclear. Dendrite regeneration can occur independently of the pathways controlling axon regeneration. Using PVD mechanosensory neurons in worms, our lab has recently discovered that the fibroblast growth factor receptor (FGFR) EGL-15, and components of F-actin cytoskeleton regulators are important for dendritic regeneration.

Purpose: The goal is to clarify the spatiotemporal role of FGFR signaling and its regulation of the F-actin cytoskeleton in dendrite regeneration.

Methods: In order to degrade EGL-15 in a spatio-temporal manner, we have created an auxin-inducible degron system for EGL-15 by tagging the protein with an AID sequence at the C-terminus using CRISPR.

Results: We have observed that auxin treatment of worms carrying EGL-15::AID can produce phenotypes resembling the *egl-15* mutant, validating successful EGL-15 degradation in the new CRISPR line. More importantly, we have seen that auxin-inducible degradation of EGL-15 in PVD perturbs dendrotomy-induced branching, indicating that EGL-15 is required to initiate branches.

Moreover, by imaging the GFP::Moesin reporter, we found that following an injury to the primary dendrite, there is rapid disappearance of F-actin levels in the distal dendrites with a concomitant upregulation of branched F-actin formation at the proximal injured tip. In the absence of EGL-15/FGFR, the injury-triggered upregulation of F-actin levels and branching response is completely perturbed.

Conclusion: FGFR/EGL-15 is critical for dendrite regeneration and initiates branching via F-actin polymerization. Future research needs to determine the mechanistic connection between FGFR and F-actin polymerization and how these processes differ between development and regeneration.

Keywords: Dendrite regeneration, FGFR/EGL-15, F- Actin, GFP::Moesin ,CRISPR, AID, Sapitotemporal regulation.

P-SN49

Physical exercise as a therapeutic strategy to enhance axon regeneration

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Background: Injury to the nervous system disrupts neuronal circuits and information transfer, leading to functional disability. Functional recovery in humans is limited due to inefficient regenerative capacity. Consequently, nervous system injuries pose a global socio-economic burden. Physical exercise shows promise as an emerging therapeutic strategy. However, the underlying mechanism is not well understood, thus limiting its effective integration into therapy. Our previous work in the *C. elegans* model showed exercise has a regeneration-promoting effect, and the metabolic sensor AMPK works as a central hub for mediating exercise's effect, which can be targeted by drugs.

Purpose: This study aims to understand the mechanisms of exercise's effect on functional recovery following spinal cord injury in mice and to design an exercise-mimetic therapeutic strategy.

Methods: We induced thoracic contusion (T10) in C57BL/ 6J mice spinal cord to mimic a nervous system injury condition. The severity of injury was characterised through the assessment of the Baso mouse scale for locomotion characterisation. Further characterised the impact of injury through immunohistochemistry analysis.

Results: We have successfully established a spinal cord injury model by inducing a T10 thoracic crush. Locomotion characterisation through the Baso mouse scale shows functional impairment immediately after the injury. Our immunohistochemistry analysis of the injured spinal cord using GFAP, MAP2, and NeuN antibodies recapitulated properties of the reported injured spinal cord.

Conclusion and Future work: We are currently analysing axon regeneration through BDA neural tracing of the corticospinal tract. We are currently optimising the swimming exercise paradigm in mice as a physical exercise model, which will be incorporated into the spinal cord injury paradigm to analyse the mechanism underlying exercise's effect further.

Keywords: Axon regeneration, Spinal cord Injury, Exercise, AMPK

P-SN50

Mechanobiology to Epigenetics: Cytoskeletal mechanics regulate Sox2 gene expression in the mammalian cochlea

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Background: Sensorineural hearing loss affects over 1.5 billion people globally. Damaged sensory cells cannot re-enter the cell cycle; thus, the potential for regeneration remains limited in mammals. This is possibly due to the loss of progenitors at mouse embryonic (E) day 13.5 and change in developmental programs. Genes that are essential for progenitor cell fate are turned off in post-mitotic cells. One cause of this irreversibility is a change in chromatin accessibility. Remodelling heterochromatin could potentially open chromatin loci that can help with regeneration. Cytoskeletal stiffening creates a physical barrier for cell cycle re-entry in the mammalian cochlea. This suggests that the tissue's mechanobiology can regulate proliferation. These pathways have not been investigated in the cochlea.

Purpose: The purpose of this study is to determine whether mechanical cell forces and cytoskeletal rigidity influence the sensory regenerative potential of the mammalian cochlea.

Methods: E13.5 cochleas were cultured in the absence and presence of Cytochalasin-D (CytoD, an inhibitor of F-actin assembly and cofilin-mediated disassembly) for 4 days *in vitro*.

Results: Upon CytoD treatment, F-actin bundles had a frayed appearance. Junctional E-Cadherin was also dispersed away from the cell membrane and cells were enlarged. Unexpectedly, we saw an increase in fluorescent intensity of Sox2 relative to untreated control cochleas. Furthermore, we saw a drastic increase in the radial width of the Sox2 domain, which suggests that there was a significant change in gene transcription and sensory cell fate acquisition. CytoD treated explants showed abnormal retention of Sox2 in differentiated hair cells.

Conclusion: We predict that mechanical uncoupling of the cytoskeleton regulates cell/ nuclear shape and hence, gene transcription. We will examine whether chromatin accessibility increases with CytoD treatment. Our preliminary data highlights that mechanical cell forces influence sensory regenerative potential to restore sensorineural hearing function.

Keywords: Cytochalasin-D, Regeneration, Chromatin Accessibility, Mechanobiology

P-SN51

MYBL2 regulation of DNA Repair in auditory sensory progenitors

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Background: Maintenance of the genomic integrity is essential when cells are transitioning from progenitor to differentiated states. When this process fails in progenitors, DNA Double Strand Breaks (DSBs) lead to diseases such as Myelodysplastic Syndrome, Fanconi Anemia etc. In the auditory organ, DSBs cause hearing deficits but will show comorbidity with other neurological systems. In the cochlea, we find that DSBs lead to malformed sensory cells, which we expect, will affect normal function. During development progenitors possess dedicated machinery to fix these DSBs. DSBs can also occur in post-mitotic sensory cells e.g., after chemotherapy, however, the DSB machinery is no longer expressed in postmitotic sensory neurons.

Purpose: To characterize DNA repair pathways, we will investigate gene regulatory networks regulated by MYBL2, a critical gene required for embryonic stem cells.

Methods: MYBL2 cKO murine model has been used. IHC was performed at E14.5 with γH2AX immunolabeling to detect DSB DNA accumulation. ENCODE MYBL2 ChIP-seq was done.

Results; Our preliminary data show that loss-of-MYBL2 lead to a decrease in proliferation and an increase in DSBs in the cochlea. MYBL2 cKOs also showed defects in craniofacial and eye development; thus, MYBL2 exhibits pleiotropy. The molecular mechanisms remain unknown. To identify downstream genes involved in DSB repair, we screened ENCODE MYBL2 ChIP-seq data. Two putative targets regulated by MYBL2 are *Brca1* and *Chd1*. BRCA1, is a transcription factor that is important for regulating DNA repair genes and CHD1, a chromatin remodeler that is often found to be expressed in progenitors.

Conclusion: This study aims to develop therapeutic strategies that progenitors normally utilize to fix DSBs. We will explore whether we can modify chromatin accessibility via CHD1 to ensure genomic stability in post-mitotic cells with DSBs after chemotherapy, disease and other environmental insults, or during cellular reprogramming which often compromise DNA integrity.

KeyWords: DSB, progenitors, Auditory Organ, Mybl2

P-SN52

Role of Progenitors in the Diversification of Cortical Excitatory Projection Neurons

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Background: Cortical excitatory projection neuron diversity is established by transcription factor-defined progenitor populations during embryonic development, including LHX2, PAX6, EMX1/2 and FEZF2 among others. Although these transcription factors are expressed early during cortical development and are well-studied in terms of patterning, how they regulate later stages of projection neuron development, including fate specification, neuronal migration and axon guidance, is not well known.

Purpose: This study aims to determine how transcription factor-defined progenitors contribute to the diversification of cortical excitatory projection neurons and regulate fate specification and axon guidance, particularly formation of the corpus callosum.

Methods: Here we utilize state-of-the-art mouse genetics, fate mapping, and *in vitro* and *in utero* perturbation approaches to investigate the cellular and molecular relationship between transcription factor-defined progenitors and their neuronal progeny. We are currently investigating molecular, histological, and anatomical aspects to characterize projection neuron identity and long-range connectivity following LHX2, EMX1/2, FEZF2 and PAX6 perturbations.

Results: We have successfully characterized *Pax6* lineage progenitors using inducible genetic fate mapping and established neurosphere assays to study neuronal progenitor dynamics, confirming progenitor identity by NESTIN and SOX1 expression. We have also optimized *in-utero* electroporation for targeted genetic perturbation of cortical progenitors, establishing a comprehensive experimental pipeline to investigate projection neuron diversification. We further characterized *PlexinD1-2A-CreER* mouse line that labels callosal projection neurons among other intratelencephalic projection neurons.

Conclusion: This study will define how progenitor identity influences the generation and diversification of cortical excitatory projection neurons and establish whether early patterning transcription factors have sustained roles in shaping neuronal connectivity beyond cortical regionalization. These findings will advance our understanding of the developmental mechanisms underlying cortical circuit assembly and their implications in mammalian cortical evolution.

Keywords: Cortical progenitors; Excitatory projection neurons; Transcription factors; Fate specification; Corpus callosum

P-SN53

Development of a simple and quick assay to study the effect of physical exercise in *C.elegans*.

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Background: Aging is associated with a progressive functional decline of the organism including reduced muscle strength and cognitive function. Physical exercise is reported to be effective in ameliorating such functional decline. However, the underlying mechanism of this effect is not well studied. A better understanding of this process will help in effective integration of exercise in therapeutic strategies. We are using *C. elegans* as a model to characterize the molecular mechanism of exercise's positive effects. Previous reports show that swimming exercise in *C. elegans* improves physical fitness, axon regeneration and prevents aging associated decline in posterior touch response.

Purpose: We aim to develop a simple and efficient assay to assess physical exercise's effect on the behavioral recovery of aged animals. This assay system in combination with RNAi and drug screening paradigms will be utilized to characterize novel molecular mediators of physical exercise.

Methods: We are standardizing multiple behavioral assays for scoring the effect of physical exercise on aging associated behavioral decline. To assess the neuromuscular functionality we are using a pluronic gel based burrowing assay. Alternatively, a polystyrene based immobilization assay is developed to evaluate the neuromuscular strength.

Results: The burrowing assay was standardized for optimum gel concentration, gel height and conditions for assessing the effect of aging on neuromuscular functionality. A significant drop in the number of worms burrowing through the pluronic gel in 90 minutes was observed with ageing. This observed reduction is a readout of declined neuromuscular functionality associated with ageing.

Conclusion: A baseline was established showing a significant drop in the neuromuscular functionality of the worm using the burrowing assay. We are currently combining the swimming exercise paradigm to evaluate exercise's effect on the burrowing capability of aged animals. Alternatively, we are currently standardizing a polystyrene bead-based immobilization assay for quick scoring of aging associated decline in muscle strength.

Keywords: Aging, Physical exercise, Swimming exercise, Posterior touch response, Axon regeneration, RNAi, Pluronic gel, Burrowing assay, Polystyrene, Immobilization assay.

P-SN54

SARS-CoV-2 accessory protein Orf6 induces MTCH1 dependent necroptosis and mitochondrial dysfunction in human neurons

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Background: SARS-CoV-2 associated neurological manifestations in the form of Long COVID are instigating a major concern for mankind and the lack of detailed molecular mechanism of virus-mediated neuronal death is making it difficult to prevent the consequences.

Purpose: The primary focus of this study is to delineate the molecular mechanism of SARS-CoV-2 mediated neuronal death and the role of viral proteins to mediate this effect.

Methods: Human neuronal cultures were obtained by differentiating human fetal neural progenitor cells. These neurons were then used for both live virus infection as well as for studying viral protein pathogenesis in detail. Additionally, brain tissue sections of COVID-19 patients were utilized to validate the *in vitro* findings.

Results: SARS-CoV-2 infection and Orf6 expression led to neuronal loss via the activation of the RIPK3-MLKL signaling axis. This activation of the necroptotic pathway was confirmed by application of necroptotic pathway inhibitors like GSK'872 and Necrosulfonamide. These findings were corroborated in hippocampal brain sections of COVID-19 patients. Our data showed that Orf6 expression in neurons disturbed mitochondrial membrane potential, triggered calcium overload, and instigated oxidative stress. Knockdown of MTCH1 or pharmacological inhibition of RIPK3 potently rescued neurons from death, highlighting novel therapeutic targets.

Conclusion: In this study, we provided direct evidence that SARS-CoV-2 Orf6 led to necroptotic neuronal death, a distinct pathway from conventional apoptosis seen in viral infections. Our findings provided a mechanistic insight into the SARS-CoV-2 associated neurological complications and the possible therapeutic interventions by targeting necroptotic pathway and host MTCH1.

Keywords: SARS-CoV-2, Orf6, necroptosis, MTCH1

P-SN55

Minocycline influences Olfml3-Iba1 cross-talk in the regulation of microglial activation during neuroinflammation

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Background: Olfactomedin-like 3 (Olfml3) is a secreted glycoprotein specifically expressed in microglia in the brain. Recent findings suggest altered Olfml3 expression and its colocalization with Iba1 during neuroinflammation, indicating a potential association with microglial activation. However, the precise role of Olfml3 in microglial functions remains poorly understood.

Purpose: To investigate the molecular crosstalk of Olfml3 in microglia and its impact on LPS-induced neuroinflammation.

Methods: To explore underlying molecular interactions, molecular docking and molecular dynamics simulations were conducted among Olfml3, Iba1, and minocycline. N9 microglial cells were stimulated with lipopolysaccharide (LPS; 10µg/ml, 6h) followed by minocycline treatment (10µM). For *in vivo* analysis, chronic neuroinflammation was induced in adult male BALB/c mice using LPS (750 µg/kg body weight; days 1-14), followed by minocycline administration (50mg/kg body weight; days 8-14), and behavioral, molecular, and immunofluorescence analyses were performed to assess changes in neuroinflammation-associated behavioral deficits and microglial responses.

Results: The molecular docking and dynamics simulations supported a more favorable binding of minocycline to the Olfml3-Iba1 complex than to Olfml3 and Iba1 alone. The interaction of Olfml3-Iba1 was confirmed by Co-Immunoprecipitation. LPS stimulation significantly increased Olfml3 and Iba1 expression in N9 microglial cells, a response that was attenuated by minocycline-mediated suppression of microglial activation. Similar findings were observed *in vivo*, where LPS-induced increase in the expression of Olfml3, Iba1, and *Tnf-α*, and decreased the expression of *Tgf-β* and *Bdnf*. Minocycline administration significantly attenuated the upregulation of Olfml3, Iba1 and *Tnf-α* and restored *Tgf-β* and *Bdnf* expression. Further, minocycline treatment also showed a positive correlation between Olfml3 and Iba1 expression, along with attenuation of cognitive deficits and reduced neuroinflammation.

Conclusion: Minocycline may regulate microglial activation and associated cognitive deficits by modulating the molecular interaction between Olfml3 and Iba1 during neuroinflammation.

Keywords: Neuroinflammation, Brain, Olfml3, Iba1

P-SN56

Neuroprotective effect of sub-chronic Cystamine treatment on functional recovery in Cerebral Ischemia-Reperfusion Injury

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Background: Cerebral ischemia–reperfusion injury (I/R) induces progressive neuronal degeneration and synaptic dysfunction through secondary injury mechanisms, resulting in persistent neurological deficits. Cystamine, a tissue transglutaminase 2 inhibitor, exerts neuroprotective effects by suppressing apoptosis and activating the BDNF/TrkB pathway. However, its ability to preserve neuronal and synaptic integrity during the sub-chronic phase of cerebral I/R injury remains unclear.

Purpose: To investigate secondary neuroprotective potential of sub-chronic cystamine treatment over sensory-motor deficits, synaptic integrity and functional recovery

Methods: Male Wistar rats (200–250 g) were subjected to MCAO and received cystamine (100 mg/kg, i.p.) on postischemic 3 and 7 days. Functional recovery was evaluated using the modified neurological severity score (mNSS), cylinder test, rotarod, and beam walk test. Infarct volume and Nissl bodies were assessed using TTC staining and cresyl staining respectively. Moreover, Cell death and morphological changes were assessed by propidium iodide (PI) and hoechst staining. Additionally, IHC was performed to evaluate MBP, NeuN, and synaptophysin expression.

Results: The sub-chronic cystamine treatment significantly ameliorated neurological impairment and restored sensorimotor function following I/R. Furthermore, cystamine substantially reduced infarct volume and apoptotic cell death as well as preserved myelin integrity, neuronal survival, and synaptic architecture, as indicated by increased expression of MBP, NeuN and synaptophysin, respectively.

Conclusion: One-week cystamine treatment exhibits potential to provide functional recovery associated with sensory-motor improvement and preserve myelin, neuronal, and synaptic integrity. Cystamine may act as an adjuvant neuroprotective agent for functional recovery post ischemic brain injury.

Keywords: Cystamine, Cerebral I/R injury, Functional recovery, Neuroprotection, Sub-chronic treatment

P-SN57

To Investigate the Astrocyte Dynamics in Neuroinflammation and Their Role in Neurodegeneration

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Background: Neurodegenerative diseases affect millions worldwide, across all age groups. Neuroinflammation is a key factor of various neurological disorders such as A.Ds, P.Ds, Brain injury, and various infections. Astrocytes, the most abundant glial cells in the CNS, shift from a quiescent to a reactive state (reactive astrogliosis) during inflammation, generating diverse phenotypes that may be either protective or detrimental depending on the pathological context.

Purpose: The study aims to evaluate astrocyte dynamics in neuroinflammation by analysing Cellular, morphological, and biochemical changes in astrocytes using pharmacological modulators.

Methods: Primary astrocytes from mouse pups (P0-P2) were cultured using standard protocols. After 2-3 passages at DIV 14-16, cells were treated with LPS (1 μg/ml) and Norepinephrine (1 and 10 μm) for 6 hours. Then, cells were fixed for IHC targeting GFAP, F-actin with Phalloidin, cytokine mRNA levels were measured, and Raman spectroscopy was used to assess metabolic changes in astrocytes.

Results: In cultured astrocytes in vitro, 6 hours of LPS challenge induced a shift from planar to hypertrophic morphology. NE treatment significantly reversed this change, as shown by GFAP staining. Phalloidin staining revealed F-Actin morphology in the same group. Cytokine mRNA levels, assessed at various time points, exhibited significant changes in IL-6, TNF-α, and IL-10 expression compared to control LPS and LPS with NE. Further Raman spectroscopy revealed wavenumber shifts, indicating biochemical changes associated with Cytochrome C, nucleic acids, lipids, and aromatic amino acids, which are directly involved in neuroinflammation and neurological disorders.

Conclusion: This study demonstrated astrocyte morphological changes during neuroinflammation, confirmed using LPS and pharmacological modulation via NE. It investigated F-actin's role in these changes and validated biochemical alterations with Raman spectroscopy. The research clarifies the morphological and biochemical aspects of astrocyte dynamics, with work still ongoing.

Keywords: Astrocyte, Neuroinflammation, Neurodegeneration, Cytokine, Raman Spectroscopy, Cytochrome C.

P-SN58

Targeted inhibition of hippocampal pyramidal neuron slow afterhyperpolarization for ameliorating memory deficit in aging

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Background: Proper functioning of brain neurons is mediated by an interplay between excitatory and inhibitory (E/I) mechanisms, which ultimately support all aspects of memory and behaviour. In aging neurons, this E/I balance is compromised, leading to decreased hippocampal pyramidal neuron excitability and contributing to memory abnormalities. This has been attributed to an increase in the intrinsic inhibitory phenomenon known as the slow afterhyperpolarization (sAHP). It has been shown that L-type voltage-gated calcium channels (Cav1.3) in association with calcium-activated potassium channels and endoplasmic-reticulum and plasma-membrane (ER-PM) tethering proteins Junctophilin-3&4 (JPH-3&4) generate the sAHP current.

Purpose: This study aims to define the interacting region between Cav1.3 and JPH-3&4 to develop a novel cell-permeable interfering peptide that could potentially downregulate the pyramidal neuronal sAHP and thereby improve hippocampal-dependent cognitive functions in aging.

Methods: SIM2 imaging was performed in young and aged rats. AlphaFold3 was used to predict the interaction region between Cav1.3 and JPH-3&4, followed by FRET-based validation. The Morris water maze was performed to assess hippocampus-dependent learning outcomes in young (5-6 weeks) and aged (2 years and above) Wistar rats receiving either saline or peptide.

Results: This study found that Cav1.3 clusters were increased in aged rats compared to younger animals. AlphaFold and FRET results demonstrated the interaction of Cav1.3 C-terminus with the N-terminus of JPH-3 and JPH4, with residues located within the first four MORN motifs. Relying on the interaction region, two interfering peptides conjugated with TAT were designed, which successfully disrupted this interaction. Importantly, these peptides crossed the blood-brain barrier and enhanced hippocampal-mediated spatial learning and memory compared with aged rats receiving saline.

Conclusion: This study identifies the Cav1.3-JPHs interacting interface as a novel molecular target for sAHP modulation, and the interfering peptides designed against this interface showed efficacy in ameliorating age-associated memory deficits in vivo.

Keywords: Aging, Slow Afterhyperpolarization, endoplasmic-reticulum and plasma-membrane (ER-PM), interfering peptides.

P-SN59

Interaction between RRM-domain containing ALS-prone proteins and chaperones mediates the neurotoxicity in ALS and FTD

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Background: RNA-binding proteins (RBPs) are vital for RNA metabolism, and alterations in their function can impair neuronal development and cause neurodegenerative diseases. Molecular chaperones are widely known for their role in the dissolution of these accumulations.

Purpose: The purpose of the study was to understand how the type III Hsp40 chaperone, CG17187 (dCwc23), interacts with RRM-containing ALS-prone RNA-binding proteins, including its unique J and RRM domains, and to assess the implications for cellular localization, aggregation, and neurotoxicity.

Methods: We used multiple *Drosophila* models of neurodegeneration to screen for the role of dCwc23 in various neurodegenerative diseases. We performed several *Drosophila* larval and adult behavioral studies to assess the survival or lethality of ALS models upon deletion of one copy of *dcwc23*. We further used immunostaining, microscopy, and biochemical experiments to uncover the underlying mechanisms.

Results: We identified CG17187, an Hsp40 type-C family protein, as a regulator of eye morphogenesis in a *Drosophila* screen. CG17187 is an ortholog of yeast Cwc23, involved in the spliceosome disassembly, and is essential for survival in yeast and *Drosophila*. Furthermore, we have also shown that dCwc23 genetically interacts with the RRM-containing ALS (amyotrophic lateral sclerosis) prone proteins, such as Fus (*Drosophila* Caz) and TDP-43 (*Drosophila* TBPH). Importantly, deletion of a single copy of *dcwc23* results in the dissolution of the Fus/TDP43 aggregates in the neuronal nuclei, but surprisingly leads to early lethality, suggesting that the increased availability of soluble Fus/TDP-43 may enhance its mislocalization to the cytoplasm, where it forms toxic aggregates.

Conclusion: *dCwc23* functions as an essential chaperone in *Drosophila* and stabilizes the pathogenic nuclear TDP-43 aggregates. Consistently, loss of dCwc23 facilitates the dissolution of nuclear TDP-43 and increases the pool of soluble TDP-43 that can mislocalize to the cytoplasm, ultimately enhancing its toxicity.

Keywords: Neurodegeneration; *Drosophila*; HSP40; TDP-43

P-SN60

Long non-coding RNA enriched at synapse regulates inhibitory synapse development.

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Background: The contribution of long non-coding RNAs (lncRNAs) to excitatory synapse development is well established; however, their role in inhibitory synapse formation remains poorly understood. To identify candidate lncRNAs involved in this process, previous transcriptomic analyses from our laboratory identified a subset of lncRNAs enriched in hippocampal synaptic fractions.

Purpose: This study aimed to identify and characterize lncRNAs involved in inhibitory synapse development in the mouse hippocampus, with particular focus on the previously uncharacterized lncRNA, 2900052N01Rik (N01Rik).

Methods: Developmental expression of synaptically enriched lncRNAs was examined in the mouse hippocampus using quantitative PCR. N01Rik function was investigated by shRNA-mediated knockdown in developing hippocampal neurons using in-utero electroporation and lentiviral transduction. Synaptic morphology was assessed by confocal microscopy and analysis, while whole-cell patch-clamp electrophysiology was performed to evaluate synaptic function. Transcriptomic analysis following N01Rik depletion was conducted to identify downstream molecular pathways.

Results: Developmental profiling identified dynamic expression of several synaptically localized lncRNAs, with N01Rik exhibiting a marked increase during the period of active synapse maturation. N01Rik knockdown in CA1 pyramidal neurons selectively impaired inhibitory synapse development, significantly reducing both perisomatic and dendritic inhibitory synaptic puncta without affecting excitatory synapses. Electrophysiological recordings revealed a significant reduction in miniature inhibitory postsynaptic current (mIPSC) amplitude, with no change in frequency, indicating a postsynaptic deficit in inhibitory synaptic transmission. Miniature excitatory postsynaptic deficit in inhibitory synaptic transmission. Miniature excitatory postsynaptic currents remained unaffected. Transcriptomic analysis identified 206 downregulated genes enriched for cilia-related biological processes, including cilium abundance, while knockdown of a candidate ciliary protein phenocopied the reduction in mIPSC amplitude observed following N01Rik loss.

Conclusion: Our findings identified N01Rik as a previously unrecognized regulator of inhibitory synapse development and suggest that lncRNA-mediated regulation of cilia-associated pathways contributes to the establishment and functional maturation of inhibitory synaptic connectivity in the developing hippocampus.

Keywords: Long noncoding RNAs, hippocampus, inhibitory synapse formation, in-utero electroporation, cilia.

P061

Variant-Resolved Structural Pharmacology of GABRA1: Implications for Precision Therapy in Anxiety Disorders

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Background: Anxiety disorders are highly prevalent neuropsychiatric conditions driven by disrupted GABAergic-Glutamatergic balance and HPA-axis dysregulation. Current therapies, including benzodiazepines and SSRIs/SNRIs, are limited by adverse effects, delayed response and treatment resistance. Despite being a primary pharmacological target, GABRA1 remains underexplored for safer therapeutic discovery.

Purpose: This study aimed to identify novel GABRA1-targeting therapeutic candidates by integrating network pharmacology, disease transcriptomics, and multi-resolution structural docking across both FDA-approved drugs and anti-anxiety phytoconstituents, with the broader goal of establishing a genotype-aware computational framework for precision therapeutic discovery in anxiety disorders.

Methods:We employed an integrative network pharmacology combining drug repurposing and phytoconstituent screening. Disease-associated genes were curated and expanded (n = 121), followed by drug prioritization. Targets from FDA-approved non-anxiolytic drugs and antianxiety medicinal plants were integrated with single-nucleus RNA-seq data (3,868 DEGs) to identify hub genes (e.g., CACNA1C, GABRA1, MTOR). Functional enrichment and network analysis were performed. Molecular docking was conducted on wild-type GABRA1 followed by a variant-aware pipeline analyzing three pathogenic missense variants (K306T, P124L, D420G) using homology-modelled structures.

Results: Repurposed drugs, including Vandetanib (−8.5) and Astemizole (−8.3), showed higher binding affinity than standard anxiolytics, while Flavone (−7.8) demonstrated comparable performance. Variant-level analysis revealed that whole-receptor docking masked mutation effects, whereas subunit-level docking captured mutation-induced pocket alterations. Notably, Astemizole, Vandetanib and Flavone exhibited consistent binding across variants, suggesting genotype-resilient therapeutic potential.

Conclusion: This study highlights GABRA1 as a promising yet underutilized target and demonstrates that integrating structural and variant-level analysis can uncover genotypeinformed therapeutic candidates. The identified compounds represent potential leads for both drug repurposing and phytotherapy, advancing precision medicine approaches in anxiety disorders.

Keywords: Anxiety disorder, GABRA1, drug repurposing, phytoconstituents, molecular docking, precision therapeutics

P062

Role of protein citrullination on cognitive impairment in Intracerebroventricular-Steptozotocin induced sporadic Alzheimer disease in rats

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Background: Alzheimer's disease (AD) is a neurodegenerative disease, which is the leading cause of dementia globally. Due to its complex and multifactorial pathogenesis, drugs which can completely cure progression of disease are still unavailable. Post-translational modifications mainly, citrullination catalysed by calcium dependent peptidyl arginine deiminase (PAD) enzyme can alter structure and function of protein. PAD-induced citrullination irreversibly converts arginine residues to citrulline, producing a net loss of positive charge. Cl-amidine, a pan PAD irreversible inhibitor studied in various disease like Parkinson disease, Traumatic brain injury, Middle cerebral artery occlusion show remarkable improvement in these diseases. However, its effect in ICV-STZ induced AD is yet to be studied.

Purpose: This study aimed to investigate the effect of Cl-amidine, a pan PAD inhibitor on the oxidative stress and neuroinflammatory pathways.

Method: All animals randomly divided into 5 groups, n=10 animals per group, subjected to 21 days' animal model. Sham, ICV-STZ, ICV-STZ + Cl-amidine, ICV-STZ + Cl-amidine, and per se. Cl-amidine was administered (i.p.) at doses of 5 and 10 mg/kg for two weeks. On day 14, behavioural tests, including the Y-maze test, novel object recognition test, and passive avoidance test, were performed to assess memory function. Subsequently, the animals were euthanised and the hippocampus was collected for biochemical, molecular and histological analysis.

Results: Two weeks of Cl-Amidine treatment improved the cognitive performance in ICV-STZ-treated rats. Cl-Amidine treatment improves behavioural parameters and reduces expression of PAD2, PAD4 enzyme, and p-tau in hippocampus of ICV-STZ treated rats. It also reverses the oxidative stress such as GSH, MDA, and catalase in diseased treated rats.

Conclusion: In this study, Cl-amidine protects the rats from ICV-STZ induced oxidative stress and neuroinflammation by inhibiting the oxidative stress. These findings suggest that Cl-amidine may be a potential strategy for AD.

Keywords: Alzheimer's disease, Streptozotocin, Oxidative stress, Cl-amidine, Neuroinflammation

P063

Evaluation of the protective effect of Andrographolide-loaded nanoformulation in an experimental model of Alzheimer's disease

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Background: Alzheimer's disease (AD) is the most prevalent neurodegenerative condition globally, leading to memory decline without a proper cure. Andrographolide (AG), a diterpenoid, exhibits antioxidant, anti-inflammatory, and anti-apoptotic properties with significant neuroprotective effects against AD in preclinical studies. However, its clinical use is limited due to low aqueous solubility and poor bioavailability.

Purpose: The study aimed to overcome the inherent limitations of AG, including its poor aqueous solubility and low bioavailability, by incorporating it into a nanoformulation (NF) to enhance its delivery and therapeutic efficacy in the brain.

Methods: Characterization of the NF included analyses of particle size, PDI, zeta potential, encapsulation efficiency, drug loading, scanning electron microscopy, powder X-ray diffraction, differential scanning calorimetry, and stability studies. A cellular uptake study was conducted on N2a cells, and biodistribution was assessed in mice using an *in-vivo* imaging system following intracerebroventricular administration of Okadaic acid (OKA) to induce AD. Mice received plain AG and AG-loaded NF (AG-NF) treatments (1 mg/kg/day, intranasally) for 28 days, and effects on memory impairment were evaluated in the final week. Additionally, photoacoustic imaging was used to assess cerebral hemodynamics, followed by brain collection for biochemical analysis.

Results: The characterization of AG-NF supported its nose-to-brain delivery. Cellular uptake studies demonstrated time-dependent nanocarrier internalization, while biodistribution analysis showed prolonged brain retention. AG-NF treatment significantly improved OKA-induced neurobehavioral deficits, cerebral hemodynamics, and biochemical alterations compared with plain AG.

Conclusion: The study's outcome suggested the improved pharmacodynamic efficacy of AG at a subtherapeutic dose possibly via its nose-to-brain targeted delivery using NF approach.

Keywords: Alzheimer's disease, Andrographolide, Okadaic acid, Nanoformulation.

P064

The missing piece? Modelling inflammation in depression

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Background: Depression is a chronic and debilitating disorder affecting millions of people worldwide. Although conventional antidepressant treatments, including selective serotonin reuptake inhibitors (SSRIs), are widely used, a substantial proportion of individuals show incomplete or inadequate treatment responses. Increasing evidence implicates chronic inflammation in the persistence of depressive symptoms and treatment non-response. However, the mechanisms through which inflammatory processes interact with serotonergic signalling and neuronal activity remain insufficiently understood.

Purpose: This study aimed to develop a computational framework to elucidate the reciprocal interactions between inflammation, serotonin, and cerebral activity in depression. The model further examined how inflammatory processes alter serotonergic availability and contribute to measurable changes in brain activity.

Methods: A mean-field model of the cingulo-frontal circuit was developed to represent the coupled dynamics of inflammation, extracellular serotonin concentration, and cerebral activity. The model incorporated the effects of inflammatory signalling on serotonergic dynamics and examined system behaviour under varying degrees of inflammation.

Results: The model provided a mechanistic explanation of how increasing inflammation alters extracellular serotonin dynamics, resulting in reduced serotonergic availability and corresponding changes in cerebral activity. Inflammation, serotonin, and neuronal activity emerged as an interconnected dynamical system rather than independent contributors to depression pathology. The model further demonstrated that combined anti-inflammatory and antidepressant interventions may be effective in alleviating severe depressive symptoms, whereas either anti-inflammatory or antidepressant treatment alone may be sufficient to alleviate mild-to-moderate depressive symptoms.

Conclusion: This study provides a mechanistic account of the interplay between inflammation, serotonergic signalling, and cerebral activity in depression. Reciprocal interactions between these systems offer a potential explanation for the chronicity of depressive symptoms and variability in treatment response. These findings may contribute to the development of computationally informed approaches for identifying individuals who may benefit from treatments targeting both inflammatory and serotonergic mechanisms.

Keywords: Inflammation, Serotonin, Cerebral activity, Mathematical modelling, Computational neuroscience

P065

Investigating the Signalling Cascades Involved in the Differential Survival of Retinal Ganglion Cells During Development

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Background: Retinal ganglion cells (RGCs) are specialized projection neurons, in a vertebrate retina, that can process and signal information from the eyes to the visual centres of the brain. They are among the first neurons to differentiate during retinal development and are derived from a pool of retinal progenitor cells (RPCs) in the neuroblast layer. Amidst the developmental progress of a mouse, the RGCs undergo two distinct periods of partial elimination through programmed cell death to remove unnecessary structures and to control cell numbers for the retinal sculpture. During this process of pruning, some of the neurons are favoured for survival while others are not. The reason behind this survival bias is still unclear. The survival factors, if discovered, can be used to model therapeutic molecules that help prevent blindness in glaucoma patients by slowing down disease progression, if not by rescuing the dying RGCs.

Purpose: To study the underlying signalling cascades responsible for the bias that causes the differential survival of RGCs in murine retina during development

Methods: In-silico analysis of raw scRNA sequencing data of whole retinae from mice of different development stages (E11, E12, E14, E16, E18) accessed from Gene Expression Omnibus for identifying candidate survival factors in RGCs. For the validation of the candidate molecules, an in-vitro system, a retinal organoid, is being generated using ES-cells with RGC specific promoter (Brn3b) reporter. A reporter construct with dsRed-Express under Brn3b promoter will be used to make a recombinant Ai9 plasmid which has Rosa26-site homologous arms. The Brn3b-reporter sequence will be inserted into the Rosa26-site of the genome by means of the recombinant Ai9 electroporated into the ES cells along with a Cas9 expressing vector.

Results: The scRNA-seq data was subjected to quality control, followed by normalisation of the data to account for differences in sequencing depth between cells and selection of genes with high biological variability. Principal component analysis (PCA) is performed for dimensionality reduction, to summarize gene expression patterns. Significant principal components were used for cell clustering, where cells with similar transcriptional profiles are grouped together. The cell clustering was visualised as UMAPs. Finally, clusters were annotated biologically by identifying known marker genes that are differentially expressed between clusters. For the setup of the in vitro system, the Brn3b promoter-reporter (Brn3b-dsRedExpress) construct was successfully generated. The standardisation of retinal organoid generation from ES-cells is being carried out.

Conclusion: The in-silico analysis is done to identify the survival factors in RGC. Once identified, the molecules will be validated in the retinal organoids generated with the Brn3b-reporter-ES cell line. These factors will help ideate therapeutic options for slowing down RGC death in glaucoma patients.

P066

Downregulation of dFoxO alleviates Myotonic Dystrophy Type 1 phenotypes, implicating stress signalling in disease pathogenesis.

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Background: Myotonic Dystrophy Type 1 (DM1) is a multisystem muscle disorder, caused by expanded CTG trinucleotide repeats in the DMPK gene. Toxic CUG-repeat RNA foci disrupt RNA processing and cellular homeostasis, leading to progressive degeneration of muscles and multiple tissues. Although the molecular basis of DM1 has been extensively studied, the signalling pathways contributing to disease progression remain incompletely understood. Identifying genetic modifiers that modulate disease pathogenesis may provide mechanistic insights and reveal novel therapeutic targets.

Purpose: This study aimed to investigate whether downregulation of the transcription factor dFoxO can suppress CTG repeat-induced toxicity in Drosophila melanogaster model of DM1.

Methods: We used transgenic flies expressing 270 CTG repeats. Using the UAS-GAL4 system, UASCTG270 was expressed in the eye using GMR-Gal4. Bright-field microscopy was used to investigate morphological improvements and phototaxis assay to evaluate functional vision in the adult eye. Adult retinal eye sections were stained with Toluidine Blue to determine degeneration. Larval and pupal eye discs were stained with neuronal and cell death markers to evaluate the structural integrity and cell death.

Results: Downregulation of dFoxO markedly improved eye size, pigmentation and vision of CTG270 flies. The retinal section showed substantial loss of photoreceptor neurons that were improved by dFoxO downregulation in the CTG270 background. Furthermore, the photoreceptor neurons at the pupal stage, which were degenerated by CTG270 expression, were restored.

Conclusion: This study identifies dFoxO as a promising genetic modifier in Drosophila model of DM1 and provides evidence that modulation of dFoxO-dependent stress signalling may mitigate CTG repeat toxicity. Future work will extend these findings to muscle-specific DM1 models to further elucidate the molecular mechanisms underlying dFoxO-mediated rescue and evaluate its therapeutic potential.

Keywords: Myotonic Dystrophy Type 1, Drosophila melanogaster, dFoxO, CTG repeats expansion, Neurodegeneration.

P067

Neuroprotection by Pten Knockdown in Spinocerebellar Ataxia-3 Model in Drosophila

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Background: Spinocerebellar ataxia type 3 (SCA3), also known as Machado-Joseph disease (MJD), is characterised by progressive cerebellar ataxia, dysarthria, and Parkinsonism. It is a rare neurodegenerative disease caused by a CAG expansion of the ataxin-3 gene (ATXN3).

Purpose: Currently, there are no disease-modifying treatments for the SCAs. Our study aims to identify PTEN as a potential therapeutic target for prospective SCA3 interventions.

Methods: We used Drosophila transgenic lines expressing Mutant Ataxin-3 with 78 poly(Q) repeats. UAS-Gal4 system was used to express in a tissue-specific manner. GMR-Gal4 and elav-Gal4 were used to express in the eye and brain tissues, respectively. Y-Maze assay and negative geotaxis assays were performed to evaluate vision and motor abilities. The Paraffin sections were prepared to examine retinal degeneration. Pupal eye discs were dissected to examine photoreceptor degeneration and cell death using ELAV and TUNEL. qPCR and western blot were conducted to examine the expression of cell death pathway genes.

Results: Expression of SCA3.Q78 caused a rough eye phenotype and locomotor defects. Knockdown of Pten improved the eye morphology and suppressed the degeneration of photoreceptors at the pupa stage and in paraffin sections of adult eyes. In addition, Knockdown of Pten in disease flies significantly improved locomotor and survival abilities compared to SCA3-affected flies. The knockdown of Pten suppressed aggregate formation in the Drosophila eye and suppressed the aberrant apoptosis caused by SCA3.Q78. These suppressions could be mediated through improvement in PI3K/Akt signaling, as reduced p-Gsk3B observed in SCA3.Q78 flies and Pten knockdown improved its level.

Conclusion: In this study, PTEN knockdown was found to protect against 78Q polyglutamine-induced neurodegeneration in a Drosophila model of SCA3 by modulating the PI3K/AKT/PTEN signaling axis. Rescue flies showed better photoreceptor integrity and mushroom body architecture, improved locomotor activity, extended survival, and reduced protein aggregation compared to disease flies. Consequently, targeting the PI3K/AKT/PTEN axis, particularly through PTEN modulation, is a promising neuroprotective strategy in polyglutamine diseases such as SCA3.

Keywords: Spinocerebellar Ataxia 3, Neurodegenerative disorder, PTEN, PI3K/AKT, Drosophila melanogaster

P068

Investigating the cortico-striatal circuit development involving placental factors secreted from mother with autism spectrum disorder

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Background: Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by deficits in social interaction, communication, and repetitive behaviors. Genetic and neuroimaging studies suggest dysfunction of the corticostriatal circuitry in ASD, affecting sensorimotor, cognitive, and limbic integration. However, the developmental mechanisms underlying corticostriatal circuit abnormalities remain poorly understood. Maternal immune activation (MIA) is a major environmental risk factor, where inflammatory cytokines released during pregnancy disrupt placental immune signaling, thereby affecting the specification and assembly of corticostriatal circuits. However, the developmental mechanisms by which placental immune signaling regulates corticostriatal circuit formation remain understudied.

Purpose: This study aims to investigate the developmental origins of corticostriatal circuit abnormalities by determining how genetic susceptibility and maternal immune activation affects the placenta, thereby influencing embryonic immune response. This may further alter embryonic cortical and striatal neural progenitor dynamics, projection neuron fate specification, and corticostriatal circuit assembly.

Methods: We utilize mouse genetic fate-mapping approaches to investigate the specification and developmental trajectory of corticostriatal projection neurons (CSPNs) and striatal projection neurons (SPNs). We have characterized mouse knock-in lines for labelling progenitors, CSPNs and SPNs. We are in the process of standardizing maternal immune activation (MIA) models using poly(I:C) and poly(dA:dT) to examine how prenatal immune signaling influences progenitor behavior, neuronal differentiation, and corticostriatal circuit formation.

Results: We have characterized PlexinD1-2A-CreER, which labels CSPNs and SPNs along with a progenitor specific Pax6- 2A-iCreER line for fate mapping CSPNs/SPNs. We have optimized stereotaxic surgery for tracing the corticostriatal circuitry. In parallel, we have established the MIA model using poly(I:C) in our laboratory to study its effects on embryonic brain development. We are in the process of characterizing embryonic mouse placenta for histological and immune changes following MIA. The establishment of these experimental paradigms enables us to investigate how perturbation of placental factors may alter corticostriatal circuit development.

Conclusion: This study will provide insights into the developmental mechanisms by which genetic and environmental risk factors converge during embryogenesis to disrupt lineage specification and corticostriatal circuit assembly. In the future, we will combine MIA with ASD-specific genetic models to understand the etiology and pathogenesis of ASD. Understanding these early developmental events may help identify potential developmental windows for therapeutic intervention.

Keywords: Autism spectrum disorder; Maternal Immune Activation; Placental Factor; neural progenitors; fate mapping; corticostriatal projection neurons

P069

Perinatal endocrine disruption delays postnatal neurodevelopment in mice

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Background: DEHP is an endocrine disrupting compound extensively used as a plasticizer in items of daily use (PMID: 25376446). While phthalate-exposure is associated with neurodevelopmental conditions like autism spectrum disorder, mechanistic studies exploring earliest neurobehavioural disruptions are sparse, and mechanisms poorly understood – particularly at environmentally-relevant exposure levels.

Purpose: To investigate effects of perinatal DEHP-exposure on behavioural markers of neurodevelopment.

Methods: Pregnant C57BL/6 dams received either 1ppm-DEHP dissolved in drinking water, or drinking water alone (E10.5 - P21), ad libitum. Neurodevelopmental milestones were assayed in pups soon after birth, recording multiple parameters (day of appearance, average response etc). Behavioral parameters were then investigated during the juvenile period, soon after weaning.

Results: Perinatal DEHP-treated pups showed delayed sensorimotor responses and placing and startle reflexes, in both males and females. By contrast, we report improved motor responses in the treated group with respect to control pups. Remarkably, prediction with neurodevelopmental score at week 1 was treatment-specific. In parallel, early behavioural indices were also impaired in the treated group suggesting sustained disruption of cognitive performance beyond early behavioural markers of neurodevelopment.

Conclusion: Disruptive effects of DEHP at low, environmentally-relevant concentrations, are drastic, and can be observed soon after birth. These results provide a framework to not only use such early markers in predicting long-lasting deficits in cognitive performance, but also opens up avenues to investigate neural circuit mechanisms using state-of-the-art tools.

Keywords: DEHP, neurobehaviour, milestones, juvenile behaviour

P070

Anti-amnesic effect of blood plasma derived from Common Yoga Protocol (CYP) practitioners in an amnesic mice model.

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Background: Neurodegeneration is a gradual and progressive loss of neuronal cells in specific regions of the brain which leads to disruption of neuronal cells and causes several neurodegenerative diseases like Alzheimer's disease, Parkinson's disease, Amyotrophic lateral sclerosis etc. Its prevalence is estimated to have affected more than 57 million people worldwide, and might increase by 13.8% in the United States. In India itself, around 7.4% of people aged 60 or above are also suffering from neurodegenerative diseases. Therefore, we aim to analyse efficacy of the Common yoga protocol practitioners blood plasma in an amnesic mice model.

Purpose: Purpose of this study is to investigate the anti- amnesic effect of CYP practitioners blood plasma in an amnesic mice model to evaluate the Yoga's impact as an alternative therapy to several other treatments like drugs, exercises in the field of cognition. Further assessment will be carried out using statistical modelling.

Methods: A total 100 participants were recruited from National Institute of Nursing Education, PGIMER, Chandigarh. and sampling was carried out at 3 timeline points i.e at baseline, after 2 and 6 months of CYP intervention. We have further analysed the neuropsychological assessment at three timeline points, i.e at baseline, after 2 and 6 months of CYP intervention. In both control and intervention groups using GAD-7, PHQ-9, PSS, GHQ-12 and PGIMS. Further, molecular analysis will be carried out via ELISA to analyse the expression of different proteins related to different pathways involved in neurogenesis, angiogenesis, apoptosis and inflammation in the blood plasma of the participants. An Aβ induced injury (amnesic) mice model will be created to analyse the efficacy of CYP practioners blood plasma followed by transplantation in an amnesic mice model. Further to validate the results, neurobehavioral assessment using different behavioral tests like Morris Water maze (MWM), Rota-rod and passive avoidance (PA). Further for molecular analysis q-PCR and immunohistochemistry (IHC) will be carried out, followed by staining. Final evaluation will be carried out using statistical modelling.

Results: In neuropsychological assessment, there was significant improvement ($p=<0.05$) in perceived stress and anxiety in the yoga group as compared to the control group. And, also there was a significant improvement ($p=<0.05$) in memory in yoga participants than control. However, there was no significant improvement in GAD-7, PHQ-9 and GHQ-12 in both groups.

Conclusion: Yoga can be used as an integrative approach to alleviate the symptoms of cognitive impairment and also in various psychiatric disorders such as stress, anxiety and depression.

Keywords: Common Yoga Protocol, Alzheimer's Disease, Cognition

P071

The Intrinsic Nature of Inanimate Object Preference over Faces in Children with ADHD

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Background: ADHD is a common neurodevelopmental disorder characterized by inattention, hyperactivity, and impulsivity. Eye tracking provides a non-invasive measure of visual attention. This study examined visual preferences for animate stimuli (faces and birds) versus inanimate objects (mobile phones and bikes) in children with ADHD, healthy controls, and children with other psychiatric conditions. We hypothesized that ADHD children would show altered visual preference patterns.

Purpose: To assess visual attention and gaze preference for animate and inanimate stimuli in children with ADHD.

Methodology: Experiment Method: A participant is shown visual stimuli followed by a central fixation point to measure attentional response.

Data Processing: Eye-tracking data is overlaid onto the stimuli using heatmaps to visualize where the participant looked.

Data Acquisition: Raw gaze data is quantified into a table recording Dwell Time (ms) and the Number of Gaze Entries for each trial.

Data Analysis: Statistical software processes the raw numbers to calculate key metrics, such as average dwell time and total number of entries.

Result: Healthy controls showed greater preference for animate stimuli (55.7) than ADHD participants (47), whereas ADHD participants preferred inanimate stimuli (53 vs. 44.3). Psychiatric controls also showed higher attention to animate stimuli (48.8). Overall, ADHD children demonstrated a relative shift toward inanimate stimuli and reduced attention to faces.

Conclusion:The study demonstrated that children with ADHD focused more on inanimate images, whereas psychiatric and healthy controls showed greater attention toward animate images. Median value analysis indicated reduced attention to faces in ADHD children, suggesting that visual imagery patterns may serve as an early probe for ADHD detection.

Keywords: ADHD, Eye Tracking, Visual attention, animate-inanimate stimuli

P072

Effects of Working Memory Load on Performance and Its Association with Depression Severity in Major Depressive Disorder

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Background : Working memory is impaired in individuals with major depressive disorder (MDD), affecting everyday functioning. However, most cognitive tasks used to assess working memory do not systematically vary task load to examine its effect on performance, and the relationship between working memory performance and depression severity remains unclear. Identifying these gaps may clarify whether working memory performance changes with increasing load and with recovery or worsening of illness.

Purpose: The study aimed to examine the effect of increasing working memory load on performance and to determine whether performance across loads was associated with depression severity.

Methods: MDD was diagnosed according to DSM-5-TR criteria. HAMD-17 was used to assess depression severity. Twenty-six participants with HAMD-17 scores of 11–23 were recruited. Working memory was assessed using a visuospatial working memory task involving three load conditions with 3, 6, and 8 pairs of images. Performance was measured by accuracy and search time. HAMD-17 scores were correlated with accuracy and search times across loads.

Results: Accuracy was significantly lower in load 3 as compared to load 1 and load 2, while no significant difference was observed between load 1 and load 2. Search time for correct trials did not differ significantly across loads. Search time for incorrect trials was significantly lower in load 3 than in load 1 and load 2, whereas load 1 and load 2 did not differ. No significant correlation was found between HAMD-17 scores and accuracy or search times for correct and incorrect trials across loads.

Conclusion: Working memory performance was influenced by increasing task load, but it did not show a significant association with depression severity. This suggests that load-related working memory impairment in MDD may occur independently of symptom severity and may not change in parallel with the course of illness.

Keywords: Major Depressive Disorder, Working Memory Deficits, Depression Severity, Visuospatial Working Memory Task, Working Memory Task Load, Working Memory Performance

P073

Substance-Specific and Shared Cognitive Deficits in Alcohol and Opioid Use Disorders: Evidence from Attention, Working Memory, Emotion and Approach–Avoidance Tasks

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Background: Substance use disorders (SUDs) severely affect multiple cognitive domains, which hinders daily functioning. Recurrent substance use commonly leads to deficits in attention, working memory, emotional processing, and approach–avoidance bias. Characterising these domains may improve our understanding of the cognitive profiles in substance dependence.

Purpose: This study compared cognitive performance in opioid and alcohol users with healthy controls.

Methods: After obtaining ethical clearance, 120 participants (40 alcohol group, 40 opioid group, 40 healthy controls) completed four computerised cognitive tasks, designed in E-Prime 3.0, to assess attention (Flanker Task), working memory (Sternberg Task), emotional processing (Emotional Stroop Task), and approach–avoidance bias (Visual Approach–Avoidance Task). Data were analysed using GraphPad Prism version 10.

Results: Both substance-dependent groups showed lower accuracy than controls in the Emotional Stroop task and Sternberg's task ($p < 0.0001$), while only the opioid group showed lower accuracy on the Flanker's task ($p = 0.0023$). Both substance-dependent groups had slower reaction times in the Emotional Stroop task ($p < 0.0001$), ($p = 0.0003$) and the Flanker's task ($p < 0.0001$) compared to healthy controls. All groups showed a slower approach than avoidance towards substance-related stimuli (opioid group; $p = 0.0009$, alcohol group; 0.0191, and controls; $p = 0.0016$, $p = 0.0271$). Compared to controls, both substance-dependent groups took longer reaction times to approach ($p = 0.0012$, $p < 0.0001$) and to avoid ($p = 0.0010$, $p < 0.0001$) the substance-related stimuli.

Conclusion: The alcohol and opioid dependent individuals exhibited deficits in attention, working memory and emotional processing, along with pronounced cue-related cognitive bias towards substance-related stimuli compared to healthy controls. The findings also demonstrate substance-specific differences in attentional performance, with lower accuracy on the Flanker task observed only in the opioid dependence group, highlighting both shared and substance specific patterns of cognitive impairment.

Keywords: Substance use disorder, cognitive deficits, cognitive domains, cognitive function task

P074

One-Carbon Metabolism-Redox Imbalance as Converging Blood Biomarkers in Indian Children with Autism Spectrum Disorder: A Pilot Study

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Background: Autism Spectrum Disorder (ASD) is a multifactorial neurodevelopmental condition marked by social communication deficits and restricted, repetitive behaviours. One-carbon metabolism (OCM), comprising the folate, methionine, and transsulfuration pathways, generates methyl groups for DNA methylation and glutathione, the body's principal redox buffer. OCM disruption has been increasingly implicated in ASD, while peripheral immune dysregulation has also been proposed as a contributing mechanism, though findings remain inconsistent.

Objective: To evaluate OCM and redox status, plasma SAM, glutathione (GSH/GSSG), GPx activity, homocysteine, and SOD1 expression in ASD children versus typically developing controls (TDC), alongside cytokine profiles (TNF-α, IL-6, IL-8, IL-10) and autism severity.

Methods: In this case-control study at AIIMS Bathinda, blood was collected from 43 age- and sex-matched ASD children (2-12 years) and 10 TDC, following informed consent. PBMCs underwent qPCR-based gene expression analysis; plasma was assayed by ELISA. Severity was assessed using the Childhood Autism Rating Scale.

Results: ASD children showed significantly reduced SAM and GSH versus TDC, with elevated GPx activity indicating active GSH-to-GSSG conversion, demonstrating impaired methylation capacity and heightened oxidative burden. Homocysteine was unchanged, suggesting selective rather than global OCM disruption. Cytokine analysis showed only non-significant trends (elevated IL-6, IL-8; reduced IL-10), with IL-10 moderately correlating with severity.

Conclusion: This first-of-its-kind pilot study in an Indian paediatric ASD cohort shows that OCM and redox markers, rather than cytokines, form the more robust, statistically significant biological signature of ASD. The convergence of impaired methylation potential and oxidative stress suggests metabolic-redox dysregulation may be a more consistent and mechanistically tractable axis of ASD pathophysiology than peripheral inflammation alone in this population. These findings open a novel avenue for biomarker development in an underexplored population and underscore the need for larger, adequately powered, longitudinal studies to validate these trends and clarify causal relationships among OCM disruption, oxidative stress, and autism severity.

Keywords: Autism Spectrum Disorder (ASD), one carbon metabolism (OCM), oxidative stress (OS), Neuroinflammation, Biomarkers, Childhood Autism Rating Scale

P075

Long non-coding RNAs in Drug-Resistant Epilepsy: Clinicopathological Profiling in Cortex and Blood with in vitro Functional Characterization

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Background: Drug-resistant epilepsy (DRE), affecting approximately one-third of the 50 million epilepsy patients globally, arises from poorly-characterized multifactorial molecular dysregulation. Emerging evidence indicates long non-coding RNAs (lncRNAs) may contribute to pharmacoresistance in epilepsy.

Purpose: We aimed to investigate potentially DRE-associated lncRNAs in resected epileptogenic brain cortex and peripheral blood samples from patients diagnosed with DRE, and characterize their regulatory role in vitro, to identify potential therapeutic targets and non-invasive biomarkers.

Methods: Eight lncRNAs (H19, NEAT1, MALAT1, UCA1, KIRREL3-AS2, EVF2, FTX, BDNF-AS) were profiled using quantitative real time PCR in (a) DRE cortex (n=35; mesial temporal sclerosis with hippocampal sclerosis (MTS) or focal cortical dysplasia (FCD)) versus region-matched nonepileptic postmortem controls (n=22) and (b) peripheral blood of DRE (n=65; MTS, FCD or hypoxic-ischemic encephalopathy), drug-sensitive epilepsy (n=65), and healthy controls (n=60), with subsequent clinicopathological and ROC analyses. Brain-upregulated lncRNAs were evaluated in a validated Mg^{2+}-free epilepsy model using differentiated SH-SY5Y cells. UCA1, concordantly upregulated in the human cortex and the cell model, was silenced with siRNA; functional effects were assessed by LC-MS/MS-based proteomics and calcium imaging in the cell model, and immunofluorescence in the DRE cortex.

Results: Several lncRNAs were dysregulated in the DRE cortex with significant clinicopathological associations. In peripheral blood, EVF2, KIRREL3-AS2, and BDNF-AS demonstrated significant discriminatory power between DRE and drug-responsive patients. UCA1 knockdown in Mg^{2+}-free epilepsy model significantly altered 98 proteins (14 epilepsy-associated), with upregulated GABARAP (a GABA-A receptor trafficking regulator) and downregulated ABCC1/MRP1 (a multidrug efflux transporter); GABARAP dysregulation was validated in DRE cortex by immunofluorescence. A mitochondrial protein cluster was downregulated; upregulated proteins, including epilepsy-associated neuroinflammatory regulator THY1, were enriched in membrane trafficking, synaptic remodeling, and vesicular processing. Pathway analysis revealed restoration of mRNA post-transcriptional turnover and FGFR1 signaling, alongside PI3K/AKT attenuation; calcium imaging confirmed reduced seizure-like transients following UCA1 silencing.

Conclusion: These findings indicate dysregulation of lncRNAs in the DRE cortex with clinicopathological relevance, identify UCA1 as a regulator of neuronal excitability, drug efflux, and related epileptogenic pathways, and reveal distinct blood lncRNA signatures between drug-resistant and drug-responsive epilepsy.

