Collaborative Program in Neuroscience (CPIN)

2026 CPIN Research Day

MEETING PROGRAM

June 19, 2026

Myhal Centre, University of Toronto

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Collaborative Program in Neuroscience (CPIN)

2026 CPIN RESEARCH DAY

Friday, June 19, 2026

Myhal Centre for Engineering Innovation & Entrepreneurship

55 St. George Street, Toronto, ON M5S 0C9

PROGRAM SCHEDULE

8:15 – 9:00 AM	**Registration, Poster Setup, Poster Viewing** *Light Refreshments*	*Myhal Centre Lobby*

Section I — Opening Remarks & Scientific Symposium I

9:00 – 9:15 AM	**Opening & Welcome Remarks** **Dr. Zhong-Ping Feng** *Director, Collaborative Program in Neuroscience (CPIN); Professor, Department of Physiology, University of Toronto*	*MY150*
	Scientific Symposium I: Invited Talks ***Moderator: Dr Bojana Stefanovic*** *(Professor, Department of Medical Biophysics, University of Toronto)*	
9:15 – 9:40 AM	**Dr. Molly S. Shoichet** *Professor, Institute of Biomedical Engineering, University of Toronto* ***"Promoting tissue and functional repair in the CNS"***	
9:40 – 10:05 AM	**Dr. Vince Tropepe** *Professor, Department of Cell and System Biology, University of Toronto* ***"Post-transcriptional Regulation of Müller Cell Reprogramming in the Regenerating Retina"***	
10:05 – 10:30 AM	**Dr. Chao Zheng** *Assistant Professor, Departments of Psychiatry, Chemistry, and Pharmacology & Toxicology, University of Toronto* ***"Seeing Synapses in the Living Brain: PET Imaging Probes for Translational Neuroscience"***	

10:30 – 10:50 AM	**Dr. Jeffrey Henderson** *Associate Professor, Leslie Dan Faculty of Pharmacy, University of Toronto* ***"Novel molecular mechanisms governing cell death in stroke"***	

Section II — CPIN Trainee Parallel Oral Presentations

10:55 – 12:00 PM	**CPIN Trainee Parallel Oral Presentations / Evaluation Session**	
	Aging & Neuro-degenerative Disorders (Translational)	*MY315*
	Aging & Neuro-degenerative Disorders (Clinical)	*MY317*
	Behavioral & Social Neuroscience	*MY320*
	Cognitive Neuroscience	*MY330*
	Developmental Neuroscience	*MY350*
	Molecular & Cellular Neuroscience	*MY360*
	Systems & Circuits Neuroscience	*MY370*
	Neuropharmacology & Drug Development	*MY380*
	Motor & Sensory Control	*MY420*

Section III — CPIN Trainee Poster Presentations & Lunch

12:00 – 1:25 PM	**CPIN Trainee Poster Presentations / Evaluation Session** *9 groups of Poster Presentations* ***Lunch will be provided***	*Myhal Centre Lobby*

Section IV — President's Remarks & Scientific Symposium II

1:30 – 1:50 PM	**President's Remarks** **Dr. Melanie Woodin** *President, University of Toronto; Professor, Cell and System Biology* ***Introduced by Dr. Zhong-Ping Feng***	*MY150*
	Scientific Symposium II: Invited Talks ***Moderator: Dr. Kaori Takehara*** *(Professor, Department of Psychology)*	
1:50 – 2:15 PM	**Dr. Carmela Tartaglia** *Professor, Department of Medine and Institute of Medical Science; Senior Scientist, Tanz Centre for Research in Neurodegenerative Diseases, University of Toronto* ***"A Paradigm Shift in Neurodegenerative Diseases: Co-Pathology the Norm, not the Exception"***	

2:15 – 2:40 PM	**Dr. Sheena Josselyn** *Professor, Departments of Psychology and Physiology, University of Toronto; Senior Scientist, Hospital for Sick Children* ***"Engrams and Memory in Mice"***	
2:40 – 3:05 PM	**Dr. Shuzo Sugita** *Professor, Department of Physiology, University of Toronto; Senior Scientist, Krembil Research Institute* ***"Exploring the Mechanistic Roles of SNARE-mediated Membrane Fusion in the Brain"***	
3:05 – 3:30 PM	**Dr. Limor Avivi-Arber** *Associate Professor, Faculty of Dentistry, University of Toronto* ***" What Good Is Walking and Writing If You Can't Chew and Swallow?"***	
3:30 – 3:55 PM	**Dr. Robert Chen** *Professor, Institute of Medical Science, University of Toronto; Senior Scientist, Krembil Research Institute* ***"Transcranial ultrasound stimulation: A novel non-invasive brain stimulation method"***	

Section V — Professional Development Workshop

	***Moderators: Irina Alymova** (PhD Candidate, CSB) **& Dr. Ain Kim** (Postdoc, Tanz Centre for Research in Neurodegenerative)*	
3:55 – 4:35 PM	**AI-assisted Coding (Vibe-coding) for Neuroscience** **Dr. Jimmy Fraigne** (*Assistant Professor, Cell and System Biology, University of Toronto*)	*MY150*
4:35 - 4:50 PM	**NeuroBriefer: A Neuroscience Literature Tool** **Dr. Damien Boorman** (*Postdoctoral Fellow, University of Toronto Mississauga*)	

Section VI — Awards Ceremony & Closing

4:50 – 5:15 PM	***Moderators: Dr. Jeffrey Henderson, Dr. Hong-Shuo Sun** (IMS & Physiology) **& Dipa Chatterjee** (PhD Candidate, PCL)* **Awards Ceremony** **Jonathan Dostrovsky Awards in Neuroscience** **CPIN Graduate Student Recognition Awards** **Trainee Oral and Poster Presentation Awards** **Awards Ceremony** **Dr. Zhong-Ping Feng** ***(Post-Event Light Refreshments)***	*MY150*

SPEAKER PROFILES

Dr. Molly S. Shoichet, *Departments of Biomedical Engineering and Chemical Engineering & Applied Chemistry*

Promoting tissue and functional repair in the CNS

Professor Molly Shoichet is University Professor, a distinction held by less than 2% of the faculty. She is the inaugural Pamela & Paul Austin Chair in Precision and Regenerative Medicine, and Scientific Director of Precision Medicine (PRiME) and BioHubNet at the University of Toronto. Shoichet served as Ontario's first Chief Scientist in 2018 where she worked to enhance the culture of science. Dr. Shoichet has published over 850 papers, patents and abstracts and has given nearly 600 lectures worldwide. She leads a laboratory of 30 and has graduated 270 researchers. Her research is focused on drug and cell delivery strategies in the central nervous system, 3D hydrogel culture systems to model cancer and colloidal drug aggregates. She co-founded four spin-off companies, actively engages in translational research and science outreach. Dr. Shoichet is the recipient of many prestigious distinctions and the first (and until recently the only) person to be inducted into all three of Canada's National Academies of Science of the Royal Society of Canada, Engineering and Health Sciences. Professor Shoichet is an Officer of the Order of Canada and holds the Order of Ontario. Dr. Shoichet is the L'Oreal-UNESCO For Women in Science Laureate for North America, 2015, Foreign Member of the US National Academy of Engineering, Fellow of the US National Academy of Inventors, recipient of the Killam Prize in Engineering, 2017 and Fellow of the Royal Society (UK). Dr. Shoichet is the NSERC Herzberg Gold Medal awardee, 2020 (the highest award in science/engineering in Canada) and recipient of the Margolese National Brain Disorders Prize. Dr. Shoichet received her SB from the Massachusetts Institute of Technology (1987) and her PhD from the University of Massachusetts, Amherst in Polymer Science and Engineering (1992).

Dr. Vincent Tropepe, *Department of Cell & Systems Biology*

Post-transcriptional regulation of Müller cell reprogramming in the regenerating retina

Dr. Vincent Tropepe is a Professor in the Department of Cell & Systems Biology and Associate Vice-President Research Oversight & Compliance at the University of Toronto. His lab investigates how neurogenesis contributes to the generation and maintenance of regional nerve cell diversity throughout life using molecular genetic techniques. Neurogenesis is a lifelong process with regional specialization that is critical for the formation of distinct functional domains in the vertebrate nervous system. Moreover, neurogenesis in the mature nervous system may contribute to the structural changes that underlie neural plasticity (crucial for sensory processing and behaviour).

Dr. Chao Zheng, *Departments of Psychiatry, Chemistry, and Pharmacology & Toxicology; Scientist, CAMH*

Seeing Synapses in the Living Brain: PET Imaging Probes for Translational Neuroscience

Dr. Chao Zheng is an Assistant Professor in the Departments of Psychiatry, Chemistry, Pharmacology & Toxicology at the University of Toronto. He is also an Independent Scientist at the Brain Health Imaging Centre and the Azrieli Centre for Neuro-Radiochemistry at the Centre for Addiction and Mental Health (CAMH). The Zheng research group focuses on the development and application of innovative radiopharmaceuticals for the diagnosis and assessment of treatment in neuropsychiatric and neurodegenerative disorders. Dr. Chao Zheng's research program has specific objectives: 1) Discovery of cutting-edge radiopharmaceuticals for brain imaging applications; 2) Developing and applying novel PET imaging methods that directly capture biochemical or phenotypic changes in vivo. This involves integrating disciplines such as medicinal chemistry, radiochemistry, quantitative PET imaging from in vitro and preclinical in vivo studies, and pharmacology.

Dr. Jeffrey Henderson, *Department of Pharmaceutical Sciences, Leslie Dan Faculty of Pharmacy*

Novel molecular mechanisms governing cell death in stroke

Dr. Jeffrey Henderson is an Associate Professor in the Department of Pharmaceutical Sciences in the Leslie Dan Faculty of Pharmacy at the University of Toronto. His research focuses on molecular mechanisms governing programmed cell death and axon guidance in the central nervous system. Abnormal PCD occurs in an array of acute and chronic neurologic disorders as well as a variety of human cancers. Understanding these processes is therefore critical to enhancing recovery from such pathologic states. Through the use of molecular genetics, stem cell technologies, and therapeutic discovery approaches, his work aims to identify novel strategies for promoting neural recovery and treating neurodegenerative disease.

President Melanie Woodin, *Department of Cell & Systems Biology, President of the University of Toronto*

President's Remarks

Professor Melanie A. Woodin, an internationally recognized neuroscientist, began her term as the University of Toronto's 17th President on July 1, 2025. A widely respected scholar, teacher, mentor and administrator, President Woodin is a Professor in the Department of Cell & Systems Biology and former Dean of the University's Faculty of Arts & Science — Canada's largest and most comprehensive faculty. During her tenure, the Faculty's Acceleration Consortium was awarded $200 million — the largest federal research grant awarded to a university in Canadian history. She also oversaw the development of new centres for African Studies and Caribbean Studies, the elevation of the Centre for Indigenous Studies and the creation of the Online Learning Academy. She supported the redesign of student spaces, expanded college-based registrarial supports, and guided the development and launch of new academic programs including the Arts & Science Internship Program.

President Woodin is renowned for her multidisciplinary approach to examining synaptic communication in the brain and has authored or co-authored more than 50 academic papers and book chapters. She and her research team are unravelling mechanisms that lead to neurological disorders and diseases, including autism spectrum disorder, Huntington's disease and ALS.

After earning a Bachelor of Science and Master of Science from U of T, President Woodin completed her PhD in neuroscience at the University of Calgary. Following postdoctoral study at the University of California, Berkeley, she joined the University of Toronto in 2004 as an assistant professor in the Department of Zoology. She was promoted to full professor in 2017 in the Department of Cell & Systems Biology and has received research funding from the Natural Sciences and Engineering Research Council of Canada, Canadian Institutes of Health Research, Simons Foundation Autism Research Initiative and Amyotrophic Lateral Sclerosis Society of Canada, among others.

President Woodin serves on the board of several organizations, including SickKids and Fulbright Canada, and is a past director of the Vector Institute and past president of the Canadian Association for Neuroscience.

Dr. Carmela Tartaglia, *Institute of Medical Science; Senior Scientist, Tanz Centre for Research in Neurodegenerative Diseases*

A Paradigm Shift in Neurodegenerative Diseases: Co-Pathology the Norm, Not the Exception

Dr. Carmela Tartaglia is a Senior Scientist at the Tanz Centre for Research in Neurodegenerative Diseases and a Professor in the Department of Medicine and Institute of Medical Science at the University of Toronto. She is a cognitive-behavioral neurologist at the UHN Memory Clinic where she sees patients with neurodegenerative diseases, and she is interested in the delayed effects of repetitive head impacts. She employs a multi-modal approach to understand the role of co-pathology across neurodegenerative diseases with the aim of advancing precision medicine and enabling targeted, early interventions. She holds the Marion and Gerald Soloway Chair in Brain Injury and Concussion Research and is the medical lead of the TWH Clinical Research Unit. She is the Executive Director of the Toronto Dementia Research Alliance.

Dr. Sheena Josselyn, *Departments of Psychology and Physiology; Senior Scientist, SickKids*

Engrams and Memory in Mice

Dr. Sheena Josselyn is a Senior Scientist at SickKids and a Professor in the Departments of Psychology and Physiology at the University of Toronto. Her research focuses on understanding how the brain encodes, stores, and retrieves memories. Her laboratory investigates the neural mechanisms underlying memory formation, with a particular interest in how specific neurons are recruited into memory traces, or engrams, and how these representations change over time and with new experiences. By uncovering the biological basis of memory, her work aims to advance our understanding of brain function and inform new approaches for treating neurological and psychiatric disorders.

Dr. Shuzo Sugita, *Department of Physiology; Senior Scientist, Krembil Research Institute*

Exploring the Mechanistic Roles of SNARE-mediated Membrane Fusion in the Brain

Dr. Shuzo Sugita is a Senior Scientist at the Krembil Research Institute and Professor in the Department of Physiology at the University of Toronto. His main area of interest is investigating mechanisms of synaptic transmission, particularly synaptic vesicle exocytosis in neurons, using C. elegans and mice as models. Recently, he started the investigation of the roles of vesicle exocytosis processes across different cell types underlying

various brain functions. These include synaptic plasticity, learning and memory, visual information processing, axon myelination and neuron-glia communications.

Dr. Limor Avivi-Arber, *Faculty of Dentistry*

What Good Is Walking and Writing If You Can't Chew and Swallow? Orofacial Function and the Brain: An Underappreciated Frontier in Neuroscience

Dr. Limor Avivi-Arber is an associate professor in the Departments of Prosthodontics and Oral Physiology at the University of Toronto Faculty of Dentistry. Her research focuses on understanding the neuroplastic changes that occur in the brain following alterations in orofacial sensory and motor function. Using animal models of tooth loss and dental implant treatment, her work investigates the central nervous system mechanisms underlying orofacial sensory and motor behaviours. Her long-term goal is to improve the prevention and treatment of maladaptive outcomes associated with tooth loss and oral rehabilitation.

Dr. Robert Chen, *Institute of Medical Science; Senior Scientist, Krembil Research Institute*

Transcranial ultrasound stimulation: A novel non-invasive brain stimulation method

Dr. Robert Chen is a Professor at the University of Toronto and a Senior Scientist at the Krembil Research Institute. His research focuses on the organization and function of inhibitory and excitatory pathways within the human motor cortex and how these circuits are altered in neurological disease. Dr. Chen investigates the mechanisms underlying neuromodulation therapies such as deep brain stimulation. Using a combination of non-invasive brain stimulation, neuroimaging, and neurophysiological approaches, his work seeks to advance our understanding of the neural circuits that govern motor function and to inform the development of more effective treatments for neurological disorders affecting movement.

TRAINEE ORAL PRESENTERS

Theme	Abstract #	Name	Theme	Abstract #	Name
Aging & Neuro-degenerative Disorders (Translational) *Room Number: MY315*	19	Justin Chia	**Aging & Neuro-degenerative Disorders (Clinical)** *Room Number: MY317*	24	Riya Dama
	22	Kevan Clifford		40	Dana Xinyue Huang
	39	Bianca Hill		88	Priya van Oosterhout
	98	Ryan Yip		68	Davina Premraj
	99	Lyanne Zhang		85	Evelyn Tjiandri
Behavioural & Social Neuroscience *Room Number: MY320*	2	Ariya Ahona	**Cognitive Neuroscience** *Room Number: MY330*	8	Alessia Alicandro
	13	Grace Burns		5	Mryam Ali
	17	Aaima Cheema		14	Candela Castro
	44	Victoria Ivakitch		36	Rayna Ghosh
	59	Megan Lozzi		45	Mehvish Jamal
	79	Sarah Smith		73	Sadhna Ramquar
Developmental Neuroscience *Room Number: MY350*	1	Tesam Ahmed	**Molecular & Cellular Neuroscience** *Room Number: MY360*	4	Alameen Alajeely
	26	Andrea De Bartolo		16	Dipa Chatterjee
	87	Rivka van Klei		47	Lauren Joe
	91	Xianxuan Wang		62	Jonathan Monteiro
	93	Hannah Whitehead		66	Lilliana Pavicic
Systems & Circuits Neuroscience *Room Number: MY370*	9	Irina Alymova	**Neuro-pharmacology & Drug Development** *Room Number: MY380*	28	Kamrani Doray
	10	Kayla Baker		37	Brooke Ginson
	18	Andrew Cheon		60	Dhvani Mehta
	50	Vittala Korann		58	Tommy Liu
	77	Rubab Shafiq		81	Omer Syed
Motor & Sensory Control *Room Number: MY420*	7	Yasma Ali-Hassan			
	29	Maryam Fazili			
	63	Pedram Mouseli			
	80	Yutong Sun			
	83	Huseyin Taskin			
	100	Zhihong Luo			

TRAINEE POSTER PRESENTERS

Theme	Abstract #	Name	Theme	Abstract #	Name
Aging & Neuro-degenerative Disorders	33	Sofia Gentile	**Cognitive Neuroscience**	23	Madeleine Coppolino
	32	Selena Gangaram		21	Annie Chu
	48	Bryan Kartono		31	Francis Fernandes
	54	Hannah Le		56	Polina Lekhnitskaia
	70	Syeda Hania Qamar		78	Stephanie Shishis
	86	Harani Uthayakumar		92	Judy Wang
Brain Development & Lifespan Neuroscience	3	Evelyn Ajayi	**Neuro-pharmacology & Drug Development**	38	Rachel Ha
	11	Mary-Claire Ball		52	Medha Krishnan
	41	Yi-Syuan Huang		64	Zahra Nasser
	43	Alena Ionova		72	Gaithtry Rameswaran
	89	Lyra Vania		74	Nikol Rybolov
	97	Maria Yang		96	Victor Xu
Pain & Sensory Disorders I	25	Sushmit Das	**Pain & Sensory Disorders II**	15	Nicole Cesca
	46	Jiyoon Jeong		27	Nathaniel De Vera
	67	Angela Praecht		61	Xianze Meng
	75	Vaidhehi Sanmugananthan		65	Melanie Niu
	82	Nadeen Tantash		94	Yik Lok Wong
Psychiatric Disorders I	35	Leen Ghanayem	**Psychiatric Disorders II**	12	Sayona Bhattacharyya
	42	Molly Hyde		34	Mark Gerlai
	55	Gia Han Le		69	Alexandra Puchiele
	57	Jino Lim		76	Andrew Sedrak
	53	Emily Kuik		90	Hsin-Yun (Angel) Hsieh
	49	John Kennedy		95	Sabrina Wong
Cellular & Systems Neuroscience	6	Muhammad Ali			
	20	Mya Chronopoulos			
	30	Madison Fedele			
	71	Areeba Qureshi			
	84	Ricardo Tello Marroquin			
	101	Thomas Sanderson			

PROFESSIONAL DEVELOPMENT WORKSHOP SPEAKERS

Dr. Jimmy Fraigne, *Department of Cell & Systems Biology*

AI-assisted coding (vibe-coding) for neuroscience

Dr. Jimmy Fraigne is an Assistant Professor in Cell and Systems Biology at the University of Toronto. His research focuses on understanding how neural circuits generate and regulate sleep and wakefulness, and how dysfunction in these circuits contributes to disorders such Narcolepsy and REM Sleep Behavior Disorder. Dr. Fraigne is also passionate about teaching and mentorship, particularly introducing students to coding and computational approaches in neuroscience. He has developed multiple courses designed to help students with little or no prior programming experience build practical coding skills and confidence in research.

Dr. Damien Boorman, *Department of Cell & Systems Biology*

NeuroBriefer: A Neuroscience Literature Tool

Damien is a CIHR postdoctoral research fellow in the Martin Pain Lab in the department of psychology at the University of Toronto Mississauga. Damien first completed a Bachelor of Arts in Philosophy from the University of Sydney in 2011. Soon after, he realized that his job prospects as a philosopher were limited and so returned to the University of Sydney to complete a Bachelor of Science in Neuroscience, graduating with first class honours and the University Medal. He then completed his PhD in neuroscience, in which he developed new animal models of placebo analgesia. In 2023, he moved to Toronto to work with Professor Loren Martin, where he currently investigates the mechanisms driving chronic pain. Over the last year, he has been developing NeuroBriefer because he wanted a better way to keep up with and share the latest neuroscience research.

EVENT MODERATORS

Dr. Zhong-Ping Feng, *Professor, Department of Physiology; Director, Collaborative Program In Neuroscience*

Event Moderator

Dr. Feng's lab studies ion channels and calcium-dependent mechanisms underlying neurodevelopment and neural plasticity, and identifies neuroprotective drug targets for brain injury and related neurological disorders.

Dr. Bojana Stefanovic, *Professor, Department of Medical Biophysics; Senior Scientist; Director of Physical Sciences, Sunnybrook Research Institute*

Scientific Symposium I Moderator

Dr. Stefanovic's lab studies in situ methods of imaging neurons, vasculature, and glia activity and metabolism in small animal models of AD, stroke and brain trauma.

Dr. Kaori Takehara-Nishiuchi, *Professor, Department of Psychology*

Scientific Symposium II Moderator

Dr. Takehara-Nishiuchi studies how the brain turns experience into knowledge to support reasoning and problem-solving. Using rodent models, her research explores how neural populations detect patterns across experiences and apply them in complex environments, and how these processes are disrupted in models of mental disorders.

Irina Alymova, *PhD Candidate, Department of Cell and Systems Biology*

Workshop Part 1 Moderator

Irina is a PhD Student in Peever-Fraigne Lab. Her project focuses on understanding the neural mechanisms that regulate arousal, a fundamental component of all animal behavior. Beyond her research, she is passionate about teaching and has helped develop coding tutorials that introduce undergraduate students to programming in an accessible and supportive way.

Dr. Ain Kim, *Post-Doctoral Fellow, Tanz Centre for Research in Neurodegenerative Diseases*

Workshop Part 2 Moderator

Dr. Ain Kim is a post-doctoral researcher at the Tanz Centre for Research in Neurodegenerative Diseases (CRND), University of Toronto. Dr. Kim's research explores the application of artificial intelligence (AI) to transform and deepen our understanding of neurodegenerative diseases, with a particular emphasis on the morphological, biochemical, and cytopathological characterization of these diseases.

Dr. Jeffrey Henderson, *Associate Professor, Department of Pharmaceutical Sciences, Leslie Dan Faculty of Pharmacy*

Awards Ceremony Moderator

Biography can be found under “Speakers”.

Dr. Hong-Shuo Sun, *Professor, Departments of Surgery, IMS, Pharmacology & Toxicology, and Physiology*

Awards Ceremony Moderator

Dr. Sun’s research is mainly focused on studying the role of ion channels in neuroprotection against cerebral ischemia and stroke, and drug development for potential treatment for stroke.

Dipa Chatterjee, *PhD Candidate, Department of Pharmacology & Toxicology*

Awards Ceremony Moderator

Dipa Chatterjee is a PhD candidate in the Beaulieu Lab, exploring how the RNA-binding protein FXR1 regulates allostatic response to stress. Her work aims to identify common downstream mechanisms underlying various psychiatric disorders.

AWARDS COMMITTEE

Jonathan Dostrovsky Award in Neuroscience:

Jeffrey Henderson, *Associate Professor, Department of Pharmaceutical Sciences, Leslie Dan Faculty of Pharmacy*
Qian Lin, *Assistant Professor, Department of Cell and Systems Biology*
Janice Robertson, *Professor, Department of Laboratory Medicine & Pathology; Senior Scientist, Tanz Centre for Research in Neurodegenerative Diseases*
Bojana Stefanovic, *Professor, Department of Medical Biophysics; Senior Scientist; Director of Physical Sciences, Sunnybrook Research Institute*
Kaori Takehara, *Professor, Department of Psychology, University of Toronto*
Chao Zheng, *Assistant Professors, Departments of Psychiatry, Chemistry, Pharmacology & Toxicology*

CPIN Graduate Student Recognition Award:

Robert Bonin, *Professor, Leslie Dan Faculty of Pharmacy*
Meghan Chenoweth, *Assistant Professor, Department of Pharmacology & Toxicology*
Kaja Jasinska, *Assistant Professor, Department of Applied Psychology and Human Development*
Junchul Kim, *Associate professor, Department of Psychology*
Loren Martin, *Professor, Department of Psychological & Brain Sciences, UTM*
Robert Rozeske, *Assistant Professor, Departments of Psychology and Cell and Systems Biology, UTSC*
Hong-Shuo Sun, *Professor, Departments of Surgery, IMS, Pharmacology, Toxicology &Physiology*

TRAINEE ORAL PRESENTATION JUDGES & MODERATORS

Chair/Judges:

Carrie Causing-Henderson, *Project Coordinator, Lunenfeld-Tanenbaum Research Institute, Sinai Health System*
Suzan Farhang-Sardroodi, *Research Associate, Department of Pharmacology and Toxicology*
Jimmy Fraigne, *Assistant Professor, Department of Cell and Systems Biology*
Francesco Leri, *Professor and Associate Vice-Principal, Research & Innovation, Department of Psychology, University of Toronto Scarborough*
Kathryn Manning, *Scientist, Hospital for Sick Children (SickKids); Assistant Professor, Department of Medical Biophysics*
Luka Milosevic, *Scientist, Krembil Research Institute; Assistant Professor, Institute of Biomedical Engineering & Institute of Medical Science*
Martin Ralph, *Professor, Department of Psychology*
Hong-Shuo Sun, *Professor, Departments of Surgery, IMS, Pharmacology & Toxicology, and Physiology*
Paul Whissell, *Assistant Professor, Department of Psychology, University of Toronto*

Moderators:

Matthew Danesh, *PhD Candidate, Department of Cell and Systems Biology*
Brittany Dugan, *PhD Candidate, Department of Cell and Systems Biology*
Angel Hsieh, *Master's Student, Department of Physiology*
Ain Kim, *Post-Doctoral Fellow, Tanz Centre for Research in Neurodegenerative Diseases*
Russell Luke, *Post-Doctoral Fellow, Department of Cell and Systems Biology*
Areeba Qureshi, *PhD Candidate, Department of Medical Biophysics*
Erin Ricaloglu, *PhD Candidate, Department of Psychology*
Jia Vedante, *Master's Student, Department of Cell and Systems Biology*
Maria Yang, *PhD Candidate, Department of Physiology*

TRAINEE POSTER PRESENTATION JUDGES

Damien Boorman, *Postdoctoral Fellow, Department of Cell & Systems Biology, UTM*

Caleb Browne, *Assistant Professor, Department of Psychiatry, University of Toronto*

Carrie Causing-Henderson, *Project Coordinator, Lunenfeld-Tanenbaum Research Institute, Sinai Health System*

Meghan Chenoweth, *Assistant Professor, Department of Pharmacology & Toxicology, University of Toronto*

Tim Corson, *Professor and Co-Director, Department of Pharmaceutical Sciences, Leslie Dan Faculty of Pharmacy, University of Toronto*

Suzan Farhang-Sardroodi, *Research Associate, Department of Pharmacology and Toxicology*

Jimmy Fraigne, *Assistant Professor, Department of Cell and Systems Biology, University of Toronto*

Jeffrey Henderson, *Associate Professor, Department of Pharmaceutical Sciences, Leslie Dan Faculty of Pharmacy, University of Toronto*

Ain Kim, *Post-Doctoral Fellow, Tanz Centre for Research in Neurodegenerative Diseases, University of Toronto*

Francesco Leri, *Professor and Associate Vice-Principal, Research & Innovation, Department of Psychology, UTSC*

Russell Luke, *Post-Doctoral Fellow, Department of Cell and Systems Biology*

Luka Milosevic, *Scientist, Krembil Research Institute and Assistant Professor, Institute of Biomedical Engineering & Institute of Medical Science*

Maxwell Shafer, *Assistant Professor, Department of Cell and Systems Biology*

Shuzo Sugita, *Professor, Department of Physiology; Senior Scientist, Krembil Research Institute*

Hong-Shuo Sun, *Professor, Departments of Surgery, IMS, Pharmacology, Toxicology & Physiology*

Yalin Sun, *Post-Doctoral Fellow, Department of Pharmacology & Toxicology*

Kaori Takehara, *Professor, Department of Psychology*

Paul Whissell, *Assistant Professor, Department of Psychology*

EVENT ORGANIZERS

Organizing Committee

Irina Alymova (Student Co-Lead)
Dipa Chatterjee (Student Co-Lead)
Zhong-Ping Feng (Chair)
Jeffrey Henderson
Ain Kim (Post-Doctoral Lead)
Janice Robertson
Bojana Stefanovic
Hong-Shuo Sun
Kaori Takehara
Tina Zhu (CPIN staff)

Award Committee

Robert Bonin
Meghan Chenoweth
Jeffrey Henderson (Co-Chair)
Kaja Jasinska
Junchul Kim
Qian Lin
Loren Martin
Janice Robertson
Robert Rozeske
Bojana Stefanovic
Hong-Shuo Sun
Kaori Takehara
Chao Zheng

Trainee Volunteers

Madeleine Coppolino
Kamy Doray
Camille Grande
Hio Ho
Hsin-Yun (Angel) Hsieh
Alena Ionova
Jiyoon Jeong
Emily Kuik
Jino Lim
Russell Luke
Joshua Olorocisimo
Erin Ricaloglu
Maria Yang
Ryan Yip
Xinyao Zhuang

Program Booklet Design

Irina Alymova
Dipa Chatterjee
Victoria Ivakitch **(Cover Design)**
Trusha Tullu
Areeba Qureshi
Tina Zhu

Moderators & Judges

Event Moderators
Oral Presentation
Poster Presentation

Sponsorship Committee

Irina Alymova
Dipa Chatterjee
Hong-Shuo Sun
Chao Zheng

Administration

Zhong-Ping Feng
Kateryna Maksymenko
Tina Zhu

CPIN PARTICIPANTING GRADUATE UNITS AND SPONSORS

Biochemistry
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Institute of Biomedical Engineering
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UNIVERSITY OF TORONTO | Department of Cell & Systems Biology

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UNIVERSITY OF TORONTO

Psychology
UNIVERSITY OF TORONTO

Rehabilitation Sciences Institute
UNIVERSITY OF TORONTO

UNIVERSITY OF TORONTO
FACULTY OF KINESIOLOGY & PHYSICAL EDUCATION

Krembil UHN

MCE® MedChemExpress

APPENDIX: ABSTRACTS

[#1] Tesam Ahmed; Institute of Medical Science

Supervisor: Dr. Daniel Felsky

Theme: Developmental Neuroscience (Oral Presentation)

IDENTIFYING SUBTRAJECTORIES OF PSYCHOTIC-LIKE EXPERIENCES (PLEs) IN ADOLESCENTS: A GROUP-BASED MULTIVARIATE TRAJECTORY (GBMT) ANALYSIS

Ahmed T1,2; Felsky D1,2,3,4*

1 Krembil Centre for Neuroinformatics, Centre for Addiction and Mental Health, Toronto, Ontario, Canada; 2 Institute of Medical Science, University of Toronto, Toronto, Ontario, Canada; 3 Department of Psychiatry, University of Toronto, Toronto, Ontario, Canada; 4 Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, Canada

Introduction: Psychotic-like experiences (PLEs) are subclinical symptoms often associated with psychopathology and increased mental health service utilization. It is important to identify PLE subtrajectories that account for symptom type and severity to identify distinguishing factors influencing impairment between groups.

Objective: The aim of this study was to identify subtype-informed PLE groups that can inform the longitudinal mental and social functioning of youth.

Methods: We analyzed data from the Adolescent Brain Cognitive Development (ABCD) study including n = 11,190 participants aged 9-10 from baseline to 6-year follow-up. Group-based multivariate trajectory (GBMT) analysis was applied to define participant subgroups using the 21-item Prodromal Questionnaire - Brief Child Version (PQ-BC). Each of 21 questions was scored 0/1/2 signifying: not endorsed, endorsed, or endorsed with notable severity (>0 on PQ-BC distress). AIC and BIC guided optimal model selection. We then analyzed associations between subtrajectories and changes in mental health functioning (CBCL), and prosocial behaviors. GBMT subgroups were compared with existing PLE subgroup definitions.

