Integrate and Fire

@ Canadian Association for Neuroscience

CAN 2026 Pre-Conference Satellite Event
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integrate and fire
Big Questions in Neuroscience
Seminar Series

CAN-ACN
CANADIAN ASSOCIATION FOR NEUROSCIENCE
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McGill | Integrated Program In Neuroscience

CIAN Centre for Integrative and Applied Neuroscience
Centre pour l'Intégration et l'Application des Neurosciences

Département de neurosciences
Faculté de médecine
Université de Montréal

SfN Society for Neuroscience Montreal Chapter

CSBN Center for Studies in Behavioral Neurobiology

Institut de recherche Centre universitaire de santé McGill
Research Institute McGill University Health Centre

nat network for applied technology

ADÉNUM Association des Étudiants en Neurosciences de l'Université de Montréal

About

Dear Colleagues,

Welcome to the Integrate and Fire CAN Satellite!

Academic research has become increasingly specialized, narrowing trainee perspectives toward the small circles equipped to understand their work. Yet major scientific problems are inherently interdisciplinary. At conferences, we tend to remain in familiar bubbles, attending talks by the same groups, networking with people we already know, while connections that could reshape our thinking go unmade.

The Integrate and Fire Satellite Symposium offers a full-day, trainee-centered event designed to foster genuine interdisciplinary connections among early-career neuroscientists before the main CAN 2026 conference. We aim to provide attendees with an established network of peers going into the main CAN conference, ready to continue their conversations and expand into each other's circles throughout the week.

Organizing Committee

Zeeshan Haqque | McGill University

Peter Fleming | McGill University

Lucia Pizzoccaro | Université de Montréal

Wanyi Lyu | York University

Schedule

8:30 AM – 9:00 AM	Registration and Welcome
9:00 AM – 9:15 AM	Opening Remarks
9:15 AM – 10:30 AM	Talks | Rethinking the Stressed Brain
10:30 AM – 11:00 AM	Coffee Break
11:00 AM – 12:15 AM	Talks | Deciphering the Hidden Mind
12:15 AM – 2:00 PM	Lunch + Clustered Poster Session
2:00 PM – 3:15 PM	Talks | Architects of Cognition
3:15 AM – 3:45 PM	Mind-Matching Speed Networking
3:45 AM – 4:00 PM	Closing Synthesis

Talk Session 1 – Rethinking Stressed Brain

9:15 AM – 10:30 AM

Fear, anxiety, depression. We know these states intimately, yet the circuits that generate them continue to surprise us. What if the real story lies in unexpected cell types, overlooked neuromodulators, or entirely new ways of thinking about vulnerability and resilience? This session explores the cellular and molecular logic of emotional regulation, and what emerging findings reveal about the limits of our current treatments.

Speakers:

Maryia Bairachnaya, PhD (Giros Lab; McGill University)
Circuit-specific noradrenergic dynamics are associated with stress susceptibility in a learned helplessness model

Houaria Adaïdi (Stellwagen Lab; McGill University)
Microglial TNF signaling is required for behavioral and cognitive deficits in a rodent model of post-traumatic stress disorder

Ossama Ghenissa (Murphy-Royal Lab; Université de Montréal)
Basolateral amygdala astrocytes encode anxiety states

Angela Zolis (Lambe Lab; University of Toronto)
When calcium fails to predict plasticity: Improving theta burst stimulation for vulnerable circuits

Talk Session 2 – Deciphering the Hidden Mind

11:00 AM – 12:15 AM

What the brain shows us is rarely the whole story. Behind every decision, feeling, and brain scan is a hidden state; a latent logic that drives what we observe but resists direct measurement. How do we get at what the mind is actually doing? This session explores how neuroscientists are learning to infer hidden mental states from the signals the brain leaves behind, pushing our understanding of neuroscience beyond the observable.

Speakers:

Meriam Zid (Ebitz Lab; Université de Montréal)
Monkeys choose to make mistakes

Darius Valevicius (Taschereau-Dumouchel Lab; Université de Montréal)
Closed-loop synthetic image evolution for affective neuroscience

Tamires Marcal (Evans Lab; McGill University)
Forecasting brain states in movie-watching with Dynamic Functional Connectivity

Kian Godhwani (Benrimoh Lab; McGill University)
Echoing Tides: A video game for psychosis risk screening

Talk Session 3 – Architects of Cognition

2:00 PM – 3:15 PM

How we learn, what we remember, and how we create are as much the products of architecture as they are of experience. From genes to networks, the brain arrives with structure, and that structure influences cognition in ways we are only beginning to appreciate. This session asks how far that architecture goes, and what it leaves for experience to write with.