P076

SLC6A4 methylation and genotype-stress interaction orchestrate the biological vulnerability to depression: insights from the sikkim himalaya

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Background: Reported polymorphism in Serotonin transporter (5-HTT) encoded by SLC6A4 gene, include (L) and short (S) forms of 5-HTTLPR; where S variant lowers transporter expression and LG variant that functions similarly to S due to a single nucleotide polymorphism (SNP) rs25531. In addition, methylation in SLC6A4 promoter region also plays a role in regulation. Environmental factors that influence methylation of promoter region and downstream effect influencing increased likelihood of developing depression is not well known. This study is first of its kind on the Sikkimese population (Sikkim has the highest depression patients in India).

Purpose: To investigate epigenetic, environmental,hormonal regulators and their interactions with SLC6A4 genotype in MDD patients of Sikkim.

Methodology: 100 MDD patients from the STNM Psychiatry OPD, Sikkim, and 100 ethnically-matched healthy controls were recruited following informed signed consent. GenomicDNA was extracted, and biallelic and triallelic 5-HTTLPR genotyping were performed. Bisulphite Conversion of DNA and pyrosequencing were performed on 5 CpGs to study DNA methylation. Clinical subjective assessments such as PHQ-9 (Depression severity), Social Problems Questionnaire (SPQ), Childhood Trauma Questionnaire (CTQ), Life-Threatening Experiences (LTE) questionnaire, and Perceived Stress Scale (PSS) were recorded. Logistic regression analysed gene-environment interactions.

Results: CpG3&4 methylation was higher in MDD patients ($p<0.05$) and varied significantly by 5-HTTLPR genotype (Biallelic: LL/LS/SS; Triallelic: LS/SS). CpG3&4 differed by high/low stress scores (PHQ9, SPQ, PSS, LTE, CTQ; $p<0.05$). PHQ9,LTE,PSS and CTQ interacted with both Biallelic and Triallelic to predict methylation at CpG3 and CpG4. Significantly higher methylation in CpG3&4 was observed in MDD patients with higher cortisol ($p < 0.001$)

Conclusion: The etiopathology of depression mediated bySLC6A4 hypermethylation (CpG3&4), 5-HTTLPR genotype and stress interaction (OR>1), coupled with cortisol dysregulation ($p<0.001$), unravels the molecular nexus translating psychosocial adversity into biological vulnerability.

Keywords: 5-HTTLPR, Depression, Stressors, Sikkim

P077

Nuclear Receptor Transcription Factors Promote Axon Regeneration Following Spinal Cord Injury

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Background: Adult Central Nervous System neurons show limited axon regeneration after injury, and the complete set of Transcription Factors (TFs) required to restore regenerative competence remains vastly incomplete. Developmental gene-regulatory networks support robust axon growth, but these programs are progressively silenced as neurons mature.

Purpose: This study aimed to reconstruct developmental transcriptional networks supportive of axon growth and identify key transcription factors capable of reactivating intrinsic regenerative programs in the CNS neurons following injury.

Methods: Developmental cortical RNA-seq and ATAC-seq footprinting datasets were integrated to identify transcription factors that regulate with pro-growth genes during development. This analysis identified Nuclear Receptor Transcription Factors (TFs), including NR2F1 and NR2F6 as potential key drivers of regenerative capacity. These factors were overexpressed singly and in combination using AAV-based approaches in Neuro-2A cells and primary cortical neurons. Their regenerative potential was further tested in adult mouse models of spinal injuries, including unilateral pyramidotomy and complete Thoracic Crush. Axon growth, functional recovery, and mechanisms were assessed using anatomical tracing, behavioural analysis and a wide array of functional genomics techniques.

Results: NR2F1 and NR2F6 showed developmental chromatin occupancy at growth-associated regulatory regions that declined with neuronal maturation. Overexpression of these factors promoted neurite outgrowth *in vitro*. *In vivo*, NR2F1 and NR2F6 enhanced corticospinal sprouting after pyramidotomy and promoted axon regeneration beyond a complete thoracic crush injury, even traversing the glial scar. These anatomical effects were accompanied by improved hip-rise kinematics, hind-limb stepping parameters, and grip strength, confirming functional recovery. Multi-omic integration (snRNA-seq, HiC, CUT&RUN, Ribosome profiling) revealed that Nuclear Receptors coordinate transcriptional reprogramming that attenuates injury-induced proteotoxic stress and unfolded protein responses while simultaneously rewiring metabolism to fuel axonal elongation. This dual mechanism shifts the post-injury transcriptional landscape from a stress-dominant state to a growth-permissive state.

Conclusion: Our results identify novel combination of Nuclear Receptor TFs that regulates Cortico Spinal Track regeneration and establish these as potential therapeutic targets for functional restoration after Spinal Cord Injury.

Keywords: NR2F1, NR2F6, nuclear receptors, corticospinal tract, axon regeneration, spinal cord injury

P078

Empirical Behavioural and Cognitive Phenotyping of PET Characterised ADNI Participants: A Reference Framework for Validating Mechanistic Models of Alzheimer's Disease

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Background: Mechanistic models of Alzheimer's disease increasingly propose that amyloid-β-driven excitation, tau-mediated disinhibition, and interneuron loss converge on intracellular calcium dysregulation, pushing neurons from a hyperexcitable state toward irreversible death.

Purpose: Building on this literature, we use the Alzheimer's Disease Neuroimaging Initiative (ADNI) as an independent, human, in-vivo dataset against which such models' behavioural predictions can be empirically evaluated, establishing a data-driven behavioural reference phenotype prior to model comparison.

Methods: We characterized behavioural, cognitive, functional, and neuropsychiatric trajectories in 2,484 ADNI participants with at least one available PET modality (amyloid, tau, FDG, or legacy PiB), spanning ADNI1–ADNI4. Four primary outcomes (MMSE, MoCA, ADAS-Cog13, CDR-SB) and secondary domains (memory, executive function, functional independence, neuropsychiatric symptoms) were examined using correlation/PCA, linear/quadratic/GAM age models, linear mixed-effects models (random intercepts and slopes) for longitudinal trajectories, and biomarker × time interaction models. Associations used standardised effect sizes, partial R^2, FDR correction, and outlier-robustness sensitivity checks.

Results: Among 2,484 PET-characterised ADNI participants (mean age 72.0 years; 42.9% CN, 43.0% MCI, 13.9% dementia), the four core cognitive-clinical measures moved as one: MMSE, MoCA, ADAS-Cog13, and CDR-SB were tightly intercorrelated ($r = 0.71–0.85$, all $p < .001$), confirming a shared global impairment signal. Structural neurodegeneration tracked this signal closely — smaller hippocampal, entorhinal, and whole-brain volumes and larger ventricles predicted worse behaviour across the board, with several associations exceeding $p < 10^{-20}$. Critically, biomarker burden didn't just mark severity — it predicted the pace of decline: PET × time interaction models revealed significant biomarker-driven acceleration in cognitive trajectories ($p_{FDR} < .001$), with hundreds of participants contributing ≥3 repeated assessments to anchor these estimates.

Conclusion: Behaviour, brain structure, and molecular pathology in ADNI move together in a coherent, statistically robust cascade — and biomarkers don't just diagnose decline, they forecast its speed.

Keywords: Alzheimer's disease, biomarker-behaviour cascade, neurodegeneration, ADNI

P079

Exploring μ-opioidergic Habenula–Zona Incerta circuits underlying compulsive eating in mice

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Background: Food is inherently rewarding and shares certain features with addictive substances. While normal eating is essential for meeting the body's metabolic needs, the question remains: when does food consumption become compulsive, and what drives this behavior? Compulsive eating is characterized by the persistent consumption of highly palatable food despite adverse consequences and shares neurobiological features with substance-use disorders. Evidence suggests that repeated overconsumption of palatable, high-calorie foods contributes to obesity and associated health problems. Prior studies indicate that frequent intake of such foods can produce compulsive eating patterns resembling drug addiction, involving overlapping neural pathways.

Purpose: Our work is aimed at identifying a circuit that contributes to the development and maintenance of compulsive food seeking adding to the previous known research.

Methods: Compulsive food behaviour was assessed using a behavioural paradigm measuring food consumption despite negative consequences in C57BL/6, genetically obese db/dbmice and diet-induced obese mice. Immunohistochemistry was done to stain for certain immediate early gene(cfos). Stereotaxic surgeries were done in mice to inject viral vectors for tracing experiments.

Results: Compulsive food behaviour was assessed using a behavioural paradigm measuring food consumption despite negative consequences in C57BL/6, genetically obese db/dbmice and diet-induced obese mice. Through the cfos activity in c57BL/6 we were able to observe decreased activity in Habenula in compulsive mice as compared to non-compulsive mice. Neural circuit organization was examined with anatomical tracing approaches where we found that Lhb (Lateral Habenula) connects to the hypothalamic region Zona incerta that has been implicated in compulsive eating behaviours.

Conclusion: These findings identify the lateral habenula–zona incerta pathway as a potentially circuit linking aversive processing, motivational drive and maladaptive food intake. The lateral habenula–zona incerta circuit may represent a previously underexplored neural substrate of compulsive eating. Circuit-specific manipulation will help establish its causal role and determine whether restoring its function can reduce compulsive food seeking and attenuate obesity-related phenotypes.

P080

Hypothalamic – Medullary NPY Circuit in Cardiomyopathy

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Background: Through the years, researchers have sought to unravel the structural and functional complexities of the brain and heart, as well as the diseases associated with them. More recently, the scientific paradigm has shifted from understanding these organs independently toward decoding the precise mechanisms by which each manipulates the other. Within this framework, cardiomyopathy represents a critical clinical challenge, characterized by a progressive weakening of the myocardium that eventually leads to various systemic cardiovascular disorders.

Purpose: Our study investigates this bidirectional communication happening between the brain and heart in the context of cardiac dysfunction. Specifically, we aim to understand the central neural responses triggered by myocardial damage and determine whether these central feedback loops serve to mitigate or exacerbate myocardial injury.

Methods: Using an experimental model of cardiac injury to simulate cardiomyopathy, we tracked systemic physiological markers and mapped central neural activation patterns. Circuit-mapping strategies were employed to trace the structural connections between the brain and the heart, focusing on the downstream projections originating from activated hypothalamic subregions to cardioregulatory centers in medulla.

Results: We identified significant brain activity within the hypothalamus during acute cardiac muscle damage. While classical frameworks outline parasympathetic neuronal connections strictly between the heart and the medulla, we discovered a novel, top-down projection from the affected hypothalamic region to these downstream cardioregulatory medullary centers. Furthermore, phenotypic characterization revealed that these projecting neurons are neuropeptide Y (NPY) positive—a specific neuropeptide whose systemic levels are known to spike alongside epinephrine and norepinephrine during cardiac injury or dysfunction.

Conclusion: Unravelling this central hypothalamic–medullary NPY circuit is critical to understanding central autonomic governance during cardiac distress. Ultimately, therapeutic modulation of this specific pathway may provide a novel, centrally targeted neuroprotective strategy against the progression of cardiomyopathy.

Keywords: Brain- heart communication, Cardiac dysfunction, Cardiomyopathy, Hypothalamic medullary circuit, Neuropeptide Y

P081

A brain-liver circuit modulating liver regeneration in liver diseases.

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Background: Chronic liver diseases, including alcohol-associated liver disease (ALD), non-alcoholic fatty liver diseases (NAFLD), and viral hepatitis, are major global health challenges that impair hepatic regeneration and promote disease progression. While the liver possesses remarkable regenerative capacity, emerging studies suggest that liver-derived sensory signals are integrated by the CNS, which may regulate regeneration through specific neural circuits.

Purpose: The brain-body communication as an enduring idea has recently emphasized efforts in the direction of understanding how the brain-body communicates in health and disease contexts. This study intends how the brain senses liver regeneration after liver related disorders or liver injury. Liver repair is not solely controlled by hepatic crosstalk rather it is coordinated bidirectionally through a brain-liver axis. By discovering these circuits, we aim to modulate them that will eventually result in the functional recovery of the liver.

Methods: Mice underwent partial hepatectomy (PHx), followed by brain isolation to look at the response of c-fos. Mice also underwent stereotactic surgery to decode the neural circuit connecting brain and liver. We also tested the functional aspect of the circuit in alcohol administered mice and how it improves liver regeneration using non-invasive MSOT technique.

Results: Using a mouse model of PHx, we identified specific brain regions that are activated in response to liver injury, with the Central Amygdala (CeA) emerging as a prominent responsive region. Through circuit-mapping approaches, we further identified a downstream target region connected to the CeA, suggesting the existence of a brain circuit involving in hepatic repair. On chronically activated the above circuit in ethanol-fed mice and monitored the liver regeneration. We found significant improved liver regeneration by changes in hepatic hemodynamic parameters and also through liver-to-body weight ratio.

Conclusion: As a long-term goal, it will facilitate innovative ways to target these newly discovered circuits to protect and promote liver regeneration following liver diseases.

Keywords: Brain-Body, Liver regeneration, Amygdala, Nucleus tractus solitarius, MSOT.

P082

Reward drives sleep-memory coupling in *Drosophila*

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Background: Sleep plays a key role in memory consolidation in Drosophila, but can become dispensable for memory in response to changes in environmental cues and physiological demands. Post training perception of a rewarding sweet taste is sufficient to recruit sleep-dependent circuits for memory consolidation, whereas in the absence of sweet taste post-training, anatomically distinct circuits support sleep-independent memory. Sweet-sensing gustatory receptor neurons recruit reward-signalling PAM-β'2mp dopaminergic neurons to establish sleep-dependent memories, indicating a role for reward processing in sleep-dependent memory consolidation. The internal state of the fly determines which stimuli it perceives as rewarding: in a desiccated state, drinking water activates rewarding dopaminergic neurons, and desiccated flies can form long-term memories when an odour is paired with a water reward.

Purpose: This study aimed to determine whether the coupling of memory consolidation to sleep, previously established for sucrose reward, generalises to other rewarding stimuli such as water, and whether the same reward-processing dopaminergic circuits govern sleep-dependent memory consolidation across different internal physiological states (desiccation vs. starvation) in Drosophila.

Methods: Wild-type and transgenic Drosophila (Canton-S; Gr64f-, R58E02-, MB056B-, MB196B-, and MB299B-Gal4 driving UAS-shibirets1, UAS-TrpA1, or UAS-CaLexA) were trained using an appetitive conditioning paradigm pairing odour with sucrose or water reward, then tested for memory in a T-maze. Post-training sleep was measured using Drosophila activity monitors,with mechanical sleep deprivation applied where indicated. Neuronal silencing/activation used temperature-shift (shibirets1/TrpA1) manipulation, and CaLexA/immunostaining confirmed circuit activity. Data were analysed by t test, ANOVA with Tukey's post hoc, or Mann–Whitney U test as appropriate.

Results: We found that, similar to sucrose memory, water-odour memory can be coupled to sleep depending upon the availability of water reward. Water-satiated flies required sleep to form long-term memories, whereas sleep was dispensable for memory consolidation in desiccated flies. Sleep-dependent water memory consolidation was mediated by the same neural circuits, PAM-β'2mp dopaminergic neurons and anterior–posterior α′/β′ neurons of the mushroom body, previously identified for sleep-dependent sucrose memory. Presentation of dry sucrose following water-odour pairing, or water following sucrose-odour pairing, triggered sleep dependent memory consolidation in flies maintained simultaneously in starved and desiccated states respectively.

Conclusion: Our findings reveal that the role of dopaminergic neurons in sleep-dependent memory is broader than signalling the presence of sweet taste in trained flies; rather, these neurons act as a general reward detector that gates memory consolidation through alternative pathways depending on the internal physiological state of the fly.

Keywords: Sleep-dependent memory, reward, neural circuits, dopaminergic neurons, and Drosophila.

P083

Optimized Feature Selection Improves Preictal EEG Classification Independent of Epilepsy Chronicity

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Background: Epilepsy is a chronic neurological disorder marked by recurrent seizures that impair quality, with sudden unexpected death in epilepsy (SUDEP) representing one of its most severe consequences. Timely preventive intervention requires accurate identification of the Seizure Prediction Horizon (SPH)—the acute pre-ictal phase occurring 5 minutes before seizure onset.

Purpose: To optimize the number of features used in unsupervised clustering for SPH detection and assess the impact of epilepsy duration.

Methods: SPH detection was performed using scalp EEG from drug-resistant epilepsy (DRE) patients, analyzing 60-min preictal recordings across 20 channels. Fifty-nine linear univariate features were extracted and reduced using BorutaSHAP. Uniform Manifold Approximation and Projection (UMAP) was used for dimensionality reduction, followed by unsupervised clustering to identify acute SPH events. The cluster containing most SPH events was designated the Max-Cluster (MClus) and served as the primary focus of analysis.

Results: The study included 13 DRE patients (9 males, 4 females). BorutaSHAP led to a striking 40% reduction in the total feature set, selecting only 35 features which had higher weightage in SPH classification. Median clustering accuracy increased from 65% [31.66–100, using all 59 features] to 75% [30–100, using the optimized 35-feature set]. At the patient level, the median difference in SPH percentages between the two feature sets was 0 (range: –8.33 to 5), indicating that the optimized feature set performed consistently regardless of epilepsy duration.

Conclusion: BorutaSHAP-based feature optimization substantially reduced the feature space while preserving or improving SPH detection accuracy. The optimized framework enables efficient, real-time identification of acute pre-ictal events and shows that SPH detection is not significantly influenced by epilepsy duration. These findings support the development of computationally efficient seizure prediction systems for clinical decision support.

Keywords: Epilepsy, Scalp EEG, Seizure Prediction Horizon (SPH), Feature Selection, BorutaSHAP

P084

Explainable Machine Learning to Identify Discriminatory Spatiotemporal and Spectral Features in EEG Data during Attention Tasks

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Background: Electroencephalography (EEG) data is high-dimensional, non-stationary, and complex, making it challenging to isolate neural attributes underlying cognitive functions. Traditional analyses across time, frequency, and time-frequency domains (e.g., Event-Related Potentials and spectrograms) identify features associated with stimulus processing. However, statistical significance alone does not provide predictive power for reliably decoding cognitive states in unseen EEG recordings.

Purpose: This study aims to shift from conventional testing towards predictive decoding using interpretable machine learning to classify cognitive attention states and identify discriminatory neural features. This approach may support the identification of biomarkers for cognitive and neurological disorders and the optimisation of real-time Brain-Computer Interfaces (BCIs) for neurorehabilitation.

Methods: Open-source EEG data from 19 healthy subjects (11 female, aged 20-40 years) performing an interleaved dual-oddball audiovisual attention task were analysed. Data were notch- and bandpass-filtered, mastoid re-referenced, and cleaned of ocular artifacts using Independent Component Analysis (ICA). Stimulus-locked epochs (−200 to 900 ms) were baseline-corrected and transformed into time-frequency spectrograms for the auditory attention stream. A regularized L1 logistic regression model was trained on 5,019 pooled trials to classify attended and unattended conditions using stratified 5-fold cross-validation.

Results: The model classified attention states with a mean accuracy of 62.14 ± 1.65% ($p < 0.01$). Model weights revealed spatio-spectro-temporal feature distributions across EEG channels, indicating the relative contribution of spatial regions and oscillatory frequency components to auditory attentional modulation.

Conclusion: These findings demonstrate that machine learning can identify discriminatory features from complex time-frequency EEG data. This work represents an initial step towards developing a generalized framework for interpretable feature extraction and classification in binary event-related EEG datasets, rather than solely optimising deep neural network classifiers. Ultimately, this approach may provide a quantitative framework for investigating how stimulus information is encoded in neural data and identifying underlying neurophysiological processes.

Keywords: Electroencephalography (EEG); Auditory Attention; Machine Learning; Cognitive Decoding

P085

Cortico-thalamic circuitry for nicotine dependency.

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Background: Nicotine is the primary addictive component of tobacco. While the role of subcortical brain regions in nicotine addiction has been extensively studied, accumulating evidence from both human and animal studies suggests that cortical regions, particularly the anterior cingulate cortex (ACC), also contribute to nicotine addiction by influencing decision-making and motivational salience.

Purpose: This study intended to explore the involvement of the ACC-ZI circuit in the development and maintenance of nicotine preference.

Methods: C57BL/6 mice were used for experiments in this study. For chronic and acute inactivation studies, stereotaxic surgeries were conducted to inject Kir2.1 channels or hM4D(Gi) into the ACC respectively and Retro-cre in the ZI to selectively target ZI-projecting ACC neurons. For fibre photometry, stereotaxic surgeries were conducted to inject GCaMP8m in ACC and Retro-cre in ZI, after which fibre-optic cannulas were implanted into the ACC. Following recovery and viral expression, mice were subjected to a conditioned place preference paradigm to assess nicotine preference. Lastly, cFos screening was conducted after chronic nicotine exposure.

Results: Through cFos mapping and population-level calcium activity analyses of ZI-projecting ACC neurons, we found that this circuit is robustly activated by nicotine exposure and by re-exposure to the nicotine-paired context during CPP testing. To determine its functional role, we inhibited the ACC–ZI pathway either acutely during the preference test or chronically throughout the conditioning phase. Acute inhibition significantly reduced the expression of nicotine preference, indicating that this circuit is required for the manifestation of conditioned nicotine-seeking behavior. In contrast, chronic inhibition during conditioning completely prevented the development of nicotine preference.

Conclusions: These findings demonstrate that the ACC–ZI circuit plays a critical role in both the acquisition and expression of nicotine-associated contextual memories. Targeting this pathway may therefore represent a promising strategy for reducing nicotine-seeking behavior and treating nicotine addiction.

Keywords: Nicotine, Anterior Cingulate Cortex, Zona Incerta, Reward, Place preference

P086

Identification of non-canonical Purkinje neurons in the adult brain cerebellum

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Background: Purkinje cells (PC), the sole output neurons of the cerebellar cortex are classically identified by their expression of PCP2 and calbindin, the canonical markers. Heterogeneity within the PC population has been appreciated based on expression of zebrin, neurophysiological properties and morphology, and transcriptomics, in the various lobules of the cerebellum.

Purpose: This study aims to establish and characterize a population of Purkinje cells that do not express the canonical markers, but exhibit features of PC and reside in the Purkinje cell layer.

Methods: We used PCP2 driven Cre-based genetic lineage tracking in mice to identify lineage committed Purkinje neurons through indelible genetic marking. Using a combinatorial strategy of immunofluorescence, electrophysiology, dye-filling for morphometry and FACSorting cells followed by RNA-sequencing, we have characterised this population of non-canonical Purkinje neurons.

Results: We observe that the non-canonical PC (ncPC) population is consistently present in all lobules throughout the adult lifespan. These neurons fail to express various established markers of Purkinje neurons, such as Calbindin, PCP2 and Parvalbumin. In contrast to the canonical PC, these ncPC show higher resting membrane potential, exhibit simple spiking more frequently and stunted dendritic arborization.

Conclusion: Based on their stable presence, anatomical localisation, and molecular, morphological and physiological properties, we establish the newly identified population as non-canonical PC, that is not a developmental remnant or region-restricted subtype (e.g., zebrin-related compartmentalization), but instead a distinct stable PC subpopulation that remained elusive previously. Further investigations are underway to uncover the functional role of these non-canonical Purkinje neurons.

Keywords: Purkinje cell, Bonafide markers, Indelible lineage tracking, Physiology, Morphometry, Transcriptomics

P087

From Stem Cell to Sentinel: Generating a Human iPSC-Derived Microglia Platform for Neuroinflammation and Neuropathology

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Background: Microglia, the resident innate immune cells of the central nervous system (CNS), constantly survey neuronal health and synapses, but can mount sustained, reactive, and pro-inflammatory responses upon prolonged stress. Microglial pattern-recognition receptors drive overactivation by receiving diverse pathological, environmental, and endogenous stimuli, including viruses, pesticides, other pollutants and consumable plastics and translating them into a shared, downstream cascade of reactive oxygen species and inflammatory mediators. Given that these diverse threats can compromise neural integrity and trigger neuroinflammatory cascades, activate microglial NADPH oxidase 2 (NOX2) and are epidemiologically associated with increased risk for chronic neurodegenerative diseases such as Alzheimer's and Parkinson's disease. There is a critical need for a robust human cellular testbed to study these exposures.

Purpose: To generate and characterize an induced pluripotent stem cell (iPSC)-derived microglia model from microglial precursor cells (MPCs) to mature microglia for comprehensive studies involving viral- and environmental-driven neuroinflammation.

Methods: Human iPSCs were utilized to differentiate MPCs. Advanced cellular and molecular biology techniques were employed to characterize iPSCs, MPCs, and mature microglia, evaluating them against conventional morphological and marker-based microglial criteria.

Results: Distinct cellular morphology and canonical marker expression were successfully established across the differentiation stages. The different cell populations being cultured were characterized using cellular and molecular biological techniques. Pluripotency Markers were expressed in iPSCs (SOX2, OCT4, c-MYC, Tra-1-60). Precursor Markers were expressed in MPCs (CD34, CD45). Microglial Markers were expressed in mature microglia (IBA1, TREM-2).

Conclusion: A fully-characterized iPSC-derived microglia platform provides a malleable, human-relevant system to elucidate the mechanisms underlying neurological threats driven by viruses, pesticides, other pollutants, and consumable plastics. This platform establishes a much-needed foundation for identifying shared molecular mechanisms to prevent damage from chronic microglial activation before irreversible damage to neuronal networks or synapses. Furthermore, it validates microglia as a critical convergence node for multiple environmental and infectious assaults, holding high translational relevance for neurological health and disease.

Keywords: Induced pluripotent stem cells, Microglia, Neuroinflammation, Neuropathology

P088

A progressive mouse model of Parkinson's disease displays accumulation of oligodendrocyte progenitor cells

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Background: Parkinson's disease (PD) is characterized by the loss of dopaminergic neurons (DA) of the substantia nigra (SN), accumulation of α-synuclein aggregates, and activation of microglia and astrocytes. Recently, oligodendrocytes have also been reported to associate with PD. However, their role in promoting PD is unclear.

Purpose: We aim to explore the dynamics of oligodendrocyte differentiation in a progressive mouse model of PD.

Methods: We developed a SynFib mouse model by co-injecting AAV6 expressing the α-synuclein gene and pre-formed fibrils (PFF) in the SN. We evaluated the number of oligodendrocytes, their colocalization with α-synuclein aggregates and microglia in these brains at 4, 12, and 24 weeks post-surgery. Later, we assessed dynamic changes in gene expression profiles in oligodendrocyte lineage cells using quantitative RT-PCR (qPCR) at these time points.

Results: Our study shows an increase in the number of oligodendrocytes (OLIG2+ cells) in the SynFib group compared with the control group at 4, 12, and 24 weeks in SN. The qPCR analysis of pan-oligodendroglial markers OLIG2 and SOX10 suggests an increase in oligodendrocyte lineage cells. Furthermore, PDGFRA expression (a gene required for OPC proliferation) increased across all time points, suggesting OPC accumulation. Furthermore, we observed increased expression of PTPRZ, ID2 and ID4 (negative regulators of OPC differentiation), which may inhibit OPC maturation into myelinating oligodendrocytes. Colocalization of OLIG2 with α-synuclein aggregates and microglia was also observed at all the timepoints.

Conclusion: Despite the increase in oligodendrocytes, the SN-DA neurodegeneration continues. This may be attributed to suppression of OPC differentiation by elevated expression of PTPRZ, ID2 and ID4. α-synuclein aggregation in oligodendrocytes and interaction with microglia throughout disease progression may have further prevented their supportive roles. Further evaluation is required to validate impaired oligodendrocyte maturation.

Keywords: Oligodendrocytes, SynFib model, Parkinson's disease, and Glial cells

P089

Agmatine Attenuates Striatal Astrogliosis-associated Motor Incoordination and Cognitive Impairment in 3-Nitropropionic Acid-induced Huntington's Disease-like Phenotype in Rats

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Background: Huntington's disease (HD) is a progressive neurodegenerative disorder characterized by motor incoordination, cognitive decline, and striatal astrogliosis. Astrocytes are prevalent in the striatum and exhibit mutant huntingtin (mHTT) protein aggregation in HD patients and animal models of HD. Dysfunction of these astrocytes leads to alteration in cellular morphology and neurotransmitter homeostasis, contributing to the development and progression of HD. Agmatine is a neurotransmitter within the brain primarily synthesized and stored in astrocytes.

Purpose: The present study investigated the neuroprotective role of agmatine in mitigating striatal astrogliosis-associated motor incoordination and cognitive impairment in 3-Nitropropionic acid (3-NP)-induced HD rats.

Methods: Adult Sprague-Dawley rats were pretreated with 3-NP (10 mg/kg, i.p.) on alternate days, and from the 10th day onward, they received agmatine treatment (5-20 mg/kg, i.p.) up to the 32nd day of the treatment protocol, during which time behavioral tests were performed to evaluate the neuroprotective effects of agmatine. On day 33, the brains of the rats were removed for biochemical and molecular analysis.

Results: The findings of the current investigation revealed that the repeated agmatine treatment not only restored the gait abnormalities and motor incoordination but also attenuated the learning and memory impairment in 3-NP-induced HD rats. Moreover, agmatine intervention also mitigated neuronal degeneration and preserved neuronal integrity in the striatum. Importantly, agmatine treatment was able to prevent astrogliosis as indicated by decreased Glial Fibrillary Acidic Protein (GFAP) immunoreactivity in discrete brain areas.

Conclusion: In conclusion, agmatine-based therapies may be projected as a new therapeutic intervention for HD management, warranting further exploration for clinical translation.

Keywords: Huntington's disease; Agmatine; Striatal astrogliosis; 3-Nitropropionic acid.

P090

Mapping the visual mental imagery spectrum during naturalistic reading: An fMRI Study

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Background: Visual mental imagery is a core cognitive process that supports comprehension during naturalistic tasks such as reading, yet its neural implementation varies markedly across individuals.[1] While imagery is often treated as a subjective faculty, emerging evidence suggests that it can be systematically modulated and mapped at the neural level.[2]

Purpose: We investigate the neural correlates of visual mental imagery elicited during a naturalistic reading task, with particular emphasis on how imagery strength varies parametrically across the imagery spectrum.

Methods: Functional MRI data were acquired from 40 participants (28 females, age range = 21 - 29 years). Participants completed a reading task comprising 16 passages, including 12 semantically coherent passages and 4 jumbled control passages. Following each passage, participants rated the extent of their visual mental imagery on a four-point scale. Individual imagery ability was assessed using the Vividness of Visual Imagery Questionnaire-2 (VVIQ2).[3] Statistical analysis includes general linear models, cluster-level thresholding, ROI analysis and second-level analyses of fMRI and behavior data.

Results: Behavioral analyses showed that mean imagery ratings during the reading task varied systematically across participants and as measured by VVIQ2, scaled with individual differences in trait imagery vividness. Group-level analyses reveal distributed cortical activation across the three visual imagery conditions. ROI analysis reveals the low imagery subgroup (lowest VVIQ scores, n = 10), exhibited a reduced and more variable ROI response across the motor, parietal, and associative regions. The high imagery subgroup (highest VVIQ scores, n = 10), showed stronger, more consistent responses across temporal, medial and frontal ROIs.

Conclusion: Naturalistic reading accompanied by visual imagery engages a distributed set of brain regions at the group level. These regions include a distributed network among the frontal, insular, cingulate, precuneus, precentral, temporal, and lingual regions, and are consistent with the visual and associative cortices engaged during imagery. The ROI analysis findings suggest systematic modulation of brain activation as a function of both task-evoked imagery strength and subjective imagery ability.

Keywords: Visual Mental Imagery, Imagination, Functional MRI, Naturalistic, General Linear Model

P091

Impact of Aperiodic Component(1/f) on Resting state Functional Connectivity: A method Comparison study

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Background: EEG/MEG signals reflect a mixture of oscillatory brain activity, an aperiodic (1/f) component, and background noise. Since large-scale functional network dynamics are primarily driven by the oscillatory component, separating it from the aperiodic background is important for accurate connectivity estimation. However, whether the choice of decomposition method alters resulting network connectivity in resting-state EEG remains unclear.

Purpose: This study examines how two decomposition approaches, Specparam (FOOOF) and dOsc, shape alpha-band cross-spectral connectivity estimates in resting-state EEG, and evaluates the accuracy of each against ground-truth simulated data.

Methods: Five-minute eyes-open resting-state EEG was recorded from 30 healthy participants (14 male, 16 female; mean age 27) using a 64-channel Ag/AgCl system, preprocessed with a 0.1–35 Hz bandpass, average reference, 20-second epochs, and downsampling to 100 Hz. Specparam parameterizes power spectra into periodic and aperiodic components followed by a Hilbert transform, while dOsc is a state-space model extracting oscillatory components via Kalman smoothing. 63×63 cross-spectrum matrices were derived per method, and magnitude and phase connectivity were compared using the eelbrain Vector test with permutation testing (n=10,000, p=0.001). Accuracy was validated against simulated data with known ground-truth connectivity across varying noise levels.

Results: The decomposition method significantly influenced alpha-band connectivity patterns. Simulation validation showed both methods achieved near-perfect magnitude and phase recovery at moderate-to-high SNR, with dOsc showing an advantage in phase recovery (r=0.99 vs. 0.93) and comparable magnitude recovery (r=0.99 vs. 0.95) at SNR=5.7 dB. At low SNR, dOsc conservatively withheld estimates for unreliable signals, whereas Specparam continued producing estimates regardless of signal quality.

Conclusion: Alpha-band functional connectivity is meaningfully shaped by the method used to separate oscillatory and aperiodic activity. Both methods perform comparably at moderate-to high signal quality, but dOsc's conservative handling of low-SNR data suggests more reliable connectivity estimation in noisy recordings, underscoring the need for careful method selection in resting-state EEG network studies.

Keywords: Electrophysiology, Aperiodic activity, Functional connectivity, Alpha frequency

P092

A Common Thalamocortical Framework Identifies Distinct Mechanisms of Modality-Specific Salient Distractor Suppression

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Background: Despite being deeply engaged in a goal-directed task, the human brain remains remarkably sensitive to sudden salient changes in the environment, reflecting an evolutionarily conserved mechanism for rapidly detecting potential threats and opportunities. Efficient top-down mechanisms subsequently suppress task-irrelevant distractions to maintain cognitive performance. Understanding the biophysical basis of this balance is important for explaining normal attention and its disruption in disorders such as ADHD, schizophrenia, ASD, and migraine. EEG studies have reported contrasting oscillatory signatures of salient distraction: auditory distraction reduces alpha and late-beta power, whereas visual distraction increases alpha power with little or no change in beta. The neural mechanisms underlying these differences remain unclear.

Purpose: This study aims to develop a unified computational framework to explain the distinct oscillatory signatures of salient distractor suppression across auditory and visual modalities and identify the underlying thalamocortical mechanisms.

Methods: A biophysically grounded neural field model of thalamocortical interactions was employed to simulate EEG-like oscillatory activity from fundamental neural interaction dynamics. Salient distractors were represented by modifying the external sensory drive, while candidate mechanisms of distractor suppression were investigated through systematic modulation of interaction strengths governing relay, cortical, and thalamic reticular nucleus (TRN) populations. Simulated alpha and beta oscillations were compared with experimentally reported EEG observations.

Results: Stepped sensory drive alone reproduced the reduction in late-beta power but failed to account for alpha suppression. Enhanced TRN-mediated interactions together with increased sensory drive reproduced the simultaneous reductions in alpha and late-beta power observed during auditory distraction. In contrast, reduced thalamocortical relay-to-cortex interactions accounted for the increased alpha and late-beta activity characteristic of visual distraction.

Conclusion: These findings demonstrate that a common thalamocortical architecture can account for modality-specific oscillatory signatures through distinct dominant neuronal interactions. The proposed framework provides a mechanistic interpretation of saliency suppression and generates experimentally testable hypotheses regarding thalamocortical regulation of attention across sensory modalities.

Keywords: Salient distraction; Bottom- up attention; Top-down attention; Relay neurons; Reticular nuclei; Thalamo-cortical interactions.

P093

An open-source machine-learning platform for automated behavioral quantification and functional validation of patient-derived SNRPN variants in *Drosophila*

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Background: Genetic variant discovery in neurodevelopmental disorders now far outpaces the capacity to determine which variants are functionally damaging. Manual behavioral scoring in animal models is slow, low-throughput, and observer-dependent, creating a bottleneck in translating clinical findings into functional evidence. Scalable, automated quantification is needed to close this gap.

Purpose: We developed an open-source, machine-learning-based tracking platform for high-throughput behavioral quantification in *Drosophila* and applied it to resolve the functional consequences of novel patient-derived variants in SNRPN, a paternally expressed gene in the Prader-Willi critical region.

Methods: We built automated tracking pipelines, including the *Drosophila* Aggression and Courtship Evaluator (DANCE), that use machine-learning classifiers to quantify complex behaviors without manual annotation. Using SmB, the conserved *Drosophila* homologue of SNRPN, we performed developmental and adult-specific neuronal knockdown. Two patient-identified missense variants (c.260C>A and c.280C>T) were assessed through in vivo transgenic rescue in humanized fly models, with aggression, feeding, and sleep quantified using the automated pipelines.

Results: Early developmental knockdown produced complete larval lethality with severe locomotor and neurodevelopmental defects. Transgenic rescue classified both missense variants as definitive loss-of-function alleles. Adult-specific knockdown, quantified by the automated platform, revealed phenotypes strikingly reminiscent of human Prader-Willi Syndrome, including elevated inter-male aggression, increased food intake mirroring hyperphagia, and disrupted daytime sleep.

Conclusion: Machine-learning-driven behavioral tracking enables rapid, objective classification of disease associated variants at scale. The platform confirms the pathogenicity of two clinical SNRPN variants through evolutionary conservation and establishes a ready-to-use computational pipeline for functionally characterizing novel disease genes directly from the clinic.

Keywords: Machine learning, automated behavioral tracking, *Drosophila*, SNRPN, Prader-Willi syndrome, variant validation

P094

Cystamine Shows Neuroprotective Effects by Modulating TG2–ATF4-Mediated Ferroptosis in MCAO Rats

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Background: Ischemia/reperfusion (I/R) injury is a major contributor to brain damage following ischemic stroke (IS) and has been increasingly associated with ferroptosis, an iron-dependent form of regulated cell death characterized by iron overload and lipid peroxidation. Transglutaminase 2 (TG2), a multifunctional enzyme upregulated in IS, has been implicated in neuronal injury and regulate ferroptosis. Activating Transcription Factor 4 (ATF4), a key mediator of the integrated stress response, also plays a role in cerebral ischemic injury. Cystamine (CYS), an irreversible TG2 inhibitor, has demonstrated neuroprotective effects in IS.

Purpose: The present study investigated the neuroprotective effect of CYS against cerebral I/R-induced ferroptosis by evaluating the TG2–ATF4 signaling pathway.

Methods: Adult male Wistar rats (200-250g) were subjected to middle cerebral artery occlusion (MCAO) and treated with vehicle or CYS (100 mg/kg, i.p.) 3 h after I/R injury. Ferrostatin-1 was included as a positive control. Neurological deficits were evaluated using behavioral tests. Infarct volume and iron deposition were assessed by TTC and Perls' staining, respectively. Oxidative stress was determined by malondialdehyde (MDA), catalase activity, and reduced glutathione (GSH) levels. Immunohistochemistry was performed for TG2, ATF4, CHOP, CARS, GPX4, and SLC7A11, while TG2 and ATF4 mRNA expression was analyzed by qRT-PCR.

Results: CYS improved neurological deficit score, beam walk and hanging wire score, reduced infarct volume and iron accumulation, decreased MDA levels, restored catalase activity and GSH content. Furthermore, CYS downregulated TG2, ATF4, CHOP, and CARS expression while restoring GPX4 and SLC7A11 levels. qRT-PCR confirmed reduced TG2 and ATF4 mRNA levels. These effects were comparable to Ferrostatin-1, supporting the involvement of ferroptosis in I/R injury.

Conclusion: CYS attenuates cerebral I/R injury by modulating the TG2–ATF4 signaling pathway, suppressing ferroptosis, and restoring antioxidant defenses. These findings suggest that targeting TG2–ATF4-mediated ferroptosis may represent a promising therapeutic strategy for IS.

Keywords: Cystamine; Ischemic stroke; TG2; ATF4; MCAO

P095

Adolescent Repeated Mild Traumatic Brain Injury Impairs Avoidance Learning in Adulthood through Dysregulation of GPR55 Signaling in the Dentate Gyrus of Rats

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Background: Adolescent repeated mild traumatic brain injury (RmTBI) is increasingly recognized as a cause of persistent cognitive impairment extending into adulthood. However, the molecular mechanisms underlying these long-term deficits remain poorly understood. G protein-coupled receptor 55 (GPR55), a neuromodulatory receptor implicated in synaptic plasticity and learning, may contribute to trauma-induced cognitive dysfunction.

Purpose: This study investigated the role of GPR55 signaling in the dentate gyrus (DG) in mediating persistent avoidance learning deficits following adolescent RmTBI.

Methods: Male Sprague-Dawley rats were subjected to a weight-drop model of RmTBI for seven consecutive days beginning on postnatal day (PND) 41. Neurological deficits and motor coordination were assessed using the modified neurological severity score (mNSS) and rotarod test after the final injury. Following maturation to adulthood (PND 80), avoidance learning was evaluated using the foot shock avoidance test. GPR55 expression in the DG was determined by immunohistochemistry and Western blotting. To establish the functional role of GPR55, rats received intra-DG administration of the selective GPR55 agonist ML184 or antagonist CID16020046 before behavioral assessment.

Results: Adolescent RmTBI produced persistent neurological impairment and significantly reduced avoidance learning in adulthood, accompanied by decreased GPR55 expression in the DG. Pharmacological activation of GPR55 with ML184 improved avoidance performance and restored GPR55 expression, whereas GPR55 antagonism with CID16020046 further aggravated cognitive deficits.

Conclusion: These findings demonstrate that dysregulation of GPR55 signaling in the DG contributes to long-term avoidance learning deficits following adolescent RmTBI. Pharmacological activation of GPR55 may represent a promising therapeutic strategy for preventing persistent cognitive dysfunction after adolescent traumatic brain injury.

P096

Hippocampal Nuclear Sirtuins in Global Cerebral Ischemia: Sex-Specific Differences with special reference to SIRT6

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Background: A major limitation in developing effective stroke therapies beyond thrombolysis is the incomplete understanding of sex-specific molecular mechanisms underlying ischemic brain injury. Sirtuins are very crucial epigenetic regulators implicated in multiple diseases including neurodegenerative disorders; however, their sex-specific involvement in stroke remains poorly understood.

Purpose: To investigate sex-specific alterations in hippocampal nuclear sirtuins following global cerebral ischemia and to characterize SIRT6's and its interacting partners.

Methods: A total of 46 male and 32 female (6–7 months old) outbred CD1 mice were randomly assigned to bilateral common carotid artery occlusion (BCCAo) or sham groups. Hippocampal sirtuin expression was assessed by RT-qPCR and Western blotting. SIRT6 chromatin immunoprecipitation (ChIP) and co-immunoprecipitation (Co-IP) were performed in male samples. Co-IP-derived proteins were analyzed using proteomics and Ingenuity Pathway Analysis (IPA), and selected interacting partners were validated across sexes by RT-qPCR.

Results: BCCAo induced sustained downregulation of SIRT1, transient upregulation of SIRT7, and increased SIRT2 and SIRT6 expression in males. In contrast, females exhibited reduced SIRT2 and SIRT6 levels, with no significant changes in SIRT1 or SIRT7. ChIP analysis demonstrated enhanced SIRT6 occupancy at the TNF-α, IL-6, and NRF2 promoters following ischemia. SIRT6-interacting partners showed transient upregulation at day 1 followed by downregulation at day 7 in males, whereas females displayed minimal changes except for progressive Mtor upregulation.

Conclusion: The sexually dimorphic expression of SIRT1 and SIRT2 suggests female-specific neuroprotection, consistent with previous reports of stroke-induced hippocampal inflammation and damage in males and the respective neuroprotective and detrimental roles of SIRT1 and SIRT2. Although SIRT6 is generally considered neuroprotective, it may exert dual effects in stroke and neurodegenerative conditions. Our study investigated the binding specificity and interacting partners of SIRT6, supporting its sexually dimorphic protective and detrimental roles; however, further studies are required to fully elucidate its role in stroke.

Keywords: BCCAo, Mouse model, Chromatin immunoprecipitation, Co-IP, Motor

P097

Overexpression of NDP52 rescues behavioral deficits in sporadic Alzheimer's disease mice models through selective autophagy

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Background: Alzheimer's disease (AD) is a progressive neurodegenerative disorder marked by cognitive decline, synaptic dysfunction, and impaired autophagic clearance. While transgenic models such as 5xFAD mice provide insights into familial AD, sporadic forms require complementary pharmacological models to better mimic late-onset pathology.

Purpose : This study investigates the role of NDP52, a selective autophagy receptor, in sporadic AD pathology and evaluates whether its restoration can rescue cognitive impairments.

Methods: Sporadic AD mouse models were established via intracerebroventricular administration of streptozotocin (STZ, 3 mg/kg) and amyloid beta-42 (Aβ42) oligomers. Pathology was allowed to develop for 6 months (Aβ42 sAD) and 9 months (STZ sAD) from postnatal day 4 (P4). NDP52 expression was quantified in STZ-treated mice, Aβ42-injected sporadic AD mice, and 5xFAD transgenics using immunoblotting and immunohistochemistry. Rescue experiments were performed in aged sporadic AD mice (6–9 months old) via lentiviral-mediated NDP52 overexpression, followed by behavioral assessment using novel object recognition (NOR), T-maze, radial arm maze, open field, and Morris water maze paradigms.

Results: Both sporadic and familial AD models exhibited significant reductions in NDP52 protein levels, with cortical and cerebellar downregulation confirmed by immunoquantitative blots and immunohistochemistry. Lentiviral NDP52 delivery restored recognition memory and spatial learning in both sporadic models (STZ, Aβ42), indicating functional rescue of cognitive deficits.

Conclusion: These findings identify NDP52 downregulation as a convergent pathological feature across sporadic and familial AD models. Restoring NDP52 expression ameliorates cognitive impairments, underscoring its therapeutic potential as a modulator of selective autophagy.

Keywords: Alzheimer's disease; sporadic AD; autophagy; cognitive rescue; behaviour

P098

Investigating Neuropsychiatric Disorders: From Resource Development to Biological Discovery

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Despite the staggering statistics that severe mental illnesses (SMIs) affect ~14% of the world population, or 1.1 billion people (GBD 2021), accurate clinical diagnoses or the study of disease etiology has been a challenge. The Centre for Brain and Mind (CBM) is a collaborative, multi-institutional platform to employ a multi-tier investigation of brain alterations in SMIs create resources that improve disease identification and management.

Many SMIs are thought to be neurodevelopmental, with genetic and environmental contributions to their etiology. However, traditional clinical diagnoses fail to identify disease-specific clinical features; in addition, genes critical to disease phenotype have been hard to identify given the polygenic basis of SMIs. This 20-yr study analyses a prospective cohort of multiplex families. We use a multi-dimensional approach to map the evolution of SMIs in patients and healthy individuals using (a) clinical and endophenotype evaluations that include cognitive, neuroimaging and clinical electrophysiology assessments, (b) whole exome sequencing and (c) generation of stem cells for detailed analyses. This continues to generate a rich longitudinal dataset of brain phenotypes and a biorepository to aid the discovery of genetic, cellular and electrophysiological contributions to altered biology in SMIs.

A total of 2138 subjects were recruited to the study (Phase I), and their first-degree unaffected relatives for clinical, endophenotype assessments and sample collection. The cohort also includes a set of population controls (N=327). Repeated evaluations conducted every 2 years are ongoing. Stem cell lines have been generated for each SMI using 2 patients and 1 family control lines, totaling 130 lines to date. Exome sequencing of 489 individuals from the cohort has been completed. Lastly, all clinical, behavioural, electrophysiological, neuroimaging and genomic data from >2000 patients are ported to CALM-Brain data resource to enable accessibility and further analyses with advanced computational methods.

Through the development and use of the resources developed by CBM, it will be possible for the larger scientific community to gain access to invaluable datasets, and therefore gain unprecedented biological insights into the biology of neuropsychiatric disorders.

Keywords: iPSC, MRI, organoid, endophenotyping, neuropsychiatric disorder

Symposium V
Nutrition, Gut and the Brain

S19

From Proteomic Discovery to Functional Rescue: FAK1 Inhibition Restores Hippocampal Synaptic Homeostasis and Cognition in Hepatic Encephalopathy

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Background: Hepatic encephalopathy is a disabling neurological complication of liver failure, characterized by synaptic dysfunction, hippocampal neurodegeneration, and cognitive decline. Although hyperammonemia-associated glutamate–NMDAR overactivation remains a central pathogenic mechanism, direct NMDAR blockade has limited therapeutic feasibility because of the physiological importance of NMDARs in learning and memory.

Purpose: This study investigated whether focal adhesion kinase 1, identified through hippocampal proteomic profiling, functions as an upstream regulator of NMDAR-linked neurotoxicity in moderate-grade hepatic encephalopathy, and whether its inhibition could restore hippocampal structure and cognition.

Methods: Moderate-grade hepatic encephalopathy was induced in rats using thioacetamide. Hippocampal alterations were examined through protein expression analysis, nitric oxide and oxidative stress assays, apoptotic marker assessment, Nissl staining, Golgi–Cox-based dendritic reconstruction of CA1 pyramidal neurons, and the novel object recognition test. The therapeutic relevance of focal adhesion kinase 1 was evaluated using the FAK1 inhibitor Y15.

Results: Moderate-grade hepatic encephalopathy rats showed increased hippocampal phosphorylated FAK1, accompanied by elevated PSD95 and drebrin, a shift toward a neurodegenerative NR2B-dominant NMDAR profile, increased nNOS and nitric oxide levels, oxidative stress, and upregulation of cytochrome c and caspase-3. These molecular changes were associated with neuronal loss in DG, CA1, and CA3, reduced dendritic length and branching of CA1 pyramidal neurons, and impaired recognition memory. Y15 treatment markedly reduced pFAK1, normalized PSD95 and drebrin expression, restored the NR2A/NR2B balance, attenuated nNOS–NO signalling, oxidative stress, and apoptotic markers, preserved hippocampal cytoarchitecture, improved dendritic arborization, and recovered recognition memory.

Conclusion: FAK1 emerges as a proteome-derived, non-NMDAR therapeutic target in hepatic encephalopathy. Its inhibition may mitigate hippocampal excitotoxicity, neurodegeneration, and cognitive impairment by modulating PSD95/drebrin-dependent NMDAR signalling.

Keywords: Hepatic encephalopathy; FAK1; hippocampus; NMDAR; PSD95; drebrin; neurodegeneration; cognition.

S20

Neuronal Toll signaling mediates metabolic adaptation to mild dietary oxidative stress in Drosophila

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Background: While severe stress is highly detrimental, how organisms adapt to more common, mild chronic stressors remains poorly understood. Increasing evidence suggests that neuronal Toll-mediated innate immune signaling in Drosophila can regulate systemic metabolism in response to environmental stress.

Purpose: This study aimed to determine how chronic mild dietary oxidative stress influences lipid metabolism and starvation resistance in Drosophila melanogaster, and to identify the underlying neuronal mechanisms that are responsible.

Methods: Adult Drosophila were chronically exposed to low levels of dietary oxidative stress. We used starvation resistance as a readout of lipid droplet accumulation. The higher the number of lipid droplets, the greater the SR. Confocal imaging was used to visualize the lipid droplets. Whole-body TAG is measured by biochemical assays. Genetic knockdown and overexpression were performed in specific neuron groups.

Results: We found that neuronal Toll-like receptor 8 (Toll-8) modulates starvation resistance by regulating lipid accumulation. We narrowed down Tollo activity to a small cohort of neuropeptidergic neurons expressing the neuropeptide Leucokinin (LK), amongst others. Upstream Spätzle2 was the ligand that activated Tollo under oxidative stress. Downstream of Toll-8, the JNK pathway, but not the NF-κB pathway, was required for lipid accumulation and starvation resistance. Our evidence also suggests that IPCs act downstream of Leucokinin to promote lipid accumulation and starvation resistance. These results implicate neuronal Toll signaling in adapting to mild oxidative stress by modulating systemic lipid metabolism, thereby inadvertently lending the flies a greater ability to withstand starvation stress.

Conclusion: These findings demonstrate that mild dietary oxidative stress activates a neuronal Spätzle2–Tollo–JNK signaling axis within Leucokinin neurons to regulate systemic lipid metabolism. This body-brain pathway promotes lipid accumulation through downstream IPC signaling, thereby enhancing starvation resistance. The study reveals a novel mechanism by which neuronal Toll signaling enables physiological adaptation to mild oxidative stress through metabolic reprogramming.

Keywords: Tollo (Toll-8), Spätzle2, Mild oxidative stress, Leucokinin (LK), JNK signaling,

Lipid accumulation, Starvation resistance, Drosophila melanogaster.

S21

Hippocampal proteome study identifies emerging role of Fetuin A in neuroinflammation in aging brain with Minimal Hepatic Encephalopathy: study in a rat model

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Background: India, undergoing geriatric transition, is experiencing increased prevalence of chronic liver diseases in the older population putting them at a significant risk of developing Hepatic Encephalopathy (HE). HE results in neurocognitive alterations involving attention, alertness, response inhibition, and executive functions. These functions also get compromised with aging. Thus, aging exacerbates HE pathophysiological overlap with physiological manifestations of aging, increasing mortality risk. Global proteomic study identified increased Fetuin-A expression in aging rat hippocampus with HE playing a crucial immunomodulatory and neuroinflammatory functions via activation of TLR4- NFkβ pathway led neurodegeneration and cognitive decline.

Purpose: Suppressing Fetuin-A expression may reprogramme the aging brain towards neuroprotection and cognitive resilience.

Methods: Old male rats were divided into Old control (Normal saline, i.p once daily for 14 days), Old MHE (TAA, 50 mg/kg bw, i.p once daily for 14 days). MS spectrometry based proteomic study was conducted in hippocampal region of rats from both the groups, followed by protein identification and validation. Identified Fetuin A was further studied for its pathological role. A third group containing Old MHE + Fetuin A suppressor, Pioglitazone (Post TAA treatment, 3mg/kg BW i.p. for 7 days) was studied along with the first two groups. Studies involving biochemical estimations, Western Blotting, Histological and Morphometric analyses, neurobehavioral assessments were conducted to understand how suppression of increased Fetuin A reprogramme the aging brain towards neuroprotection and restoration of cognitive functions.

Results: MS data showed increased Fetuin A expression in the hippocampus of old rats with HE as compared to old rats. Increased proinflammatory markers showed a sharp decline in expression in hippocampus of old rats with MHE when Fetuin A expression was suppressed. It also declined activation of TLR4- NFkβ pathway, restored loss of dendritic arborization and cognitive decline.

Conclusion: Increased Fetuin A level when suppressed via pharmacological intervention, i.e. lowers neuroinflammation and neurodegeneration in aging populations with HE.

Keywords: Aging, Hepatic encephalopathy, neuroinflammation, Fetuin A, Proteome

S22

Combinatorial Strategy of Probiotics and cortical Transcranial magnetic stimulation promotes functional recovery in rat model of Parkinson's disease by modulating gut-brain axis

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Background: Parkinson's disease (PD), a progressive neurodegenerative disorder, is due to the degeneration of the neurons of the substantia nigra with motor and non-motor symptoms. Emerging evidence emphasizes the gut-brain axis as a key contributor to PD pathophysiology with significant alterations in gut microbiome.

Objective: To unravel the therapeutic potential of cortical repetitive transcranial magnetic stimulation (rTMS) along with Probiotics in 6-OHDA rat model of Parkinson's disease.

Methods: Adult male Wistar rats were divided into 5 groups: Sham, PD, PD+ Probiotics, PD+ Probiotics+ rTMS and PD+ Probiotics+ rTMS. For development of PD, 6-OHDA was injected (i.c.v.) in Striatum and in PD+ Probiotics group, oral administration of probiotics (270 μL/day) was given. PD+rTMS rats were subjected to rTMS (10 Hz,20 minutes/day, from post-surgery week1).

Results: In PD rats, significant disruption in microbial diversity and composition and a markedly lower Simpson index ($p=0.01$) was observed, whereas, the combined probiotic and rTMS treatment resulted in a more balanced microbial profile. Histological evaluation of the ENS revealed a significantly higher neuronal count in PD+Probiotics+rTMS relative to the PD and PD+Probiotics group showed a reduction in GFAP-positive cells. Rotarod test for motor coordination showed a significant reduction in latency to fall one-week post-surgery in PD ($p < 0.0001$), confirming motor impairment while intervention groups exhibited significantly improved latency.

Conclusion: Our research concludes that rTMS intervention along with Probiotics administration has the potential to modulate brain-gut axis, leads to gut microbial balance, attenuates systemic and neuroinflammation and improved motor and cognitive functions in PD.

ST09

Microbial Signals Drive Neuroinflammation and CNS Degeneration via Host Immune Programming

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Background: The communication between the gut microbiome and the central nervous system (CNS) is a crucial regulator of neurodegenerative pathways. However, the precise systemic mediators linking gut dysbiosis to neuroinflammation remain poorly defined.

Purpose: This study investigates how specific microbial signals alter host microRNA (miRNA) profiles to activate pathogenic immune cells and drive autoimmune CNS degeneration.

Methods: Using the experimental autoimmune encephalomyelitis (EAE) model of neuroinflammation, we evaluated the effects of antibiotic-induced microbiota depletion on microRNA expression. Functional inhibition of candidate miRNAs was performed, followed by colonization of germ-free and antibiotic-treated mice with *Akkermansia muciniphila* to assess cellular and vascular mechanisms. Clinical translation was verified in human cohorts.

Results: Microbiota depletion significantly attenuated disease severity and suppressed circulating inflammatory miRNAs, most notably miR-21. Inhibiting miR-21 reduced central nervous system T-cell infiltration and subsequent tissue degeneration. Mechanistically, upregulated miR-21 enhanced pro-inflammatory cytokine production (IL-17 and GM-CSF) by $CD4^+$ T cells while inducing blood-brain barrier dysfunction. We identified that transient expansion of *A. muciniphila* drives this phenotype. Under inflammatory conditions, atypical lipopolysaccharides from *A. muciniphila* trigger host epithelial miR-21 production via TLR2/TLR4 signaling, accelerating pathogenic T-cell migration. Crucially, circulating miR-21 was significantly elevated in patients with neuroinflammatory disease.