Results: We identified 5 latent classes: Perceptual/Cognitive-Negative (n = 1,861; 16.6%), Low-Stable (n = 5,176; 46.3%), High-Persistent-Multisymptomatic (n = 818; 7.3%), Sensory-Grandiose (n = 948; 8.5%), and Visual-Ideational (n = 2,387; 21.3%). Compared to existing trajectory definitions according to Karcher et al. (2022) - based on threshold aggregate Z-scores using an identical clinical subsample (N = 9,118), GBMT-defined classes explained significantly more variance in prosocial behavior across baseline (R2 = 0.12 vs 0.002), 6-year follow-up (R2 = 0.003 vs 0.001), and longitudinal change (R2 = 0.009 vs 0.003). The High-Persistent-Multisymptomatic group remained the most impaired in mental health functioning at the final visit compared to all other classes ($p < 0.001$).

Conclusion: This study has identified novel type and severity-informed PLE subtrajectories that improve prediction of functional changes in youth over time.

[#2] Ariya Ahona; Department of Pharmacology & Toxicology

Supervisor: Dr. Meghan J. Chenoweth

Theme: Behavioural and Social Neuroscience (Oral Presentation)

GENOME-WIDE INTERACTION STUDY REVEALS RISK LOCI FOR HEAVIER SMOKING AMONG CANNABIS USERS

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Introduction: Tobacco smoking is highly heritable and the leading cause of preventable disease and death worldwide. Co-use with cannabis is common and associated with greater dependence, heavier use and poorer cessation in both substances.

Objective: Using a genome-wide interaction study (GWIS), we tested whether cannabis use moderates genetic influences on tobacco smoking heaviness.

Methods: Analyses were conducted in tobacco smokers of European ancestry from the Pharmacogenetics of Nicotine Addiction Treatment (PNAT, NCT01314001; n=916) trial and UK Biobank (UKB; n=4,187). Current cannabis use was self-reported. GWIS tested SNP-by-cannabis use interaction effects on cotinine (COT) in PNAT, and on cigarettes smoked per day (CPD) in UKB. COT, the major metabolite of nicotine, and CPD are an established biomarker and self-reported measure of smoking heaviness, respectively. Cannabis use was defined as current use in PNAT and ever use in UKB. Models adjusted for SNP and cannabis use main effects, age, sex, and the first four principal components of ancestry. Top SNPs were annotated using Functional Mapping and Annotation of Genome-Wide Association Studies (FUMA).

Results: The top PNAT SNP-by-cannabis use interaction on COT was rs467683 (P=7.9e-8) near STXBP5L. The T (vs. G) allele showed no main effect on COT but was associated with higher COT levels among current cannabis users. STXBP5L (syntaxin binding protein 5L) inhibits vesicle trafficking, including neurotransmitter release, and was previously identified in a GWAS of cigarette smoking initiation. The UKB top SNP-by-cannabis use interaction on CPD was rs4495669 (P=5.0e-7) near LMX1A and PBX1. The A (vs. G) allele showed no main effect on CPD but was associated with higher CPD among ever cannabis users. LMX1A (LIM homeobox transcription factor 1 alpha) is involved in embryonic development of dopaminergic neurons. PBX1 (pre-B-cell leukemia homeobox 1), a transcription factor also involved in developmental processes, was previously identified in a GWAS of cigarette smoking initiation.

Conclusion: Although tobacco smoking rates are decreasing in the general population, increasing cannabis use, in part due to its ongoing legalization, may worsen smoking cessation outcomes and tobacco-related health burden. Our GWIS findings highlight potentially susceptible subgroups (e.g., individuals with the r4676831 T allele or rs4495669 A allele) where cannabis use may amplify the risk of heavier tobacco smoking.

[#3] Evelyn Ajayi; Institute of Medical Science
Supervisor: Dr. Jennifer Crosbie
Theme: Brain Development and Lifespan Neuroscience (Poster Presentation)

EFFECT OF PHYSICAL AND SOCIAL ENVIRONMENTAL EXPOSURES ON NEURODEVELOPMENTAL DISORDERS IN ONTARIO CHILDREN AND YOUTH

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Introduction: Childhood physical (e.g., air pollution) and social (e.g., socioeconomic status) environmental factors have been linked to diagnoses of neurodevelopmental disorders (NDD) such as ADHD, OCD and autism. However, past studies have looked at individual environmental factors (e.g., nitrogen dioxide - NO2; fine particulate matter - PM2.5; social and material deprivation) rather than the combined effects of these factors and have ignored potential confounders such as increased distance to mental health care. Further, to understand the relationship between physical and social environmental factors and NDDs, population-based samples that look at quantitative traits of NDDs, rather than diagnosis alone, will boost power and improve the generalizability of findings.

Objective: This study aimed to (1) test the association of individual physical environment (greenspace deprivation, PM2.5, NO2) and the social environment (material deprivation, social deprivation,) exposures during childhood with quantitative NDD traits (ADHD, autism, OCD) (2) test the combined effect of physical and social exposures during childhood on each NDD trait, and (3) to test whether proximity to care mediates the relationship of physical and social exposures during childhood on NDD traits. It was hypothesized that greater environmental risk exposure will be associated with higher NDD traits in univariable and multivariable models. It was also hypothesized that distance to care will partially or fully mediate associations between environmental exposures and NDD traits.

Methods: Spit for Science is a general population sample (ages 6-17 years; N = 22,041) with quantitative measures of ADHD traits, autism traits, OCD traits, as well as postal Codes at the time of data collection. In a sub-sample (n = 15,728), postal codes were geospatially linked to environmental and Census data to derive physical (greenspace deprivation, PM2.5, NO2) and social (material and social deprivation) exposures and proximity to care. Univariable and multivariable regressions assessed associations between exposures and NDD traits, with mediation analyses examining distance to care for significant associations.

Results: In univariable analyses, reduced greenspace deprivation, PM2.5, and NO2, but increased material deprivation and social deprivation were each significantly associated with higher ADHD traits ($p < 0.01$), while only increased material deprivation was significantly associated with higher autism trait scores ($p < 0.01$). In the multivariable analyses, for ADHD traits, the same pattern of effects was found across exposures ($p < 0.01$). For autism traits, higher material deprivation ($p < 0.01$) and social deprivation ($p < 0.05$), but reduced NO2 was significantly associated with higher traits ($p < 0.05$). Finally, proximity to care completely mediated the relationship between NO2 and ADHD trait scores but partially mediated the association for greenspace deprivation, PM2.5, material deprivation, social deprivation and ADHD trait scores. Distance to healthcare did not mediate the association between any of the environmental variables and autism traits.

Conclusion: All physical and social exposures were differentially associated with ADHD and autism traits but were not associated with OCD traits. Despite some unexpected findings,

material and social deprivation were clearly linked to neurodevelopmental disorders. Improving exposure measurement precision to understand environmental influences further may enhance risk prediction, guide interventions, and inform policies supporting Canadian children and families.

[#4] Alameen Alajeely; Department of Pharmaceutical Sciences

Supervisor: Dr. Robert Bonin

Theme: Motor & Sensory Control (Oral Presentation)

ANALGESIC EFFECT OF MDMA IN MOUSE MODELS OF ACUTE SPONTANEOUS PAIN

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Introduction: The classic psychedelic, 3,4-Methylenedioxymethamphetamine (MDMA) has displayed analgesic properties in humans with pain disorders and in preclinical models; however, the mechanisms, efficacy, and possible sex-dependence of MDMA analgesia remain unclear. Here we investigate the analgesic properties of MDMA in mouse pain assays, specifically, the Formalin Assay (FA) and Acetic Acid Writhing Assay (AAWA). Experiments were performed across male and female mice to investigate potential sex differences.

Hypothesis: MDMA administration will decrease pain expression behaviour in mouse models of spontaneous pain

Methods: Male and female C57BL/6J mice aged 10-12 weeks old received either 2.5 mg/kg, 5.0 mg/kg, or saline control systemically 30 minutes prior to behavioural assays. FA involves the intraplantar injection of 2.5% formaldehyde in dH2O to induce biting and licking of the injected paw. Biting and licking occur in two phases after injection: phase 1 from 0-10 minutes and phase 2 from 15-60 minutes. AAWA involves intraperitoneally injecting 1% acetic acid in dH2O to induce 'writhing' behaviour - a contortion of the abdomen and extension of the hind limbs. Mouse behaviour in both assays was video recorded and manually assessed.

Results: Across assays and sexes, 5.0 mg/kg MDMA significantly decreased the expression of pain behaviour compared to saline controls. Time binned analysis within FA further revealed significant decreases in biting and licking in mice which received 2.5 mg/kg and 5.0 mg/kg MDMA during phase 1, but only mice that received 5.0 mg/kg displayed a significant decrease in phase 2. In AAWA, male and female mice that received 5.0 mg/kg MDMA spent significantly less time writhing compared to saline controls. Notably, female but not male mice that received 2.5 mg/kg MDMA also displayed significantly less time writhing.

Conclusions: Our work has revealed promising analgesic effects of MDMA in multiple mouse models of tonic pain and expands on earlier findings of MDMA-analgesia in both humans and rodents. This work offers an animal model in which the biological mechanisms of this novel treatment can be studied. Future work will investigate the potential spinal and supraspinal sites of MDMA analgesia and explore whether the effects of this drug involve distinct subtypes of dorsal horn 5-HT receptors. The development of novel pain therapies based on serotonergic psychedelics is promising and offers potential alternative treatments for pain disorders.

[#5] Mryam Ali; Department of Psychology

Supervisor: Dr. Benjamin T. Dunkley

Theme: Cognitive Neuroscience (Oral Presentation)

MULTIVARIATE ASSOCIATIONS BETWEEN RESTING STATE MEG OSCILLATORY AND APERIODIC SPECTRAL FEATURES AND PTSD SYMPTOM DIMENSIONS

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Introduction: Posttraumatic stress disorder (PTSD) is increasingly understood as involving disruptions across distributed neural systems supporting memory and cognitive regulation rather than reflecting a single fear-based condition. However, most electrophysiological studies continue to rely on categorical diagnostic comparisons and univariate approaches that cannot capture how continuous symptom dimensions relate to coordinated variation in large-scale brain activity. Multivariate models integrating oscillatory rhythms with the aperiodic structure of neural signals provide a principled framework for examining brain–symptom relationships across the spectrum
of trauma-related symptom expression.

Objective: This study examined whether continuous dimensions of posttraumatic stress symptoms (PTSS) are associated with coordinated variation in periodic and aperiodic resting-state
magnetoencephalography (MEG) spectral features using canonical correlation analysis (CCA).

Methods: Resting-state MEG data were collected from 151 trauma-exposed members and veterans of the Canadian Armed Forces (CAF) during a five-minute eyes-open recording. Symptom severity was measured using the PTSD Checklist Military Version (PCL-M). Anxiety (GAD-7), depression (PHQ-9), and concussion diagnosis were included as covariates. Source-resolved oscillatory power across canonical frequency bands, together with parameterized aperiodic slope and offset components, was analyzed to capture complementary aspects of large-scale neural population dynamics. CCA was used to identify multivariate relationships linking symptom dimensions with coordinated patterns of neural activity across individuals.

Results: Significant multivariate relationships linked reexperiencing, avoidance or withdrawal, and hyperarousal symptom dimensions to coordinated variation in delta, theta, beta, and low gamma oscillatory activity, together with regional differences in aperiodic slope and offset. Multiple statistically significant canonical functions revealed partially separable symptom-specific electrophysiological signatures rather than a single shared neural disturbance, indicating that distinct symptom dimensions map onto dissociable patterns of large-scale neural activity variation.

Conclusion: These findings demonstrate that variability in PTSS expression maps onto coordinated oscillatory and aperiodic neural dynamics across distributed brain systems supporting memory coordination and cognitive regulation. Rather than reflecting a unitary fear-

based neural disturbance, distinct canonical functions revealed symptom-specific alterations across large-scale neural systems. Together, these results provide electrophysiological support for a dimensional systems-level framework of trauma-related symptom expression and identify resting-state MEG spectral features as candidate markers of symptom-specific neural variation across trauma-exposed individuals

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Supervisor: Dr. Zhong-Ping Feng
Theme: Cellular & Systems Neuroscience (Poster Presentation)

GLP-1R AGONIST CONFERS NEUROPROTECTION AND PRESERVES BLOOD–BRAIN BARRIER INTEGRITY FOLLOWING HYPOXIC-ISCHEMIC BRAIN INJURY IN NEONATAL MICE

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Introduction & Hypothesis: Hypoxic-ischemic brain injury (HIBI) is a leading cause of mortality and long-term neurological deficits. Treatments such as therapeutic hypothermia are only partially effective in severe injuries. Secondary injury mechanisms involving proinflammatory cascades and dysregulation of the BBB exacerbating neuronal apoptosis leading to worse clinical outcomes. Experimental models of neurological injuries show that diabetes drug semaglutide, a glucagon-like-1-receptor agonist (GLP-1R), exerts neuroprotective effects. However, the neuroprotective effect of semaglutide in neonatal HIBI and the associated mechanisms by which it mediates neuroprotection remains elusive. Here we assess the neuroprotective effect of GLP-1R agonists in neonatal HIBI via BBB preservation and anti-inflammation.

Methods: The modified Vannucci model of HIBI in neonatal mice was used to assess the effect of Semaglutide (given by i.p), a GLP-1R agonist. Neurofunctional outcomes were assessed through short term behavioral assays and infarct volume was quantified using triphenyltetrazolium chloride staining. Western blot was performed for molecular analysis. Transcriptional analysis of publicly available RNA sequencing data for identifying potential molecular mechanisms. We also will perform Evans Blue to assess vascular leakage.

Results: Semaglutide significantly reduced infarction volume, increased pAkt/Akt ratio and decreased MMP-9/MMP-2 ratio in HIBI mice relative to vehicle-treated controls, suggesting the neuroprotective effect is associated with activation of the PI3K-Akt pro-survival pathways, and reduction of MMP-driven BBB disruption. Transcriptomic analysis further indicates Semaglutide modulates inflammatory and neurogenic signaling pathways.

Conclusions: Semaglutide provides significant neuroprotection against HIBI through preserving BBB integrity and regulating inflammatory responses. These effects are mediated through activation of downstream pro-survival and anti-inflammatory signaling pathways.

[#7] Yasma Ali-Hassan; Department of Rehabilitation Sciences
Supervisor: Dr. Kristin Musselman
Theme: Motor & Sensory Control (Oral Presentation)

STIMULATING POSTURAL CONTROL TO AUGMENT REHABILITATION AFTER CEREBRAL STROKE (SPARC): A PILOT TRIAL

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Introduction: Impaired balance control is a major factor limiting safe mobility after stroke. Reactive balance training (RBT), which involves repeated practice of reactive stepping following a loss of balance, has been shown to reduce fall risk in people with stroke. However, some individuals, particularly those with moderate to severe sensorimotor impairments, may have difficulty performing the repetitive reactive stepping required for RBT. A possible technique to improve the efficacy of RBT for individuals with stroke is transcutaneous spinal stimulation (TSS), a non-invasive neuromodulation technology involving electrical stimulation of nerves around the spinal cord to increase the excitability of the spinal circuitry during rehabilitation.

Objective: The Stimulating Postural control to Augment Rehabilitation after Cerebral stroke (SPARC) is a pilot, assessor-blinded, randomized, sham-controlled trial. The objectives of this trial are to: 1) Describe and compare clinical and biomechanical outcomes between individuals with stroke who receive the balance intervention with TSS and those who receive the balance intervention with sham TSS; 2) Determine the acceptability of balance intervention combined with TSS. We hypothesize that participants receiving the balance intervention with TSS will demonstrate greater changes in measures of upright balance control, balance confidence and reactive stepping ability,

than participants receiving the balance intervention with sham TSS. We also hypothesize that participants will perceive the balance intervention with TSS as useful and easy to use.

Methods: Sixteen individuals >1 year post-stroke will be randomly allocated to one of the following intervention groups: 1) RBT + TSS and 2) RBT + sham TSS. Participants in each group will attend three 60-minute sessions/week for four weeks, with TSS or sham TSS applied to the lumbar spinal cord throughout each session. RBT will involve repetitive practice of reactive stepping in response to external perturbations (i.e. pushes/pulls by trainer) while the participant is attached to an overhead harness for safety. Measures of reactive stepping ability (Lean-and-Release test), upright balance control (mini-BESTest) and balance confidence (Activities-specific Balance Confidence (ABC) Scale) are collected at baseline, immediately post-intervention, and three months post-intervention. To evaluate intervention acceptability, participants will complete the Technology Acceptance Model 2 (TAM2) Questionnaire at the post- intervention assessment. Descriptive and inferential statistics

will be used to interpret the study outcomes.

Results: To date, five participants (three in RBT + TSS group) have completed the study. All three participants in the RBT + TSS group showed a greater proportion of single step responses on the Lean-and-Release Test,

whereas the two participants in the RBT + sham TSS group did not. All participants showed clinically meaningful improvements in mini-BESTest scores. Regarding balance confidence, one participant in the RBT + TSS group and in both participants in the RBT + sham TSS group showed a clinically meaningful change. All participants completed the TAM2 questionnaire post-intervention which will be analyzed descriptively

Conclusion: Impaired upright balance following stroke can substantially reduce independence in mobility leading to significant personal, social, and health impacts. Effective balance interventions are therefore needed to promote the recovery of safe functional mobility. Early findings of the SPARC trial suggest that TSS can be integrated into balance interventions for individuals with stroke. By advancing evidence for tech-based balance rehabilitation, the SPARC pilot study has the potential to expand stroke rehabilitation practices.

[#8] Alessia Alicandro; Department of Cell and Systems Biology

Supervisor: Dr. Kaori Takehara

Theme: Cognitive Neuroscience (Oral Presentation)

COMPARISON OF COLLATERALIZATION AND PROJECTION DENSITY OF PREFRONTAL CORTEX NEURONS PROJECTING TO THE LATERAL ENTORHINAL CORTEX

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Introduction: The prefrontal cortex (PFC) mediates diverse cognitive and affective functions through subregions with distinct cortical and subcortical projections. Particularly, the role of the PFC in learning and memory relies on interactions with the lateral entorhinal cortex (LEC). However, the anatomical organization supporting this connection is incompletely understood.

Objective: We compared the density of projections to the LEC originating from four subregions of the PFC: the medial orbitofrontal cortex (ORBm), prelimbic cortex (PL), infralimbic cortex (IL), and anterior cingulate cortex (ACC), followed by investigating the presence of collateralizations to alternative brain regions in mice.

Methods: To visualize PFC cells projecting to the LEC, retrograde AAV carrying EGFP was infused into the LEC. Following this anterograde AAV carrying mCherry was infused in the ORBm and PL respectively and analyzed in the LEC. Finally, to determine whether LEC-projecting PFC neurons affect additional brain regions via axon collaterals, we examined their distribution patterns by injecting a retrograde AAV cre recombinase into the LEC, and cre-inducible anterograde AAV mCherry tracer into the PL or ORBm.

Results: Among the examined PFC subregions, the highest density of retrograde GFP labeled cells was detected in the superficial ORBm. Anterograde tracing intensity measures modelled that both ORBm and PL subregions primarily project to the deep layers of the LEC. Furthermore, both PL and ORBm subjects displayed axon collaterals to the perirhinal cortex and amygdala from LEC-projecting cells.

Conclusion: These findings reveal that the PFC subregions exhibit distinct patterns in the density of efferents to the LEC and contribute to

a larger network circuit involving subcortical structures. These anatomical differences may underlie the varying involvement of PFC subregions across the different stages of memory processes and content, while coordinating activity across multiple downstream regions.

[#9] Irina Alymova; Department of Cell and Systems Biology

Supervisor: Dr. John Peever and Dr. Jimmy Fraigne

Theme: Systems and Circuits Neuroscience (Oral Presentation)

HYPOTHALAMIC DOPAMINE AND HISTAMINE CIRCUIT REGULATES AROUSAL

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Introduction: Dopamine and histamine are neurotransmitter systems that promote arousal. Supporting this, dopaminergic drugs are prescribed to combat daytime sleepiness, and anti-histaminergic allergy medications induce drowsiness. However, we still do not fully understand how these neurotransmitter systems interact to orchestrate arousal. Our lab previously identified a group of dopamine neurons in the A11 hypothalamic nucleus that regulate arousal. These cells are active during wakefulness, and activation of these neurons promotes arousal from sleep. However, the downstream mechanisms by which dopaminergic A11 neurons promote wakefulness is still unclear.

Objective: Here, we hypothesized that A11 neurons control wakefulness by interacting with the histamine neurons of the tuberomammillary nucleus (TMN).

Methods: To test if the A11→TMN circuit is involved in arousal, we used a genetically encoded dopamine sensor (i.e., GRABDA) to record dopamine release in the TMN.

Results: We found that dopamine release was highest during wakefulness and lowest during NREM and REM sleep (One-Way ANOVA, $p < 0.05$, $n = 8$). Additionally, dopamine release was higher in prolonged wake bouts (>20 s) compared to shorter bouts (<20 s) (paired t-test, $p < 0.05$, $n = 8$). Next, to assess the functional role of the A11→TMN circuit, we optogenetically activated A11 axon terminals in the TMN. Activating the A11→TMN pathway prolonged periods of wakefulness by 87% compared to controls (Two-Way Anova, $p < 0.05$, $n = 7$). Lastly, we showed that the A11→TMN pathway is dependent on dopamine receptor 2 (D2R)-mediated neurotransmission, as D2R antagonism abolished the wake-promoting effects of A11→TMN activation (paired t-test, $p < 0.05$, $n = 5$).

Conclusion: These findings show that the A11→TMN dopamine-histamine circuit functions to sustain wakefulness, which will help identify potential drug targets for sleep disorders, such as insomnia, narcolepsy, or idiopathic hypersomnia.

[#10] Kayla Baker; Institute of Medical Science

Supervisor: Dr. Gaspard Montandon

Theme: Systems and Circuits Neuroscience (Oral Presentation)

A MIDBRAIN CIRCUIT COORDINATING RESPIRATION WITH BEHAVIORS IN RODENTS IN VIVO

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Introduction: Breathing is an essential process controlled by the brainstem breathing centers; still, it is also highly flexible and can be synchronized with behaviours requiring activation of respiratory muscles. Respiratory neural circuits receive projections from many brain regions, allowing respiratory muscles to be modulated to accommodate various motor behaviours. The periaqueductal grey matter (PAG), located in the midbrain, sends projections to the medulla and can coordinate autonomic functions such as breathing with behaviours. However, the types of PAG neurons involved in breathing and their functions remain unclear.

Objectives: Somatostatin (SST) is an inhibitory neuropeptide located in the ventrolateral PAG (vlPAG), and we aim to if SST vlPAG neurons can modulate respiratory rhythm and if it is coordinated with behaviour. We used optogenetics to selectively activate SST vlPAG cells by expressing channelrhodopsin in SST cells using cre-lox recombination.

Methods: We measured respiratory activity with whole-body plethysmography and recorded motor behaviours in freely-behaving mice while photostimulating SST cells.

Results: We observed that activation of SST vlPAG cells stimulates breathing and also initiates a simultaneous increase in locomotor activity. Additionally, as the PAG is a key region in the descending pain pathway, activating SST vlPAG cells decreased the latency to tail flick, thereby facilitating the nociceptive response.

Conclusion: Our results suggest that stimulation of SST vlPAG neurons independently modulated respiratory, motor activity, and nociception. These cells may be involved in modulating respiratory muscle activity to produce non-respiratory behaviours or in coordinating breathing with other behaviours.

[#11] Mary-Claire Ball; Department of Applied Psychology & Human Development

Supervisor: Dr. Kaja Jasińska

Theme: Brain Development and Lifespan Neuroscience (Poster Presentation)

NEURAL ACTIVATION DURING READING: EVIDENCE FROM MULTILINGUAL COMMUNITIES IN RURAL CÔTE D'IVOIRE

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Introduction: 200 million children around the world are learning to read in a new language at school (UNESCO, 2016). In rural Côte d'Ivoire, children speak one, two, or more Ivorian languages at home but learn to read in French at school (Jasińska & Guei, 2023). The mismatch between home and school languages is a contributing factor to poor reading outcomes (Alkateb-Chami, 2024), since children leverage spoken language skills (e.g., phonological

awareness, vocabulary) for reading. As such, language processing regions in the brain, particularly left hemisphere frontal and temporo-parietal regions, are active during reading tasks (Jasińska et al., 2016). Previous research has found differences in neural activation patterns between monolingual and bilingual children. Bilingual children demonstrate more robust activation in left hemisphere language processing regions (Jasińska & Petitto, 2013; 2014; Kovelman et al., 2008a), the prefrontal cortex, as well as right hemisphere regions, during reading tasks (Jasińska & Petitto, 2013; 2014). Further, activation patterns change depending on reading skill level. Proficient readers rely less on sounding out words letter-by-letter and therefore show greater activation in semantic processing areas (Jasińska & Petitto, 2014). Importantly, behavioural research conducted in both Global North contexts (Jasińska & Petitto, 2018; Kovelman et al., 2008b) and rural Côte d'Ivoire has found that bilingual children demonstrate better language and reading skills than their monolingual peers (Ball et al., 2022; under review; submitted). However, few neuroimaging studies have examined neural activation for reading among monolingual and bilingual children in low-literacy and multilingual Global South contexts, like rural Côte d'Ivoire.

Objective: To better understand how neural activation relates to reading skill in low-literacy and multilingual contexts, we asked: 1) What patterns of neural activation are associated with better reading in rural, multilingual communities? 2) Do monolinguals and bilinguals differ in activation patterns during reading tasks? Based on previous neuroimaging and behavioural studies, we predicted that both bilinguals and better readers would show more robust activation in the left hemisphere language processing regions, particularly in semantic processing regions, with additional recruitment of right hemisphere regions.

Methods: Children (N=75, M age=9.43, SD age=1.41) completed standardized French language and literacy assessments from the Early Grade Reading Assessment (RTI International, 2015) and a French print speech task while undergoing functional near-infrared spectroscopy. The print speech task randomly presented stimuli in a block design; within the print condition, children were shown familiar French words, pseudowords, and false fonts. Within the speech condition, children heard familiar French words, pseudowords, or vocoded speech sounds.

Results & Conclusion: Preliminary findings suggest that better readers have increased activation in the left inferior and middle frontal gyri as well as the right middle temporal gyrus. Differences in neural activation patterns between monolinguals and bilinguals are currently being analyzed; findings and implications will be shared at Research Day.

[#12] Sayona Bhattacharyya; Department of Psychology

Supervisor: Dr. Robert Rozeske

Theme: Psychiatric Disorders II (Poster Presentation)

INVESTIGATING THE EFFECTS OF PRIOR STRESS AND THREAT AMBIGUITY ON CONTEXT-BASED FEAR DISCRIMINATION

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Introduction: Context-based fear discrimination is the ability to distinguish between safe and threatening environments. A hallmark of post-

traumatic stress disorder (PTSD) is the intrusive re-experiencing of traumatic memories in non-threatening contexts, reflecting impaired context processing. Medial prefrontal cortex dysfunction underlies this deficit. To inform the development of targeted therapeutics, we examined, how trans-situational effects of stress and threat ambiguity shape context fear discrimination.

Objectives: We used a novel augmented-reality fear conditioning "teleporter" apparatus to determine if experiential factors alter context-based fear discrimination. We had two hypotheses: (1) intermittent restraint stress would produce impaired fear discrimination and (2) context ambiguity would produce dynamic changes in fear discrimination across days.

Methods: In study 1, mice were exposed to restraint stress for 1 hour across 2 consecutive days, before testing discrimination between a safe and threatening context over 3 days. In study 2, mice were tested during gradual transitions between the safe ↔ ambiguous ↔ threatening contexts. Freezing behaviour was used to quantify fear expression in both studies.

Results: Intermittent restraint stress produced fear generalization that disappeared upon subsequent tests. Alternatively, mice exposed to gradual threat transitions showed improved context discrimination across days. Within transition periods, mice shifted their freezing behaviour as a function of context ambiguity.

Conclusion: These findings indicate that stress history and context threat ambiguity affect fear discrimination in a time-dependent manner, motivating future studies to track prefrontal cortex neuronal population changes over days.

[#13] Grace Burns; Department of Medical Biophysics

Supervisor: Dr. Kathryn Manning

Theme: Behavioural and Social Neuroscience (Oral Presentation)

CHILD BRAIN IMAGING OUTCOMES FOLLOWING THE VID-KIDS PROGRAM FOR IMPROVING INTERACTIONS BETWEEN DEPRESSED MOTHERS AND THEIR INFANTS

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Introduction: Postpartum depression affects an estimated 12–15% of mothers globally and is associated with reduced mother-infant interaction quality and altered child development. The VID-KIDS program is a nurse-delivered video-feedback intervention designed to enhance 'serve and return' interactions by improving depressed mothers' sensitivity and responsiveness to infant cues. Characterizing how maternal depression shapes the developing brain, and whether early supportive interventions, like VID-KIDS, can

meaningfully alter developmental trajectories, is crucial for improving long-term outcomes for families. Evidence from electroencephalogram (EEG) studies links right-frontal asymmetry, a marker associated with depression, to children exposed to maternal depression, and positive mother-infant interactions have been shown to mitigate this asymmetry. However, MRI-based investigations of how parenting interventions may shape developing neural circuits remain limited.

Objective: This project will employ multi-modal MRI to characterize group-level differences between children of depressed mothers who received the VID-KIDS intervention and controls who did not. Based on observations from previous EEG studies, differences are expected in lateralized networks such as the frontal-parietal network, with children whose mothers received the VID-KIDS intervention showing less right-lateralization than the control group.

Methods: The VID-KIDS randomized controlled trial enrolled 140 mother–infant dyads (75 intervention, 65 control) (5). Interaction quality (Parent-Child Interaction Teaching Scale), maternal depressive symptoms (EPDS), and child developmental outcomes (ASQ-3) were assessed at baseline, immediately post-intervention, and at a two-month follow-up. A neuroimaging subset comprised 48 children aged 3 to 8 (31 intervention, 17 control, 30 male, mean age = 4.9 years). Child behavioural outcomes at the MRI timepoint were assessed using the Child Behaviour Checklist (CBCL) and the Behavior Rating Inventory of Executive Function - Preschool Version (BRIEF-P). Resting-state functional MRI (fMRI) and diffusion tensor imaging (DTI) data will be preprocessed using FSL software. The frontal-parietal functional network will be uncovered using independent component analysis, and nodes will serve as seeds for diffusion tractography. Imaging and survey data of children whose mothers received the VID-KIDS treatment will be compared to those of children whose mothers did not. To further uncover the mitigating effects of this intervention, the treated group will also be compared to age-matched participants in a parallel study who were not exposed to maternal depression.

Results: Significantly higher mother-child interaction scores were observed in the intervention group compared to the control, both immediately post-test and 2 months post-intervention. Images from 36 participants (23 intervention, 13 control, 23 male, mean age = 5.3 years) were successfully collected. Group differences in the functional and structural connectivity and lateralization of the frontal-parietal network will be quantified. Linear mixed-effects models will be used to determine relationships between maternal symptoms, child behaviour, and brain connectivity.

Conclusion: VID-KIDS improves early mother–infant interaction quality among mothers experiencing postpartum depression. We will integrate behavioral outcomes of mothers and children with functional and diffusion-based MRI findings to explore how early interventions influence the organization and early development of brain network connectivity.

[#14] Candela Castro; Department of Music

Supervisor: Dr. Michael Thaut

Theme: Cognitive Neuroscience (Oral Presentation)

COGNITIVE INTERACTIONS AND TRANSFER EFFECTS BETWEEN MUSICAL WORKING MEMORY AND LANGUAGE: A THREE-STUDY RESEARCH PROTOCOL

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Introduction: Music and language rely on the real-time processing of sequential information, and working memory (WM) is a key mechanism supporting both domains. Growing evidence suggests a partial overlap of cognitive and neural mechanisms between musical and verbal WM, and musicians often outperform non-musicians on WM tasks. It is still unclear whether musical WM advantages transfer to broader language functions. In post-stroke aphasia, WM impairments are common and have been shown to predict language outcomes and therapy response, although it is not always explicitly targeted in language rehabilitation. This research protocol investigates musical and verbal WM interactions as a potential mechanism for music-based aphasia rehabilitation.

Objective: This project aims to examine the extent to which musical and verbal WM share underlying cognitive resources, whether musical WM performance transfers to language functions, and whether music-based WM training can improve verbal WM and language outcomes in individuals with post-stroke aphasia. It is hypothesized that musical and verbal WM rely on partially overlapping mechanisms, and that auditory musical WM may serve as a cognitive scaffold to support verbal WM and language processing in aphasia.

Methods: This research protocol includes three complementary studies. Study 1 is a cross-sectional, between-subjects study comparing 100 healthy adult musicians and non-musicians. Participants will complete measures of verbal WM, auditory WM, musical WM, visuospatial WM, and language performance, including Digit Span, Listening Span, Nonword Repetition, tonal and rhythmic musical WM tasks, n-back tasks, sentence comprehension, and phonemic fluency.

Study 2 is a cross-sectional pilot study with at least 10 adults with chronic post-stroke aphasia and verbal WM deficits. This study will characterize musical WM profiles in aphasia and examine their relationship with verbal WM and language measures, including Digit Span, verbal n-back, nonword repetition, sentence repetition, musical WM, visuospatial WM, sentence comprehension, and language repetition.

Study 3 is a single-arm delayed-start waitlist pre-post pilot intervention study with individuals with chronic aphasia. The intervention will use a Neurologic Music Therapy protocol focused on Auditory Perception Training to target auditory musical WM. Outcomes will include feasibility measures, such as recruitment, retention, adherence, and acceptability; target engagement measures of verbal and musical

WM; and transfer outcomes, including sentence comprehension and language repetition.