Speakers:

Chiara Bramati (Di Cristo Lab; Université de Montréal)
Human-specific gene SRGAP2C improves learning by promoting information-seeking

Javad Karimi, PhD (Brandon Lab; McGill University)
An intrinsic evolving hippocampal scaffold guides the encoding of novel spatial memories

Sofiya Zbaranska (Josselyn Lab; University of Toronto)
Telling Friends from Foes: Contributions of the medial amygdala to social memory

Posters

A1. Erinn M. Grigsby | Université de Montréal

Cognitive flexibility exacts a measurable neural energy cost in prefrontal cortex.

A2. Gabrielle Dufresne | Université de Montréal

Exploration drives reward-dependent long-term memory.

A3. Sophie Bourgeault | Université de Montréal

Effects of Optogenetic Stimulation of Central Amygdala Neurons on Sucrose Seeking Guided by Discriminative and Conditioned Stimuli.

A4. Zijing Wu | McGill University

The basal ganglia as a distributed reinforcement learning system computing general values.

B1. Léonie Jean | Université de Montréal

Modulation de la plasticité corticale par stimulation theta-burst.

B2. Mryam Ali | University of Toronto

Multivariate Associations Between Resting State MEG Oscillatory and Aperiodic Spectral Features and PTSD Symptom Dimensions.

B3. Avin Sharma | Krembil Brain Institute, UHN

Cerebellar Modulation of Motor Preparatory Dynamics Using Low-Intensity Focused Ultrasound Stimulation.

B4. Joaquim Streicher | Université de Montréal

A scalable EEG framework for monitoring anesthesia depth and nociceptive responses.

C2. Polina Vishnyakova | Université de Montréal

L'association du polymorphisme Val66Met du gène BDNF avec les caractéristiques des ondes lentes chez les personnes âgées avec et sans trouble cognitif léger.

C3. Subhasri Viswanathan | Université de Montréal

Cannabis and alcohol show dissociable effects on adolescent functional brain network development and receptor architecture: A longitudinal study.

C4. Vasvi Dhir | McGill University

Multi-voxel pattern analysis for characterizing functional connectivity underlying grit in cognitively unimpaired older adults at-risk for Alzheimer's disease.

D1. Carlos Zavaleta Zamora | Universidad Nacional Autónoma de México

Differential expression of neurotransmitter synthesis genes in aminergic neurons is associated

D2. Jorge Ramírez-Ruiz | Université de Montréal

The ability to structure the world drives the developmental self-organization of behavioral and neural niches.

D3. Wanyi Lyu | York University

Factorial Analysis of Ensemble Representation of Attention and Decision-making in Prefrontal Cortex of Macaque Monkeys.

D4. Eric G. Ceballos | McGill University

Organization of neuropeptide systems in the human brain.

E1. Anne-Catherine Chouinard | Université de Montréal

Cortical specificity matters: Targeted hindlimb cortical stimulation enhances locomotor recovery after spinal cord injury.

E2. Ashkan Karimi | York University

Prefrontal and Parietal Local Field Potentials Employ Different Visuospatial Codes for Reach: A Complex-Valued Network Classification Approach.

E3. Chen Jiang | McGill University

Population structure of reward-induced remapping in the hippocampal CA1.

E4. Simon Alvado | Université de Montréal

Early functional immaturity of the reinnervated neuromuscular junction.

F1. Eve Honoré | McGill University

Unravelling Non-Canonical Subicular Circuits: Projecting Somatostatin Cells Anatomy and Function in Memory.

F2. Julie O'Reilly | McGill University

Traumatic brain injury activates vasopressin and oxytocin neurons of the supraoptic nucleus, causing hyponatremia.

F3. Mahgol Darvish | Concordia University

Spontaneous and miniature excitatory postsynaptic currents in medium spiny neurons of the dorsomedial striatum in Bmal1 knock-out mice.

F4. Clara Ireland | Université de Montréal

Role of Astrocytes in Regulation of CRH Neurons and the HPA Axis.

G1. Cassandra Souleles | McGill University

Cognitive Trajectories During Cannabis Abstinence in Individuals With Attention-Deficit/Hyperactivity Disorder Symptoms.

G2. Gurpreet Khurme | McGill University

Unlocking Antidepressant Response: Early Insights from Astrocyte-Derived Extracellular Vesicle microRNAs.

G3. Stefanie A. Tremblay | McGill University

A Canadian guidance framework for integrating social determinants of health in aging and Alzheimer's disease research.

G4. Harjeev Sudan | University of British Columbia

Toward parity in brain health: Characterizing neuroprognostication practices after drug-associated cardiac arrest.