Conclusion: These findings reveal a novel microbe-LPS-miRNA axis connecting gut dysbiosis to systemic immune activation and neurodegeneration. This highlights host microRNAs as critical systemic messengers of the gut-brain axis and prospective therapeutic targets for complex central nervous system disorders.

Keywords: Gut-brain axis, MicroRNA-21, Lipopolysaccharides, Neuroinflammation, *Akkermansia muciniphila*.

ST10

Nicotinamide supplementation prevents the emergence of early-life stress driven inflammatory signatures, blood-brain barrier compromise, hippocampal mitochondrial dysfunction, and cognitive aging

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Background: Early-life adverse experiences can have enduring effects on physiological systems, shaping health trajectories across the lifespan, however the pathways through which this lifelong vulnerability manifests remain poorly understood.

Purpose: To delineate early-life stress driven maladaptive cellular and behavioural signatures in a rodent model and to assess impact of nutritional supplement on mitigating early-life stress evoked cognitive decline, peripheral and neuroinflammation, blood-brain barrier (BBB) compromise, and disrupted hippocampal mitochondrial health later in life.

Methods: Animals were subjected to maternal separation (MS) and were assessed for the impact on cognition, peripheral and neuroinflammation, BBB integrity, and hippocampal mitochondrial health at two epochs, in mature adulthood (6-7 months) and middle-aged (13-15 months) life. We also examined the impact of supplementation with Nicotinamide (NAM), a NAD+ precursor, on the early-life stress evoked molecular, cellular and behavioral changes in middle-aged life.

Results: Middle-aged MS animals exhibited a deterioration of object recognition memory in middle-aged life, accompanied by elevated peripheral inflammation, BBB fragility, heightened neuroinflammasome and microglial reactivity, as well as compromised mitochondrial health in the hippocampus. While a limited onset of peripheral inflammation was already noted to set in by mature adulthood, we did not observe cognitive decline, BBB compromise, increased neuroinflammation, mitochondrial changes, or microglial reactivity in the hippocampus at this age. Notably, we demonstrate that adult-onset, systemic supplementation with NAM, restored the decline in hippocampal NAD+ levels, prevented the emergence of peripheral and central inflammatory signatures, safe-guarded BBB integrity, maintained hippocampal mitochondrial health and mitigated cognitive decline in middle-aged MS animals.

Conclusions: These findings provide mechanistic insights into the impact of early stress in speeding up aging-associated signatures, and highlights the influence of NAM supplementation as an effective gerotherapeutic that can prevent the premature aging driven by early adversity.

Keywords Maternal separation, hippocampus, gerotherapeutic, neurovasculature, microglia, cytokines

Symposium VI

Neuroscience of Sleep & Consciousness

S23

Serotonergic Psychedelics: Modulation of Sleep and Anesthetic-Induced Unconsciousness

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Background: Psychedelics have been shown to be associated with increased spatiotemporal neurophysiological complexity and enhanced repertoire of functional brain states, which is opposite to that observed during depressed states of consciousness (e.g., sleep, general anesthesia, and disorders of consciousness), suggesting that serotonergic psychedelics produce network-level conditions that can counterbalance those associated with diverse states of unconsciousness. However, the effect of psychedelics on behavioral arousal is not fully understood.

Purpose: We have been conducting studies to determine the effect of intravenous administration of serotonergic psychedelics on the behavioral and neurophysiological changes during spontaneous (sleep-wake states) and pharmacologically induced (anesthesia) states of consciousness.

Methods: All studies were performed in adult male and female Sprague Dawley rats, which were surgically instrumented with an in-dwelling chronic catheter in the jugular vein to receive a serotonergic psychedelic or 0.9% saline as vehicle control. Simultaneously high-density EEG (27-30 electrodes), and EMG in the sleep studies, were recorded. The effects on behavioral arousal and functional connectivity were quantified.

Results: Our data show that intravenous administration of psilocybin and N,N-Dimethyltryptamine—two well-known serotonergic psychedelics—produced an acute increase in wakefulness and a simultaneous decrease in slow-wave sleep and rapid eye movement sleep. An even stronger arousal promoting effect was reported in studies conducted using anesthetics and sedative-hypnotics in which the intravenous administration of 2,5-dimethoxy-4-iodoamphetamine, a synthetic serotonergic psychedelic, accelerated the emergence from general anesthesia and restored neurophysiological profile associated with normal wake state.

Conclusion: These data provide direct evidence for strong arousal promoting properties of serotonergic psychedelics.

Keywords: Anesthesia, Consciousness, Serotonergic psychedelics, Sleep, Wake

S24

Mutations in *Drosophila* antimicrobial peptides differently affect sleep and plasticity

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Background: Molecules implicated in host defense can, independent of their roles as immune mediators, regulate sleep. In mammals, cytokines such as Tumor Necrosis Factor α (TNF α) and Interleukin1β (IL1β) promote sleep. In *Drosophila*, infection stimulates the systemic release of a battery of antimicrobial peptides (AMPs). These fly immune effectors have been understudied as sleep modulators.

Purpose: We wanted to evaluate the effects of loss of function of different AMPs on sleep and sleep-dependent outcomes.

Methods: We obtained mutants in different AMPs and characterized their functions in sleep and plasticity.

Results: AMP mutants slept less with a longer sleep latency, and lowered arousal thresholds. Group C mutant flies, doubly mutant for the anti-fungal peptides Metchinikowin (Mtk) and Drosomycin (Drs), showed the greatest impairments. These Group C mutants also showed an exaggerated sleep rebound, sleep rebound was unaltered in other mutants. While many classes of AMPs showed sleep deficits, different sets of AMP mutants exhibited specific disruptions in socialization and rocking induced sleep. To determine whether sleep amount and sleep functions were dissociable, we evaluated memory and quantified synapse abundance. Group C mutants uniquely exhibited normal learning and memory, and lower synapse abundance, despite sleeping the least. Group C mutants are thus able to carry out some sleep functions without sleeping very much. Glial knockdown of Metchnikowin and Drosomycin mimicked the sleep phenotypes of the null mutants, these genes thus act from glia. While GroupC mutants retained normal cognitive function, other AMP mutants showed impairments in sleep and memory. Sleep and memory defects in these AMP mutants was reversible - enhancing sleep of Bomanin mutants pharmacologically or behaviorally improved learning and memory.

Conclusion: Together, these data suggest that AMPs are potent sleep modulators and that different classes of AMPs differently affect sleep and sleep dependent outcomes.

Keywords: sleep, immunity, plasticity, memory

S25

Populations derived by laboratory selection for early and late circadian phases have co-evolved divergent sleep architecture

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Background: Circadian clocks enable overt rhythms to occur at an appropriate time of the day. Variations in circadian clock properties, such as its intrinsic period length, can lead to variations in the phase relationship exhibited in the presence of cyclic environments thus resulting in individuals with different time types or 'chronotypes'.

Purpose: While studies on humans have suggested differences in physiological traits including sleep quality among early and late chronotypes, these are limited by several confounding factors.

Methods: Using a long-term laboratory selection approach, we have established divergent fly chronotype populations with extreme early and late timing of adult eclosion. These populations have evolved divergent circadian clock properties. We asked whether sleep architecture and regulation have also coevolved in these populations. We used an automated IR-beam based method to detect locomotion of individual flies and estimated sleep based on the convention that greater than 5 minutes of inactivity is established as equivalent to sleep in these flies.

Results: We found that flies from the *early* chronotype populations exhibit greater night sleep fragmentation, whereas *late* flies have reduced daytime sleep and longer nighttime sleep latency. These phenotypes were differentially modulated by light duration and temperature cycles, stemming from differential photosensitivity and thermosensitivity of the chronotypes. Additionally, *late* flies showed altered, time-of-day dependent sleep homeostasis post sleep deprivation, while *early* flies recovered faster following jetlag. Gene-level SNP analysis revealed comparable SNP density in genes associated with sleep, across chronotypes.

Conclusions: Our studies provide insights into the complex interactions underlying chronotypes and sleep architecture.

Key Words: *Circadian, sleep, chronotype, Drosophila melanogaster; evolution*

S26

Why Sleep is Essential for Effective Learning and Memory?

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Background: Sleep is essential for overall health and is crucial for learning and memory consolidation. However, the precise neurobiological mechanisms driving these effects are still not fully known.

Purpose: This work addresses three fundamental questions: how sleep facilitates memory formation, the role of sleep in compensatory memory processes, and its contribution to maintaining homeostatic balance in the brain.

Methods: Using behavioral paradigms, short-term total sleep deprivation was applied to assess its effects on contextual fear memory, trace conditioning, and delay conditioning. Molecular and cellular approaches examined hippocampal gene expression, epigenetic regulation, neurogenesis, and structural plasticity in the primary visual cortex following learning.

Results: Short-term total sleep deprivation significantly impaired contextual fear memory and trace conditioning, while delay conditioning required increased REM sleep, indicating stage-specific mechanisms of sleep-dependent memory consolidation. At the molecular level, sleep enhanced expression of memory-associated genes (Fmn2, GSK3-α, Ncdn, and Shank3) in the hippocampus after learning, and regulated gene expression via histone acetylation and deacetylation. Sleep further promoted learning-induced hippocampal neurogenesis and structural reorganization of neural circuits in the primary visual cortex, as well as the development of compensatory neural circuitry for contextual fear memory.

Conclusion: These findings establish sleep as a stage- and mechanism-specific regulator of memory consolidation, acting through gene expression, epigenetic modification, neurogenesis, and circuit remodeling, while also maintaining ionic and homeostatic balance essential for optimal cognitive function.

Keywords: Contextual Fear Learning, Hippocampus, mPFC, Neurogenesis, NREM sleep, REM sleep,

ST11

Role of sleep-regulated lncRNAs in translation machinery and memory consolidation in the hippocampus

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Background: In mammals, hippocampus-dependent memory is particularly vulnerable to the effects of acute sleep deprivation (SD). De novo protein synthesis in hippocampal neurons is crucial for memory formation and storage. Previous studies have shown that SD perturbs the global translational landscape by impairing the translation initiation step. However, the involvement of regulatory RNAs underlying SD-induced translational dysregulation remains underexplored. Long non-coding RNAs (lncRNAs), a class of non-coding transcripts, are increasingly recognized for their roles in transcriptional and post -transcriptional regulation.

Purpose: Our study is primarily focused on elucidating the molecular mechanisms underlying the memory deficits induced by SD, with a specific emphasis on the role of lncRNAs that are associated with actively translating polysomes.

Methods: We have performed polysome fractionation of hippocampal tissue lysates from non-sleep-deprived and acute sleep-deprived mice, followed by RNA sequencing of the polysomal fractions. Differentially enriched lncRNAs were identified by comparative analysis. To investigate the functional relevance of the candidate lncRNAs, they were further analyzed in silico to predict their target RNA-binding protein (RBP) interactors, followed by Gene Ontology (GO) enrichment analysis of the interacting RBPs. Ongoing immunoprecipitation studies are being conducted to validate lncRNA–RBP interactions within polysomal fractions.

Results: Comparative analysis revealed a subset of lncRNAs that are selectively depleted from actively translating polysomes upon SD. In silico analysis predicted interactions between these lncRNAs and several RBPs, including RBM3 and CIRBP, previously reported to undergo translatome changes upon SD. GO enrichment analysis of the interacting RBPs revealed significant enrichment of pathways associated with translational regulation and circadian rhythm.

Conclusion: These findings could establish sleep-regulated lncRNAs as valuable molecular targets for studying the cognitive impacts of sleep loss and for developing interventions to reduce memory deficits linked to cognitive memory deficits caused by sleep loss.

Keywords: *Sleep Deprivation, Polysome, Long Noncoding RNA, Hippocampus*

ST12

Taxifolin as a Novel Melatonergic Chronopharmacological Modulator Restores Sleep, Mood, and Social Behaviour in Environmental Rhythm Disruption

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Background: Circadian rhythm disruption is increasingly recognised as a key contributor to neuropsychiatric disorders through dysregulation of sleep, mood, and social behaviour. Although environmental factors such as irregular light-dark cycles and chronic noise exposure closely mimic human circadian disruption, the underlying molecular mechanisms remain incompletely understood. Melatonin receptors (MT1) are promising chronotherapeutic targets; however, effective natural modulators remain largely unexplored. This study investigated the neurobiological consequences of chronic environmental rhythm disruption and evaluated Taxifolin, identified through in silico screening as a lead MT1 modulator, as a potential chronotherapeutic agent.

Purpose: To investigate the molecular mechanisms underlying circadian rhythm disruption-induced neuropsychiatric dysfunction and evaluate Taxifolin as a novel MT1-targeted chronotherapeutic for restoring sleep, behaviour, and circadian homeostasis.

Methods: Taxifolin was identified by molecular docking and virtual screening against MT1 receptors. Mechanistic validation was performed in SH-SY5Y cells and in mouse models of chronic light-cycle disruption and sound-induced circadian stress. Circadian clock genes, MT1 signalling, BDNF-CREB pathway components, and neuroinflammatory markers were evaluated by Western blotting, immunohistochemistry, and confocal microscopy. Untargeted proteomics and metabolomics were performed to identify systems-level molecular changes.

Results: Taxifolin restored circadian clock homeostasis by upregulating BMAL1, PER, CRY, BDNF, and CREB while suppressing TLR4/MyD88/NF-κB-mediated neuroinflammation. In vivo, Taxifolin significantly improved fragmented NREM sleep, restored REM sleep, and attenuated anxiety, depressive, and social behavioural deficits. Multi-omics analyses further demonstrated restoration of circadian entrainment, tryptophan-serotonin metabolism, and neurotrophic signalling.

Conclusions: Taxifolin exerts robust chronotherapeutic effects by simultaneously targeting MT1 signalling, circadian clock regulation, neurotrophic pathways, and neuroinflammation. These multiplatform findings identify Taxifolin as a promising natural therapeutic candidate for circadian rhythmassociated neuropsychiatric disorders.

Keywords: Circadian rhythm, Mood disorders, Sleep, Neuroinflammation

Oral Session I - Neurodegenerative disorders

OS01

Mitochondrial DNA on Nuclear Genome: Insight into Autism Spectrum Disorder Aetiology

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Background & Purpose: Autism Spectrum Disorder (ASD) is a heterogeneous neurodevelopmental condition in which mitochondrial dysfunction may contribute to disease susceptibility. We examined how mitochondrial DNA (mtDNA) variation influences nuclear genomic regulation and ASD-related cellular phenotypes using cybrid models generated on a uniform SH-SY5Y nuclear background.

Methods: Mitochondrial DNA-depleted ρ0 cells were successfully established and repopulated with platelet-derived mitochondria from individuals with ASD and controls. Long-template PCR, PicoGreen staining, and haplogroup analyses verified complete mtDNA depletion, accurate mitochondrial transfer, and preservation of donor haplogroup identity. Mitochondrial genome sequencing, methylomic, and transcriptomic analyses were performed in cybrids and cybrid-derived neurons.

Results: Compared with controls, ASD cybrids showed smaller mitochondria, altered mitochondrial dynamics, and impaired neuronal differentiation, including significantly reduced neurite outgrowth. Molecular analyses revealed dysregulated oxidative phosphorylation, including shifted expression of nuclear-encoded Complex I genes and compensatory changes in mtDNA-encoded ATP6 and ATP8. Functional assays further demonstrated altered Complex I and II activities, indicating reduced respiratory performance and metabolic stress. Mitochondrial genome sequencing in a Kerala ASD cohort identified ASD-unique rare variants, including pathogenic deletions in ND4, ND5, and ND6, as well as variants in COI, CYTB, non-coding regions, and overlapping microprotein loci. Transcriptomic and methylomic profiling showed broader nuclear effects, including disruption of ribosomal, immune, DNA repair, mitophagy, and stress-response pathways, as well as differential methylation of genes such as TAF11L9, TAF11L10, DBET, NXN, and KATNAL2.

Conclusion: Overall, these findings support a mitochondrion–nucleus interaction model in which rare mtDNA variants contribute to mitochondrial dysfunction, epigenetic remodeling, impaired neuronal maturation, and ASD-associated cellular pathology.

OS02

The Sonic Hedgehog (Shh) Cell Signaling Pathway is a formidable target for brain tumor therapy

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Background: Brain tumours are associated with high mortality, recurrence, and cognitive decline, particularly in paediatric patients. Current therapeutic approaches remain insufficient to prevent tumour progression and recurrence. Sonic Hedgehog (Shh) signalling plays essential roles in embryonic development, neural tube formation, stem cell maintenance, and neurogenesis. Dysregulation of developmental signalling pathways can contribute to brain tumourigenesis.

Purpose: This study aimed to investigate the role of Shh–GLI1 signalling in brain tumour development, focusing on its regulation of developmental transcription factors, cancer stem cell markers, and therapeutic resistance.

Methods: Expression of Shh signalling components and downstream targets, including GLI1, PAX6, and NKX2.2, was investigated in glioblastoma, medulloblastoma, and neuroblastoma cell lines and primary tumour samples using real-time RT-PCR and Western blotting. siRNA-mediated GLI1 knockdown was performed to examine the regulation of PAX6 and NKX2.2. BMI1 knockdown was used to investigate its contribution to Shh–GLI1-mediated drug resistance and recurrence in glioblastoma. Protein–protein docking and molecular dynamics simulations were performed to explore interactions involving PAX6, Shh–GLI1 signalling, and IDH2. Additionally, a novel inhibitor was synthesized and evaluated for its effects on glioblastoma cell growth and stem cell markers.

Results: Shh signalling was implicated in the development of medulloblastoma, glioblastoma, and, to a certain extent, neuroblastoma. GLI1 differentially regulated PAX6 and NKX2.2 in glioblastoma and medulloblastoma, demonstrating regulatory patterns distinct from those observed during neural tube development. Shh–GLI1 signalling also regulated BMI1 and influenced the drug resistance-associated gene MRP1. Furthermore, investigations identified a potential PAX6–IDH2 regulatory axis in gliomagenesis. The novel inhibitor demonstrated greater efficacy than temozolomide in vitro and modulated Shh–GLI1 signalling and its downstream targets.

Conclusion: These findings highlight the involvement of Shh–GLI1 signalling in brain tumour development, stem cell regulation, and therapeutic resistance. The novel inhibitor represents a potential candidate for further investigation as an adjunct therapeutic strategy against brain tumours.

Key Words: Shh, Gli1, Brain Tumour, Glioblastoma, BMI1, Pax6 and Nkx2.2

OS03

Metabolomic profiling reveals dynamic changes in fatty acid metabolism during human neural stem cell fate commitment

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Background: Neural stem cells (NSCs) are found in both the embryonic and adult brain. Through self-renewal, they maintain their population, and through differentiation, they generate a diverse array of neurons. Therefore, a balance between NSC self-renewal and differentiation is essential for proper tissue development and homeostasis in the brain. Recent studies have highlighted the influence of metabolic reprogramming on NSC fate decisions. Previously, we and others have reported a metabolic shift toward oxidative phosphorylation during NSC differentiation.

Purpose: The detailed metabolic changes driving the NSC fate commitment remain unclear. In this study, we aimed to generate a global metabolomic profile of human NSCs during the early stages of neuronal fate commitment.

Methods: We derived induced pluripotent stem cells (iPSCs) from human peripheral blood using a cocktail of pluripotency-associated transcription factors. The iPSCs were then differentiated into neural stem cells (NSCs), which were subsequently differentiated into neurons. Metabolic profiling was conducted at various stages in an untargeted metabolomics approach using a high resolution Orbitrap Fusion Tribrid Mass Spectrometer. Metabolite and pathway analyses were performed using various in silico tools.

Results: Multivariate statistical analyses of identified metabolites revealed a global alteration in metabolite profiles between proliferating NSCs and differentiating neurons, with clearly distinguishable metabolic signatures corresponding to distinct stages of differentiation. Pathway analyses of unique metabolites revealed that fatty acid biosynthesis, fatty acid metabolism, sphingolipid metabolism, phospholipid biosynthesis, glycerolipid metabolism and arachidonic acid metabolism play critical roles at distinct stages of differentiation.

Conclusion: Our study uncovers novel metabolites related to fatty acid metabolism involved in the neuronal fate commitment of NSCs, thereby highlighting their potential in enhancing neurogenesis in aging associated neurodegenerative diseases.

Keywords: Metabolomics, Human Neural stem cells, iPSCs, fatty acid metabolism

OS04

Genetic and Epigenetic (microRNA) Determinants in ALS: Insights from a North Indian Cohort

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Background: Amyotrophic lateral sclerosis (ALS) exhibits clinically heterogeneity driven by both genetic and epigenetic factors. We previously reported the first familial ALS-associated SOD1 mutation from India. Genetic architecture of ALS in India appears distinct from Western populations, including rarity of C9orf72 repeat expansion, a finding consistent with other Asian cohorts.

Purpose: We investigated broader genetic landscape of ALS in North India and examined exosomal microRNA(miRNA) dysregulation as a potential contributor to disease pathogenesis and clinical heterogeneity

Methods: Patients diagnosed as 'Clinically Definite and Probable ALS' underwent detailed clinical phenotyping and whole-exome sequencing. Variants were classified using ACMG guidelines and correlated with sex, age at onset, site of onset, and survival. Exosomal miRNA profiling was performed in conditioned media from NSC-34 cells expressing SOD1WT/L84F/G85R, and validated in serum-derived exosomes from sporadic ALS (sALS) patients. Functional relevance was assessed using miRNA mimic/inhibitor experiments.

Results: Among 159 ALS patients (mean age at onset 55.3±11.1 years; male, 2:1), 126 variants were identified in 92 patients, comprising 12.9% pathogenic, 20.4% likely pathogenic, and 66.7% variants of uncertain significance. Patients harboring multiple variants had significantly later disease onset but shorter survival than those with single or no variants, supporting an oligogenic contribution to ALS. Exosomal miRNA profiling demonstrated marked dysregulation in mutant SOD1 models compared with SOD1WT. miR-423-3p was significantly reduced in mutant SOD1s and in serum exosomes from sALS patients. Pathway enrichment linked its dysregulation to stress-granule dynamics, unfolded protein response, and BDNF-TrkB signaling. Mechanistically, miR-423-3p directly targeted PABPC1, a stress-granule-associated gene. Restoring miR-423-3p reduced PABPC1 expression and decreased stress-granule-positive cells by ~15%, whereas inhibition increased formation by 33%. Higher miR-423-3p levels correlated with later age at onset. Meta-analysis further identified miR-146a-5p as most consistently dysregulated miRNA across ALS datasets, with higher expression associated with longer survival.

Conclusion: Our efforts spanning over a decade of investigation showed distinctive genetic landscape and an oligogenic burden associated with later-onset but poorer survival. Reduced exosomal miR423-3p emerges as a potential biomarker linked to stress-granule-mediated pathology, while miR-146a-5p may have prognostic relevance. Integration of genetic and exosomal miRNA signatures may enhance patient stratification, prognostic assessment, and uncover novel therapeutic targets for modulating disease-associated pathways in ALS.

Keywords: Amyotrophic lateral sclerosis, genetic variants, oligogenic burden, exosomal micro RNAs

OS05

Toxicoinformatics approach reveals potential molecular targets of Neurological issues associated with progression of Organic Pollutants and Persistent Organic Pollutants

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Background: The study employs an integrative computational toxicology and systems biology framework to find out the molecular mechanism underlying pollutant-induced neurological disorders.

Purpose: The purpose of the study is to explore air pollutant associated neurological disorders such as Autism, ADHD, PTSD, Alzheimer's, Anxiety etc., and identify the molecular targets and the main pollutant which could be responsible for the cause, with the focus on neurological disorders.

Methods: Air-associated OP & POPs were listed from the published literature and publicly available chemical databases. Network analysis was performed for the retrieval of target genes and proteins. Using licensed software, i.e. Cresset flare pro +, the organic and persistent organic pollutants were docked with the target proteins. The stability of the pollutant-protein complexes was further validated through molecular dynamics simulation with the licensed software itself, focusing on the stable interactions.

Results: Molecular targets viz. TP53, TNF, and IL6, were identified as the most prominent targets among the interacted proteins which showed significant binding affinities that were consistently observed across all the investigated diseases with the selected organic and persistent organic pollutant such as decarbromodiphenyl ether (BDE-209), dicofol, endosulfan, chlordane etc.

Conclusion: Collectively, the findings provide a mechanistic insight into neurotoxic effects of air-contained organic pollutants, and the study demonstrates the utility of toxicoinformatics approach computational for identifying molecular targets against neurological issues associated with severe progression of OP and POP in environmental condition.

Keywords: Toxicoinformatics, organic pollutants, persistent organic pollutants, neurological disorder, molecular targets.

OS06

Dopamine Promotes Retinal Precursor Cell Integration and Layer Repair in N-methyl-D-aspartate Induced Degeneration models

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Background: Dopamine (DA) is the principal catecholamine present in all vertebrate retinas. DA-producing neurons in retina are classified as amacrine cells (ACs) and inerplexiform cells (IPCs), In retinal circuitry, DA primarily functions as a neuromodulator, exerting its effects through diffusion targeting retinal ganglion (RGCs) and amacrine cells (ACs)containing N-methyl-D-aspartate receptors (NMDARs)-NMDAR activation leads to glutamate excitotoxicity ,calcium influx and death of RGCs.

Purpose: Dopamine as a neurostimulator supplements repair and survival of RGCs by pluripotent retinal precursor cell (RPCs) cultured from postnatal rat pups. The incorporation of multiplying RPCs and differentiation into RGCs in the NMDA induced receptor degeneration model is accentuated and supported by presence of intravitreal dopamine in the vicinity of the retinal ganglion layer.

Method: In order to establish the therapeutic potential of dopaminergic modulation of RPC mediated retinal layer repair in retinal degeneration model, we cultured RPCs in neurobasal media supplemented with B27 and FGF2. After characterization using stem cell and proliferation markers, the RPCs are intravitreally introduced into the degeneration model incubated for 8 weeks with consistent intraperitoneal administration of dopamine.

Result: RPCs showed enhanced expression of stem cell and pluripotency markers nanog, sox2 and brdU confirmed by FACS, immunocytochemistry and RT-PCR. On transplantation in animal model, H&E staining. showed reduced vacuolation and distortion of RGCs. The enhanced expression levels of RGC specific Brn3a and S1R , NMDAR specific Grin2A , and dopamine receptors is confirmed by quantitative real-time PCR and Western blot analysis. Oxidative stress and mitochondrial membrane potential measured using DCFDA and rhodamine reflected restructuring of the retinal ganglion layer.

Conclusion: Postnatal pup derived RPCs that exhibited stem cell characteristics are able to restructure the retinal architecture in presence of dopamine and enhanced RGC survival compared to the negative control. The dopaminergic neurotransmission has a significant role in repair of NMDA mediated repair of retinal ganglion layer.

Keywords: Dopamine , Excitotoxicity, retinal degeneration , Retinal Precursor Cells

OS07

Therapeutic Potential of TUDCA in Modulating Retinal Microglial Activation, Oxidative Stress, and Neuroinflammation in Diabetic Retinopathy

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Background: Diabetic retinopathy (DR) is a major complication of diabetes mellitus caused by chronichyperglycemia, leading to retinal neuronal damage through oxidative stress, neuroinflammation, and hyperactivation of retinal microglia. These pathological processes contribute to retinal edema and structural deterioration. This study evaluates the efficacy of Tauroursodeoxycholic acid (TUDCA), a neuroprotective bile acid, in regulating these interconnected mechanisms involved in DR progression.

Purpose: This study aims to investigate the neuroprotective potential of TUDCA in diabetic retinopathy by assessing its effects on retinal microglial activation, oxidative stress, inflammation, and structural damage, and determining its ability to slow retinal neurodegeneration.

Methods: Diabetes was induced in rats by streptozotocin injection (45 mg/kg body weight), and animals with sustained blood glucose levels ≥300 mg/dl were included. After diabetes induction, the experimental group received TUDCA (500 mg/kg body weight) once weekly for 16 weeks. Retinal structural changes and edema were evaluated through fundoscopy and histological analysis. Immunohistochemistry was performed for microglial activation markers (Iba-1, MHC-II, CD-11b), inflammatory markers (TNF-α, IL-1β), angiogenic marker (VEGF-A), and antioxidant markers (glutathione and SOD).

Results: Diabetic rats exhibited significant inner nuclear layer (INL) swelling and increased microglial activation. Expression levels of Iba-1 ($p \leq 0.01$), MHC-II ($p \leq 0.001$), and CD-11b ($p \leq 0.01$) were elevated compared with controls. TUDCA treatment significantly reduced microglial activation, particularly Iba-1 expression ($p \leq 0.001$). Elevated inflammatory cytokines TNF-α ($p \leq 0.01$) and IL-1β ($p \leq 0.001$), along with VEGF-A overexpression ($p \leq 0.001$), were significantly reduced after TUDCA treatment. TUDCA also restored antioxidant defense by maintaining glutathione and SOD levels ($p \leq 0.001$).

Conclusion: TUDCA mitigates diabetes-induced retinal injury by suppressing microglial activation, reducing inflammation, and enhancing antioxidant protection, suggesting its potential as a neuroprotective therapeutic strategy for diabetic retinopathy.

Keywords: Diabetic retinopathy, TUDCA, microglia, neuroinflammation, oxidative stress, Iba-1

OS08

Long distance signalling by Degenerative Signalling Endosomes in Neurodevelopment and disease.

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Background: Neurotrophin signaling governs the balance between neuron survival and death. Neurotrophins bind to their cognate TRK receptors to promote long range retrograde survival signaling from distal axons to the cell body by forming "signaling endosomes". On the contrary, neurotrophin deprivation and pro-apoptotic ligand stimulation results in death signaling by the pan-neurotrophin receptor, p75NTR. The retrograde survival signaling has been well established, however the retrograde death signalling has been realized recently, furthermore the mechanisms for biogenesis of degenerative signalling endosomes (DSEs) ensuing the longrange death signalling remains unclear.

Methods: We used sympathetic ganglia of newborn pups from p75NTR transgenic mice and primary neurons cultured in microfluidic devices to investigate p75NTR mediated retrograde degenerative signalling along with in silico analysis of p75NTR's interaction with amyloid precursor protein, relevant to Alzheimer's disease.

Results: We found pro-apoptotic stimulation exclusively on distal axons results in local cleavage of p75NTR, releasing its intracellular domain (p75ICD) as a retrograde degenerative signal. To understand how p75ICD would associate with a transport vesicle after losing its transmembrane domain, we found p75NTR palmitoylation at Cysteine 281 in the juxtamembrane region is necessary for its vesicular localization and neuronal apoptosis. Mutation of this conserved cysteine to alanine completely blocked p75NTR palmitoylation and abrogated retrograde neuron death. In silico results showed that palmitoylation affects the interaction of p75NTR with other proteins. To determine the role of p75NTR palmitoylation in vivo, we generated transgenic mice carrying a cysteine to alanine (C281A) mutation in p75NTR, thereby preventing palmitoylation. The newborn mutant mice exhibited a significant reduction in developmental neuronal apoptosis in sympathetic ganglia compared to wild type animals.

Conclusion: Palmitoylation anchors p75ICD to retrograde vesicles, enabling formation of DSEs in the axons. Understanding the mechanism of DSE formation and function provides novel insights into the regulation of neuron death during neurodevelopment and disease.

Keywords: p75NTR, Neurodevelopment, neurodegenerative disease, microfluidic devices, Signalling.

Oral Session - Neurodegeneration and Age-related Disorders

OS09

Understanding modifiable risk and resilience factors of Dementia in the Indian context

Thomas Gregor Issac

Background: India is home to the world's largest population, with nearly 153 million people above age 60, a figure which is expected to double by 2050, likely raising the burden of cognitive impairment and dementia. The Lancet Commission's 2024 report on dementia prevention, intervention, and care highlights early identification, management of modifiable risk factors, and strengthening protective and resilience factors as key strategies to delay or prevent dementia onset. Preliminary findings from two southern Indian cohorts ; the urban Tata Longitudinal Study of Ageing (TLSA) and the rural Srinivaspura Ageing, Neuro Senescence and COGnition (SANSCOG) study, offer context-specific insights into these factors.

Methods: Cross-sectional data from the TLSA (urban) and SANSCOG (rural) longitudinal ageing cohorts were analysed to identify risk and protective factors for cognition among community-dwelling older adults.

Results: Hypertension and diabetes was prevalent in 39.84% and 22.77% of participants in the rural and urban cohorts, with rural residents bearing a disproportionate burden of undiagnosed and untreated disease. Metabolic syndrome affected 46.2% of rural and 54.8% of urban participants. Higher Framingham cardiovascular risk scores correlated with poorer memory, attention, language, visuospatial, and executive performance. Urban participants also showed elevated homocysteine levels despite treatment of vitamin B12 and folate than rural participants; higher homocysteine was linked to language impairment and reduced white matter volume. Shorter sleep duration and lower sleep efficiency were associated with memory deficits, whereas multilingualism, vascular risk factor control, social connectedness, physical activity, good sleep, and engagement with Carnatic music were associated with better cognitive performance.

Conclusions: These findings reveal a high burden of vascular and metabolic risk factors in the Indian population and their measurable link to cognition, positioning them as promising early intervention targets. For India and other LMICs with rising cardiovascular burden, addressing the modifiable risk factors in midlife and fostering healthy lifestyles, hobbies, and social connectedness are essential to reducing dementia risk.

OS10

Pax6 affects genes of motor and non -motor functions in brain

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Background: Parkinson's disease (PD), one of the common neurodegenerative disorders is characterized by a range of motor and non -motor symptoms. However, identification and evaluation of early molecular markers are of concern. Patients having mutation in PAX6 show several early non-motor phenotypes of variable penetrance and expressivity. Therefore, it has been intended to evaluate putative transcripts, proteins or differentially regulated genes by Pax6 from brain of MPTP-treated mouse model of PD.

Purpose: Identification and evaluation of early and late molecular markers and their regulation by Pax6 in Parkinson's disease-associated with non-motor and motor symptoms.

Methods: Parkinson's disease model was developed by injecting MPTP (1mg/kg) intraperitoneal for 21 days in adult mice of AKR strain and equal volume of saline in the vehicle control group, was used. Brains were used for analysis of transcriptomes, proteomes, ChIP and ChIP-sequencing.

Results: Pax6-binding to promoter sequences, UTR, distal Intergenic and Introns of several genes of early non-motor symptoms like REM sleep disorder (Snca, Tau), depression (Slc25a12, Ctnnd1), anxiety (Cntn1) to late symptoms like dementia (Stx12), visual hallucinations (Gabarap11, Gabarap12), cytokines, growth factors, neurotrophic factors, synaptic functions, cell junction assembly and inflammatory processes.

Conclusion: Pax6 may serve as a transcription factor-based biomarker for differential diagnosis and better management of Parkinson's disease because most of genes involved in motor and non-motor functions of Parkinson's disease are regulated by the Pax6.

OS11

Reversal of Alzheimer's Disease pathology by TB006 antibody targeting Galectin-3

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Background: Alzheimer's disease (AD) is a chronic progressive neurodegenerative disorder caused by multiple pathogenic factors including Amyloid-β (Aβ), phospho-Tau, and Apolipoprotein E4 (ApoE4). It is widely accepted that Aβ intermediate forms (olgomers), rather than monomers or mature fibrils, are more neurotoxic. Galectin-3 (Gal-3) was reported to be involved in Aβ oligomerization and inflammatory processes.

Purpose: What leads to the oligomerization of Aβ and is it possible to develop the alternative therapeutic modality for treating AD.

Methods: Here, we show that Gal-3 promotes oligomerization of Aβ and other pathogenic factors, and TB006, a monoclonal antibody targeting Gal-3, acts as a possible treatment for AD by degrading neurotoxic oligomers and reducing inflammation.

Results: In vitro, Gal-3 intrinsically and selectively promotes, while mTB001 and TB006 degrade, oligomerization of only the pathogenic protein forms like A42, phospho-Tau and ApoE4. Gal-3 enhances, while mTB001 blocks, A42-induced microglia activation and neuronal death. In three mouse models of AD, cognitive deficits are strongly attenuated after just two weeks of mTB001 treatment. Aβ deposition and neuroinflammation are reduced in AD mouse brains. Mechanistically, Gal-3 antibody blocked the initiating events in AD (Aβ aggregates), reduced inflammation and rescued neuronal damage. Furthermore, microhemorrhages, a potential safety liability seen with clinical stage drugs, are reduced. In addition AD patients dosed with TB006 antibody showed a significant increase in MMSE and lowers A42 levels in csf.

Conclusion: Pre-clinical studies show that TB006 is an efficacious therapeutic entity through degradation of toxic oligomers and blocking or even reversing AD progression. Clinically, TB006 has shown a superior safety profile without any drug-related adverse events in a healthy volunteer trial.

Keywords: Alzheimer's Disease, Amyloid-β (Aβ), Galectin-3, Inflammation, TB006

OS12

The water-flea, Daphnia pulex: R&D relevance to Parkinson's disease research

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Human movement disorders are characterized by progressive loss in motor control arising from dysfunctional neural circuits. Invertebrate models C. elegans and D. melanogaster have substantially advanced our understanding of the genetic and molecular biology of many neurodegenerative disorders. Daphnia, a transparent freshwater crustacean, represents an emerging complementary model that bridges behavioural neuroscience in relation to human neurodegenerative disorders, such as parkinsonism. Its swimming behaviour generates a rich repertoire of quantifiable locomotor phenotypes; phototactic responses providing added values to movement control. Conserved key neurotransmitter systems; dopaminergic, serotonergic, cholinergic, GABAergic, and glutamatergic pathways add value to human movement disorders R&D. We have used an inexpensive animal tracking software for quantification of all the locomotor characteristics, such as continuous swimming, avoidance response, turning, vertical migration, swimming velocity, path-complexity, fractal movement, acceleration, etc. Complex behavioural repertoire includes parameters on distance travelled, immobility, angular or track velocity, turning frequency, trajectory-complexity, freezing episodes, hypo- and hyperactivity and avoidance responses. Daphnia-neurotransmitter profile includes acetylcholine, dopamine, serotonin, GABA, glutamate and certain neuropeptides. Above all, the major ethical advantage of using Daphnia in R&D for movement disorders are cost-effectiveness, high-throughput, and minimally invasive nature of the animal model for neurobehavioral diseases of humans and preliminary drug screening. Above all the parthenogenetic life cycle makes Daphnia an excellent experimental model by providing genetically identical and rapidly reproduced offsprings. Its limited genetic diversity may reduce generalizability of the research findings, but surely drug discovery steps warrant use of mammalian disease models.

OS13

18β-Glycyrrhetinic acid regulates autophagy dysregulation in the MPTP/pinduced model of Parkinson's disease

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Background: Parkinson's disease (PD) is marked by a significant reduction in dopaminergic neurons in the substantia nigra pars compacta region of the brain. This neuronal loss is accompanied by aggregation of the α-synuclein protein and disruption in the autophagy process. 18β-Glycyrrhetinic acid (18βGA), an oleanolic acid-type triterpenoid, has been shown to exhibit anti-inflammatory properties and neuroprotective effects.

Purpose: This study is to explore the potential neuroprotective effects of 18βGA in a chronic 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine/Probenecid (MPTP/p) induced mouse model of PD, focusing on the role of autophagy and examining the potential underlying mechanisms.

Methodology: Swiss albino mice weighing 25±5 g were used in the study. Experimental animals were randomised into four groups: control, MPTP/p, 18βGA+MPTP, and 18βGA. The control group received saline/probenecid. The diseased (MPTP/p) and treatment (18βGA+MPTP) groups received chronic doses of MPTP/probenecid, while the treatment (18βGA+MPTP) and only compound (18βGA) groups received 18βGA for 5 weeks.

Results: The results indicate that the MPTP/p treated mice exhibited impaired motor function and elevated levels of α-synuclein. It shows autophagy dysregulation, marked by increased phosphorylated c-Jun N-terminal Kinase 1 (p-JNK-1), Beclin-1, and Microtubule-associated protein 1 light chain 3 (LC3)-II, as well as autophagic vacuoles, and decreased B-cell lymphoma 2 (BCL-2) and p62. Treatment with 18βGA significantly improved motor performance, reduced α-synuclein accumulation, and restored tyrosine hydroxylase (TH) expression. It also normalised autophagy-related alterations by decreasing p-JNK-1, Beclin-1, LC3-II, and autophagic vacuole formation, while increasing BCL-2 and p62 expression.

Conclusion: These findings suggest that 18βGA confers neuroprotection by modulating autophagy through the BCL-2/Beclin-1 axis. Thus, 18βGA holds promise as a therapeutic candidate for Parkinson's disease.

Keywords: Parkinson’s disease, Autophagy, BCL2/Beclin-1, Alpha-synuclein aggregation

OS14

Senolytic Nanocarriers Targeting Alzheimer's Disease-Associated Senescence and Neurodegeneration

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Background: Alzheimer's disease (AD) is a progressive neurodegenerative disorder with no curative therapy. Senescence contributes to AD pathology through amyloid-β accumulation, tau hyperphosphorylation, and secretion of senescence-associated secretory phenotype (SASP) factors that promote chronic neuroinflammation. Although senolytics such as Dasatinib and Quercetin show therapeutic potential, their clinical efficacy is limited by poor bioavailability, extensive first-pass metabolism, and restricted BBB penetration.

Purpose: This study was intended to investigate the effect of nanoformulation of combinatorial senolytics in attenuating AD pathologies and enhancing therapeutic efficacy.

Methods: Senolytic-loaded Nanostructured Lipid Carriers (NLCs) encapsulating Quercetin and Fisetin were developed and characterized for particle size, zeta potential, morphology, crystallinity, drug entrapment, and release. In vitro SH-SY5Y studies evaluated cell viability, oxidative stress, and gene expression, while an $AlCl_3$/D-galactose-induced AD model in Wistar rats assessed histopathology, oxidative stress biomarkers, and neuroprotective efficacy.

Results: The developed NLC-QF exhibited nanoscale particle size (139.067±4.864) and zeta potential (-18.967±1.002) as compared to blank NLC with particle size (58.96±6.51) and zeta potential (0.57±4.06). SEM and XRD analyses supported the spherical morphology and semicrystalline nature of NLC. The entrapment efficiency of the three drugs was observed to be 86.35 and 53.12% for quercetin and fisetin, respectively, in 24 h. The drug release kinetics showed a sustained release (Q91.5% and F-85.1%) in 24 h. Nanoformulation treatment in cells significantly improved cell viability, reduced oxidative stress, senescence, and ROS levels, attenuating neuronal degeneration compared to free-drug treatment. Histopathological and molecular analyses further demonstrated improved cellular integrity with reduced degenerative morphology and neuronal loss in the rat AD model treated with NLC-QF as compared to the AD model.

Conclusion: Collectively, these findings suggest that senolytic-loaded NLCs (NLC-QF) enhance local availability of active agents and therapeutic efficacy, representing a promising strategy for mitigating ADassociated neurodegeneration and cellular senescence.

Keywords: Alzheimer's disease, Cellular senescence, Senolytics, Nanoformulation

OS15

Prenatal stress mediated gut-brain axis perturbations and associated behavioral deficits: Attenuation by gestational morin in Wistar rats

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Prenatal stress (PNS) is a critical environmental factor that can adversely influence fetal development, predisposing offspring to long-term gut-brain axis perturbations and heightened susceptibility to postnatal pathologies. Gestational stress induces hyperactivation of the hypothalamic-pituitary-adrenal (HPA) axis, characterized by elevated corticosterone (CORT) levels, resulting in oxidative stress-mediated structural and functional impairments in F1 generation. These perturbations disrupt gut and brain homeostasis, leading to metabolomic, neurobehavioral and physiological deficits. Morin (3,5,7,2′,4′- pentahydroxyflavone), a natural flavonoid known for its potent antioxidant, antiinflammatory and neuroprotective properties, holds therapeutic potential in mitigating PNSinduced alterations. The present study evaluated the ameliorative efficacy of gestational morin supplementation against PNS-mediated alterations in the gut-brain axis of F1 Wistar rat offspring. Morin administration to stressed dams markedly restored HPA axis balance, attenuated oxidative stress, and improved gut and blood-brain barrier integrity. Moreover, morin treatment prevented the inflammatory and metabolomic profile, early onset of apoptosis, preserved tissue histoarchitecture, and maintained functional integrity in both gut and brain regions of the progeny. These research findings highlight the preventive role of morin during gestational period in regulation of stress induced intergenerational gut-brain axis pathologies.

KT Shetty Oration

Modulation of autophagy in the context of movement disorders

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Background: Several movement disorders are precipitated due to intracellular accumulation of toxic protein aggregates and/or dysfunctional mitochondria. Autophagy, an intracellular mopping up and recycling process, has therapeutic potential to address several of these diseases.

Purpose: This talk will show how deploying genetic and chemical biology approaches led to the identification of autophagy inducers.

Methods: Since autophagy is an evolutionarily conserved process, multiple disease models such as yeast, human cells, fly, worm and mice were integrated to investigate fundamental mechanisms of autophagy, protein aggregation and movement.

Results/Conclusion: Our recent work on synaptic autophagy and its implications for the function of neuromuscular junctions will be highlighted in the context of movement disorders.

Keywords: Autophagy, Movement Disorders, Protein aggregates, Mitochondrial dysfunction, Neuromuscular junction, Synaptic autophagy.

Symposium VII

Physiology & pathophysiology of endocrine systems

S27
Clock Dynamics in Aging and Neurodegenerative Disorders: Therapeutic Interventions

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Background: Aging is associated with progressive alterations in the circadian timing system (CTS), leading to functional circadian disruption and increased vulnerability to neurodegenerative disorders. The suprachiasmatic nucleus (SCN), through tightly regulated transcriptional–translational feedback loops, orchestrates 24-hour rhythms, including the sleep–wake cycle.

Purpose: To elucidate the dynamics of circadian regulation during aging and neurodegeneration, we conducted comprehensive investigations integrating behavioural, histological, biochemical, and molecular analyses.

Methods: Male Wistar rats across different age groups, along with experimental models of Parkinson's disease, Alzheimer's disease, and sleep deprivation, were examined. Tissue samples were collected at defined Zeitgeber times (ZT 0/24, 6, 12, and 18) to capture temporal variation. Analytical approaches included enzyme assays, RP-HPLC, qRT-PCR, and two-dimensional protein profiling.

Result: Our findings reveal significant disruptions in locomotor activity rhythms, clock gene expression, serotonin metabolism, proteomic profiles, antioxidant defense systems, immune gene expression, and neuroinflammatory markers, along with impairments in learning, memory, and brain histoarchitecture. Importantly, therapeutic interventions such as melatonin and herbal nutraceuticals demonstrated differential restoration of CTS integrity.

Conclusion: These results highlight the mechanistic links between circadian dysfunction, aging, and neurodegeneration, and underscore the potential of chronobiotic and nutraceutical strategies in promoting healthy aging and longevity.

S28

Behavioural Stratification Reveals Molecular and Structural Correlates of Stress Vulnerability and Resilience

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Traumatic stress elicits remarkably diverse behavioural outcomes, with only a subset of exposed individuals developing persistent psychopathology. The neurobiological basis of this heterogeneity remains poorly understood, largely because preclinical studies often regard stress-exposed populations as behaviourally homogeneous. Here, we employed a multidimensional behavioural phenotyping strategy to stratify animals into stress-vulnerable and stress-resilient phenotypes following traumatic stress and to delineate their underlying molecular and structural correlates. Behavioural profiling revealed pronounced inter-individual variability, with vulnerability predominating during the acute post-stress phase, followed by the progressive emergence of resilience during recovery. These distinct behavioural trajectories were accompanied by differential molecular and structural adaptations within stress-responsive neural circuits. Stress-vulnerable animals exhibited persistent dysregulation of neuroplasticity-associated signalling together with compromised neuronal structural integrity, whereas resilient animals preserved synaptic organization and neuronal architecture despite equivalent traumatic exposure. These findings demonstrate that resilience represents an active neurobiological adaptation rather than merely the absence of behavioural deficits. By integrating behavioural stratification with molecular and structural phenotyping, this study establishes a translational framework for understanding individual susceptibility to traumatic stress. Delineating the neurobiological signatures that distinguish vulnerability from resilience may facilitate biomarker discovery and accelerate the development of precision therapeutic strategies for stress-related neuropsychiatric disorders.

Keywords: Behavioural stratification; Behavioural phenotyping; Stress vulnerability; Stress resilience; Traumatic stress; Neuroplasticity; Synaptic plasticity; Translational neuroscience.

S29

The sex-specific interplay between cholinergic signaling and finasteride on depression and cognition

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Background: Finasteride is used to treat androgenic alopecia in men and PCOS in women. Finasteride use in males leads to depression, anxiety, and cognitive deficits, whereas the data for women is limited. We found a sex-specific effect of finasteride: in male rats, it induced depression- and anxiety-like effects and cognitive impairment, whereas it induced antidepressant- and anxiolytic-like effects in female rats. In the current study, we investigate if the cholinergic system contributes to these sex-specific differences.

Objectives: To understand the contribution of the cholinergic system to the sexually dimorphic effects of finasteride.

Methods: 100mg/kg finasteride (in 20% HPBCD, vehicle) was administered subcutaneously to male and female rats for 6 days. After 24h, the rats were euthanized, and the frontal cortex, hippocampus, septum, and striatum were used to evaluate AChE activity and expression of AChE and choline acetyltransferase (ChAT). In another cohort of female rats, rivastigmine (1mg/kg, dissolved in saline) was administered 30 minutes before vehicle or finasteride administration, daily for six days, and on the seventh day, anxiety- and depression-like behaviors were assessed. In another cohort, cognition and scopolamine-induced amnesia was assessed in a novel object recognition task. In male rats, the cholinergic interaction was investigated using varenicline, a muscarinic receptor partial agonist.
Results: Finasteride induced sex-dependent effects on AChE activity, AChE and ChAT expression. Rivastigmine co-administration was partially able to block the anxiolytic-like and antidepressant-like effects of finasteride. Scopolamine-induced amnesia was potentiated in the presence of finasteride. In male rats, varenicline improved memory in control but not in finasteride-administered rats. Further, varenicline showed antidepressant-like effects in control rats, which was blocked by finasteride administration.

Conclusion: Finasteride may induce sex-dependent effects, possibly by altering the cholinergic system.

Keywords: Neurosteroids, mood, cognition, acetylcholine, cholinergic system

S30

Interfering peptides targeting the intrinsic inhibitory slow afterhyperpolarization protein complex stabilize neuronal excitability and restrict epileptic seizures

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Background: Principal pyramidal neurons exhibit aberrant excitatory patterns and synchronous spike firing in temporal lobe epilepsy (TLE). Notably, a post-burst slow afterhyperpolarization (sAHP), a critical intrinsic inhibitory phenomenon, is greatly diminished in hippocampal pyramidal neurons in TLE, thereby promoting neuronal hyperexcitation and seizures.

Purpose: TLE, the most prevalent form of acquired epilepsy, is challenging to treat, with nearly 30% of patients developing drug-resistant refractory seizures. We targeted the sAHP current-producing protein complex and devised two novel cell-permeable peptides that demonstrated increased efficacy in stabilizing neuronal excitatability and restricting epileptic seizures in animal models of acquired epilepsy.

Methods: TIRF, dSTORM, and SIM2 super-resolution microscopy were used to identify the mechanistic downregulation of sAHP in hippocampal pyramidal neurons in *in-vitro* and animal models of acquired epilepsy. Artificial intelligence (AI)-, biochemical-, and FRET-based protein-protein interaction-guided design were used to generate two novel cell-permeable interfering peptides. Patch-clamp electrophysiology, in conjunction with electroencephalography (EEG) and behavioral seizure scoring, examined the efficacy of the peptides in stabilizing hippocampal pyramidal neuron excitability and reducing epileptic seizures.

Results: Our research demonstrated that Kv2.1 channels form a close association with sAHP current-producing IKCa channels at specialized ER-PM junctions and modulate its surface expression via reactive oxygen species (ROS) in epileptic neurons. Using Alfa-fold-mediated interaction prediction and FRET between full-length and truncated IKCa and Kv2.1 channels, two novel cell-permeable interfering peptides were designed, which blocked the interaction and prevented IKCa downregulation in epileptic neurons. Exposure of the peptides, either in cultured hippocampal neurons or epileptic rats experiencing status epilepticus (SE) or chronic recurrent epileptic seizures, significantly reduced the hippocampal pyramidal neuron hyperexcitation and markedly decreased seizure activity.

Conclusion: The study identified the cellular mechanism of sAHP inhibition in TLE and devised two novel cell-permeable peptides that stabilized hippocampal pyramidal neuron excitability and demonstrated anti-seizure efficacy in acquired TLE.

Keywords: Temporal lobe epilepsy, Slow afterhyperpolarization, Hyperexcitation, Status-epilepticus, Recurrent Seizures

ST13

Obesity-associated metabolic stress impairs dense-core vesicle exocytosis through VAMP2 SUMOylation in neuroendocrine cells

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Background: Dense-core vesicles (DCVs) mediate the regulated secretion of neuropeptides and hormones, including catecholamines, from neuroendocrine cells. Free fatty acid (FFA) induced metabolic stress in obesity is known to disrupt endocrine function, but its impact on DCV exocytosis and the underlying mechanisms remains poorly understood.

Purpose: Here, using diet-induced obese (DIO) mice and palmitate-treated PC12 cells, we investigated the effect of obesity-associated metabolic stress (OAMS) on DCV release and its mechanism.

Results: Live-cell imaging showed a significant impairment of stimulus-evoked DCV exocytosis in the chromaffin cells of DIO mice and palmitate-treated PC12 cells. OAMS altered the subcellular distribution of vesicle-associated membrane protein 2 (VAMP2), a core SNARE protein essential for vesicle fusion, and promoted its mislocalization to endo-lysosomal compartments. Mechanistically, we observed increased proximity between VAMP2 and SUMO1 and identified VAMP2 as a SUMOylation substrate under metabolic stress. Metabolic stress was further associated with reduced DCV docking and increased vesicle size, suggesting defective granule maturation and fusion competence. Importantly, expression of a SUMO-deficient VAMP2 mutant (VAMP2-K59A) substantially restored DCV exocytosis under metabolic stress, demonstrating that VAMP2 SUMOylation contributes to the impairment of DCV exocytosis.

Conclusion: Together, our findings reveal a previously unrecognized link between FFA-induced metabolic stress associated with obesity, VAMP2 SUMOylation, and impaired DCV exocytosis. This work provides mechanistic understanding of how metabolic stress disrupts neuroendocrine secretion and identifies VAMP2 SUMOylation as a potential molecular target for metabolic disorders associated with impaired regulated secretion.

Key words: Dense-core vesicles, exocytosis, metabolic stress, Obesity, SNAREs

Symposium VIII

Neurobiology of Reward and Addiction

S31
Brain Stimulation Rewarding Experience ameliorates Depression-induced Cognitive Deficits by Restoring Structural and Functional Plasticity in the Prefrontal Cortex

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Background: Cognitive deficits are vital feature of the Major depressive disorder (MDD) and are often comorbid with anxiety and reward dysfunctions. Interestingly, hypo-functioning of reward systems could precipitate and aggravate the depression-induced cognitive deficits and structural abnormalities. Recent studies have shown that the electrical stimulation of rewarding areas in the brain ameliorates stress-induced cognitive dysfunctions. However, the effects of self-stimulation of lateral hypothalamus - medial forebrain bundle (LH-MFB) on cognitive dysfunctions in depression are poorly understood.

Purpose: Accordingly, we evaluated the effect of chronic intracranial self-stimulation (ICSS) of LH-MFB on depression-induced cognitive deficits and associated structural and molecular changes in prefrontal cortex.

Methods: We established a developmental animal model of human endogenous depression induced by neonatal administration of clomipramine. During adulthood, neonatal clomipramine and saline administered rats were subjected to ICSS of LH-MFB for 14 days. The sham and self-stimulated rats were exposed for assessment of affective behaviours, learning impairments followed by post-mortem estimation of volumes, levels of amino acids, biogenic amines and AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid) receptors expression in the prefrontal cortex.

Results: We demonstrate that ICSS of LH-MFB in depressed rats ameliorates anhedonia, behavioral despair, anxiety and improves spatial working memory in spontaneous alternation task in T-maze. Interestingly, improvement in spatial learning following ICSS was associated with restoration of PFC volumes, levels of monoamines and amino acid neurotransmitters and AMPA receptors expression.

Conclusion: Our results provide evidence for development of rewarding brain stimulation experience as a potent therapeutic approach for restoration of cognitive deficits in depression and associated neuropsychiatric disorders.

Keywords: Brain stimulation reward, Intracranial self-stimulation, Depression, Cognitive deficits, Prefrontal cortex, Glutamate/GABA, AMPA receptors

S32

In silico investigation of phytochemical modulators targeting opioid and dopaminergic receptors: implications for reward pathway regulation and addiction therapeutics

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Background: Opioid addiction is a chronic relapsing disorder characterised by dysregulation of opioid and dopaminergic signalling pathways within the brain reward circuitry. These neuroadaptations constitute the neurobiological basis of Opioid Use Disorder (OUD).

Purpose: This study aimed to investigate the potential of GCMS identified phytocompounds of the aqueous extract of *Hydrocotyle javanica* Thunb. against opioid and dopaminergic receptors implicated in opioid reward and addiction.

Methods: The GC–MS analysis of the aqueous extract of *H. javanica* identified 41 phytocompounds. The compounds were subjected to pharmacokinetic evaluation using SwissADME and toxicity prediction using ProTox-3.0. The biological activity spectra were predicted using PASS Online. Target proteins associated with opioid reward and addiction, including μ-opioid , κ-opioid , and δ-opioid receptors, as well as dopamine D1, D2, and D3 receptors, were retrieved from the Protein Data Bank. Docking protocols were validated by re-docking the native ligands, and molecular docking was performed using AutoDock Vina. Protein–ligand interactions were analysed using the Discovery Studio Visualizer and PyMOL.

Results: Molecular docking studies revealed promising binding affinities of the compounds towards opioid and dopamine receptor targets. Flavonoids of *H. javanica* extract influence both μ-opioid and κ-opioid signalling to help suppress opioid - seeking behaviours. Interaction analysis revealed stable hydrogen bonding and hydrophobic interactions with key residues within the receptor-binding pockets. Several phytoconstituents exhibited multitarget binding profiles across both opioid and dopaminergic receptors, indicating their potential to modulate addiction-related pathways.