Results: The proposed studies are expected to generate a detailed map of auditory, musical, verbal, and visuospatial WM profiles in musicians and non-musicians; provide the first detailed characterization of musical WM in aphasia; and offer preliminary evidence regarding the feasibility and potential transfer effects of an NMT-based WM intervention for aphasia rehabilitation.

Conclusion: This research program will clarify the extent of overlap and dissociation between musical and verbal WM systems and examine whether musical WM can support language processing in aphasia. It will also inform the development of mechanism-driven, music-based interventions for post-stroke aphasia rehabilitation.

[#15] Nicole Cesca; Department of Rehabilitation Sciences

Supervisor: Dr. Kristin Musselman

Theme: Pain and Sensory Disorders II (Poster Presentation)

GAZE BEHAVIOUR AND SPATIOTEMPORAL METRICS DURING WALKING TASKS IN AMBULATORY INDIVIDUALS WITH SPINAL CORD INJURY

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Introduction: Individuals with incomplete spinal cord injury (SCI) often have difficulty with complex walking tasks (e.g., obstacle negotiation) due to impaired gait adaptability (i.e., ability to adjust walking pattern to task demands). This limitation increases the risk of falls and limits community walking. Visual input is critical for modulating walking patterns; yet, how individuals with SCI use vision (i.e., gaze behaviour) during walking remains poorly understood.

Objective: To compare gait adaptability metrics including eye gaze behaviour (e.g., number of fixations, fixation duration) and spatiotemporal gait parameters (e.g., step length, width) during gait adaptability tasks between individuals with SCI and age- and gender-matched individuals without SCI.

Methods: This cross-sectional study included seven walking tasks: 1) navigating around a 32-gallon cylindrical trash can, 2) stepping over a 3-inch Styrofoam obstacle, 3) stepping onto a 7.75-inch wooden platform, 4) crossing a perpendicular carpet, 5) dual-task walking, 6) walking along a parallel carpet, and 7) straight-line walking. Gaze behaviour was recorded at 200 Hz using Pupil Invisible glasses© and analyzed in Pupil Cloud© to identify fixations (i.e., steady gaze) and define common areas of interest (AOIs) (i.e., regions of directed gaze). Gaze metrics (i.e., average fixation duration, number of fixations, proportion of fixation time on AOI) were calculated for the two steps preceding tasks 1-4 and during all steps for walking tasks 5-7. Footfall timing was recorded using the Zeno™ Walkway system to align gaze with step events and to measure step length and width during each task. Walking speed was measured with a stopwatch. Mann-Whitney U and independent t-tests were used for group comparisons.

Results: Fifteen individuals with SCI (53.8 ± 17.2 years; 8 women) and 12 without SCI (51.4 ± 15.7 years; 7 women) participated. The SCI

group walked more slowly ($p<0.0001$) and had shorter step lengths ($p<0.03$) for all tasks. The SCI group showed increased gaze behaviour on the walking path beside the trash can ($p < 0.01$), wooden platform ($p = 0.029$), walking path during the walking task, and the carpets during the carpet tasks ($p < 0.05$).

Conclusions: These findings contribute to characterizing gait adaptability after SCI and suggest that gaze behaviour may represent a relevant target for assessment and rehabilitation aimed at improving safe and effective community walking.

[#16] Dipa Chatterjee; Department of Pharmacology & Toxicology

Supervisor: Dr. Martin Beaulieu

Theme: Molecular & Cellular Neuroscience (Oral Presentation)

PREFRONTAL NEURONAL FXR1 REGULATES STRESS-INDUCED ALLOSTATIC BALANCE AND RESILIENCE

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Introduction & Objective: Mechanisms that maintain allostasis under chronic stress are key regulators of mental stability, and its dysregulation contributes to depression/anxiety-related disorders. The RNA-binding protein FXR1 (FMR1 autosomal homolog 1) has been implicated in stress-sensitive conditions (sleep deprivation, schizophrenia, and bipolar disorder) and modulating synaptic homeostasis. FXR1 is also regulated by lithium, suggesting a role in its therapeutic and prophylactic effects. However, the direct impact of prolonged environmental stress on FXR1 remains unknown.

Methods: Here we characterized the effects of chronic stress on FXR1 (and vice-versa) by subjecting C57BL/6J mice to chronic restraint stress (CRS: 1h, 2-times/day, for 5 weeks). Subsequently, FXR1 overexpression or knockout (via CRISPR) viruses were injected into the prefrontal cortex (PFC) bilaterally, followed by CRS. Various behavioural and molecular/cellular measurements were taken.

Results: CRS reduced FXR1 levels in the PFC without altering its X-linked homolog FMRP. Additionally, BDNF increased, while Corticosterone decreased, FXR1 protein levels. Knocking out FXR1 increased anxiety-like behaviours at baseline but did not exacerbate stress-induced effects. Conversely, overexpression of FXR1 rescued overall emotionality and restored select molecular mechanisms following chronic stress exposure.

Conclusion: Together, our results suggest that chronic stress reduces FXR1 levels in the PFC, while overexpressing PFC FXR1 enhances resilience. These findings implicate FXR1 in stress regulation and homeostatic control, and highlights FXR1 rescue as a potential therapeutic strategy.

[#17] Aaima Cheema; Institute of Medical Science

Supervisor: Dr. Katharine Dunlop

Theme: Behavioural and Social Neuroscience (Oral Presentation)

BEHAVIOURAL CORRELATES OF IRRITABILITY AND SUICIDALITY IN MAJOR DEPRESSIVE DISORDER

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Introduction: Suicide is a leading cause of death in North America. In Major Depressive Disorder (MDD), understanding the behavioral link between irritability and suicidal thoughts/behaviors may help identify risk factors. Prior studies indicate that irritability may be associated with heightened suicidality in individuals with MDD, potentially through maladaptive responses to interpersonal conflict (e.g., peer rejection). No prior study has directly tested whether this conflict explains the link between irritability and suicidality in adults with MDD.

Objective/Hypothesis: The primary objective of this study is to investigate whether irritability varies across MDD with a history of a suicide attempt (MDD+SA), MDD with no history of a suicide attempt (MDD–SA), and healthy controls (HC). Additionally, the study aims to determine whether irritability correlates with social decision-making following experimentally induced social exclusion.

Methods: We enrolled 95 eligible participants (18-65 years, 60 female): 30 MDD individuals with a past suicide attempt (MDD+SA), 31 MDD individuals with no past suicide attempt (MDD-SA), and 34 healthy controls (HC). All participants completed an interview, self-report questionnaires, and two fMRI paradigms assessing irritability following social exclusion and retaliation against excluders. Group differences were tested using covariate-adjusted models (ANCOVA), controlling for age, sex, anxiety, and depression severity.

Results: MDD+SA exhibited significantly higher baseline irritability than MDD-SA ($p=.045$, $\eta p^2=.075$). Irritability increased significantly from pre- to post-exclusion across all groups ($p < 0.001$, $\eta p^2 = 0.329$), but this increase did not differ between MDD groups. All groups made more costly choices during Exclusion than Inclusion, especially MDD+SA (OR = 9.26). Irritability increases predicted greater costly choice in MDD+SA ($p < 0.001$).

Conclusion: Irritability was elevated at baseline in MDD+SA and increased following exclusion. Prior suicide attempt and increases in irritability are linked to greater costly retaliation toward excluders. These recently analyzed findings indicate that baseline irritability and interpersonal conflict responding may be a behaviorally informative correlate of suicide risk in MDD.

[#18] Andrew Cheon; Department of Medical Biophysics

Supervisor: Dr. Junchul Kim

Theme: Systems and Circuits Neuroscience (Oral Presentation)

ANTERIOR OLFACTORY NUCLEUS ACTIVITY DYNAMICS IN CONTEXT-DEPENDENT ODOR MEMORY

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Introduction: The anterior olfactory nucleus (AON) is a central component of early olfactory processing. It modulates odor-guided behaviours by integrating bottom-up olfactory bulb (OB) inputs with top-down hippocampal (HPC) inputs. We previously demonstrated the necessity of HPC-AON circuits for episodic odor memory, highlighting the AON as a repository for odor-context engrams. However, it remains

unknown how odor-context memory processes can be represented by the spatiotemporal dynamics of AON activity.

Objective: We hypothesize that contextual cues reminiscent of prior odor experiences reactivate hippocampal engrams, which then reactivate odor-context representations in the AON.

Methods: First, we coupled in vivo fiber photometry with our olfactory go/no-go paradigms to identify subregion-specific AON activity signatures correlated with odor memory processes. Next, we integrated stGtACR2-mediated optogenetic inhibition with our olfactory go/no-go tasks to test the necessity of task-associated AON activity signatures for odor-guided behaviours. Finally, we integrate one-photon Ca2+ imaging with passive odor exposure paradigms to record spatially-explicit ensemble dynamics at cellular resolution, which enables us to analyze how AON populations represent odor identity and spatiotemporal context, and how this code reorganizes with experience.

Results: Dual-site fiber photometry experiments revealed that distinct AON subregions showed distinct temporal dynamics of activity depending on task complexity: mAON shows robust pre-odor activation across context-independent and context-dependent tasks, whereas dAON shows significant activation selectively in the context-dependent task. Optogenetic inhibition of non-odor-window dAON activity impairs context-dependent odor memory encoding and retrieval, but spares context-independent odor memory. Finally, preliminary one-photon Ca2+ analyses suggest that AON activity contains structured information about odor identity through correlated response patterns, indicating that AON population responses reflect odor relationships.

Conclusion: Together, our findings support our hypothesis that odor-context memory is represented in unique AON activity signatures, particularly in the dAON. Future work will leverage optogenetic manipulation and one-photon calcium imaging approaches to further characterize the necessity of AON activity across olfaction-guided behaviours, which will deepen our understanding of how the brain processes sensory elements of episodic memory.

[#19] Pou Hong Justin Chia; Department of Pharmacology & Toxicology

Supervisor: Dr. Chao Zheng

Theme: Aging and Neurodegenerative Disorders (Translational) (Oral Presentation)

TRACKING SYNAPTIC DENSITY LOSS IN THE SPINAL CORD OF EXPERIMENTAL AUTOIMMUNE ENCEPHALOMYELITIS MICE AND PILOT EVALUATION OF SV2A PET IN PATIENTS WITH MULTIPLE SCLEROSIS

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Introduction: Synaptic loss is a critical pathological feature of multiple sclerosis (MS) associated with long-term disability and cognitive decline. We previously reported widespread cerebral synaptic density loss in the experimental autoimmune encephalomyelitis (EAE) mouse model using synaptic vesicle glycoprotein 2A (SV2A) PET imaging. However, despite the spinal cord being a primary and often early site of inflammatory and neurodegenerative pathology in both EAE and MS, in vivo quantification of synaptic density in this region has not yet been reported. This knowledge gap limits our understanding of the full topographic extent of synaptic pathology across the central nervous system (CNS). This study addresses this unmet need by validating [18F]SynVesT-1 PET for the specific assessment of spinal cord pathology in EAE mice. Furthermore, to provide a translational context for these preclinical findings, we present a pilot clinical PET research study using [11C]UCB-J to assess synaptic density in patients with MS.

Methods: Experimental autoimmune encephalomyelitis (EAE) was induced in C57BL/6J mice (n=18/group; 10 females, 8 males) via MOG35-55 immunization, with PET imaging reserved for animals reaching a clinical score ≥3. Dynamic 90-minute [18F]SynVesT-1 acquisitions were performed on a Mediso nanoScan PET/CT scanner. Spinal cord regions of interest (cervical, thoracic, lumbar, and sacral) were manually defined on co-registered CT images guided by a CT atlas. The total volume of distribution (VT) was quantified using Logan graphical analysis (t* = 10–15 min) with a radiometabolite-corrected image-derived input function. Thin-section autoradiography (ARG) binding assay was performed on post-mortem fresh-frozen coronal spinal cord sections from EAE and naive mice (n=2/group/sex) to assess tracer binding. Non-specific binding was evaluated using levetiracetam, a known ligand for the SV2A. Preclinical data were analyzed using a two-way ANOVA to assess differences in PET and in vitro metrics between groups. To provide translational context, dynamic [11C]UCB-J PET imaging was performed in a pilot cohort of MS patients (n=6) and healthy controls (n=6). Human kinetic modeling utilized metabolite-corrected arterial plasma input functions to generate parametric VT maps for regional quantification. Human PET data were compared using two-tailed, unpaired Welch's t-tests, with no multiple comparison correction applied due to the limited sample size.

Results: In EAE mice, [18F]SynVesT-1 PET successfully detected significant segment-specific reductions in synaptic density within the spinal cord. VT analysis demonstrated robust decreases in the cervical (-27.7%, $p < 0.0001$) and lumbar (-21.7%, $p < 0.01$) segments. These in vivo deficits were corroborated by in vitro ARG study, which revealed parallel reductions in SV2A protein expression in the cervical and lumbar regions. In the human PET study, MS patients exhibited a significant 16.4% reduction in global cortical [11C]UCB-J binding compared to healthy controls ($p = 0.026$). Widespread reductions were also observed in subcortical and spinal cord regions, including the caudate (-26.0%) and thalamus (-19.4%), mirroring the extensive synaptic pathology seen in the preclinical model.

Conclusion: This study demonstrates that SV2A PET can successfully detect and quantify synaptic pathology in the spinal cord of EAE mice. The concordance between these preclinical spinal cord findings and the widespread synaptic loss observed in MS patients supports SV2A PET as a sensitive,

translational biomarker capable of assessing neurodegenerative burden across the entire central nervous system. Future work will focus on validating these spinal cord findings in larger longitudinal preclinical model and MS patient cohorts.

[#20] Mya Chronopoulos; Institute of Medical Science

Supervisor: Dr. Caleb Browne

Theme: Cellular & Systems Neuroscience (Poster Presentation)

DYNAMIC REGULATION OF SEROTONIN RELEASE IN THE MESOLIMBIC DOPAMINE CIRCUIT DURING MOTIVATED BEHAVIOUR

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Introduction: Motivation enables organisms to initiate and sustain goal-directed behaviour necessary for survival. Dysregulation of motivational processes underlies many major psychiatric conditions, most notably depression. While the mesolimbic dopamine system – particularly projections from the ventral tegmental area (VTA) to the nucleus accumbens (NAc) – is well established as a core driver of motivated behaviour, the role of serotonin within this circuit remains poorly understood. Pharmacological and genetic manipulations that increase serotonin activity reliably suppress reward-seeking behaviour, suggesting that serotonin exerts an inhibitory influence on motivation. This effect is hypothesized to arise through serotonergic modulation of mesolimbic dopamine circuitry. However, this prior work has relied largely on static manipulations of serotonin, leaving how endogenous serotonin is regulated during real-time motivated behaviour largely unknown.

Objective: This study aimed to characterize the real-time dynamics of serotonin release in the NAc across systematically increasing levels of effort and reinforcement uncertainty during motivated behaviour. We hypothesized that NAc serotonin signaling would exhibit distinct phase-specific dynamics during reward seeking and consumption, and that these temporal patterns would be preserved but qualitatively modulated as motivational demand and uncertainty increased.

Methods: In vivo fiber photometry, combined with operant responding for water in mice, was used to monitor NAc serotonin release. Mice received stereotaxic delivery of a genetically encoded serotonin sensor (AAV9-hSyn-GRAB-5-HT3.0) and optic fiber implantation targeting the NAc. Following recovery, animals progressed through an escalating paradigm of reinforcement schedules designed to systematically increase motivational demand and reward uncertainty. Serotonin signals were normalized, aligned to lever pressing and reward delivery, and analyzed for peri-event changes in activity using an area under the curve approach.

Results: Across reinforcement schedules, a robust biphasic serotonergic release pattern was observed. Serotonin release increased at the time of lever pressing, followed by a pronounced reduction during reward consumption, and a rebound in activity upon

completion of reward consumption. This temporal structure was conserved across reinforcement schedules; however, qualitative differences in signal magnitude and timing were observed as motivational demand and reward uncertainty increased. These findings suggest that serotonin signaling in the NAc is not static, but dynamically structured according to behavioural state and reinforcement contingencies.

Conclusion: These findings suggest that serotonin signaling in the mesolimbic dopamine system is tightly coupled to motivated behaviour. Ongoing studies will further refine causal contributions of serotonin to motivational control. Together, this will advance our understanding of neuromodulatory regulation of goal-directed behaviour and lay critical groundwork for understanding motivational dysfunction in psychiatric disorders.

[#21] Annie Chu; Department of Music

Supervisor: Dr. Michael Thaut

Theme: Cognitive Neuroscience (Poster Presentation)

MUSICAL MNEMONIC TRAINING IN MANDARIN: A DIALOGUE ON DYNAMIC BRAIN NETWORKS AND CLINICAL PRACTICES OF MEMORY CONSOLIDATION IN AGING

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Introduction: With the rising prevalence of MCI globally, effective non-invasive interventions for promoting cognition are crucial among elderly.

Objective: This study investigates the efficacy and neural mechanisms of Musical Mnemonic Training (MMT) in enhancing verbal memory among native Mandarin speakers.

Methods: 32 native Mandarin speakers (aged 55–85) in Taipei were randomly assigned to MMT or spoken conditions for the Chinese Verbal Learning Task (CVLT). fMRI data were collected (figure 1) and analyzed using Python, SPM, and CONN to examine regional brain activation and functional connectivity (FC) differences. T-test was conducted between two groups with significance level of 0.05.

Results: Preliminary analyses indicate significantly higher memory retention in the MMT group than that in the spoken group ($n=16$ each group, $p<0.05$) (figure 2a). fMRI results reveal that MMT enhances FC between the language network and the bilateral putamen, right frontal pole, and anterior cingulate (FDR-corrected $p < 0.05$) (figure 2b & c). This supports the role of "Temporal Priming" and "Dual Coding" in strengthening memory encoding.

Conclusions: The findings suggest that MMT facilitates a dynamic transition from short-term encoding to long-term memory consolidation by modulating network connectivity. These results provide neurobiological evidence that music serves as a robust neuro-mnemonic scaffold, facilitating the dynamic consolidation of memory for Mandarin-speaking older adults. By bridging the gap between initial sensory processing and long-term cognitive representation, this study offers a promising

direction for cross-cultural clinical practice and international dialogue in music therapy education.

[#22] Kevan Clifford; Institute of Medical Science

Supervisor: Dr. Yuliya Nikolova

Theme: Aging and Neurodegenerative Disorders (Translational) (Oral Presentation)

CROSS-SPECIES NEUROSTRUCTURAL AND COGNITIVE EFFECTS OF A NOVEL AGE-DEPENDENT EXTRACELLULAR MATRIX PATHWAY CENTERED ON THE FREM3 GENE

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Introduction: The human extracellular-matrix-related FREM3 gene is strongly age-dependent and implicated in neurodegenerative disorders. To establish translationally relevant causal evidence for FREM3's roles in brain structure and cognition, we developed an excitatory-neuron-specific Frem3 knockout (Frem3-enKO: Frem3flox/flox;Camk2Cre/+) mouse model and computed FREM3 genetically regulated expression (FREM3-GReX) in humans, enabling convergent cognitive and neurostructural characterizations.

Objective: Lower Frem3/FREM3 expression will be associated with reduced brain volume in mice and reduced cortical surface area in humans, particularly in age-sensitive regions, alongside worse cognitive performance.

Methods: Frem3-enKO and control mice (n=6-8/genotype, ages=4-6-months, 50% female) completed memory and executive function-like tasks (Y-maze, reversal learning, novel object recognition). A cohort of young-adult (5-month-old) and late-middle-aged (12-month-old) mice (n=16/genotype, 50% female) completed ex-vivo MRI with deformation-based morphometry. ANCOVAs and linear models assessed effects of genotype and age-by-genotype interactions, respectively, on cognition and brain volume (total and 180 regions), controlling for sex. In the UK Biobank (n=31,384; $\bar{x}$=64.1y; ~50% female), PrediXcan-derived FREM3-GReX was tested against cognition and cortical surface area (total and 62 regions), including age interactions. Covariates included demographics, 10 genetic PCs, site, and eTIV; regional results corrected at FDR 5%.

Results: Frem3-enKO mice performed worse across all behavioural tasks (all $p<0.05$), and showed widespread lower regional brain volume in middle-age vs young adulthood (98/180 regions, $pFDR<0.05$; interaction $p<0.05$ in 24 regions) strongest in the frontal association cortex, with no age effects in control mice ($pFDR>0.05$). In humans, lower FREM3-GReX predicted lower total surface area ($pFDR=0.006$) driven by occipital and isthmus cingulate regions ($pFDR<0.05$) with trend-level left pars triangularis and precentral ($pFDR=0.055$-0.056) effects.

Conclusion: We provide the first causal evidence linking reduced Frem3 expression to cognitive and neurostructural deficits alongside converging human associations, informing targeted molecular follow-up of FREM3-related pathways.

[#23] Madeleine Coppolino; Department of Rehabilitation Sciences

Supervisor: Dr. Tijana Simic

Theme: Cognitive Neuroscience (Poster Presentation)

COMPARING LANGUAGE LEARNING IN APHASIA AND HEALTHY CONTROLS: A SYSTEMATIC REVIEW OF THE EVIDENCE

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Introduction: Language learning research has identified principles of learning in young adults, but older adults remain understudied. Further, our understanding of language learning in older adults with cognitive impairments, such as post-stroke aphasia, is even more constrained. Emerging evidence suggests that people with aphasia (PWA) can learn new vocabulary, though performance is variable and often reduced compared to healthy older controls (HC). Improving baseline understanding of language learning across these populations is critical for personalizing aphasia therapy to individual learning profiles and optimizing treatment outcomes.

Objective: The proposed study aims to systematically review the current best evidence (and evidence gaps) on language learning in older adults with and without aphasia.

Methods: We aim to conduct a systematic review of the literature, in line with the gold-standard Cochrane framework, comparing language learning ability in HCs and PWA. We will search six databases: MEDLINE, Embase, PsycINFO, CINAHL, and CENTRAL, using search terms centered on operational definitions of "aphasia," "healthy controls," and "language learning." Accepted studies (reviewed by two independent raters) will report: a) original research, b) comparing language learning in HC vs PWA, c) with N>3 adults per group (i.e., at least 90% of participants are >40 years), and d) with at least 90% of aphasia cases attributable to stroke. We will extract data on participant demographics, language learning tasks, primary learning outcomes, and quantitative data comparing HCs and PWA. Accepted articles will be appraised for risk of bias using the Cochrane ROBINS-I tool. If appropriate, we will conduct a meta-analysis of findings.

Results: Preliminary review findings reveal this is an area with limited evidence. Current evidence indicates variability in language learning ability among HC and PWA, with differences observed across various language learning tasks. Study limitations include small sample sizes and no direct comparisons of word learning ability across learning tasks.

Conclusion: This review will synthesize our current understanding of language learning in older adults with and without aphasia, supporting the development of more personalized and effective aphasia therapies, particularly for individuals who do not show improvement using current interventions.

[#24] Riya Dama; Institute of Medical Science

Supervisor: Dr. Tom Schweizer

Theme: Aging and Neurodegenerative Disorders (Clinical) (Oral Presentation)

GREY-TO-WHITE MATTER SIGNAL INTENSITY RATIO AS A BIOMARKER FOR AGE-RELATED CORTICAL CHANGES

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Introduction: There are age-related alterations in brain microstructure that precede overt neurodegeneration and measurable cortical atrophy. The grey-to-white matter signal intensity ratio (GWR) has emerged as a promising but underexplored neuroimaging metric that may capture these subtle microstructural changes associated with aging. Prior work in neurodegenerative disease cohorts suggests that GWR demonstrates distinct spatial patterns of abnormality even in the absence of detectable cortical thinning, highlighting its potential sensitivity to early brain changes not captured by conventional structural measures. However, the characterization and validation of GWR across the healthy aging span remain limited. Examining how GWR varies with age and cognitive performance may help to establish how this metric changes under normal aging, validating its use in abnormal aging cohorts.

Objective: To investigate the relationship between GWR, age and cognitive performance throughout the brain, with cognitive performance assessed using the Montreal Cognitive Assessment (MoCA).

Methods: A total of 103 healthy adults (33% female, aged 27-85) were included in this study. High-resolution structural MRI data were acquired on a 3T Siemens Magnetom Skyra scanner, and cognitive functioning was assessed through MoCA. GWR values were calculated across 148 cortical regions. Region-wise general linear models were used to examine associations between cortical GWR, age, sex, and MoCA score.

Results: 38 cortical regions demonstrated significant associations between age and regional GWR following false discovery rate (FDR) correction ($p < 0.05$). The observed effects showed a highly dispersed pattern, with t-statistics ranging from $|2.57|$ to $|4.25|$. Negative associations were observed primarily in occipital and medial temporal regions, including the cuneus, lingual cortex and occipital pole. In contrast, positive associations were more widely distributed across frontal, temporal, and insular cortices, including prefrontal regions (superior, middle, and inferior frontal gyri), orbitofrontal cortex, anterior cingulate, insula, and superior temporal regions. In the age and sex-adjusted analysis of MoCA-related effects, 18 cortical regions showed nominal significance ($p < 0.05$ uncorrected), with t-statistics ranging from $|1.99|$ to $|3.08|$. However, none of these associations survived FDR correction for multiple comparisons. The observed effects were predominantly negative in direction, suggesting lower GWR with higher MoCA scores across most regions. These associations were distributed across frontal, temporal and parietal cortices, including the paracentral gyrus, temporal pole, superior temporal cortex,

orbitofrontal regions, and parietal association areas.

Conclusion: GWR showed significant, widespread associations with age across distributed cortical regions, supporting its sensitivity to age-related brain changes. In contrast, associations between GWR and cognitive performance (MoCA) were observed only at the nominal level and did not survive correction for multiple comparisons. These findings highlight age as a primary driver of cortical GWR variation, while its relationship with cognitive performance may be more nuanced and requires further investigation.

[#25] Sushmit Das; Institute of Medical Science

Supervisor: Dr. Karen Davis

Theme: Pain and Sensory Disorders I (Poster Presentation)

DISENTANGLING PERIODIC AND APERIODIC ALPHA ACTIVITY IN THE DYNAMIC PAIN CONNECTOME OF YOUNG HEALTHY ADULTS

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Introduction: Resting-state alpha activity has been proposed to be related to acute pain sensitivity and chronic pain, including alpha power and peak alpha frequency (PAF). However, band-limited power spectral density (PSD) metrics can reflect true oscillatory peaks and/or shifts in the aperiodic (1/f-like) background. This complicates interpretation across studies, cohorts, and interventions.

Objectives: Here, we investigated whether PSD-based alpha metrics and spectral parameterization yield similar estimates of alpha activity, or whether they differ in ways that could change conclusions.

Methods: Healthy young adults (under 40 years old) underwent resting-state magnetoencephalography. Spectra were computed using a standard PSD pipeline across 19 regions of interest (ROIs) in the dynamic pain connectome spanning ascending and descending nociceptive pathways, salience and default mode networks. We applied spectral parameterization to separate the aperiodic (1/f) background from periodic alpha peaks. From both approaches, we extracted PAF and total 8–13 Hz alpha power for each participant.

Results: PSD- and parameterization-based estimates of PAF differed significantly across all ROIs, showing the methods are not interchangeable. PSD total alpha power also differed significantly from parameterized periodic-only alpha peak power after removing the 1/f background.

Conclusion: These findings highlight the importance of spectral analysis method which can shape inferences about alpha-band activity. PSD-based alpha power effects may partly reflect background spectral changes, whereas parameterization yields separable periodic and aperiodic features that improve interpretability and comparability. Therefore, reporting both parameterized alpha peak and aperiodic measures provide key information to disambiguate alpha power and PAF from aperiodic shifts.

[#26] Andrea De Bartolo; Psychology

Supervisor: Dr. Kaja Jasinska

Theme: Developmental Neuroscience (Oral Presentation)

DEFAULT MODE NETWORK AND CENTRAL EXECUTIVE NETWORK NEURAL CONNECTIVITY IN SYRIAN REFUGEE YOUTH

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Introduction: This study investigated how the developmental timing of adversity (conceptualized as age and duration of displacement) among Syrian refugee children and youth is associated with resting-state functional connectivity in the default mode network (DMN) and the central executive network (CEN). The DMN and CEN are brain networks within the frontal, temporal, and parietal cortices that are involved in adaptive behaviours (e.g., self-reflection, social interaction, emotional regulation; Gusnard et al., 2001; Moreno-López et al., 2020). The functional connectivity of these networks is suggested to be affected by adversity and can undermine behaviours that help individuals overcome adversity and cope with stress (Holtz et al., 2023; Lopez et al., 2024; Tooley et al., 2020). Adversity-related experiences are associated with decreased functional connectivity within the DMN and CEN (Bluhm et al., 2009; DiGangi et al., 2016; Koch et al., 2016). However, existing research is limited in its application to populations (Sato et al., 2014; Sherman et al., 2014), as it does not encompass the range of adverse experiences faced by children globally, nor does it account for how the timing of adversity can alter the functional integration of these networks. Recent studies have found that the developmental timing of displacement among Syrian refugee youth is related to altered neural network organization, specifically in terms of how effectively networks connect (Abdulrasul et al., 2025). Displacement represents the discrete onset and duration of adversity, allowing for the examination of developmental vulnerability to adversity.

Objective: The current study aims to answer the following question: a) How does the developmental timing of displacement relate to functional connectivity between and within the DMN and CEN? We expect to find that those who are displaced at an older age and for a longer duration will have lower functional connectivity within each network.

Methods: Syrian refugee youth (N = 83, Mage = 13.7) resettled in Canada participated in this study. Resting-state functional near-infrared spectroscopy (rsfNIRS) scans were used to conduct region-of-interest analysis of the DMN and CEN.

Results: Preliminary results suggest that migration experiences are associated with neural functioning. Specifically, the longer duration of displacement for refugee youth is associated with less functional connectivity within the DMN (β = -.01, SE = .00, $p < .05$).

Conclusion: This study offers an opportunity to advance understanding of the neural mechanisms that link the developmental timing of adversity to the ability to adapt and enhance psychological well-being. Canada has provided refuge to over 100,000 Syrian refugees since 2015, providing insights into a large, highly vulnerable population often underrepresented in neurodevelopmental studies.

[#27] Nathaniel De Vera; Dentistry

Supervisor: Dr. Massieh Moayedi

Theme: Pain and Sensory Disorders II (Poster Presentation)

CHALLENGING THE OROFACIAL PAIN DOGMA: FACIAL SKIN IS LESS SENSITIVE THAN FOREARM SKIN TO NOXIOUS HEAT

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Introduction: Orofacial pain is often considered to be more intense and unpleasant than pain elsewhere on the body, due to the centrality of the mouth and face in physiological and social functions (e.g., eating, communicating). However, there is no empirical evidence to support this.

Objective: Here, we aimed to investigate whether heat pain on the face is more unpleasant and intense than on the volar forearm.

Methods: Sixty participants consented to procedures approved by the local Research Ethics Board. First, they underwent an individually calibrated heat pain protocol administered to the skin territory of the mental nerve (below the lower lip) and volar forearm, and provided pain intensity and pain unpleasantness ratings for each stimulus on a 0-100 computerized visual analogue scale.

We performed two analyses to compare heat pain sensitivity between the face and forearm: a linear mixed model, and curve parameter comparisons using MANCOVAs based on sigmoid stimulus response function (4-parameter logistic; 4PL) fit parameters to pain intensity and pain unpleasantness. Significance at $p<0.05$.

Results: Forearm heat stimulations were perceived as more painful (intense) and more unpleasant than heat stimuli on the face based on linear mixed models ($p<0.05$).

Sigmoid curve fit comparisons revealed a similar effect: the minimum (lower asymptote) was higher and inflection point temperatures was lower for the forearm than the face for both pain intensity and pain unpleasantness (all $p<0.05$).

Conclusion: Facial skin below the lower lip is less sensitive to noxious heat than the forearm skin. Future research should also investigate whether these findings are consistent across stimulus modalities and tissues. Furthermore, the structural and functional bases of these differences in sensitivity warrant investigation.

[#28] Kamrani Doray; Pharmacology & Toxicology

Supervisor: Dr. Laurie Zawertailo

Theme: Neuropharmacology and Drug Development (Oral Presentation)

FEASIBILITY AND ACCEPTABILITY OF HOME-BASED TRANSCRANIAL DIRECT CURRENT STIMULATION COMBINED WITH VARENICLINE FOR SMOKING CESSATION

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Introduction: Tobacco use remains a leading cause of preventable death and disease

worldwide. Although evidence-based smoking cessation interventions exist, their implementation in routine clinical practice is often limited by barriers including access to specialized clinics, travel burden, and challenges with treatment adherence. Transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation technique that targets the prefrontal cortex, enhancing cognitive control and reducing craving, showing promise as an adjunctive treatment for nicotine dependence. However, the feasibility and acceptability of home-based tDCS delivery in smoking cessation populations remain underexplored.

Objective: The objective of this study is to evaluate the feasibility and acceptability of home-based tDCS delivered in combination with varenicline within an ongoing randomized controlled trial (RCT) for smoking cessation. It is hypothesized that the predefined feasibility benchmarks will be met, including adequate recruitment, retention, adherence, and no serious device-related adverse events. It is hypothesized that participants will report high acceptability of the tDCS treatment.

Methods: This study is embedded within a double-blind, sham-controlled RCT evaluating tDCS combined with varenicline. Feasibility outcomes included recruitment, retention, adherence, and safety. Recruitment was defined as enrollment rate (benchmark ≥3.5 participants/month). Retention was defined as the proportion completing daily tDCS sessions (≥80%), and adherence as the proportion of prescribed sessions completed (≥80%). Safety was defined as the occurrence of serious device-related adverse events. Acceptability was assessed using the Acceptability of Intervention Measure (AIM), an 11-item, 5-point Likert scale, with high acceptability defined as ≥70% of participants rating items as strongly agree or agree. Optional open-ended responses captured qualitative feedback.

Results: As of May 2026, 76 participants have been enrolled over 13 months (5.8 participants/month), exceeding the target rate. Of these, 62 (82%) completed home-based tDCS. Adherence was high, with a mean completion rate of 97% of prescribed sessions. No serious device-related adverse events have been reported. Acceptability data collection is ongoing.

Conclusion: Preliminary findings suggest that home-based tDCS combined with varenicline is feasible and well-tolerated in a smoking cessation population. Ongoing analyses will evaluate acceptability and further investigate the potential for remote tDCS to improve accessibility and implementation of smoking cessation treatments.

[#29] Maryam Fazili; Cell and Systems Biology

Supervisor: Dr. Loren Martin

Theme: Motor & Sensory Control (Oral Presentation)

INVESTIGATING THE ROLE OF EW-CCK NEURONS IN PAIN MODULATION

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Introduction: Chronic pain affects approximately 20% of the global population and remains a leading cause of disability worldwide. Although the Periaqueductal Gray (PAG) has historically been the primary midbrain region studied in pain modulation, emerging evidence suggests that other midbrain nuclei may also contribute to pain processing. The Edinger–

Westphal nucleus (EW), particularly its cholecystokinin (CCK)-expressing neuronal population, has been implicated in stress-responsive and affective behaviors but remains largely unexplored in the context of chronic pain.

Objective: This study aimed to investigate the role of EW-CCK neurons in pain-related behaviors under both uninjured and neuropathic pain conditions. We hypothesized that modulation of EW-CCK neuronal activity would differentially influence nociceptive and affective behaviors depending on injury state.

Methods: To examine the functional role of EW-CCK neurons, CCK-Cre mice underwent stereotaxic viral injections targeting the EW with either excitatory (hM3Dq), inhibitory (hM4Di), or control (mCherry) DREADD constructs. Uninjured and injured (spared nerve injury (SNI)) models were included in the experimental design to record any behavioral shift in pain state models. Chemogenetic manipulation was achieved using clozapine-N-oxide (CNO), followed by behavioral testing including hot plate, von Frey, open field, and conditioned place preference assays. Histological analyses were performed to confirm injection localization, assess c-Fos expression, and characterize EW-CCK circuitry.

Results: Chemogenetic excitation of EW-CCK neurons increased c-Fos expression relative to inhibitory and control groups, confirming successful neuronal modulation. Behavioural effects of EW-CCK manipulation were limited under uninjured conditions. However, in neuropathic pain paradigms, activation of EW-CCK neurons reduced hind paw withdrawal duration during hot plate testing and increased preference in the conditioned place preference assay, suggesting a potential modulatory effect on pain sensitivity and affective pain processing. Preliminary circuit tracing further revealed that EW-CCK neurons both receive input from and project to multiple brain regions implicated in pain modulation.

Conclusion: These findings identify EW-CCK neurons as a previously underexplored component of chronic pain circuitry. The differential effects observed between uninjured and injured paradigms suggest that EW-CCK neurons may become selectively recruited during neuropathic pain states. This work expands current understanding of supraspinal pain modulation beyond the PAG and highlights the EW as a potential therapeutic target for chronic pain.

[#30] Madison Fedele; Cell and Systems Biology

Supervisor: Dr. Laura Corbit

Theme: Cellular & Systems Neuroscience (Poster Presentation)

ATP ADMINISTRATION ENHANCES SENSITIVITY TO OUTCOME DEVALUATION IN THE DORSOMEDIAL BUT NOT DORSOLATERAL STRIATUM IN RATS

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Introduction: Increasing evidence suggests that neuroinflammation can alter behavioural flexibility; however, the mechanisms through which inflammatory signalling affects corticostriatal circuits remain unclear. Microglia become activated during chronic neuroinflammatory states, including diet-induced obesity, and release ATP, which acts on purinergic receptors and influences glutamatergic transmission.

Objective: This study aimed to determine whether ATP signalling within the dorsal striatum is sufficient to alter behavioural control and whether these effects are region-specific. It was hypothesized that increased ATP signalling would impair goal-directed behaviour and promote behavioural inflexibility.

Methods: Adult male Long-Evans rats were trained on an instrumental outcome devaluation task to distinguish goal-directed from habitual behaviour. Localized ATP or saline infusions were administered into either the dorsomedial striatum (DMS) or dorsolateral striatum (DLS), and sensitivity to outcome value was assessed following devaluation testing.

Results: Contrary to the hypothesis, ATP infusion into the DMS did not disrupt goal-directed behaviour. Instead, ATP-treated rats showed enhanced sensitivity to outcome devaluation relative to saline controls ($F(1,5)=11.749$, $p=0.019$). In contrast, ATP infusion into the DLS tended to reduce sensitivity to devaluation ($F(1,6)=4.063$, $p=0.09$), suggesting region-specific effects of ATP signalling on behavioural control.

Conclusion: These findings demonstrate dissociable effects of ATP signalling within dorsal striatal subregions and suggest that ATP alone is insufficient to explain inflammation-related behavioural inflexibility. ATP is expected to produce mild microglial activation, whereas LPS induces robust inflammatory changes, supporting the idea that broader neuroimmune processes may be required to disrupt behavioural flexibility.

[#31] Francis Fernandes; Institute of Medical Science

Supervisor: Dr. Tom Schweizer

Theme: Cognitive Neuroscience (Poster Presentation)

CHOROID PLEXUS & LATERAL VENTRICULAR VOLUME AS POTENTIAL BIOMARKERS OF CUMULATIVE BLAST EXPOSURE

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Introduction: Repetitive blast exposure (BE) is a common occupational hazard among military personnel and has been increasingly linked to persistent neurological symptoms and structural brain alterations, even in the absence of overt traumatic brain injury. While prior neuroimaging studies have largely focused on parenchymal abnormalities, structures within the ventricular system may be especially vulnerable to blast-related biomechanical and inflammatory effects.

Objective: This study examined whether choroid plexus and lateral ventricles may serve as possible biomarkers of cumulative BE in a cohort of military and police personnel and hypothesize that choroid plexus and lateral ventricular volume will be associated to BE, independent of age and additional neurobehavioural variables.

Methods: Sixty-one male participants with structural magnetic resonance imaging (MRI), neurobehavioral, psychiatric, and BE data were examined. Cumulative BE was quantified using the generalized blast exposure value (GBEV). Structural T1-weighted MRI was used to derive lateral ventricular volumes through FreeSurfer segmentation, while choroid plexus volumes were refined using a Gaussian mixture model-based method with manual correction. Separate Bayesian linear regression models were used to examine associations of BE, age, psychiatric symptoms, traumatic stress exposure, concussion history, and concussion-related symptoms with nCPV and nLVV.

Results: Age was positively associated with both nCPV (median = 0.418, Probability of Effect [P] = 99.84%) and nLVV (median = 0.469, P > 99%). Greater cumulative BE was also positively associated with nCPV (median = 0.165, P = 89%) and nLVV (median = 0.296, P = 99%). Higher concussion symptom burden was negatively associated with both outcomes, whereas concussion history, traumatic stress exposure, anxiety, and PTSD symptoms were not credibly associated (P < 85%).

Conclusion: These findings suggest that the choroid plexus and lateral ventricles may represent sensitive neuroanatomical correlates of cumulative BE. Ventricular and cerebrospinal fluid-related structures may therefore provide accessible MRI-based markers of the neurological impacts of BE in military populations.

[#32] Selena Gangaram; Medical Biophysics

Supervisor: Dr. Bradley MacIntosh

Theme: Aging and Neurodegenerative Disorders (Poster Presentation)

INVESTIGATING HOW WHITE MATTER HYPERINTENSITY PROGRESSION IN CEREBRAL SMALL VESSEL DISEASE IMPACTS CEREBRAL BLOOD FLOW AND COGNITION

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Introduction: Identifying markers of early cognitive decline is crucial for detecting and intervening in neurodegenerative diseases, prior to the emergence of clinical symptoms. Earlier detection may allow for interventions that might slow or prevent disease progression. Investigating cerebral small vessel disease (CSVD) has become increasingly important as it may occur prior to the emergence of Alzheimer's Disease (AD) and dementia. CSVD involves damage to arterioles and capillaries in the brain, which in turn, can disrupt cerebral blood flow (CBF). As such, these vascular changes from CSVD can manifest as several neuroimaging markers in the brain with white matter hyperintensities (WMH) serving as a key imaging feature. WMH progression is therefore considered an important indicator of CSVD advancement and may indicate a potential

window for interventions, targeting modifiable vascular risk factors (e.g., diabetes, hypertension, etc.).

Objective: This study will examine the association between WMH progression and CBF leveraging the Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset. Specifically, the primary aim will examine how WMH accumulation overtime may be linked to CBF changes in CSVD vulnerable brain regions, including the bilateral thalamus, insula, and parietal lobes.

Methods: Participants will include cognitively normal individuals and those who are mildly cognitively impaired. Both CBF and WMH volumes will be obtained from the ADNI dataset, with CBF estimates derived from arterial spin labelling (ASL) MRI scans. A Linear Mixed Effects statistical model will be used to assess the association between WMH progression and CBF estimates.

Conclusion: Overall, using the ADNI dataset to assess change in WMH progression in association with CBF may reveal important insight into underlying pathology in CSVD progression and cognitive implications.

[#33] Sofia Gentile; Laboratory Medicine and Pathology

Supervisor: Dr. Naomi Visanji & Dr. Michael Pollanen

Theme: Aging and Neurodegenerative Disorders (Poster Presentation)

SPATIAL IMMUNE PROFILING OF PROGRESSIVE SUPRANUCLEAR PALSY BRAIN USING IMAGING MASS CYTOMETRY

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Introduction: Progressive supranuclear palsy (PSP) is a rare and fatal neurodegenerative disease, the etiology of which remains largely unknown. The disease is characterised by the presence of insoluble, hyperphosphorylated tau aggregates, in the form of 3 distinct cytopathologies – Neurofibrillary tangles, tufted astrocytes, and oligodendroglial coiled bodies. Although chronic inflammation and immune activation are increasingly recognized as important contributors to the pathology of many neurodegenerative diseases, their specific role in the pathogenesis of PSP remains relatively underexplored.

Imaging Mass Cytometry (IMC), is a novel multiplexed tool, originally developed to enable high-dimensional immune cell profiling. Combining metal-conjugated antibodies and mass cytometry principles IMC enables the visualization and spatial analysis of 40-plus markers on single sections. Here we employ IMC to map the immune microenvironment in the brains of patients with PSP.

Objectives: Perform a quantitative mapping of immune system involvement in the frontal cortex of PSP patients using multiplexed analysis of post-mortem brain tissue to observe and quantify immune activation and neuroinflammation

Methods: The frontal cortex of 6 patients with a clinical and neuropathologic diagnosis of PSP were stained using a custom designed 38-marker IMC antibody panel. The panel included markers of tissue architecture, vasculature, neural cell phenotyping, hyperphosphorylated tau and a range of immune cell and inflammatory markers, including myeloid and lymphoid subsets and complement proteins.

Results: Immunostaining using conventional immunohistochemical methods in serial sections confirmed equivalent staining patterns to IMC-generated images for several markers including for hyperphosphorylated tau (AT8) and complement pathway (C1q). Multiple regions of interested were selected and ablated for downstream analysis that will integrate quantitative and spatial profiling of immune markers in relation to tau aggregates across PSP cytopathologies.

Conclusions: Future work will apply quantitative measures and spatial analysis of markers of interest in relation to pathogenic tau protein aggregates in each of the three distinct cytopathologies, allowing for a deeper understanding of their contribution to disease pathogenesis. A more detailed understanding of the immune landscape in PSP could provide novel insights into disease pathobiology and identify potential novel therapeutic targets.

[#34] Mark Gerlai; Physiology

Supervisor: Dr. Jiannis Taxidis

Theme: Psychiatric Disorders II (Poster Presentation)

HIPPOCAMPAL INTERNEURON DYSFUNCTION DURING WORKING MEMORY IN A MOUSE MODEL OF SCHIZOPHRENIA

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Introduction: Schizophrenia is characterized by cognitive impairments including working memory (WM) deficits. WM deficits may be underpinned by aberrant inhibitory signaling from major interneuron classes like parvalbumin (PV) and somatostatin (SST) interneurons. Aberrant PV/SST activation and morphology in the CA1 have been reported in the DF16A mouse model of the human 22q11.2 chromosomal deletion, the strongest genetic predictor of schizophrenia. However, physiological deficits of these fast-spiking inhibitory cells are poorly understood in-vivo, while finer morphological deficits have not been explored.

Methods: We performed in-vivo voltage imaging on double transgenic PV-Cre Df16A and SST-Cre Df16A mice, during an olfactory WM task, followed by in-vitro confocal imaging. We recorded action potentials and subthreshold activity of multiple CA1 PV/SST cells in parallel, at high temporal resolution and across days.

Results: Ongoing analyses suggest Df16A PV cells are hypoactive and SST cells are hyperactive during odor encoding. Additionally, Df16 PV and SST phase locking to intracellular theta oscillations is significantly weaker. Such dysfunction in the inhibitory microcircuit may contribute to noisy stimuli encoding and poor WM maintenance. Indeed, Df16A mice exhibited learning deficits compared to littermate controls. Sholl analysis on fixed Df16A PV cells revealed significant decreases in dendritic complexity compared to controls,

perhaps underpinning observed intrinsic PV activity deficits.

Conclusion: These experiments reveal how interneuron physiological and morphological dysfunction leads to disruption of WM in schizophrenia, with implications for CA1 inhibitory circuits as future therapeutic targets.

[#35] Leen Ghanayem; Institute of Medical Science

Supervisor: Dr. Sakina Rizvi

Theme: Psychiatric Disorders I (Poster Presentation)

DIFFERENTIAL NEURAL CORRELATES OF WORKING MEMORY DYSFUNCTION IN TREATMENT-RESISTANT VERSUS TREATMENT-RESPONSIVE DEPRESSION

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Background: Treatment-resistant depression (TRD), defined as non-response to at least two adequate antidepressant trials, affects one-third of individuals with major depressive disorder (MDD). TRD is associated with greater cognitive impairment, particularly in working memory, compared to treatment-responsive depression (non-TRD). Neuroimaging studies suggest altered activation in the frontoparietal network (FPN) and default mode network (DMN) during working memory performance in TRD; however, direct comparisons to non-TRD remain limited.

Objective: To examines group differences in task-related functional connectivity within the FPN and DMN across TRD, non-TRD and healthy controls (HCs). At higher cognitive loads, worse working memory performance in TRD will be associated with reduced suppression of the DMN, weaker FPN functional connectivity and weaker FPN-DMN segregation.

Methods: Participants with TRD (n = 7), non-TRD (n = 3) and HCs (n = 2) completed a functional magnetic resonance imaging scan during an N-back task. Reaction time and accuracy were examined in relation to functional connectivity within the FPN and the DMN across groups.

Results: Preliminary analyses indicated behavioural accuracy showed near ceiling for 0- and 1-back conditions and greater variability at 2-back. Reaction time increased with load across groups and showed the largest spread at 2-back. Connectivity-behaviour coupling differed by group. In HC and non-TRD groups, greater FPN-DMN segregation was associated with higher accuracy, while in TRD stronger FPN-DMN coupling was correlated with slower reaction times. Associations involving within-network connectivity in both the DMN and FPN were weak or inconsistent.

Conclusions: Early evidence suggests that network segregation between FPN and DMN, rather than within-network connectivity, relates to working memory performance in TRD. Given the small sample size, results remain exploratory and require replication in the full sample. Nonetheless, this pattern provides preliminary evidence of neural differences between TRD and non-TRD that may inform future studies of treatment response.

[#36] Rayna Ghosh; Institute of Biomedical Engineering

Supervisor: Dr. Kei Masani

Theme: Cognitive Neuroscience (Oral Presentation)

ASSESSING CORTICOBULBAR EXCITABILITY FOLLOWING FACIAL FUNCTIONAL ELECTRICAL STIMULATION THERAPY

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Introduction: Facial muscles play a central role in emotional expression and social communication and are closely linked to neural systems involved in affective processing. Facial movements can influence emotional states through sensorimotor feedback mechanisms. Functional electrical stimulation therapy (FEST) has been widely used in neurorehabilitation to induce neuroplastic changes in limb motor pathways. However, the neurophysiological effects of facial FEST on facial motor pathways in the context of mood regulation remain unknown.

Objective: The objective of this study was to investigate whether facial FEST modulates corticobulbar excitability in facial motor pathways. We hypothesized that facial FEST would alter transcranial magnetic stimulation (TMS)-evoked motor potentials, reflected by increased motor evoked potential (MEP) amplitudes and reduced MEP latencies in facial muscles.

Methods: To date, five healthy participants completed two separate experimental sessions consisting of facial FEST and sham stimulation. In the facial FEST condition, muscle stimulation was paired with voluntary contraction of orbicularis oculi and zygomaticus major induced by expressive smiling. In Sham, stimulation was below motor threshold at a sensory level coupled with expressive smiling. Prior to and following each intervention, transcranial magnetic stimulation was delivered over the motor cortex to MEPs. Surface electromyography recorded MEP responses from the orbicularis oculi and zygomaticus major muscles. Pre- to post-intervention changes in MEP amplitude and latency were analysed.

Results: Following facial FEST, participant-level analyses showed reduced MEP latencies in 3/5 participants for orbicularis oculi and 4/5 participants for zygomaticus major. Motor evoked potential amplitudes increased in 2/5 participants for orbicularis oculi and 4/5 participants for zygomaticus major. Group-level analyses demonstrated trends toward modulation of zygomaticus major MEP latency and amplitude following facial FEST, while no consistent changes were observed for orbicularis oculi.

Conclusion: These preliminary findings suggest that facial FEST may influence corticobulbar excitability, particularly in the zygomaticus major muscle. This approach may provide a novel neuromodulatory tool for probing and modulating neural circuits underlying facial motor control and emotional expression.

[#37] Brooke Ginson; Psychology

Supervisor: Dr. Francesco Leri

Theme: Neuropharmacology and Drug Development (Oral Presentation)

POST-TRAINING HEROIN MODULATES PERFORMANCE IN A DOSE- AND TASK-DEPENDENT MANNER

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Introduction: Enhancement of memory consolidation is critical to all reinforcing stimuli, and many drugs of abuse have memory-enhancing properties as demonstrated experimentally using the post-training administration method. In fact, our laboratory has demonstrated consistent evidence for enhanced memory consolidation by post-training heroin for episodic memories. However, others have found robust opioid-mediated memory impairments, particularly in inhibitory avoidance tasks.

Objective: The present experiments aimed to better characterize the reinforcing effects of the opioid heroin when administered post-training to male Sprague-Dawley rats following two distinct learning situations: drug place conditioning and escape training. It was hypothesized that post-training heroin would facilitate drug compartment bias in place conditioning after fewer conditioning sessions and decrease escape latency after fewer training sessions in the Barnes maze.

Methods: In study 1 and 2, rats underwent drug place conditioning with 1 mg/kg heroin (n=48; Study 1) or 20 mg/kg cocaine (n=30; Study 2) and received immediate post-conditioning injections of vehicle, 1 mg/kg heroin, or 1 mg/kg heroin + 3 mg/kg naloxone. Animals were tested after 1 pairing (test 1) and 4 pairings (test 2). Study 3 tested the effects of 0, 1, or 2 mg/kg heroin on consolidation of escape training in the Barnes maze. Rats (n=60) were trained to find a fixed escape box over 10 sessions and at the end of training, they were tested on a probe trial during which the escape hole was relocated.

Results: In both place conditioning studies, post-training 1 mg/kg heroin attenuated the drug compartment bias, and this effect was blocked by naloxone. In study 3, while escape latency was gradually reduced in all groups during training, post-training 1 mg/kg heroin uniquely enhanced original target investigation during training, and increased escape latency, target investigation, and target quadrant locomotion during the probe trial. Conversely, escape latency was not changed on the probe trial in the post-training 2 mg/kg heroin group, and target investigation was reduced.

Conclusion: These studies suggest that post-training drug administration does not limit their effects to memory consolidation. Instead, post-training heroin may modulate behaviour through the incidental conditioning of central motivational states, and these states may differ with post-training dose and interact with the unique response requirements of the task. This possibility should be carefully considered when using the post-training method and when interpreting previous studies of post-training reinforcers.

[#38] Rachel Ha; Pharmaceutical Sciences

Supervisor: Dr. Robert Bonin

Theme: Neuropharmacology and Drug Development (Poster Presentation)

THE ROLE OF NON-IONOTROPIC NMDA RECEPTOR SIGNALING IN SYNAPTIC DEPOTENTIATION IN THE MOUSE HIPPOCAMPUS

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Background: N-Methyl D-Aspartate receptors (NMDARs) play a key role in hippocampal

synaptic plasticity by modulating long-term potentiation (LTP), long-term depression (LTD) and depotentiation (DEP). Recently, non-ionotropic NMDARs (NI-NMDARs) have been discovered to be necessary for LTD, but their role in modulating DEP remains under-investigated. Here, we aim to assess its role in the DEP of spaced and compressed LTP.

Methods: NMDAR glycine site antagonists 7-chlorokynurenic acid (7-CK) and L689,560 (L689,560) were applied to hippocampal brain slices harvested from C57BL/6J mice aged 6-12 weeks during electrophysiology recordings to assess the requirement of NI-NMDAR signaling in depotentiation of spaced and compressed LTP.

Results: Depotentiation of compressed LTP (cLTP-DEP) appeared to persist in the presence of glycine site antagonists 7-CK and L689, suggesting that NI-NMDAR signaling is sufficient and necessary for compressed DEP. However, sLTP-DEP was blocked by 7-CK, but not L689.

Conclusion: Results suggest that there may be a diverging requirement for the NI-NMDAR between cLTP-DEP and sLTP-DEP, but effects differ depening on the pharmacological agent used. Future work involves repeating the experiments with CGP-78608, another glycine site antagonist that is more potent and specific to NMDARs, to re-assess the role of NI-NMDARs in both cLTP-DEP and sLTP-DEP.

[#39] Bianca Hill; Immunology

Supervisor: Dr. Veronique Miron

Theme: Aging and Neurodegenerative Disorders (Translational) (Oral Presentation)

MYELOID REGULATORS OF CENTRAL NERVOUS SYSTEM REMYELINATION

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Introduction: Multiple sclerosis (MS) is a neurodegenerative disease considered to result from T-cell mediated damage to myelin, the membrane surrounding axons in the central nervous system (CNS). Myelin is made by oligodendrocytes following myelin loss in MS, termed 'remyelination.' Remyelination eventually fails in MS, causing neuronal dysfunction and loss. Our recent work uncovered that inflammatory monocytes impair remyelination, yet the underlying mechanisms remain unclear.

Objectives: To determine how infiltrating monocytes and monocyte-derived myeloid cells impair remyelination.

Methods: Our lab uses transgenic mice that lack circulating inflammatory monocytes (CCR2-/-). We induce focal demyelinating lesions in the white matter tract, corpus callosum, and assess myelin repair, glial cell activity, and myeloid cell responses using single-cell RNA sequencing (scRNAseq), immunofluorescence, and flow cytometry.

Results: ScRNAseq analysis of brain lesions indicate that monocytes differentiate into dendritic cells at the onset of myelin repair. At this time, oligodendrocytes were found to adopt an altered transcriptional profile previously detected in MS lesions (Serpina3n+). These Serpina3n+ oligodendrocytes are greatly reduced in Ccr2-/- mice compared to controls. To identify mechanisms by which monocyte-derived dendritic cells influence oligodendrocytes, we performed bioinformatic pathway analysis on the genes enriched in

Serpina3n+ oligodendrocyte population, which predicted interferon signaling. We validated this by staining for the interferon signaling molecule, STAT1, which colocalized with Serpina3n+ oligodendrocytes, and was reduced in Ccr2-/- mice. We also identified infiltration of T-cells into fully repaired lesions, which was completely ablated in Ccr2-/- mice, indicating a potential autoimmune response to changes in oligodendrocytes and myelin.

Conclusions: These findings indicate that infiltrating myeloid populations hinder myelin repair, through direct changes in oligodendrocyte profiles, and potentially indirectly through induced autoimmunity. Our discovery reveals the importance of myeloid cells in regulating myelin repair, revealing them to be novel therapeutic targets for MS.

[#40] Dana Xinyue Huang; Institute of Medical Science

Supervisor: Dr. Tom Schweizer

Theme: Aging and Neurodegenerative Disorders (Clinical) (Oral Presentation)

STRUCTURAL BRAIN CHANGES ARE RELATED TO AUTONOMIC SYMPTOMS IN RADIOLOGICALLY ISOLATED SYNDROME

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Introduction: Radiologically isolated syndrome (RIS) is a diagnosis that refers to individuals who have magnetic resonance imaging (MRI) findings suggestive of multiple sclerosis (MS), but without overt, clinical symptoms. As a preclinical stage of MS, individuals with RIS often report subtle non-MS specific symptoms. There is growing recognition that autonomic dysfunction is highly prevalent in MS, but its neural mechanisms remain poorly understood. Studying structural brain changes related to autonomic symptoms in people with RIS may provide important insights into these debilitating experiences.

Objective: To evaluate the relationship between autonomic symptoms and grey matter volume in individuals with RIS, targeting areas of the central autonomic network (CAN), which are involved in autonomic regulation.

Materials and Methods: 59 adults with RIS (mean age = 44.5 years +/- 11.8 years, 78% female) and 32 healthy controls (mean age = 40 years +/- 9.8 years, 69% female) were recruited from a large academic MS center. All participants underwent a 3.0T MRI of the brain. Hierarchical Bayesian regression modelled volumetric differences between groups, and assessed the relationship between autonomic symptom scores (Composite Autonomic Symptom Score-31, COMPASS-31) and volumes of CAN regions, adjusted for age, sex, and intracranial volume.

Results: Most participants with RIS (n=57, 97%) endorsed autonomic symptoms (scored greater than 0 on COMPASS-31), with a median score of 18. They also demonstrated volumetric reductions in all CAN regions compared to healthy controls (all >99% probability of

direction, PD). However, higher endorsement of autonomic symptoms was associated with greater left thalamic (88% PD), left amygdala (86% PD), and right pallidum (85% PD) volumes.
Conclusion: These findings provide first evidence for the prevalence of autonomic symptoms and associated structural brain changes in RIS, expanding our understanding of RIS as a preclinical form of MS. Future multimodal MRI studies would provide further insights into the biological basis of dysautonomia in RIS.

[#41] Yi-Syuan Huang; Institute of Physiology
Supervisor: Dr. Zhong-Ping Feng
Theme: Brain Development and Lifespan Neuroscience (Poster Presentation)
MATERNAL DIABETES: A CRITICAL DRIVER OF HIE RISK AND SEVERITY
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Introduction & Objective: Maternal diabetes mellitus affects more than 14% of pregnancies worldwide and is increasingly recognized as a key driver of neonatal brain vulnerability. While hypoxic–ischemic encephalopathy (HIE) remains a leading cause of neonatal death and long-term disability, it is still unclear why infants of diabetic mothers (IDMs) experience disproportionately severe injury. We propose a ""two-hit"" hypothesis: the diabetic intrauterine environment serves as the first hit, priming the fetal brain through oxidative stress, neuroinflammation, and epigenetic changes; intrapartum hypoxia–ischemia acts as the second hit, triggering exacerbated damage.
Methods: We synthesized evidence from a range of animal and cellular models alongside clinical cohort data from PubMed and MEDLINE The analysis focused on linking specific diabetes subtypes to HIE risk and severity, with a particular emphasis on the role of abnormal calcium signalling as a central mediator of brain injury in IDMs.
Results: Clinically, diabetes-exposed HIE infants experience more frequent neonatal hypoglycemic episodes, longer ventilatory support requirements, and prolonged NICU stays with severe short-term outcomes. These pathological changes are further evidenced preclinically, driven by maternal diabetes, oxidative injury, neuroinflammatory priming, mitochondrial dysfunction, and disturbed calcium balance, collectively contributing to shaping the deteriorated HIE vulnerability.
Conclusion: To address these challenges, we outline a translational disease stratification framework. By combining diabetes subtypes, continuous glucose monitoring metrics, and calcium-related neonatal biomarkers, we provide a pathway toward precise neuroprotection. This approach ultimately aims to improve clinical outcomes through better risk identification and targeted interventions for this high-risk patient group.

[#42] Molly Hyde; Institute of Medical Science
Supervisor: Dr. Sakina Rizvi
Theme: Psychiatric Disorders I (Poster Presentation)
FUNCTIONAL CONNECTIVITY IN REWARD CIRCUITRY AND ANHEDONIA IN ADULTS WITH VARYING DEGREES OF SUICIDE RISK
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Introduction: Anhedonia and impaired reward processing may contribute to the transition from suicidal ideation to action. Reward processing encompasses multiple facets, including interest, motivation, effort, and pleasure. Yet, how these components are reflected in underlying neural circuitry and altered among suicide attempters needs to be established.

Objective: We examined differences in reward network connectivity and the relationship with subjective anhedonia in depressed adults with varying degrees of suicide risk.

Methods: This cross-sectional study evaluated neuroimaging and clinical data from suicide attempters (n=60) and non-attempters (n=30) with Major Depressive Disorder, and healthy controls (n=30). Functional magnetic resonance imaging (fMRI) was acquired at rest and anhedonia ratings were collected using the Dimensional Anhedonia Rating Scale (DARS), a self-report scale that measures levels of hedonic function across domains (i.e., hobbies, social activities, food/drink, and sensory experience). The following reward network nodes were selected as regions of interest: bilaterial ventral striatum, ventromedial prefrontal cortex, posterior cingulate cortex (PCC), ventral tegmental area (VTA), bilateral thalamus, presupplementary motor area, bilateral anterior insula (AI).

Results: Compared to NA, SA showed greater connectivity between left AI and left/right dorsolateral prefrontal cortices (DLPFC; p<.001-<.01), and between VTA and left posterior cingulate cortex (PCC; p<.01). SA had reduced connectivity between the AI and dorsal anterior cingulate cortex (dACC; p<.01). NA individuals with stronger VTA – Left PCC connectivity had lower global anhedonia (p=0.038), lower social anhedonia (p=0.008) and lower sensory anhedonia (p=0.019). DARS scores did not significantly differ between groups (p>.05).

Conclusions: Greater AI–DLPFC connectivity in suicide attempters may reflect stronger coupling between salience detection and cognitive-control systems, whereas greater AI–dACC connectivity in non-attempters may reflect stronger salience-conflict/affective monitoring. Despite comparable self-reported anhedonia, suicide attempters exhibited divergent connectivity patterns within key reward-related neural circuits. These alterations may reflect neurobiological vulnerabilities that facilitate the transition from suicidal ideation to action, highlighting potentially viable brain-based markers of suicide risk and future targets for intervention.

[#43] Alena Ionova; Medical Biophysics

Supervisor: Dr. Kathryn Manning

Theme: Brain Development and Lifespan Neuroscience (Poster Presentation)

MATERNAL PHYSICAL ACTIVITY AND THE NEURODEVELOPMENT OF PROGENY

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Introduction: During pregnancy there is a dramatic formation of neurons in the fetal brain and compromised maternal health may disrupt this process. While physical activity (PA) has broad benefits, only recently has it been explored during pregnancy for its effects on the mother. Prenatal PA (pPA) has been shown to reduce odds of complications like preeclampsia, preterm delivery, and even of depression and anxiety. However, less is known of its effects upon the developing child. In animal models, pPA reduces offspring anxiety, increases neurotrophic factors, and buffers consequences of prenatal stress. In humans, pPA has been associated with increased infant cerebral maturation and cortical thickness, but not hippocampal volume in older children, as measured via Magnetic Resonance Imaging (MRI). The hippocampus is particularly sensitive to changes in the internal environment, making it a focal region for further investigation. In all, it is still unclear how pPA affects child behavioural and early brain development.

Objective: This study examined if pPA is associated with (a) maternal outcomes and (b) offspring neurodevelopment, with a focus on hippocampal structure and connectivity in infancy. We hypothesized that higher pPA levels would correlate with improved maternal mental health and sleep, better child development scores, and more mature hippocampal structure and connectivity.

Methods: Data from the Pregnancy during the Pandemic study was used, with minutes of moderate-to-strenuous pPA (Godin-Shephard Leisure-Time Exercise Questionnaire; GLTEQ) as the main predictor. Maternal data, excluding those with substance use (n>8,000), included measures of mental health (Edinburgh Postnatal Depression Scale; EPDS, Patient-Reported Outcomes Measurement Information System (PROMIS) anxiety), sleep duration, and delivery outcomes, was analyzed with mixed-effects models, while controlling for household income. Child development was assessed via sleep (Brief Infant Sleep Questionnaire; BISQ), infant behaviour (Infant Behaviour Questionnaire; IBQ), and milestones (Ages and Stages; ASQ), with linear models evaluating associations with pPA.