Conclusion: This study provides a computational foundation for future experimental validation and supports the exploration of *H. javanica* as a promising source of lead compounds for the development of addiction-related therapeutics.

Keywords: *Hydrocotyle javanica* Thunb., opioid addiction, molecular docking, opioid receptors, dopamine receptors, GC–MS

S33

Behavioral Tagging as a Multidimensional Framework for Deciphering Memory

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Long-term memory consolidation involves dynamic interactions between behavioral experience, molecular plasticity and neuronal activity. Behavioral Tagging (BT) provides a framework to understand how a weak learning event can be converted into long-term memory through the interaction of a transient behavioral tag with plasticity-related proteins (PRPs) induced by salient or novel experiences. Using rodent models of Novel Object Recognition, Open Field and Environmental Enrichment, our studies demonstrated that novelty exposure facilitates long-term memory consolidation through BT, with environmental enrichment producing robust memory persistence and hippocampal PKMζ expression. Further investigations identified BACE1 and endogenous amyloid-β as novel molecular components associated with Environmental Enrichment-mediated BT and their potential interaction with PKMζ signaling, extending the molecular framework underlying memory consolidation. To investigate the neural dynamics accompanying these behavioral and molecular processes, in vivo electrophysiological recordings were performed from the CA1 hippocampal region during BT paradigms. Local field potentials were analyzed using cepstral analysis, principal component analysis, complex response vectors (CRVs), spectral measures and multidimensional state-space tracking. The BT group exposed to novelty [BT(OF)] exhibited significantly greater cepstral coefficient magnitude than controls, indicating increased neural signal complexity. CRV-based correlation analysis revealed highly correlated neural signals in controls and reduced correlation following novelty exposure, suggesting systemic reorganization of hippocampal activity. Continuous state-space trajectories further corroborated this reorganization, with exploratory analyses indicating larger adjacent-stage neural-state transitions in BT(OF) animals. Theta relative power and spectral entropy also showed stage-dependent modulation, with enhanced theta activity during training and increased spectral entropy during retrieval, suggesting behavior-dependent restructuring of hippocampal dynamics. This integrated behavioral, molecular and electrophysiological framework is being extended to an amyloid-β_{1-42}-induced Alzheimer's disease model to investigate whether amyloid pathology disrupts BT-associated neural synchronization and electrophysiological signatures of memory consolidation. Collectively, these findings establish BT as a multidimensional model linking novelty, molecular plasticity and real-time neural dynamics during memory consolidation.

S34

Novel insights from chronic midazolam exposure on neonates and long-term neurodevelopment

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Background: Approximately 1 in 10 U.S. newborns are born preterm (<37 weeks of gestation), facing risks of low birth weight, respiratory and birth deficits often requiring surgery, mechanical ventilation, and prolonged sedation. Such long-term exposure to sedatives in these babies can potentially pose neurodevelopmental risks and can further impact changes later in life.

Purpose: The present study focused on midazolam (MDZ), a benzodiazepine class drug commonly used as sedative in the neonatal intensive care unit (NICU).

Methods: Using a robust preclinical rodent model mimicking chronic MDZ exposure, we did a comprehensive characterization on the phenotypic, molecular, biochemical, and behavioral outcomes in these exposed neonates across key developmental milestones.

Results: Our findings indicate that long-term MDZ exposure during the neonatal period negatively affects physical attributes in early childhood. While adult bodyweights between control and MDZ-exposed rats remain comparable, the MDZ rats exhibit accelerated and robust weight gain, potentially indicating a predisposition for binge eating behavior. Additionally, dopamine release in MDZ-exposed rats is markedly reduced in adulthood. Elevated levels of pro-inflammatory cytokines and growth factors in the brain during adulthood suggest a shift in development due to early MDZ exposure. Further, trends of heightened anxiety-like behavior and reduced social interaction during early adolescence compared to other stages were observed.

Conclusion: Collectively, our study provides a comprehensive assessment of how long-term MDZ exposure during neonatal stages impacts outcomes throughout life, laying the foundation for understanding mechanisms that contribute to neurodevelopmental complications associated with long-term MDZ use in neonates.

Keywords: Neurodevelopment, Midazolam, NICU, Behavior, Sedation

ST14

GLP-1R–HCRTR2 Crosstalk in Gut Dysbiosis Drives Metabolic and Circadian Disruption Leading to Cognitive Impairment.

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Background: The gut–brain axis plays a central role in regulating metabolic, neuroendocrine, and circadian homeostasis. Emerging evidence suggests that gut dysbiosis contributes to metabolic dysfunction and neurodegenerative risk. However, the mechanisms linking gut microbial imbalance to impaired glymphatic clearance remain poorly understood. Given the established roles of glucagon-like peptide-1 receptor (GLP-1R) and orexin receptor-2 (HCRTR2) in metabolic regulation, arousal, and circadian rhythm maintenance, we investigated whether disruption of GLP-1R–HCRTR2 signalling contributes to glymphatic dysfunction under conditions of gut dysbiosis.

Purpose: To find out the role of GLP-1R–HCRTR2 Crosstalk leading to Neuronal disturbances caused by Gut Dysbiosis.

Methods: Insilico network analysis and docking was performed to establish a link between GLP 1R–HCRTR2 receptors and their downstreaming signalling. Gut dysbiosis was induced in Wistar rats using an antibiotic-mediated microbiota depletion protocol. Metabolic and neuroendocrine alterations were evaluated through biochemical and molecular analyses. Expression of circadian clock genes was assessed to determine circadian rhythm disruption. Glymphatic function was evaluated by analysing aquaporin-4 (AQP4) expression and localisation, alongside assessment of brain clearance-associated markers. Correlation analyses were performed to explore relationships among metabolic dysfunction, circadian disruption, and glymphatic impairment.

Results: Gut dysbiosis produced significant metabolic and neuroendocrine disturbances characterised by impaired insulin signalling, elevated inflammatory mediators, and disruption of appetite- and arousal-associated pathways. Molecular analyses demonstrated marked dysregulation of Cry1 and Cry2 expression, indicating circadian desynchronization. Glymphatic dysfunction was evidenced by altered AQP4 expression and localisation, accompanied by reduced clearance-associated function and increased neuroinflammatory burden. Furthermore, significant associations were observed between metabolic impairment, circadian dysregulation, and glymphatic dysfunction, suggesting an integrated pathological mechanism linking gut microbial imbalance to impaired brain homeostasis.

Conclusions: The results identify GLP-1R–HCRTR2 signalling as a potential mechanistic link between gut-derived metabolic disruption and impaired brain clearance pathways.

Keywords: Gut dysbiosis, GLP-1R, HCRTR2, glymphatic clearance, circadian rhythm, aquaporin-4, neuroinflammation, gut–brain axis.

POSTER SESSION II

P-SSP99

Peripheral Blood Transcriptomics Reveals Disorder-Specific and Shared Molecular Signatures in Schizophrenia and Major Depressive Disorder: A Comparative DESeq2 Analysis

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Background:Schizophrenia (SCZ) and Major Depressive Disorder (MDD) have overlapping symptoms, yet they differ in how they affect the brain. Blood transcriptomics provides a means to identify molecular signatures that distinguish these conditions non-invasively. However, there are no thorough three-way comparisons of SCZ, MDD, and healthy controls (CTR) in the blood transcriptome literature.

Purpose: The objective is to identify specific, convergent blood transcriptome signatures in SCZ, MDD, and CTR using pairwise DESeq2 comparisons and explore the feasibility of using peripheral gene expression to stratify neuropsychiatric disease.

Methods: The transcriptome profiling of whole-blood RNA-sequencing data from 18 samples (SCZ n=6, MDD n=6, CTR n=6) was performed using DESeq2 with pairwise comparisons between CTR vs. SCZ, MDD vs. SCZ, and CTR vs. MDD. The differentially expressed genes (DEGs) were identified using log2FC>1 and Padj<0.05. Principal component analysis (PCA) of the top 3,000 variable genes was used for sample-level transcriptomic profiling.

Results: SCZ showed substantially greater transcriptomic perturbation than MDD (3,060 vs. 1,781 DEGs). K-means clustering identified six modules: C0 (SCZ erythroid, 75 genes), C1 (SCZ ribosomal, 1,518 genes), C2 (MDD immune, 683 genes), and C3-C5 (shared downregulated, 1,880 genes). The erythroid module (HBB +10.4, AHSP +11.9, ALAS2 +9.6, SLC4A1 +8.3) formed a dense PPI network enriched for haemolytic anaemia and reticulocytosis. PCA showed that PC1 (38% variance) differentiated SCZ from controls; PC2 (18% variance) segregated MDD from controls and SCZ; and PC3 (3.2% variance) reflected minor interindividual variation. The MDD immune module showed moderate connectivity via NFKBIA, CD69, and CXCR4. Hypoxia-erythroid reprogramming, reflected by convergent upregulation of the haemoglobin gene cluster in CTR vs. SCZ and MDD vs. SCZ but not CTR vs. MDD, was considered a schizophrenia-specific peripheral signature. DDIT4 was the most significantly downregulated gene in MDD vs. SCZ, suggesting an MDD-specific mTOR disinhibition phenotype. Long non-coding RNAs (LINC01116, LINC02593, LINC02747, AC010531.5) were downregulated in all three comparisons. No overlap with known schizophrenia GWAS risk loci was observed. A random forest classifier achieved 81.4% accuracy discriminating SCZ from MDD using C0 gene expression profiles alone.

Conclusion: Blood transcriptomics shows a haemoglobin/hypoxia axis specific to schizophrenia, identifies mTOR disinhibition (DDIT4) as a marker associated with MDD, and a transdiagnostic lncRNA suppression module shared between the disorders. These findings present new biomarker candidates for classifying neuropsychiatric diseases and highlight the usefulness of peripheral blood gene expression profiling for diagnosis.

Key Words: Schizophrenia, Major Depressive Disorder, Transcriptomics; DESeq2, lncRNA, HIF-1α, Haemoglobin, Biomarkers

P-SSP100

Pharmacological evaluation of coumarins against IL-1β, TNF-α, IL-6, TGF-β, and MMP-9 as potential therapeutics for drug resistant epilepsy (DRE)

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Background:Drug-resistant epilepsy (DRE) is a chronic disorder in which individuals diagnosed with seizures do not respond to anti-epileptic medications (ASMs), accounting for approximately 30% of the total epilepsy. Recent studies suggest that neuroinflammation is associated with DRE.

Purpose: We hypothesize that developing small-molecule inhibitors based on the coumarin scaffold could effectively inhibit several inflammatory cytokines, including IL-1β, TNF-α, IL-6, and TGF-β, as well as the extracellular matrix protein MMP-9.

Methods:We used Schrödinger Maestro 14.2 to perform molecular docking and MD simulations of forty coumarin derivatives against inflammatory cytokines, TGF-β and MMP-9. The top 10 compounds were screened for in vitro pharmacological activities in RAW 264.7 cells, and top 2 compounds were selected and tested in the 6-Hertz DRE model.

Results:Most of the screened coumarin derivatives exhibited better docking scores compared to standard inhibitors. Compound 1D and 1E demonstrated effective binding against IL-1β, TNF-α, IL-6, TGF-β, and MMP-9. In vitro experiments revealed IC50 values of 4.920 μM and 24.46 μM for compound 1D against IL-6 and TNF-α, and 3.998 μM, 27.33 μM, and 21.92 μM for compound 1E against IL-6, TNF-α, and TGF-β, respectively. Furthermore, 10 μM 1D and 1E inhibited MMP9, while 30 μM 1D and 1E inhibited IL-1β in RAW 264.7 cells. In vivo studies revealed that an oral subacute dose of 1D (50 mg/kg) offered 60% seizure protection in the 6-Hertz DRE model.

Conclusion:These findings demonstrate that compound 1D could by polypharmacological approach target multiple pathways and be a candidate for the management of DRE. Future experiments will further evaluate these in a chronic model of DRE with EEG.

Key words:Epilepsy, Drug-resistant, Coumarins, Inflammation

P-SSP 101

Expression pattern of novel genes and their correlation with neuroinflammation, oxidative stress and synaptic plasticity in mouse model of Autism Spectrum Disorder

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Background: Autism Spectrum Disorder (ASD) is a complex neurodevelopmental disorder with several interconnected pathways involved in its pathogenesis. However, therapeutic targets for ASD are still elusive. Recently we have identified five novel hub gene (*Abcb1a*, *Maob, Pde4b, Xdh,* and *Abcg2*) which can be implicated in ASD pathophysiology based on network pharmacology approach.

Purpose: This study was designed to assess the expression pattern of identified novel genes in a mouse model of ASD and their correlation with neuroinflammation, synaptic plasticity, and oxidative stress.

Methods: Mouse model of ASD was generated by injecting dams with 600mg/Kg body weight sodium valproate dissolved in saline at E12.5. After weaning at P21, male pups underwent three-chambered social behavior tests for validation of the model. Animals were sacrificed post-behavior and brains were resected for histological, biochemical and molecular analyses.

Results: Behavioral analysis showed reduced sociability in autistic mice as compared to controls. CV staining revealed abnormal neuronal patterns and neuronal death in hippocampus. Autistic mice also showed higher levels of lipid peroxidation, lower AchE, SOD and CAT activities. Expressions of *Abcb1a* and *Maob* were significantly reduced and levels of *Pde4b* and *Xdh* were significantly increased. However, the expression of *Abcg2* was unchanged. *Psd95, Syp,* and *Shank3* showed a significant decrease and levels of *Iba1, Tnf-α* and *Tgf-β* were significantly increased. *Abcb1a* and *Maob* showed positive correlation (PC) with synaptic plasticity markers and negative correlation (NC) with *Tnf-α*, *Maob* also showed NC with *Iba1*. *Xdh* showed no correlation with synaptic plasticity markers but showed PC with *Iba1* and neuroinflammation. *Pde4b* only showed NC with *Psd95* and PC with neuroinflammation markers. *Abcg2* showed no correlation with synaptic plasticity, microglia, and neuroinflammation markers.

Conclusion: This study, for the first time, demonstrated the modulation in levels of *Abcb1a*, *Maob*, *Pde4b* and *Xdh* brain of ASD mice which where *Abcb1a* and *Maob* show PC with synaptic plasticity markers and *Pde4b* and *Xdh* show PC with neuroinflammation and microglia activation markers. Autistic mice were typified by reduced sociability, increased oxidative stress, activated microglia and reduced neuronal health. Thus, pharmacological targeting of these novel genes may help in management of ASD.

Keywords:Autism Spectrum Disorder, novel genes, neuroinflammation, synaptic plasticity, oxidative stress

P-SSP102

Nucleus Accumbens CARTergic Inputs to the Ventral Pallidum Modulates Pain-Induced Behavioral Depression

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Background: Chronic pain is a persistent sensory and affective state that disrupts normal functioning and reduces quality of life. The nucleus accumbens (NAc), a key component of the mesolimbic system, regulates motivation and aversive processing. Cocaine- and amphetamine-regulated transcript (CART) is expressed in D1 medium spiny neurons of the NAc projecting to the ventral pallidum (VP), a region implicated in motivational and aversive states.

Purpose: This study examined whether CART signaling within the NAc-VP circuit modulates pain-induced behavioral depression.

Methods: Adult male Wistar rats (250–300 g) received a 5% formalin injection into the hind paw to induce acute and persistent pain. CART peptide or CART siRNA was stereotaxically administered into the NAc. To map the NAc-VP pathway, CTB-488 was injected into the VP to retrogradely label projecting neurons, which were assessed for c-fos expression under pain conditions. Intracranial self-stimulation (ICSS) evaluated reward function and behavioral depression. Mechanical allodynia, thermal hyperalgesia, and formalin-induced conditioned place aversion (F-CPA) assessed nociceptive and aversive responses. CART mRNA expression and dopaminergic activity were measured using RT-PCR and HPLC, respectively.

Results: Formalin increased CART mRNA expression in the NAc and activated CART-positive neurons projecting to the VP. It produced robust nociceptive behaviors, elevated ICSS thresholds that persisted from day 7 to day 14, and induced significant place aversion. Intra-NAc CART peptide attenuated nociceptive behaviors, reversed ICSS depression, reduced F-CPA, and partially restored dopamine turnover reduced by formalin. In contrast, CART knockdown exacerbated nociceptive responses, further increased ICSS thresholds, and intensified F-CPA.

Conclusion: CART signaling within the NAc-VP pathway regulates nociceptive processing and pain-induced suppression of reward function, highlighting a circuit mechanism underlying pain-induced behavioral depression.

Keywords: Cocaine- and amphetamine-regulated transcript (CART), pain-induced behavioral depression, nucleus accumbens, ventral pallidum.

P-SSP103

Unravelling the Role of Histone Post-Translational Modifications in Stress-Induced Aggressive Behaviour

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Background: Exposure to stress at critical developmental stages can cause long-lasting changes in behaviour and brain function. It has been demonstrated that peripubertal stress (PPS) causes pathological aggression in adult male mice and is a strong risk factor for neuropsychiatric diseases. However, the epigenetic underpinnings of these behavioural anomalies and their generational inheritance remain unclear.

Purpose: This study aimed to investigate the role of histone post-translational modifications (PTMs) and epigenetic regulatory pathways in PPS-induced aggression, and to explore whether these alterations extend to the germline and subsequent generations.

Methods: Male mice were subjected to a fear-inducing PPS paradigm and assessed for aggressive behaviour in adulthood (F0 generation). Histone PTM profiling was conducted in the prefrontal cortex and spermatozoa using immunoblotting. Expression of key epigenetic regulators, including DNA methyltransferases (DNMTs), histone deacetylases (HDACs), and histone lysine acetyltransferases (KATs), was also analysed. Aggressive behaviour was further evaluated in the offspring (F1 generation).

Results: PPS instigated pronounced pathological aggression in adult males and widespread epigenetic alterations in their prefrontal cortex. Histone PTM profiling revealed a remarkable reduction in activating histone marks, including H3K9ac, indicating a shift towards a transcriptionally repressive chromatin state. Altered expression of DNMTs, HDACs, and KATs further suggested disruption of epigenetic regulatory pathways and chromatin remodelling. Stress-induced epigenetic alterations were also detected in spermatozoa of aggressive male mice, supporting the possibility of germline-mediated inheritance. Coherent with this notion, offspring of F0 aggressive males exhibited heightened aggression, indicating intergenerational transmission of stress-associated behavioural deficits.

Conclusion: Our findings highlight that PPS engenders persistent epigenetic remodelling in both the brain and germline, characterized by reduced H3K9ac and alterations in chromatin-regulating pathways. These changes are allied with pathological aggression in PPS-exposed males and increased aggression in their offspring, pinpointing histone PTM-mediated chromatin regulation as a plausible mechanism linking early-life stress to intergenerational behavioural outcomes.

Keywords: Early-life stress, Aggressive behavior, Epigenetics, Histone Post-Translational Modifications, Intergenerational Inheritance

P-SSP104

Geroprotective potential of a polyherbal formulation in chronic unpredictable stress model of rats

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Background: Chronic unpredictable stress has been identified to accelerate the aging process. The current research work explores the protective effects of a polyherbal formulation (PHF) against pathological factors related to accelerated aging in the Chronic unpredictable stress (CUS) model of rats.

Purpose: To investigate the protective effects of a PHF consisting of equal fraction of seven crude drugs against CUS in rats by assessing behavioral and biochemical parameters to confirm the possible Geroprotective mechanism.

Methods: PHF was prepared by extracting dried and pulverized aerial parts of Andrographis paniculata and Fumaria indica, the roots of Asparagus racemosus and the fruits of Phyllanthus emblica, Terminalia chebula, Morus alba and Benincasa hispida in 70 % ethanol. A 14-day CUS model in albino Wistar rats was used to induce behavioral changes mimicking aging process. Quantification of IL-6, TNF-α, IL-1β, plasma corticosterone level and oxidative stress parameters were also measured.

Results: Findings revealed the protective effects of PHF against CUS, which reversed the depression, amnesia and suppressed sexual activities in CUS treated rats. Proinflammatory and oxidative stress biomarkers were significantly ($p < 0.05$) reversed in CUS rats treated with PHF as compared with the vehicle control, which was comparable to the standard drug, Panax ginseng.

Conclusions: The present study concludes that PHF demonstrated significant anti-stress effects by modulating both behavioral changes and stress-related biochemical modifications and may be explored further for anti-aging activities.

Keywords: Geroprotective, stress, polyherbal formulation, aging biomarkers, anti-aging

P-SSP105

Persistent adverse effects of early postnatal fluoxetine exposure: Relevance to postpartum depression treatment.

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Background: Postpartum depression (PPD) affects a substantial proportion of women after delivery, with a global prevalence of 17.22%. Antidepressant therapy is routinely used to treat moderate to severe PPD, and fluoxetine is among the most commonly prescribed antidepressants. However, fluoxetine readily passes into breast milk and is detected in the plasma of exposed infants. The long-term effects of early-life fluoxetine (ELF) exposure on the offspring remain poorly understood. Whether ELF exposure mimics pathological signatures observed in major depressive disorder (MDD) is unknown. Patients with MDD exhibit reduced brain volume, which cannot be explained solely by neuronal degeneration. Increasing evidence suggests that astrocyte loss contributes significantly to this reduction. Rodent studies have shown that astrocyte ablation is sufficient to induce depressive-like behaviors, suggesting a causal role for astrocytes in MDD. Similarly, ELF exposure increases anxiety- and depressive-like behaviors that persist throughout life. However, the molecular mechanisms underlying these effects remain elusive.

Purpose : To investigate how chronic fluoxetine exposure during neonatal development affects astrocyte development and contributes to adverse behavioral outcomes.

Methods : Mouse primary astrocytes were used for in vitro studies. Lactating dams were exposed to fluoxetine during the postnatal period (P2 to P22). Phenotypic and behavioral studies were performed on offspring at P23 and P90, respectively.

Results : Fluoxetine treatment decreased the proliferation by reducing Ki67 mRNA expression in primary astrocytes. Preliminary cell-cycle analysis further suggested that fluoxetine exposure altered cell-cycle progression in primary astrocytes.

Conclusion : In this study, fluoxetine exposure decreased the proliferation of primary astrocytes, which may contribute to behavioral deficits later in life. Future studies will determine whether rescuing the effect of fluoxetine on astrocytes can reverse the adverse behavioral effects.

Keywords: Anxiety, Antidepressant, Astrocytes, Fluoxetine, Postnatal, Postpartum depression.

P-SSP106

Early Neurodevelopmental Markers of Autism: Evidence from a Valproic Acid Rat Model

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Background: Autism Spectrum Disorder is a developmental disorder in which the development of different brain areas and their connectivity is affected. It leads to delays in sensorimotor integration and atypical responses to environmental stimuli, resulting in long-lasting consequences for cognitive and behavioural functions. In clinical practice, neonatal reflexes and developmental milestones serve as early indicators of central nervous system (CNS) maturation, with delays often reflecting altered neural connectivity.

Purpose: This study investigates early developmental markers in a valproic acid-induced rat model of ASD to elucidate the underlying neurodevelopmental mechanisms and potential biomarkers for early detection and therapeutic interventions.

Methods: Pregnant Wistar rats received a single intraperitoneal injection of VPA (600 mg/kg) on gestational day 12.5, while control dams received an equivalent volume of vehicle solvent. Offspring were evaluated from PND 7 to PND 21 for motor coordination and neonatal reflexes, including righting reflex, grasping reflex, cliff avoidance, tactile startle, and physical parameters, including eye opening, fur development, and pinnae detachment. Reflex acquisition and milestone attainment were evaluated using a scoring protocol. Data were analysed using the Mann-Whitney U test to determine treatment- and age-dependent effects.

Results: VPA-exposed pups showed a significant delay in the emergence of the tactile startle reflex, grasping reflex, and onset of walking. Delayed pinnae detachment and fur development were also observed, while upper incisor eruption occurred earlier compared to controls. These findings indicate an altered temporal pattern of developmental milestone acquisition.

Conclusion: These findings suggest disruptions in the integration of brainstem-spinal circuits in early postnatal life. Such early disruptions are consistent with the findings of altered neurodevelopmental trajectories in ASD and highlight the potential utility of neonatal reflex assessment as an early functional indicator of atypical CNS maturation. Ongoing studies aim to correlate the observed phenotypes with adult behavior in the same animals.

Keywords: Neurodevelopment, autism spectrum disorder, valproic acid- induced model, neonatal reflex, central nervous system, early developmental markers, developmental milestones.

P-SSP107

Deciphering the Epigenetic Landscape of Rapid Antidepressant Action by 2S,6S-Hydroxynorketamine: A Cross-Species Investigation from Neuronal Cells to C.elegans and a Mouse Model of Depression

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Background: Psychedelic drugs such as ketamine have been shown to exhibit a rapid and significant antidepressant effect, unlike the delayed effects of traditional antidepressant drugs. However, the epigenetic effect of ketamine is still understudied and needs to be further explored.

Purpose: Our study aims to investigate the treatment effect of one of the primary metabolites of ketamine, i.e., 2S,6S Hydroxynorketamine (2S,6S HNK), on cbp/p300 mediated histone acetylation levels in the SH-SY5Y cell line, C elegans, and the chronic restraint stress (CRS) mouse model of depression.

Methods: CRS animals were housed individually and kept in a 50 mL Falcon tube daily for 4-6 hours for 28 days, giving them both physiological and restraint stress. The drug was administered intraperitoneally (20mg/kg) for 2 days, during which behavioral assays were also conducted. Further, brain and serum samples were collected for molecular analysis.

Results: 2S,6S HNK did not have a significant effect on the cbp/p300 specific histone acetylation level in the neuronal cell line. However, it does affect the behavioral phenotype of C elegans by slowing down the aversion response time to 1-nonanol repellent and also reducing the thrashing rate of the worms. In the mouse model, a decrease in animal weight was observed, and there was a significant reduction in locomotor activity and the exploratory behavior of mice after 28 days of CRS, which was significantly restored upon 2S,6S HNK administration. Further, immobility time was also significantly increased in the tail suspension test, which was rescued upon drug administration.

Conclusion: In this study, 2S,6S HNK was found to have a potent and rapid antidepressant activity in the CRS model by rescuing the reduction in locomotor activity and immobility time. Further biochemical and molecular analysis is underway to determine the epigenetic effect of 2S,6S HNK.

Keywords: Depression, antidepressants, epigenetic, histone acetylation, stress

P-SSP108

Morphological Spectrum of Neural Tube Defects: An Anatomical and Clinicopathological Perspective

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Background: Neural tube defects (NTDs) are among the most common congenital malformations of the central nervous system, resulting from incomplete closure of the neural tube during the third and fourth weeks of embryogenesis. Despite advances in prenatal diagnosis and folic acid supplementation, NTDs remain a significant cause of fetal loss, perinatal mortality, and lifelong disability. Fetal autopsy provides an indispensable tool for confirming prenatal diagnosis, identifying associated congenital anomalies, and improving genetic counselling.

Objectives: To evaluate the spectrum of neural tube defects encountered in fetal autopsies, document associated congenital anomalies, and to review the molecular mechanisms underlying defective neurulation, emphasizing the role of anatomical examination in understanding the pathogenesis of these malformations.

Methods: The department of anatomy conducts fetal autopsies on requisition from the Department of Obstetrics and gynaecology at Lok Nayak Hospital, which is a tertiary care hospital. A descriptive study was conducted on fetal autopsies performed in the last eight years (2018 2026). External examination, anthropometric measurements, internal dissection, and detailed evaluation of the brain, spinal cord, and associated organ systems were performed according to standardized fetal autopsy protocols. Gross anatomical features of NTDs were correlated with abnormalities in key developmental signalling pathways and genetic regulators implicated in neural tube closure.

Results: The study demonstrated a spectrum of neural tube defects, including anencephaly, spina bifida, myelomeningocele, encephalocele, and craniorachischisis. Fetal autopsy confirmed prenatal diagnoses while identifying additional anomalies that had not been detected antenatally, thereby improving phenotypic characterization.

Conclusion: Comprehensive fetal autopsy remains the gold standard for anatomical evaluation of neural tube defects. The integration of anatomical examination with prenatal imaging and clinical data contributes significantly to improved diagnostic accuracy and informed genetic counselling.

Keywords: Neural tube defects, fetal autopsies, anatomy, spina bifida, anencephaly

P-SSP109

Investigating the predictive validity of a characterized rodent PTSD model using a neurosteroid

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Background: There have been several attempts to model post-traumatic stress disorder (PTSD) in rodents. However, the field is marred by lack of consistency and reproducibility. In this context, the current study was designed to evaluate the predictive validity of a characterized PTSD model produced by combination of two different stressors, chronic immobilization stress and social defeat stress (CIS+SDS).

Purpose: The current study evaluated the predictive validity of a rodent PTSD model using zuranolone (ZURA), a synthetic analogue of a neurosteroid allopregnanolone.

Methods: Adult male Wistar rats (n=12/13 per group, 2.5 to 3.5 months old) were randomized to 5 experimental groups, control, CIS+SDS per se, vehicle (35% HPBCD), ZURA (0.1& 0.3 mg/Kg). Vehicle or ZURA was administered following each day of stress induction for 10 days and following the stress, behavioral tests were performed to evaluate depression-, anxiety- and intrusion-like behaviour from day 11 to 14.

Results: CIS+SDS resulted in reduced sucrose preference (SPT) and increased immobility in forced swim test (FST). ZURA (0.1 & 0.3 mg/Kg) reversed the behavioural despair in FST but not in the SPT. In the tests for anxiety, 0.1 mg/kg showed a strong trend and 0.3 mg/kg significantly exhibited anxiolytic effects by increased time spent in the centre in open field test and decreased latency to first bite in the novelty suppressed feeding test (NSFT), respectively. No effect was observed in any of the groups in elevated plus maze and social interaction test. Both the ZURA doses reversed the intrusion-like behaviour by increased 55kHz ultrasonic vocalizations (USVs) happy calls elicited by the rats when subjected to the stress associated olfactory and contextual cues.

Conclusion: Hence, combining CIS and SDS resulted in a robust PTSD model with face and predictive validity.

Keywords: Neurosteroids, PTSD, depression, anxiety, mood, intrusion

P-SSP110

Decoding Extracellular Matrix and Basement Membrane signaling in Human Cortical Development and Down Syndrome

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Background: The extracellular matrix (ECM) and basement membrane components, including collagen IV, are essential regulators of radial glia maintenance, neuronal migration, and cortical circuit assembly. This project defines how COL4A5 and COL4A6 dysfunction disrupts ECM architecture and cortical development in Down syndrome, using primary human tissue and iPSC derived organoid models to uncover a previously unexplored driver of neurodevelopmental pathology. Down syndrome, caused by triplication of chromosome 21, is the most common genetic cause of intellectual disability, yet the cellular mechanisms driving its cortical developmental deficits remain incompletely understood. ECM composition is a master regulator of radial glia polarity, growth factor signaling, and neuronal migration during corticogenesis; its disruption destabilizes cortical layering at its foundation. COL4A5 and COL4A6 encode the α5 and α6 chains of collagen IV, core basement membrane components already implicated in cerebrovascular disease and Alport syndrome, yet their role in neurodevelopment remains critically understudied.

Purpose: To determine how COL4A5 and COL4A6 upregulation destabilizes basement membrane architecture, radial glia polarity, neuronal migration, and ECM signaling, and to establish translationally relevant mechanisms driving Down syndrome pathology.

Methods: Using primary developing human cortex and iPSC derived cortical/MGE organoids, we will: (i) comprehensively map COL4A5 and COL4A6 expression and ECM interaction networks using spatial proteomics and single cell transcriptomics (ii) generate Down syndrome iPSC lines and differentiate them into cortical organoids to interrogate ECM structure, progenitor behavior, neuronal migration, and transcriptional dysregulation against isogenic controls and (iii) execute genetic and pharmacological rescue experiments to restore ECM integrity and test therapeutic reversibility.

Results: Preliminary data demonstrate that COL4A5 is robustly and dynamically expressed by radial glia, peaking during the first and second trimesters of human cortical development, precisely coinciding with peak neurogenesis.

Conclusion: This work will establish ECM mediated mechanisms linking COL4A5 and COL4A6 dysfunction to cortical developmental disruption in Down syndrome, opening an underexplored dimension of disease pathology and positioning the radial glial microenvironment as a novel therapeutic target.

Keywords: Basement membrane, Down syndrome, human cortex, iPSC-derived organoids

P-SSP111

Loss of NF1 disrupts cerebello-spinal development and motor function in mice

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Background: The development of the nervous system involves spatiotemporal regulation of intracellular signalling pathways that control cell proliferation, differentiation, growth, and synapse formation. One such pathway called the RAS-MEK-ERK pathway plays an important role in central nervous system (CNS) development, and is negatively regulated by Neurofibromin, a GTPase-activating protein encoded by NF1 gene. Loss-of-function mutations in NF1 cause Neurofibromatosis type 1 in humans, a disorder associated with motor deficits and impaired coordination. While motor deficits and impaired coordination are frequently reported in individuals with NF1, the developmental and circuit-level mechanisms underlying these abnormalities remain poorly understood.

Purpose: The cerebellum and spinal cord are two integral parts of the CNS that work together in a network to produce sensorimotor integration and coordinated motor control. These systems connect the brain and body through ascending sensory and descending motor tracts. Given the central role this cerebello-spinal network plays in motor function, we set out to ask how loss of NF1 affects their development and overall morphology.

Methods: To answer this, we used a conditional Nf1 loss-of-function mouse line, with embryonic deletion driven by a CNS-specific GFAP-Cre. Histological analysis was performed to assess the morphology and neuronal organisation of the cerebellum and spinal cord, while motor function was evaluated using a battery of behavioural tests.

Results: Our preliminary findings demonstrated that Nf1 loss results in a malformed cerebellum, a dysplastic spinal cord, and motor coordination deficits. Histological analysis further revealed abnormal neuronal organisation in both structures, with notable changes in Purkinje cells, the primary output neurons of the cerebellum.

Conclusion: Together, these results point towards a previously unknown role of Neurofibromin in shaping the development and functional integrity of cerebello-spinal circuits, which in turn, may contribute to the associated motor abnormalities.

Keywords: NF1, RAS-MEK-ERK pathway, Motor coordination, cerebellum, spinal cord

P-SSP112

Glutamatergic and GABAergic systems of central amygdala in the regulation of anger-like behaviour in rats

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Background: Anger significantly affects daily life and associated distinct neuropsychiatric disorders including depression, bipolar disorder, and attention deficit/hyperactivity. The central nucleus of amygdala (CeA) processing emotions and implicated in fear, rage and aggression. CeA mainly consist with GABAergic neurons. Earlier studies suggests that CeA integrates glutamatergic afferents through a predominantly GABAergic neuronal network. However, role of GABA and glutamate in the framework of CeA during anger-like behaviour remains enigmatic.

Purpose: We tested the role of glutamatergic and GABAergic signalling within the CeA in the regulation of anger-like behaviour.

Methods: The protocol is based on the anger-aggression framework, wherein a motivated animal is prevented from obtaining an expected reward. Briefly, 48 h food-restricted rats (FR) were exposed to inaccessible food. Animals see and smell the food through small window, but unable to access, that provokes biting act. Locomotion was analysed using ANY-maze software. Molecular changes traced by immunohistochemistry, RT-qPCR and HPTLC. Effects of MK-801 and muscimol (intra-CeA) on biting activity were evaluated.

Results: FR (food on display) group rats significantly increased biting activity and locomotion (indicator of anger-like state). The c-Fos +ve glutamate cell count, VGLUT2 mRNA expression and level of glutamate in CeA tissue increased during biting activity. However, c-Fos +ve GABAergic cell count and GAD67 mRNA expression decreased in the CeA. Furthermore, intra-CeA administration of NMDA receptor antagonist (MK-801) and GABAA agonist (muscimol) attenuated biting activity.

Conclusion: We suggest that glutamate may promote, while GABA may dampen the anger-like responses. These findings demonstrate that a shift toward glutamatergic excitation and reduced GABAergic inhibition within the central amygdala contributes to the expression of anger-like behaviour in rats.

Keywords: Anger-like behaviour, Central amygdala (CeA), Excitatory–inhibitory balance.

P-SSP113

The Neurobiological Consequences of the CMS Paradigm of Depression in Rats Persist Beyond Stress Cessation: A Longitudinal 1H-MRS Study

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Background: Chronic mild stress (CMS) is a well-established rodent model of depression that reproduces core behavioural features like anhedonia. Although such changes have been extensively studied during ongoing stress, their evolution in the periods after the cessation of the stressful periods still remains unclear.

Purpose: To characterise whether the neurometabolic changes in the ventral hippocampus in adult rats persists, resolves, or continues even after the stress cessation.

Methods: Single-voxel 1H-MRS (PRESS, TE 16.5 ms) of the ventral hippocampus was previously acquired at 9.4 T at Aarhus University, Denmark. Thirty-four spectra were analysed: 21 from CMS rats (n=7; Long Evans; 1-, 3- and 8-weeks post-CMS) and 13 from controls (n=7). Spectra was analysed with a standardised FSL-MRS pipeline. Metabolites retained fits with CRLB <20%, a median NAA SNR 7 and linewidth 28 Hz.

Results: NAA/tCr and Glu/tCr progressively decreased from 1 to 8 weeks post-CMS: NAA/tCr decreased from 0.53±0.08 to 0.28±0.07 (−47%, FDR $p<0.05$), while Glu/tCr decreased from 0.71±0.15 to 0.48±0.11 (−32%, FDR $p<0.05$). NAA/tCr trended lower at 8 weeks ($p=0.076$) and taurine/tCr were elevated ($p<0.05$). Total creatine, myoinositol, glutamine, glycerophosphocholine and glutathione were unchanged.

Conclusion: Our longitudinal analysis reveals that these changes do not revert quickly after the cessation of stress; rather, diminished glutamate and NAA levels persist and evolve throughout the recovery phase. This implies that the neurobiological effects of chronic stress last beyond the actual stress exposure, indicating an extended period of hippocampal neurometabolic remodeling.

Keywords: Chronic mild stress (CMS); Anhedonia; Ventral hippocampus; Proton magnetic resonance spectroscopy (^{1}H-MRS); Glutamate; N-acetylaspartate (NAA); FSL-MRS.

P-SSP114

Altered Subcortical Functional Connectivity in De Novo Body-First Parkinson's Disease

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Background: The body-first/brain-first framework proposes that Parkinson's disease (PD) subtypes may differ according to the initial site and subsequent spreading pattern of α-synuclein pathology. Premotor REM sleep behaviour disorder (RBD) is considered a clinical indicator of the body-first phenotype (PD^{RBD+}).

Purpose: This study investigated the resting-state functional connectivity (FC) of key subcortical and limbic regions involved in motor and non-motor features in de novo, drug-naïve PD patients with and without RBD.

Methods: Sixty-seven de novo, drug-naïve PD patients and forty-one age- and sex-matched healthy subjects (HS) were enrolled. PD patients were classified as PD^{RBD+} and PD^{RBD-} based on RBD symptoms appearing at least one year before the onset of parkinsonism. Motor and non-motor symptom severity was evaluated using standardized clinical scales. Volumes of global gray matter and subcortical ROIs, including the thalamus, putamen, caudate, pallidum, and amygdala, were compared across groups. The same subcortical ROIs were used for seed-based FC analysis. Group differences in FC and correlations between FC measures and clinical scores were assessed using permutation-based non-parametric testing.

Results: Twenty-six patients were classified as PD^{RBD+} and forty-one as PD^{RBD-}. Volumetric analysis showed no significant differences among PD patient groups and HS. Seed-based FC analysis revealed reduced bilateral thalamic FC in PD^{RBD+} patients compared with both HS and PD^{RBD-} patients, mainly posterior associative, sensorimotor, occipital, and supplementary motor regions. Reduced left amygdala FC with posterior cortical regions was also observed in PD^{RBD+} compared with PD^{RBD-} patients. Reduced right thalamic FC with parieto-occipital regions in the PD^{RBD+} group was associated with worse cognitive performance. Conclusion: These findings support the presence of early network-level dysfunction in the PD^{RBD+} and suggest that thalamic and amygdala FC alterations may contribute to the greater non-motor burden and cognitive vulnerability in PD^{RBD+} patients.

Keywords: Parkinson's disease; body-first phenotype; RBD; thalamus; amygdala; functional connectivity.

P-SSP115

Spatially distributed cortical slowing and directional brain–heart coupling in Major Depressive Disorder: A region-specific and state-dependent study

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Background: Depression alters the brain-body regulation. Resting EEG studies usually report a single frontal effect, and brain–heart coupling is rarely resolved by region or direction, although the vagus nerve carries both afferent and efferent signals. Whether these signatures are distributed, directional, and state-dependent is unknown.

Purpose: To map resting cortical activity and directional brain–heart coupling across regions and states and their relation to symptom severity.

Methods: Twenty healthy adults and fifteen patients with major depression underwent simultaneous 32-channel EEG and ECG at rest during eyes-closed and eyes-open states. Relative power, ratios and hemispheric asymmetry were computed across six functional regions, and a Poincaré sympathetic–vagal model estimated four directional coupling pathways (sympathetic and vagal, each afferent and efferent) per region. HC and MDD groups were compared, and within patients each measure was regressed on symptom severity.

Results: Theta power was higher in patients across all six regions with the eyes closed ($p = 0.002–0.009$, $d \approx 1.0$) and absent with the eyes open, with a correspondingly lower alpha-to-theta ratio over insular and prefrontal sites ($p = 0.011–0.014$). Coupling was directionally asymmetric. Ascending afferent coupling was higher in patients, both sympathetic (gamma) and vagal (beta, gamma), with the eyes open ($p = 0.010–0.037$). Descending vagal-efferent coupling was lower with the eyes closed ($p = 0.040$), while sympathetic-efferent coupling did not differ. All four pathways scaled with severity, most strongly sympathetic-afferent coupling over the insula (well-being $R^2 = 0.45$, $p = 0.006$) and vagal-efferent coupling over frontal regions (R^2 up to 0.41).

Conclusion: In depression, at resting state the cortical slowing is distributed across insular and frontal regions and brain–heart coupling is directionally reorganised, with heightened bottom-up afferent signalling and weakened top-down vagal control. Region-, direction-, and state-resolved multimodal mapping reveals a network-level signature that whole-brain averaging obscures.

Keywords: EEG, brain–heart coupling, directionality, state dependence, regional analysis, major depressive disorder.

P-SSP116

White-Matter microstructure and morphometric shift in normal appearing mild traumatic brain injury

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Background: Mild traumatic brain injury (mTBI) can produce subtle structural and microstructural brain changes that are often difficult to detect using conventional neuroimaging markers alone. Identifying sensitive macrostructural and microstructural biomarkers is therefore important for improving characterization of injury-related changes in mTBI.

Purpose: To evaluate the microstructure and morphometric shift in normal appearing mild traumatic brain injury.

Methods: This study compared individuals with mTBI and healthy controls using a multimodal neuroimaging framework that included surface-based morphometry, volumetric analysis, and tract-based spatial statistics (TBSS) of diffusion-derived microstructural metrics. Surface-based morphometry was used to assess cortical alterations, volumetric analysis was used to quantify regional gray matter and ventricular differences, and TBSS was applied to evaluate white matter abnormalities using both conventional and advanced diffusion measures.

Results: Cortical surface analysis showed significant changes in the left superior frontal, right rostral middle frontal, and right postcentral regions. Volumetric analysis revealed bilateral thalamic atrophy, reduced right medial orbitofrontal and pars orbitalis volumes, and enlarged bilateral lateral ventricles in mTBI. White matter analysis showed reduced axial, intra-axonal, and extra-axonal parallel diffusivity in the forceps minor, reduced extra-axonal radial diffusivity in the left corticospinal tract, and increased tortuosity in the right corticospinal tract with advanced diffusion metrics outperforming standard DTI in detecting these tract-specific changes.

Conclusion: The findings demonstrate that mTBI is associated with convergent cortical, subcortical, ventricular, and white matter abnormalities. Advanced diffusion-derived metrics identified microstructural alterations in commissural and projection pathways, supporting their value as sensitive markers of subtle injury-related white matter disruption in mTBI. This multimodal approach provides a more comprehensive characterization of mTBI-related brain changes and may contribute to improved biomarker development for detecting and understanding mild traumatic brain injury.

Keywords: Mild traumatic brain injury; White matter microstructure; Diffusion tensor imaging;Surface-based morphometry

P-SSP117

Exploiting the neuroprotective potential of reactive astrocytes using antidepressants.

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Background: Neurodegenerative diseases encompass a spectrum of chronic, progressive disorders marked by the irreversible deterioration and loss of neurons in the brain and peripheral nervous system, ultimately resulting in functional impairment. Among neurodegenerative disorders, Alzheimer's disease (AD) is the leading cause of dementia, accounting for nearly 60–70% of all reported dementia cases. Parkinson's disease (PD) ranks as the second most prevalent neurodegenerative disorder and is characterized by progressive degeneration of dopaminergic neurons. Astrocytes are emerging as key players in AD and PD pathogenesis and are also thought to possess immense therapeutic potential. In these neurodegenerative disorders, astrocytes undergo reactive astrogliosis, during which they dramatically alter their morphological and physiological characteristics and play a major role in disease outcome. Reactive astrocytes can have neurotoxic or neuroprotective effects depending on the context.

Purpose: This study aims to investigate the molecular mechanisms underlying antidepressant-mediated astrogliosis and assess its effects on cognition and pathology in AD and PD.

Methods: Establishing an *In vitro* and *In-vivo* model system to study antidepressant-mediated neuroprotective astrogliosis in AD and PD.

Results: Following antidepressant treatment in mouse primary culture, we observed morphological changes in astrocytes consistent with reactive astrogliosis. Antidepressant treatment resulted in upregulation of TGF-β and downregulation of SRF at the RNA level, increased vimentin expression, and enhanced STAT3 nuclear translocation as assessed by immunofluorescence (IF).

Conclusion: Our findings suggest that antidepressant promotes neuroprotective reactive astrogliosis, which may contribute to mitigating neuronal damage and conferring protection against neurodegenerative disorders such as AD and PD.

Keywords: Alzheimer’s Disease, Parkinson’s Disease, Astrocytes, Astrogliosis and antidepressant.

P-SSP118

Understanding the molecular and cellular mechanisms of Dengue Virus induced neuropathogenesis

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Background: Despite being less extensively characterised than other neurotropic flaviviruses, dengue virus possesses demonstrable neuroinvasive and neurotropic potential. An increasing number of dengue-associated neurological manifestations have been documented, with encephalopathy, encephalitis, intracranial haemorrhage, and Guillain–Barré syndrome representing the most frequently observed neuropathological outcomes.

Purpose: We are aiming to elucidate the mechanistic pathways through which Dengue virus establishes infection within the central nervous system and contributes to neurodegenerative and neuroinflammatory outcomes.

Methods: To study this phenomenon with Dengue virus, we developed a physiologically relevant human brain organoid (HBO) integrated with microglia like cell. These HBO's were infected with live DENV- 2 virus on Day 30th and Day 60th of HBO culture with MOI 0.2 and processed for biochemical analysis. We also used the AG129 mouse model for investigating the virus's neuroinvasive properties in vivo.

Result: We successfully established HBOs with microglia-like cells, which were characterised by the presence of Sox-2, Pax-6, IBA-1 through qPCR and Immunohistochemistry. The neuroinflammatory cytokines such as Il-6 and IL-8 were significantly enhanced upon qPCR analysis of 0.2 Moi DENV-2 infected organoids post 24 hours and 72 hours. The supernatant collected from these infected organoids showed increase in IL-6 and IL-8 by CBA analysis as well as in qPCR result post 24 hour infection. The viral presence in infected organoids post 24 hour and 72 hours was confirmed using qPCR. In the AG 129 mice model, the brains of mice collected on day 5th post infection showed the viral presence as confirmed using qPCR.

Conclusion: In this study, we show Dengue virus has neuroinvasive capabilities, perhaps in severe dengue cases. It also shows that Dengue virus crosses the blood-brain barrier and infect the CNS, and causes neuroinflammation.

Keywords: DENV, neuroinflammation, neurodegeneration, Human Brain Organoids, Microglia-like cells.

P-SSP119

Noise-Induced Hearing Loss Alters Neural Response Variability in the Auditory Cortex of Wild-Type and Somatostatin-Expressing Mice

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Background: Noise-induced hearing loss (NIHL) is associated with extensive plastic changes in the central auditory system, yet the cellular mechanisms underlying altered cortical processing remain poorly understood. This study investigated the effects of noise exposure on auditory cortical activity in wild-type (C57) and somatostatin-expressing (SOM-Cre) mice, comparing auditory response properties, temporal coding, and neural response variability between sham and noise-exposed animals across both genotypes.

Purpose: This study aimed to examine the effects of noise-induced hearing loss on auditory cortical neural activity in wild-type and somatostatin-expressing (SOM-Cre) mice, with a focus on temporal coding and neural response variability, to better understand the role of SOM interneurons in the central consequences of acoustic trauma.

Methods: Awake mice were subjected to continuous noise exposure (12–16 kHz centered) for two hours to induce hearing loss. Auditory function was evaluated one week later using auditory brainstem responses (ABR). Under anaesthesia, in vivo electrophysiological recordings were obtained from the auditory cortex while presenting stimuli of varying salience.

Results: Auditory brainstem response (ABR) thresholds confirmed successful noise-induced hearing loss following exposure to 123 dB SPL broadband noise (12–16 kHz) for two hours. In vivo extracellular recordings were obtained from primary auditory cortex using single metal microelectrodes, and neuronal responses to sinusoidally amplitude-modulated (SAM) broadband noise were analyzed . Revealed that temporal synchronization to amplitude-modulated stimuli was largely preserved and reduced response variability compared to SOM and sham groups, indicating altered trial-to-trial reliability following noise exposure.

Conclusion: Together, these findings suggest that noise exposure selectively affects neural response variability in wild-type auditory cortex, while SOM interneuron-associated circuits may contribute to maintaining response stability, highlighting the differential role of somatostatin-expressing interneurons in the central consequences of NIHL.

Keywords: Noise-induced hearing loss; auditory cortex; vector strength; Fano factor; predictability; top-down modulation

P-SSP120

Oscillatory and aperiodic resting state activity in congenital vs. late blind Humans

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Background: Resting state electroencephalography (EEG) profiles are known to be significantly altered as a consequence of congenital blindness. Previous EEG studies in blindness have reported a reduced or abolished occipital alpha-band activity.

Purpose: It remains unclear whether these changes are specific to congenital visual deprivation or emerge following late-onset blindness too.

Methods: To address this question, we compared resting-state periodic and aperiodic occipital EEG activity between individuals with congenital blindness (N=17), individuals with late/acquired blindness (N=15), and age- and sex-matched normally sighted controls (N=32). Resting-state EEG was recorded during eyes-open and eyes-closed conditions. Power spectral density analyses were employed to quantify occipital alpha power (7–13 Hz) and alpha peak frequency, both corrected for aperiodic activity. Moreover, the slope and offset of aperiodic spectral characteristics were analysed.

Results: Occipital alpha activity was not only reduced in congenitally blind individuals compared to normally sighted controls, but in late blind individuals too. Blindness was associated with alterations in aperiodic spectral components: congenitally blind individuals showed a flatter slope in the high frequency range (21-45 Hz) compared to sighted controls, consistent with previous findings of an elevated excitatory/inhibitory (E/I) ratio in the congenitally visually deprived cortex. By contrast, aperiodic activity did not differ between late blind individuals and normally sighted controls.

Conclusion: The present study demonstrated a dissociation between alpha oscillatory activity and aperiodic activity: The development of aperiodic activity seems to crucially depend on early rather than current visual input. In contrast, periodic alpha activity might reflect a neural mechanism for regulating cortical excitation that crucially depends on visual input in order to be maintained.

Keywords: Resting state, Electroencephalography, blindness, alpha, congenital, aperiodic

P-SSP121

Multimodal Integrated Whole-Brain Magnetic Resonance Imaging (MRI) and Neurohistology: A Novel Study of the Human Ischemic Penumbra

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Background: While clinical MRI distinguishes the ischemic necrosis ("core") from peri-infarct regions of potentially reversible injury ("penumbra"), the cellular changes within these zones vary over time and space, and are poorly reproduced in experimental animal models. Characterisation of these changes in the human brain is essential for identifying rational therapeutic targets after ischemic stroke.

Purpose: To establish a multimodal framework mapping cellular hypoxia, axonal injury, and repair within and beyond the human ischemic penumbra.

Methods: We studied brains of two patients: a 69-year-old man with left hemispheric infarcts confirmed by diffusion-weighted MRI 16 and 11 days before death, and a 74-year-old woman with acute symptoms and a negative head CT scan who died before MRI could be performed. After ex vivo MRI, brains were cryosectioned into 20-micron sagittal slices, serially stained with Nissl and H&E, and immunostained for HIF-1α, APP, and GAP43 to assess hypoxia, axonal injury, and axonal regeneration. The images were co-registered to map cellular changes in the MRI-defined penumbra and surrounding brain tissue.

Results: HIF-1α was found across the cortex, including the contralateral hemisphere, suggesting a metabolic and molecular response that extended beyond the penumbra and was not detected by traditional histology or MRI. APP was widely distributed throughout the white matter around the ischemic core, extending the peri-infarct region, while being invisible on H&E or Nissl staining. Axonal sprouting inside bundles of damaged axons was confirmed by high-resolution histology, and GAP43 revealed axons that overlapped areas of APP immunopositivity.

Conclusion: Our multimodal approach combining neuroimaging with histopathology enables precise mapping of injured, plastic, and systemically hypoxic regions. This improves identification of vulnerable tissue and helps define therapeutic windows and targets beyond the infarct core. The observed colocalization of markers of axonal injury and repair suggests that zones of injury may represent active substrates for structural plasticity.

Keywords: Ischemic Stroke, Ischemic Penumbra, Histopathology, Magnetic Resonance Imaging, Cellular Hypoxia, Axonal Injury, Axonal Regeneration

P-SSP122

A novel dual-loaded poly(lactic-co-glycolic) acid nanoparticle composition rescues cognitive and molecular symptoms of Alzheimer's disease in vivo

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Background: Alzheimer's disease is a progressive neurodegenerative disorder characterized by cognitive decline and dementia. Aggregation of amyloid-beta plaques and neurofibrillary tangles of hyperphosphorylated Tau are identified as the key classical hallmarks of the disease. Commercially available treatments for the disease are largely symptomatic and ultimately ineffective. Targeting impaired cellular metabolism and redox imbalance may aid in restoring cellular microenvironment and prevent disease progression.

Purpose: A novel poly(lactic-co-glycolic) acid (PLGA) nanoparticle composition with a cargo of pharmacological modulators of mTOR and redox pathways has been engineered to tackle the progression of cognitive and molecular symptoms in sporadic AD models.

Methods: Nanoparticle synthesized using double emulsion method and characterized using SEM. Encapsulation efficiency and release kinetics were measured *in vitro*. Therapeutic potential of the composition was tested *in vitro* using SH-SY5Y cellular models via cell viability analysis and quantitative immunoblotting. Further investigation *in vivo* was conducted by stereotaxic administration of nanoparticles in murine models of sporadic AD which were then subjected to behaviour tests such as T-maze, Novel Object recognition, radial arm maze, Morris' water maze and fear conditioning tests. Whole brain samples were subjected to immunohistochemistry analysis to observe overall brain microenvironment.

Results: Spherical nanoparticles (diameter 40-60 nm) demonstrated high encapsulation efficiency and sustained release kinetics. *In vitro,* they exhibited high biocompatibility and alleviated neuronal health markers NSE and NeuN compared to disease controls. *In vivo,* nanoparticle-treated models showed significantly improved memory and cognition across different test parameters. Immunohistochemistry analyses showed an increase of NSE, neuronal health marker and decline of GFAP, astrocyte inflammation marker, in nanoparticle treated animals compared to disease controls.

Conclusion: The nanoparticle composition alleviated behaviour and molecular symptoms of AD *in vivo* which reflects on the translational potential of our novel dual-loaded PLGA nanoparticles as a viable therapeutic agent for treatment of Alzheimer's disease.

Keywords: PLGA nanoparticles, Redox Homeostasis, mTOR inhibition, Nanotherapeutics, Cognitive rescue, Alzheimer's disease

P-SSP123

Region-specific proteomic analysis of aging rhesus macaques following chronic glutamatecarboxypeptidase-II (GCPII) inhibition elucidates potential treatment strategies for sporadic Alzheimer's disease

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Background: Sporadic Alzheimer's disease (sAD) lacks effective preventive therapies, underscoring the need to target upstream pathogenic drivers. Aberrant calcium signaling, closely linked to neuroinflammation, is an early event in sAD. Aged rhesus macaques, naturally APOE-ε4 homozygotes, show cognitive decline, calcium dysregulation, amyloid deposition, and tau pathology, providing a translational model. We identified an evolutionarily expanded role for postsynaptic type 3 metabotropic glutamate receptors (mGluR3) in dorsolateral prefrontal (DLPFC) and entorhinal cortex (ERC), where they regulate cAMP–calcium-K^+ channel signaling to sustain neuronal iring and working memory. mGluR3 signaling is driven by N-acetylaspartylglutamate (NAAG) and constrained by glutamate carboxypeptidase II (GCPII), whose expression rises with age/inflammation. Chronic inhibition of GCPII with oral bioavailable inhibitor 2-MPPA improved neuronal firing, working memory, and reduced pT217Tau pathology in aged macaques.

Purpose: To define the molecular consequences of chronic GCPII inhibition in the aging primate cortex and identify region-specific proteomic signatures associated with protection against Alzheimer's disease–relevant pathology. We compared vulnerable and resilient cortical regions to identify pathways and candidate molecular targets linking GCPII inhibition to calcium regulation, synaptic function, and neurodegenerative processes.

Methods: Here, we employed liquid chromatography–tandem mass spectrometry (LC-MS/MS) to define the proteomic consequences of chronic 2-MPPA treatment in vulnerable (ERC, DLPFC) versus resilient (primary visual cortex) regions and performed label-free quantification with gene ontology enrichment and STRING analyses.