A subset of children (n=109) had MRI scans acquired at 3 months of age on a 3T scanner at the Alberta Children's Hospital. FSL software will be used for standard preprocessing before the segmentation and quantification of the hippocampal volume. Functional and structural connectivity of the hippocampus with hubs of the default mode network will then be assessed using dual regression and tractography. Group differences by pPA levels will be assessed using general linear models with multiple-comparison correction.

Results: Of the larger maternal cohort (mean age = 31.8±4.4 years), 34.1% met physical activity guidelines of 150 minutes of moderate-to-strenuous activity per week, at intake. Preliminary analyses suggest that minutes of pPA per week had a weak negative association with maternal sleep duration (β=-0.05, $p<.01$) and mental health symptoms (β=-0.08, $p<.001$), while having no significant associations

observed for delivery method (β=-0.04, p=.33) or child sleep scores at 3 months (β=0.11, p=.63).

Conclusion: Up until the 1970s, women were recommended to remain as sedentary as possible during pregnancy. Emerging research contrarily suggests various benefits to the mother and child, however, benefits to the child are less understood. This project investigates these effects of pPA on the child which has the potential to support the development of future health policies and intervention strategies.

[#44] Victoria Ivakitch; Cell and Systems Biology

Supervisor: Dr. Rutsuko Ito

Theme: Behavioural and Social Neuroscience (Oral Presentation)

REINFORCER VOLUME INFLUENCES PUNISHMENT-RESISTANT ETHANOL SEEKING IN MALE AND FEMALE RATS

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Introduction: In preclinical models of alcohol misuse, compulsive-like behaviour, a key clinical feature of alcohol use disorder (AUD), is assessed by pairing an ethanol reward with an aversive stimulus to measure the persistence of ethanol-seeking despite punishment. However, as females typically weigh less than males, delivering a fixed ethanol dose to both sexes results in females receiving a proportionally larger dose per reinforcement. Therefore, while females typically exhibit greater aversion-resistant phenotypes, this may be partly attributable to sex differences in ethanol exposure in standard paradigms.

Objective: To address this limitation, we implemented a sex-adjusted ethanol self-administration paradigm in adult Long-Evans rats, in which reinforcer volumes approximated equivalent g/kg ethanol exposure across sexes (20% v/v ethanol; 0.10 mL for males and 0.06 mL for females). **Methods:** Animals were trained under fixed-ratio schedules (FR1 followed by FR3) and subsequently assessed under extinction and punishment conditions to evaluate ethanol-seeking behaviour when reinforcement was either withheld or paired with increasing, mild footshock intensities (0.2-0.4 mA).

Results: Females exhibited greater baseline responding and ethanol intake during unpunished self-administration. While both sexes showed comparable reductions in responding during extinction, males maintained higher levels of responding during punishment sessions, indicating greater resistance to aversive consequences under sex-adjusted conditions.

Conclusion: Together, these findings demonstrate that ethanol dose is an important factor influencing operant self-administration and should be considered when interpreting sex differences in punishment-resistant responding.

[#45] Mehvish Jamal; Rehabilitation Sciences

Supervisor: Dr. Tijana Simic

Theme: Cognitive Neuroscience (Oral Presentation)

ASSESSING NEUROLOGICAL DEFICITS IN POST-COVID-19 CONDITION USING AUTOMATED LANGUAGE ANALYSES

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Introduction: Post-COVID-19 Condition (PCC) affects 2.1 million Canadians, causing debilitating multisystemic symptoms including fatigue, post-exertional malaise and cognitive-communication (C-C) difficulties. Standard assessments inadequately capture these impairments. Language sampling may be more sensitive however, manual "gold-standard" analysis is time consuming and costly.

Objective: This study aims to develop and validate automated analysis (AA) of an engineered speech- and language feature set as a biomarker in PCC.

Methods: Participants with PCC (N=34) and age-matched controls (N=30) were recorded retelling the Cinderella Story. Recordings were automatically transcribed using Whisper AI large v3. A speech-language feature set (n=17) was built using existing literature in PCC and related conditions assessing fluency, syntax, vocabulary, and informativeness. Automated extraction of these linguistic features was completed in Python using the spaCy library. To ascertain reliability of the AA method, 20% of the dataset (n=14) was compared against the gold standard, manual transcription and feature extraction, guided by Quantitative Production Analysis methodology.

Results: An average 96% agreement was found between manual and automated transcripts. Comparisons of AA and manual methods indicate moderate reliability on average (combined Intraclass Correlation Coefficient (3,1) of 87%). Preliminary Mann-Whitney U comparisons of the narrative productions using the reliability dataset reveal a significantly lower main verb production in PCC than in controls ($U_{min}=42$, $p<0.05$). Descriptive statistics indicate a wider range of scores and lower group means for the PCC group however, this did not equate to a significant difference for the remaining features.

Conclusion: Analyses are ongoing to improve reliability of certain features, compare CC performance across the complete dataset, and to evaluate the clinical correlates of automatically extracted features.

[#46] Jiyoon Jeong; Psychology

Supervisor: Dr. Matthias Niemeier

Theme: Pain and Sensory Disorders I (Poster Presentation)

ACTION INTENTIONS PARSE OBJECTS INTO BEHAVIOURALLY RELEVANT SEGMENTS

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Introduction: It is often assumed that during grasping, attention splits into multiple foci near the intended grasp-points, whereas during reaching, attention is directed toward the object's centre of gravity.

Objective: Here we revisited this distinction by asking participants to grasp or reach for objects that differed in local geometry near grasp-points, coloured surface patches, and object orientation.

Methods: To decode feature representations underlying these two action types, we used electroencephalography (EEG) combined with Support Vector Machine (SVM) classifiers applied to event-related potentials (ERPs).

Results: Classification accuracy for grasp-point geometry was significantly higher during grasp planning compared to reach planning (234–332 ms), as was accuracy for object orientation (308–371 ms), consistent with previous studies. However, contrary to the classical split-attention account, classification accuracy for central colour was significant regardless of action intention, suggesting that central colour is processed independently of the planned action.

Conclusion: Taken together, these findings suggest that action-dependent attention does not split into isolated foci at the contact points, but instead parses objects into behaviourally relevant units that are defined by the motor demands of the task at hand.

[#47] Lauren Joe; Laboratory Medicine and Pathology

Supervisor: Dr. Janice Robertson

Theme: Molecular & Cellular Neuroscience (Oral Presentation)

TARGETING THE LIMK-COFILIN PATHWAY TO RESTORE SYNAPTIC DYSFUNCTION IN C9ORF72 HAPLOINSUFFICIENCY

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Introduction: Amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD) are neurodegenerative disorders that represent two extremes of a shared disease spectrum. Patients rapidly develop progressive motor paralysis and cognitive decline, with death typically occurring within 2–5 years of diagnosis, highlighting the urgent need for disease-modifying therapies. Hexanucleotide (G4C2) repeat expansion (HRE) in intron 1 of chromosome 9 open reading frame 72 (C9orf72) represent the most common genetic cause of ALS and FTD, and carriers may develop ALS, FTD, or both (C9-ALS/FTD). Synaptic dysfunction and loss are early events in C9-ALS/FTD, however the mechanisms driving this impairment remain unclear. C9orf72 HREs cause haploinsufficiency through transcriptional downregulation of C9orf72 mRNA and diminished protein expression. The precise function of C9orf72 remains unclear, yet it has been shown to interact with the actin-binding protein cofilin, a critical regulator of actin dynamics. C9orf72 loss leads to increased cofilin inactivation through phosphorylation by LIM domain kinase 1 (LIMK1) and recent work from our laboratory demonstrates that C9orf72 haploinsufficiency perturbs synaptic function through dysregulation of the LIMK-cofilin signaling pathway. Notably, C9orf72 knockout (C9KO) mice exhibit enhanced postsynaptic GluA1 (but not GluA2) expression in the hippocampus, increased phosphorylated cofilin, and cortical hyperexcitability, features previously implicated in ALS/FTD pathogenesis.

Objective: Given that C9orf72 reduction increases cofilin dysregulation and synaptic GluA1 levels, I hypothesize that reducing excessive LIMK signaling to restore cofilin

activity will normalize postsynaptic GluA1 levels and rescue synaptic dysfunction.

Methods: Field electrophysiological recordings were performed in the Schaffer collateral-commissural pathway of C9KO mice to test whether elevated GluA1 expression promotes calcium-permeable AMPA receptor (CP-AMPAR)-dependent synaptic plasticity. To elucidate underlying mechanisms, IEM-1460, a selective CP-AMPAR antagonist, and LIMKi3, an ATP-competitive LIMK inhibitor, were applied to hippocampal slices during recordings. Western blotting was performed to assess phosphorylated cofilin, total cofilin, phosphorylated LIMK, and total LIMK levels at baseline and following LIMKi3 treatment.

Results: C9orf72 reduction selectively enhances long-term potentiation 2 (LTP2), a CP-AMPAR-dependent form of synaptic plasticity. Pharmacological inhibition of CP-AMPARs normalized the elevated LTP2 observed in C9KO mice to wild-type levels. Inhibition of LIMK signaling restored phosphorylated cofilin and phosphorylated LIMK levels, and also normalized elevated LTP2.

Conclusion: Together, these findings uncover a novel role for C9orf72 haploinsufficiency in modulating CP-AMPAR and LIMK-cofilin-dependent synaptic plasticity and identify potential therapeutic targets for synaptic dysfunction in ALS and FTD.

[#48] Bryan Kartono; Laboratory Medicine and Pathology

Supervisor: Dr. Janice Robertson

Theme: Aging and Neurodegenerative Disorders (Poster Presentation)

ULTRASTRUCTURAL CHARACTERIZATION OF PRESYNAPTIC ARCHITECTURE IN THE CONTEXT OF C9ORF72 HAPLOINSUFFICIENCY

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Background: The most common genetic cause of amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD) is a hexanucleotide repeat expansion in C9orf72. While toxic gain-of-function mechanisms have been extensively studied, increasing evidence suggests that reduced C9orf72 protein expression may contribute to early synaptic dysfunction. Synaptic alterations are thought to precede overt neurodegeneration in ALS/FTD; however, the presynaptic ultrastructural consequences of C9orf72 loss remain elusive. Given the proposed role of C9orf72 in membrane trafficking and vesicle dynamics, detailed structural analysis of presynaptic compartments may provide insight into early synaptic vulnerability. Here, we perform an ultrastructural characterization of presynaptic architecture across genotypes in a mouse model of C9orf72 deficiency.

Methods: Mice were generated by crossbreeding C9orf72+/– animals. At 3 months of age, brain tissue was collected and processed using high-pressure freezing and freeze substitution for transmission electron microscopy. Regions of interest included the hippocampal CA1 stratum radiatum and CA3 stratum lucidum. Ultrathin sections were imaged at high resolution, and presynaptic terminals were analyzed using quantitative morphometric approaches. Parameters assessed included total synaptic vesicle density, the number of docked vesicles at the active zone, and vesicle size.

Results / Future Directions: Preliminary analyses reveal genotype-dependent differences in presynaptic organization at 3 months of age. Alterations in synaptic vesicle distribution and active zone-associated vesicle pools were observed with reduced C9orf72 expression, suggesting early remodeling of presynaptic architecture. Most notably, mossy fiber boutons (MFBs) within the CA3 stratum lucidum were markedly depleted in C9orf72-deficient mice, indicating substantial structural disruption of this specialized presynaptic compartment. In addition, C9orf72-deficient mice exhibited reduced synaptic vesicle size compared to wild-type controls, further supporting altered presynaptic vesicle morphology associated with loss of C9orf72. Future work will extend this characterization to aged cohorts to assess whether presynaptic structural changes progress over time.

Conclusions: This study provides foundational ultrastructural characterization of presynaptic architecture in C9orf72-deficient mice. Structural alterations, including marked depletion of mossy fiber boutons in CA3 and reduced synaptic vesicle size in knockout mice, were evident at 3 months of age. These findings indicate that presynaptic remodeling occurs early following loss of C9orf72. Defining these structural features establishes a framework for understanding how C9orf72 deficiency influences synaptic organization and may shape early circuit-level changes relevant to ALS/FTD.

[#49] John Kennedy; Psychology

Theme: Psychiatric Disorders I (Poster Presentation)

CROSS-SECTIONS IN DRAWING DEVELOPMENT: DRAWINGS BY NOVICES WHO ARE BLIND

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Introduction: In Clark (1897), sighted children drew an apple with a pin stuck though it. Some drew the entire shaft of the pin, seeds, cores and indentations in the apple's profile.

Objective: These might be cross-sections implying the observer's vantage point. If so, drawing novices who create apple-pin cross-sections should produce other vantage-point drawings. If they offer consistent cross-sections, would they draw a cube and a pineapple to suit a vantage point? If not consistent, would these be drawn without a vantage point e.g. the cube as if folded out and the pineapple's texture outside an O shape?

Methods: In a drawing class in Bergamo, Italy, adults who were blind and novices at drawing made raised-line sketches of the apple and the pin, a cube and a pineapple.

Results: Two of the adults drew apple-pin cross-sections, i.e. with indentations top or bottom and lines all the way through the interior of the apple-shape (see top left & right). Their cube drawings used Y junctions for vertices facing the observer and their lines for texture crossed the O of the pineapple. These are vantage-point drawings. In contrast, one adult's apple-pin drawing was inconsistent, with both indentations and a line stopping inside the O for the apple (see below, right). As shown, this accompanied a foldout version of a cube and a pineapple sketch with texture drawn on the perimeter of the O and not in the interior! In theory (Kennedy & Carboni, 2024), the interior stands for the insides of the pineapple.

Conclusion: Drawing development may be similar in the sighted and blind, with cross-sections as vantage-point schemes.

[#50] Vittala Korann; Institute of Medical Science

Supervisor: Dr. Mahavir Agarwal

Theme: Systems and Circuits Neuroscience (Oral Presentation)

DEVELOPMENT AND VALIDATION OF A SEMI-AUTOMATED ABDOMINAL FAT QUANTIFICATION PIPELINE USING FAT FRACTION MRI WITH NON-RIGID MOTION CORRECTION IN PSYCHOTIC SPECTRUM DISORDERS

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Introduction: Most of the clinical studies needed the estimation of abdominal fat distribution for evaluating patients' metabolic health. Despite this important need, the literature on reliable automated fat segmentation remains limited, as manual approaches are time-consuming and labor-intensive.

Objective: Developing a semi-automated toolbox for abdominal fat quantification based on motion corrected fat fraction (FF) images acquired from patients with psychotic spectrum disorders (PSDs).

Methods: We made use of MRI abdominal data from 35 patients with PSDs. After manually removing arm, fat-only (FO) and water-only (WO) images were non-rigid motion corrected and then combined to generate FF images. The resultant motion corrected FF (FF-MC) images were given to segmentation and quantification pipeline.

Results: Non-rigid motion correction considerably improved mean correlation between slices in both FO ($t(34) = 8.23$, $p < 0.001$), Cohen's $d = 1.39$) and WO ($t(34) = 12.22$, $p < 0.001$, Cohen's $d = 2.07$) images compared to their respective non-motion corrected (NMC) images. Comparing the fat quantification between FO-NMC and FF-MC images, we found all three i.e. total fat (t-stat = 2.053, $p<0.049$, Cohen's $d = 0.34$, 95% CI [50.19 66.16]), subcutaneous fat (t-stat = 2.157, $p<0.038$, Cohen's $d = 0.36$, 95% CI [2.90 97.22]), and visceral fat (t-stat = 12.029, $p<0.001$, Cohen's $d = 2.03$, 95% CI [318.61 448.15]) significantly improved after motion correction. Finally, FF-MC images have significantly improved subcutaneous (+5.52%) and visceral

fat (+77.92%) percentage changes when compared to conventional FO-NMC images-based fat quantification.

Conclusion: The proposed pipeline applies non-rigid motion correction to fat and water images to generate a robust fat fraction, improving the accuracy and reliability of abdominal fat quantification, a must needed for most of clinical applications to assess patients' metabolic health.

[#51] Mohammad Sadegh Kord Ali; Laboratory Medicine and Pathology

Supervisor: Dr. Carol Schuurmans

Theme: Neuropharmacology and Drug Development (Oral Presentation)

OPTIMIZING ADENO-ASSOCIATED VIRUS DELIVERY OF REPROGRAMMING FACTORS FOR RETINAL REPAIR

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Introduction: Direct neuronal reprogramming, in which a fully differentiated cell is converted into an induced neuron (iNeuron), holds significant therapeutic promise for a wide range of neurodegenerative disorders, including those of the retina. However, despite evidence of Müller glia-to-neuron conversion in vivo, major challenges remain. Particularly, current adeno-associated viruses (AAVs), the primary vectors for delivering neurogenic transcription factors (TFs), face two major limitations: (1) off-target neuronal expression, due to the loss of GFAP promoter specificity when linked to neurogenic TFs, and (2) persistent transgene activity, which can cause incomplete neuronal maturation or increase the risk of tumorigenesis.

Objective: I hypothesize that incorporating neuron-specific miR-124 target sites (124T) and a Cre-mediated time-delayed off-switch into Müller glia-selective AAV8-GFAP vectors will minimize off-target neuronal expression via post-transcriptional silencing and temporally restrict Ascl1 expression to permit Müller glia-to-neuron conversion without inducing aberrant proliferation.

Methods: We used AAV-GFAP vectors to express neurogenic TFs in Müller glia. To ensure glial specificity and detarget neurons, we incorporated four 124T repeats into the 3'-UTR of an Ascl1(SA6)-mCherry transcriptional unit. Additionally, we devised a Cre-based "off-switch" to prevent continuous gene expression, predicated on the intrinsic delay of Cre-mediated recombination. To confirm the glial origin of iNeurons, we pre-labeled Müller glia via tamoxifen administration in Slc1a3-CreERT;Rosa-zsGreen mice prior to transduction with AAV-GFAP vectors.

Results: Immunofluorescence analysis demonstrated a significant reduction in Sox9-cell transduction with the Ascl1(SA6)-124T compared to Ascl1(SA6), confirming effective neuronal de-targeting. Notably, the addition of 124T repeats significantly enhanced the proportion of Crx+ cells generated while concurrently reducing Pax6+ cells, suggesting a fate shift toward bipolar- and/or photoreceptor-like neurons. Furthermore, Ascl(SA6) produced a marked increase in Brn3a+ retinal ganglion cell-like neurons relative to wild type Ascl1, an effect that was substantially attenuated by 124T co-expression, further supporting 124T's role as a neuronal subtype

fate switch rather than a general modulator of reprogramming efficiency.

Conclusion: These findings suggest that 124T serves a dual purpose, enhancing reprogramming precision while influencing iNeuron fate toward photoreceptor-like identities, supporting its potential as a strategy for safer and more targeted AAV-based therapies.

[#52] Medha Krishnan; Laboratory Medicine and Pathology

Supervisor: Dr. Gerold Schmitt-Ulms

Theme: Neuropharmacology and Drug Development (Poster Presentation)

BUILDING ON A 1ST GENERATION CRISPR-CAS9 ALL-IN-ONE RECOMBINANT AAV-DELIVERED PRP LOWERING GENE THERAPY FOR PRION DISEASES

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Introduction: Prion diseases are fatal neurodegenerative disorders affecting several mammalian species. First identified in sheep as scrapie, later in cows as bovine spongiform encephalopathy (BSE), and in humans as Creutzfeldt-Jakob disease (CJD), these diseases are driven by infectious prions (PrPSc). PrPSc acts as a template, inducing the normal cellular prion protein (PrPC) to undergo a conformational change to PrPSc. Any therapy that profoundly reduces the brain levels of PrPC should be effective for the treatment of prion diseases. This project builds on the specific hypothesis that recent advances in the virus-mediated delivery of gene therapies can be harnessed for this objective.

Objective: The aims of the study are to establish a 2nd generation all-in-one recombinant adeno-associated virus (rAAV) vector whose payload can potently induce a functional knockout of the prion gene.

Methods: This project builds on a 1st generation implementation of an all-in-one rAAV vector that codes for a prion gene-specific guide RNA and a high-fidelity SlugCas9 endonuclease which was used to generate proof-of-concept data. To improve efficacy benchmarks of this original vector, the ongoing research program is pursuing three avenues of optimization: 1) The payload composition is being revised and optimized. 2) An unbiased comparative screen of gRNA is being conducted. 3) The method of assembly and purification of AAVs is being refined.

Results: First generation proof-of-concept prion gene editing experiments have been successfully conducted. A robust pipeline has been implemented that makes use of an affinity capture methodology for producing high titre preparations of rAAVs. This first iteration of the therapeutic vector had limited PrP lowering efficacy. Second generation payloads have been assembled that drive the expression of SauCas9 from one of several promoters with potent expression in neurons. To further increase potency, regulatory elements of the payload have been replaced. An array of payloads has been assembled to identify the most potent gRNAs. The method AAV purification has been amended to increase the full-to-empty ratio of rAAV vector preparations.

Conclusion: The key components of an rAAV-delivered gene therapy that generates a functional knockout of the prion gene are in place. Improvements to the first-generation

payload are currently being assessed. Future work will need to establish the relative efficacy and safety of this approach for the treatment of prion diseases.

[#53] Emily Kuik; Pharmacology & Toxicology

Supervisor: Dr. Jeffrey Meyer

Theme: Psychiatric Disorders I (Poster Presentation)

EFFECTS OF SEX, TREATMENT RESISTANT DEPRESSION, AND ANTIDEPRESSANT TREATMENT ON MONOAMINE OXIDASE B TOTAL DISTRIBUTION VOLUME

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Introduction: Monoamine oxidase B (MAO-B) is a high-density protein that influences mitochondrial function and the transition to astrogliosis, and produces hydrogen peroxide while metabolizing non-serotonergic monoamines. Its level is elevated in several common neuropsychiatric diseases, including the prefrontal cortex (PFC) of major depressive episodes (MDE) and the cortex of persistent traumatic brain injury, long COVID, and Alzheimer's disease.

Objectives: The aims of the present study are to examine the effect of sex, treatment-resistant depression, and antidepressant treatment on MAO-B total distribution volume ($[^{11}C]$SL25.1188 V_T), an index of MAO-B level. We hypothesize that $[^{11}C]$SL25.1188 V_T will be lower in females compared to males; elevated in individuals with MDE and history of treatment-resistance (TRD) compared to individuals with MDE and no history of treatment-resistance (NTR-MDE); and lowered after treatment with rasagiline or phenelzine but not duloxetine.

Methods: $[^{11}C]$SL25.1188 PET was applied in 95 participants (29 with NTR-MDE, 26 with TRD, and 40 healthy). A subset of NTR-MDE and TRD were scanned before and after treatment (once daily for 4-6 weeks) to determine the effects of phenelzine, rasagiline, and duloxetine.

Results: $[^{11}C]$SL25.1188 V_T was significantly higher in females compared to males (13.3%, $F_{1,91} = 16.263$, $p < .001$) in prioritized grey matter regions (including PFC, anterior cingulate cortex, and hippocampus), and in TRD compared to NTR-MDE in the PFC (6.0%, $F_{1,52} = 4.78$, $p = .033$). Occupancy of rasagiline and

phenelzine was approximately 94%, but duloxetine had negligible effects.

Conclusion: These findings raise important implications, including whether sex differences in MAO-B level may contribute to sex differences in the prevalence or course of diseases associated with elevated MAO-B levels; consideration of targeting MAO-B in some TRD states; and whether rasagiline should be assessed in clinical trials for use beyond Parkinson's Disease given its comparably high MAO-B occupancy to phenelzine.

[#54] Hannah Le; Pharmacology & Toxicology

Supervisor: Dr. Chao Zheng

Theme: Aging and Neurodegenerative Disorders (Poster Presentation)

INVESTIGATING THE ASSOCIATION BETWEEN P2Y12 RECEPTOR, SV2A, AND TAU EXPRESSION IN POSTMORTEM AD AND CONTROL BRAINS USING IN VITRO AUTORADIOGRAPHY

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Introduction: Alzheimer's disease (AD) is a prevalent form of dementia and involves a wide range of neurodegenerative and neuroinflammatory factors that contribute to the disease progression and associated cognitive impairment. Synaptic vesicle glycoprotein 2A (SV2A), a biomarker for synaptic density; purinergic receptor P2Y12R, a marker of microglia activation; and hyperphosphorylated tau have been extensively studied in their contribution to the disease progression, with attention shifting towards investigating how these factors can enhance one another, thereby causing compounding effects or potential acceleration of the disease's symptoms.

Objective: The purpose of this work is to carry out in vitro autoradiography (ARG) studies to evaluate the expression and distribution of P2Y12R, SV2A, and tau using [^{3}H]PSB-0413, [^{3}H]UCB-J, and [^{18}F]MK-6240, respectively, in human postmortem AD versus healthy individual brain tissues.

Methods: [^{3}H]PSB-0413 and [^{3}H]UCB-J were custom synthesized (Novandi AB, Sweden), while [^{18}F]MK-6240 was synthesized following our reported protocol. 4 Thin section ARG binding assays were performed on post-mortem hippocampal/BA28 tissues from cognitively normal healthy controls (NC) (n = 3) and AD patients (n = 5). Radiotracer binding was quantified using digital ARG in regions of interest (ROI), and non-specific binding was determined through homologous blockage with 10 µM of Suramin, Levetiracetam, and cold MK-6240, known ligands for P2Y12R, SV2A, and tau, respectively.

Results: [^{3}H]PSB-0413 autoradiography had significantly decreased binding in sub-hippocampal regions including in the subiculum (SUB) (AD: 1.29 ± 0.61 µCi/g, n = 4 vs. NC: 2.56 ± 1.0 µCi/g, n = 3) and entorhinal cortex (EC) (AD: 1.41 ± 0.6 µCi/g, n = 5 vs. NC: 3.02 ± 0.86 µCi/g, n = 3). Similarly, [^{3}H]UCB-J ARG revealed a significant decrease in the dentate gyrus (DG) (AD: 82.6 ± 23.6 µCi/g, n = 4 vs. NC: 153.5 ± 8.5 µCi/g, n = 2) and CA1 (AD: 84.9 ± 17.9 µCi/g, n =

4 vs. NC: 132.3 ± 18.2 µCi/g, n = 3), alongside the EC (AD: 136.5 ± 68.1 µCi/g, n = 5 vs. NC: 157.4 ± 35.2 µCi/g, n = 3). [^{18}F]MK-6240 ARG showed strong binding to tau aggregates throughout the hippocampus, with little to no off-target binding in NC, with a significant increase in binding observed in AD patients in the CA1 (AD: 3.62 ± 2.7 µCi/g, n = 4 vs. NC: 0.46 ± 0.31 µCi/g, n = 3) and SUB (AD: 5.01 ± 3.5 µCi/g, n = 4 vs. NC: 1.95 ± 0.65 µCi/g, n = 3). Both [^{18}F]MK-6240 and [^{3}H]UCB-J showed high specific binding when displaced in AD (74.5 ± 1.8%, n = 4 for [^{18}F]MK-6420 and 90.3 ± 5.5%, n = 5 for [^{3}H]UCB-J), but the latter showed an ~50% higher specificity when displaced in NC (43.9 ± 2.5%, n = 2 for [^{18}F]MK-6240 and 91.8 ± 0.72%, n = 3 for [^{3}H]UCB-J). On the other hand, [^{3}H]PSB-0413 shows modest specificity in AD (25.5 ± 7%, n = 5) and NC (43.4 ± 9.7%, n = 3) in comparison to the previous two tracers. Overall, SV2A and P2Y12R showed a negative correlation with tau in postmortem human tissues based on ARG. The correlation between SV2A decrease and tau accumulation is consistent with known human PET studies.

Conclusions: This study demonstrates that SV2A levels decrease while tau accumulations increase in AD brains with [^{3}H]UCB-J and [^{18}F]MK-6240 respectively, and our data is consistent with in vivo human PET imaging studies of SV2A and tau. We also showed that P2Y12R is decreased in AD brains with [^{3}H]PSB-0413 and these results can be used to guide future human PET studies with this tracer. These findings reinforce the utility of these tracers for AD clinical PET imaging research. Ongoing immunohistochemistry and additional assays are underway to further corroborate the autoradiography findings and deepen our understanding of these associations and will be presented.

[#55] Gia Han Le; Institute of Medical Science

Supervisor: Dr. Roger McIntyre

Theme: Psychiatric Disorders I (Poster Presentation)

RESTING-STATE APERIODIC EEG MARKERS OF SUICIDALITY AND DEPRESSIVE SYMPTOM SEVERITY IN TREATMENT RESISTANT DEPRESSION: PRELIMINARY BASELINE DATA FROM TWO ONGOING CLINICAL TRIALS

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Introduction: Symptom-based and clinician-rated assessments are indispensable in psychiatry but offer limited mechanistic specificity, motivating the search for biomarkers that index underlying neurobiology and support target engagement studies. Aperiodic electroencephalographic (EEG) activity has emerged as a candidate marker of psychopathology; however, its clinical relevance remains undercharacterized.

Objective: Investigate aperiodic parameters (APs) as correlates of suicidal ideation (SI) burden and depressive symptom severity in treatment-resistant depression (TRD).

Methods: Resting-state eyes-closed and eyes-open EEG data from two studies were pooled

(NCT06480500, n = 37; NCT06341426, n = 32). Power spectra (1-45 Hz) were parameterized with Fitting Oscillations & One-Over-F to extract APs (offset and exponent). SI burden was indexed using Columbia-Suicide Severity Rating Scale. Linear models tested whether binary and categorical SI severity, and depressive symptom severity (Montgomery-Åsberg Depression Rating Scale score), predicted APs after adjustment for age, sex, and study. False discovery rate-adjusted q-values are reported.

Results: Compared with the no-SI group, participants with SI showed greater aperiodic offset and exponent in both eyes-closed (offset: β=0.295, p=0.00256, q=0.00776; exponent: β=0.270, p=0.00929, q=0.00929) and eyes-open (offset: β=0.257, p=0.00851, q=0.00851; exponent: β=0.274, p=0.00793, q=0.00851). Omnibus effects across SI severity categories were significant for both APs in eyes-closed (all q≤0.000178) and eyes-open (all q≤0.00386). Depressive symptom severity was positively associated with offset in eyes-closed (β=0.0124, p=0.00313, q=0.00938), while exponent showed weaker trends. Eye-state interactions were non-significant.

Conclusion: Higher symptom severity was associated with increased aperiodic offset and modest changes in exponent. APs may represent a neurophysiological marker of clinical severity, potentially reflecting altered large-scale network dynamics in TRD.

[#56] Polina Lekhnitskaia; Institute of Medical Science

Supervisor: Dr. Daniel Felsky

Theme: Cognitive Neuroscience (Poster Presentation)

PLANUM POLARE AMONG POTENTIAL BIOMARKERS FOR COGNITIVE-COMMUNICATION DISORDER AND RESILIENCE

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Introduction: Cognitive Communication Disorder (CCD) involves communication difficulties driven by impairments in cognitive processes rather than primary speech or language deficits. CCD is highly prevalent, with approximately 1.4 million stroke-related cases annually, 1–2 million pediatric post-traumatic cases each year, and Alzheimer's-related CCD projected to affect 31.2 million people globally by 2050. Despite this burden, CCD remains under-recognized due to often normal performance on standard language tests, limited large-scale epidemiological data, and a lack of studies examining resilience mechanisms.

Objective: This project aimed to identify biopsychosocial determinants of risk and resilience in CCD, using a proxy definition. We hypothesized that integration of biological, cognitive, genetic risk, and neuroimaging features would predict resilience and define distinct CCD profiles, with shared neural substrates across studies.

Methods: Using UK Biobank data, we compared 597 individuals with probable CCD to 597 demographically and etiologically matched resilient individuals identified through ICD-10 codes. CCD classification required: (1) presence of a neurological condition, (2) no aphasia diagnosis, and (3) self-reported communication difficulties. Resilience was defined as absence of cognitive and language symptoms. Logistic regression with standardized preprocessing and mean 5-fold cross-validation was applied. The

study used an 80/20 train-test split. Predictors included vocabulary level, fluid intelligence, social functioning measures, diffusion MRI, polygenic risk scores for neurodegenerative disease, and regional gray matter volumes.

Results: Median classification accuracy was 0.62 (95% CI 0.534 – 0.703), median precision - 0.577 (95% CI 0.493 – 0.660), median recall: 0.612 (95% CI 0.505 – 0.719). Volume of grey matter in Planum Polare right and Mean FA in inferior cerebellar peduncle on fractional anisotropy skeleton left had the strongest effect on resilience classification (B=-0.70, $p<0.05$; B=-0.60, $p<0.05$).

Conclusion: Grey matter volumes in the Planum Polare may contribute to the prediction of CCD phenotypes or resilience, highlighting their potential utility as neuroanatomical markers. This region is implicated in higher-order auditory processing, including the integration of prosodic and rhythmic acoustic features, and serves as a functional interface between primary auditory perception and semantic interpretation.