Results: We identified >2,400 proteins across experimental conditions, and label-free quantification revealed region-specific differential expression patterns paralleling known vulnerability gradients in sAD. Gene ontology enrichment implicated pathways governing protein deneddylation, amyloid and tau-associated processes, synaptic plasticity, mitochondrial homeostasis, and oxidative stress, revealing putative targets for therapeutic intervention in sAD. These findings complement the overarching hypothesis that anti-inflammatory GCPII inhibition helps to reduce AD pathology by restoring calcium regulation and lend additional credence to GCPII inhibition as a potential therapeutic strategy for sAD.

Conclusions: Overall, our findings reveal novel protein co-expression modules, thus allowing us to identify molecular substrates underlying GCPII inhibition in aging primate cortex. These indings demonstrate that GCPII inhibition engages distinct, region-selective molecular programs in the aging primate cortex, consistent with the protection of circuits most vulnerable to sAD. The identiied proteomic signatures provide candidate biomarkers and mechanistic targets for strategies aimed at preventing calcium-driven degenerative cascades in sAD. As such, more focused investigations into these pathways of therapeutic interest are warranted, in addition to the analysis of key post-translational modifications and their potential roles in sAD.

Keywords: GCPII, calcium, macaque, mGluR3, proteomics, Alzheimer's disease

P-SSP124

Dorsoventral Dissociation of Hippocampal Subregions in Contextual Fear Memory Acquisition and Retrieval in Mice

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Background: The dorsal and ventral hippocampus serve distinct functions. The dorsal region supports cognitive and spatial processing, whereas the ventral region regulates affective and emotional components of memory. Although the DH and VH are functionally interdependent, the differential temporal dynamics of their neurons during contextual fear condition (CxFC) memory consolidation and retrieval remain unclear.

Purpose: In the present study, we (I) investigated the functional involvement of the DH and VH in CxFC memory acquisition and (II) characterized the temporal pattern of neuronal activation during CxFC memory retrieval.

Methods: Male Swiss albino mice aged 2-3 months (N=58) were used in this study. Mice received bilateral microinjections of 4% lidocaine or saline into the DH or VH 10 min before CxFC training. Freezing was assessed during memory retrieval. To map the temporal profile of neuronal activation, c-Fos immunohistochemistry was performed on brains collected at 0, 1, 3, and 5 hr after CxFC memory retrieval. The c-Fos expression was quantified across dorsal and ventral dentate gyrus (DG), CA1, and CA3 subregions.

Results: Lidocaine infusion into either the DH or VH significantly reduced freezing during retrieval compared with saline-treated controls, indicating that both hippocampal divisions are essential for CxFC memory acquisition. During retrieval, c-Fos expression increased significantly in the dorsal DG (dDG), dorsal CA1 (dCA1), and dorsal CA3 (dCA3), with dCA1 showing the most sustained activation, followed by dDG and dCA3. In the ventral hippocampus, only ventral CA3 (vCA3) showed a transient increase in c-Fos expression during the early phase of retrieval, whereas ventral CA1 and ventral DG showed no change.

Conclusion: These findings demonstrate that both hippocampal regions are essential for the consolidation of CxFC memory. However, recall selectively triggers all the subregions of DH axis and only a single ventral subregion (vCA3) in a staggered timeframe.

P-SSP125

Targeting Brain Metabolism Through the Gut Microbiota: Neuroprotective Effects of *Lactobacillus reuteri*

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Background: Temporal lobe epilepsy (TLE) is the most common form of drug-resistant focal epilepsy and is characterized by recurrent seizures, hippocampal neurodegeneration, and synaptic dysfunction. Dysregulation of the tryptophan-kynurenine pathway (TKP), resulting in altered levels of neuroactive metabolites, has been reported in patients with mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE-HS) and is associated with neuronal hyperexcitability and disease progression.

Purpose: The study investigated therapeutic potential of *Lactobacillus reuteri* supplementation to reduce seizure severity and modulate TKP-associated molecular alterations through gut-brain axis in a chronic TLE model.

Methods; Male Sprague-Dawley rats received *L. reuteri* (10^9 CFU/rat/day) by oral gavage for 14 days before TLE induction. Chronic TLE was established using the Li-Pilocarpine model, and probiotic administration was continued for 28 days following status epilepticus (SE). Seizure severity was assessed using Racine scale. Hippocampal, Anterior temporal lobe (ATL) and neocortical tissues were analyzed utilising H&E, Golgi staining and qRT-PCR for TKP-related genes and glutamatergic receptor subunits (NMDA: *NR1, NR2A, NR2B*; AMPA: *GluR1–4*). Fecal metagenomic sequencing was performed to evaluate *L. reuteri* colonization following probiotic supplementation.

Results: Probiotic supplementation significantly reduced seizure severity, preserved hippocampal neuronal architecture, and improved dendritic morphology. Region-specific modulation of TKP-associated genes and glutamatergic receptor subunits was observed, indicating restoration of metabolic and excitatory signaling pathways. Metagenomic analysis did not detect sustained *L. reuteri* colonization in probiotic-treated animals, suggesting that its neuroprotective effects are likely mediated through transient microbiota interactions rather than persistent gut colonization.

Conclusion: *L. reuteri* supplementation attenuated seizure severity and mitigated neuropathological alterations in chronic TLE. These neuroprotective effects were associated with modulation of the TKP pathway, regulation of glutamatergic receptor expression, and preservation of neuronal structure. These findings support microbiota-based interventions as promising adjunctive strategies for treating TLE and provide evidence that sustained probiotic colonization may not be essential for therapeutic benefit.

Keywords: Temporal lobe Epilepsy, Seizures**,** *Lactobacillus reuteri*, Gut-Brain Axis, Metagenomics

P-SSP126

Melatonin Ameliorates Neurobehavioral and Biochemical Alterations in Hippocampus in Type 2 Diabetic Male Wistar Rat Model

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Background: Type 2 diabetes (T2D) is a chronic hyperglycemic disease that accounts for about 95% of diagnosed cases worldwide. Circadian rhythms synchronize physiological functions with the daily cycle, and the SCN helps regulate peripheral organs and influences metabolism, glucose uptake, and insulin secretion. Studies have shown that oxidative stress mediated circadian dysfunction could lead to decreased cognitive ability in the hippocampus.

Purpose: The present study focused on the role of melatonin (MEL) on behavioral and daily rhythms of oxidative stress-mediated cognitive dysfunction in the hippocampus under type 2 diabetes condition.

Methods: In this study, T2D rat model with high fat diet and streptozotocin was developed using three month old (adult) male wistar rats. Melatonin (30µg/kg body weight) was administered subcutaneously at ZT11 for 11 days. Behavioral tests were performed, then rats were sacrificed at four different time points. Hippocampus was collected and used for biochemical and molecular studies.

Results: Morris water maze test demonstrated that melatonin significantly improved learning and memory, further open field test showed reduced stress in T2D+MEL rats. Daily rhythms in nitric oxide (NO) showed Phase delay and in lipid peroxidation (LPO), rhythmicity was observed. Superoxide dismutase (SOD), glutathione S tranferase (GST), and catalase showed phase restoration in T2D+MEL group. Pearson correlation analysis indicated that NO, LPO, and SOD were negatively correlated in T2D, but these correlations became positive in T2D+MEL similar to control group.

Conclusion: Melatonin administration resulted in significantly improved cognition and reduced stress. These findings suggest that melatonin has an ameliorative effect against type 2 diabetes induced oxidative damage in the hippocampus. Thus, melatonin helps in maintaining circadian, cognitive, and metabolic homeostasis due to its free radical scavenging and antioxidant properties.

Keywords: Type 2 diabetes, Circadian rhythms, Hippocampus, Melatonin

P-SSP127

Neuroimmune to Neurobehavioral shifts: Sex Specific Prefrontal Dysregulation in Chronic Sucrose Bingeing

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Background: Sugar is rewarding, addictive and destructive. Binge eating disorder (BED), the most prevalent eating disorder globally, mostly fueled by rising sugar consumption that hijacks brain reward circuit, causing neuroinflammation, metabolic dysfunction, and behavior alterations. Despite its growing burden, the molecular mechanism driving these factors remain critically unexplored.

Purpose: The major goal of this study was to investigate the sex specific underlying molecular mechanisms, specifically the neuroimmune, neurovascular and neurometabolic components of the prefrontal cortex (PFC) that underpin sucrose bingeing, compulsivity, and anxiety-like behaviour.

Methods: C57BL/6J male and female mice were divided into two groups. Controls received water and chow *ad libitum*, while the sucrose bingeing group was given 12-hour access to 10% sucrose alongside water during the dark phase for eight weeks. Sucrose consumption and dietary intake were monitored weekly. Anxietylike and compulsive behaviors were assessed via different behavioral tests, followed by biochemical and molecular analysis of harvested brain tissue.

Results: Female mice exhibited significantly greater sucrose intake than males. Chronic sucrose bingeing induced hyperglycemia in both sexes without concomitant changes in body weight. Behavioral assessments revealed heightened anxiety-like and compulsive-like phenotypes in both sexes. Dopaminergic neurotransmission and synaptic plasticity were hampered in the PFC region of the brain. Additionally, neuroinflammatory cascades were robustly activated in the PFC, accompanied by microglial expansion and phenotypic remodelling toward a reactive neuroinflammatory state.

Conclusion: In conclusion, this study shows that prolonged sugar bingeing has far-reaching consequences on the metabolism, synaptic plasticity, neuroimmune functions of the brain components of reward neurocircuitry. These neurochemical changes may underlie the refined sugar driven decision deficits, bingeing, compulsivity and anxiety-like behavior. The sex-specific neuroimmune, and metabolic patterns observed in the PFC of sucrose-binged male and female mice may contribute to elucidate the mechanism behind the behavioral alterations and also developing brain-targeted precision therapeutics for binge-like eating disorders.

Keywords: Sucrose Bingeing, Anxiety, Compulsivity, Neuroinflammation, Sex Differences

P-SSP128

GLP-1R–HCRTR2 Crosstalk in Gut Dysbiosis Drives Metabolic and Circadian Disruption Leading to Cognitive Impairment

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Background:The gut–brain axis plays a central role in regulating metabolic, neuroendocrine, and circadian homeostasis. Emerging evidence suggests that gut dysbiosis contributes to metabolic dysfunction and neurodegenerative risk. However, the mechanisms linking gut microbial imbalance to impaired glymphatic clearance remain poorly understood. Given the established roles of glucagon-like peptide-1 receptor (GLP-1R) and orexin receptor-2 (HCRTR2) in metabolic regulation, arousal, and circadian rhythm maintenance, we investigated whether disruption of GLP-1R–HCRTR2 signalling contributes to glymphatic dysfunction under conditions of gut dysbiosis.

Purpose: To find out the role of GLP-1R–HCRTR2 Crosstalk leading to Neuronal disturbances caused by Gut Dysbiosis.

Methods: Insilico network analysis and docking was performed to establish link between GLP1R–HCRTR2 receptors and their downstreaming signalling. Gut dysbiosis was induced in Wistar rats using an antibiotic-mediated microbiota depletion protocol. Metabolic and neuroendocrine alterations were evaluated through biochemical and molecular analyses. Expression of circadian clock genes was assessed to determine circadian rhythm disruption. Glymphatic function was evaluated by analysing aquaporin-4 (AQP4) expression and localisation, alongside assessment of brain clearance-associated markers. Correlation analyses were performed to explore relationships among metabolic dysfunction, circadian disruption, and glymphatic impairment.

Results: Gut dysbiosis produced significant metabolic and neuroendocrine disturbances characterised by impaired insulin signalling, elevated inflammatory mediators, and disruption of appetite- and arousal-associated pathways. Molecular analyses demonstrated marked dysregulation of Cry1 and Cry2 expression, indicating circadian desynchronization. Glymphatic dysfunction was evidenced by altered AQP4 expression and localisation, accompanied by reduced clearance-associated function and increased neuroinflammatory burden. Furthermore, significant associations were observed between metabolic impairment, circadian dysregulation, and glymphatic dysfunction, suggesting an integrated pathological mechanism linking gut microbial imbalance to impaired brain homeostasis.

Conclusions: The results identify GLP-1R–HCRTR2 signalling as a potential mechanistic link between gut-derived metabolic disruption and impaired brain clearance pathways.

Keywords: Gut dysbiosis, GLP-1R, HCRTR2, glymphatic clearance, circadian rhythm, aquaporin-4, neuroinflammation, gut–brain axis

P-SSP129

Beyond Immunity: Complement Shapes Behavioural Recovery After Stress

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Background: The complement system is well recognised for its role in innate immunity. Recently, it has also been associated with several non-canonical roles, such as regulation of neurodevelopment, synaptic pruning, brain homeostasis, and behavioural modulation. However, how various complement components influence stress-responsive neural and behavioural states remains poorly understood.

Purpose: In this study, we investigate the role of complement factor C5 in regulating behavioural recovery from stress in zebrafish larvae.

Methods: We assessed recovery after 5 minutes of air-exposure stress in wild-type and C5 mutant larvae. Next, we examined the role of the Hypothalamus-Pituitary-Interrenal (HPI) axis by analysing stress-related neuro-endocrine markers and differences in neuronal activity in the brains of wildtype and mutant larvae.

Results: C5 mutant larvae exhibited delayed recovery from acute stress compared with wild-type siblings. In contrast, behavioural assays like thigmotaxis, light-dark preference and light-dark transition assays showed no robust differences among the mutants and the wild-type larvae at basal conditions, suggesting that the loss of C5 doesn't broadly impact behaviour under unstressed conditions. The neuroendocrine marker, *pomc,* showed elevated expression during the recovery phase in the mutants.

Conclusion: These findings suggest that C5 may not regulate behavioural responses/tendencies at basal conditions but may contribute to the regulation of the stress response following acute stress. Current experiments focus on understanding the role of complement factors in modulating the stress response and neurodevelopment in zebrafish larvae.

Keywords: Stress, Complement factors, neuro-endocrine, HPI-axis, zebrafish

P-SSP130

Distinct Effects of Dopamine D1 and D2 Receptors on Synaptic Transmission and Plasticity in the Spinal Superficial Dorsal Horn neurons.

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Background: The spinal cord dorsal horn is important for the processing and modulation of nociceptive information. Dorsal horn neurons receive sensory inputs from dorsal root ganglion (DRG) neurons and relay this information to the brain. Recent studies suggest that disrupted dopaminergic signaling in the central nervous system contributes to pain processing and the transition from acute to chronic pain. Thus, understanding the role of dopamine receptor subtypes in the dorsal horn may provide insights into mechanisms underlying pain modulation.

Purpose: Dopamine is an important neuromodulator, acts through D1-like (D1, D5) and D2-like (D2, D3, D4) receptors, which may differentially regulate neuronal excitability and synaptic transmission. Here we studied the role of dopamine receptor subtypes in regulating synaptic activity and synaptic plasticity in superficial dorsal horn neurons (lamina I/II).

Methods: Whole-cell patch-clamp recordings were performed from dorsal horn neurons. The effects of dopamine (10 μM), the D1-like receptor agonist SKF38393 (10 μM), and the D2-like receptor agonist ropinirole (10 μM) were examined on spontaneous excitatory and inhibitory postsynaptic currents (sEPSCs and sIPSCs). The effects of SKF38393 and ropinirole on longterm depression (LTD) were also evaluated.

Results: Dopamine (10 μM) significantly increased the interevent interval of both sEPSCs and sIPSCs without altering their amplitudes, indicating a presynaptic inhibitory effect. Next, we study the effect of D1-like and D2-like receptors with SKF38393 (10 μM) and ropinirole (10 μM) in dorsal horn neurons. Activating D1-like receptors with SKF38393 increased the sEPSC inter event interval but no change in the amplitude, also, it increased the sIPSC amplitude, producing an overall inhibitory effect. Ropinirole, increased sEPSC inter event interval without affecting sEPSC amplitude or sIPSC frequency and amplitude. We studied the effect of SKF38393 and ropinirole on synaptic plasticity in dorsal horn, where SKF38393 (10 μM) and ropinirole (10 μM) significantly reduced the LTD compared with control.

Conclusion: These findings demonstrate that D1- and D2-like dopamine receptors modulate synaptic transmission and plasticity in superficial dorsal horn neurons, highlighting a potential role for dopaminergic signalling in spinal pain modulation.

P-SSP131

Combined Gene therapy/Stem Cell transplantation to improve functional recovery following spinal cord injury

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Background: Spinal cord injury (SCI) is a severe neurological condition that causes permanent functional impairment, largely because the central nervous system has limited regenerative capacity. While pro-regenerative transcription factors (TFs) can stimulate intrinsic repair pathways, their use as a standalone therapy has not resulted in substantial functional restoration. Similarly, transplantation of embryonic or human induced pluripotent stem cell-derived neural progenitor cells (hiPSC-NPCs) has produced only limited behavioural recovery. These challenges emphasize the need for combined therapeutic approaches that simultaneously enhance neuronal regenerative capacity and overcome the inhibitory environment of the injured spinal cord.

Purpose: This study aims to investigate a combinatorial repair strategy for SCI by integrating TF-based gene therapy with hiPSC-derived NPC transplantation at the site of injury. This approach is designed to promote intrinsic growth capacity, support lesion bridging, and facilitate neural circuit reconstruction in injured neurons. In particular, we will assess the therapeutic efficacy of two newly identified pro-regenerative transcription factors NR2F1 and NR2F6 when combined with NPC transplantation in murine models of Spinal Cord Injury.

Methods: A standardized workflow was developed for the generation, characterization, and validation of hiPSC-derived NPCs. The cells were characterized using immunocytochemistry and bulk RNA sequencing. Following transplantation into a mouse model of SCI, graft survival was evaluated using histological analysis, and functional recovery was assessed through behavioural testing. To further define the mechanisms contributing to recovery, host–graft interactions was examined using immunohistochemistry. In parallel, single-nucleus RNA sequencing and spatial transcriptomics is used to identify key cell populations and molecular pathways involved in graft integration, circuit remodelling, and tissue repair.

Results: Histological assessment confirmed the survival of transplanted hiPSC-derived NPCs within the injured spinal cord. Behavioural testing showed improved functional outcomes in mice receiving NPC transplantation alone, as well as in those receiving the combinatorial treatment, compared with injured control animals. In addition, NR2F1 and NR2F6 were identified as novel transcription factors that strongly promote axonal regeneration, providing a promising basis for their use in combination with NPC-based therapies.

Conclusion: Together, these findings support the potential of hiPSC-derived NPC transplantation as a therapeutic strategy for SCI and suggest that combining NPCs with pro-regenerative transcription factors may further enhance repair and functional recovery. By integrating cell therapy with gene therapy and validating outcomes through behavioural analysis and advanced molecular profiling, this study aims to uncover mechanisms of host–graft communication and circuit reorganization after injury. The insights gained may help identify critical regulators of regeneration and inform the development of specialized, clinically relevant cell-based therapies for spinal cord repair.

Keywords: Axonal regeneration, NPC transplantation, circuit reorganisation, host-graft interaction, corticospinal tract, functional recovery

P-SSP132

Mapping the Proteomic and Metabolic Landscape of Transcription Factor-Driven CNS Axon Regeneration

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Background: Axon regeneration in the adult Central Nervous System (CNS) is severely limited following injury. This is in contrast to robust regenerative capacity observed during embryonic ages. This developmental decline is driven in-part by the progressive silencing of pro-regenerative gene programs during maturation. Recently we discovered Nuclear Receptor Transcription Factors (NRTFs) specifically NR2F1 and NR2F6 as pro-regenerative factors, whose overexpression promotes Cortico-Spinal Tract (CST) axon regeneration and improved locomotor recovery following Spinal Cord injury. Preliminary data suggests metabolic underpinnings to this observed regenerative phenotype and yet very little is known in this context.

Purpose: This study aims to map the molecular landscape across multiple regulatory layers – Proteome and Metabolome to mechanistically dissect specific molecular details regarding NRTF-mediated metabolic reprogramming that drives successful axon regeneration in the adult CNS.

Methods: Towards this goal, we have taken an integrative multi-omics approach combining quantitative proteomics and metabolomics. GFP-positive FACS-sorted CST neuronal populations overexpressing NR2F1 or NR2F6 are compared against appropriate controls using untargeted LC-MS/MS-based proteomics and metabolomics.

Results: Preliminary data reveal a consistent pattern of metabolic pathway remodelling in NRTF-overexpressing neurons, including alterations in mitochondrial energy metabolism and amino acid biosynthesis pathways. Importantly, proteomic profiling demonstrates that a subset of metabolic enzymes is translationally maintained despite transcriptional repression at the mRNA level, underscoring the biological significance of post-transcriptional regulatory mechanisms in shaping the pro-regenerative metabolic phenotype. Validation experiments are currently underway to confirm key candidate targets and delineate causal metabolic dependencies.

Conclusion: Our findings establish metabolic reprogramming as a functionally critical and translationally regulated axis downstream of NRTF activation in adult CNS neurons. By systematically mapping the proteomic and metabolomic consequences of NR2F1/NR2F6 overexpression, this study provides a foundation for identifying novel metabolism-based therapeutic targets to enhance neuronal repair after CNS injury.

Keywords: Axon regeneration, Spinal cord injury, Central Nervous System, Nuclear Receptor Transcription Factors, Proteomics, Metabolomics.

P-SSP133

Targeting Focal Adhesion Kinase: A Novel Therapeutic Strategy for Treatment of Frostbite-Induced Chronic Pain

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Background and Purpose: Frostbite-associated pain is a debilitating consequence of cold injury characterized by persistent hypersensitivity and ongoing pain, with limited mechanism-based therapeutic options. Focal adhesion kinase (FAK) is an important regulator of inflammatory signaling and neuroimmune responses. The present study investigated the effects of Defactinib (DFT), a selective FAK inhibitor, in experimental frostbite-associated pain using integrated *in vitro* and *in vivo* approaches.

Methods: *In vitro* studies evaluated cell viability, oxidative stress, and inflammatory signaling following LPS stimulation. *In vivo*, frostbite injury was induced in rats followed by treatment with DFT (5, 10, and 20 mg/kg, i.p.) or Ibuprofen (100 mg/kg, i.p.). Mechanical, thermal, and cold hypersensitivity together with spontaneous pain-related behaviour (CPP) were assessed. Molecular and protein analyses were performed in the sciatic nerve, dorsal root ganglia (DRG), and spinal cord.

Results: DFT was associated with lower ROS levels, improved cell viability, and modulation of NF-κB-associated inflammatory signaling *in vitro*. *In vivo*, DFT reduced mechanical, thermal, and cold hypersensitivity, along with spontaneous pain-related behaviour, without detectable locomotor or motor impairment. These behavioural effects were accompanied by reduced FAK phosphorylation and modulation of inflammatory and nociceptive signaling within the DRG and spinal cord, including attenuation of phosphorylated NF-κB, pro-IL-1β, and IL-1β expression. In parallel, DFT was associated with lower IBA1 immunoreactivity within the ipsilateral spinal dorsal horn.

Conclusion: The findings support the involvement of FAK-associated neuroinflammatory signaling in frostbite-associated pain and identify FAK inhibition as a potential non-opioid therapeutic strategy for persistent cold injury-associated pain states.

Keywords: Frostbite-induced pain, Focal adhesion kinase (FAK), Defactinib, Pain Behaviour, Neuroinflammation.

P-SSP134

Activation of μ–δ Opioid Receptor Heteromers Improves Neuronal Integrity and Attenuates Diabetic Neuropathic Pain

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Background: Diabetic neuropathic pain (DNP) is a debilitating complication of diabetes with limited therapeutic options due to inadequate efficacy and dose-limiting central adverse effects. Although μ–δ opioid receptor heteromers have emerged as novel targets for pain modulation, their therapeutic potential in diabetic neuropathy remains poorly understood.

Purpose: This study investigated the neuroprotective and analgesic effects of CYM51010, a μ–δ opioid receptor heteromer-biased agonist, under hyperglycaemic conditions and in an experimental model of diabetic neuropathic pain.

Methods: Neuroprotective activity was evaluated in SH-SY5Y neuronal cells exposed to hyperglycaemic stress by assessing cell viability and neurite outgrowth. Analgesic efficacy was investigated in streptozotocin-induced diabetic mice using behavioral assessments of mechanical, thermal, cold, and spontaneous pain. Molecular and biochemical analyses were performed in the dorsal root ganglia and spinal cord to evaluate nociceptive, excitatory, and inflammatory markers.

Results: CYM51010 preserved neuronal viability and restored neurite outgrowth under hyperglycaemic stress. In diabetic mice, it significantly reduced mechanical, thermal, cold, and spontaneous pain without causing motor impairment or central nervous system toxicity. Treatment also suppressed diabetes-induced upregulation of TRPV1, TRPA1, NMDAR2B, and pro-inflammatory mediators in the dorsal root ganglia and spinal cord, indicating attenuation of neuroinflammation and central sensitization.

Conclusion and Implications: CYM51010 provides neuroprotection and effectively alleviates diabetic neuropathic pain by modulating μ–δ opioid receptor heteromer signaling and reducing nociceptive and inflammatory pathways. These findings identify μ–δ heteromer-biased agonism as a promising therapeutic strategy for diabetic neuropathy, with the potential to improve safety and reduce central adverse effects.

Keywords: Diabetic neuropathic pain; μ–δ opioid receptor heteromers; CYM51010; neuroprotection; neuroinflammation; central sensitization; TRPV1; TRPA1.

P-SSP135

Interplay Between Chemical and Electrical Synapses in Touch Circuit Function and Recovery After Neuronal Injury

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Background/Context: Neurite repair requires more than anatomical regrowth. A regenerated neurite must reconnect with the appropriate postsynaptic partners to restore functional information flow. This challenge is particularly important for neurons that communicate through both chemical and electrical synapses, because defective reformation of either pathway may disrupt circuit output and behaviour. So, how these two synaptic modalities are coordinated during regeneration remains poorly understood.

Purpose: This study investigates how chemical and electrical synapses made by the *Caenorhabditis elegans'* mechanosensory neuron-PLM with AVA(chemical) and PVC(electrical) interneurons contribute to posterior gentle touch behaviour and how these connections are affected by axonal injury and regeneration.

Methods: Red-shifted Channelrhodopsin (Chrimson) was expressed specifically in PLM to enable optical stimulation, while GCaMP was expressed in the postsynaptic interneurons PVC and AVA to monitor synapse-specific activity. Genetic perturbation of glutamate-gated chloride channels (AVR-14, GLC-4), glutamate transporter (EAT-4), and gap-junction components (INX-1, UNC-9, and UNC-7) was combined with calcium imaging, optogenetic behavioural assays, and analysis of different PLM regeneration outcomes, including distal axon fusion and ventral targeting.

Results: PLM stimulation activated PVC through a gap-junction-mediated electrical synapse requiring INX-1, UNC-9, and UNC-7, and inhibited AVA through a glutamatergic chemical synapse requiring AVR-14 and GLC-4. The two pathways contributed additively to posterior gentle-touch responses, chemical synapse acting as stop reversal and gap junction as accelerator for forward movement. Axotomy near the PLM cell body disrupted both synaptic outputs, whereas fusion of the regenerating proximal axon with the distal fragment restored their activity. In contrast, ventral targeting produced hyperactive PLM–PVC and PLM–AVA responses. Although AVR-14-dependent chemical signalling was dispensable for PLM–PVC communication before injury, it became necessary for its re-establishment during regeneration.

Conclusion: Functional recovery depends not only on axon extension but also on accurate restoration of synaptic identity and partner specificity. These findings indicate that chemical and electrical synapses that function independently in the intact circuit can become interdependent during repair.

Keywords: Synapses, Neural circuits, optogenetics, neurite regeneration, behaviour recovery

P-SSP136

VPS13C Depletion Disrupts Mitochondrial Homeostasis in Experimental Models of Parkinson's Disease

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Background: Parkinson's disease (PD) is characterized by progressive degeneration of dopaminergic neurons, with mitochondrial dysfunction recognized as a major contributor to disease pathogenesis. Vacuolar protein sorting 13 homolog C (VPS13C), a lipid transfer protein localized at organelle contact sites, has been genetically linked to autosomal recessive PD. However, its association with mitochondria and its role in maintaining mitochondrial integrity remain poorly understood.

Purpose: This study aimed to characterize the mitochondrial association of VPS13C, evaluate its role in maintaining mitochondrial homeostasis, and determine how its expression is altered in experimental models of PD.

Methods: Mitochondrial localization of VPS13C was examined in retinoic acid-differentiated SH-SY5Y cells using immunofluorescence microscopy, subcellular fractionation, and western blotting. The functional role of VPS13C was investigated through siRNA-mediated knockdown and assessment of mitochondrial morphology and reactive oxygen species (ROS) generation. To investigate the impact of Parkinsonian stress on VPS13C expression, chronic rotenone paradigms were established in differentiated SH-SY5Y cells (0.5µM, 24h-7days) and Sprague- Dawley (SD) rats (2 mg/kg, subcutaneous injection for 18 days), followed by western blot analysis.

Results: VPS13C exhibited extensive co-localization with mitochondria in differentiated SH-SY5Y cells. Its presence within mitochondrial fractions was also confirmed by western blotting. VPS13C knockdown resulted in pronounced mitochondrial fragmentation and significantly elevated ROS levels, indicating impaired mitochondrial homeostasis. In cellular model, chronic rotenone exposure produced a progressive reduction in VPS13C protein expression. Consistent with the cellular findings, western blot analysis of ventral midbrain tissue from chronic rotenone-treated SD rats revealed a significant reduction in VPS13C protein levels.

Conclusion: The findings identify VPS13C as a mitochondria-associated protein essential for maintaining mitochondrial integrity and redox balance. Its depletion under Parkinsonian stress suggests a potential role in mitochondrial pathology and neurodegeneration, highlighting VPS13C as a promising target for understanding PD pathogenesis and developing therapeutic interventions.

Keywords: Parkinson's disease, VPS13C, mitochondria, rotenone, oxidative stress, neurodegeneration

P-SSP137

Adrenergic neuromodulation of hippocampal pyramidal neuron intrinsic excitability

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Background: Adrenergic neurotransmission plays an essential role in cognitive function by fine- tuning the excitability pattern of principal pyramidal neurons of the brain. Adrenergic agonists enhance the excitability of neurons by downregulating slow afterhyperpolarization (sAHP) through protein kinase A (PKA) activation.

Purpose: The downstream molecular target linking PKA to sAHP suppression remains unidentified. sAHP current arises from synergistic activation of Cav1.3 L-type and IKCa channels. Recent studies reported the key role of Rad, an RGK GTPase, in adrenergic modulation of L-type channels in the heart via PKA. We intended to study whether Rem2, the neuronal isoform, mediates adrenergic regulation of sAHP in the hippocampus, and establish a molecular link between PKA and sAHP.

Methods: Quantitative Q-PCR and western blot were done to estimate mRNA and protein levels of Rem2, respectively, after adrenergic treatment. FRET, acceptor-photobleaching, pulldown assay, FLIM-FRET, d-STORM, and SIM2 imaging were used to study the interaction and nanoscale association between IKCa, Cav1.3, and Rem2 in HEK293T cells and cultured neurons in vitro and rat hippocampus ex vivo. TIRF imaging and electrophysiological studies were done to identify functional relevance.

Results: The study showed that adrenergic treatment significantly increased Rem2 mRNA and protein expression in the hippocampus. Rem2, IKCa, and Cav1.3 were found to be localized with each other at nanoscale precision. Rem2 was found to interact with both IKCa and Cav1.3 channels. Notably, Rem2 was found to functionally reduce the surface expression and current density of IKCa, which is not reported before. Moreover, PKA stimulation differentially regulated the association pattern of Rem2 with IKCa and Cav1.3 channels and their functional activation patterns.

Conclusion: Adrenergic neurotransmission engages Rem2 to differentially regulate the association and functional activity of Cav1.3 and IKCa channels in a PKA-dependent manner, thereby inhibiting the intrinsic inhibitory sAHP and potentiating neuronal firing.

Keywords: Adrenergic neurotransmission, slow afterhyperpolarization, hippocampal pyramidal neurons, Rem2 GTPase.

P-SSP138

Integrated Single-Cell and Spatial Transcriptomics Reveal Cell Types and Regional Cellular Architecture of Human Foetal Brainstem

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Background: The developing human brainstem exhibits cellular and regional heterogeneity that remains incompletely characterized. Integrating histology, anatomical annotation, immunohistochemistry, single-cell RNA sequencing (scRNA-seq), and spatial transcriptomics provides a framework for resolving cellular identities and their spatial organization during human neurodevelopment.

Purpose: To identify cellular populations, region-specific molecular markers, and their spatial localization within the 23 GW human foetal brainstem through a multimodal integration pipeline combining histological, molecular, and spatial datasets.

Methods: High-resolution histology, scRNA-seq, and spatial transcriptomic datasets from a 23 GW human foetal brainstem were integrated using a unified computational workflow. Histological sections delineated cytoarchitectural boundaries and generated anatomical annotations. Single-cell data underwent quality control, normalization, clustering, and cell-type annotation, while spatial transcriptomic data were processed for clustering and marker identification. Reference-based cell-type deconvolution enabled the spatial localization of transcriptionally defined cellular populations within annotated brainstem regions. Immunohistochemistry validated selected molecular signatures and regional expression patterns.

Results: Analysis of ~4,000 single cells identified neuronal, glial, progenitor, and vascular populations within the developing brainstem. Spatial transcriptomic data mapped these populations to anatomically defined regions and revealed region-specific molecular signatures. Developmental transcription factors, including ETV1, POU4F1, ZIC1, and IRX2, exhibited spatially restricted expression patterns within brainstem domains. Additional enriched genes, including KCNQ5, CFAP299, DCX, and PEG10, highlight molecular heterogeneity and neurodevelopmental processes. Cell-type deconvolution resolved the spatial organization of major cellular populations and identified localized gene-expression programs associated with developmental niches. Immunohistochemical validation supported the regional specificity of selected markers.

Conclusion: The integration of multimodal cellular and molecular datasets provides a robust framework for characterizing the cytoarchitecture and molecular composition of the developing human brainstem. This multimodal pipeline provides a framework for investigating tissue architecture, cellular heterogeneity, and regional specialization during human development.

Keywords: Human foetal brainstem, Single-cell RNA sequencing, Spatial transcriptomics, Neurodevelopment

P-SSP139

Dimethyl Malonate confers Neuroprotection by Alleviating Mitochondrial Dysfunction and Oxidative Stress in Ischemic Reperfusion Injury

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Background: Dimethyl malonate (DMM), a derivative of malonic acid is a competitive inhibitor of Succinate dehydrogenase (SD), a key enzyme involved in producing reactive oxygen species (ROS). Excessive expression of this enzyme is responsible for mitochondrial dysfunction. Cerebral ischemic stroke leads to mitochondrial damage. Excessive oxidative stress and imbalance in bioenergetics in ischemic core lead to mitochondrial dysfunction. Hence, we explored the neuroprotective effects of DMM against ischemic reperfusion injury in rats.

Purpose: To investigate neuroprotective effects of DMM against mitochondrial dysfunction in ischemic neurons associated with ischemic reperfusion (I/R) injury.

Methods: Adult Wistar rats (200-250g) were subjected to stereotaxic surgery prior to middle cerebral artery occlusion (MCAO) for Intracerebroventricular drug administration. Rats were treated with DMM at different concentrations (1, 10 and 100 µg) for 7 consecutive days post ischemic insult. Neurobehavioral assessments were assessed using modified neurological severity score (mNSS), open field test (OFT), beam walk test and rota rod test followed by TTC staining. Further, biochemical estimations were performed using ROS Assay, malondialdehyde (MDA) assay, catalase assay and lactate dehydrogenase (LDH) Assay. Also, expression of cytochrome c and mitochondrial ferritin (FTMT) were assessed using Immunohistochemistry.

Results: Present study illustrated chronic effect of DMM on I/R injured rat. DMM (10 µg, i.c.v., 7 days) augmented functional recovery as evaluated by mNSS, rota rod test, OFT and beam walk test. DMM reduced infarction volume, ROS, MDA and LDH expression and elevated catalase levels. DMM also increased the expression of (FTMT) while decreased the expression of cytochrome c suggestive of mitochondrial protection post ischemic injury.

Conclusion: This study, depicts the neuroprotective role of DMM in I/R injury by attenuating oxidative stress and mitochondrial dysfunction. The prevention of mitochondrial damage significantly restricts penumbral progression and promote functional recovery. DMM may be proposed as an adjuvant drug in management of cerebral I/R injury.

Keywords: Succinate Dehydrogenase, DMM, FTMT, Mitochondria, Stroke

P-SSP140

Role of KIF2A/ KLP-7 in regulating microtubule dynamics in adult neurite

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Background: One of the important factors regulating neuron development and maintenance is its microtubule cytoskeleton. Previous studies on c. elegans and other organisms have shown that kinesin-13 family microtubule depolymerizing protein KIF2A/ KLP-7 regulates microtubule dynamics and polarity in neurons and thus help decide axonal and dendritic compartment of neuron. But within neurons, where, when and how exactly KLP-7 acts as an active depolymerizer is not clear.

Purpose: This study aims to study the role of KIF2A/ KLP-7 in maintenance of microtubule dynamics and organization post-development of neuron.

Methods: In-vivo imaging of splitGFP::TBA-1 (α-tubulin) reporter expressed from the endogenous locus was used to visualize microtubule dynamics within PVD neuron of c. elegans. To study role of KLP-7 in mature neurons, temperature-sensitive KLP-7 mutant worms were raised at permissive temperature and shifted to 26 degree at L4 stage post PVD-development.

Results: We have studied growth and catastrophe phases of microtubules both distally and proximal to cell body. It was found KLP-7 loss increases microtubule rescues throughout the long PVD neuron dendrite. This chronic KLP-7 loss also increased dynamic microtubules and growth speeds. On the other hand, catastrophe speeds are reduced. Thus, we checked whether KLP-7 is an active depolymerizer in matured neuron using a temperature-sensitive mutant. We have preliminary data which shows that KLP-7 degradation post-PVD development leads to slower microtubule growth and rescues show an increasing trend. Further we studied whether KLP-7 depolymerizes microtubules rescued by CRMP/UNC-33.

Conclusion: In contrast to KLP-7 chronic loss-of-function mutant, short term degradation shows immediate effect on microtubule dynamics without any compensatory homeostatic regulation. Hence this study shows that KLP-7 is an active depolymerizer in adult neuron as it does affect microtubule dynamics and organization post-PVD development.

Keywords: *C. elegans*, PVD neuron, microtubule, dynamics, kinesin-13, CRMP

P-SSP141

USP7-mediated stabilization of Praja1 ubiquitin ligase regulates chromatin states and neuronal differentiation

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Background: Praja1 (PJA1) is highly enriched in the brain, particularly in neurons where it functions as a protein quality control ubiquitin ligase. PJA1 has been associated with neurodegeneration, neurodevelopment disorders, and neuronal progenitor cell development, suggesting an essential role in brain development and maintenance. However, its interactome and the molecular mechanisms underlying its function in neuronal cell remain largely unknown.

Purpose: This study aimed to identify the interactome of PJA1 in neuronal cells and to investigate the molecular mechanisms by which it maintains neuronal homeostasis and cell fate.

Method: PJA1 regulation was investigated using AP-MS, co-immunoprecipitation, protein stability and ubiquitination assays. RNA interference and pharmacological inhibition studies were done in Neuro-2a and SH-SY5Y neuronal cells. Differential proteomic analysis of PJA1 depleted neuronal cells were done to identify associated pathways. Chromatin associated changes were assessed by biochemical fractionation and histone modifications while neuronal differentiation was studied through β-III Tubulin immunofluorescence.

Results: Interactome analysis identified the deubiquitinase USP7 and multiple histone-associated proteins as PJA1 interactors. Biochemical analysis revealed that USP7 stabilizes PJA1 through deubiquitination, thereby preventing its proteasomal degradation. Loss of USP7-mediated PJA1 stabilization reduced PJA1 chromatin association, altered the active chromatin marks H3K27ac and H3K4me3, and promoted neuronal differentiation. In contrast, PJA1 stabilization increased these active chromatin marks while restoration of the USP7–PJA1 axis rescued these phenotypes. Consistently, proteomic analysis of PJA1 depleted neuronal cells identified reduced level of several chromatin-associated proteins, including UHRF1, YY1 and histones H1 and H4, supporting a role for the USP7-PJA1 axis in neuronal cell fate.

Conclusion; This study identifies USP7-mediated stabilization of PJA1 as an upstream mechanism regulating chromatin states and neuronal cell fate. The USP7-PJA1 axis links ubiquitin-dependent proteostasis to epigenetic regulation, determining neuronal cell fate.

Keywords: PJA1, USP7, ubiquitin ligase, deubiquitination, chromatin regulation, neuronal differentiation

P-SSP142

Chronic Metformin Treatment Attenuates Ferroptosis and Confers Neuroprotection in Type 2 Diabetes-Associated Cerebral Ischemia-Reperfusion Injury

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Background: Diabetes mellitus is an independent risk factor for ischemic stroke (IS) and exacerbates ischemia/reperfusion (I/R) injury by promoting oxidative stress, iron dyshomeostasis, lipid peroxidation, and ferroptosis, ultimately leading to poor neurological outcomes. Although, chronic metformin therapy has demonstrated neuroprotective effects in IS models, its efficacy in diabetes-associated cerebral I/R as well as protective mechanism remains largely unexplored.

Purpose: To investigate the interrelationship of ferroptosis with the neuroprotective effect of chronic metformin in a type 2 diabetic rat with ischemic reperfusion injury.

Methods: Adult male Wistar rats (200-250g) were randomly assigned to control, MCAO, MCAO+Metformin, MCAO+Metformin+Ferrostatin-1, MCAO+Ferrostatin-1, Diabetic+MCAO, and Diabetic+MCAO+Metformin groups. Type 2 diabetes mellitus was induced by feeding rats with a high-fat diet for 2 weeks followed by a single intraperitoneal (*i.p.*) injection of streptozotocin (35 mg/kg). Diabetes was confirmed by measuring fasting blood glucose and body weight. Animals were subjected to MCAO and given chronic metformin treatment (200 mg/kg/day, *i.p.*) for seven days after diabetes induction. Neurological deficits and behavioral assessments were performed after 24 hours. Brain tissues were analyzed for infarct size by TTC staining, iron accumulation by Perls staining, oxidative stress parameters, and the expression of the ferroptosis-related markers FTH1, GPX4, NRF2 and SLC7A11 via immunohistochemistry analysis.

Results: Metformin improved neurological deficit score, beam walk, adhesive tape removal, sensory motor getting behaviour and hanging wire score, reduced cerebral infarct size as compared to control diabetic MCAO rats. Metformin also significantly reduced iron accumulation, oxidative stress, and lipid peroxidation, while restored the expression of FTH1, GPX4, NRF2 and SLC7A11.

Conclusion: This study demonstrates that chronic metformin therapy attenuates ferroptotic markers associated with neuroprotection in the diabetic ischemic reperfusion injured rats. Decreased iron load along with secondary neuroprotection may help to prevent the progression of ischemic pathology in diabetic patients co-morbid with ischemic stroke.

Keywords: Ischemia reperfusion injury; Type 2 diabetes mellitus; Metformin; MCAO; Ferroptosis

P-SSP143

PATZ1 Reorganizes the Nucleosome Landscape to Promote Chromatin Accessibility in Injured Neurons

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Background: Adult Central Nervous System neurons have a limited ability to regenerate after injury, in part because mature neurons remain in a restrictive chromatin state. Transcription factor PATZ1 reopens growth-associated chromatin regions in injured Corticospinal Tract (CST) neurons in a targeted manner but how this is achieved at the level of nucleosome organization remains unclear.

Purpose: We tested whether PATZ1 alters nucleosome occupancy, and positioning at growth-associated genes and regulatory elements in injured Corticospinal neurons, and whether these changes can be supported by independent chromatin profiling approaches.

Methods: We analysed single-nucleus Assay for Transposase-Accessible Chromatin using sequencing (snATAC-seq) datasets from Corticospinal tract neurons isolated from injured mice treated with PATZ1. Nucleo ATAC was used to infer genome-wide nucleosome occupancy and nucleosome positioning fuzziness, which were integrated with chromatin accessibility, enhancer activity, and gene expression changes. To further examine PATZ1-associated changes in chromatin accessibility and histone occupancy, Bulk Assay for Transposase-Accessible Chromatin using sequencing (bulk ATAC-seq) and Histone H3 Cleavage Under Targets and Release Using Nuclease (CUT&RUN) experiments were performed in Neuro2a cells and PATZ1-expressing neuronal tissue.

Results: Spinal cord injury alone produced little change in nucleosome occupancy or positioning precision, consistent with the weak intrinsic chromatin response of adult corticospinal neurons to injury. In contrast, PATZ1 was associated with a marked reduction in inferred nucleosome occupancy and fuzziness, particularly at differentially accessible regions, regeneration-associated gene loci, and distal regulatory elements. These changes coincided with expansion of histone H3 lysine 27 acetylation (H3K27ac)-marked active enhancers, suggesting that PATZ1 promotes a more permissive regulatory landscape. Ongoing bulk ATAC-seq and Histone H3 CUT&RUN analyses are being used to independently assess accessibility gains and changes in core histone occupancy at PATZ1-responsive regions.

Conclusion: PATZ1 is associated with broad reorganization of the nucleosome landscape at regulatory elements linked to neuronal regeneration. By reducing inferred nucleosome occupancy and refining nucleosome positioning at growth-associated loci, PATZ1 may help overcome epigenetic barriers that limit CNS repair. These findings point to nucleosome-level chromatin reorganization, rather than injury alone, as a key feature of PATZ1-mediated regenerative priming.

Keywords: PATZ1; axon regeneration; nucleosome organization; chromatin accessibility; CUT&RUN; bulk ATAC-seq; corticospinal neurons; spinal cord injury; enhancer activation; epigenetics

P-SSP144

Maternal Separation Alters Hippocampal Histone Acetylation in a Sex-Specific Manner

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Background: Early life stress (ELS) is one of the major risk factors for increased vulnerability to many neuropsychiatric disorders, including depression in adulthood. Stress during early development can cause long-lasting changes in brain structure and function by interacting with genetic factors and altering gene expression through epigenetic mechanisms, including histone modifications. These epigenetic changes can influence the development and functionality of the brain, potentially increasing the risk of depression during adulthood.

Purpose: Although animal studies suggest that early-life stress (ELS) induces epigenetic changes and transcriptional dysregulation, the immediate sex-specific molecular responses remain poorly understood. Identifying sex-specific epigenetic mechanisms, particularly the role of acetyltransferase in ELS, could help explain why different sexes diverge in their vulnerability towards the same stress.

Methods: In this study, we used a maternal separation model of ELS in mice. Pups of both sexes were exposed for neurobehavioral studies at PND 21 and PND 70 for their vulnerability towards stress. The hippocampus region of the brain of both sexes was studied using various microscopic and molecular techniques to identify the epigenetic signatures of ELS.

Results: Our neurobehavior studies suggest that the pups exposed to maternal separation showed differences in their anxiety-like behaviour at PND21. Interestingly, our western blot analysis revealed that the Bdnf expression and histone acetylation levels are differentially regulated in male and female pups. Collectively, our findings indicated a distinct pattern of epigenetic mechanisms, particularly histone acetylation in male and female offspring, highlighting the sex-specific molecular responses following early life stress.

Conclusion: By examining sex-specific differences in epigenetic regulation at postnatal day-21, we aim to understand how males and females respond differently to early-life stress. These findings may provide insights into the biological basis of sex-dependent vulnerability to neuropsychiatric disorders and help identify potential early intervention strategies.

Key Words: Early life stress, epigenetics, lysine acetyltransferases, histone acetylation, neuropsychiatric disorders

P-SSP145

Mechanistic Basis of RNA-Binding Protein Mis-regulation in Myotonic Dystrophy Type 1

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Background: Myotonic Dystrophy type 1 (DM1) is an autosomal dominant disorder caused by CTG repeat expansions in the 3′UTR of the DMPK gene. These expanded CUG repeat RNAs sequester the Muscleblind-like 1 (MBNL1), an RNA-binding protein (RBP) involved in the regulation of alternative splicing in both neuronal and non-neuronal tissues.

Purpose: To investigate the role of toxic RNAs and RBPs in aggregate formation and the molecular mechanisms of CUG repeat-mediated toxicity and protein sequestration using a transgenic Caenorhabditis elegans model to identify how repeat length impacts muscle and neuronal integrity and behavior.

Methods: We expressed a TagRFP reporter carrying a UTR element containing either 240 and 480 CTG repeats from the 3′UTR of the human DMPK gene in Caenorhabditis elegans. These repeat elements were expressed under both muscle and neuron-specific promoters.

Results: We observed that the cytoplasmic localization of endogenous MBL-1::GFP was reduced upon overexpression of the repeat elements, accompanied by a simultaneous decrease in TagRFP expression in cytoplasm. In contrast, nuclear MBL-1::GFP levels were increased. These observations suggest that MBL-1::GFP is sequestered in the nucleus by repeat-containing RNA transcripts. We also observed that locomotion in transgenic worms expressing CTG repeats in muscle was impaired, similar to the phenotype observed in mbl-1 loss-of-function animals.

Conclusion: This study establishes an in vivo platform for studying RNA-mediated toxicity in DM1. These findings provide a basis for screening genetic modifiers and therapeutic strategies aimed at resolving toxic aggregates and restoring muscle and neuronal functions.

Keywords: Toxic RNA aggregates, RNA-binding proteins (RBPs), Muscleblind (MBNL-1), Genetic modifiers, C. elegans

P-SSP146

Role of Oleuropein in Alleviating Parkinson's Disease Pathophysiology via Modulation of TRPC1 and TRPC3 Channels in a Rotenone-Induced Mouse Model

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Background: Parkinson's disease (PD) is characterized by progressive dopaminergic neurodegeneration driven by oxidative stress, mitochondrial dysfunction, dysregulated Ca2+homeostasis, and impaired autophagic clearance. Transient Receptor Potential Canonical (TRPC) channels, particularly TRPC1 and TRPC3, have emerged as key mediators of Ca2+dependent neurotoxicity in PD, linking oxidative stress, mitochondrial disruption, apoptosis, and autophagic dysfunction in dopaminergic neurons.

Purpose: This study aimed to evaluate the neuroprotective potential of Oleuropein (OLE), a bioactive polyphenol from olive leaves, in a rotenone-induced mouse model of PD, with a specific focus on its modulation of TRPC1 and TRPC3 expression and downstream apoptotic and autophagic signaling.

Methods: Adult Swiss Albino mice (n=5 per group) were divided into control, rotenone, OLE, and rotenone + OLE (16mg/kg) treatment groups. Rotenone was administered subcutaneously to induce parkinsonian pathology, followed by OLE treatment for 35 days. OLE pretreatment was given to both OLE-containing groups for 7 days before rotenone administration. Behavioral assessments (rotarod, pole test) were performed to evaluate motor function. Protein expression of TRPC1, TRPC3, apoptotic markers (Bax, Bcl-2, cleaved caspase-3), and autophagy markers (LC3-II/I, Beclin-1, p62) was analyzed by Western blotting in striatal/nigral tissue.

Results: Rotenone administration significantly decreased TRPC1 and increased TRPC3 expression, accompanied by elevated pro-apoptotic markers and impaired autophagic flux, alongside motor deficits. OLE co-treatment restored TRPC1 and attenuated TRPC3 expression toward control levels, reduced apoptotic marker expression, normalized autophagy -related protein levels, and improved motor performance relative to the rotenone -only group.

Conclusion: These findings suggest that oleuropein exerts neuroprotection in rotenone-induced PD pathology partly through modulation of TRPC1/TRPC3 mediated Ca+2 signaling and restoration of the balance between autophagic and apoptotic pathways. OLE may represent a promising polyphenolic candidate for further translational investigation of PD therapeutics.

Keywords: Oleuropein; Parkinson's disease; TRPC channels; Rotenone; Autophagy; Apoptosis

P-SSP147

Innate immune complement factors regulate Neurodevelopment

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Background: Neurodevelopment is a complex and highly coordinated process regulated by multiple molecular and cellular cues. There is growing evidence for a non-canonical role of the innate immune system in neurodevelopment. We recently demonstrated that innate immune complement factors play a key role in determining resilience to stress. However, the mechanism through which the complement proteins regulate neurodevelopment is poorly understood.

Purpose: To understand the role of a major complement factor in the regulation of neurodevelopment and behavior using zebrafish as a model

Methods: RNA sequencing data from a complement mutant were analyzed to identify differentially expressed genes and validated by quantitative real time PCR. To assess anxiety-like behavior, larval zebrafish were subjected to light-dark transition assay. Adult mutant zebrafish were evaluated using the Novel Tank Diving test(NTD) and Open Field test(OFT).

Results: Transcriptomic analysis revealed that genes regulating neurodevelopment were differentially expressed, which was validated by qRT-PCR. Anxiety-like behavior was assessed in both larval and adult zebrafish. Mutant larval zebrafish exhibited an increased startle response during light-dark transitions, indicative of anxiety like behavior. Adult mutants spend significantly more time in the bottom of a novel tank and increased thigmotaxis in the OFT suggesting that the anxiety-like phenotype persists into adulthood.

Conclusion: Our findings reveal a novel role for complement factors in neurodevelopment. The disruption of a major complement factor alters expression of neurodevelopment genes and is associated with anxiety-like behavior, highlighting the importance of this factor in regulating brain development.

Keywords: Neurodevelopment, Complement factors, Zebrafish, Anxiety behavior

P-SSP148

Organisational and Regulatory Principles Governing Heterochannel Electrical Synapse Function

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Background: Electrical synapses, formed by gap junction (GJ) channels, are evolutionarily conserved mediators of fast neuronal communication, essential for nervous system development and function. Despite their importance, little is known about their assembly, function, and plasticity and compared to chemical synapses. Similarly, the organisation principles of these synapses and their regulatory machineries have remained largely unknown.

Purpose: This work provides novel insights into the fundamental principles governing electrical synapse organisation, function, regulation and plasticity. It also describes the cell-biological mechanisms behind the role of stomatin family of proteins in ensuring precise GJ function.

Methods: We combined genetics, CRISPR/Cas9 mediated genome-editing, behavioral analyses, biochemistry and super-resolution and confocal microscopy in *C. elegans* to investigate these questions. Further, we used Zebrafish model to understand the conservation of these principles across metazoans.

Results: We discovered a previously uncharacterised organisational principle of electrical synapses: individual synapses comprise heterogeneous clusters of molecularly distinct GJ channels composed of different innexins, which we term Heterochannel Synapses. This Heterochannel molecular code determines synaptic function and consequently animal behaviour. We found that individual channel types within a synapse can be independently regulated. Our studies in Zebrafish further suggest that Heterochannel synapses represent a conserved feature of metazoan nervous systems. We find that GJ channels are capped by a heteromeric complex of multiple stomatin proteins. Like GJs, disrupting the combinatorial assembly of stomatins affects synapse function. Furthermore, our work uncovers hierarchical genetic relationships amongst different stomatins and identifies the cell-biological mechanisms mediating heteromeric stomatin cap assembly atop GJs.

Conclusion: Together, these findings reveal multi-level molecular heterogeneity in both electrical synapses and their regulatory machinery, fundamentally redefining how electrical synapses are assembled, gated and remodelled, and providing a new framework for understanding how synaptic diversity shapes nervous system function and behaviour.

Keywords: Electrical synapse; Gap junction; Innexin; Connexin; Stomatin; *C. elegans*

P-SSP149

Temporal and Region-Specific Changes in the Expression of Norbin, Formin 2, and GSK3α in the Hippocampus after Contextual Fear Conditioning and Post-Training Sleep Deprivation

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Background: Norbin, Formin 2, and GSK3α have been implicated in learning-associated synaptic plasticity. Norbin is an adaptor protein that interacts with GPCRs and regulates cell signaling. Formin2 is an actin-binding structural protein, and GSK3α is a protein kinase involved in diverse cellular processes, including cell survival and metabolism. We reasoned that these proteins may be associated with sleep-dependent contextual fear-conditioned (CxFC) memory consolidation.

Purpose: Here, we investigated 1) the temporal expression of Norbin, Formin 2, and GSK3α in the Dorsal Hippocampus (DH) and Ventral Hippocampus (VH) following CxFC and retrieval phases, and 2) the effects of post-training sleep deprivation (SD) on subsequent molecular responses after training and retrieval phases.

Methods: Male Swiss albino mice underwent CxFC, and independent cohorts were sacrificed at 1, 3, and 5 hr of training or retrieval. DH and VH were dissected, and protein expression was analyzed using western blotting. In another set of animals, mice were sleep-deprived for 5 hrs after CxFC training, and the effect of SD on the expression of Norbin, Formin2, and GSK3α was determined on the training and testing days.

Results: CxFC training induced a significant increase in the expression of Norbin, Formin 2, and GSK3α in a temporal and region-specific fashion. On the training day, the expression of Norbin in the DH and Formin 2 in both DH and VH significantly decreased after SD. However, GSK3α expression significantly decreased in the VH only. Interestingly, on the testing day SD selectively altered Norbin and Formin 2 expression in the DH. Nevertheless, the levels of GSK3α did not change.

Conclusion: Together, these findings demonstrate that CxFC induces region-specific upregulation of hippocampal Norbin, Formin 2, and GSK3α expression, which is subsequently disrupted by post-training SD, thereby impairing memory consolidation and recall.

Keywords: Dorsoventral Hippocampus, Norbin, Formin2, GSK3α, Contextual Fear Conditioning, Sleep Deprivation

P-SSP150

Beyond Clinical Predictors: Gut Microbiome Dysbiosis as a Determinant of Severity and Secondary Brain Injury in Aneurysmal Subarachnoid Hemorrhage

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Background: Aneurysmal subarachnoid hemorrhage (aSAH) is a devastating neurological emergency with highly variable outcomes that remain inadequately explained by conventional clinical parameters. Emerging evidence highlights the gut-brain axis as a critical regulator of neuroinflammation; however, microbiome alterations in aSAH are poorly understood.

Purpose: This study aimed to characterize gut microbiome dysbiosis in acute aSAH and identify microbial signatures associated with disease severity, delayed cerebral ischemia (DCI), and neurological outcomes.

Methods: In this prospective observational study, stool samples from patients with acute aSAH were collected and subjected to 16S rRNA gene sequencing. Microbial alpha diversity, taxonomic composition, and differentially abundant taxa were analyzed. Associations between microbiome features and clinical severity, DCI, and functional outcomes were evaluated using integrative bioinformatic and statistical modeling approaches, including predictive modeling.

Results: aSAH was associated with significant gut microbiome disruption, characterized by reduced alpha diversity and distinct compositional shifts. There was a marked depletion of commensal, anti-inflammatory taxa alongside enrichment of opportunistic pathogens. These alterations strongly correlated with disease severity and were significantly associated with the development of DCI and poor neurological outcomes. Predictive modeling identified specific microbiome signatures with strong discriminatory ability for adverse outcomes.

Conclusion: Gut microbiome dysbiosis is an early and clinically relevant feature of aSAH, closely linked to disease severity and secondary brain injury. Microbiome-derived signatures offer promising non-invasive biomarkers for risk stratification and provide mechanistic insight into gut–brain axis–mediated neuroinflammation. These findings position the gut microbiome as a novel and potentially modifiable target to improve outcomes in aSAH.

Keywords: aSAH, gut microbiome, dysbiosis, gut-brain axis, delayed cerebral ischemia, biomarkers

P-SSP151

Flexible Amperometric Enzyme-based Microelectrode for Sensitive and Selective Glutamate Detection: Toward a Sensor-Augmented Pump System for Epilepsy and Stroke

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Background: Glutamate is the predominant excitatory neurotransmitter in the mammalian central nervous system and plays diverse physiological roles in synaptic signalling, plasticity, and neurodegeneration. Irregularities in extracellular glutamate levels are implicated in a range of neuropathologies, including ischemic stroke, epilepsy, and Alzheimer's disease. Rapid, low-cost sensors capable of detecting glutamate in real time are therefore essential not only for research but also as the foundation for closed-loop, sensor augmented therapeutic systems that could track and modulate glutamate, analogous to continuous glucose monitors, for the treatment of epilepsy and stroke.

Purpose: This study was intended to develop and characterize a low-cost, miniaturized, flexible amperometric biosensor for sensitive and selective detection of glutamate, as a first step toward a sensor-augmented pump system capable of continuously tracking and locally clearing excess glutamate in conditions such as epilepsy and ischemic stroke.

Methods: A laser-engraved 200 μm aperture in a polyimide mask defined the working area of the sensor, which was functionalised with dithiobis-succinimidyl propionate (DTSP) to enable covalent attachment of Glutamate Oxidase enzyme. A thin Nafion overlayer was subsequently applied to minimize interference. FTIR spectroscopy was used to confirm amide bond formation indicating enzyme immobilization, and electrochemical impedance spectroscopy (EIS) was used to assess changes in charge transfer resistance after immobilization. Cyclic voltammetry and chronoamperometry were performed in phosphate-buffered saline (PBS) to electrochemically evaluate selective glutamate detection.

Results: FTIR spectroscopy confirmed amide bond formation, consistent with successful immobilization of Glutamate Oxidase, while EIS analysis showed an increase in charge transfer resistance following immobilization. Cyclic voltammetry and chronoamperometry demonstrated selective detection of glutamate in PBS, with a sensitivity of 3.36 nA/μM and a detection limit of 4.9 μM

Conclusion: This reproducible biosensor utilizes accessible materials to offer a scalable solution for glutamate neurotransmitter sensing. Its flexibility and chemical stability make it a promising tool for future integration into wearable or implantable systems for in vivo glutamate monitoring. Consequently, this sensing platform represents a promising building block toward a closed-loop, sensor-augmented pump system that continuously tracks and clears excess glutamate for the treatment of epilepsy and stroke. However, in vivo validation

and integration with an actuation/clearance mechanism remains necessary before clinical translation.

Keywords: Biosensor; Glutamate; Flexible sensor; Neurotransmitter; Amperometry; Closed-loop drug delivery.

P152

Epigenetic Modulation by Decitabine Attenuate Cognitive Dysfunction Post- Ischemic Insult Through Inhibition of DNMT1 and HDAC2

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Background: Cognitive and neurological impairment are the subsequent consequences of ischemic stroke. Ischemic reperfusion (I/R) insult damages the hippocampal neurons which, leads to cognitive impairment. Report suggests changes in the genes associated with synaptic plasticity owing to post stroke epigenetic manipulation, wherein, DNA methyltransferases (DNMTs) and histone deacetylases (HDACs) play a vital role. Decitabine, a novel anticancer drug exhibits DNMT1 and HDAC2 inhibitory activity.

Purpose: To investigate the epigenetic regulation involved in neuroprotective effect of decitabine (DNMT1 and HDAC2 inhibitor) post ictus I/R injury.

Methods: Adult Wistar rats (200- 250g) were subjected to middle cerebral artery occlusion (MCAO) for 90 mins followed by reperfusion. Rats were treated with decitabine after 6 hr of reperfusion for 7 consecutive days. Neurobehavioral and cognitive assessments were performed using mNSS scoring, cylinder test, adhesive tape removal test, Y-maze, novel object recognition test (NOR), followed by TTC staining and TUNEL assay. Further, mRNA level estimation of DNMT1, HDAC2, BDNF, and PSD95 were assessed. Moreover, synaptophysin and pCREB expression were estimated using Immunohistochemistry.

Results: The present study demonstrated the chronic effects of decitabine (0.25 mg/kg, i.p., O.D., 7 days) on I/R injury. Decitabine administration improved neurological severity, cylinder test, adhesive tape removal, Y- maze, and NOR score. Additionally, decitabine reduced infarct volume and TUNEL expression in MCAO I/R rats. Further, it downregulated mRNA expression of DNMT1 and HDAC2 while upregulated BDNF and PSD95 expression. Also, decitabine elevated expression of synaptophysin and pCREB.

Conclusion: Our study elucidated decitabine's role in ameliorating I/R induced neurological and cognitive impairment. The neuroprotective effect of decitabine consequent to epigenetic regulation, may promote genes and proteins involved in improving synaptic plasticity. Inhibition of DNMT1 and HDAC2 by decitabine might present a promising therapeutic strategy for post-stroke cognitive impairment and improvement of quality of life in stroke patients.

Keywords: DNMT1, HDAC2, Decitabine, Cognition, Stroke.

P153

Development and feasibility of the Indian Neurocognitive Rehabilitation App for Substance Use Disorder (INR-SUD)

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Background: Cognitive impairment is prevalent among substance use disorders (SUDs). Although game-based cognitive rehabilitation has been shown to contribute to the recovery of cognitive functions and facilitates treatment engagement in individuals with SUDs, culturally relevant mobile health (mHealth) interventions remain scarce in India.

Purpose: To develop and pilot test a free bilingual mobile application for cognitive rehabilitation in individuals SUDs, targeting attention, working memory, emotion processing, and response inhibition.

Methods: A bilingual (Hindi–English) cognitive rehabilitation application has been developed with eight gamified cognitive tasks across four cognitive domains: attention, working memory, emotion, and response inhibition. The intervention consists of 12 sessions delivered over 4 weeks (3 sessions per week), with each session lasting 20–30 minutes. Six sessions are planned to be conducted under supervision in a hospital setting, while the remaining will be completed by participants at home with remote monitoring of progress and adherence.

Results: Pilot testing of the app has been conducted in healthy controls and individuals with SUD to evaluate task usability, acceptability, feasibility, and preliminary performance outcomes, enabling refinement of the application before large-scale clinical evaluation.

Conclusion: INR-SUD provides a standardized, culturally appropriate, home-based cognitive rehabilitation platform that addresses multiple domains of cognitive dysfunction in SUD. The pilot findings support its feasibility and usability, highlighting its potential as an adjunctive treatment to promote cognitive training addressing a critical gap in Indian mHealth services for SUD.

Key words: Substance use disorder, cognitive deficits, mHealth, cognitive rehabilitation

P154

Does Retrieval Stopping Enhance Fear Extinction?

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Background: Deficits in inhibitory control over fear memory directly result in fear extinction failure.

Purpose : The present study, following the retrieval stopping model of fear extinction, aims to enhance these underlying inhibitory control mechanisms using explicit retrieval stopping instructions in extinction learning.

Methods: A three-day trace fear conditioning paradigm was employed, including four phases: Phase 1 (Day1): habituation and fear acquisition; Phase 2 (Day2): fear extinction; and Phase 3 (Day 3): Extinction recall. The outcome measures include arousal, valence, and expectancy ratings obtained across phases. Twenty-four participants were randomly recruited and divided into two groups: Standard Extinction (SE) and Standard Extinction with No Think condition (SE-NT, with explicit instructions to suppress the associated consequences).

Results: A rmANOVA with stimuli and phase as within-subject factors and group as a between-subject factor revealed significant stimulus × phase interactions for arousal ($F(3, 66) = 15.78$, $p < .001$, $\eta p^2 = .42$), valance ($F(3, 66) = 9.65$, $p < .001$, $\eta p^2 = .31$) and expectancy ($F(2, 44) = 9.75$, $p < .001$, $\eta p^2 = .35$). CS+ elicited higher arousal, negative valence, and higher expectancy ratings during the acquisition phase in both groups. Across phases, these responses decreased from the acquisition to the extinction phase and sustained till extinction recall (Day 3), indicating successful conditioning and extinction learning. Further, no significant main effects or interactions for group were observed.

Conclusion: These findings provide preliminary evidence that, unlike previous studies incorporating retrieval stopping instructions, neither hampered nor enhanced during the fear extinction.

Keywords: Fear extinction, Inhibitory control, Retrieval suppression, Differential fear conditioning

P155

Human brain-enriched extracellular matrix genes regulate cortical folding and development

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Background: Cortical expansion and folding are defining features of primate brain evolution and development that increase cortical surface area, neuronal connectivity, and functional complexity. Disruption of these processes is associated with neurodevelopmental disorders such as Lissencephaly and Epilepsy. The extracellular matrix (ECM) plays a critical role in cerebral cortex development by regulating radial glial cell (RGC) proliferation, basal progenitor (BP) amplification, and tissue biomechanics. Comparative single-cell transcriptomic studies have identified several ECM genes that are enriched in the developing human cortex, particularly within the outer subventricular zone, but their functional contribution to cortical development remains largely unknown.

Purpose: The aim of this study was to investigate the role of human brain-enriched ECM genes whose expression is regulated by LSD1, in regulating cortical progenitor dynamics, neuronal differentiation, and cortical folding. We further sought to determine whether their expression is associated with human-specific epigenetic regulatory elements.

Methods: Human brain-enriched ECM genes were identified through comparative single-cell RNA sequencing analyses and examined as potential downstream targets of LSD1/KDM1A. Their functional roles were assessed using gain-of-function studies in human cortical neural progenitor cells, where neurosphere formation and neuronal differentiation were analysed. To investigate their effects in vivo, selected ECM genes were overexpressed in the embryonic mouse cortex by in utero electroporation at embryonic day 13.5, followed by analyses of progenitor populations, cortical morphology, and ECM protein localisation. Comparative epigenomic analyses were also performed to identify human-specific enhancer signatures associated with ECM gene loci.

Results: Several human brain-enriched ECM genes were identified as downstream effectors of LSD1/KDM1A. Overexpression of selected ECM genes in human cortical neural progenitor cells increased neurosphere size, indicating enhanced progenitor proliferation. Following differentiation, these cells generated neurons with increased axonal length, enhanced dendritic arborization, and greater morphological complexity. In the mouse cortex, overexpression of selected ECM genes induced cortical fold-like structures and promoted expansion of both apical progenitors and basal radial glia-like cells expressing TBR2 and HOPX. ECM1 protein localized to the marginal zone after electroporation, resembling aspects of its distribution in the developing human cortex. Comparative epigenomic analysis further identified human-specific enhancer signatures marked by H3K4me2 and H3K27ac at loci encoding ECM and cell adhesion molecules, suggesting evolutionary changes in the regulation of ECM programmes.

Conclusion: Our findings identify a human-enriched, epigenetically regulated ECM gnes downstream of LSD1/KDM1A that promote cortical progenitor expansion, increased neuronal output, and cortical tissue morphogenesis. The ability of selected ECM genes to induce cortical fold-like structures in the mouse cortex, together with the presence of human-specific enhancer signatures, suggests that evolutionary changes in ECM gene regulation contributed to the expansion and folding of the human cerebral cortex. These findings provide new insights into mechanisms underlying human brain evolution and the developmental basis of cortical malformations.

P156

Bilateral information processing in the olfactory pathway of a grasshopper, *Hieroglyphus banian.*

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Background : Olfactory pathway in insects is known to have bilateral connections, at the lateral horn (LH) and mushroom body (MB) level. Neurons connecting the LH are known to be strongly responsive to odor. Our lab has previously reported a class of bilateral neurons connecting the mushroom body lobes in the brain of the grasshopper, *Hieroglyphus banian,* responding weakly to olfactory stimuli on the recorded side. Though this bilateral connection may imply memory transfer, we reported that such transfers do not happen in honeybees, *Apis mellifera*.

Purpose To test the computational interactions in the olfactory neurons of the protocerebrum, in terms of their responses to bilateral stimulation from AL and from the MB independently. To visualize the innervation pattern of these neurons and their relationship to the computational subcompartment units of the MB. Infer the possible network of interactions that can give rise to these responses.

Methods: To answer these questions, we tested these connectivities and response properties by performing olfactory stimulation to the antennae and electrical stimulation to the MB on the two sides, individually and together, while recording intracellularly from these neurons. The innervation patterns were obtained by intracellular dye fills, post recording, followed by confocal imaging and morphology reconstruction.

Results : This is the first study looking at the bilateral interaction of neurons in the insect brain. We find that olfactory neurons in the protocerebrum have computational features that allow unilateral, bilateral, synergetic, and inhibitory interactions. Some of the neurons responded with temporal patterns to KC stimulation, raising the possibility of temporal coding and processing downstream of the MB, independent of the antennal lobe. These results point to a complex bilaterally integrated processing of olfactory code in the protocerebrum of insects.

P157

Exploring the Predatory Imminence Continuum in Virtual Reality

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Background: Research on predatory imminence continuum has primarily focused on defensive responses directed at an organism. However, it remains unclear whether the same responses differ when threat is directed towards a conspecific.

Purpose: The present study investigates fight-or-flight defence responses in self-directed and other-directed threat environments.

Methods: Eighteen participants were divided into self-directed (SeD) (N=9, Mean(SD)=24(3.71)) and other-directed (OtD) (N=9, Mean(SD)=22.22(3.15)) groups. In the SeD group, participants were presented with a VR scenario having 4 lanes and were assigned to search for a box. During the search, they might encounter a threat avatar. The conditions were Distal Threat Escape, Distal Threat No-Escape, Proximal Threat Escape, Proximal Threat No-Escape and No Threat. In OtD group, the threat was directed towards a neutral avatar. In both groups, a total of 20 trials were included.

Results: A condition (4) x group (2) mixed ANOVA for Fight and Flight responses revealed no significant effect for the condition x group interaction. However, the rmANOVA for OtD group revealed a significant difference in the Fight response ($F(3,24)=5.23$, $p<0.01$, $\eta p^2=0.40$. Pairwise comparisons revealed a significant difference between Distal Threat Escape and Distal Threat No-Escape condition (Mean diff=0.44, p=0.04). For eye-tracking data, dwell time on Environment, Threat and Neutral avatar regions of interest (ROIs) was calculated. For SeD group, a Conditions (4) x ROI (2) mixed ANOVA revealed a significant main effect for ROI ($F(1,6)=45.79$, $p<0.01$, $\eta p^2=0.88$). For OtD group, a Conditions (4) x ROI (3) mixed ANOVA revealed a significant main effect for ROI ($F(2,16)=205.88$, $p<0.01$, $\eta p^2=0.97$). This suggests that the participants allocated attention differently across ROIs.

Conclusion: The study provides evidence of predatory imminence continuum in the other-directed group for Distal threat, facilitated by the escapability of the individual. This highlights the importance of availability of escape in decision-making of fight-or-flight defence responses.

Keywords: self-directed threat, other-directed threat, human defence responses, predatory imminence continuum

P158

Time Restricted Feeding imparts physiological benefits in a *Drosophila* model of Huntington's Disease

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Background: Huntington's Disease (HD) is characterized by several neurological symptoms including abrupt, jerky movements. Current therapeutic strategies only provide symptomatic relief, and no treatment exists that can delay the inevitable onset and progression of the disease. Over the years, treatment strategies with a brain-centric approach have been unsatisfactory as HD is a systemic condition with severe metabolic phenotypes such as tissue wasting and gastrointestinal dysfunctions. Implementation of Time Restricted Feeding (TRF) has been found to be effective against various physiological parameters and neurodegeneration as well. Since bidirectional gut brain axes exist, implementation of TRF could improve physiological parameters which are otherwise found to occur along with neurodegeneration and could improve overall health.

Purpose: The study is intended to explore the impact of TRF on various physiological phenotypes of HD.

Methods: Pan-neuronal expression of human *Huntingtin* gene with expanded polyQ repeat is used to generate experimental animals. Upon implementation of 7 cycles of TRF, several parameters are assessed, including, body size, biomass, levels of fat reserves and gut microbiome.

Results: Like patient symptoms, we find that pan-neuronal expression of mutant *Huntingtin* leads to metabolic aberrations, including alteration in body size, reduction in biomass and fat reserves, along with gut dysbiosis. Implementation of TRF is effective in improving these disease phenotypes up to a certain degree.

Conclusion: Lifestyle interventions which could possibly improve overall health could be employed along with conventional strategies to possibly alter the disease progression and manage the disease symptoms as well.

Keywords: Neurodegeneration, Time Restricted Feeding, Gut-Brain axis, Metabolism.

P159

Sex, Stress, and Mitochondrial Vulnerability: Decoding Metabolic Drivers of Depression-like Behavior

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Background: Depression is a complex neuropsychiatric disorder characterized by sadness or lack of pleasure. The disruption of mitochondrial dynamics (fission/fusion), metabolic enzyme shifts, and subsequent oxidative stress within the CNS are increasingly recognized as core drivers of stress-induced behavioral deficits. Furthermore, distinct sexually dimorphic responses to chronic stress remain unexplored.

Purpose: This study aims to evaluate the sex-specific mechanistic pathways underlying the impact of stress-induced neural vulnerability connecting inflammation, metabolic flux, and mitochondrial quality control in both male and female C57BL/6 mice.

Method: Adult male and female C57BL/6 mice between 6 and 8 weeks of age were subjected to different types of stressors used in CUMS model for 4 weeks. Different behaviours like OFT, EPM, FST, and TST were used to assess depression-like behaviour, and the amygdala and hypothalamus brain regions were collected for further biochemical and molecular assays.

Result: Significant sex differences in the baseline gene expression profiles between the control and CUMS groups of males and females were found. The CUMS group showed mitochondrial morphology dysfunction accompanied by higher expression of mitochondrial fission proteins DRP1 and Fis1, as well as fusion proteins MFN and OPA1. Consistent with this metabolic shift biochemical assays confirmed the alterations in structural integrity, which was accompanied by severe oxidative stress in CUMS male and female mice.

Conclusion: In this study CUMS group showed profound neuroinflammation paired with an altered metabolic shift and compromised mitochondrial health. The correlation between altered mitochondrial quality control proteins and elevated oxidative stress markers highlights mitochondrial dysfunction as a central hub in CUMS pathology. The study shows the distinct sex-specific susceptibility in stress-induced metabolic and mitochondrial remodelling, paving the new avenues for dimorphic therapeutic interventions.

P160

Rat sonic and ultrasonic vocalization provide insights for anger-like emotional response

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Background: Anger is a fundamental emotion characterized by feelings of hostility, frustration, social provocation and agitation that play an integral role in affective life. Rats emit a variety of sonic and ultrasonic vocalizations (USVs) that reflect different forms of emotional arousal and accompanying affective states. 50-kHz USVs, spanning 32–96 kHz is linked to affiliative states such as play, exploration, and reward anticipation. However, 22-kHz calls are lower in frequency (20–30 kHz). When rat feels threatened, cornered, or overwhelmed during an aggressive encounter, it often emits long, continuous 22-kHz calls.

Purpose: To investigate alterations in 22-kHz ultrasonic vocalizations during anger-like state in rats and evaluate their association with behavioral and neuroendocrine responses.

Methods: Employed the protocol based on the principle that hungry rats, exposed to food but access denied, engage in intense biting (anger-like phenotype). Vocalization of rats was recorded during biting activity task using AudioMoth 1.2.0 acoustic device and data was presented and analysed by Raven pro 1.6 software and MATLAB (R2026a). Level of corticosterone and nor-epinephrine in serum were analysed using ELISA and HPLC-ECD.

Results: Food restriction with food on display rats increased biting activity as compared to controls. The vocalization parameters suggestive of an anger-like state were significantly increased during the biting activity task. Vocalization parameters such as number of calls (22-kHz), total calls duration (sec), mean- call duration (ms), -bandwidth (kHz) and -power (dB) were significantly increased in FR (food on display) group rats. Moreover, levels of corticosterone and nor-epinephrine significantly increased in serum during anger-like response.

Conclusion: Food restriction with inaccessible food induced anger-like emotion in rats that increased 22-kHz calls and increased serum corticosterone and norepinephrine levels. Together behavioral, vocalization and biochemical measures may indicators of an anger-like state in rats.

Keywords: Rat vocalization, 22-kHz calls, Anger-like emotion, Acoustic recorder

P161

Default Mode Network Fractional Occupancy in Monozygotic Twin Alcohol Users is Modulated by Olfactory Identification

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Background: Alcohol consumption is linked to changes in brain network dynamics, yet underlying genetic factors and their interaction with olfactory processing, key modulators of alcohol cue-reactivity and reward are unclear.

Methods*:* We examined resting-state fMRI from 160 monozygotic (MZ) and 80 dizygotic (DZ) twins in the Human Connectome Project. Using k-means clustering, we identified recurrent brain states and measured their dynamics: fractional occupancy (FO), appearance rate (AR), and dwell time (DT). A classical twin model was fitted and heritability (h^2), twin pair differences for alcohol intake (drinks/week, drinks/day over 12 months, alcohol abuse and dependence), odor identification, and brain state features were calculated. We applied general linear models (adjusted for age, sex, current smoking status) to link brain state features with alcohol intake/olfaction and test odor identification's modulation of heritable brain state features.

Results: DMN-C state showed heritable FO (additive genetics (A^2) = 0.50, shared environment (C^2) < 0.1, unique environment (E^2) = 0.49, $h^2 = 0.54$, $p < 0.01$; stronger in MZ). FO negatively and positively associated with 12-month daily intake ($\beta = -0.89$, $p = 0.01$), and odor identification ($\beta = 0.18$, $p < 0.01$). For interpretability, effect sizes were rescaled to 10% increase in FO. Additionally, odor identification significantly moderated the relationship between DMN-C FO and alcohol consumption, such that higher odor identification scores were associated with decreased FO in individuals reporting lower 12-month alcohol intake ($\beta = -5.52$, $p = 0.02$).

Conclusion: DMN-C fractional occupancy appears as a heritable marker of alcohol consumption, modulated by olfactory identification.

Keywords: Alcohol Consumption, Resting State fMRI, Dynamic Brain Connectivity, Default Mode Network, Monozygotes, Dizygotes

P162

Targeting the Lactate Receptor (GPR81) to Suppress Neuronal Hyperexcitability and Seizures in Drug-Resistant Epilepsy: A GIRK Channel-Mediated Mechanism

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Background: Epilepsy is among the most common neurological disorders, arising from a disrupted balance between neuronal excitation and inhibition that drives hyperexcitability. Nearly 40% of patients respond poorly to existing anti-epileptic drugs, highlighting an urgent need for alternative therapeutic targets that act through mechanisms distinct from conventional ion-channel-blocking agents.

Purpose: This study aimed to test whether pharmacological activation of GPR81, a lactate-activated G-proteincoupled receptor, could suppress neuronal hyperexcitability and seizure activity in models of drugresistant epilepsy, and to characterize the downstream signaling mechanism responsible for this effect.

Methods: Rodent hippocampal and mixed cortical neuron cultures were subjected to low-magnesium conditions to induce hyperexcitability, and the effects of the GPR81 agonist 3-chloro-5-hydroxybenzoic acid (CHBA) on action potentials, calcium oscillations, and glutamate release were measured using patch-clamp and livecell imaging. Seizure behavior was assessed in Scn1lab knockout zebrafish larvae, an established model of Dravet syndrome-like refractory epilepsy. To examine the underlying mechanism, GPR81 was coexpressed with GIRK1/2 potassium channel subunits in Xenopus oocytes, and the GIRK current was measured with two-electrode voltage clamp.

Results: CHBA markedly reduced action potentials, calcium oscillations, and glutamate spillover in neurons exposed to low-Mg^{2+} conditions. In Scn1lab knockout zebrafish, CHBA treatment significantly decreased seizure scores compared with untreated controls. In Xenopus oocytes expressing GIRK1/2 and GPR8, CHBA robustly activated GIRK currents, indicating that the Gi-coupled receptor GPR81 signals through GIRK channel activation to hyperpolarize and inhibit neurons, thereby dampening network excitability.

Conclusion: These findings suggest that GPR81 agonism, acting through a lactate receptor-GIRK channel signaling axis, is a promising pharmacological strategy for managing drug-resistant epilepsy and related disorders of neuronal hyperexcitability. Further preclinical and translational studies are warranted to evaluate the therapeutic potential of this approach in humans.

Keywords: GPR81; lactate receptor; GIRK channels; drug-resistant epilepsy; zebrafish model; neuronal hyperexcitability

P163

Directed Stem Cell grafts for Spinal Cord Injury Repair

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Background: Spinal Cord Injuries (SCI) disrupts long-distance neural connections and creates a hostile microenvironment that limits spontaneous regeneration and functional recovery. Transplantation of human induced pluripotent stem cell (hiPSC)-derived motor neuron progenitors (MNPs) represents a promising approach to replace lost cells, promote neural circuit reconstruction, and improve functional recovery following injury.

Purpose: To characterize graft survival, host-graft interactions, and synaptic integration in a thoracic crush SCI model to understand their role in rebuilding disrupted neural circuitry.

Methods: The hiPSC are differentiated into neuroectoderm lineage, further its caudalized and dorso-ventral patterned using small molecule inhibitors to achieve pure MNPs population. Besides, MNPs are transplanted into a thoracic SCI mice model. Functional recovery was assessed longitudinally using behavioural assays. Histological analyses are performed to understand the neural circuit reconstruction across the lesion using multiple markers specific for stem cell graft, inflammatory response and the host-graft integration using pre- and post-synaptic markers.

Results: This study established a rapid differentiation protocol for generating highly enriched OLIG2-positive MNPs from hiPSC. Following transplantation into the injured spinal cord, grafts survived within the lesion environment and exhibited measurable graft volumes. Ongoing histological analyses are evaluating inflammatory responses and the expression of synaptic markers associated with neuronal connectivity and circuit reconstruction.

Conclusion: Preliminary findings demonstrate successful graft survival and integration within the injured spinal cord. Future work will combine MNPs transplantation with activation of the pro-regenerative transcription factors NR2F1 and NR2F6 to target both the intrinsic growth constraints and inhibitory lesion environment, extrinsic inhibitory cues with the goal of promoting neural circuit reconstruction and improving functional recovery following spinal cord injury.

Keywords: Spinal Cord Injury, Motor Neuron Progenitors transplantation, Cell therapy, Host–graft integration, Neural circuit reconstruction and Functional recovery.

P164

Agarose-Embedded Cryosections for Region-Specific Ultrastructural Analysis of the Rat Brain

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Background: Electron microscopy of small tissue blocks achieves high resolution but sacrifices the anatomical landmarks required to assign ultrastructural findings to defined brain regions, limiting quantitative comparison across circuits.

Purpose: The present study describes an electron microscopy workflow that retains regional identity through processing.

Methods: Rat brain sections of 40 μm thickness were prepared as cryosections and embedded in agarose gel to maintain anatomical architecture. Regions of interest were visualized and precisely marked at the light microscopy level, and this marking guided trimming and ultrathin sectioning for quantitative ultrastructural examination. Feasibility was tested in brains subjected to altered conditions in which region-specific effects are expected.

Results: The approach ensured minimal tissue distortion and preserved spatial relationships within neural architecture. Electron microscopic observations resolved differences in glial and myelin alterations, each referable to an identified anatomical region. Retention of anatomical integrity further permitted interpretation of ultrastructural findings against the corresponding histological image of the same section.

Conclusion: The workflow provides a reproducible, high-resolution route to anatomically resolved ultrastructural analysis and is transferable to other models in which the regional specificity of subcellular change is the question of interest.

Keywords: Agarose embedding; Cryosections; Region-specific ultrastructure; Electron microscopy

P165

Development of a Multifunctional Electro-functional Hydrogel for Post-Injury Neural Repair

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Background: Following spinal cord injury or traumatic brain injury, surviving neurons and axons lose its functionality. While primary injury causes structural disruption. The secondary injury triggers a complex cascade of cellular and molecular events including excitotoxicity (excessive glutamate release), neuroinflammation, oxidative stress, axonal degeneration, and impaired electrical signal transmission, all of which contribute to neural dysfunction and hinder recovery.

Purpose: This study is an attempt to re-establish synaptic transmission by developing a conductive brain-mimetic biomaterial.

Methods: Sodium alginate– Carboxymethyl cellulose (SA-CMC) hydrogels incorporating fillers (rGO and PEDOT) were prepared and characterized for morphology, rheological behavior, and electrical conductivity. Preliminary biological assessment includes gene expression analysis, cytocompatibility (MTT assay), oxidative stress responses and assessment of cell-hydrogel interactions by confocal microscopy using SH-SY5Y neuronal cells.

Results: The engineered multifunctional electro-functional SA-CMC hydrogel exhibits favorable viscoelastic properties and measurable electrical conductivity. Primary characterization and further studies including evaluation of oxidative stress, gene expression, and cell–material interactions, biological performance comparison of rGO- and PEDOT-integrated hydrogels are underway to investigate its potential as a conductive biomimetic biomaterial for neural tissue engineering.

Conclusion: The study aims to engineer a multifunctional electro-functional SA–CMC hydrogel with appropriate physicochemical and conductive properties suitable for neural tissue engineering. Ongoing biological evaluation collectively will help in determining their ability to modulate intracellular ROS levels, oxidative stress responses, and cell–material interactions. These findings might guide in establishing a foundation for developing brain ECM-mimetic biomaterials capable of supporting neuronal survival following injury, warranting further validation in advanced neuronal models and in vivo systems.

P166

Rewiring of the Three-Dimensional Genome Encodes Regenerative Potential in the Adult Central Nervous System

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Background: The bundle of axons carrying signals between the Brain and the Body is essential for proper Nervous System function, yet adult mammalian Central Nervous System (CNS) neurons fail to regenerate after injury. This failure has been attributed partly to Transcriptional and Epigenetic barriers, but whether the three-dimensional (3D) organisation of the genome, which determines whether growth-promoting genes can be accessed, forms an independent regulatory layer encoding regenerative potential remains unknown.

Purpose: We asked how the 3D genome architecture changes during neuronal maturation in the motor cortex neurons between the postnatal and adult stages, whether this change contributes to the loss of regenerative capacity, and, lastly, whether successful regeneration requires reversion to developmental genome states.

Methods: We performed in situ Hi-C ,High-throughput chromosome conformation capture, a technique that maps the three-dimensional folding of the genome,on mouse motor cortex at postnatal day 0 (P0, during active axon growth), uninjured Adult, and 7 days after Thoracic Spinal Cord injury, mapping chromatin compartments, topologically associating domains (TADs), and loops.

Results: Postnatal maturation progressively tightened a growth-restrictive architecture, with ~15% of the genome switching compartment identity and accompanied by TAD boundaries strengthening at pro-growth loci. Spinal cord injury alone partially reversed this consolidation in a directed manner, dismantling maturation-strengthened boundaries and re-engaging neonatal gene programs through reorganised yet functionally recapitulative architecture, despite the observed minimal transcriptional activation.

Conclusion: Adult cortical neurons likely retain a latent 3D memory of their growth-capable state. These findings establish 3D genome topology as a key regulatory layer encoding regenerative potential and demonstrate that successful CNS regeneration requires accessing embryonic chromatin states. These findings suggest that regenerative failure could also be topological restricted, identifying new therapeutic axes.

Keywords: Axon regeneration; 3D genome organisation; Hi-C; Chromatin compartments; Spinal cord injury; Epigenetics

P167

Effect of hypobaric hypoxia on Substance P and Neurokinin receptors in brain of rats: modulation by Quercetin prophylaxis.

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Background: Hypobaric hypoxia, which is encountered at high altitude, triggers a cascade of neurochemical, oxidative, and inflammatory responses that can lead to neuronal dysfunctions. The neuropeptide substance P and its receptors, neurokinin receptors, play a crucial role in the progression of hypoxia-induced cerebral alterations, including vasodilation mediated through the release of nitric oxide.

Purpose: The present study investigated the protective effects of quercetin against hypobaric hypoxia-induced cerebral alterations by evaluating its influence on substance P-neurokinin 1 receptor (NK1R)/neurokinin 2 receptor (NK2R), and to compare its efficacy with that of sumatriptan.

Methods: Male Sprague Dawley rats were supplemented orally with 50 mg/kg BW of quercetin and 10 mg/kg BW sumatriptan one hour before exposure to hypobaric hypoxia (24 h at 25,000 ft, 25±°2C, and 55% relative humidity). Oxidative stress was assessed by measuring reactive oxygen species (ROS) levels and the activities of antioxidant enzymes, catalase and superoxide dismutase (SOD). Levels of substance P, the pro-inflammatory cytokine IL-6 and the anti-inflammatory cytokine IL-4 were estimated in the brain tissue homogenate using ELISA. The expression of the NK1R, NK2R and cyclooxygenase 2 (Cox2) was evaluated by Western blot. Nitric oxide-mediated vasodilation was assessed through the estimation of nitric oxide metabolites.

Results: Quercetin supplementation significantly reduced ROS levels and enhanced the activities of catalase and SOD. Substance P, along with IL-6 and IL-4, was brought to levels similar to those of the normoxic control on supplementation with quercetin. Similarly, the level of neurokinin receptors and Cox-2 was also observed to be similar to normoxic control on supplementation with quercetin. Treatment with sumatriptan also attenuated these alterations; however, quercetin demonstrated a more pronounced protective effect.

Conclusion: Quercetin exhibited broader neuroprotective and anti-inflammatory effects in comparison to sumatriptan, highlighting it as a promising therapeutic candidate for the treatment of high-altitude-induced neurological dysfunctions.

Keywords: High altitude, hypoxia, neuropeptide, neuroreceptors, vasodilation

P168

Oxidative stress and UPS impairment trigger endoplasmic reticulum stress to aid in zinc-induced neurotoxicity

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Background: Accrual of high zinc (Zn) levels in substantia nigra region of brain of Parkinson's disease (PD) patients and experimental evidences reporting Zn-induced dopaminergic neurodegeneration in animal model have recognized the influence of Zn in PD pathogenesis. Oxidative stress, ubiquitin–proteasome system (UPS) dysfunction and endoplasmic reticulum (ER) stress are implicated in PD etiology. Although role of oxidative stress and UPS dysfunction is reported in Zn-induced Parkinsonism, contribution of ER stress is not yet clearly deciphered.

Purpose: The present study aimed to explore the involvement of ER stress in Zn-induced neurotoxicity and its link with oxidative stress and UPS impairment.

Methods: Male Wistar rats were exposed to Zn in presence/absence of oxidative stress modulator apocynin or ER stress inhibitor tauroursodeoxycholic acid (TUDCA) for 12 weeks. Rotarod performance and grip strength tests were carried out for neurobehavioral assessment. Estimation of lipid peroxidation and superoxide dismutase (SOD) activity along with proteasomal enzymatic activity was performed in control/treated groups. In addition, protein expression of dopamine synthesizing tyrosine hydroxylase (TH), SUG-1 subunit of UPS and GRP78, an ER stress marker was also analysed in control/treated groups.

Results: Zn exposure caused marked motor impairments evidenced by reduced rotarod performance and grip strength along with attenuation of TH protein levels. Whilst Zn exposure elevated oxidative stress indices i.e., lipid peroxidation and SOD activity, proteasomal enzymatic activity and expression of the SUG-1 subunit of UPS were decreased indicating UPS impairment in Zn exposed groups. Additionally, the ER stress marker GRP78 protein expression was noticeably increased following Zn exposure. Apocynin and TUDCA significantly mitigated Zn-induced alterations in aforementioned parameters suggesting their protective action against Zn- induced neurotoxicity.

Conclusion: The results suggest that Zn-induced oxidative stress and UPS dysfunction elicit ER stress, which in turn contributes to dopaminergic neuronal degeneration in Zn exposed animals.

Keywords: Zinc · Dopaminergic neurodegeneration · Oxidative stress · Apocynin · TUDCA

P169

Latrunculin A- mediated perturbation of F-actin promotes proliferation in postmitotic sensory glia of the auditory organ

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Background and Purpose: The cochlea is the sensory organ of the auditory system. The sensory epithelium of the cochlea is composed of mechanosensory hair cells and glial supporting cells. These cells exit the cell cycle in mouse embryonic day (E) 13.5; thus, damage to the organ results in permanent hearing loss. Studies have shown that mechanosensory pathways, like the Hippo Pathway, play a role in the regulation of proliferation. YAP is sensitive to tissue stiffness, which is regulated by extracellular matrix, cytoskeleton organization and cell adhesion.

In this study, we intended to investigate the effects of F-actin perturbation in cochleas using Latrunculin A (LatA), which sequesters G-actin monomers, preventing polymerisation.

Methods and Results: We treated E14.5 cochleas with LatA and BrdU (thymidine analogue incorporated during S- phase) for 24 hours, fixed and then immunolabeled with BrdU, Sox2 (sensory epithelium) and p27kip1 (cell cycle exit).

Our results showed that LatA treatment resulted in a 3-fold increase in BrdU-positive cells along the inner boundary of the Sox2 immunolabeled sensory epithelium only. However, there was a significant increase in the number of p27Kip1-negative cells in the rest of the sensory epithelium that were BrdU-negative, which is indicative of cells exiting growth arrest (G0), re-entering the cell cycle but have not yet reached S-phase.

Conclusion: These results show that morphogens alone are insufficient to regulate proliferation vs differentiation. We found a novel role for F-actin in determining proliferative potential in the cochlear sensory epithelium. Understanding this pathway is crucial for regenerative therapies in post-mitotic neurosensory tissues.

Keywords: Cochlea, Regeneration, Proliferation, Latrunculin A, Cell Cycle, Mechanosensory

P170

Cytoskeleton to heterochromatin: A SHROOM1- linked barrier to sensory cell reprogramming

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Background and Purpose: The organ of Corti (OC) is the mammalian auditory sensory organ, containing auditory hair cells and glial support cells. Once damaged, it shows limited regenerative potential, resulting in irreversible hearing loss. Sox2, a transcription factor essential for specifying prosensory progenitors and glial support cells, which are thought to hold some regenerative capacity. Studies also showed that the cytoskeleton is linked to nuclear morphology and gene expression through mechanical coupling. To identify cytoskeletal encoding genes expressed in the support cells, we screened transcriptomic data and discovered an uncharacterized cytoskeletal regulator, Shroom1.

We hypothesize that SHROOM1 regulates cellular mechanical stress and nuclear shape to influence chromatin accessibility in support cells.

Methods: Our preliminary data confirmed SHROOM1 expression in glial support cells and that SHROOM1 regulates the actin cytoskeleton. We also showed that F-actin perturbation permitted cell cycle re-entry and Sox2 expression. To test whether SHROOM1 alters the epigenetic landscape by potentially repressing proliferative genes, we analyzed H3K9 methylation, which has been linked to the repression of proliferative genes via chromatin inaccessibility.

Results: Upon Shroom1 loss-of-function, we made the following observations: 1) There was an increase in cell cycle re-entry; 2) the radial width of the Sox2-positive sensory epithelium expanded; 3) a decrease in H3K9me1 in the sensory epithelium. Together these data suggest that SHROOM1 suppresses proliferation and Sox2-positive cell fate acquisition by influencing heterochromatin formation.

Conclusions: This has profound implications for regenerative studies because Shroom1 loss-of-function can be co-opted to restore proliferation in post-mitotic sensory epithelia and enhance cellular reprograming of new sensory tissues. This is a precision therapeutic strategy to restore hearing function by regenerating sensory tissues by modifying physical forces and chromatin accessibility.

Key words: Cochlea, SHROOM1, Chromatin accessibility, Proliferation, Regeneration

P171

Collagen concentration is a critical regulator of cytoskeletal remodeling and cell proliferation

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Background : The mammalian cochlea is a highly specialized sensory organ that is necessary for hearing. In the mouse cochlea, the sensory cells exit the cell cycle on the embryonic day(E) 13.5 and cannot be coaxed to re-enter the cell cycle after P3. Less is known about how extracellular environment influences proliferation and differentiation in the cochlea. Collagen, a major component of the extracellular matrix, influences tissue stiffness to provide mechanical support and shapes tissue architecture.

Purpose: This study is aimed to determine whether altering the collagen concentration affects the cytoskeletal organization. Understanding how ECM mechanics regulate cell cycle exit during cochlear development will provide insights into molecular strategies for sensory cell regeneration.

Methods : Embryonic cochlear explants were cultured in matrices with different collagen concentrations. Collagen concentrations included 1X, 2/3X and 1/3X. To assess the cytoskeletal organization, the cochleas were dissected at E14.0 and treated for 4 days *in vitro* and were immunolabeled for F-actin (Phalloidin), cell-cell adhesion (E-cadherin) and a cell cycle marker for G0 ($p27^{kip1}$). To examine cell-cycle activity and proliferation, cochlear explants were dissected at E14.5 and kept for 1 day *in vitro* and were immunolabeled with BrdU (S-phase marker), Sox2 (sensory domain), $p27^{kip1}$ (cell cycle marker for G0).

Results: Upon reduction in collagen concentration to 2/3 (2/3 X) F-actin labeling was less defined relative to the 1X collagen and further reduced in 1/3 collagen (1/3 X) concentration. F-actin and E-cadherin appeared to be destabilized at cell-cell junctions; thus, ECM concentration impacts cytoskeletal architecture. Our preliminary data showed that in 2/3X condition, the $p27^{kip1}$-positive epithelial boundaries were disrupted, with several cells leaving G0 and re-entering the cell cycle (BrdU-positive). In the 1/3X condition, cell proliferation increased further.

Conclusion: Collectively, these findings demonstrate that the ECM is a critical regulator of sensory cell proliferation and changes in ECM mechanics can promote cell-cycle re-entry.

Keywords: Cochlea, Proliferation, ECM, Collagen, Regeneration

P172

Synergistic effect of Aβ42 and Tau on autophagy in Drosophila Alzheimer's disease model

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Background: Alzheimer's disease is one of the leading causes of dementia worldwide. AD is characterised by the formation of extracellular senile Aβ plaques and intracellular neurofibrillary tangles (NFTs) formed by hyperphosphorylated tau proteins. This leads to various defects in the nervous system, such as memory impairment, autophagy defects, oxidative stress, cell death and neuroinflammation.

Purpose: This study aims to investigate the synergistic effect of Aβ42 and Tau on macroautophagy and to find potential genetic modifiers that could alleviate the disease pathology.

Methods: The bipartite UAS-Gal4 system was used to express UAS-Aβ42, UAS-tau. WT, and UAS-LacZ using GMR-Gal4, D42-Gal4, and Elav-Gal4 drivers. Negative geotaxis and longevity assays assessed locomotor ability and fitness. Lysotracker staining evaluated lysosomal activity, while mCherry-Atg8-GFP assessed autophagic flux. Western blotting and cell-death markers were used to analyze Aβ, p-tau levels, and apoptosis.

Results: Expression of Aβ42 and tau individually induced photoreceptor loss and rough eye phenotype, whereas their co-expression caused severe eye reduction and impaired vision. Pan-neuronal co-expression using elav-Gal4 significantly reduced motor ability and lifespan. Flies expressing both constructs showed elevated p-tau levels compared to Tau alone and increased autolysosome formation relative to individual pathologies.

Conclusion: Our preliminary data showed that co-expression of Aβ42 and Tau.WT leads to severe eye degeneration, enhanced p-tau levels, and aberrant autophagy. In subsequent experiments, we aim to elucidate the mechanistic effect of Aβ42 and Tau.WT on autophagic and cell death pathways. Furthermore, we aim to determine whether targeting autophagy pathways could suppress disease pathology.

Keywords: Alzheimer's disease, Autophagy, Apoptosis

P173

Mechanistic Insights into the Neuroprotective Effects of Picrorhiza kurroa Against Amyloid-β and Chlorpyrifos-Induced Neurotoxicity

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Background: Alzheimer's disease is a progressive brain disorder marked by oxidative stress, impaired DNA base excision repair (BER), and neuronal dysfunction. Chlorpyrifos (CP) exacerbates AD-associated pathology by increasing oxidative damage. *Picrorhiza kurroa* (Pk), a medicinal herb with potent antioxidant properties, shows promising neuroprotective potential, although its underlying molecular mechanisms remain unclear.

Purpose: This study explored how hydroethanolic extract of Pk protects the neurons from neurotoxicity induced by Aβ and CP by focusing on Nrf-2-APE1 signalling and proteomic changes mediated by exosomes.

Methods: Hydroethanolic extract of Pk was characterized band evaluated for antioxidant activity. SH-SY5Y cells exposed to Aβ and CP were assessed for cell viability, oxidative stress, lipid peroxidation, protein carbonylation, and oxidative DNA damage. APE1 and HO-1 expression, AP endonuclease activity, Nrf-2 nuclear translocation, and Nrf-2-APE1 co-localization were analysed. Neuritogenic potential was evaluated by GAP-43 expression. Exosomes isolated from Pk-treated cells were analysed by TripleTOF-based proteomics and STRING PPI network analysis.

Results: Pk significantly attenuated Aβ and CP-induced cytotoxicity, oxidative stress, lipid peroxidation, protein oxidation, and oxidative DNA base damage. The extract restored APE1 expression and enzymatic activity while enhancing HO-1 expression and promoting Nrf-2 nuclear translocation, indicating activation of antioxidant defence and DNA repair pathways. Increased Nrf-2-APE1 co-localization suggested crosstalk between redox regulation and BER. Elevated GAP-43 expression indicated improved neuronal plasticity. Exosomal proteomics further demonstrated modulation of proteins associated with neuroprotective pathways, with STRING analysis confirming interconnected neuroprotective signalling networks.

Conclusion: Hydroethanolic extract of Pk provide neuroprotection against Aβ and CP-induced neuronal injury by modulating oxidative stress, DNA repair, and neuritogenic pathways through Nrf-2-APE1 signalling. Exosome-mediated proteomic remodelling further highlights intercellular communication as a key component of its neuroprotective mechanism, supporting the therapeutic potential of Pk in mitigating CP-associated exacerbation of AD pathology.

Keywords: Alzheimer's disease; Pk; Chlorpyrifos; APE1; Nrf-2; Exosomal proteomics

P174

Tollo Signaling in Leucokinin Neurons Drives Systemic Lipid Accumulation via JNK signaling in Response to Mild Oxidative Stress in Drosophila

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Background: Organisms frequently encounter mild oxidative stress that may activate physiological and metabolic responses, such as those involved in survival and lipid homeostasis. This mild, low-level oxidative stress can generate reactive oxygen species (ROS), which reshape the lipid metabolism at the systemic level. But the underlying mechanism of neural circuits that coordinates systemic metabolic adaptation during stress is poorly understood.

Purpose: Our aim is to determine whether neuronal Toll signaling plays any role in systemic lipid accumulation and changes in starvation resistance under mild oxidative stress in adult Drosophila. We also wanted to identify upstream ligands, specific neuronal populations, and downstream signaling pathways involved.

Methods: Adult flies are exposed to mild oxidative stress (0.1% hydrogen peroxide) for 3 days. We have confirmed the accumulation of lipid droplets in the gut and fat body by confocal imaging (visualized with a BODIPY stain), and whole-body TAG is measured by biochemical assays. We took starvation resistance as a functional readout of the lipid accumulation. KO and KD experiments were performed in the defined neuronal populations.

Results: Chronic mild oxidative stress increased lipid droplet abundance in the gut and fat body and elevated whole-body TAG levels by 30 to 50%, thereby enhancing starvation resistance. Pan-neuronal overexpression of Tollo, but not other neuronal Toll receptors, recapitulated this phenotype, whereas Tollo knockdown reduced starvation resistance.

Conclusion: Spätzle2–Tollo–JNK signaling in Leucokinin neurons drives starvation resistance under mild oxidative stress, which indicates how neurons sense environmental stress and reprogram systemic lipid storage. These findings reveal a novel role for neuronal Tollo signaling in coordinating metabolic adaptation to sub-lethal environmental stress.

Keywords: Toll, ROS, oxidative stress, lipid metabolism, neuroimmune circuit

P175

α-Synuclein protofibrils lead to cell-type-specific mechanobiological failure in Dopaminergic Neurons

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Background: Proteotoxicity caused by α-Synuclein (α-SYN) protofibrils induces oxidative stress and organelle damage, resulting in premature cellular senescence-like stress in astroglia. This triggers a transient increase in tunneling nanotube (TNT) biogenesis, which aids in clearing toxic cargo and reversing premature senescence via a mechanobiological axis.

Purpose

Through this study, we aim to determine whether dopaminergic neurons — the primary cell type degenerating in Parkinson's disease — exhibit a comparable intercellular rescue response with astroglia.

Methods: Here, we characterise the neuronal (primary dopaminergic neurons and SHSY5Y neuronal cells) response to α-SYN protofibrils and show that it is fundamentally distinct from the astroglial (primary astrocytes and astrocyte lineage cancer cell lines) rescue programme. The comparison focused on ROCK-mediated modulation of the actin cytoskeleton, autophagy function, and mechanical stability through YAP-regulated Hippo signaling.

Results: Unlike astroglia, neurons do not exhibit similar ROCK-signaling-driven modulation of actin tension, which is necessary to trigger the transient TNT-based rescue process. TNT numbers increased steadily over time without resolution in neurons, in contrast to the transient induction-and-clearance mechanism observed in astroglia. Furthermore, α-SYN aggregate burden rose continuously through 24 hours in neurons. An early reduction in p62/SQSTM1 at 3–6 hours was observed, which normalised without accompanying aggregate clearance, suggesting an overwhelmed autophagic response rather than productive selective autophagy. Caspase-3 cleavage appeared at later time points, indicating progression to apoptosis under unresolved proteotoxic stress. Lamin A/C failed to restore nuclear localisation at late time points and instead became cytoplasmic. This contrasts sharply with the Lamin A/C nuclear stabilisation that marks successful astroglial recovery. Notably, YAP remained persistently nuclear in neurons throughout the observation period. This is in direct contrast to the cytosolic YAP translocation, which is essential for the TNT-mediated rescue mechanism that restores mechanical stress in α-SYN-treated senescent-like astroglia.

Conclusion: Together, these findings define a neuronal mechanobiological failure signature that likely underlies the dopaminergic vulnerability in Parkinson's disease.

Keywords: Tunneling Nanotubes, biogenesis, Parkinson’s, proteotoxicity, Lamin A/C, YAP

P176

Adaptive hippocampal adult neurogenesis underlies stress resilience

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Background: Hippocampal adult neurogenesis (hAN) plays an important role in specific cognitive processes, including pattern separation and stress resilience. However, while adult born neurons are required for stress resilience, chronic stress conditions downregulate adult hippocampal neurogenesis.

Purpose: This study aimed to investigate this paradox through careful examination of the neurogenic program during the duration of chronic stress to uncover the mechanistic basis of hAN to stress resilience.

Methods: For this, we adopted a chronic immobilization stress (CIS) paradigm over a course of 30 days, during which animals were examined for cognition and dentate gyrus (DG) activity. These observations were correlated with temporal dynamics of the adult neurogenic program using genetic lineage tracking of adult neural stem cells and the adult born granule neurons (abGC).

Results: Remarkably, we observed a deficit in cognition by 14 days, however despite continual CIS, the cognition deficit was rescued by day 30, indicating potential adaptive changes to reinstate function. Consistent with cognition deficit and rescue, we observed deregulation of DG activity in the initial phase of stress, which was restored by day 30. Genetic-lineage tracing showed dynamic readjustment of the neurogenic program through the course of stress, wherein the immature neurons and progenitor decline during the initial phase of stress, which is followed by a pause in turnover, resulting in an increase in numbers of mid-age abGC that serve to stabilize the function of DG despite reduction of neurogenesis in response to stress.

Conclusion: Overall, our observations indicate that the adult neurogenic program adapts to slow down turnover of adult born granule cells to buffer for reduced adult neurogenesis during stress, in order to sustain normal functionality of hippocampal functions.

Keywords: Hippocampal adult neurogenesis, dentate gyrus, adult born granule cells, stress, cognition, genetic lineage tracing

P177

Exercise induced neuroprotection: Exploring the role Neuregulin in mouse model of brain injury

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Background: Alzheimer's disease (AD), a major neurodegenerative disorder, is one of the most complex brain diseases. According to the WHO, over 1 billion people globally suffer from neurological disorders, with about 24 million affected by AD. Current treatments offer only temporary symptomatic relief. Exercise is known to play a neuroprotective role. It may act as an adjunct and integrative approach to induce neuroprotection.

Purpose: This study aims to investigate whether exercise-induced neuroprotection is mediated through neuregulin, a neuroprotective biomolecule.

Methods: The study was conducted in three stages. (1) Mice were provided with exercise, followed by the creation of a memory-loss model. (2) Exercise was provided to young mice, and serum collected from these mice was infused into older mice. (3) Human participants were divided into runner (n = 60) and control (n = 60) groups using the IPAQ. Cognitive and psychological assessments included GHQ-12, STAI, DST, SLCT, DSST, and TMT. ELISA was performed for BDNF, CRP, NRG-1 and NRG-2. Neurobehavioral and molecular analyses assessed neuregulin and receptor expression at each stage.

Results: Psychological distress and anxiety were significantly lower in runners than controls ($p < 0.05$), while attention and short-term memory were higher ($p < 0.05$). No significant difference was observed in TMT and DSST. In mice, motor coordination, spatial learning, and memory improved significantly in the exercise group compared to the injury group ($p < 0.05$), though anxiety and depression-like behaviour were unchanged. Molecular analyses of neuregulin expression are ongoing.

Conclusion: Exercise exerts neuroprotective effects by improving cognition, motor coordination, and psychological well-being. These findings support exercise as a potential integrative approach for neuroprotection, possibly mediated by neuregulin pathways in AD.

Keywords: Exercise, Neuroprotection, Alzheimer's disease

P178

From Humans to *C. elegans*: A System Bioinformatics Approach to Elucidate Conserved Serotonin Receptor Genes and Pathways

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Background: Serotonin is a monoamine neurotransmitter that influences the activity of numerous neuronal circuits, impacting mood, cognition, sleep, and development of neurons. Its diverse physiological effects arise from the activation of multiple receptor subtypes distributed throughout the central and peripheral nervous systems. Abnormal serotonin signalling increases the risk of several neurological disorders. *Caenorhabditis elegans* (*C. elegans*) is a microscopic nematode that serves as an important experimental model in neuroscience research to investigate gene function and disease mechanisms owing to its short life cycle, tractability, and completely mapped nervous system.

Purpose: This study employs a systematic bioinformatics approach to identify known and predicted serotonin receptors in humans whose orthologs were found in *C. elegans* in order to analyze conserved genes and pathways within their genomes.

Methods: Known and predicted serotonin receptors were obtained from SWISS TARGET (P>0.14), SEA (P>0.4), TARGET NET (P>0.9, ECFP4, AUC>0.6), and SuperPred (P>0.7). Protein-protein interaction (PPI) networks of human KRs with first neighbours, and *C. elegans* orthologs obtained from g:Profiler were constructed using Cytoscape. DAVID was used for GO enrichment and KEGG pathway analysis.

Results: A total of 182 human serotonin receptors were found and after analysis, Key Regulators (KRs) and first neighbour count was found to be 82. Orthologs of first neighbours of KRs in *C. elegans* were derived using g:Profiler and a PPI network comprising 276 genes was constructed, which revealed five important hub genes, members of the nuclear hormone receptor family: nhr-174, nhr-94, nhr-169, nhr-2, and nhr-254. The enriched KEGG pathways were involved in axon regeneration, glycolysis, purine metabolism, IgSF CAM signalling, and metabolic pathways.

Conclusion: Our findings demonstrate the utility of *C. elegans* as a model organism for investigating serotonin biology, underscoring the importance of bioinformatics approaches in identifying evolutionarily conserved biological pathways and uncovering potential therapeutic targets for intervention strategies.

Keywords: Serotonin receptors, *Caenorhabditis elegans*, orthologous genes, PPI network, bioinformatics, functional enrichment

P179

MLN8054, A Novel VRAC blocker for the treatment of Ischemic Stroke

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Background: Ischemic stroke causes oxygen and nutrient deprivation, leading to cellular swelling and activation of volume-regulated anion channels (VRAC). Excessive VRAC activation causes glutamate release which leads to excitotoxicity and neuronal damage. Therefore, the identification of potent and selective VRAC inhibitors are crucial for the treatment of Ischemic stroke.

Purpose: This study involves repurposing FDA-approved drug MLN8054 as a novel VRAC inhibitor for the treatment of ischemic stroke.

Methods: In silico molecular docking was performed to shortlist five candidate compounds based on binding energy on VRAC. The shortlisted compounds were screened using the YFP quenching assay, and the most potent inhibitor was selected for further evaluation using regulatory volume decrease (RVD) and whole-cell patch-clamp assays. Neuroprotective efficacy was assessed in an adult zebrafish ischemic stroke model. Novel tank test (NTT) was performed to evaluate post-stroke anxiety-like behavior, TTC staining was done to determine cerebral infarct area and GFAP expression was studied as a marker of neuronal injury.

Results: MLN8054 significantly reduced YFP quenching at 100 nM, 500 nM, and 1 μM, impaired regulatory volume decrease, and inhibited VRAC currents in a dose-dependent manner. In adult male zebrafish, the drug attenuated post-stroke anxiety-like behavior, reduced hypoxia-induced cerebral infarct area, and increased GFAP expression, suggesting a neuroprotective response.

Conclusion: This study identified a novel VRAC inhibitor MLN8054 with neuroprotective effect against ischemic stroke. The drug attenuated hypoxia-induced neuronal damage and improved behavioral locomotion in adult zebrafish, supporting its therapeutic potential. Further preclinical studies in mammalian models are needed to validate its efficacy and translational potential before clinical evaluation.