[#57] Jino Lim; Institute of Medical Science

Supervisor: Dr. Katharine Dunlop

Theme: Psychiatric Disorders I (Poster Presentation)

IDENTIFYING BRAIN AGE-BASED SUBTYPES OF MAJOR DEPRESSIVE DISORDER

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Introduction: Major Depressive Disorder (MDD) is associated with accelerated brain aging. However, the regional volumetric contributions to brain aging, and how inter-individual clinical heterogeneity relates to brain aging in MDD remain unknown.

Objectives: To address these challenges, we will generate latent brain age-based symptom dimensions, which identify structural deviations contributing to brain aging correlated with depressive symptoms.

Methods: We extracted 145 brain regions from preprocessed structural scans of 385 adult MDD participants (62.6% female) across four studies in the COORDINATE-MDD consortium. SHapley Additive exPlainations (SHAP) was used to estimate each region's contribution to predicted brain age. The SHAP values for all 145 brain regions were generated from a previously defined brain aging model. Leveraging the 17-item Hamilton Rating Scale for Depression, we used canonical correlation analysis (CCA) to generate symptom-brain latent dimensions. Significant dimensions were identified using Wilks' lambda at $p < 0.05$. Dimension weights were characterized, and multiple comparisons were corrected using the false discovery rate.

Results: CCA identified two significant symptom-brain latent dimensions. Dimension 1 ($p = .003$; correlation = 0.749) was positively correlated with insomnia, anxiety, and hypochondriasis. Higher symptom severity for this dimension was negatively associated with SHAP values in the left middle cingulate, temporal lobe, and bilateral angular gyrus. Dimension 2 ($p = .046$; correlation = 0.732) was positively associated with guilt, suicide, and gastrointestinal symptoms. Higher symptom severity for this dimension was positively associated with SHAP values in the right planum polare, inferior occipital gyrus, and cerebellum.

Conclusion: We identified two distinct symptom-brain dimensions, supporting brain aging-based indices as promising biomarkers for neurobiologically meaningful subtypes. These

subtypes could inform targeted interventions and may improve clinical outcomes. Future work will incorporate regularization and clustering efforts to delineate subtypes.

[#58] Tommy Liu; Rehabilitation Sciences
Supervisor: Dr. Deryk Beal
Theme: Neuropharmacology and Drug Development (Oral Presentation)
IN-VIVO ROBOTIZED AND NAVIGATED MOTOR CORTEX MAPPING TO MEASURE INDIVIDUALIZED 80-EFFECTIVE SPREAD OF SINGLE TRANSCRANIAL MAGNETIC STIMULATOR PULSES: A PROTOCOL
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Introduction: TMS is a widely used brain stimulator whose applications range from diagnosing motor diseases, treating psychiatric disorders, to aiding surgical planning. Prior to stimulation, the energy field is often modelled in-silico, and the model is relied upon to determine which brain regions are affected. However, modelled averaged reach spread (MARS) may not truthfully reflect the affected brain regions, as it is not empirical and does not take into account fine details of individual anatomy nor phenomena such as activation propagation, unlike observed individualized effective spread (OIES). While effective spread has been empirically measured, only one study has done so, and without 1) robotization, 2) navigation, 3) individualization, or 4) an area as output.
Objectives and Methods: This current design aims to address these four gaps by using robotized and navigated motor cortex mapping to measure 80-effective spread of single TMS pulses in a health adult.
Conclusion: A better understanding of OIES may inform stimulation choices, from energy source to intensity, and thus improve stimulation outcome. Future Directions: The current study may pave the way for future ones exploring 1) individualized effective depth (an adjacent field property to spread), 2) congruity between modelled individualized reach spread and observed individualized effective spread, and 3) post-hoc analysis of between- and within-subject determinants affecting effective spread.

[#59] Megan Lozzi; Psychology
Supervisor: Dr. Robert Rozeske
Theme: Behavioural and Social Neuroscience (Oral Presentation)
ROLE OF LATERAL PERIAQUEDUCTAL GREY IN FLEXIBLE DEFENSIVE STRATEGIES
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Introduction: Generating context-appropriate defensive responses to threat is essential for survival. While defensive behaviour is often operationalized as freezing, animals express a repertoire of behavioural strategies, including avoidance and risk assessment. The periaqueductal gray (PAG) organizes expression of defensive behaviour along its dorsal-ventral axis, but the specific contribution of the lateral PAG (lPAG) to threat-related behaviour is less understood.
Methods: We systematically varied threat intensity experience in a context fear avoidance task. We used deep learning–based pose estimation approaches to characterize defensive behaviour patterns beyond the

traditional freeze/no-freeze binary. We then performed calcium imaging in the lPAG with fiber photometry during our task. To test causality, we chemogenetically inhibited lPAG neurons with DREADDs and observed differential effects on freezing and avoidance.

Results: We observed a range of defensive phenotypes across experimental groups and found that behaviour expressed during the conditioning phase of the task predicted freezing and avoidance strategies during the test phase. lPAG activity dynamically tracked defensive responses, including entry and exits into the threatening context.

Conclusion: Together, these data identify the lPAG as a potential node for flexible defensive behaviour selection across individuals.

[#60] Dhvani Mehta; Institute of Medical Science

Supervisor: Dr. Victor Tang

Theme: Neuropharmacology and Drug Development (Oral Presentation)

FEASIBILITY AND TOLERABILITY OF BILATERAL INSULA-PFC RTMS USING THE MMC-140 COIL IN CANNABIS USE DISORDER

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Background: Repetitive transcranial magnetic stimulation (rTMS) has demonstrated considerable efficacy for many substance use disorders, thought its application for cannabis use disorder (CUD) remains promising but under-explored. A crucial first step in adapting this intervention for CUD is establishing feasibility and tolerability.

Objective: As part of an ongoing blinded, randomized trial, we sought to evaluate the feasibility of delivery bilateral insula-prefrontal cortex (PFC) rTMS in individuals with CUD and examine how stimulation parameters (e.g., intensity) influence tolerability and adherence.

Methods: Forty CUD participants were randomized to receive 20 daily sessions of high- or low-frequency bilateral rTMS targeting the insula-PFC at F5/F6 regions using the MMC-140 circular coil. Analyses were blinded to allocation. Feasibility was assessed via session completion and attainment of the target intensity (120% motor threshold (MT)). Tolerability was measured using session-level pain/discomfort ratings (0-10) and adverse events. Linear mixed-effects models examined longitudinal changes in pain and associations with stimulation parameters.

Results: Seventy-eight percent of participants completed all sessions. At the session level, 120% MT was achieved in 31.9% of right-sided and 26.8% of left-sided sessions. At the participant level, 50% reached target intensity on the right and 37.5% on the left ($p=0.384$), typically by sessions 8-9. Right-sided stimulation was associated with slightly higher pain/discomfort ($p=0.03$) and intensity ($p<0.001$). Mean pain/discomfort decreased overtime, from 5.34 (SD = 1.90) at session 1 to 3.19 (SD = 2.51) at session 20, indicating habituation ($\beta=-0.256$, $p<0.001$). Early pain/discomfort did not predict adherence. Adverse events were generally mild, most commonly headache (58.5%), dizziness (20.3%), and nausea (15.4%).

Conclusion: Bilateral insula-PFC rTMS with the MMC-140 coil is feasible and well tolerated in CUD. However, due to challenges with tolerating the standard stimulation intensity of 120% RMT, future studies should consider exploring the efficacy, safety, and neurobiological effects of using lower intensity stimulation.

[#61] Xianze Meng; Institute of Medical Science

Supervisor: Dr. Karen Deborah Davis

Theme: Pain and Sensory Disorders II (Poster Presentation)

HEAT- VS. MECHANICAL-BASED TEMPORAL SUMMATION OF PAIN IN HEALTHY INDIVIDUALS AND PEOPLE WITH NEUROPATHIC PAIN

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Introduction: Temporal summation of pain (TSP) refers to increased pain evoked by a series of brief noxious stimuli; thought to reflect dorsal horn neuronal windup and central sensitization. Experimental studies of TSP have used heat or mechanical stimuli but it is unclear whether TSP is modality-independent.

Objective: The aim of our study was to compare heat- versus pressure-based TSP in healthy individuals (HCs) and those with neuropathic pain (NP). We hypothesize that TSP is modality-dependent in HCs and NP because heat- and mechanical nociception involve distinct receptors and nociceptive pathways.

Methods: In each HC and NP study participant, we delivered a series of 10 brief stimuli at 0.3Hz to evaluate heat (48 °C, TSA II, Medoc) and mechanical (256 mN probe, MRC Systems) TSP. TSP was quantified based on % and absolute change to peak pain from the first stimulus. We conducted group and within-subject comparisons of heat and mechanical-based TSP.

Results: In HCs, mechanical-based TSP was significantly less than heat-based TSP. However, in the NP group, there was no significant difference between mechanical versus heat TSP.

Conclusion: These data indicate that TSP may be modality-dependent in healthy individuals but is modality-independent in people with chronic pain. The findings provide support for using mechanical devices to evaluate TSP in chronic pain which also has the benefit of simplicity and low-cost.

[#62] Jonathan Monteiro; Immunology

Supervisor: Dr. Véronique Miron

Theme: Molecular & Cellular Neuroscience (Oral Presentation)

MICROGLIA PREVENT SPONTANEOUS RECURRENT CENTRAL NERVOUS SYSTEM DEMYELINATION

Monteiro J, 1,2; Rose J, 3; Hugues N, 4; McNamara NB, 5,6; Wever D, 5,6; Ouk K, 7; Craig GA, 1-3; Hoffman A, 1-3; Hill BM, 1,2; Holloway RK, 1,2; Bradshaw H, 8; Cui QL, 9; Munro DA, 3; Pridans C, 10; Antel JP, 9; Priller J, 3,7,11,12; Huitinga I, 5,6; Luo Y, 4; Miron VE, 1-3

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Introduction: Multiple sclerosis (MS) is characterized by recurrent bouts of central nervous system (CNS) demyelination. While remyelination occurs efficiently in youth, demyelination often recurs and becomes chronic by middle-age, associated with progressive disability. Although peripheral autoimmunity is widely considered to cause demyelination, recent work has suggested that microglia could play a complementary role. In MS, microglia lose their homeostatic profiles at sites where demyelination is initiated (normal appearing white matter) or becomes chronic (mixed lesion rim). However, the underlying mechanisms by which loss of microglia homeostasis may contribute to demyelination in MS is not understood.

Objectives: We asked whether loss of microglia homeostasis is sufficient to induce age-dependent demyelination. We hypothesize that microglia regulate oligodendrocyte health in homeostasis, and that loss of homeostatic microglia functions may trigger demyelination by compromising oligodendrocyte health.

Methods: We combined MS tissue analysis, single cell RNA sequencing, and experimental modeling of microglia dysregulation and loss of homeostasis in mice where microglia are absent (Csf1rFIREΔ/FIREΔ), or their homeostasis is disrupted (Cx3cr1CreERT2;Tgfb1fl/fl).

Results: We discovered that modeling loss of microglia homeostatic function is sufficient to trigger spontaneous and recurrent demyelination and oligodendrocyte loss in an age-dependent manner. Single cell RNA sequencing revealed that demyelination was associated with the emergence of an oligodendrocyte state vulnerable to death by ferroptosis, which we also detected at sites of increased demyelination in MS. We identified STAT3 activation as a driver of this oligodendrocyte state, with STAT3 inhibition preventing oligodendrocyte ferroptosis and demyelination.

Conclusion: We demonstrate that loss of homeostatic microglia function is sufficient to model the dynamics of myelin pathology observed in MS. These findings uncover a novel role for homeostatic microglia in maintaining oligodendrocyte health and preventing repeated and worsening demyelination with age, positioning loss of microglia homeostasis as upstream of increased oligodendrocyte heterogeneity and dysfunction during demyelination. We also identify a novel therapeutic target to reduce this dysfunction

and prevent progressive white matter pathology in MS.

[#63] Pedram Mouseli; Dentistry

Supervisor: Dr. Iacopo Cioffi; Dr. Massieh Moayedi

Theme: Motor & Sensory Control (Oral Presentation)

LENS: A GENERALIZABLE PERIPHERAL NEUROMUSCULAR SIGNATURE FOR MUSCULOSKELETAL PAIN

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Introduction: Musculoskeletal pain is the leading cause of years lived with disability worldwide. While patient self-report remains the gold standard for pain assessment, its reliance on episodic and subjective input limits the potential for continuous monitoring and scalable, objective clinical care.

Objective: We aimed to develop and validate LENS (Latent sEMG Neuromuscular Signature), a novel deep learning-based biomarker designed to predict subjective orofacial pain using only surface electromyography (sEMG). We hypothesized that a model trained to uncover hidden neurovascular features from sEMG could robustly predict acute pain and generalize to individuals with chronic pain conditions.

Methods: Following REB approval, we collected a 72.5-hour dataset from 183 adult participants (healthy controls and individuals with chronic myogenic temporomandibular disorders [TMD]). Participants performed a repeated tooth-clenching task to induce acute facial pain. We developed LENS using a cross-modal self-supervised learning strategy that reconstructs muscle oxygenation from sEMG alone, effectively extracting a hidden neurovascular representation without requiring optical sensors at inference. The pipeline integrated label-free test-time adaptation to tailor these latent representations to individual physiology.

Results: LENS robustly predicted experimentally-induced acute pain in healthy individuals ($\rho \approx 0.50$). Crucially, the model successfully generalized to the unseen chronic pain cohort (TMD). The use of label-free test-time adaptation allowed the model to tailor its latent representations to pathological physiology without requiring any prior exposure to pathological data during training. Mechanistically, LENS revealed that this signature of pain is preferentially encoded in high-frequency (150–400 Hz) motor patterns.

Conclusion: We present LENS, the first sEMG-derived deep learning biomarker capable of

predicting subjective orofacial pain across healthy and chronic pain states. By reconstructing neurovascular representations from sEMG alone, LENS offers a non-invasive, low-cost tool that overcomes the limitations of episodic self-reporting. This framework uncovers hidden physiological mechanisms of pain and provides a scalable tool for continuous remote patient monitoring and objective endpoints in clinical trials.

[#64] Zahra Nasser; Laboratory Medicine and Pathology

Supervisor: Dr. Gerold Schmitt-Ulms

Theme: Neuropharmacology and Drug Development (Poster Presentation)

INVESTIGATING THE MECHANISMS OF EFFECTIVE BRAIN-WIDE DELIVERY OF ADENO-ASSOCIATED VIRUSES FOR THE TREATMENT OF NEURODEGENERATIVE DISEASES

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Introduction: The biggest challenge in gene therapy remains the identification of vehicles that can deliver therapeutic constructs efficiently and safely to the human brain. Adeno-associated viruses (AAVs) have emerged as one of the most promising tools for the delivery of disease-relevant gene therapies into the CNS. Engineered capsids such as receptor-targeted BI-hTFR1 aim to enhance endothelial engagement and brain delivery. Despite immense interest in selecting the most brain-penetrant capsids, early host cell responses during endothelial entry remain poorly defined. Here, we undertook a deep dive into proteomic changes that manifest in a human endothelial (hCMEC/D3) cell paradigm upon viral exposure to a recombinant AAV known to cross these cells by TFR1-mediated transcytosis.

Objective: Elucidate the molecular mechanisms by which engineered AAV capsids, particularly BI-hTRF1, interact with and traverse the blood–brain barrier using proteomics, in vitro BBB models, and fluorescence-based trafficking analyses to identify factors that influence CNS transduction efficiency.

Methods: Human brain microvascular endothelial cells grown on Transwells were exposed to brain-penetrant BI-hTFR1 capsids with a payload encoding an EGFP reporter. Whole-cell lysates were collected at 30 minutes, 3 hours, and 48 hours post-exposure. Using an Astral Orbitrap instrument in data independent acquisition mode, the relative abundances of more than 8,000 proteins were captured. Proteins whose abundance levels differed from vehicle treated control cells consistently across biological replicates were analyzed using pathway enrichment tools.

Results: The cellular response to BI-hTFR1 transduction was more complex than previously anticipated. A surprising 239 proteins underwent rapid changes exceeding 40% in their levels as early as 30 minutes post-transduction, returning to baseline levels by 48 hours. This pattern suggests early, reversible proteomic remodeling upon AAV docking and entry. In contrast, 110 proteins remained unchanged at early timepoints but displayed steady-state changes exceeding 40% by 48 hours. Together, this data points toward a model that distinguishes early cellular responses to rAAV entry that do not require protein synthesis versus late morphogenetic adaptations based on protein translation.

Conclusion: Our data demonstrate that rAAV exposure induces rapid and transient proteome shifts within 30 minutes of exposure. These early proteomic shifts must rely on a reservoir of nascent proteins that cells can deploy rapidly, reflect early morphological changes, or contribute to cellular signaling upon receptor-mediated rAAV entry. Within two days of virus uptake, endothelial cells undergo a major reprogramming of their cellular proteome. Further delineation of changes essential for rAAV penetrance as opposed to secondary or bystander effects will be needed to derive strategies for manipulating brain uptake of rAAVs.

[#65] Melanie Niu; Physiology

Supervisor: Dr. Zhong-Ping Feng

Theme: Pain and Sensory Disorders II (Poster Presentation)

DETECTING IONIC MECHANISMS UNDERLYING AERIAL-BREATHING BEHAVIOURAL CHANGES IN THE HYPOXIA-TOLERANT LYMNAEA STAGNALIS

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Introduction: While mammalian neurons are highly vulnerable to prolonged hypoxia (low oxygen), the central nervous system of Lymnaea Stagnalis (L. stagnalis), a freshwater pond snail, demonstrates marked hypoxia tolerance. A bimodal breather, L. stagnalis obtains oxygen via cutaneous respiration and atmospheric air through pneumostome opening. Network-level control of aerial respiration is mediated by a well-characterized central pattern generator (CPG) comprising three ganglia, with the interneuron RPeD1 serving as a key respiratory rhythm initiator, and the IP3 interneuron generates the expiratory phase and VD4 mediates closure. However, the mechanisms triggering the transition from cutaneous to aerial breathing during hypoxia remain unexplored.

Objectives: Since ion channels are major regulators of neuronal excitability and have been extensively characterized in L. stagnalis, we hypothesize that hypoxia-dependent modulation of ion channel activity favours the switch to aerial breathing in this hypoxia-tolerant species.

Methods: L. stagnalis were exposed to normoxic and variable controlled hypoxia conditions. Pneumostome opening frequency and duration were quantified under various oxygen conditions using standardized video tracking. A biologically based computational model was built to model the rhythm generation based on ion channel kinetics.

Results: Hypoxia significantly increased aerial respiratory behavior in L. stagnalis. Compared with normoxia, hypoxia produced an increase in pneumostome opening frequency and duration. Animals demonstrated distinct behaviour pattern under normoxia and hypoxia. The computational model reproduces characteristic firing pattern of the central pattern generator.

Conclusions: Controlled hypoxia reliably modulates pneumostome opening frequency and duration in L. stagnalis. This framework provides a platform to test how specific conductance changes alter the rhythmic firing behavior of the L. stagnalis respiratory central pattern generator, how this regulation is modified under hypoxia, and how these mechanisms contribute to the species' hypoxia tolerance.

[#66] Lilliana Pavicic; Cell and Systems Biology

Supervisor: Dr. Jaideep Bains and Dr. Melanie Woodin

Theme: Molecular & Cellular Neuroscience (Oral Presentation)

CHARACTERIZING KCC2 PROTEIN INTERACTIONS IN HUNTINGTON'S DISEASE

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Introduction: KCC2 is the neuron specific member of the K+ Cl- cotransporter family that maintains a low intracellular Cl- concentration required for fast synaptic inhibition mediated by GABA in the central nervous system. Several neurological disorders including Huntington's disease (HD), exhibit impaired synaptic inhibition and Cl- dysregulation due to decreased KCC2 expression and function. KCC2 activity is regulated by post-translational modifications and protein-protein interactions (PPIs), making the KCC2 interactome a valuable target for understanding its functional regulation.

Objective: We hypothesize that HD is associated with alterations in the KCC2 interactome during early postnatal development, contributing to Cl- dysregulation and impaired inhibition prior to symptom onset.

Methods: Affinity purification-mass spectrometry (AP-MS) was performed on brain tissue from HD and wildtype (WT) mice. Comparative interactome analyses were used to identify disease-specific alterations in KCC2 PPIs. Ongoing studies are examining the biochemical and functional relationships of altered PPIs.

Results: The KCC2 interactome was successfully characterized in both HD and WT early postnatal mouse brain. Comparative analyses revealed disease-specific alterations in KCC2 protein networks in HD.

Conclusion: These findings provide the first characterization of the KCC2 interactome in a disease model and suggest that disrupted KCC2 PPIs during neurodevelopment may contribute to early Cl- dysregulation in HD. Ongoing work aims to define how these alterations impact KCC2 function and inhibitory signaling.

[#67] Angela Praecht; Institute of Medical Science

Supervisor: Dr. Matthew Sloan

Theme: Pain and Sensory Disorders I (Poster Presentation)

PAIN INTERFERENCE ACROSS SUBSTANCE USE DISORDERS

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Introduction: Pain is common among individuals with substance use disorders (SUDs) and predicts poorer treatment outcomes, yet it remains unclear which SUDs are associated with pain and how strong these associations are. Prior research has mainly focused on opioids or examined substances in isolation, limiting opportunities to estimate whether the prevalence of pain differs by SUD diagnosis.

Objective: We hypothesized that individuals with alcohol use disorder (AUD), cannabis use disorder (CUD), opioid use disorder (OUD), and stimulant use disorder (StUD) will show stronger associations with pain interference compared to control without substance use disorders (SUDs).

Methods: Using nationally representative data from the National Epidemiologic Survey on Alcohol and Related Conditions-III (n=36,309), we examined associations between past-month pain interference and past-year DSM-5 diagnoses of AUD (n=4321), CUD (n=343), OUD (n=152), and StUD (n=59). Hierarchical ordinal logistic regression models compared cases to controls accounting for progressively adjusted covariates, including sociodemographic variables, medical and psychiatric comorbidities.

Results: OUD was associated with markedly greater pain interference across all models (fully adjusted OR [aOR]=4.37, 95%CI: 2.93–6.53, p<0.001), with nearly one-quarter of participants with OUD reporting extreme interference. AUD showed weaker but significant associations after full adjustment (aOR=1.13, 95%CI: 1.03–1.23, p<.05). The association for CUD was dependent on covariate inclusion and was no longer significant after adjusting for medical and psychiatric comorbidities. StUD was not significantly associated with pain interference.

Conclusion: Our findings suggest that while OUD and AUD are associated with pain, CUD and StUD are not after accounting for covariates. This underscores the importance of considering concurrent disorders when evaluating pain-SUD relationships. Integrated treatment approaches addressing pain, substance use, and comorbid disorders concurrently may be particularly helpful to address pain in SUD patients.

[#68] Davina Premraj; Institute of Medical Science

Supervisor: Dr. Maria Carmela Tartaglia

Theme: Aging and Neurodegenerative Disorders (Clinical) (Oral Presentation)

PERSISTING SYMPTOMS OF CONCUSSION ARE MOSTLY SIMILAR IN OLDER VS. YOUNGER ADULTS -- A RETROSPECTIVE OBSERVATIONAL STUDY

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Introduction: Concussions are a concern in ageing populations, as head injuries may elevate the risk of developing dementia. While there have been recent advancements in investigating the persisting symptoms of concussion profiles in younger adults, these remain poorly defined in older adults.

Objective: To achieve a better understanding of how the persisting symptoms of concussion (according to the SCAT6) manifest in older adults and how it compares to the well-studied profile in younger adults.

Methods: Patients aged 18-49 (n=32, mean age = 33.75+/- 7.20 years old) and 50+ (n=55 (18 males, 37 females), mean age =61.84+/-8.14 years) who were seen at the Canadian Concussion Clinic in Toronto, ON with a concussion diagnosis one month to three years were included. All data were systematically collected via REDCap, and all patients provided informed consent.

Results: Overall, there were no statistically significant differences with reported: headache,, gait/balance problems, sensitivity to

light, sensitivity to noise, feeling like in a 'fog', difficulty concentrating, memory issues, vertigo, restlessness, and anxiety ($p>0.05$). Although trends suggested that younger adults report more neck pain, nausea or vomiting, blurred vision, fatigue/low energy, confusion, irritability, disinhibition, and sex effects of depression between younger and older patients, and that older adults experience increased dizziness and sleep disturbance, these were not significant ($p<0.30$).

Conclusion: Symptoms of persisting concussion in younger vs. older adults are similar. Replication of these findings in a larger cohort is necessary to confirm these findings.

[#69] Alexandra Puchiele; Institute of Medical Science

Supervisor: Dr. Benjamin Goldstein

Theme: Psychiatric Disorders II (Poster Presentation)

POLYGENIC RISK FOR INSOMNIA IN RELATION TO NEUROCOGNITION IN YOUTH WITH AND WITHOUT BIPOLAR DISORDER

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Introduction: Insomnia, the most common sleep disturbance, is prominent in bipolar disorder (BD) and contributes to reduced neurocognitive function. Focusing on the genetics of insomnia enables evaluation of putative mechanisms underlying its association with neurocognition.

Objective: We aimed to extend the literature by examining insomnia polygenic risk (insomnia-PRS) in relation to neurocognition in youth with and without BD. We hypothesized that higher insomnia-PRS would be associated with reduced neurocognition, particularly in youth with BD.

Methods: 132 youth aged 13-20 years (74 BD, 58 controls) completed the Cambridge Neuropsychological Test Automated Battery. Insomnia-PRS was computed based on adult genome-wide association study data. A global neurocognitive composite score was generated by averaging z-scores for six frontal-executive cognitive tasks. Linear regression tested the association of insomnia-PRS with global neurocognitive composite scores in the overall sample and in diagnostic subgroups, controlling for age, sex, IQ, current depression severity, and genetic principal components. Exploratory analyses evaluated individual cognitive domains and subtests.

Results: Insomnia-PRS was not associated with the neurocognitive composite in the overall sample or in diagnostic subgroups. Higher insomnia-PRS was associated with poorer quality of decision making in the Cambridge Gambling Task in the overall sample ($\beta=-0.21$, $p=0.02$) and in youth with BD ($\beta=-0.28$, $p=0.02$) but not controls ($\beta=-0.02$, $p=0.91$). These findings were not significant after correction.

Conclusions: Overall, insomnia-PRS was not strongly associated with neurocognition. Youth with BD may be differentially susceptible to greater insomnia-PRS, based on tentative evidence that insomnia-PRS is associated with subdomains of executive function. Further research with larger sample sizes is warranted.

[#70] Syeda Hania Qamar; Institute of Medical Science

Supervisor: Dr. Carmela Tartaglia

Theme: Aging and Neurodegenerative Disorders (Poster Presentation)

SEX DIFFERENCES IN CEREBROSPINAL FLUID INFLAMMATORY BIOMARKERS ACROSS NEURODEGENERATIVE DISEASES

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Background: Sex differences influence susceptibility, progression, and clinical presentation of neurodegenerative diseases, yet the contribution of sex-specific inflammatory biology remains incompletely understood. Cerebrospinal fluid (CSF) inflammatory biomarkers provide insight into shared and sex-dependent mechanisms of neurodegeneration. However, inflammatory markers have been studied mainly within single disease contexts, and no studies have systematically evaluated large panels of CSF inflammatory biomarkers transdiagnostically to identify shared sex-dependent mechanisms across neurodegenerative diseases.

Objective: To systematically evaluate a large panel of CSF inflammatory biomarkers transdiagnostically to identify shared sex-dependent mechanisms across neurodegenerative diseases.

Methods: CSF inflammatory biomarkers were quantified using OLINK proximity extension assay and analyzed as normalized protein expression (NPX) values. Participants included individuals with Alzheimer's disease (58 females (F), 32 males (M)), Frontotemporal Lobar Degeneration (FTLD)-Tau-related-syndromes (23F, 24M), FTLD-TDP43-related-syndromes (34F, 29M), yielding a total neurodegenerative disease cohort of 200 participants. Healthy controls (HC; 28F, 27M) were analyzed separately. Over 420 biomarkers were assessed. For each, NPX was modeled using linear regression with sex as the primary predictor, adjusting for age, assay plate, and diagnosis to account for heterogeneity. Multiple testing was corrected using the Benjamini–Hochberg procedure, and biomarkers showing sex effects in HC were excluded to isolate neurodegenerative disease-related differences.

Results: Across the neurodegenerative disease cohort, 35 inflammatory biomarkers showed significantly higher expression in males compared with females. In HC, 48 biomarkers were significantly upregulated exclusively in males, with no biomarkers significantly higher in females. After excluding biomarkers associated with sex in HC, 14 inflammatory biomarkers remained associated with sex in the neurodegenerative disease cohort. Levels of SIT1, GZMA, and PZP were higher in females, whereas ANGPTL2, AGRP, CFHR5, ANGPTL4, CCL23, CR1, EDAR, PON1, FSTL3, MEPE, and APOA1 were higher in males.

Conclusions: These findings identify sex-associated inflammatory signatures in CSF that are present across neurodegenerative diseases and are independent of diagnostic-specific effects. Differential inflammatory biomarker regulation by sex may contribute to variability in disease pathogenesis and clinical manifestation between males and females. Characterizing shared, sex-dependent inflammatory pathways may inform the development of targeted, disease-modifying therapies and support sex-informed precision medicine approaches in neurodegenerative diseases.

[#71] Areeba Qureshi; Medical Biophysics

Supervisor: Dr. Iacovos Michael

Theme: Cellular & Systems Neuroscience (Poster Presentation)

CHARACTERIZING THE ROLE OF HMGB3 IN MODULATING TUMOUR-IMMUNE INTERACTION IN BREAST CANCER BRAIN METASTASIS

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Introduction: Brain metastases, most commonly arising from lung, breast, and melanoma cancers, are associated with limited therapeutic options. A major challenge for treatment is understanding how cancer cells adapt to the brain microenvironment. High Mobility Group Box 3 (HMGB3), a non-histone chromatin-binding protein, is upregulated across multiple cancers. Analysis of RNA-sequencing data demonstrates that HMGB3 is significantly upregulated in brain metastasis compared to matched primary breast tumours,

and its expression correlates with poor patient survival. Notably, recurrent tumours emerging from dormancy in immunocompetent Tol mice exhibited elevated HMGB3 expression.

Objectives: I hypothesize that HMGB3 promotes brain metastasis by modulating tumour-immune interactions, enabling cancer cells to adapt to immune-selective pressures within the brain.

Methods: To investigate the role of HMGB3 in tumour progression and immune modulation, breast cancer cells with HMGB3 upregulated were implanted intracranially into both immunocompetent Tol and immunocompromised SCID mice. Tumour growth was monitored using bioluminescence imaging and survival analysis was conducted. Flow cytometric analysis of tumours was conducted in Tol mice.

Results: HMGB3 overexpressing breast cancer cells enhanced tumour growth in immunocompetent mice, demonstrated by a robust increase in bioluminescence signal and marked reduction in survival relative to controls. In contrast, this phenotype was completely abolished in immunocompromised mice. Furthermore, flow cytometric analysis in immunocompetant mice indicated an increase in the immune cell population at the tumour site as compared to the contralateral hemisphere. These findings indicate that HMGB3-driven tumour progression is dependent on an intact adaptive immune system. Ongoing studies will define how HMGB3 shapes immune cell composition and function within the brain-tumour microenvironment.

Conclusion: This work provides important insight into the interaction between epigenetic regulation of cancer cells and the tumour-immune microenvironment, and may inform the development of therapies that target immune evasion and metastatic progression.

[#72] Gaithtry Rameswaran; Medical Biophysics

Supervisor: Dr. Bradley MacIntosh

Theme: Neuropharmacology and Drug Development (Poster Presentation)

MULTIMODAL IMAGE ANALYSIS OF CEREBRAL ARTERIAL MORPHOLOGY USING DEEP LEARNING-BASED SEMANTIC SEGMENTATION

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Introduction: The circle of Willis (CoW) is the primary arterial anastomosis network supplying cerebral blood flow and a key site for intracranial aneurysm formation, particularly within the anterior circulation. However, CoW morphology varies substantially across individuals presenting a challenge for accurate automated segmentation. Two commonly used angiography approaches are Computed Tomography Angiography (CTA) with an endogenous Iodine-based contrast agent and Time of Flight MR Angiography (TOF-MRA) with or without a Gadolinium-based contrast agent.

Objective: The project aims to develop and evaluate a deep learning-based semantic segmentation of the CoW across both CTA and TOF-MRA, as a means of quantifying arterial morphology and relating it to established aneurysm hotspot regions in the anterior circulation.

Methods: Deep learning models offer the potential for highly time-efficient arterial

segmentation. This imaging information can help characterize morphological features, such as branching patterns, bifurcation angles, and vessel lengths. Understanding the brain's vasculature in better detail can lead to more precise treatment planning and provide additional diagnostic information during time-critical situations. Data from open-source repositories, Sunnybrook Health Science Centre, and partner hospitals will be used to train the model's ability to perform semantic segmentation. To further improve the detection of small vessels, 7 Tesla TOF-MRA data from healthy participants will also be incorporated. The segmentations derived from this method will be further validated by clinician experts based on clinical samples.

Conclusion: This work aims to bridge the gap between advanced imaging methods and their clinical application in neurovascular disease diagnosis and treatment.

[#73] Sadhna Ramquar; Rehabilitation Sciences

Supervisor: Dr. Robin Green

Theme: Cognitive Neuroscience (Oral Presentation)

COGNITIVE EFFECTS OF SLOW-PACED BREATHING IN HEALTHY ADULTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Slow-paced breathing (SPB), defined as breathing at fewer than 10 breaths per minute, has emerged as a promising non-invasive intervention for improving cognitive function. Previous studies have reported improvements in attention, memory, executive functioning, and processing speed following SPB interventions; however, findings have remained heterogeneous due to variability in intervention protocols, cognitive outcome measures, and study methodologies. A comprehensive synthesis was therefore needed to clarify the cognitive effects of SPB and investigate optimal intervention parameters.

Objective: This systematic review aimed to synthesize evidence examining the effects of SPB across cognitive domains in healthy adult populations and explore intervention parameters associated with cognitive benefits. It was hypothesized that SPB would demonstrate domain-specific effects on cognition, with stronger effects anticipated across executive functioning and attention-related outcomes, and that these effects would vary depending on intervention parameters such as breathing rate.

Methods: A search strategy developed with an information specialist was conducted across MEDLINE, Embase, Cochrane CENTRAL, PsycINFO, CINAHL, and Web of Science. Eligible studies included randomized, quasi-randomized, and non-randomized controlled interventions involving healthy adults. Primary outcomes included standardized cognitive measures grouped into executive-function accuracy, executive-function reaction time, attention, and processing speed domains. Two independent reviewers completed screening, data extraction, and risk-of-bias assessments using Covidence and the RoB 2 and ROBINS-I

tools. A narrative synthesis was conducted, with meta-analysis using RevMan performed where appropriate based on study homogeneity.

Results: 7,275 abstracts and 52 full-text articles were screened, with 5 studies meeting inclusion criteria. While a large number of studies examined breathing-based interventions, many were excluded due to insufficient cognitive outcome reporting, lack of baseline data, interventions or control groups that did not meet predefined slow-paced breathing criteria, use of non-standardized cognitive tests, or failure to report intervention breathing rate. Although some individual studies reported improvements in cognitive outcomes following SPB-related interventions, pooled effects were not statistically significant across executive-function accuracy, executive-function reaction time, attention, or processing speed. Non-significant pooled effects may reflect heterogeneity in intervention protocols and durations. Although several studies demonstrated significant pre- to post-intervention improvements, similar improvements were often observed in control groups, suggesting potential practice effects associated with repeated cognitive testing. Among the included studies, Sutarto et al. employed the most intensive intervention protocols in terms of overall duration and session frequency and demonstrated the most consistent cognitive improvements, with benefits observed in two of the three cognitive domains assessed (attention and executive-function reaction time, but not executive-function accuracy).

Conclusion: SPB is a low-cost, accessible, and scalable intervention with potential to improve cognitive function. While our meta-analysis did not identify significant overall cognitive improvements following SPB, this likely reflects substantial heterogeneity in intervention duration, session length, and breathing protocols across studies. Notably, the most intensive intervention protocol demonstrated significant improvements in two of the three cognitive domains assessed. The observed variability across studies highlights the importance of optimizing SPB intervention parameters. This review will inform a planned RCT further investigating the role of intervention duration and session length in driving cognitive improvements associated with SPB.

[#74] Nikol Rybolov; Institute of Medical Science

Supervisor: Dr. Isabelle Boileau

Theme: Neuropharmacology and Drug Development (Poster Presentation)

INVESTIGATING TAUOPATHY IN CANADIAN ARMED FORCES MEMBERS USING A NOVEL POSITRON EMISSION TOMOGRAPHY RADIOPHARMACEUTICAL

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Introduction: Canadian Special Operations Forces (SOF) personnel are frequently exposed to repetitive blast overpressure (ReBOp), yet the effects of this on long term brain health remains poorly understood and no in vivo diagnostic test exists. An estimated 20-30% of Canadian Armed Forces (CAF) personnel with blast-related mild traumatic brain injury (mTBI) experience persistent cognitive, physical, and psychological symptoms which often go unrecognized in operational settings. While limited in vivo studies, including our own preliminary findings (Lora et al., 2026), suggest tau pathology may occur following blast exposure, its presence in SOF members remains unclear. Our team at CAMH developed a next-generation pan-tau positron emission tomography (PET) radiopharmaceutical (Lindberg et al., 2024; Murrell et al., 2025), [^{18}F]OXD-2314, which shows disease-relevant uptake patterns in early studies of patients with progressive supranuclear palsy and preliminary studies in individuals with repeated subconcussive exposures.

Objective: The primary objective of this study is to evaluate [^{18}F]OXD-2314 for detecting tau pathology in CAF members with a history of ReBOp exposure.

Methods: We are recruiting 20 SOF members with extensive ReBOp exposure and 10 unexposed CAF controls. Participants undergo comprehensive characterization of blast exposure history, alongside cognitive, physical, and psychological symptoms. Participants receive an intravenous injection of 185 MBq (±10%) of [^{18}F]OXD-2314 followed by a 120-minute dynamic PET scan, with MRI acquired for delineation of regions of interest. PET data are processed using PMOD (v4.28), and binding (BPND) will be estimated using SRTM2 with the cerebellum as reference. Group differences across regions of interest are assessed using ANOVA.

Results: To date, 5 male participants have been enrolled, including 3 SOF members with ReBOp exposure and 2 CAF controls. The blast-exposed participants have a mean age of 52.7 ± 4.5 years and 20.3 ± 3.5 years of exposure to blast. Controls have a mean age of 38.5 years. PET and MRI data acquisition has been completed in these participants. Image processing and kinetic analyses are currently underway to quantify [^{18}F]OXD-2314 binding and evaluate group differences in regional uptake.

Conclusion: This study will evaluate [^{18}F]OXD-2314 as a novel imaging biomarker of tau pathology in individuals with occupational blast exposure. By characterizing in vivo binding, regional distribution, and clinical correlates, this work has the potential to advance the detection of blast-related brain injury in both military and civilian populations. This study is ongoing and analyses are pending.

[#75] Vaidhehi Sanmugananthan; Institute of Medical Science

Supervisor: Dr. Karen Davis

Theme: Pain and Sensory Disorders I (Poster Presentation)

PAIN ATTENUATION DURING TASK; A NEW SCORING METRIC TO CAPTURE INDIVIDUAL DIFFERENCES IN CHRONIC PAIN CHANGES BY TASK ENGAGEMENT

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Introduction: Distraction based coping strategies are a benefit to some people living with chronic pain. However, there is no established method to capture the individual effect of distraction from pain through task engagement that considers fluctuations in pain, does not focus on group-level changes in pain, and considers the clinical relevance of these changes.

Objective: Here we present a new scoring system that aims to capture individual differences in the effect of distraction through task engagement in the context of chronic pain, that takes into consideration these different aspects. We hypothesized that those with better performance on the attention-demanding tasks (i.e., more engagement in the task) would exhibit greater pain attenuation than those with lower performance, and that this relationship would be prominent in the more difficult task.

Methods: Participants with chronic pain (n=27) underwent a simple and difficult version of a cognitive numeric task consisting of 3 blocks of trials. Task engagement was measured using reaction time (RT) mean, RT standard deviation (SD) and percent accuracy. Chronic pain intensity and unpleasantness ratings were acquired from each participant before and between task blocks. A chronic pain attenuation during task (PAT) score was calculated for each participant based on the largest percent change of pain from baseline (pre-task) to during the task blocks.

Results: There was a significant negative correlation between PAT intensity scores and mean RT in the simple task indicating that those with greater pain attenuation had faster task performance. Those with positive PAT scores had a significantly lower group-level median of painDETECT scores than those with negative PAT scores.

Conclusion: Our new PAT scoring system can be used to capture the impact of engagement in a task to attenuate an individual's chronic pain. The findings also suggest that there may be pain-related characteristics in PAT sub-groups that require further exploration. Therefore, the PAT scoring system may have clinical utility to help guide decision making of the potential benefit from attention-based pain management approaches (e.g. cognitive behavioural therapy) to manage chronic pain.

[#76] Andrew Sedrak; Department of Pharmacology and Toxicology

Supervisor: Dr. Albert Wong

Theme: Psychiatric Disorders II (Poster Presentation)

FROM TEMPORAL PRECISION TO DELUSION FORMATION: GAMMA SYNCHRONY AND PERCEPTUAL DEFICITS IN SCHIZOPHRENIA

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Introduction: Altered gamma-band synchrony is a core neurophysiological abnormality in schizophrenia and may contribute to disruptions in the perception of brief time intervals. Disrupted sub-second timing may, in turn, relate to the mechanisms underlying delusion formation.
Objective: This study investigates whether two novel behavioural paradigms, the Time Perception Accuracy Task (TPAT), and an auditory interval-discrimination task, Drew's Hoots, can quantify perceptual timing deficits in schizophrenia. Given evidence that gamma synchrony supports timing precision, we hypothesized that performance on both tasks would be associated with individual variability in gamma-band phase-locking.
Methods: Individuals with schizophrenia spectrum disorders (SSD; n=28) and healthy controls (HC; n=32) were recruited. TPAT presents physically valid sphere collisions or collisions with artificial temporal delays; participants detect invalid collisions. Drew's Hoots tests sub-second interval judgments while minimizing reliance on working memory or counting. Separately, EEG was recorded during the presentation of 40-Hz click trains to examine whether behavioural timing measures were associated with gamma (40 Hz) auditory steady-state phase-locking factor (PLF) and evoked power at Fz.
Results: On TPAT, accuracy increased monotonically with delay length in both groups, with no significant between-group differences overall (all $p > .08$). SSD and controls had differences approaching significance with medium ($t = 1.78$, $p = .082$, $d = 0.49$; SSD > HC) and long delay ($t = -1.68$, $p = .099$, $d = -0.46$; HC > SSD). On Drew's Hoots, SSD showed a trend toward lower overall accuracy ($t = 1.89$, $p = .074$, $d = 0.74$) and elevated false-alarm rates at short durations (125 and 250 ms; both $p < .10$), consistent with lower temporal resolution. EEG analyses revealed that SSD exhibited significantly lower 40 Hz PLF at Fz than HC ($t(9.7) = 3.62$, $p = .005$, $d = 1.57$), while evoked power did not differ between groups ($p = .147$).. PLF predicted Drew's Hoots accuracy in HC ($r = 0.65$, $p = .083$) but not SSD ($r = -0.05$, $p = .826$), suggesting disrupted neural-behavioural coupling in the clinical group. There was a significant interaction between TPAT delay and PLF on accuracy in the TPAT (trend $r = 0.70$, $p = .003$),. Performance on TPAT and Drew's Hoots was not significantly correlated within either group (all $p > .12$), suggesting the tasks capture distinct aspects of temporal processing.
Conclusion: Together, TPAT and Drew's Hoots reveal different types of timing deficits in schizophrenia spectrum disorders and some relationship to EEG 40 Hz phase locking. time perception Ongoing work to increase sample size will help to determine whether gamma synchrony mediates the relationship between timing precision and psychotic symptoms.

[#77] Rubab Shafiq; Institute of Medical Science
Supervisor: Dr. Yuliya Nikolova

Theme: Systems and Circuits Neuroscience (Oral Presentation)

NEUROSTRUCTURAL SIGNATURES OF STRESS IN A NOVEL KNOCKOUT MOUSE MODEL OF THE DEPRESSION-RELATED FREM3 GENE

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Introduction: Depression is the leading cause of disability worldwide. It is a multifactorial disorder influenced by many factors including, environment and genetic influences. Chronic stress is a major environmntal risk factor for depression and can induce structural changes in the brain. Fras1-related extracellular matrix 3 (FREM3) is a promising candidate gene linked to depression, predominantly expressed in excitatory neurons, and believed to support long-range brain connectivity in humans. However the role of Frem3 and its contribution to stress-related brain vulnerability remains poorly understood.

Objective: The objective of this work is to evaluate the neurostructural effects of a novel Frem3 conditional knockout (Frem3-cKO) mouse model in the context of chronic stress; a major risk factor for depression.

Methods: Mice (n = 8/condition, 4-6 months old, 50% female) underwent a chronic restraint stress paradigm and were assessed for coat state deterioration. Following the paradigm, mice underwent ex vivo MRI. Brain images were mapped to an atlas to derive regional volumes. Linear models were applied to test the main effects of genotype, stress and stress-by-genotype interaction effects on regional brain volume, controlling for sex and total brain volume; FDR correction was applied. Exploratory genotype-stratified analyses were conducted to assess nominally significant interaction effects.

Results: Nominal stress-by-genotype interaction effects were identified in six regions in the limbic, cerebellum and brainstem. Exploratory follow-up analyses showed that stress was associated with smaller hypothalamic and amygdala-related regions in wildtype mice, while Frem3-cKO mice had reduced hypothalamic volume at baseline. Frem3-cKO mice also showed reduced baseline volume in the superior olivary complex, suggesting genotype-dependent differences in both baseline structure and stress responses.

Conclusion: Our exploratory analyses suggest that the loss of Frem3 in excitatory neurons alters baseline and region-specific responses to stress across limbic, cerebellar and brainstem systems. The results highlight Frem3 as a potential modulator of stress-related brain plasticity, providing a foundation for future studies.

[#78] Stephanie Shishis; Department of Cell and Systems Biology

Supervisor: Dr. Junchul Kim

Theme: Cognitive Neuroscience (Poster Presentation)

THE INVESTIGATION OF CORTICAL LAMP5 INTERNEURONS USING AN INTERSECTIONAL CRE-BASED APPROACH

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Introduction: Cortical interneurons synchronize the activity of the central nervous system by inhibiting neuronal circuits and reducing neuronal excitability. However, imbalances in excitatory-inhibitory circuits and dysfunction of the GABAergic system can critically affect learning and memory processes, contributing to disorders such as Alzheimer's Disease. My proposed project focuses on the LAMP5 interneuron, a relatively understudied GABAergic cardinal interneuron subtype found predominantly in the cortex and hippocampus. Within this population, the majority of LAMP5 cortical interneurons consist of putative neurogliaform cells (NGFCs). Growing evidence implicates NGFCs as key effectors of inhibitory circuits, contributing to network function through volume transmission, a unique synaptic modality that provides widespread, non-specific inhibitory effects on nearby neurons. The role of cortical GABA volume transmission in cognitive function remains poorly understood, as does the behavioural contribution of LAMP5 interneurons despite their distinct cellular identity.

Objective: To address this, I will investigate the role of prefrontal cortical LAMP5 interneurons specifically in working memory. Based on the well-established role of the prefrontal cortex (PFC) in working memory, coupled with the specialized volume transmission employed by NGFCs, I hypothesize that LAMP5 interneurons in the PFC play a significant role in working memory.

Methods: By utilizing a LAMP5-Cre mouse driver line combined with a Cre-responsive AAV-Dlx virus to selectively target LAMP5 interneurons, I will conduct various behavioural, chemogenetic, optogenetic and fiber photometry experiments integrated within a spatial working memory paradigm. This intersectional Cre-based approach will enable visualization and functional manipulations of LAMP5 interneurons.

Results: To date, I have established baseline behaviour in the spatial working memory paradigm, demonstrating robust delay-dependent decay of working memory. However, preliminary chemogenetic data reveals no disruptive effects on working memory, and additional data is required before conclusions can be made.

Conclusion: Ultimately, this intersectional Cre-based targeting approach will allow assessment of the functionality and contributions of LAMP5 interneurons, providing critical insight into specific neural mechanisms with significant clinical relevance, furthering our understanding of distinct cognitive and behavioural processes.

[#79] Sarah Smith; Institute of Medical Science

Supervisor: Dr. Sidney Kennedy, Dr. Katharine Dunlop

Theme: Behavioural and Social Neuroscience (Oral Presentation)

EARLY IRRITABILITY IMPROVEMENT IN MALES PREDICTS DLPFC-RTMS ANTIDEPRESSANT RESPONSE

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Introduction: While repetitive transcranial magnetic stimulation (rTMS) is an effective treatment for treatment-resistant depression (TRD), heterogeneous clinical responses highlight the need to identify reliable predictors of treatment outcome. Early improvement in irritability may predict long-term antidepressant

outcomes. However, robust sex differences in the clinical presentation and biological correlates of irritability impede our understanding of its relation to rTMS response.
Objective: This study aimed to determine whether early irritability change predicts treatment outcomes in males and females and to identify baseline resting-state functional connectivity correlates of irritability in both sexes.
Methods: 157 adults with TRD (ages 19-60, 92 female) from the CARTBIND trial received 30 days of rTMS targeting the bilateral subgenual anterior cingulate cortex (sgACC). Irritability was measured using the restlessness and irritability items of the General Anxiety Disorder-7, with early improvement evaluated at treatment day 10. Sex-stratified linear regressions assessed the relationship between early irritability improvement and post-rTMS depression severity. Covariates included age, baseline anxiety, irritability, depression severity, and early change in depression severity. We used whole-brain seed-to-voxel resting state functional connectivity (RSFC) from the left sgACC to identify baseline neural correlates of early irritability improvement.
Results: Early irritability improvement was significantly correlated to post-rTMS depression severity in males (β=1.964, p=.011), but not in females (β=-0.020, p=.980). In males, higher baseline irritability is correlated with greater RSFC between the sgACC and the dorsomedial prefrontal cortex (DMPFC).
Conclusion: Early change in irritability predicts rTMS outcomes in males, and baseline sgACC-DMPFC RSFC correlates with increased baseline irritability in both males and females. Evaluating sex differences can reveal biological and clinical factors, potentially supporting personalized and effective treatment.

[#80] Yutong Sun; Department of Medical Biophysics
Supervisor: Dr. J. Jean Chen
Theme: Motor and Sensory Control (Oral Presentation)

HEMODYNAMIC RESPONSES IN WHITE MATTER: REDUCED BLOOD FLOW IN DEEP WM DURING HYPERCAPNIA REVEALED BY MULTI-DELAY PCASL

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Introduction: Hypercapnia refers to an increased arterial concentration of carbon dioxide (CO2) as a potent vasodilator which modulates the extracellular pH to cause relaxation of vascular smooth muscle and reduced vascular resistance1. Because its effects are largely non-neuronal, hypercapnia is widely used in studying cerebrovascular reactivity. Although hypercapnia is often assumed to produce a relatively uniform 30-50% increase in cerebral blood flow (CBF) across the brain2, multiple studies suggest a more complex MR signal response. For example, some studies report a more subdued and sluggish response of the blood-oxygenation level-dependent (BOLD) fMRI signal in the white matter (WM)3, while others have reported a potential vasoconstriction in diseased white matter4. Given that little is known about the neurovascular mechanisms in the white matter, it is unclear if the WM's response to

hypercapnia conforms to expectations based on the grey matter.

Objective: In this study, we assessed the hypercapnia-evoked hemodynamic responses in the WM using multi-delay pseudo-continuous arterial spin labelling (pCASL).

Methods: 25 healthy young adults (age=25.04±3.89 years, 12M/13F=8/10) underwent controlled hypercapnia by inhaling 4% CO2 through a custom-built gas delivery system to ensure stable gas delivery (Figure 1a). The end-tidal CO2, breathing rate and heart pulse were monitored in real time to confirm reliable induction of hypercapnic states. Considering that hypercapnia may alter arterial transit times (ATT), which is particularly long in the WM5, with post labelling delays of 0.4, 0.9, 1.4, 1.9, 2.4 s to enable ATT-corrected CBF quantification, pCASL data was collected under both baseline and hypercapnic conditions using labeling duration=1.5s, TR/TE=3.95s/0.019s, 2.5x2.5mm resolution, and 2.81mm slice thickness, with field maps acquired on AP+PA directions. The resulting data was corrected for susceptibility-induced distortion then converted into quantitative CBF in units of (mL/100g/min) via the general kinetic model (Figure 1b). Percent CBF changes due to hypercapnia was calculated and tested using voxelwise t-test followed by significance thresholding using threshold-free cluster enhancement.

Results: Representative slices from a single subject (figure 2a) demonstrate an overall CBF increase in cortical grey matter (GM) and a heterogeneous CBF response to hypercapnia in WM. This spatial pattern on effect polarity was consistent across subjects. Group-level region-of-interest (ROI) analysis showed significant CBF increases of 29.15%±12.15% in cortical GM ($p=0.0026$) and 10.12%±14.90% in WM ($p<0.0001$, Figure 2b), with the net CO2 effect being negative for 4 subjects. Voxelwise analysis detected significant CO2-induced CBF changes predominantly in cortical GM, with a gradual attenuation of effect magnitude toward deeper tissue layers (figure 2c). After segmenting brain volume into cortical GM, superficial WM, deep WM, subcortical GM, and periventricular regions (figure 2d), pairwise comparisons were significant (all $p<0.0001$) except for cortical GM versus subcortical GM (figure 2e).

Conclusion: Although the WM vascular response to hypercapnia has been assumed to follow that of the GM, our findings reveal that deep WM can exhibit negative CBF changes during hypercapnia, inversely related to the GM CBF response, challenging the conventional assumption of uniformly increased perfusion due to vasodilation. There could be several possible mechanisms contributing to this observation. One of them is the “Robin Hood” redistribution hypothesis, which suggests that vascular branches with greater CO2 reactivity lower their resistance more substantially during hypercapnia, diverting blood flow away from branches of higher-resistance. Another theory is vessel-size-dependent dilation, implying that larger arteries undergo greater absolute diameter increases than small penetrating vessels, leading to the depth-dependent perfusion redistribution (presuming that deep white matter contains smaller arteries). Importantly, although the negative CBF responses observed in deep WM did not reach voxelwise significance at the group level, this does not diminish their physiological relevance. The lack of significance could be due to the high spatial variability in the precise locations of negative voxels across subjects, exacerbated by potentially imperfect inter-subject co-registration. The key takeaway is that negative CBF responses commonly exist across subjects

in their WM, which indicates that this phenomenon is robust. Indeed, prior literature also illustrated spatial correspondence between regions showing negative CO2-induced BOLD-CVR and regions affected by leukoaraiosis (4), suggesting negative CVR could arise from weakened vascular tone. To summarize, our results uncovered a hypercapnia-induced CBF reduction in the deep WM that has never before been shown in healthy adults, and highlight the importance to not assume the similar hemodynamic responses in the GM and WM.

[#81] Omer Syed; Institute of Medical Science
Supervisor: Dr. Peter Giacobbe
Theme: Neuropharmacology and Drug Development (Oral Presentation)

HARMED BY EXPECTATION: THE NOCEBO EFFECT ACROSS KETAMINE DEPRESSION TRIALS

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Introduction: Growing interest surrounds ketamine and esketamine as pharmacological interventions for difficult-to-treat depression. While preclinical and human neuroimaging studies have strongly linked es/ketamine's therapeutic effects to their pharmacological properties, the influence of the placebo effect driving therapeutic effects is a popular topic of discussion. However, the inverse of the placebo effect, the nocebo effect, receives little attention yet potentially carries substantial clinical relevance. It is theorized that expecting negative effects, such as those surrounding es/ketamine's side effects, may exacerbate the severity of these adverse experiences during treatments, and may even manifest among blinded study participants receiving an inactive placebo treatment.

Objective: First, quantify the nocebo effect within placebo-controlled trials of ketamine and esketamine treatments for depression. Second, assess the proportion of adverse events (AEs) reported by participants receiving es/ketamine which can be attributed to nocebo instead of pharmacological effects.

Methods: The electronic databases of PubMed, Embase, and PsychINFO were searched on April 6, 2026, without applying any search filters or restrictions. Randomized controlled trials administering ketamine or esketamine for depression with saline comparator were included in this review. Data from the adverse events forms for each study were extracted to calculate proportions of participants reporting ≥1 AE, as well as reports for individual specific AEs. The nocebo effect was defined as the proportion of participants reporting treatment-emergent AEs who received an inactive placebo. The nocebo-attributable fraction was defined as the proportion of AEs reported by the es/ketamine receiving participants which can be attributed to nocebo instead of a pharmacological effect.

Results: The meta-analysis included 18 clinical trials with 2682 participants. Most studies (k=15) employed a parallel trial design and administered an adjunctive antidepressant treatment alongside es/ketamine (k=10). The observed nocebo rate across studies were consistent around 50%, and the proportion of AEs in the es/ketamine group attributable to the nocebo effect was approximately 67.6%. The es/ketamine groups consistently reported higher likelihoods of experiencing AEs

compared to the inactive placebo groups, with a consistently higher estimated risk ratio of approximately 1.5.

Conclusion: An estimated two-thirds of adverse events reported within ketamine and esketamine depression trials can be attributed to the nocebo effect instead of the treatment's pharmacological effect. Clinicians and study investigators should reflect carefully in their communication of adverse effects of treatments as they may influence patient expectancy and potentially lead to a greater nocebo effect.

[#82] Nadeen Tantash; Institute of Medical Science

Supervisor: Dr. Karen Davis

Theme: Pain and Sensory Disorders I (Poster Presentation)

BRAIN-BEHAVIOR RELATIONSHIP BETWEEN RESILIENCE AND ALPHA OSCILLATIONS IN THE ANTINOCICEPTIVE PATHWAY AND SALIENCE NETWORK IN CHRONIC PAIN

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Introduction: Resilience is a protective factor that can mitigate pain and its effect on activities of daily living (ADL). The neural mechanisms underlying resilience in chronic pain are not understood. Our lab has linked resilience to increased gray matter in the dynamic pain connectome (DPC) and reported peak alpha (8–13 Hz) frequency (PAF) slowing and altered alpha power, sometimes with sex-specificity, in people with chronic pain. Neural oscillations provide a framework to examine functional underpinnings of DPC abnormalities associated with chronic pain and resilience. Alpha oscillations may be involved in attention regulation, sensory inhibition, and pain.

Objectives: The study aims were to determine the impact of 1) resilience on alpha oscillations in the DPC, chronic pain and ADL; and 2) sex. We hypothesized that 1) lower resilience will correlate with greater impact on ADL and abnormal alpha; and 2) the AS group will show alpha/PAF abnormalities, with possible sex differences.

Methods: Participants with chronic pain associated with ankylosing spondylitis (AS) (25M/15F) and age-/sex-matched healthy controls underwent resting-state magnetoencephalography to quantify PAF and alpha power in the antinociceptive pathway (subgenual anterior cingulate cortex), and salience network (right dorsolateral prefrontal cortex, anterior insula (rAINS), temporoparietal junction (rTPJ)). We also assessed pain over the last month, ADL (Bath Ankylosing Spondylitis Functional Index), and resilience (RS-25).

Results: In the chronic pain group, resilience was negatively correlated with rAINS peak and total alpha power. Sex differences in AS were: 1) rTPJ peak alpha power in males correlated with pain, 2) lower resilience correlated with greater impact on ADLs in males.

Conclusion: Thus, alpha oscillations within the salience network may underlie sex-specific impact of resilience on pain and function in AS.

[#83] Huseyin Taskin; Institute of Medical Science

Supervisor: Dr. Robert Chen

Theme: Motor and Sensory Control (Oral Presentation)

CEREBELLAR NEUROMODULATION WITH TRANSCRANIAL ULTRASOUND

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Introduction: The cerebellum has traditionally been studied in the context of motor control and learning. However, converging evidence suggests that its role extends beyond motor functions. Imaging methods such as functional MRI (fMRI) have been used to non-invasively investigate functional localization within the cerebellum; however, fMRI findings remain largely correlational. Non-invasive neuromodulation offers a complementary approach by enabling causal investigation of cerebellar function. A major limitation of conventional neuromodulation techniques, such as transcranial magnetic and electrical stimulation (TES/TMS), is their limited spatial specificity due to widespread current distribution within the cerebellum. Transcranial ultrasound stimulation (TUS) is a novel and rapidly developing neuromodulation technique that provides relatively high spatial precision and deeper penetration compared with conventional non-invasive methods.

Objective: The aim of this study was to examine whether ultrasound sonication of motor regions of the cerebellum can modulate motor cortex excitability through cerebello-cortical connections, similarly to traditional neuromodulation methods.

Methods: TUS (PRF = 1000 Hz, duty cycle = 10%) was applied to cerebellar lobules V–VIII and the dentate nucleus for 0.5 s. A TMS pulse was delivered to M1 0.5 s after ultrasound stimulation to assess motor cortex excitability. Multiple sham conditions were included to control for auditory confounds associated with ultrasound transducer noise.

Results: On average, motor cortex excitability was inhibited following ultrasound sonication of lobules V and VIII. In contrast, dentate nucleus sonication produced variable effects, with excitation observed in some cases and inhibition in others, possibly due to inadvertent activation of cerebellar white matter. Sham conditions produced effects similar to baseline.

Conclusion: These findings demonstrate that ultrasound sonication of the cerebellum can modulate motor cortex excitability. Given the increased focality afforded by TUS, this technique may provide a valuable tool for functional investigation of the cerebellum.

[#84] Ricardo Tello Marroquin; Department of Cell and Systems Biology

Supervisor: Dr. Robert Rozeske

Theme: Cellular and Systems Neuroscience (Poster Presentation)

THE EFFECTS OF RHYTHMIC SENSORY STIMULATION ON FEAR EXTINCTION

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Introduction: Exposure therapy is a common treatment for trauma-related disorders that is based on principles of extinction learning theory. Yet extinction to trauma-associated cues that arise in different contexts remains a challenge for clinicians. Ideally, fear extinction should reduce defensive responses to trauma-associated cues while preserving discrimination between threat and safety signals. This balance is thought to involve coordinated medial prefrontal cortex–amygdala activity, which is exemplified by specific frequencies of neural oscillations during fear expression and fear extinction.

Objective: Here we test if rhythmic sensory stimulation (RSS), a non-invasive patterned light stimulation, alters fear extinction behaviour. We hypothesize that RSS will bias endogenous prefrontal–amygdala oscillatory activity, which will reduce fear expression during extinction.

Methods: C57BL/6J mice underwent discriminative auditory fear conditioning. Mouse fear was probed in several tests and RSS was administered afterwards. The cumulative and long-term effects of RSS on fear expression were examined during longer fear tests. DeepLabCut was used to track behaviour and quantify freezing, a behavioural correlate of fear. Freezing was compared across control and multiple RSS groups.

Results: Mice acquired fear conditioning and discriminated dangerous CS+ (conditioned stimulus +) auditory cue from neutral CS- auditory cue during probe tests. During the first long fear test we observed that faster RSS protocols reduced freezing to CS-, but slower RSS protocols reduced freezing to CS+. These effects were not observed 1 week later during a fear test.

Conclusion: These findings suggest that RSS can reduce fear behaviour during extinction yet preserves neutral and dangerous cue discrimination. This work provides a framework for testing the behavioural specificity and circuit mechanisms by which non-invasive sensory stimulation may influence fear regulation.

[#85] Evelyn Tjiandri; Department of Music

Supervisor: Dr. Michael Thaut

Theme: Aging and Neurodegenerative Disorders (Clinical) (Oral Presentation)

AGE-RELATED SHIFTS IN PITCH-CATEGORY MAPPING IN ABSOLUTE PITCH: BEHAVIOURAL EVIDENCE FROM CIRCULAR ERROR ANALYSIS

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Introduction: Absolute pitch (AP) provides a highly quantifiable behavioural phenotype for examining age-related changes in the representation and access of pitch categories. AP is the ability to identify or produce a musical pitch without an external reference. By combining conventional pitch-labelling accuracy with circular chroma-error patterns, we examined whether reduced performance with aging reflects random perceptual failure or structured shifts in pitch-category organization.

Objective: This study examined whether age-related changes in self-reported AP reflect simple accuracy decline or structured changes in pitch-label mapping. We hypothesized that older AP participants would show lower conventional accuracy and more systematic chroma-error patterns. We also explored

whether pitch-labelling time-outs were associated with broader response-speed differences, measured by Go/No-Go reaction time.

Methods: Self-reported AP participants (n = 61) completed an online pitch-labelling task and Go/No-Go task. Conventional AP performance was quantified using pitch-class labelling accuracy and time-out count. For circular error analysis, signed chroma errors were computed and used to identify each participant's dominant pitch-class shift and dominant-shift proportion. Age-group differences were tested using the Kruskal–Wallis and chi-square tests, and Spearman correlations were used to examine age-related trends. Pearson correlation tested the association between pitch-labelling time-outs and Go/No-Go mean correct reaction time.

Results: Older self-reported AP participants showed lower conventional accuracy and more time-outs than younger participants. Adults aged 50+ showed the highest proportion of systematic pitch-class shifts [10/16; 62.5%], followed by ages 35–49 [3/14; 21.4%] and 18–34 [4/31; 12.9%]. Shift classification differed by age group [χ^2 p = .0013] and increased with age [Spearman's ρ = .386, p = .0021]. Kruskal–Wallis analysis also supported age-group differences [p = .0036]. Time-outs correlated modestly with slower Go/No-Go reaction time [r = .28, p = .028].

Conclusion: Conventional accuracy measures indicated age-related AP decline, but circular error analyses showed that lower accuracy often reflected consistent pitch-label displacement rather than random errors alone. The association between pitch-task time-outs and Go/No-Go reaction time suggests that nonresponses may also reflect reduced response efficiency beyond pitch-specific uncertainty. Together, these findings suggest that aging in AP may involve both systematic shifts in pitch-label mapping and changes in task-related response speed.