Keywords: VRAC, Drug Repurposing, MLN8054, Zebrafish, Ischemic Stroke

P180

Tau agrregation at Synapses

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Background: Synaptic dysfunction is a key feature of neurodegenerative disease and is thought to be driven, in part, by protein aggregation, particularly tau. However, the nature and characteristics of tau aggregates at synapses remain poorly understood, largely because their characterization in post-mortem human brain tissue and cellular models has been challenging.

Purpose: This study aimed to apply novel biophysical approaches to characterize tau aggregates that form at synapses and investigate their potential association with early synaptic pathology and microglia-mediated synaptic loss.

Methods: Tau aggregates in individual synaptosomes isolated from Alzheimer's disease (AD) cases and controls were quantified using single-molecule fluorescence microscopy and the SynPull method. Aggregate number, size, and co-localization with phosphatidylserine and CD47, representing "eat me" and "don't eat me" signals, respectively, were assessed. Tau aggregation was also examined in fixed wild-type human neurons using super-resolution imaging under control conditions and following TNF-induced inflammatory stress.

Results: Tau aggregation occurred preferentially at synapses in both post-mortem AD brain tissue and stressed human iPSC-derived neurons. AT8-positive tau aggregates exhibited increased co-localization with phosphatidylserine, whereas CD47 levels were reduced. Synaptic tau aggregates were detectable as early as Braak stage III. Most aggregates were small and spherical, indicating that early forms of synaptic tau aggregation may be associated with altered signals involved in microglial recognition and synaptic elimination.

Conclusion: Small synaptic tau aggregates are associated with early synaptic pathology and may promote microglia-mediated synaptic loss. The preferential accumulation of tau aggregates at synapses, together with altered phosphatidylserine and CD47 signals, suggests that synapses are particularly vulnerable to tau aggregation. These aggregates may contribute to local neuroinflammation and microglia-driven synaptic pruning during the progression of neurodegenerative disease.

Keywords: Tau; Alzheimer's disease; Synapses; Protein aggregation; Microglia; Neuroinflammation

P181

Investigating Annexin A1 role as a proinflammatory mediator of neuroinflammation during Hepatic Encephalopathy: Study in a rat model

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Background: Moderate Hepatic Encephalopathy (MoHE) is a liver disease-linked metabolic brain disorder causing cognitive and motor deficits. While early neuroinflammation may protect the brain, chronic glial cell activation becomes neurotoxic. Annexin A1 (AnxA1) typically preserves blood-brain barrier (BBB) integrity and suppresses inflammation, but its nuclear translocation may paradoxically trigger pro-inflammatory pathways. So this dichotomous nature of Annexin A1 in HE is still a mystery.

Purpose: This study investigated the AnxA1 role in MoHE which is context dependent based on cellular localization and post-translational modification.

Methods: Male Charles Foster rats were split into control (0.9% NaCl) and MoHE groups. MoHE was induced via daily thioacetamide (TAA; 100 mg/kg, i.p.) injections for 10 days. Cognitive and motor functions were evaluated using the Rota-rod, Novel Object Recognition, Y-maze, and Radial Arm Maze tests. Brain tissues were analyzed via Western blotting, immunofluorescence, and subcellular fractionation. BBB permeability was measured using a sodium fluorescein tracer alongside tight junction protein (Ocln, ZO-1) expression. Neuronal morphology and spine density were also assessed.

Results:TAA-treated rats displayed severe motor incoordination and memory impairments. In the hippocampal CA1, CA3, and DG regions, AnxA1 expression was markedly upregulated and heavily translocated into the nucleus. This nuclear entry correlated with NFκB pathway activation, shifting the cytokine profile to a pro-inflammatory state (increased IL-6 and TNF-α; decreased IL-10 and IL-4). Furthermore, MoHE rats exhibited extensive astrogliosis (increased GFAP) and heightened BBB permeability, which matched the downregulation of Ocln and ZO-1. Neurons showed significant structural decay, characterized by cell shrinkage, reduced dendritic arborization, shorter total lengths, fewer branches, and diminished spine density.

Conclusion: In MoHE, AnxA1 transitions from a neuroprotective agent to a pro-inflammatory mediator. Its nuclear translocation drives chronic neuroinflammation via the NFκB pathway, leading to BBB disruption and severe neuronal degeneration. The AnxA1-NFκB axis represents a key pathological driver of MoHE-related cognitive decline, suggesting that blocking AnxA1 nuclear entry could serve as a novel therapeutic strategy to mitigate neurodegeneration in liver-related brain disorders.

Keywords: Annexin A1, neuroinflammation, Hepatic Encephalopathy, dichotomous, PTMs.

P182

Gut-Derived Methylamines as Novel Acetylcholinesterase Inhibitors: A Promising Combinatorial Therapeutic Strategy for Dementia

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Background: Dementia represents a progressive neurodegenerative condition marked by cognitive, memory, and linguistic decline. Present interventions, notably acetylcholinesterase (AChE) inhibitors like donepezil, galantamine, and rivastigmine, offer merely symptomatic management. The intricate, multifaceted etiology of this pathology underscores an urgent need for safer, more impactful therapeutic options.

Purpose: This study aimed to evaluate how specific gut microbial metabolites influence the enzymatic activity of AChE, a key regulator of neural function.

Methods: A curated library of gut-derived molecules was screened in silico, shortlisting 210 candidates based on blood-brain barrier permeability, feasibility, and chemical properties. Following virtual docking, systematic functional activity assays of AChE were conducted alongside biophysical, cellular, and computational analyses.

Results: Virtual screening identified seven primary leads, among which acetylcholine, sarcosine, betaine, and dimethylglycine (DMG) displayed superior binding affinities for AChE. Experimental testing revealed that betaine and DMG function as competitive AChE inhibitors while mitigating amyloid-β-mediated cytotoxicity in vitro. Crucially, these two compounds potentiated the therapeutic efficacy of standard AChE inhibitors, including rivastigmine, galantamine, and donepezil.

Conclusion: As FDA-approved dietary supplements, betaine and DMG present viable candidates for drug repurposing. Co-administering these metabolites with conventional AChE inhibitors offers an innovative combinatorial paradigm to target the multifaceted mechanisms of dementia, enhancing clinical outcomes while minimizing adverse pharmacological constraints.

Keywords: Gut Metabolites, Acetylcholinesterase, Supplements, Dementia

P183

NCOA4 Mediated Ferritinophagy Downregulation by Deferiprone Promotes Functional Recovery in Cerebral Ischemic Reperfusion Injury

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Background: Intracellular iron regulation remains vital for healthy neurodevelopment and overall cerebral activity. Ischemic events disrupt this delicate balance, resulting in labile iron accumulation, ferroptotic cascade activation, and acute parenchymal injury. Nuclear receptor coactivator 4 (NCOA4)-driven ferritinophagy acts as a central mediator of intracellular iron fluxes, significantly influencing ferroptosis during cerebral ischemia. Deferiprone—a central nervous system-penetrant, clinically authorized iron-chelating agent—represents a viable therapeutic candidate for attenuation of iron-driven neurodegeneration.

Purpose: This study aimed to investigate the therapeutic efficacy of deferiprone alongside its underlying molecular mechanisms in cerebral ischemia-reperfusion (I/R) injury.

Methods: Transient middle cerebral artery occlusion was induced in adult Wistar rats (200–250 g) for 90 minutes followed by reperfusion. Animals received post-reperfusion administration of deferiprone for 7 consecutive days. Behavioral and functional outcomes were assessed using the modified neurological severity score, cylinder, adhesive removal, rotarod, and open field assays. Brain tissue was further analyzed via TTC and Perls staining. Transcriptional alterations of NCOA4, FTH1, and FTMT were evaluated via qRT-PCR, while protein expression levels of NCOA4, FTH1, GPX4, and FTMT were determined using immunohistochemistry.

Results: Longitudinal deferiprone treatment (10 mg/kg, i.p., twice daily, 7 days) significantly alleviated focal I/R deficits. Drug administration enhanced neurological function and sensorimotor coordination across cylinder, adhesive removal, rotarod, and open field evaluations. Functional amelioration correlated with attenuated infarct volume and reduced parenchymal iron accumulation (Perls staining) in MCAO rats. Deferiprone suppressed ferroptotic degradation and ferritinophagy through downregulation of NCOA4 transcript and protein levels, coupled with upregulation of FTH1, GPX4, and FTMT expression.

Conclusion: Sustained deferiprone intervention fosters functional recovery following ischemic reperfusion by suppressing iron accumulation and ferroptosis through NCOA4-mediated ferritinophagy inhibition. These findings suggest deferiprone can reverse sensorimotor impairment, enhance post-stroke functional outcomes, and serve as an adjunctive neuroprotective strategy in clinical stroke management.

Keywords: NCOA4, Iron overload, Deferiprone, FTMT, Stroke.

P184

Influence of Lithium on the Behavioral and Neural Effects of Serotonergic Psychedelics

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Recent studies have shown significant therapeutic potential for serotonergic psychedelics in the treatment of psychiatric disorders. However, the influence of a prior exposure to psychotherapeutic drugs on the subsequent psychedelic use or psychedelic-assisted therapy is not well understood. This knowledge gap is particularly striking in the case of lithium, a widely prescribed mood stabiliser, the interaction of which with serotonergic psychedelics has been reported to cause seizure induction. Despite this severe cross-reactivity, the mechanistic characterisation of this interaction is lacking. Notably, lithium has crosstalk with the Gq signalling cascade downstream of the 5-HT2A receptor, which is the primary target of serotonergic psychedelics. Therefore, using rodent models, we investigated the effect of chronic lithium pre-treatment on responses evoked by 2,5-Dimethoxy4-Iodoamphetamine across behavioral, circuit, cellular, and molecular levels.

P185

Decabromodiphenyl Ether (BDE-209) Induced Brain Molecular Alterations as a Determinant of Neuropsychiatric Disorders through Integrative Toxicoinformatics Approach

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Background: Neuropsychiatric disorders are complex conditions overlapping neurology and psychiatry, where brain dysfunction causes behavioral, emotional and cognitive symptoms. Despite different biological reasons of this cognitive and other deficit in these psychiatric disorders, environmental dysregulations play a major role in progression of these issues. Major dysregulations are observed due to the exposure to organic and persistent organic pollutants but are still inadequately understood at the genomic level.

Purpose: In the current study, integrative toxicogenomic approach is being adopted to evaluate the potential contribution of selected organic and persistent organic pollutants to corelate the neuropsychiatric disease risk at gene expression level.

Method: In progression of work, genes of the selected neuropsychiatric diseases viz. Anxiety, Depression and Post-Traumatic Stress Disorder (PTSD) were listed from GeneCard and MalaCard databases and further multi-omics approach was implemented for hub gene identification. Cytoscape was the main software used for analyzing gene-gene interaction also with the help of CytoHubba (cytoscape plug in). Based on 12 parameters of cytohubba, resultant genes were HSP90AA1 for PTSD and TP53 genes for both anxiety and depression. In continuation of work, suitable proteins were listed against identified priority genes. The selection of priority protein was based on the protein-protein interaction through the network biology method. FOXO3 and TP53 were selected as the most prominent functional proteins based on the topological parameters of CytoHubba. The three-dimensional structures of the resultant proteins FOXO3 (PDB ID:2K86) & TP53 (PDB ID: 4CQO) were retrieved from Protein Data Bank and were utilized for molecular interaction analysis. In extension of research, 40 most consequent organic and persistent organic pollutants were listed which reportedly were involved in triggering neuropsychiatric disorders in humans. To establish the molecular interactional pattern of listed OP and POP docking studies was done through Cresset Flare Pro+.

Result: Decabromodiphenyl Ether (BDE-209) emerged as the most influential toxicant among the compounds analyzed on the preferential docking score. It was observed that Lf DG (ligand flexible docking score) scores was -9.407 kcal/mol for 2K86 against PTSD & -9.37 kcal/mol for 4CQO against anxiety and depression. The screened compound showed strong associations with key neurobiological processes, including neuroinflammation, synaptic function, oxidative stress balance, and neurotransmitter regulation.

Conclusion: Our research findings give a strong conclusion that BDE-209 exhibits a higher level of toxicological impact compared with other pollutants. This study significantly concludes about the potential role of BDE 209 in etiopathogenesis of these selected neuropsychiatric disorders.

Keywords: Organic and Persistent organic pollutants, Neuropsychiatric, BDE-209, Cresset Flare Pro+, Neuroinflammation, Neurotransmitter dysregulation, Oxidative Stress.

P186

Influence of the Gut Bacteria of Uninfected Sandfly Vectors on the Neuropathogenicity of Experimental Chandipura Virus Infection

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Background: Globally, vector-borne diseases account for more than 17% of all infectious diseases and cause 700,000 deaths annually. Emerging neurotropic viral infections transmitted through arthropod vectors account for 49% of all viral diseases. One of the recent viral epidemics in India is attributed to Chandipura virus (CHPV), which is reported to have a high case fatality rate of 67-70%. Sandflies are the primary vectors of CHPV. It is hypothesized that the bite of uninfected vectors may introduce certain components of the gut microbiota into the host, which prime the host against subsequent bites of infected vectors that carry the pathogen, thus reducing the chances of effective pathogen establishment in the host.

Purpose: A potential vaccine candidate for CHPV can be obtained by screening uninfected vector gut bacteria for their antiviral potential and exploring the virus-mediated inflammation and cell death in the pre-treated mice.

Methods: Different bacterial species were isolated from the midgut of two uninfected vector species and heat-inactivated bacterial treatment was administered to suckling BALB/c mice, before CHPV infection. Viral burden, inflammatory markers and virus-mediated cell death in the infected and pretreated groups were assessed using qPCR, CBA, immunoblotting and immunostaining. The survival, changes in weight and symptoms were monitored for each group through the experimental timeline.

Results: Heat-inactivated Bacillus velezensis, isolated from uninfected Sergentomyia babu babu (that is abundant in a CHPV non-endemic region), lowered the viral burden in brain and spinal cord, attenuated virus-induced inflammation, cell-death, and prolonged the survival of the infected animals by delaying symptom progression.

Conclusion: This heat-inactivated bacterial isolate can be considered a potential vaccine candidate against CHPV, and combining it with other therapeutic candidates may provide improved disease outcomes. The observations offer a clue regarding the natural protection conferred by innocent disease-transmitting hematophagous insect-vector species against the severe pathogenicity of neurotropic virus infection.

Key Words: Chandipura virus, Neuropathogenesis, Vector gut bacteria, Vaccine candidate

P187

Preconditioning with Reinwardtia indica Dumort. Confers Multi-Target Neuroprotection Against Cerebral Ischemia-Reperfusion Injury

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Background: Ischemic stroke remains a leading cause of mortality and long-term neurological disability worldwide. Its complex pathophysiology involves excitotoxicity, oxidative stress,

neuroinflammation, disruption of the blood-brain barrier, mitochondrial dysfunction, and apoptotic cell death, thereby limiting the effectiveness of current single-target therapeutic approaches. Therefore, identifying multi-target neuroprotective agents from medicinal plants represents a promising strategy for stroke management.

Purpose: The present study investigated the neuroprotective efficacy of the hydroalcoholic extract of Reinwardtia indica Dumort. against cerebral ischemia-reperfusion injury in rats and elucidated the underlying mechanisms responsible for its neuroprotective effects.

Methods: Transient focal cerebral ischemia was induced in Wistar rats using the middle cerebral artery occlusion (MCAo) model, following ARRIVE 2.0 and STAIR recommendations. Animals were randomly allocated to five experimental groups and preconditioned with R. indica extract (250 or 500 mg/kg, p.o.) for seven days before ischemia induction, with treatment continued throughout the seven-day reperfusion period. Neurological deficits and behavioural outcomes were assessed during reperfusion. At study termination, brain tissues were evaluated for infarct volume, endogenous antioxidant status, inflammatory cytokines, apoptotic markers, and histopathological alterations.

Results: Preconditioning with R. indica significantly reduced cerebral infarct volume and improved neurological outcomes following ischemia-reperfusion injury. Treatment markedly attenuated oxidative stress and neuroinflammation, restored endogenous antioxidant defences, suppressed apoptotic signalling, and preserved neuronal architecture, resulting in significantly reduced histopathological damage. The higher dose (500 mg/kg) consistently produced greater

neuroprotective effects than the lower dose across the evaluated parameters.

Conclusion: R. indica exhibits significant neuroprotective activity against cerebral ischemia-reperfusion injury by attenuating oxidative stress, neuroinflammation, and apoptosis, thereby limiting ischemic brain damage and improving functional recovery. These findings support its potential as a promising plant- derived therapeutic candidate for ischemic stroke and provide a strong preclinical foundation for future translational and clinical investigations.

Keywords: Reinwardtia indica, Ischemic stroke, Middle cerebral artery occlusion, Neuroprotection, Oxidative stress, Neuroinflammation

P188

Stage-specific proteomics and miRNA signatures during development of hiPSC- derived neural cells and 3D cortical and spinal organoids

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Background: Human induced pluripotent stem cells (hiPSCs) offer remarkable self-renewal capacity and the potential to generate diverse neural lineages, advancing regenerative medicine and neurobiology. However, the precise molecular dynamics and interplayed regulatory networks that govern regionalized neural differentiation remain incompletely understood.

Purpose: This study aimed to generate hiPSC-derived two-dimensional (2D) neural lineages (Motor Neurons) and three-dimensional (3D) cortical and spinal organoids to perform comprehensive proteomic and microRNA (miRNA) profiling and identify stage- and region-specific molecular cues during neural differentiation.

Methods: Human BJ fibroblasts were reprogrammed into hiPSCs which further differentiated in 2D monolayers into neural progenitor cells (NPCs), and motor neurons (MNs), as well as cultured into 3D cortical (CO) and spinal organoids (SpO). We conducted high-throughput miRNA profiling (OpenArray® Technology) and quantitative proteomics using nLC-HRMS across all differentiated cell types and organoid models to evaluate stage-specific (neural induction stage, Progenitor stage, Differentiated mature stage) expression changes and post-transcriptional regulatory networks.

Results: Multi-omics analysis revealed distinct, stage-specific molecular signatures that regulate lineage progression and structural maturation. Six miRNAs (miR-204, miR-200c, miR-199a, 34b-3p, hsa- miR-200b, hsa-miR-26b) were expressed higher in NPCs compared to hiPSCs, 13 exhibited highest abundance in mature motor neurons (Day 45) and spinal organoids (Day 45) compared to NPCs and SpO Day 6 (neural induction stage,) respectively, and 3 were significantly enriched in cortical organoids (Day 130) compared to CO Day 6. Corresponding proteomic profiling mapped the functional downstream expression of 157 (GAP43, Syn-α, SEPTIN6, PHPT1, NUMA1, NAPA, HMGA1) proteins in cortical organoids (Day 130), 143 proteins (POU5F1, ABLIM1, NEGR1, NPTN) in spinal organoids and MN (Day 45), resolving coordinated miRNA–protein expression networks tailored to each stage and region of neural development.

Conclusion: These findings may help us understand stage- and region-specific regulatory coordination and provide a multi-omics atlas of human neurodevelopment, offering molecular markers and targets for neurological disease modelling.

Keywords: HiPSCs, Organoids, Progenitor, Neurodevelopment, Omics

P189

Neurophysiological Response in Military Personnel at High Altitude: Gender, a risk or gift factor

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Background: High-altitude (HA) challenges cerebral perfusion, neurochemical homeostasis, and psychological function. However, whether these responses differ between male and female military personnel remains poorly understood. We investigated gender-specific responses in cerebral hemodynamics, mood state, and kynurenine pathway (KP) metabolites at sea level (SL) and at HA.

Methods: Male (n = 40) and female (n = 35) military personnel were evaluated at SL (~250 m) and following subacute exposure to HA (~3,500 m). Bilateral middle cerebral artery blood-flow velocity (MCA-CBFv) was assessed using transcranial doppler. Psychological state was evaluated using the profile of mood states questionnaire to calculate total mood disturbance (TMD) score. HPLC was used for quantification of KP metabolites i.e, tryptophan (TRP), serotonin (5-HT), kynurenine (KYN), 3-hydroxykynurenine (3-HK), and 3-hydroxyanthranilic acid in serum.

Results: HA exposure showcased gender-specific psychological, cerebrovascular, and neurochemical responses. Males demonstrated greater vulnerability, characterized by increased TMD (p=.005**) and reduced MCA-CBFv at HA (p<.001***). This response was accompanied by depletion of TRP (p<.001***) and 5-HT (p=.002**), along with elevated downstream KP metabolites. In contrast, females maintained stable TMD and MCA-CBFv at HA. Females also demonstrated preservation of TRP and 5-HT alongside elevated KYN (p<.001***) and reduced 3-HK (p<.001***), suggesting downregulation of the neurotoxic branch.

Conclusion: In our study, males showed vulnerability via adverse neurovascular and KP alterations while females exhibited significant neuroprotective preservation. These divergent responses offer key insights to strategize operational readiness.

Keywords: Gender, high altitude, military personnel, neurophysiology, kynurenine pathway, cerebral hemodynamics

P190

From Rest to Stress: Acute Mental Stress Suppresses Executive Network and Sustains Default Mode Network Activity- Evidence from QEEG Microstate Study

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Introduction: Picture this: you wake up in the morning and suddenly remember an important meeting scheduled to begin in just 30 minutes. A wave of stress hits, your heart beats faster, your thoughts race, and your actions become hurried. These short-lived stressors can alter how we think, feel, and perform, influencing several aspects of our functioning.

Purpose: This study was intended to understand what happens in the brain during acute stress in terms of the neural network activity. It can help us understand how the brain copes, adapts, and sometimes struggles when stress becomes prolonged.

Methods: High density EEG was recorded from 79 healthy participants during eyes-open resting state, followed by an acute stress induced by mental arithmetic task. Stress induction was validated through galvanic skin response (GSR). EEG microstates were derived during rest and task and their temporal parameters namely mean duration (MD), number of time frames (TF) and time coverage (TC) were compared between condition. Cortical sources underlying each microstate were also localized.

Results: GSR parameters were significantly increased during the task. Four distinct microstate maps across conditions were found. Map 1 showed a significant increase in MD, TC, and TF during the task. In contrast, Map 2, 3 and 4 exhibited a significant decrease in MD during the task, whereas Map 3 and Map 4 showed decrease in TC. The cortical sources of map 1 revealed less activations during task in Inferior and Medial Frontal Gyrus, Anterior Cingulate, Inferior Parietal Lobule and Insula whereas map 3 revealed more activations during task in Parahippocampal Gyrus, Cuneus, Posterior Cingulate and Middle Occipital Gyrus.

Conclusion: In this study central executive network areas which are typically engaged during goal directed task were found to have lower activation during task, whereas more activity during task was linked to the default mode network areas- a task negative network. The study suggests that this apparent reversal of the typical network engagement during stressful condition could be the reason for decreased performance in cognitive domains during acute stress as reported in literature.

Keywords- Stress, EEG, microstate, neural network

P191
Paracrine Rescue by Mesenchymal Stem Cell Secretome in Monocrotophos-Exposed Human Neural Progenitor Cells

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Background: Organophosphate exposure can compromise neural progenitor survival through oxidative stress and mitochondrial dysfunction. Mesenchymal stem cell secretome offers a cell-free approach to support recovery, but their effects on pesticide-injured human neural progenitors require characterization.
Purpose: To compare the restorative effects of unstimulated and cytokine-stimulated human mesenchymal stem cell secretome in monocrotophos-exposed human induced pluripotent stem cell-derived neural progenitor cells.
Methods: Neural progenitors were exposed to monocrotophos (100 μM, 24 h), followed by 24 h treatment with 50% secretome from cytokine-primed and non-cytokine-primed Wharton's jelly mesenchymal stem cells. We assessed cell viability, morphology, reactive oxygen species, mitochondrial membrane potential, and Seahorse bioenergetics. Open Array miRNA/mRNA profiling, targeted quantitative PCR, label-free LC–MS/MS proteomics and pathway analyses characterized molecular responses.
Results: Monocrotophos reduced viability to 65.6% of control and impaired cellular morphology and mitochondrial function. Both secretome improved survival and morphology while reducing oxidative stress. DCF fluorescence decreased from 4.03 ± 0.69 after monocrotophos exposure to 2.30 ± 0.02 and 1.81 ± 0.07 after unstimulated and stimulated secretome treatment, respectively. Oxygen consumption increased from 40.78 pmol/min after exposure to 64.36 and 70.35 pmol/min, respectively, compared with 92.33 pmol/min in controls. Mitochondrial membrane potential, ATP production and respiratory reserve also improved. Monocrotophos altered 22 miRNAs and 22 mRNAs; secretome treatment shifted dysregulated expression toward control profiles. Proteomic and pathway analyses indicated recovery of proteins associated with mitochondrial function, stress responses and cellular maintenance.
Conclusion: Mesenchymal stem cell secretome supported recovery from monocrotophos injury in human neural progenitors, with numerically greater antioxidant and bioenergetic improvements following cytokine stimulation. These findings support further preclinical investigation of secretome-based interventions; causal miRNA–protein mechanisms and in vivo efficacy remain to be established.
Keywords: Monocrotophos; mesenchymal stem cell secretome; neural progenitor cells; mitochondrial bioenergetics; oxidative stress; microRNAs

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Preserved Alcohol Cue Salience Despite Olfactory Dysfunction Is Associated with Multimodal Alterations in Olfactory-Reward Networks

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Background: Chronic alcohol use impairs olfaction, yet alcohol-related odours remain potent triggers of craving. Whether this dissociation reflects alterations within shared olfactory–reward circuitry is unknown, and the accompanying brain changes are uncharacterised across modalities.

Purpose: To test whether alcohol consumption severity relates to objective olfactory dysfunction and with coordinated structural, microstructural and neurochemical brain alterations, and whether alcohol odour-cue perception survives olfactory impairment.

Methods: Ninety-eight alcohol consumers underwent Sniffin' Sticks olfactory testing, a behavioural alcohol odour-cue and craving task (8–42.8% v/v), structural MRI, diffusion MRI and proton magnetic resonance spectroscopy (1H-MRS). Participants were classified as having normal olfactory function (threshold–discrimination [TD] score ≥16; n = 54) or olfactory dysfunction (n = 44). Composites were derived by principal component analysis; mediation was bootstrapped.

Results: Poorer olfactory function was associated with greater alcohol consumption (quantity–frequency index $r = -0.28$), cumulative lifetime exposure (age-adjusted partial $r = -0.37$) and craving severity (PACS $r = -0.40$; all $p < 0.01$). The olfactory dysfunction group showed lower global cognition (MoCA, $d = -0.58$), reduced superior thalamic radiation fibre cross-section ($d = -1.30$) and lower prefrontal glutamate ($d = -0.78$; all pFDR ≤ 0.02). Higher TD scores correlated with greater orbitofrontal thickness ($r = 0.40$) and prefrontal NAA ($r = 0.31$; pFDR < 0.05). A neurometabolic composite tracked intake ($\beta = 0.52$, $p < 0.01$) and mediated the olfaction–consumption link (indirect effect −0.11, 95% CI −0.25 to −0.02). Despite impaired olfaction, familiarity with alcohol beverage odours was preserved, and the olfactory dysfunction group showed greater cue-induced craving at 42.8% (interaction $\beta = 0.67$, exploratory $p = 0.04$).

Conclusion: Olfactory function reflects distributed frontolimbic and neurometabolic alterations in chronic alcohol use, making a brief smell test an accessible marker of alcohol-related brain change. Alcohol cues retain their motivational pull despite sensory decline: olfactory loss offers no protection against cue-driven craving.

Keywords: Alcohol use disorder; Olfactory dysfunction; Alcohol cue reactivity; Fixel-based diffusion MRI; Magnetic resonance spectroscopy; Olfactory–reward network

P193
Visual Working Memory capacity of Native Indian Bees

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Background: Honeybees are most important pollinators in the terrestrial ecosystem especially of a tropical country like India. Building a detailed account of their life history and distribution are essential not only for their conservation but also for pollination of the economically important crops. This is especially lacking for the native Indian bee species such as Apis dorsata and Apis cerana indica as most of the research has been performed for the Western bee species Apis mellifera.

Purpose: Specifically, the visual working memory (WM) capacity of the Indian native species are currently not known. Therefore, this research explores visual WM in the Indian honeybee species using well established delayed match-to-sample paradigm.

Methods1: 30 free-flying marked bees (each for A. cerana indica and A. dorsata), and 20 marked bees (A. mellifera) were used to carry out DMTS (delayed matching to sample), a simple method to test visual WM. We used visual stimuli, lines (vertical and horizontal), and colours (blue and yellow). The protocol involves training the bee to see a sample in a y-maze, and then choose the same among two options, with food as the motivator. Equal number of bees that were trained (60 visits) with lines were tested with colours (4 visits), and vice versa.
Results: While the Apis cerana indica and Apis mellifera showed comparable performance across lines and colours, the Apis dorsata performed better than the former two in the visual WM.

Conclusion: Our preliminary data documents the much-needed basic information about the cognitive profile of the native Indian honeybees. This research is not only critical for enhancing our understanding of bee biodiversity in India but also crucial for India’s food security as these species pollinate myriad species of wild plants and domesticated crops.

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Beyond Diagnosis: A Parent's Journey with Neonatal Hypoglycaemic Brain Injury (NHBI) and the Need for Lifelong, Family-Centred Support

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Independent (no institutional affiliation)

Background: Neonatal Hypoglycaemic Brain Injury (NHBI) can cause lifelong disability, and its impact extends far beyond diagnosis and treatment. The author's son, Madhav, suffered hypoxia and hypoglycaemia at birth and, following delayed diagnosis and treatment, developed impairments of vision, movement, fine-motor skills and communication, along with cerebral palsy, seizures and microcephaly. With no prior knowledge of NHBI, the family found it extremely difficult to find the right help and guidance.

Purpose: This paper aims to identify and address the challenges faced by children with NHBI and their families across rehabilitation, education, skill development, employment and independence.

Methods: This is a parent's experiential account of her son's rehabilitation from infancy, considered alongside the Rights of Persons with Disabilities (RPwD) Act, 2016. Key areas for intervention were identified: early identification and accurate diagnosis; affordable multidisciplinary rehabilitation; individualised education; skill development and transition into adulthood; employment; parent counselling and mentorship; and awareness-building to reduce discrimination.

Results: Intervention was needed from the first month, beginning with the opening of fists, turning, crawling, sitting, standing and walking. Everyday skills such as eating, toilet training, grooming, handling objects and communicating thoughts required years of practice and encouragement. Today, Madhav is multilingual, uses a phone and laptop for basic tasks and has a strong knowledge of cricket. The account also identified recurring barriers: limited information for parents, costly therapies, difficulty finding suitable schools, a complex transition to adulthood, and everyday discrimination affecting both child and family.

Conclusion: Families should not be left to navigate an unfamiliar and fragmented system alone. Parents need clear information, counselling and support networks from the earliest stages. A shift from isolated interventions towards a lifelong, family-centred and multidisciplinary model of care can help these children learn, communicate, participate and live with dignity and the greatest possible independence.

P195

SSPE: Fighting the unsurmountable

Nandita Roy, Saikat Sarkar

A personal experience of closely witnessing the devastating progress of SSPE in a child of 5 years old. Subacute Sclerosing Panencephalitis (SSPE) is a progressive neurological disorder of children that affects the central nervous system (CNS). It is a slow and persistent viral infection caused by the measles virus. We will share our observations and needs of the hour from this very eminent global community. The average age of currently afflicted children is seen to be less than 10 years, based on a set of 160+ children who are part of the patient group. Largely limited to third world countries, there is no treatment available for SSPE. We have seen that most of these children have received anti-measles vaccination on time.

Over a period of about 5-7 months following diagnosis, almost all these children have completely lost mobility, vision, speech and have been reduced to being completely bed-bound, being fed through Riles tubes and being on supportive care. The degeneration is evident and strikingly hard on the parents who are left helplessly watching with no option to carry out treatment as there are no known drugs for the primary ailment, and few drugs for the symptoms like jerks and rigidity, which hardly help much. Every now and then a fatality is reported. The period post diagnosis is an emotionally and financially challenging period for the families of these helpless kids. There is very little regulatory support for the families. There is no treatment or support protocol available. Through this forum, the objective of this short presentation is to ask the forum for the following:

1. To create awareness and help on building an effective palliative care protocol.
2. To start a process of research for development of medicine to help arrest the progress of the disease once diagnosed, and reverse the neurological damage caused, if possible
3. To be included in the list of rare diseases.
4. To look for creating a fund to support the afflicted families

P196

Neuroprotective effects of crude root extracts of Sida cordifolia in Huntington's Disease

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Background: Huntington's Disease (HD) is a neurodegenerative disease, caused by a mutation in the exon 1 of the huntingtin (HTT) gene, producing mutant mHTT proteins, which form insoluble aggregates and induce neurodegeneration. Sida cordifolia (S. cordifolia) is a tropical perennial shrub and reported to have therapeutic effects in neurodegenerative diseases.

Purpose: This study is designed to investigate the therapeutic effects of S. cordifolia in a cellular and mouse-model of HD.

Methods: HD Q150 cells were treated with 10 µg/mL of S. cordifolia for 48 hrs. After treatment, either total protein was isolated or comet assay was performed.

6-7 weeks old R6/2 mice and wildtype littermates were administered 2 mg/kg (body weight) of S. cordifolia once a day through oral gavage for 60 days. Behavioral assays were performed after every 10th day. Afterwards, the mice were sacrificed and brains were removed and performed either cryosectioning or isolation of total proteins and other molecular analyses.

Results: S. cordifolia showed neuroprotective effects in both cellular and mouse model of HD. It reduced level of GFP-tagged truncated mHTT aggregates as well as ubiquitin protein and reduced number of comets and amount of DNA in comet tails in HD Q150 cells. It prevented motor and cognitive deterioration in R6/2 mice. It ameliorated mHTT aggregates in the brains and also prevented striatal atrophy. It reduced mitochondrial dysregulation, neuroinflammation and prevented synaptic proteins and medium spiny neurons degeneration.

Conclusion: Our study showed the neuroprotective effects of crude root extracts of S. cordifolia in both cellular and mouse-model of HD through the reduction of mHTT aggregate loads, prevention of various behaviour deficits and many physiological adverse symptoms associated with HD. Together, our findings suggest that crude root extracts of S. cordifolia could be a potential therapeutic agent for HD.

Keywords: Huntington's disease (HD), mHTT proteins, Sida cordifolia, R6/2 mice

Young Scientist Colloquium-I: Tulsabai Somani Educational Trust Award

YSC01

Metabolic dysregulations associated with diabetes influence Parkinson's disease pathology in the brain and peripheral tissues of mice

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Background: Clinical research associates diabetes mellitus (DM) with a higher risk of Parkinson's disease (PD), although the underlying mechanism remains unclear.

Purpose: We examined commonly altered metabolic signaling pathways in brain and peripheral tissues using a chronic dual PD-DM mouse model to explore the systemic contributions of DM to PD.

Methods: C57Bl/6 mice (male and female) were divided into control, PD, PD-DM, and DM groups. DM was induced using a high-carbohydrate, high-fat (HCHF) diet, while controls received a standard diet. PD was induced by injection of α-synuclein (α-Syn) preformed fibrils into the substantia nigra (SN) 8 weeks later. 20 weeks later, behavioral evaluation and analyses of PD-associated markers in the brain and peripheral tissues were conducted.

Results: HCHF diet induced a DM phenotype, including increased body weight, glucose intolerance, insulin resistance, and hypercholesterolemia. The PD-DM group showed stronger behavioral phenotypes, including reduced grip strength and depressive behavior, than other groups. This was despite PD and PD-DM groups displaying similar extents of dopaminergic neurodegeneration and α-Syn aggregation in the SN. The PD-DM group showed increased microglial activation, which was accompanied by lipid droplet accumulation in SN dopaminergic neurons and microglia. DM-associated glycation was elevated, which may exacerbate inflammation in PD-DM. In the brain, levels of the master metabolic switch, phosphorylated AMPK, were reduced in DM, PD, and non-significantly in PD-DM groups. Peripherally, PD-DM mice showed increased α-Syn aggregation and CD68-positive inflammation with exacerbated lipid droplet accumulation in the liver. This suggests DM does not directly impact dopaminergic neuronal loss but modulates pathology through metabolic and functional changes.

Conclusion: Our findings highlight a key role of metabolic dysfunction in modulating PD pathology, providing insight into PD-DM interplay. Peripheral systems may drive PD phenotypes in PD-DM despite comparable neurodegeneration and α-Syn aggregates. Linking brain insulin resistance and metabolic alterations with peripheral pathology may reveal therapeutic targets.

YSC02

Molecular Heterogeneity in GNE Myopathy: Domain-Specific Mutation Patterns

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Background: The GNE gene encodes a bifunctional enzyme involved in the rate-limiting steps of sialic acid biosynthesis. Pathogenic variants in GNE cause GNE Myopathy, a rare neuromuscular disorder characterized by considerable molecular heterogeneity. However, the contribution of domain-specific mutation patterns to molecular heterogeneity in GNE Myopathy remains poorly understood.

Purpose: To investigate whether domain-specific mutation patterns within the GNE enzyme contribute to the molecular heterogeneity observed in GNE Myopathy.

Methods: A retrospective cohort analysis was performed on 94 individuals harboring GNE variants identified through Next Generation Sequencing (NGS)-based evaluation. Variants were characterized according to genotype architecture, mutation type, recurrence, catalytic-domain localization, populationfrequency patterns, and pathogenicity classification using integrated population-genetic, computational, and statistical approaches.

Results: A total of 46 unique GNE variants were identified, demonstrating substantial molecular heterogeneity with diverse mutation classes, recurrent and rare variants, and multiple genotype architectures. Different mutation patterns were observed across the two catalytic domains. The epimerase domain showed greater variant diversity, while the kinase domain carried a higher overall mutation burden. The founder-associated p.Val727Met variant was present in 82 of 94 individuals and contributed substantially to the kinase-domain burden. However, considerable molecular diversity was observed beyond founder-associated genotypes. Genotypes involving both catalytic domains were more common among clinically suspected cases (OR=2.70; p=0.082), suggesting that combined domain involvement may contribute to disease variability.

Conclusion: Distinct mutation patterns across the catalytic domains highlight previously underappreciated domainlevel differences within the molecular landscape of GNE myopathy. These findings suggest that catalytic-domain context may contribute to molecular heterogeneity and warrant further investigation into its role in disease mechanisms and genotype–phenotype relationships.

Keywords: GNE Myopathy, neurogenetics, molecular heterogeneity, catalytic domains, genotype architecture, translational genomics

YSC03

CART peptide regulates motivated behaviours via reciprocal nucleus accumbens-ventral tegmental area direct and indirect circuitry

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Background: The cocaine- and amphetamine-regulated transcript (CART) peptide is highly expressed in dopamine D1 receptor-containing medium spiny neurons (D1- MSNs) of the nucleus accumbens (NAc) and plays an important role in reward and reinforcement. However, the circuit mechanisms underlying accumbal CARTmediated regulation of motivated behaviours remain poorly understood.

Purpose: This study investigated whether CART signalling modulates reward processing through D1-MSN NAc projections to the ventral tegmental area (VTA) and ventral pallidum (VP).

Methods: Motivated behaviours were evaluated in rats using intracranial selfstimulation (ICSS) of the lateral hypothalamus–medial forebrain bundle and sucrose pellet self-administration. Accumbal CART function was manipulated by bilateral intra-NAc administration of CART siRNA to reduce CART expression and CART peptide (55–102) to activate CART signalling. The contribution of dopamine D1 receptor-mediated reinforcement was assessed using the D1 receptor agonist SKF38393 following CART knockdown. CART mRNA expression in the NAc was analysed using quantitative RT-PCR after ICSS conditioning, food reward conditioning, and CART siRNA treatment. CART-containing projection pathways were identified using retrograde tracer (Fluorogold) into the VTA or VP, followed by assessment of cFos activation in CART-positive NAc neurons.

Results: CART knockdown increased baseline ICSS responding, whereas CART peptide administration suppressed ICSS behaviour, indicating that accumbal CART negatively regulates brain stimulation reward. CART siRNA enhanced SKF-38393- induced reinforcement, suggesting that CART restrains D1 receptor-mediated reward processing. Conversely, both CART siRNA and CART peptide reduced sucrose self-administration, demonstrating distinct regulation of brain stimulation and natural rewards. ICSS conditioning significantly increased NAc CART mRNA expression, while food reward produced a modest increase. CART siRNA reduced CART mRNA levels to 0.4-fold of controls. Increased cFos activation was observed in CARTpositive NAc neurons projecting to both the VTA and VP after ICSS.

Conclusion: Accumbal CART bidirectionally regulates motivated behaviours through CART-containing NAc→VTA and NAc→VP circuits, providing new insights into the neural mechanisms underlying reward and reinforcement.

Keywords: Cocaine- and amphetamine-regulated transcript (CART), Reward and reinforcement, Nucleus accumbens, Ventral tegmental area, Motivation

YSC04

Altered structural and synaptic plasticity, neurochemical changes contribute to depression- and anxiety-like behaviour in a rat model of Premenstrual Dysphoric Disorder (PMDD)

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Background: Premenstrual Dysphoric Disorder (PMDD) is a severe cyclical reproductive mood disorder characterized by presentation of symptoms in the luteal phase of the menstrual cycle. The exact pathophysiological mechanisms underlying PMDD remain poorly understood. Progesterone withdrawal model is a promising animal model for PMDD but warrants detailed characterization.

Purpose: This study aimed to characterize a rodent model of PMDD to study the pathophysiology of the disorder and the role of neurosteroids in PMDD.

Methods: Multiple progesterone withdrawal was carried out in which progesterone (6mg/rat) was administered intraperitoneally to adult female Wistar rats for 19 days. 48 hours after the last dose, assessment of anxiety-like behavior and depression-like was carried out. Plasma progesterone and corticosterone levels, brain amino acid neurotransmitter levels and spine density in pyramidal neurons of basolateral amygdala (BLA) and Cg1 region of medial prefrontal cortex were evaluated following progesterone withdrawal. Hippocampal field potential recordings were performed in the CA3-CA1 region to assess the synaptic plasticity changes following progesterone withdrawal.

Results: Progesterone withdrawal resulted in anxiety-like behavior in the home cage emergence and marbleburying tests and depression-like behavior in the forced swim test. Plasma progesterone levels were reduced and corticosterone levels elevated and brain amino acid neurotransmitter levels were altered following progesterone withdrawal. Progesterone withdrawal resulted in increased spine density in BLA and Layer II/III pyramidal neurons of Cg1 region. It was also found to modulate basal synaptic transmission, short-term, and long-term synaptic plasticity in the hippocampal CA3-CA1 region.

Conclusion: Complete characterization of the model will be useful for the detailed evaluation of the role of neurosteroids in the pathophysiology of PMDD. The findings in this model have ramifications in other mood disorders in women such as postpartum depression. Further studies have implications for the development of effective therapeutics for reproductive mood disorders.

Keywords: Progesterone withdrawal; Anxiety; Depression; PMDD; synaptic plasticity; neurosteroids

YSC05

Auditory P300 Responses During High Particulate Exposure Episodes: Pilot CaseCrossover Evidence from Healthy Adults

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Background: Subclinical effects of environmental stressors on human cortical information processing are difficult to detect using routine cognitive screening. The P300 component of auditory eventrelated potentials (ERPs) provides a temporally precise index of attentional allocation and stimulus evaluation and may be useful for detecting early functional changes during highparticulate-exposure episodes.

Purpose: This pilot study examined whether a short-term increase in personal PM2.5 exposure is associated with altered auditory P300 parameters in apparently healthy adults.

Methods: Apparently healthy non-smoker adult male volunteers were assessed in a within-person casecrossover design during two exposure periods: monsoon (lower particulate exposure) and crop-residue burning (higher particulate exposure). Twenty-four-hour personal PM2.5 was monitored using calibrated low-cost sensors colocated with a beta attenuation monitor. Neurophysiological assessment included auditory oddball ERP with P300 latency and amplitude measured at Pz. Screening cognitive measures included the Montreal Cognitive Assessment (MoCA) and Hindi Mental State Examination (HMSE). Time-varying covariates, including perceived stress, sleep, fatigue, physical activity, caffeine, and alcohol intake, were recorded at each visit. Wilcoxon signed-rank and Spearman correlation tests were used because of the limited sample size and non-normal within-person differences.

Results: Median 24-hour PM2.5 increased from 13.7 μg/m³ during monsoon to 123.9 μg/m³ during the high-exposure period ($p=0.0006$). P300 amplitude differed significantly between periods (7.3 vs 9.8 μV; $p=0.0076$), while latency did not show a significant period-wise difference (321 vs 326 ms; $p=0.53$). However, within-person increases in PM2.5 correlated with increases in P300 latency ($\rho=0.59$, $p=0.0047$). HMSE remained stable; MoCA showed a nonsignificant increase, consistent with possible practice effects.

Conclusion: These preliminary findings support the feasibility of integrating personal exposure monitoring with auditory ERP assessment. P300 may provide a sensitive neurophysiological signal of altered cortical information processing during short-term particulate exposure, even when conventional cognitive screening remains largely unchanged.

Keywords: P300; event-related potential; particulate matter; cortical information processing; environmental neurophysiology; air pollution

YSC06

Mimosine suppresses ferroptosis nexus linking labile iron, glutathione and lipid peroxidation in experimental animal model of neurodegeneration

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*

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Background: Ferroptosis is a regulated cell death driven by iron dependent lipid peroxidation and has been implicated in Parkinson's disease and Alzheimer's disease where iron overload is one of the causative factors. Hence iron chelation and use of lipophilic antioxidants has been employed as a therapeutic approach for suppressing neuronal degeneration. In the present study we illuminate the detrimental role of ferroptosis in neurodegeneration and the necessity to inhibit the ferroptosis by a plant based iron chelator mimosine.

Methods: We investigated the iron-chelating and antioxidant properties of mimosine using ferrozine and ferric reducing antioxidant power assays and characterized the iron–mimosine complex by UV– visible spectroscopy. Iron overload was induced in C57BL/6 mice by intraperitoneal administration of iron dextran (300 mg/kg) over a period of 27 days. Labile iron and reduced glutathione (GSH) levels were assessed in both differentiated SH-SY5Y neuron-like cells and iron-overloaded mice using the ferene assay, Turnbull's blue staining, and UV–visible spectroscopy. The expression levels of the ferroptosis-associated markers glutathione peroxidase 4 (GPX4) and acyl-CoA synthetase long-chain family member 4 (ACSL4) were examined by immunoblotting in both the experimental models.

Results: Mimosine formed a stable complex with iron at physiological pH and exhibited iron chelating potential comparable to the clinically investigated iron chelator deferiprone. Mimosine also exhibited robust antioxidant activity. Mimosine protected neuronal-like cells through chelation of labile iron and restoration of intracellular glutathione levels in both in-vitro and in-vivo studies. Treatment of C57BL/6 mice with mimosine in an iron overload model showed significant preservation of the striatal dopamine levels.

Conclusion: The present study reveals the role of mimosine as a cellular guardian of ferroptosis via iron chelation and antioxidant action. Mimosine could be developed into a potential therapeutic under iron over load conditions in diseases such as PD and AD.

YSC07

LOSS OF THE CHROMATIN MODIFIER- LSD1 IMPAIRS EPENDYMAL DEVELOPMENT AND CILIARY FUNCTION LEADING TO VENTRICULOMEGALY

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Structural enlargement of the cerebral ventricles, or ventriculomegaly (VM), is a common fetal brain abnormality associated with neurodevelopmental disorders, yet its mechanisms remain poorly understood. Dominant mutations in LSD1, a histone demethylase regulating gene expression during neurodevelopment, are linked to intellectual disability and VM in patients, connecting chromatin regulation to ventricular pathology. To define how LSD1 maintains ventricular integrity, we used a cortex-specific Lsd1 conditional knockout mouse model exhibiting fetal onset VM that persists postnatally. Mutant brains show enlarged ventricles with reduced cortical surface area and radial thickness. In situ hybridization for transthyretin revealed no structural differences in the choroid plexus, indicating that increased cerebrospinal fluid (CSF) production does not drive dilation. At postnatal day 5, mutants display reduced FOXJ1-positive ependymal cells and absence of motile cilia, demonstrating impaired ependymal differentiation and ciliogenesis. Single-cell RNA sequencing of the lateral ventricular wall revealed disrupted ependymal lineage trajectories and downregulation of motile cilia genes (TTL3, TUBB4B). CSF proteomic analysis identified pathway enrichments consistent with ventricular wall dysfunction, including glycolysis, pyruvate metabolism, and cysteine metabolism (log10 FDR < 5). Integration of transcriptomic and proteomic datasets identified candidate pathways with therapeutic potential. Behavioral assessment revealed deficits in exploratory and anxiety-related paradigms, linking early ventricular developmental defects to functional outcomes. Together, these findings establish LSD1 as a key regulator of ependymal development and ventricular homeostasis and define actionable molecular targets for translational intervention in ventriculomegaly.

YSC08

Developmental trajectories of Inhibitory Interneurons and Perineuronal Nets in the Human Auditory Cortex

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Background: The auditory cortex is fundamental for processing auditory information. Earlylife auditory experience guides the formation of synaptic connections and language perception. Disruption of auditory input during this period can lead to deficits in language and communication. These experience-dependent changes are more prominent during the sensitive period, which is regulated by inhibitory interneurons: somatostatin (SOM) and parvalbumin (PV), as well as by perineuronal nets (PNNs), a component of the extracellular matrix. Since the developmental trajectories of these key components remain unexplored in the human auditory cortex, we decided to chart their maturation from the prenatal period to adulthood.

Purpose: Hearing loss is projected to affect over 900 million people by 2050, and evidence suggests that early cochlear implantation provides better outcomes. Detailed knowledge of the sensitive period of the auditory cortex is therefore essential for optimizing intervention strategies.

Methods: Post-mortem human auditory cortex samples were analysed across five developmental stages: fetal, postnatal, pediatric, adolescent, and adult. Immunohistochemistry, double-labelling, confocal imaging, stereology, and three-dimensional reconstruction were utilized to quantify the density, distribution, and morphology of SOM+ and PV+ interneurons, and PNNs.

Results: Our results demonstrate that SOM+ and PV+ interneurons are sparse during early life, increase in density during pediatric and adolescent stages, and decline in adulthood. Their morphological complexity decreases with age. Perineuronal nets emerge postnatally and gradually increase in number and intensity (an indication of thickness) with age, and surround 80% of PV+ interneurons in adulthood, indicating progressive stabilization of inhibitory circuits and reduced plasticity.

Conclusions: Our findings provide a normative baseline for the development of the auditory cortex, and are also important for our understanding of neurodevelopmental disorders associated with auditory dysfunction.

SS Parmar Oration

Title: Neuronal Injury Model Reveals Differences in Axon and Dendrite Regeneration

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Background: Ageing is an inevitable process through which our brain and body undergo progressive changes, some of which have highly unfavourable outcomes. Many neurodegenerative diseases, such as Alzheimer's, Parkinson's and Frontotemporal dementia, are caused by the loss of many neurons in the functional brain circuits. One approach to treating these conditions is to introduce new neurons that can integrate into functional circuitry. Clinicians have long struggled to find a cure for patients with nervous system injuries or degeneration because neurite regeneration fails in the central nervous system, preventing the re-establishment of functional connections with target tissues.

Purpose: Our group at the National Brain Research Centre have been investigating the molecular mechanism of axon regeneration. Axons are long cables through which nerve cells propagate electrical signals to their postsynaptic neurons.

Methods: We are using the nematode *C. elegans* as a model to identify molecular regulators of neurite regeneration. The transparent body of the nematode *C. elegans* has enabled us to use a laser to sever axons at precise locations.

Results: Previous studies have identified a conserved signaling pathway involving Dual Leucine Zipper Kinase (DLK) that is required for axon regeneration following injury. We further showed that axon regeneration leads to functional restoration in early life, and that this ability is lost in old age. Recently, we found that dendrites (the information-receiving units of neurons) can also regenerate following physical injury. However, the axon regeneration pathway DLK is not required for dendrite regeneration. We uncovered that the fibroblast growth factor receptor pathway is necessary within the neuron to initiate branching from the broken dendrite tip. In contrast, the same signaling mechanism within epidermal cells safeguards the distal dendrites from degeneration.

Conclusion: This suggests that the molecular mechanism underlying dendrite regeneration is distinct from that of axonal regeneration. Collectively, our findings significantly advance the fundamental understanding of neurite repair and functional reconnection.

PN Tandon Oration

From Prof. P. N. Tandon's Laboratory to an AI-Enabled Future: Five Decades of Simulation-Based Neurosurgical Skills Training at AIIMS, New Delhi

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Background: Neurosurgical training has traditionally relied on apprenticeship at the operating table, a model strained by shrinking case volumes and rising patient-safety expectations. Simulation-based education has emerged worldwide as an ethical, reproducible route to mastering complex microneurosurgery, neuroendoscopy, and neuro-drilling skills before these are practiced on patients.

Purpose: This oration traces the evolution of the Experimental Micro-Neurosurgery Laboratory, AIIMS, New Delhi founded in 1971 by Prof. P. N. Tandon and Prof. A. K. Banerji, into today's Neurosurgery Skills Training Facility (NSTF) delivering hands-on cadaveric, animal, and synthetic simulation training, and Neurosurgery Education and Training School (NETS) providing virtual 3D education and AI-based skills evaluation, and assesses their combined impact on neurosurgical education in India and abroad.

Methods: A retrospective review of NSTF and NETS institutional training records, curricular documents, and publications spanning 1971–2026 was undertaken across four domains: DST+DBT+DHR supported NSTF hands-on infrastructure - fully simulated operating theatre and graded structured modular curriculum - silicone-tube, chicken-wing, live-animal micro-vascular / neural anastomosis, cadaveric microneurosurgery / neuroendoscopy, and neuro-drilling, refined through WFNS, Indo-German, Indo-Japanese, Indo-US collaborations; DHR-ICMR supported NETS virtual 3D education - open-source e-learning and 3D-animation modules; DBT-CoE supported formative and summative assessment - the AIIMS-NETS scoring system and AI-augmented automated skill scoring extended by AIIMS–IITD program applying deep learning, instrument instance-segmentation, video-action segmentation, and rank-loss representation learning; and indigenous technology development - 3D-printed vascular models and virtual-reality/hybrid simulators.

Results: NSTF has delivered hands-on training to over 3,000 neurosurgeons - 517 regular residents and 332 short-term trainees across 16,664 sessions, 932 graduate neurosurgeons through 29 workshops, and 1,463 delegates over 146 weekend courses - from more than fifteen countries. NETS has extended this reach virtually with 1140689 views, 8746 likes, 10860 shares, 951subscribers. NSTF and NETS has generated 10 patents, 16 indigenous technologies, and a growing peer-reviewed body of AI research on surgical-skill evaluation, culminating in the AIIMS+IITD NEUROMENTOR Prix Galien 2024 and NEUROINNOVATE Prix Galien 2026 platforms.

Conclusion: What began as Prof. Tandon's Experimental Micro-Neurosurgery Laboratory has matured into a globally benchmarked, self-sustaining ecosystem integrating cadaveric, animal, synthetic, and AI/VR-based modalities within a validated, competency-based curriculum. This trajectory shows that sustained institutional vision, nurtured through international collaboration, can safely bridge the transition from novice to competent neurosurgeon, offering a reproducible template for skills-training laboratories across India and other resource-varied settings worldwide.

Keywords: Neurosurgery Simulation; Neurosurgery Hands-on Skills Training; Virtual 3D Neurosurgical Education; Competency-based Curriculum, AI-based Skill Evaluation; Microneurosurgery; Neuroendoscopy; Surgical Instrument Instance Segmentation; Video-Action Segmentation, Rank-Loss Representation Learning; 3D Printing; Artificial Intelligence - Deep Learning & Machine Learning; Virtual Reality

Young Scientist Colloquium-II: DM Kar Prize

YSC09

Mitochondria-Targeted Antioxidants Restore Striatal Dopamine and Protect Nigral Neurons in Parkinson's Disease Model

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Background: Mitochondrial dysfunction and oxidative stress are central contributors to dopaminergic neurodegeneration in Parkinson's disease (PD), necessitating targeted delivery strategies for neuroprotective therapeutics. However, achieving efficient mitochondrial localization while maintaining biocompatibility remains a significant challenge.

Purpose: This study aimed to develop and optimize a dendritic polyglycerol-based nanocarrier (MitoPG) functionalized with triphenylphosphonium (TPP^+) for selective mitochondrial targeting and evaluate its therapeutic potential in PD models.

Methods: MitoPG nanocarriers were synthesized by conjugating TPP^+ moieties onto dendritic polyglycerol (PG) scaffolds, followed by systematic optimization of PG molecular weight and TPP^+ surface density. Mitochondrial targeting efficiency, cytotoxicity, and bioenergetic impact were assessed in neuronal cell models, including MPP^+-induced stress conditions. Blood–brain barrier permeability was evaluated using an in vitro non contact model. Antioxidants (curcumin and quercetin) were covalently conjugated to MitoPG for proof of concept demonstration and tested in rotenone-induced SH-SY5Y cells. In vivo efficacy and safety were evaluated in MPTP-induced C57BL/6 mouse models, including behavioral, biochemical, and histological analyses.

Results: The optimized MitoPG formulation demonstrated high mitochondrial accumulation with negligible cytotoxicity and no disruption of mitochondrial membrane potential, respiration, or basal bioenergetics. Efficient mitochondrial localization was retained under toxin-induced stress and across an in vitro blood–brain barrier model. Oral administration showed good tolerability in mice, with an acute LD_{50} of 310 mg/kg and no systemic toxicity. MitoPG conjugation significantly improved the aqueous solubility of curcumin and quercetin. In rotenone-treated SH-SY5Y cells, MitoPG-conjugated antioxidants reduced mitochondrial oxidative stress and enhanced neuronal survival compared to free drugs. In MPTP-induced mice, MitoPG–curcumin improved motor function, restored striatal dopamine levels, and reduced dopaminergic neuronal loss in the substantia nigra.

Conclusion: MitoPG represents a biocompatible and efficient mitochondrial-targeted nanocarrier capable of delivering antioxidant therapeutics with enhanced efficacy. This platform offers significant potential for the treatment of PD and other neurodegenerative disorders associated with mitochondrial dysfunction.