[#86] Harani Uthayakumar; Institute of Medical Science

Supervisor: Dr. Corinne Fischer and Dr. Tom Schweizer

Theme: Aging and Neurodegenerative Disorders (Poster Presentation)

SEX-SPECIFIC GENETIC AND HORMONAL DETERMINANTS OF PSYCHOSIS SYMPTOMS IN ALZHEIMER'S DISEASE

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Medicine and Pathobiology, Temerty Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada; 11 Division of Pathology, Unity Health Toronto, Toronto, Ontario, Canada; 12 Temerty Faculty of Medicine, Division of Neurosurgery, University of Toronto, Toronto, Ontario, Canada; 13 Department of Psychiatry, Temerty Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada.

Introduction: Psychosis, characterized by the presence of hallucinations and/or delusions, affects up to 50% of individuals with Alzheimer's Disease (AD) and is associated with accelerated cognitive decline and substantial caregiver burden. While the APOE4 allele is a well-established genetic risk factor for AD, its association with psychosis in AD has produced inconsistent findings across studies. One possible explanation for this variability may reflect sex-specific biological mechanisms, as psychosis symptoms are more prevalent in females with AD. Estrogen has been proposed as one plausible contributor, given its role in modulating dopaminergic signaling within prefrontal and striatal brain regions implicated in psychosis. However, the extent to which estrogen influences psychosis risk in AD, particularly in relation to APOE4 status, remains poorly understood.

Objective: We examined the influence of APOE4 homozygosity, sex, and estrogen hormone therapy (EHT) on psychosis symptoms in AD. Consistent with evidence suggesting that female APOE4 homozygotes have an increased likelihood of Lewy body-related processes, we hypothesize that APOE4 homozygosity increases hallucinations in females, while EHT reduces psychosis prevalence.

Methods: Data from 29,195 individuals diagnosed with AD were obtained from the NACC Uniform Dataset. Psychosis was defined by the presence of hallucinations and delusions, as assessed using the NPI-Q, as well as clinically meaningful behavioural changes related to visual hallucinations, auditory hallucinations, and abnormal and false beliefs drawn from the Clinician Judgment of Symptoms forms. Stepwise generalized additive models were used to examine the effects of APOE4 status and EHT (in females), adjusting for age, education, and MMSE scores. Analyses were stratified by sex to explore potential differences in psychosis outcomes.

Results: APOE4 homozygosity was associated with significantly greater odds of delusions in both males (OR = 1.23 $p < .05$) and females (OR = 1.26 $p < .01$). In females only, APOE4 homozygosity was significantly associated with hallucinations (OR = 1.29, $p < .05$). EHT was associated with lower risk of hallucinations in females (OR = .40, $p < .05$).

Conclusion: Findings demonstrate sex and symptom-specific associations of APOE4-homozygosity with psychosis phenotypes in AD. Given that Lewy body pathology is strongly associated with hallucinations, the observed females-specific susceptibility to these symptoms provides further support for the possibility that the APOE4 homozygous effect may be mediated, at least in part, through Lewy body co-pathology. EHT's association with reduced hallucination risk may indicate a symptom-specific effect of estrogen in AD-related psychosis. Results emphasize the need for sex-and hormone-informed approaches over one-size-fits-all models in addressing psychosis symptoms in AD.

[#87] Rivka van Klei; Institute of Medical Science

Supervisor: Dr. Dan Felsky

Theme: Developmental Neuroscience (Oral Presentation)

GENETIC ESTIMATES OF BRAIN RESERVE TRAJECTORIES IN MID-LIFE PREDICT COGNITIVE RESILIENCE IN LATE-LIFE

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Introduction: Brain reserve, a neuroanatomic resource, supports cognitive resilience against late-life cognitive decline despite accumulation of Alzheimer's disease-related neuropathology. However, brain reserve development throughout the lifespan and its effect on late-life cognitive resilience remain unknown.

Objective: To examine where in the brain and at what age brain development impacts late-life cognitive resilience the most.

Methods: We analyzed data from 1,473 participants from the Religious Orders Study and Rush Memory and Aging Project (ROS/MAP, mean age at death: 90.1±6.6 years; 67% women), with antemortem cognitive, genotype, and postmortem neuropathology measures. Age-dependent polygenic scores (PGSs), indexing propensity for non-linear change in brain structural trajectories (Brouwer et al.,2022), were calculated at 5-year intervals from ages 5-80. Cognitive resilience was defined as the residual of observed antemortem cognitive performance regressed on 12 brain-wide postmortem neuropathologies. Linear models tested associations between each age-specific brain-change PGS and resilience, correcting for false discovery rate (q=0.05). Sex-by-PGS interactions and post-hoc PGS-to-neuropathology analyses were also explored.

Results: PGSs reflecting slower cortical atrophy during midlife were most strongly associated with late-life cognitive resilience. Suggested effects were observed for slower hippocampal volume decline between ages 30-60 (age 50, p=0.04), total brain volume between 15-50 (age 25, p=0.04), and cerebellar cortical volume between 25-50 (age 50, p=0.02). No sex interactions remained significant after multiple testing. Midlife reserve PGSs were specifically associated with cerebral atherosclerosis and β-amyloid burden.

Conclusion: Genetic influences on cortical atrophy rates may partly determine brain reserve, conferring protection against AD-related cognitive decline, decades before typical dementia onset.

[#88] Priya van Oosterhout; Institute of Medical Science

Supervisor: Dr. Yuliya Nikolova

Theme: Aging and Neurodegenerative Disorders (Clinical) (Oral Presentation)

SUBSTANTIA NIGRA INTEGRITY, AGING, AND COGNITION IN SUBSTANCE USE DISORDERS: PRELIMINARY FINDINGS FROM THE COGNITIVE DYSFUNCTION IN THE ADDICTIONS RESEARCH PROGRAM

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Introduction: Substance use disorders (SUDs) are associated with increased risk for age-related cognitive decline and dementia, potentially driven by accelerated biological aging. Age-sensitive dopaminergic nuclei, such as the Substantia Nigra (SN), may be impacted by chronic substance use. However, the cognitive implications of these structural alterations remain unexplored.

Objective: The goal of this project was to determine the relationships between SN structural integrity, aging, and cognition. We hypothesized that greater chronological age would be associated with altered structural indices, consistent with accelerated aging in the SN. Furthermore, we hypothesized that these age-associated patterns would be associated with lower cognitive performance and general functioning.

Methods: This analysis uses data from the Cognitive Dysfunctions in the Addictions (CDiA) study, a naturalistic cohort of adults seeking treatment for SUDs. Participants (n=107, mean age: 39 +/- 11 years, range: 18-60) underwent neuromelanin-sensitive magnetic resonance imaging to assess SN structure, indexed via contrast-to-noise ratios (CNR). Multiple voxel-wise linear regressions were used to evaluate the link between CNR, age, and cognitive performance, measured via the Neurocognition Index from the Central Nervous System – Vital Signs battery of tests. Diagnosis was determined using the Diagnostic Assessment Research Tool. Cluster-level significance was determined via permutation testing (n=5000).

Results: There was no significant effect of having a specific SUD diagnosis or having multiple SUDs (all p>0.75). In the full sample, age was associated with higher CNR and lower CNR in non-overlapping subdivisions of the SN (cluster-level p=0.0196). Better cognitive performance was further associated with lower CNR (p= 0.0168), in clusters partially overlapping those associated with younger age.

Conclusion: Age and cognitive scores were both significantly associated with SN CNR, in line with previous evidence suggesting this nucleus is both age-sensitive and involved in cognitive processes. Interestingly, there was no significant effect of substance use, suggesting that the observed effects are independent of SUD type.

[#89] Lyra Vania; Department of Pharmacology & Toxicology

Supervisor: Dr. Amy Ramsey

Theme: Brain Development and Lifespan Neuroscience (Poster Presentation)

GENE-BASED THERAPY FOR GRIN DISORDER USING A LIPID NANOPARTICLE-BASED DELIVERY PLATFORM

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Introduction: Grin1 disorder arises from de novo mutations in the GRIN1 gene, which

encodes the GluN1 subunit of the NMDA receptor, a protein critical for neurodevelopment. Symptom presentation can vary between patients, and includes seizures, cognitive impairments, autism spectrum disorder, and movement disorders.

Objective: We hypothesized that delivering wild-type GRIN1 can rescue the behavioral and physiological phenotypes observed in transgenic GRIN1-deficient mice. To investigate this, 8-10-week-old GRIN1 knockdown mice received WT Grin1 messenger RNA (mRNA) bilaterally via intracerebroventricular injection, encapsulated in lipid nanoparticles (LNPs). Given that LNP formulation can dictate tissue selectivity, we screened brain-targeting LNPs using in vitro and in vivo luciferase-based assays. Histological analysis further provided an anatomical map of treatment delivery in the brain.

Methods: To quantify delivery of treatment mRNA, RT-qPCR was used to measure treatment-derived mRNA levels in brain tissue, and single-cell flow cytometry determined gene transfer efficiency and cell-type bias of the LNP vectors. Finally, behavioural assays are performed to demonstrate if functional NMDA receptor rescue can translate to phenotypic improvements.

Results: Preliminary data show moderate to mild rescue of hyperactive and anxiety-like behavior in mRNA-treated GRIN1 knockdown mice, with further behavioral studies ongoing. Separately, our work demonstrates that modulating LNP formulation can shift cell-type targeting even within different brain cell types.

Conclusion: While previous publications on these LNP formulations focused on peripheral organ selectivity, we posit that this novel brain delivery approach has broad potential for gene therapy in other neurological disorders.

[#90] Hsin-Yun (Angel) Hsieh; Department of Physiology

Supervisor: Dr. Evelyn Lambe

Theme: Psychiatric Disorders II (Poster Presentation)

DOES INDUCTION CALCIUM RELATE TO PLASTICITY OUTCOME OF SPACED THETA BURST STIMULATION?

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Introduction: Prefrontal cortex dysfunction is a hallmark of major depression. Increasing attention is devoted to treatments that strengthen the connections that activate prefrontal cortex, such as theta burst stimulation. Clinically effective theta burst patterns are delivered in discrete episodes separated by stimulus-free intervals, and many questions remain about the optimal spacing of episodes in the prefrontal cortex.

Objective: Here, we focus on 3-episode spaced TBS protocols to investigate how the spacing of theta burst intervals affects induction calcium and the resulting plasticity in the prefrontal cortex. We hypothesize that the strengthening of connections in the prefrontal cortex will depend on the peak level of calcium achieved during theta burst induction.

Methods: We use wide-field calcium imaging in brain slices from adult Thy1-GCaMP6f mice which label the major output neurons, including their apical dendritic arbors, in the prefrontal cortex. We use calcium imaging to monitor the recruitment of this brain region by test stimuli before and after the theta burst induction. In addition, we visualize the calcium increase during each episode of theta burst stimulation to assess the impact of changing the duration of the intervening stimulus-free intervals.

Results: We observed a dissociation between peak induction calcium and subsequent potentiation of prefrontal cortex recruitment. The briefest inter-episode interval (10 s) increased theta burst calcium the most yet did not show the greatest potentiation. A longer inter-episode interval (20 s) yielded an intermediate induction calcium peak but the strongest synaptic potentiation. The longest inter-episode interval (30 s) gave the lowest outcomes in both domains.

Conclusion: These findings suggest greater induction calcium rise does not guarantee greater plasticity outcome. Future work will extend the results and probe the mechanism driving the improved plasticity of the optimal spaced TBS protocol.

[#91] Xianxuan Wang; Department of Physiology

Supervisor: Dr. Hong-Shuo Sun

Theme: Developmental Neuroscience (Oral Presentation)

CURCUMIN ATTENUATES NEONATAL HYPOXIC-ISCHEMIC BRAIN INJURY THROUGH REGULATION OF MITOCHONDRIAL THERMOMETABOLISM

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Introduction: Neonatal hypoxic–ischemic (HI) brain injury is a major cause of mortality and long-term neurodevelopmental disability, and therapeutic hypothermia remains partially effective. Curcumin is a polyphenolic compound with reported anti-inflammatory, anti-oxidant and neuroprotective properties, but its role in thermometabolic regulation after neonatal HI is unclear.

Methods: Using the Rice–Vannucci model in postnatal day 7 mice, we evaluated the effects of curcumin administered either before HI (100–300 μg/g, i.p.) or after HI (200 μg/g within 3 h).

Results: Curcumin significantly reduced infarct volume, improved survival and body-weight recovery, and accelerated restoration of sensorimotor and cognitive function. Infrared thermography and rectal temperature monitoring showed that HI induced focal lesion-side hyperthermia accompanied by an increase in core temperature, whereas curcumin reduced both during the acute post-insult period. Bioinformatics analyses identified a mitochondrial thermometabolic signature among HI-related genes, with glutaminase 2 (GLS2) and nicotinamide phosphoribosyltransferase (NAMPT) emerging

as central nodes. Molecular docking supported favorable binding of curcumin to GLS2 and NAMPT, and enzymatic analyses further showed that curcumin suppressed HI-associated GLS activity, reduced recombinant NAMPT catalytic activity, and mitigated disruption of intracellular NAD+/NADH homeostasis. **Conclusion**: These findings suggest that curcumin confers neuroprotection in neonatal HI, at least in part, through regulation of mitochondrial thermometabolic pathways and support further development of curcumin-based strategies for neonatal hypoxic–ischemic encephalopathy.

[#92] Judy Wang; Department of Rehabilitation Sciences

Supervisor: Dr. Yana Yunusova

Theme: Cognitive Neuroscience (Poster Presentation)

SPEECH LANGUAGE PATHOLOGY SERVICES FOR MANAGEMENT OF BULBAR SYMPTOMS IN MYASTHENIA GRAVIS: A SCOPING REVIEW

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Introduction: Myasthenia gravis (MG) is a chronic autoimmune neuromuscular disorder characterized by fluctuating weakness of voluntary muscles that worsens with activity and improves with rest. Bulbar manifestations of MG, affecting speech and swallowing muscles, involve communication challenges, swallowing difficulties, and respiratory issues that significantly impair patient quality of life, mental health, and social participation. Currently, there is a growing demand for MG care and services, yet no standardized guidelines addressing bulbar symptoms in MG. Though speech language pathologists (SLPs) are routinely involved in the care pathway for other neurological disorders, there is evidence that SLP services are underutilized in this patient population. Mapping the existing research on SLP involvement in the MG care pathway can inform the creation of practice measures that address barriers to care, improve early identification of bulbar symptoms and support targeted interventions.

Objective: The objective of this scoping review is to synthesize available evidence on the current literature regarding the access, usage, and effectiveness of SLP assessments and treatments for MG.

Methods: Databases and organizational websites were comprehensively searched using Medical Subject Headings, including peer-reviewed studies and grey literature published before February 2026. Interventions within SLP scope of practice were considered across three areas: dysarthria, dysphagia, and respiration in the context of airway clearance.

Results: Of 525 peer-reviewed and 229 grey literature articles screened, 50 met the inclusion criteria for independent dual reviewer data extraction. Studies to date are limited to low quality evidence such as case studies, and barriers to SLP referrals include cost and difficulty accessing clinics. However, SLP treatments are effective in reducing aspiration severity and improving voice quality in MG via compensatory speaking and swallowing strategies, as well as respiratory muscle training. Further research may target remote

interventions to improve accessibility, and address SLP awareness towards bulbar MG as a rare disease.

Conclusion: Therefore, this review highlights the importance of SLP involvement in MG. It also emphasizes the need for high rigor studies exploring standardized and accessible interventions that mitigate barriers to MG care.

[#93] Hannah Whitehead; Applied Psychology & Human Development

Supervisor: Dr. Kaja Jasińska

Theme: Developmental Neuroscience (Oral Presentation)

NEUROCOGNITIVE DEVELOPMENT OF NUMERACY AND MATHEMATICS IN CONTEXTS WITH LIMITED EXPOSURE TO NUMBER DIGITS

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Introduction: In the Minority World, children are exposed to number symbols early in life (e.g., television, toys, store signage). In these contexts, both symbolic (e.g., 3 vs. 4) and nonsymbolic (e.g., ∵ vs. ∷) magnitude processing, at both behavioural and neural levels, relate to mathematics skills, with stronger associations between symbolic magnitude and mathematics. However, little is known about the neurocognitive development of numerical processing in contexts where children have minimal exposure to number digits prior to formal schooling.

Objective: We aimed to understand how variation in exposure to number digits relates to magnitude processing and mathematics skills. We hypothesized that, given the minimal exposure to number digits, children may leverage nonsymbolic skills for mathematics more than symbolic skills in this context. We expected symbolic skills may be associated with mathematics for children in older grades (i.e., those with greater exposure to number digits). At the neural level, we hypothesized, based on previous work, that inferior parietal activation for both nonsymbolic and symbolic skills would be related to mathematics.

Methods: We assessed symbolic and nonsymbolic magnitude processing in a sample of 142 rural Ivorian children (M=9.23, SD= 1.44) using a magnitude comparison task. Participants were instructed to select the larger magnitude within pairs of dot arrays (nonsymbolic) and number digits (symbolic). Behavioural performance was calculated using reaction time and accuracy; neural activation was measured using functional near-infrared spectroscopy (fNIRS). Mathematics skills were assessed using subtests from the Early Grade Mathematics Assessment.

Results: Overall, mathematics skills were low, including in the oldest children (11-13), who still struggled with single- and double-digit addition and subtraction. Despite minimal exposure to number digits prior to formal schooling, at the behavioural level, symbolic magnitude skills were predictive of mathematics. In line with our hypothesis, we found a positive interaction such that for children in older grades, symbolic skills were more predictive of mathematics than for those in younger grades. At the neural level, there were no main effects of neural activation on mathematics skill. However, age-related neural sensitivity to magnitude was related to

how children leveraged symbolic skills for mathematics. More specifically, greater magnitude sensitivity in the right inferior parietal (specifically, angular gyrus) in younger, but not older, children was associated with stronger links between symbolic skills and emergent mathematics.

Conclusion: Results suggest developmental sensitivity for successfully leveraging symbolic skills for mathematics. In line with a neuroconstructivist framework, our findings emphasize the complex interplay between development, neural processing of magnitudes, and symbolic magnitude skills in supporting mathematics.

[#94] Yik Lok Wong; Department of Pharmaceutical Sciences

Supervisor: Dr. Rob Bonin

Theme: Pain and Sensory Disorders II (Poster Presentation)

EFFECT OF MDMA ON NOCICEPTION IN ACUTE, INFLAMMATORY AND NEUROPATHIC PAIN

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Objective: Psychedelics, including MDMA, have been explored as a new treatment option for pain. MDMA has been shown in male rodents to have an analgesic effect in certain assays. In this study, we explore the effect of MDMA on a wide range of pain models in both sexes to better characterize its analgesic properties and effects on mechanical sensitivity.

Methods: 8-11 week-old male (n = 30) and female C57BL6 mice (n = 30) were given an intraplantar injection of capsaicin or CFA under anesthesia to induce acute or inflammatory pain respectively, or spared nerve injury surgery to induce neuropathic pain. Then, an i.p. injection of either saline or MDMA (2.5mg/kg or 5.0mg/kg) was given. Paw withdrawal thresholds were then measured using Von Frey filaments to assess tactile hypersensitivity.

Results: MDMA had no effect on paw withdrawal thresholds in the pain models that were tested. Uninjured females exhibited a transient thermal sensitivity when given MDMA.

Conclusion: This work demonstrates that MDMA has no effect on evoked pain in these pain models. This is partly in contrast with previous work, and may indicate that MDMA acts to inhibit affective rather than sensory components of pain.

[#95] Sabrina Wong; Department of Pharmacology & Toxicology

Supervisor: Dr. Roger McIntyre

Theme: Psychiatric Disorders II (Poster Presentation)

Association Between Glucose-Insulin Homeostatic Disturbances and Suicide Risk in Treatment-Resistant Depression: A Preliminary Analysis of a Phase II Randomized Controlled Trial

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Introduction: Conditions characterized by insulin resistance (IR) and beta-cell dysfunction (e.g., treatment resistant depression (TRD), polycystic ovarian syndrome) have been

associated with suicidal ideation (SI). However, the relative contributions of insulin resistance and beta-cell dysfunction to suicide risk are not well characterized.

Objective: Herein, we investigated the associations between IR and beta-cell function with SI severity in individuals with TRD.

Methods: We conducted an exploratory analysis of baseline data from an ongoing randomized controlled trial investigating ketamine and internet-based cognitive behavioural therapy for suicidality in TRD (NCT06480500; n=24). IR and beta-cell function were assessed using the homeostatic model assessment of insulin resistance (HOMA-IR) and beta-cell function (HOMA-B). SI severity was measured using Columbia Suicide Severity Rating Scale (C-SSRS) items 1-5. Ordinal regression models estimated the effects of HOMA-IR and HOMA-B on C-SSRS scores, adjusting for demographics, body mass index, past psychotropic medications, and depressive symptom severity.

Results: Higher IR was associated with increased odds of greater SI severity (OR = 9.87, 95% CI 0.36-270, p = 0.18), with similar trends observed for beta-cell function (OR = 3.20, 95% CI 0.12-87.85, p = 0.31). A HOMA-IR and HOMA-B interaction suggested that impaired metabolic compensation conferring greater SI (β = -3.36, OR = 0.035, 95% CI 0.0013-0.96, p = 0.17).

Conclusion: Although nonsignificant, our results highlight an emerging role for glucose-insulin dysregulation in TRD pathophysiology. Routine metabolic assessment should be integrated into psychiatric evaluation. Preclinical characterization of metabolic effects of emerging psychotropic agents prior to clinical implementation is warranted.

[#96] Victor Xu; Department of Chemistry

Supervisor: Dr. Chao Zheng

Theme: Neuropharmacology and Drug Development (Poster Presentation)

RADIOSYNTHESIS AND PRELIMINARY PET STUDIES OF 18F-CVN636 FOR IMAGING METABOTROPIC GLUTAMATE RECEPTOR 7 IN THE BRAIN

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Introduction: Metabotropic glutamate receptors (mGluRs) are seven transmembrane domain receptors that play crucial roles in excitatory neurotransmission in the central nervous system (CNS). mGluR7, a member of the group III mGluRs, is localized in the presynaptic zone, with functions in neurotransmitter regulation and early neuronal development. Due to its wide expression in the CNS, with high density in different regions of the brain, the mGluR7 has emerged as a key theragnostic target of interest in neurodevelopmental and neurodegenerative diseases. However, the lack of suitable PET radioligands has limited the in vivo investigation of mGluR7 pathophysiology. We herein report on the radiosynthesis and preliminary PET imaging studies 18F-CVN636, a mGluR7-selective allosteric agonist and CNS penetrant.

Methods: 18F-(S)-2-(4-fluorophenyl)-N-((3S,4S)-4-(methylsulfonyl)chroman-3-yl)propen-amide was synthesized from the boronic ester precursor, (S)-N-((3S,4S)-4-(methylsulfonyl)chroman-3-yl)-2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-propanamide via a modified Cu-catalyzed deborylative fluorination reaction. The reaction was performed in a 2:1 mixture of DMA:BuOH with freshly prepared tetrakis(pyridine)copper (II) triflate complex and heated to 120 oC for 20 minutes using tetraethylammonium triflate (eluted as [18F]-tetraethylammonium fluoride). Dynamic PET images were acquired for 90 min on a Mediso nanoScan PET-CT scanner in adult Sprague-Dawley (SD) rats (n = 2/gender) following the injection of [18F]CVN636 through a lateral tail vein catheter using a syringe pump (GenieTouch, Kent Scientific). Time-activity curves (TACs) of 64 brain regions were extracted from the dynamically reconstructed images using PMOD 4.203.

Results: The successful automated radiosynthesis afforded [18F]CVN636 in 3% radiochemical yield (RCY) and a molar activity of 49 GBq/mmol. The isolated radiolabeled compound was confirmed by analytical radio-HPLC co-injection with reference standard, CVN636. The product was formulated in a 10 mL mixture of 9:1 saline: ethanol, with a percentage purity of 99.5% confirmed by analytic rad-HPLC. Preliminary PET imaging using male and female SD rats (n = 2/gender) showed a very low uptake and fast washout of the radioligand in the brain. The standard uptake values (SUVs) however showed a slight but insignificant uptake in the female rat compared to the male.

Conclusion: We successfully automated the radiosynthesis of 18F-CVN636 and performed preliminary PET imaging with SD rats. Future work with the radioligand will include metabolite, efflux and receptor occupancy studies, as well as autoradiography assays to determine the binding affinity of the radioligand. Furthermore, we will continue to modify the structure of the lead compound to obtain radioligands with high brain penetrability and as targets for imaging mGluR7.

[#97] Maria Yang; Department of Physiology
Supervisor: Dr. Zhong-Ping Feng
Theme: Brain Development and Lifespan Neuroscience (Poster Presentation)

TARGETING RYR2-MEDIATED CALCIUM DYSREGULATION PROTECTS AGAINST HYPOXIC-ISCHEMIC BRAIN INJURY THROUGH MODULATION OF AUTOPHAGY AND MITOPHAGY PATHWAYS

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Introduction: Hypoxic-ischemic brain injury (HIBI) is a major contributor to neonatal neurological morbidity and is associated with intracellular calcium dysregulation, mitochondrial impairment, and altered autophagic signaling. Ryanodine receptor 2 (RyR2), an intracellular calcium release channel, has been implicated in secondary injury progression following hypoxia-ischemia.

Objective: This study investigated the neuroprotective potential of R-carvedilol (RCV), a selective inhibitor of RyR2-mediated calcium release, in a neonatal mouse model of HIBI.

Methods: HIBI was induced in postnatal day 7 mouse pups. RCV was administered intraperitoneally either before or after injury induction. Acute injury was assessed by TTC

staining, while long-term structural outcomes were evaluated using whole-brain imaging. Neurological recovery was examined through short- and long-term neurobehavioral assessments. Dose-response and therapeutic window studies were performed using TTC-based infarct measurements. Western blot analysis was used to examine autophagy- and mitophagy-related pathway alterations.

Results: RCV administration before injury or at 1 h post-HIBI significantly decreased infarct volume and improved neurological outcomes in both acute and long-term assessments. Neuroprotection was dependent on both dose and treatment timing, supporting the presence of a defined therapeutic window. Mechanistically, RCV mitigated HIBI-associated alterations in autophagy signaling and increased mitophagy-related protein expression, consistent with improved mitochondrial homeostasis.

Conclusions: Selective inhibition of RyR2-mediated calcium release by RCV provides significant structural and functional protection following neonatal HIBI. The observed therapeutic window, dose-dependent efficacy, and modulation of mitochondrial quality control pathways support the translational potential of RCV as a therapeutic strategy for calcium-driven secondary brain injury.

[#98] Ryan Yip; Department of Cell and Systems Biology

Supervisor: Dr. Ina Anreiter

Theme: Aging and Neurodegenerative Disorders (Clinical) (Oral Presentation)

THE ROLE OF M6A-MEDIATED CHAPERONE EXPRESSION IN NEUROINFLAMMATION OF THE DROSOPHILA BRAIN

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Introduction: N6-methyladenosine (m6A) is one of the most well-studied post-transcriptional modifications in eukaryotic mRNA, regulating various stress responses. In the brain, stress responses are crucial to maintain neuronal and cognitive function short and long-term. Objective: Thus, understanding how m6A facilitates cellular homeostasis in the brain in response to stress may provide valuable insights to stress-induced neurodegenerative phenotypes. Here we use heat shock as a primer to investigate the role of m6A in regulating brain-stress response. We show that m6A levels in the brain increase upon heat stress. **Methods**: Through immunoblotting, we also show sex-specific chaperone expression patterns and functionally link these to METTL3, the core enzyme that deposits m6A.

Results: METTL3 knockout female mutants have increased levels of Hsp70 expression in the brain and higher resilience to heat stress. Interestingly, Hsps showed delayed response in METTL3 KOs upon heat shock, demonstrating METTL3 is a key regulator in maintaining brain health upon stress.

Conclusion: Overall, our data suggest m6A modification in Drosophila has a negative influence on stress resilience and this mechanism shows sex differences.

[#99] Lyanne Zhang; Institute of Medical Science

Supervisor: Dr. Pushpal Desarkar and Dr. Sanjeev Kumar

Theme: Aging and Neurodegenerative Disorders (Clinical) (Oral Presentation)

INVESTIGATING BRAIN CRITICALITY AND FUNCTIONAL EXCITATION/INHIBITION BALANCE IN ALZHEIMER'S DISEASE

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Introduction: Disruption of the neural excitation/inhibition (E/I) balance has been proposed as a key neurobiological mechanism driving the progression of Alzheimer's disease (AD). The functional and cognitive consequences of E/I imbalance can be investigated through the framework of brain criticality, which defines the optimal dynamical state for information processing in neural networks.

Objective: Our study investigated brain criticality and functional E/I balance in healthy controls (HC) and patients across the AD clinical continuum: mild cognitive impairment (ADMCI) and dementia (ADD). We hypothesized that ADMCI and ADD groups would show reduced criticality and a shift toward over-excitation, both of which would correlate with poorer cognitive performance.

Methods: We analyzed the alpha band activity from resting-state electroencephalography (EEG) data from 175 older adults (51HC; 36ADMCI; 88ADD). Brain criticality was inferred via long-range temporal correlations (LRTCs) using the detrended fluctuation analysis (DFA) algorithm, while E/I balance was quantified using a functional E/I metric.

Results: Compared to the HC group, alpha-band LRTCs were significantly reduced in both ADMCI and ADD groups, with no significant differences observed between ADMCI and ADD. In contrast, functional E/I balance did not differ significantly across groups. Furthermore, reduced LRTCs predicted lower cognitive performance in ADD group, whereas functional E/I balance showed no correlation with cognitive performance.

Conclusion: The collapse of alpha-band criticality may serve as an early, predictive biomarker of cognitive impairment within the Alzheimer's continuum. Notably, this loss of criticality occurs independently of shifts in functional E/I balance.

[#100] Zhihong Luo; Department of Cell and Systems Biology

Supervisor: Dr. Minoru Koyama

Theme: Motor & Sensory Control (Oral Presentation)

BEHAVIORAL ROLES OF SPINAL V2a NEURONS UNCOVERED BY IMPROVED GENETIC ABLATION IN LARVAL ZEBRAFISH

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Introduction: Physiological and anatomical studies of spinal V2a neurons across vertebrate models indicate that this interneuron type plays an important role in generating rhythmic motor output during locomotion. However, their behavioral contribution to rhythmic locomotor output remains controversial. Genetic ablation of V2a neurons by diphtheria toxin A-chain (DTA) in mice leaves rhythm generation intact, but results in behavioral deficits in limb coordination during locomotion. On the other hand, two-photon ablation of a portion of spinal V2a neurons in larval zebrafish increases

induction threshold of swimming activity under fictive preparation, suggesting a role of this cell type in rhythm generation. These studies differ not only in the model systems employed but also in the techniques used, each with a different set of caveats. For example, all the V2a neurons including the ones in the hindbrain and eyes are killed in the mouse studies, which may confound the interpretation on behavioral roles of spinal V2a neurons.

Objective & Methods: To pinpoint their exact behavioral roles, we restricted DTA expression to the spinal cord using an intersectional approach via Cre-loxP system in larval zebrafish.

Results: Behavior experiments showed that the treatment group can still produce rhythmic locomotor output, but with significant effects on both the amplitude and interval of body bend. Notably, the treatment group exhibits significantly slowed propagation of locomotor activity along the rostral-caudal body axis, strongly suggesting their contribution to intersegmental coordination.

Conclusion: Hence, we provide new insights into the behavioral roles of spinal V2a neurons that may be conserved across vertebrates.

[#101] Thomas Sanderson; Department of Physiology

Theme: Cellular & Systems Neuroscience (Poster Presentation)

THE CENTRE FOR OPTOPHYSIOLOGY

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The Centre for Optophysiology (CfO; www.optophysiology.ca) is a CFI-ORF funded platform that is located at two custom renovated sites; one in the Department of Physiology at UofT and one in The Centre for Phenogenomics (TCP), a state-of-the-art CFI-funded animal facility jointly run by SHS and HSK. These sites were chosen for their suitability and to provide focus for in vitro and in vivo experiments, respectively. The CfO is designed to meet the critical need for resources to manipulate and image optogenetic tools (both actuators and reporters) over the full range of preparations used in modern physiology research, from in vitro cell culture to the awake behaving animal. The equipment on offer was designed to facilitate neuroscience research, but are applicable to multiple areas in physiology and so the centre is of utility to physiology researchers with a variety of specialisms. Equipment includes:

1) Three multiphoton microscopes for imaging deep (~1.5 mm) within biological tissue
2) A stimulated emission depletion (STED) super resolution microscope
3) Wide field imaging for both in vitro and in vivo research.

Distinguishing features of our facility include the inclusion of dedicated light paths to enable activation of optogenetic probes while simultaneously imaging reporters, as well as the availability of electrophysiology and behavior equipment. In addition, optical stimulation of multiple targets can be performed simultaneously using a spatial light modulator (SLM) and the response of optogenetic reporters can be interrogated by measuring subtle changes in their function using fluorescence lifetime imaging (FLIM). This equipment allows researchers to take advantage of the burgeoning list of new optogenetic tools that have become available. These tools range from new voltage sensors (that open up the possibility of all-optical

electrophysiology) to reporters that provide real time readouts on molecular signaling processes with high specificity. Our equipment can complement more traditional electrophysiology and biochemical techniques available in PIs labs, as our imaging approach provides important spatial and temporal information, critical to fully understand physiological processes in health and disease