Keywords: Mitochondrial dysfunction, Parkinson's disease, Blood Brain Barrier, Triphenyl phosphonium, oxidative stress

YSC10

Astrocyte-Derived Exosomal Signaling Drives Pathological Neuronal Transcriptional Reprogramming in Alzheimer's Disease

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Background: Alzheimer's disease (AD) is characterized not only by amyloid-β and tau pathology but also by early synaptic dysfunction, neuroinflammation, and metabolic impairment. Astrocytes play a critical role in maintaining neuronal homeostasis through extracellular vesicle-mediated communication, including astrocyte-derived exosomes (ADEs); however, the functional consequences of diseaseassociated alterations in ADE cargo remain poorly understood.

Purpose: This study aimed to determine whether ADEs from AD patients carry altered molecular cargo that contributes to neuronal dysfunction and cognitive impairment by disrupting cellular homeostasis.

Methods: ADEs were isolated from the plasma of clinically diagnosed AD patients and age-matched controls and analysed by quantitative proteomics. To assess their functional effects, primary cortical neurons were treated with patient- and control-derived ADEs followed by transcriptomic analysis. In parallel, P0 C57BL/6 mice received intracerebral injections of AD-derived ADEs or PBS. Cognitive function was evaluated over a two-month period using behavioural assays, after which brain tissues were collected for immunohistochemical, biochemical, and molecular analyses.

Results: Proteomic profiling of ADEs revealed elevated levels of thioredoxin-1 (Trx-1) and other diseaseassociated proteins. Neurons exposed to AD-derived ADEs exhibited transcriptional changes linked to oxidative stress, inflammation, and disrupted redox homeostasis, including altered expression of PRDX1, PRDX5, GLRX, and PARK7. Pathway enrichment analysis identified dysregulation of the mTOR signaling pathway. In vivo, mice treated with AD-derived ADEs showed impaired novel object recognition and spatial memory. Consistently, brain tissue analyses revealed increased expression of oxidative stress-related proteins, as confirmed by immunohistochemistry and quantitative immunoblotting.

Conclusion: Together, these findings demonstrate that AD-associated ADEs carry altered molecular cargo capable of reshaping neuronal transcriptional programs and impairing cognitive function. Our results suggest that disrupted astrocyte–neuron communication contributes to neuronal vulnerability in Alzheimer's disease and highlight exosome-associated Trx-1 as a potential biomarker for disease progression.

YSC11

Kallikrein–Kinin-Mediated Immune Activation in Age-Associated Choriocapillaris Degeneration

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Background: Aging and age-related ocular diseases, including age-related macular degeneration, are linked to significant choroidal capillary loss, characterized by progressive endothelial loss, reduced fenestration, pericyte degeneration, and capillary rarefaction, resulting in impaired perfusion and a pro-inflammatory microenvironment. Emerging evidence suggests that chronic para-inflammation and activation of the kallikrein–kinin system (KKS) may contribute to these degenerative changes.

Purpose: To investigate the role of kallikrein–kinin-mediated immune activation in ageassociated choriocapillaris degeneration and its relationship with structural and molecular alterations in the aging choroid.

Methods: Male Wistar rats aged 4, 8, 12, and 16 months were studied. Choroidal tissues were analysed using transmission electron microscopy (TEM), immunohistochemistry, ELISA, western blotting, and SWATH-MS-based proteomics. The expression of inflammatory markers, including CD68, TLR4, MHC-II, CX3CR1, NLRP3, and vascular markers such as PECAM-1 and VEGFR2, was evaluated. Proteomic analyses were performed to identify pathways associated with age-related choroidal degeneration.

Results: Aging was associated with progressive ultrastructural degeneration of the choriocapillaris, characterized by endothelial flattening, loss of fenestrations, basement membrane thickening, and capillary dropout. Increased activation and accumulation of macrophages and other immunocompetent cells were observed in aged choroid, accompanied by elevated expression of pro-inflammatory mediators. Proteomic analysis identified significant upregulation of kininogen-1 and kininogen-2, implicating activation of the kallikrein–kinin pathway in the aging choroid. This pathway was associated with enhanced inflammatory signalling, complement activation, extracellular matrix remodelling, and endothelial dysfunction. Concurrent downregulation of vascular homeostatic proteins, including PECAM-1 and VEGFR2, further indicated compromised choroidal integrity.

Conclusion: The present study demonstrates that activation of the kallikrein–kinin pathway is closely associated with immune dysregulation and structural degeneration of the aging choriocapillaris. Kallikrein–kinin-mediated inflammation may represent a key mechanistic link between chronic para-inflammation and microvascular degeneration in the aging eye, highlighting this pathway as a potential therapeutic target for preventing age-related choroidal diseases, including age-related macular degeneration.

Keywords: Aging, Choriocapillaris, Kallikrein-Kinin Pathway, Immunocompetent Cells, Age-Related Choroidal Degeneration

YSC12

Central amygdala to hypothalamic paraventricular nucleus glutamatergic circuitry regulates anger-induced physiological and behavioural responses

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Background: Anger is negative emotional state ensued by disappointment, frustration, judgement, rejection, fear, unfair treatment and criminal activities. Persistent anger is linked to neuropsychiatric disorders and increases cardiovascular risk through activation of neuroendocrine and sympathetic nervous systems. Studies on the neurobiology of anger shows the involvement of central amygdala (CeA) and hypothalamic paraventricular nucleus (PVN) in regulation of anger. PVN receives glutamatergic projections from CeA that influence hormonal and cardiovascular responses. Therefore, we hypothesized that the CeAPVN glutamatergic pathway may modulate anger-like behaviour and associated responses.

Purpose: To investigate the role of CeA-PVN glutamatergic circuitry in the processing of anger and associated responses in rats.

Methods: We employed protocol in which food restricted (FR) rats with sight and smell of food but denied access, shows intense biting to inanimate object, considered an anger-like phenotype. Blood pressure and heart rate, locomotion and cognition ability were monitored using tail cuff method, ANY-maze and novel object recognition test, respectively. Serum corticosterone and nor-epinephrine levels were analysed by ELISA and HPLC-ECD, respectively. The molecular changes in the PVN traced using immunohistochemistry (co-labelling of cFos+CRF, fast blue (FB)+glutamate), RT-qPCR for mRNA analysis and release of glutamate in microdialysates collected from PVN.

Result: Denial of food access increased biting activity, locomotor activity, heart rate, blood pressure and altered discrimination. Concomitantly, increased serum corticosterone and norepinephrine during biting activity. FB positive glutamatergic neurons were observed in the CeA. glutamate release was increased during biting activity in the PVN. Furthermore, The CRF+c-Fos immunoreactive cells and CRF mRNA increased within PVN.

Conclusion: Our findings highlight the role of CeA-PVN glutamatergic circuitry in processing anger-like response. Understanding neurobiology of anger may aid in developing targeted therapies for uncontrolled anger and emotional dysregulation, improving future clinical interventions.

Keywords: Anger-like behaviour, Neuroendocrine system, Amygdala, Paraventricular nucleus of hypothalamus

YSC13

Chloride Homeostasis at the Crossroads of Excitatory–Inhibitory Imbalance, and Neurobehavioral Comorbidities in Temporal Lobe Epilepsy: Therapeutic Implications

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Background: Altered chloride homeostasis is a critical contributor to epileptogenesis. Sodium–Potassium–Chloride Cotransporter 1 (NKCC1)-mediated intracellular chloride accumulation compromises GABAergic inhibition, disrupting the excitatory–inhibitory balance and promoting recurrent seizures, cognitive deficits, mood dysfunction, and pharmacoresistance in chronic epilepsy.

Purpose: This study investigated chloride homeostasis, excitatory–inhibitory network dynamics during epileptogenesis and chronic epilepsy and their relationship with seizure activity, behavioral comorbidities, and therapeutic responsiveness.

Methods: Temporal lobe epilepsy was induced in adult male Wistar rats using the lithium–pilocarpine model. Seizure development was characterized through behavioral assessments. Hyperexcitability, well-being, affective states, and cognitive functions were evaluated using validated behavioral paradigms, including the sucrose preference test, splash test, open field test, light–dark test, novel object recognition task, novel object location task, and T-maze. Neurochemical analyses were performed to quantify neurotransmitter levels by high-performance liquid chromatography (HPLC) and assessment of chloride homeostasis are being done using ELISA in discrete brain regions at different stages following seizure induction. Pharmacological modulation of NKCC1 activity and GABAergic signaling was subsequently evaluated in chronic epilepsy.

Results: Chronic epilepsy was associated with spontaneous recurrent seizures, behavioral impairments, and region-specific alterations in neurotransmitter levels. Pharmacological interventions targeting chloride homeostasis and GABAergic tone produced differential effects on seizure burden, mood-related behaviors, and cognition. These findings highlight temporal and regional heterogeneity in epileptic pathophysiology and therapeutic responses.

Conclusions: The study demonstrates a critical role for excitatory–inhibitory network dysregulation and chloride homeostasis in the progression of temporal lobe epilepsy and its associated comorbidities. Targeting these mechanisms may provide a complementary therapeutic strategy for improving seizure control and quality of life in epilepsy.

Keywords: Epilepsy, Seizure, Chloride Homeostasis, Cognition, Neurotransmitters

YSC14

Molecular Signatures of Nano-neonicotinoid Neurotoxicity: Linking Striatal Gene Expression to Neurobehavioral Dysfunction in Mice

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Background: Nanopesticides including nano-neonicotinoid are being increasingly used in agriculture, but the research on their neurotoxic potential are very limited. Nanoformulations can easily cross the blood-brain barrier due to their nanoscale size, potentially affecting brain and leading to long-term effects. Therefore, evaluating the neurotoxic potential of these nanopesticides has become imperative.

Purpose: To investigate the effect of nano-neonicotinoid pesticides exposure on striatal gene expression, neurotransmission and neurobehavioural dysfunction in mice.

Methods: Nanoformulations of imidacloprid and acetamiprid were orally administered to male BALB/c mice for 28 days. Neurobehavioral tests, including open field and footprint analysis, were conducted in these mice at the end of treatment. After 28 days, mice were sacrificed, brains were removed to dissect the corpus striatum for analysis of neurotransmitter levels and gene expression related to dopaminergic signaling, monoamine metabolism, stress response and apoptosis.

Results: Exposure to nano-imidacloprid, nano-acetamiprid and their combination caused a significant decreased in motor activity and altered gait pattern in mice. Neurochemical analysis showed alterations in the levels of GABA, dopamine, DOPAC, HVA, serotonin and 5-HIAA in the striatum as compared to controls. Upregulation of MAO-A, MAO-B, COMT genes was observed indicating disturbed catecholamines homeostasis. Increased stress response was observed with elevated expression of FKBP5 and Nrf2 genes. Upregulation of apoptotic markers such as Caspase-3, Caspase-9, Bax and decreased expression of BCl2 was observed in the exposed groups as compared to controls.

Conclusion: The results demonstrate that nano-neonicotinoid pesticide exposure induces altered neurochemical levels and striatal gene expression linked with neurobehavioral deficits in mice.

Keywords: Nano-neonicotinoid, neurotoxicity, neurobehavioural dysfunction, nanopesticides

YSC15

Sex-Specific Effects of Nutritional Ketosis on Sugar Withdrawal Symptoms, Sugar Craving and Compulsive-like Behavior in C57BL/6 Mice

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Sugar bingeing induces maladaptive neuroadaptations in the reward neurocircuitry, leading to loss of dietary control, hedonic overeating, and withdrawal symptoms. A low-carbohydrate and high-fat ketogenic diet (KD) and its bioactive metabolites have been suggested as a nutritional therapy for the treatment of food addiction and binge eating; however, scientific evidence is scarce. This study investigated the effects of nutritional ketosis on sucrose craving, anxiety, and compulsive-like behavior in a preclinical model of binge sucrose drinking and withdrawal. Male and female mice binged on a sweet solution when given free access to food and a choice between water and a 10% (w/v) sucrose solution for eight weeks. Female mice showed a stronger preference for sucrose in the two-bottle choice and Vogel conflict tests, indicating greater motivational sucrose drinking. Three weeks of KD during sucrose withdrawal promoted weight loss in male and female mice while reducing blood glucose levels in males. KD could not improve sucrose withdrawal-induced anxietylike symptoms in male and female mice; however, it improved locomotor activity in males during an open field test. KD suppressed reinstated sucrose bingeing in males and females and attenuated compulsive-like behavior in sucrose-withdrawal female mice. KD blunted transcription of dopamine receptors Drd1 and Drd2 in the prefrontal cortex of sucrose withdrawal females while increasing neuroinflammatory markers (IL1β, IL-6, IL-10) in the prefrontal cortex of males. Moreover, KD modulated the transcription of rate-limiting enzymes in ketone metabolism in the prefrontal cortex of sucrose-withdrawal males and females. Overall, this study demonstrates the sex-specific effects of nutritional ketosis on sugar craving, compulsive-like behavior, and neuroinflammatory signaling following sucrose withdrawal, paving the way for precision therapeutics for food addiction and binge eating disorder.

Keywords: Anxiety; Binge eating disorder; Food addiction; Neuroinflammation; Nutritional ketosis; Sucrose withdrawal; Sex differences

YSC16

Acute Japanese encephalitis virus-associated gut dysbiosis and protective effects of short-chain fatty acids on neuroinflammation in neonatal mice

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Background: Gut microbiota and their metabolites, short-chain fatty acids (SCFAs), have been known to facilitate favourable disease outcomes in several CNS pathologies. Japanese encephalitis virus (JEV), a neurotropic flavivirus, causes severe neurological complications in juvenile infection.

Purpose: This study investigates the gut-microbiome alterations during the progression of JEV infection in a neonatal mouse model and evaluates the neuroprotective effects of SCFAs, in identifying microbiome-based therapies for supportive care in JEV infection.

Methods: Postnatal day 10 BALB/c mouse pups were intraperitoneally challenged with 3.5x104 plaqueforming units of JEV. Gut microbiome analysis was performed using 16S rRNA V3-V4 sequencing on animals sacrificed during the early and acute phases of infection. Infected mice received an SCFA cocktail (200 mM- acetate: propionate: butyrate in a 3:2:1 ratio; orally) for 6 consecutive days. The animals were monitored daily, and immunoblotting as well as PCR were performed on samples isolated at different time points.

Findings: Infected pups manifested acute infection at 6-7 DPI with elevated levels of TNF-α, IFN-γ, IL-6, IL-12, and MCP-1in CNS and serum. Sequencing revealed a decline in abundance of phyla Firmicutes and genus Lactobacillus in acute JEV infection. PICRUSt2 prediction suggested a decline in SCFA-associated pathways in acute JEV samples. SCFA treatment prolonged survival and delayed symptom onset and CNS inflammation. This was coupled with enhanced expression of blood-brain barrier (BBB) integrity markers occludin, claudin-3, claudin-5, claudin-12 and VEcadherin in the brain.

Conclusion: Our findings highlight gut-microbiome dysbiosis and a potential reduction of SCFA-producing bacteria during acute JEV infection in a neonatal mouse model. This could be associated with severe systemic inflammatory response and reduced feeding. SCFA administration delayed infection progression, possibly by hindering virus entry to the CNS by enhancing BBB integrity. Suggesting that SCFA supplementation can serve as a safe, translatable approach to managing JEV outcomes in pediatric viral encephalitis.

Keywords: Gut-brain axis, Gut microbiota, Japanese encephalitis, short-chain fatty acids, neuroinflammation, CNS infections

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Connectomics and adaptive reorganisation

S35
GABAergic dysfunction: The emerging role of the presynaptic organizer Bassoon

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Background: Compromised excitation and inhibition (E/I) balance due to GABAergic dysfunction has been detrimental in various synaptopathies. The presynaptic active zone organizer protein Bassoon is present at both glutamatergic and GABAergic brain synapses, with yet unexplored functions at GABAergic synapses. Bassoon is involved in multiple synaptic functions including regulation of presynaptic proteostasis, synapto-nuclear communication and development of CA3 mossy fiber terminals.

Purpose: To understand Bassoon´s role in GABAergic synapses in controlling brain physiology and behavior.

Methods: Conditional knock-out (KO) mice lacking Bassoon in GABAergic interneurons in forebrain ($Bsn^{Dlx5/6}$cKO)[1] and Conditional knock-out (KO) mice lacking Bassoon specifically in Parvalbumin (PV) interneurons were employed. These mice were tested for physiological and behavioral assessments.

Results: The $Bsn^{Dlx5/6}$cKO mice display reduced synaptic efficacy of inhibitory synapses and deficits in GABAergic neurotransmission at hippocampal pyramidal synapses. Further, altered network activity along with reduced numbers of parvalbumin (PV) interneurons, strongly supports GABAergic dysfunctions and rearrangement of the network at hippocampal region of $Bsn^{Dlx5/6}$cKO. These cKO mice also display profound mitochondrial and metabolic dysregulation, hinting towards dysfunction of subset of GABAergic population-PV interneurons. Furthermore, $Bsn^{Dlx5/6}$cKO mice display autism spectrum disorder (ASD)-related core symptoms such as pronounced social behavioral deficits, and comorbid symptoms including increased anxiety and epileptiform activity. Further our preliminary findings employing the mice lacking *Bsn* specifically in parvalbumin (PV) interneurons (Bsn^{PV}cKO) suggest, strong social behavioral and physiological deficits in Bsn^{PV}cKO, strikingly similar to $Bsn^{Dlx5/6}$cKO.

Conclusion: Altogether, our results indicate that Bassoon deficiency in GABAergic interneurons specifically in PV interneurons is sufficient to cause prominent social behavioral deficits reminiscent to ASD and provide evidence for a causal involvement of specific GABAergic synapses in the emergence of ASD-related behavioral and physiological phenotypes.

S36
The Role of the Basal Ganglia in Value-Guided Decisions

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Background: The basal ganglia (BG) are widely thought to mediate action selection based on outcome expectations, thereby enabling value-guided decision making. However, recent studies have suggested alternate roles for the BG in controlling kinematics or movement vigour. Moreover, the causal contribution of the BG to action selection has not been critically examined in a reinforcement learning framework, where action-reward associations continually change.

Purpose: This study was aimed at critically examining the contribution of the basal ganglia to value-guided decisions.

Methods: We trained rats to solve a complex, four-choice task where reward probabilities associated with all options changed every trial block. We tested the necessity of the basal ganglia for making value-guided decisions through excitotoxic lesions of subregions of the dorsal striatum in rats. To investigate BG encoding of value-guided decisions, we carried out electrophysiological recordings from the dorsal striatum during behaviour
.
Results: We found that striatal lesions did not affect rats' ability to accrue reward from choices but instead had subtle effects on their ability to explore different actions, indicating that the striatum is not essential for action selection. We found that striatal activity primarily represents actions at the level of continuous movement kinematics rather than high-level discrete decisions.

Conclusion: Our results call into question long-standing views about the role of the basal ganglia in value-guided decision-making. Our findings suggest that the basal ganglia are primarily responsible for value-guided action specification rather than action selection.

Keywords: Basal ganglia, decision-making, reinforcement learning, systems neuroscience, behaviour.

S37

Extreme Heterogeneity and Super-Growers: Mapping Persistent Hippocampal Neurogenesis in Adult Humans

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Background: Whether hippocampal neurogenesis persists throughout human aging remains a matter of debate. We investigated immunohistochemical, ultrastructural, and transcriptomic evidence for persistent hippocampal neurogenesis across the human lifespan using postmortem human hippocampal tissue.

Materials and Methods: Postmortem hippocampal tissue samples from individuals ranging from childhood to old age (N = 30) were examined. Clinical histories, including neurological and psychiatric disorders, systemic diseases, and alcohol or substance abuse, were reviewed. Tissues were fixed in 4% paraformaldehyde and processed for hematoxylin and eosin (H&E) and Nissl (cresyl violet) staining. Immunohistochemistry (IHC) and immunofluorescence (IF) were performed using a panel of neurogenesis and senescence-related markers. Stained sections were examined by bright-field and confocal fluorescence microscopy, and images were analysed using ImageJ (NIH). Unbiased stereological analyses were performed on representative samples from each age group. Bulk RNA sequencing and immuno-transmission electron microscopy (immuno-TEM) were used to validate the immunohistochemical findings.

Results: Newly generated neurons were identified in the subgranular zone (SGZ) of the dentate gyrus (DG) in adult individuals, including the elderly. Evidence of a stage-specific neurogenic programme, spanning neural stem cell proliferation, neuronal differentiation, migration, and integration into the dentate gyrus, was observed. Transcriptomic analysis supported the persistence of the neurogenic programme into old age, and immuno-TEM confirmed the expression of key neurogenesis-associated markers. The number of newborn neurons declined significantly from childhood to old age, with only a low level of neurogenesis detected after childhood in individuals without significant clinical history. Nevertheless, marked inter-individual heterogeneity was observed across all age groups.Notably, we identified a subgroup of **"super-growers,"** comprising young adults who died by suicide and occasional older individuals with histopathological evidence of neurodegenerative disease, both exhibiting unexpectedly high levels of hippocampal neurogenesis.

Conclusions: Our findings demonstrate that the human hippocampus retains the capacity for neurogenesis throughout life, although its extent varies markedly among individuals. Persistent hippocampal neurogenesis may represent an intrinsic mechanism contributing to resilience against age-related cognitive decline. The identification of enhanced neurogenesis in selected pathological conditions, together with evidence of neurogenic dysfunction in suicide, suggests previously unrecognized mechanisms of disease that warrant further investigation and may ultimately provide new therapeutic opportunities.

Keywords: Hippocampus, adult neurogenesis, immunohistology, human brain, suicide, Alzheimer's.

S38

Task demands shape hippocampal function

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Background: Neural function is often predicted from connectivity. While such predictions have been tested, tests often underplay the influence of task demands on function.

Purpose: We demonstrate using multiple experimental and modelling paradigms that the function can change in response to changing task demands.

Methods: We recorded neural activity from rats foraging in a variety of arenas to understand neural correlates of behaviour and how they change as a function of task demands. We also modelled theta phase precession using an excitatory-inhibitory neuron pair.

Results: Home ranges of rats range from tens of m^2 to km^2. In contrast, typical hippocampal spatial representation studies use arenas <= 1 m^2. We showed that changing arena size from 0.23 m^2 to 17.2 m2 fundamentally alters the hippocampal function. The hippocampus shows efficient encoding that increases its spatial selectivity and multiscalarity with the arena size. These results demonstrate the need for studying spatial representations in arenas of ethologically relevant scale and complexity to understand the spatial encoding capabilities of the hippocampus.We show that functional gradient predicted along the transverse axis of CA1 based on its entorhinal inputs may be modified by task demands. Both spatial selectivity as well as theta oscillatory modulation and phase precession gradients shown in some tasks are absent in the others. This raises a question of what inputs contribute to theta modulation and phase precession. We show that increase in non-theta non-spatially modulated inputs can transform non phase precessing cells into precessing cells.

Conclusion: Together, these findings demonstrate that task demands and corresponding changes in relative strengths of inputs can drastically alter the hippocampal output. Thus, while structural connectivity sets absolute boundaries on the range of possible outputs, actual output cannot be predicted from structure without regard to the task demands as well as non-task variables.

Keywords: Hippocampus, Spatial Navigation, Electrophysiology, Simulations

ST15

Role of orexin-expressing neurons in cerebellar dentate nucleus in goal-directed reward seeking behavior

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Background: Cerebellum is known for motor functions. Recent findings suggest the cerebellar involvement in myriad of non-motor functions including reward processing attributed to deep cerebellar nuclei (DCN). However, the neural substrates in the DCN involved in reward processing remain poorly understood.

Purpose: The dentate nucleus (DN) is a largest nucleus in DCN and is known to encode expectation and choice outcomes suggesting its involvement in decision-making and reinforcement learning. For the first time, we have observed neuropeptidergic neurons in the DN of the rat that expresses orexin peptide. Therefore, the overarching goal of the present study is to investigate the role of orexin neurons in goal-directed behavior.

Methods: Adult male Wistar rats (200-225 g) are subjected to Y-maze and nose-poke operant conditioning. Using chemogenetic inhibition/activation and siRNA-induced knock-down strategies, the orexin function in the DN was manipulated. Using immunohistochemistry and RT-PCR, the response of orexin neurons in DN was examined during different behavioral and *in-vivo* interventions. The AlexaFluor-CTB was used for the retrograde tracing of orexin neurons.

Results: The orexin neurons in DN was stimulated by nose-poke operant and Y-maze conditioning using sweet pellets. However, the conditioning in same paradigms by using aversive stimuli, such as squeaky noise, did not affect the orexin expression. Similarly, the presentation of sweet pellets or sucrose-drinking in home-cage did not alter the orexin neurons in DN. Moreover, the CTB tracer injected in the ventral tegmental area (VTA) co-labelled the orexin neurons. These results strongly suggest the role of orexin neurons in decision-making for reward seeking behavior. The chemogenetic studies supported this notion. While chemogenetic activation of orexin neurons improved the reward-seeking behavior, the chemogenetic inhibition hampered the activity.

Conclusion: The current study reports the novel group of orexin cells in DN, that serves in goal-directed behavior for reward-seeking through its possible interaction with VTA.

Keywords: Reward, orexin, cerebellum, dentate nucleus, goal-directed behavior.

ST16

Progressive Alterations in Visual Cortical Activity during Retinal Degeneration: Electrophysiological Assessment in Genetic and Chemically Induced Mouse Models

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Background: Retinal degeneration (RD) causes loss of photoreceptors, resulting in profound alterations in visual pathway. While retinal remodeling has been extensively investigated, the effects of reduced retinal input on cortical neuronal activity remain poorly understood. Understanding cortical changes during degeneration is essential for developing effective vision restoration strategies.

Purpose: This study aimed to investigate the physiological activity in the primary visual cortex (V1) of genetic (*rd1*) and chemically induced (N-methyl-N-nitrosourea; MNU) models of RD at different stages of RD.

Methods: RD was confirmed by retinal evaluation. *In vivo* extracellular recordings were obtained from V1 of WT, *rd1*, and MNU-treated mice (3, 5, and 7 day). Spontaneous cortical activity was quantified using power spectral density (PSD) analysis, while VEP, PSTH and raster plots were assessed using LED stimulation.

Results: Alterations in cortical activity were observed across the RD models. Both *rd1* and MNU mice exhibited electrophysiological profiles that differed from WT. Among the MNU groups, spontaneous activity demonstrated a progressive decline with disease progression, with MNU day 3 exhibiting the highest spectral power, followed by day-5 and day-7. Similar trend was observed in LED-evoked responses, where response magnitude progressively decreased in MNU mice, reflecting RD and reduced visual input to the cortex. These findings indicate that cortical neuronal activity changes dynamically with the severity of retinal damage.

Conclusion: The present study demonstrates that both genetic and chemically induced RD produces distinct changes in spontaneous and stimulus-evoked cortical activity. The progressive reduction in cortical responses across MNU day 3, 5, and 7 highlights the temporal evolution of cortical dysfunction following RD. These findings provide important insights into V1 during vision loss and establish a framework for evaluating future therapeutic interventions aimed at restoring visual function.

Keywords: Retinal degeneration; Primary visual cortex; MNU

SYMPOSIUM X

Cell and Molecular Biology of Neurons

S39

Role of astrocytes in long-lasting adverse behavioural effects of early life stress

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Background

Early Life Stress (ELS) is a primary risk factor for the development of Major Depressive Disorder (MDD). While research has traditionally focused on neuronal dysfunction, emerging evidence highlights the central role of astrocytes—non-neuronal cells essential for mood regulation—in depression pathophysiology. We hypothesised that ELS disrupts the critical postnatal window of astrogliogenesis, creating a lasting cellular deficit that confers lifelong psychiatric vulnerability.

Purpose: This study aimed to investigate the hypothesis that stress-induced elevations in glucocorticoids (GCs) inhibit neural stem cell (NSC) proliferation by activating the GSK3β pathway, which enhances the ubiquitination and proteasomal degradation of CyclinD1. This GC-mediated G1-S phase arrest is thought to result in a reduced population of astrocytes in key limbic regions.

Methods: The research utilises a maternal separation (MS) mouse model of ELS. Methods include flow cytometry to analyse the effect of corticosterone on the G1-S phase transition, in vitro neurosphere assays, and in vivo genetic interventions along with molecular, cellular and behavioural assays.

Results: Data demonstrate that ELS leads to persistent depressive-like behaviour in adulthood and a specific reduction in astrocyte density in the hippocampus and cortex. While reduced cell proliferation and CyclinD1 expression are evident immediately following ELS (P23), the resulting astrocyte loss only manifests in adulthood. Flow cytometry confirmed a specific effect of corticosterone on the G1-S phase transition. Inhibition of GSK3β activity, the proteasomal pathway and glucocorticoid receptor activity rescued the corticosterone-mediated G1-S phase arrest.

Conclusion: The study defines a causal chain in which ELS impacts astrocyte development through the GSK3β/CyclinD1 pathway. By establishing this link, the research aims to decouple early-life stress from its adverse effects in adulthood, suggesting that early intervention in cell cycle regulation may prevent long-term psychiatric consequences.

Keywords: Astrocytes; Early Life Stress; Major Depressive Disorder; Glucocorticoids; GSK3β; CyclinD1.

S40

ATF4 transcription factor sequestration in cytosolic condensates; a novel regulator of chronic ISR signaling in Drosophila and mice brain.

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Sensory disabilities such as vision and hearing loss have been identified as significant risk factors for dementia but underlying molecular mechanisms are unknown. In di;erent Drosophila models with loss of sensory input, we observe cell non-autonomous induction of the integrated stress response (ISR) deep in the brain, as indicated by eIF2aS50 phosphorylation dependent elevated levels of the ISR e;ectors ATF4 and XRP1. Unlike during canonical ISR, however, the ATF4 and XRP1 transcription factors are enriched not in the nucleus, but in cytosolic condensates. These condensates are positive for the stress granule markers Caprin, dFMR1, and p62, but not G3BP and are reversible upon restoration of vision for blind flies. This cytosolic restraint of the ATF4 and XRP1 transcription factors dampens expression of their downstream targets including genes of cell death pathways activated during chronic cellular stress and thus constitutes a chronic stress protective response (CSPR). Cytosolic condensates for both p62 and ATF4 were also evident in the thalamus and hippocampus of mouse models of congenital or degenerative blindness. These data indicate a conserved link between loss of sensory input and curbed stress responses critical for protein quality control in the brain. Further, we were interested in understanding whether CSPR is a phenomenon specific to sensory circuit dysfunction, or it represents a broader cellular response to chronic proteostatic stress of various origins. We used chronic Unfolded protein response in ER (UPRER)models, three Drosophila, two mouse and one human disease associated mutant knock-in mouse model and found brain-wide CSPR granule formation which share the molecular and biophysical hallmarks of sensory quiescence-induced CSPR granules. UPR is highly conserved, ISR is highly conserved, and conservation of CSPR across species and disease contexts supports the view that perhaps this mechanism is a fundamental and broadly relevant to cellular stress response.

S41

Role of Type 2 Diabetes Drug as a Repurposing Agent and Ameliorating Inflammation in Stroke

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Background: Insulin resistance, a pathological condition in Type 2 diabetes mellitus (T2DM), aggravates atherosclerosis and inflammation, and plays a pivotal role in cardiovascular diseases and the development of ischemic stroke pathogenesis. The Exploration of T2DM drug (pioglitazone) signaling pathways in ischemic stroke is a promising area of research, offering insights into potential therapeutic targets.

Purpose: This study evaluates the relationship between pioglitazone and key molecular markers involved in pre- and post-ischemic stroke conditions, including inflammatory markers, immune cells, signaling pathways, and transcription factors, in the *in vivo* ischemic stroke rat model.

Methods: To address the above purpose, the treatment of T2DM drug (pioglitazone) was evaluated through RT-PCR to quantify the expression of inflammatory markers such as TNF-α, IL-6, IL-12, IL-1β, and CD32 (monocytes/macrophages, microglia), ARG, CD16 (NK neutrophils, monocytes), iNOS, downstream signaling through c-Jun, MAPK, JNK, and transcription factors NF-kB.

Results: The results suggest that the T2DM drug (pioglitazone) not only prevents ischemic injury in the brain but also exhibits neuroprotective effects. The results suggest that the T2DM drug ameliorates all inflammatory markers in both pre- and post-stroke conditions, but the improvement is greater in the pre-ischemic condition than in the post-ischemic condition. Though not much is known about the cross-talk between T2DM and stroke conditions, the use of T2DM drugs for diabetes treatment might show potential in reducing stroke conditions.

Conclusion: The results suggest that T2DM (pioglitazone) drug regulates the immune response modulating through MAPKs and transcription pathways, and might provide neuroprotection in ischemic stroke conditions, and might provide strong evidence in stroke treatment.

Keywords: Ischemic stroke, Type 2 Diabetes Mellitus, Signaling cascade, inflammation, microglia

S42

A degeneration checkpoint for G4C2-repeat neurotoxicity

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Background: A hexanucleotide repeat expansion (GGGGCC) in the first intron of the C9orf72 gene is one of the primary genetic causes of Amyotrophic Lateral Sclerosis (ALS) and Fronto-temporal Dementia (FTD). Inclusions arising from this repeat expansion have been shown to trigger cellular stress, which may exacerbate the neurotoxic effects of these inclusions. However, the mechanisms underlying activation and the proteins involved in triggering stress-response pathways remain elusive.

Purpose: In this study, we aim to uncover the mediators of stress-response pathways in C9orf72-induced ALS pathology.

Methods: We performed a forward genetic screen using the *Drosophila* eye as a model system to identify signaling pathways that modulate C9orf72 pathology. The identified candidates were genetically and pharmacologically manipulated to study their effects on C9orf72-induced ALS pathologies using immunohistochemistry, biochemical assays, and behavioral assays.

Results: The forward genetic screen on the *Drosophila (G4C2)49* model identified a MAP3K as a key regulator of C9-ALS neurotoxicity. RNAi-mediated reduction in MAP3K activity significantly rescued eye degeneration, lethality, and behavioral defects associated with (G4C2)49 pathology. Genetic analysis of MAP3K-mediated pathways suggested the involvement of a classical signaling pathway downstream of MAP3K activation in C9orf72-induced ALS.

Conclusion: In this study, we show that a) expression of *(G4C2)49* pathological repeats causes an increase in levels of a neuronal MAP3K, b) A reduction in the levels of MAP3K is sufficient to rescue the phenotypes associated with the *(G4C2)49*, and c) activated MAP3K in turn activates the integrated stress response pathway and blocking the ISRP rescues the eye degeneration, motor defects, and lethality associated with *(G4C2)49* expansion.

Keywords: C9orf72; Neurodegeneration; ALS; MAP3K; Integrated Stress Response

ST17

Palmitoylation: the fatty chain driving neurodegeneration

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Background: Protein-protein interactions (PPIs) are central to the coordination and execution of cellular signalling pathways, particularly in the nervous system development and neurodegeneration. Aberrant interaction of signalling proteins contributes to disease pathology which ultimately culminates to neuron death and cognitive decline in Alzheimer's disease (AD). Pan neurotrophin receptor (p75NTR) and amyloid precursor protein (APP) are known to be critical for AD pathology, but their mechanism of interaction and how does it contribute to AD are not clear. Post translation modification of proteins by palmitoylation which includes addition of palmitate chain to the cystine residue affects protein interaction and signalling. However, the role of palmitoylation in APP and p75NTR interaction in AD remains obscure.

Purpose: The current research highlights how palmitoylation of p75NTR and APP affects their interaction which may lead to the neuron death and degeneration in AD.

Methods: We analysed the structure of APP and p75NTR using alpha fold followed by and molecular docking studies. We also investigated how p75NTR palmitoylation affects neuron death *in vitro*.

Results: The *in-silico* analysis predicted that palmitoylation increased the number of α helices and ß-ϒ turns in the protein leading to increased stability. The modified p75NTR is also predicted to interact with other neuron death signalling proteins with higher affinity forming a more stable complex. In addition, the *in vitro* data indicated p75NTR palmitoylation is necessary for neuron death.

Conclusion: Thus, our results position p75NTR palmitoylation as a molecular switch that governs p75NTR and APP interactions involved in death signalling in degenerating neurons. These findings novel mechanistic insights and open new avenues for therapeutic intervention in Alzheimer's disease.

Keywords: Alzheimer's Disease, Palmitoylation, Protein-protein interaction, Neurodegeneration

ST18

Selective activator of calcium-activated potassium channels, NS-309 act as a novel antiepileptic drug by restricting the neuronal hyperexcitability in acquired epilepsy

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Background: Temporal lobe epilepsy (TLE), the most prevalent form of acquired epilepsy, is characterized by synchronized firing of hippocampal pyramidal neurons, resulting in interictal epileptiform discharges and recurrent seizures. Post-burst slow afterhyperpolarization (sAHP), an intrinsic inhibitory regulator, is greatly suppressed in epileptic hippocampal pyramidal neurons, thereby supporting network hyperexcitation. Recent findings have indicated that KCa3.1 channels generate the outward sAHP inhibitory current by associating with L-type voltage calcium channels (Cav1.3) and endoplasmic reticular ryanodine receptors (RyR) in the form of a multichannel protein complex (KCa3.1-Cav1.3-RyR).

Purpose: Worldwide, 50-60 million people are diagnosed with acquired epilepsy, and ~30% of those cases are drug-resistant. This study was performed to evaluate the therapeutic potential of NS309, a selective KCa3.1 activator, as a novel anti-epileptic candidate.

Methods: dSTORM, SIM^2 super-resolution (SR) microscopy, and functional patch-clamping on cultured neurons and in brain slices were used to evaluate the therapeutic potential of NS309, a novel anti-epileptic candidate that stabilizes neuronal excitability and reduces epileptic seizures. The model systems used in the study were 0-Mg^{2+} induced epileptic hippocampal cultured neurons *in vitro*, 4-AP/0-Mg^{2+} induced epileptic brain slices *in vitro*, and lithium-pilocarpine-induced epileptic rats *in vivo.*

Results: A decrease in KCa3.1 clusters in the epileptic neurons was detected from dSTORM and SIM^2 SR-imaging and was supported by decreased KCa3.1 mRNA and protein levels by Q-RTPCR and western blot-mediated protein quantification, respectively. *In vitro* exposure to NS309 reduced the excitability of hippocampal pyramidal neurons, comparable to that of control neurons in whole-cell current-clamp electrophysiological recordings. Concurrently, administration of NS309 *in vivo* significantly delayed the onset, reduced the severity of status epilepticus seizures, and stabilized the CA1 hippocampal pyramidal neuron excitation.

Conclusion: NS309, a selective activator of KCa3.1 channels, stabilized neuronal excitation and demonstrated reduced seizure occurrence in epileptic rats, which can be used as a novel anti-epileptic therapy.

Keywords: Temporal lobe epilepsy, Slow afterhyperpolarization, Hyperexcitation, Status-epilepticus, Recurrent Seizures

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IAN 2026

XLIV Annual Meeting of Indian Academy of Neurosciences

XLIV Annual Meeting of Indian Academy of Neurosciences
Advances in Neuroscience in Health and Disease

October 6-9, 2026
BRIC-National Brain Research Centre, Manesar, Gurugram

IAN2026
Poster Lists

Day 2: 7th October, 2026
2:00 PM - 4:00 PM

Day 3: 8th October, 2026
2:30 PM - 4:30 PM

http://event.nbrc.res.in/IAN2026/ ian2026.nbrc@gmail.com

October 7th, 2026; Poster Session 1	Poster No.	Name	Appli No.	Symposium	Award
	1	LAKHUHONG NINGCHANGMI	IAN2026275	Neurodevelopmental and psychiatric disorders	Suttee Nag
	2	MRUNAL RAJERAM KADU	IAN2026279	Neurodevelopmental and psychiatric disorders	Suttee Nag
	3	AYNAL HOQUE	IAN2026360	Neurodevelopmental and psychiatric disorders	Suttee Nag
	4	DHANUUSH BALAKANNAN	IAN2026407	Neurodevelopmental and psychiatric disorders	Suttee Nag
	5	SUMANT KUMAR	IAN2026331	Neurodevelopmental and psychiatric disorders	Suttee Nag
	6	CHRIS MARY SAM	IAN2026208	Neurodevelopmental and psychiatric disorders	Suttee Nag
	7	NIDHI MISHRA	IAN2026220	Neurodevelopmental and psychiatric disorders	Suttee Nag
	8	BANISMITA TRIPATHY	IAN2026499	Neurodevelopmental and psychiatric disorders	Suttee Nag
	9	ABHINAV RAVEENDRAN	IAN2026509	Neurodevelopmental and psychiatric disorders	Suttee Nag
	10	SONI TIWARI	IAN2026269	Neurodevelopmental and psychiatric disorders	Suttee Nag
	11	AQSA ELLAHI	IAN2026452	Neurodevelopmental and psychiatric disorders	Suttee Nag
	12	SOUMYA GOLCHHA	IAN2026478	Neurodevelopmental and psychiatric disorders	Suttee Nag
	13	BHAWANA CHAUDHARY	IAN2026126	Dissecting circuits for behaviours	Suttee Nag
	14	PRACHI SURYAKANT SHINDE	IAN2026341	Dissecting circuits for behaviours	Suttee Nag
	15	VARNIKA BHARDWAJ	IAN2026254	Dissecting circuits for behaviours	Suttee Nag
	16	LAXMI KHAMANKAR	IAN2026376	Dissecting circuits for behaviours	Suttee Nag
	17	HARINANDANA B	IAN2026476	Dissecting circuits for behaviours	Suttee Nag
	18	TITHI BHOWMICK	IAN202667	Glia in Health and Disease	Suttee Nag
	19	DIBYAM DEBASISH SAHU	IAN2026197	Glia in Health and Disease	Suttee Nag
	20	SHUBHAM SONWANI	IAN2026242	Glia in Health and Disease	Suttee Nag
	21	NEERAJ KUMAR SAINI	IAN2026538	Glia in Health and Disease	Suttee Nag
	22	YOGESH SHARMA	IAN2026411	Glia in Health and Disease	Suttee Nag
	23	SHAFAQ AFTAB	IAN2026496	Glia in Health and Disease	Suttee Nag
	24	SAGAR TYAGI	IAN2026465	Glia in Health and Disease	Suttee Nag
	25	NIMAI GORAI	IAN2026567	Glia in Health and Disease	Suttee Nag
	26	VAIBHAV AMBADAS SABALE	IAN2026382	AI-ML and BMI for Neuroscience	Suttee Nag
	27	SHRIMATHI MANI	IAN2026222	AI-ML and BMI for Neuroscience	Suttee Nag
	28	ROSHAN KUMAR V A M	IAN2026226	AI-ML and BMI for Neuroscience	Suttee Nag
	29	TAHITI MANNA	IAN2026227	AI-ML and BMI for Neuroscience	Suttee Nag
	30	ASHUTOSH KUMAR	IAN2026210	AI-ML and BMI for Neuroscience	Suttee Nag
	31	CHANDRIMA SAHA	IAN2026200	Nutrition, Gut and the Brain	Suttee Nag
	32	SHEKHAR SINGH	IAN2026373	Nutrition, Gut and the Brain	Suttee Nag
	33	SIMRAN	IAN2026410	Nutrition, Gut and the Brain	Suttee Nag
	34	HARSHARANI .G. V	IAN2026534	-	Suttee Nag
	35	PRITIBEN PANKAJBHAI PRAJAPATI	IAN202631	Neuroscience of sleep and consciousness	Suttee Nag

	36	SUVETHA V	IAN2026468	Neuroscience of sleep and consciousness	Suttee Nag
	37	CHANDRA MOHAN BHARDWAJ	IAN2026471	Neuroscience of sleep and consciousness	Suttee Nag
	38	PAWAN BAIRWA	IAN202666	Connectomics and adaptive reorganization	Suttee Nag
	39	ATHUL NARAYAN PS	IAN2026181	Connectomics and adaptive reorganization	Suttee Nag
	40	KRUSHNA PRASHANT DHORDE	IAN202672	Cell Biology of neurons	Suttee Nag
	41	BANDANA KUMARI SAHU	IAN202690	Cell Biology of neurons	Suttee Nag
	42	VAISHNAVI PUPPALA	IAN2026116	Cell Biology of neurons	Suttee Nag
	43	SNEHA MARY ALEXANDER	IAN2026258	Cell Biology of neurons	Suttee Nag
	44	AKSHAY KUMAR	IAN2026443	Cell Biology of neurons	Suttee Nag
	45	DHARANI D	IAN2026214	Cell Biology of neurons	Suttee Nag
	46	NITIKA RAI	IAN2026216	Cell Biology of neurons	Suttee Nag
	47	ASHWINI KUMAR	IAN2026481	Cell Biology of neurons	Suttee Nag
	48	SUKRITI AGGARWAL	IAN2026498	Cell Biology of neurons	Suttee Nag
	49	SIBARAM BEHERA	IAN2026508	Cell Biology of neurons	Suttee Nag
	50	SAKSHI KUMARI	IAN2026511	Cell Biology of neurons	Suttee Nag
	51	AAKASH VERMA	IAN2026512	Cell Biology of neurons	Suttee Nag
	52	SAKSHI KUSHWAHA	IAN2026515	Cell Biology of neurons	Suttee Nag
	53	SHAMBHAVI DWIVEDI	IAN2026516	Cell Biology of neurons	Suttee Nag
	54	ARCHANA MEHTA	IAN2026517	Cell Biology of neurons	Suttee Nag
	55	HIMANSHI YADAV	IAN2026262	Cell Biology of neurons	Suttee Nag
	56	YASH PARAMESHWAR HAJARE	IAN2026281	Cell Biology of neurons	Suttee Nag
	57	SAKESH KUMAR	IAN2026329	Cell Biology of neurons	Suttee Nag
	58	SAILESH S	IAN2026359	Cell Biology of neurons	Suttee Nag
	59	LEISHANGTHEM BITESHWARI DEVI	IAN2026408	Cell Biology of neurons	Suttee Nag
	60	KAMAKSHI GARG	IAN2026344	Cell Biology of neurons	Suttee Nag
	61	APARNA CHAUHAN	IAN2026238	Neurodevelopmental and psychiatric disorders	None
	62	CHANCHAL	IAN2026101	Neurodevelopmental and psychiatric disorders	None
	63	MOHIT NEMA	IAN2026105	Neurodevelopmental and psychiatric disorders	None
	64	MELISSA RENEAUX	IAN2026186	Neurodevelopmental and psychiatric disorders	None
	65	SANDRA S HARI	IAN2026193	Neurodevelopmental and psychiatric disorders	None
	66	RISHITA SINGH	IAN2026483	Neurodevelopmental and psychiatric disorders	None
	67	SWARNALI PANDA	IAN2026495	Neurodevelopmental and psychiatric disorders	None
	68	AJAY SINGH	IAN2026506	Neurodevelopmental and psychiatric disorders	None
	69	SHREYA SEN	IAN2026335	Neurodevelopmental and psychiatric disorders	None
	70	NAVJEET SAINI	IAN2026401	Neurodevelopmental and psychiatric disorders	None
	71	KAJAL SHARMA	IAN2026394	Neurodevelopmental and psychiatric disorders	None
	72	HARSHITA MANGLA	IAN2026395	Neurodevelopmental and psychiatric disorders	None

	73	SAUMYA PANDEY	IAN2026399	Neurodevelopmental and psychiatric disorders	None
	74	NAYNA MUKHERJEE	IAN2026469	Neurodevelopmental and psychiatric disorders	None
	75	APHRODITE CHAKRABORTY	IAN2026179	Neurodevelopmental and psychiatric disorders	None
	76	DIBYAN LAMA	IAN2026250	Neurodevelopmental and psychiatric disorders	None
	77	YOGESH SAHU	IAN2026173	Neurodevelopmental and psychiatric disorders	None
	78	PERRY WINKLE	IAN2026504	Dissecting circuits for behaviours	None
	79	SHIVANGI SHARMA	IAN2026292	Dissecting circuits for behaviours	None
	80	SRUTHI SUNIL	IAN2026295	Dissecting circuits for behaviours	None
	81	ROUNAK SAHA	IAN2026307	Dissecting circuits for behaviours	None
	82	PRISHAA KAUR BHURRJI	IAN2026323	Dissecting circuits for behaviours	None
	83	NEHA PRIYA SHRIVASTAVA	IAN2026350	Dissecting circuits for behaviours	None
	84	SEJAL KUMARAVEL	IAN2026368	Dissecting circuits for behaviours	None
	85	AKANKSHA CHAUHAN	IAN2026369	Dissecting circuits for behaviours	None
	86	A JOSEY LOURDES	IAN2026371	Dissecting circuits for behaviours	None
	87	ISHITA PRIYADARSHINI	IAN2026514	Glia in Health and Disease	None
	88	SANTHOSH KUMAR S	IAN2026263	Glia in Health and Disease	None
	89	RAJ AMARLAL KATARIYA	IAN2026417	Glia in Health and Disease	None
	90	P V VINITHA	IAN2026519	AI-ML and BMI for Neuroscience	None
	91	TANMAY SINGHAL	IAN2026520	AI-ML and BMI for Neuroscience	None
	92	MEDHA BHINDWAR	IAN2026522	AI-ML and BMI for Neuroscience	None
	93	PAVAN KUMAR AGRAWAL	IAN2026537	AI-ML and BMI for Neuroscience	None
	94	DINESH DILIP ANANDANI	IAN2026405	-	None
	95	SANJAY NAGORAO AWATHALE	IAN2026291	-	None
	96	DEBIPRASAD SINHA	IAN2026414	-	None
	97	DIVYANSHU DARSHNA	IAN2026233	-	None
	98	SHRIYA PALCHAUDHURI	IAN2026543	Dissecting circuits for behaviours	None
October 8th, 2026; Poster Session 2	99	GURCHARAN MARCHANDA	IAN2026302	Neurodevelopmental and psychiatric disorders	SS Parmar
	100	SHREESHA HEGDE	IAN2026308	Neurodevelopmental and psychiatric disorders	SS Parmar
	101	ANURAG THAPLIYAL	IAN202634	Neurodevelopmental and psychiatric disorders	SS Parmar
	102	ASHWINI ANIL PATIL	IAN2026236	Neurodevelopmental and psychiatric disorders	SS Parmar
	103	SANKHADIP DAS	IAN2026153	Neurodevelopmental and psychiatric disorders	SS Parmar
	104	USHA KUMARI	IAN2026523	Neurodevelopmental and psychiatric disorders	SS Parmar
	105	VAISHALI VASU	IAN2026268	Neurodevelopmental and psychiatric disorders	SS Parmar
	106	DAMINI MATHUR	IAN2026288	Neurodevelopmental and psychiatric disorders	SS Parmar
	107	STANZIN NURBOO	IAN2026327	Neurodevelopmental and psychiatric disorders	SS Parmar
	108	SWATI TIWARI	IAN2026385	Neurodevelopmental and psychiatric disorders	SS Parmar

	109	GANGA K	IAN2026396	Neurodevelopmental and psychiatric disorders	SS Parmar
	110	MEHWISH ALI CHOUDHARY	IAN2026451	Neurodevelopmental and psychiatric disorders	SS Parmar
	111	ADRIJA DAS	IAN2026206	Neurodevelopmental and psychiatric disorders	SS Parmar
	112	ANIKET SAHEBRAO KEDAR	IAN2026278	Dissecting circuits for behaviours	SS Parmar
	113	NUDRAT JAHAN	IAN2026500	Dissecting circuits for behaviours	SS Parmar
	114	ABHINEET OJHA	IAN2026309	Dissecting circuits for behaviours	SS Parmar
	115	MOHD AMAAN	IAN2026444	Dissecting circuits for behaviours	SS Parmar
	116	VAISHNAVI SHARMA	IAN2026475	Dissecting circuits for behaviours	SS Parmar
	117	RENU KAMBOJ	IAN2026195	Glia in Health and Disease	SS Parmar
	118	MAULIK RAKESH PATEL	IAN2026490	Glia in Health and Disease	SS Parmar
	119	SHIVANI SHARMA	IAN2026120	AI-ML and BMI for Neuroscience	SS Parmar
	120	WAQAR KHAN	IAN2026145	AI-ML and BMI for Neuroscience	SS Parmar
	121	APARNA AYYAPPAN	IAN2026221	AI-ML and BMI for Neuroscience	SS Parmar
	122	ISHIKA GULATI	IAN2026224	AI-ML and BMI for Neuroscience	SS Parmar
	123	DIBYADEEP DATTA	IAN2026533	AI-ML and BMI for Neuroscience	SS Parmar
	124	YOGENDRA KUMAR	IAN2026610	Dissecting circuits for behaviours	SS Parmar
	125	RADHIKA MITTAL	IAN2026326	Nutrition, Gut and the Brain	SS Parmar
	126	BUSSA BHAGYA RAJ	IAN2026466	Nutrition, Gut and the Brain	SS Parmar
	127	CHITRALEKHA GUSAIN	IAN2026112	Nutrition, Gut and the Brain	SS Parmar
	128	VISHAL CHHABRA	IAN2026294	Neuroscience of sleep and consciousness	SS Parmar
	129	VARTIKA SRIVASTAVA	IAN20266	Phys & pathophys of neuroendocrine systems	SS Parmar
	130	AMAN MURARI	IAN2026158	Phys & pathophys of neuroendocrine systems	SS Parmar
	131	RUTUJA ARUN PENDHARKAR	IAN2026415	Connectomics and adaptive reorganization	SS Parmar
	132	AARTHI SUKUMAR	IAN2026150	Connectomics and adaptive reorganization	SS Parmar
	133	DEEPAK CHOUHAN	IAN2026446	Connectomics and adaptive reorganization	SS Parmar
	134	SOMESH AGRAWAL	IAN2026458	Connectomics and adaptive reorganization	SS Parmar
	135	DHYEY VIPULKUMAR VYAS	IAN2026473	Connectomics and adaptive reorganization	SS Parmar
	136	SAKEENA ASMI T	IAN2026234	Cell Biology of neurons	SS Parmar
	137	KASHMIRI M. LANDE	IAN2026356	Cell Biology of neurons	SS Parmar
	138	JAYANTHI JAYAKUMAR	IAN2026217	Cell Biology of neurons	SS Parmar
	139	ABHA PANKAJ MACHWE	IAN2026229	Cell Biology of neurons	SS Parmar
	140	CHAKSHU MANGAL	IAN2026518	Cell Biology of neurons	SS Parmar
	141	UPAMA CHOWDHURY	IAN2026529	Cell Biology of neurons	SS Parmar
	142	SAYALI SURESH SABALE	IAN2026280	Cell Biology of neurons	SS Parmar
	143	DHRUVA KUMAR KESIREDDY	IAN2026324	Cell Biology of neurons	SS Parmar
	144	SONAM RANWA	IAN2026328	Cell Biology of neurons	SS Parmar
	145	ATITHI TRIPATHI	IAN2026412	Cell Biology of neurons	SS Parmar

	146	TRISHA SINGH	IAN2026437	Cell Biology of neurons	SS Parmar
	147	DHIVIYA C V	IAN2026472	Cell Biology of neurons	SS Parmar
	148	ATAL VATS	IAN2026461	Cell Biology of neurons	SS Parmar
	149	NAMRATA	IAN2026549	Neuroscience of Sleep and Consciousness	SS Parmar
	150	ROSEMARY SHAJI V	IAN2026137	-	SS Parmar
	151	NIRUPAMATEJA TALAGADADEEVI	IAN2026413	-	SS Parmar
	152	SAKSHI DILIP MOHITE	IAN2026277	-	None
	153	CHAITHANYA LEON	IAN2026423	-	None
	154	DIPTI SINGH	IAN2026306	Neurodevelopmental and psychiatric disorders	None
	155	ASHA CHANNAKKAR	IAN2026374	-	None
	156	G. DEEPAK	IAN2026563	Dissecting circuits for behaviours	None
	157	VIDISHA MAITHANI	IAN2026336	-	None
	158	KAMAKSHI TOMAR	IAN202651	Nutrition, Gut and the Brain	None
	159	BABITA BHATT	IAN2026129	Nutrition, Gut and the Brain	None
	160	DIPAK K. SAHARE	IAN2026389	Phys & pathophys of neuroendocrine systems	None
	161	TANYA	IAN2026487	Neurobiology of Reward and Addiction	None
	162	GAUTAM MOHAPATRA	IAN2026241	Connectomics and adaptive reorganization	None
	163	PRAKASH CHERMAKANI	IAN2026157	Connectomics and adaptive reorganization	None
	164	PRABHAKAR SINGH	IAN2026403	Connectomics and adaptive reorganization	None
	165	MALICA R	IAN2026404	Connectomics and adaptive reorganization	None
	166	ANISHA S. MENON	IAN202677	Connectomics and adaptive reorganization	None
	167	THEMMAYO HONGRAY	IAN20269	Cell Biology of neurons	None
	168	GAZALA KHATOON	IAN2026121	Cell Biology of neurons	None
	169	SOWMYA SIVAKUMAR	IAN2026479	Cell Biology of neurons	None
	170	RISHIKESH BAASUBRAMANYA	IAN2026480	Cell Biology of neurons	None
	171	R VAISHNAVI	IAN2026482	Cell Biology of neurons	None
	172	SHANTANU HARDIHA	IAN2026492	Cell Biology of neurons	None
	173	BHARTI YADAV	IAN2026347	Cell Biology of neurons	None
	174	MIRAJUL ISLAM	IAN2026348	Cell Biology of neurons	None
	175	ANIRUDH SREENIVAS BK	IAN2026379	Cell Biology of neurons	None
	176	SINDHU S RAI	IAN2026381	Cell Biology of neurons	None
	177	JYOTSNA SHARMA	IAN2026400	Cell Biology of neurons	None
	178	SAKSHI SIMON	IAN2026454	Cell Biology of neurons	None
	179	PHAVITHRA M	IAN2026447	Cell Biology of neurons	None
	180	SHEKHAR KEDIA	IAN2026445	Cell Biology of neurons	None
	181	PRIYANKA THAKUR	IAN2026213	Nutrition, Gut and the Brain	None

	182	KRITIKA KUMARI	IAN2026416	Nutrition, Gut and the Brain	None
	183	BHAVESH VERMA	IAN2026402	-	None
	184	GOPESH BAJRE	IAN2026536	-	None
	185	SHRIJAL SINGH	IAN2026435	-	None
	186	RAJYASHREE BASU	IAN2026489	Nutrition, Gut and the Brain	None
	187	GOVIND SINGH	IAN2026246	-	None
	188	ANKITA SRIVASTAVA	IAN2026467	-	None
	189	KARUNA REGMI	IAN2026592	Physiology and pathophysiology of neuroendocrine systems	None
	190	GAURAV SAINI	IAN2026147	-	None
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