H1. Amélie Mainville-Berthiaume | Université de Montréal

Role of neuronal projections from the prelimbic cortex to the nucleus accumbens in cocaine seeking triggered by discriminative cues.

H2. Tessa Parker | York University

Investigating the anxiolytic effect of exercise on neuronal stress circuits in people with Parkinson's Disease.

H3. Kathleen Ngo | Université de Montréal

Loosening the Nets: Psychedelics Unlock Hidden Plasticity.

H4. Joseph Farrugia | McGill University

Imaging Endocannabinoid Signalling in Individuals with Nicotine Dependence.

I1. Helia Mirabi | McGill University

Optimization of SEEG electrodes implantation guided by MEG source imaging and anatomical constraints: a simulation study.

I2. Ali Gharbienne | Université de Montréal

Combined cortical and peripheral stimulation alleviates locomotor deficits in a feline model of incomplete spinal cord injury.

I3. Mustaali Hussain | McMaster University

Exploring neural signatures for the development of chronic postsurgical pain using electroencephalography.

I4. Clara Pic Roca | Université de Montréal

Cortical switching dynamics shape delta activity under propofol anesthesia.

J1. Maïka Doré | Université de Montréal

From synaptic instability to serum biomarkers: NMJ-derived protein change in ALS.

J2. Caitlyn Mourcos | McGill University

Investigating tumour-oligodendrocyte lineage cell interactions in invasive melanoma brain metastases.

J3. Amandine Even | Université de Montréal

Development of a neuro-immune co-culture model to better understand the mechanisms involved in the neuronal death in Parkinson's disease.

J4. Aly Muhammad Salim | University of Calgary

Neuroprotective Effects of Remote Ischemic Conditioning in a Mouse Model of Repetitive Mild Traumatic Brain Injury.

K1. Coralie Godbout | Université de Montréal

The Effects of D-amphetamine Maintenance Treatment During IntA Cocaine on Discriminative Stimulus- and Conditioned Stimulus-Induced Cocaine Seeking Behaviour.

K2. Saba Bashir | Université de Montréal

Machine Learning-Enhanced Surface-Enhanced Raman Spectroscopy for Neurotransmitter Detection and Quantification.

K3. Layla Sadafi | Simon Fraser University

Re-examining ATP and Norepinephrine Signalling in Sympathetic Neurotransmission.

K4. Soraya Paquereau-Gaboreau | Université de Montréal

Phasic axonal dopamine release appears to involve mechanisms beyond synaptotagmin-1.

L1. Emma Clini | Université de Montréal

Health-related quality-of-life in patients with pediatric low-grade glioma: Findings from the initial phase of the TRAM-01 Study.

L2. Nour Eltaani | Université de Montréal

Scalable 3D longitudinal tumor monitoring in pediatric low-grade glioma using a Slicer-embedded nnU-Net.

L3. Laurence Paquet | Université Laval

Bio-imaging strategy to follow the infectious pathway of adeno-associated viruses inside neurons.

Talk Abstracts

Circuit-specific noradrenergic dynamics are associated with stress susceptibility in a learned helplessness model

Maryia Bairachnaya[1], J. Marshall[1], E. Isingrini[2], B. Giros[1]; [1]The Douglas Research Center. - Department of Psychiatry, McGill University, [2]CNRS UMR 8002 - INCC - Université de Paris-Cité

Stress exposure is a major risk factor for depression and related disorders, yet the neuromodulatory mechanisms that bias individuals toward resilience or vulnerability remain incompletely understood. The locus coeruleus-noradrenergic (LC-NE) system broadly innervates cortical and limbic circuits involved in coordinating cognitive and emotional responses to stress. To dissect the circuit-specific contributions of LC-NE signaling, we combined fiber photometry and chemogenetic approaches in a mouse learned helplessness model, in which animals are exposed to inescapable stress followed by testing of escape behavior. Using fluorescent sensors, we monitored real-time noradrenaline signals simultaneously in the medial prefrontal cortex and the amygdala during behavior. Animals that developed helpless behavior showed a marked reduction in noradrenaline signaling in the prefrontal cortex, whereas signals in the amygdala were similar across groups. This identifies a selective deficit in prefrontal noradrenaline associated with maladaptive coping. To further examine the involvement of this circuit, we selectively reduced activity in projections from the locus coeruleus to the prefrontal cortex using chemogenetic inhibition. This manipulation increased the proportion of animals displaying helpless behavior, demonstrating that noradrenaline input to the prefrontal cortex is required for adaptive responses to stress. These findings suggest that stress susceptibility may reflect an imbalance in noradrenergic engagement across prefrontal and limbic circuits, with potential implications for understanding neuromodulatory targets in stress-related mood disorders.

Microglial TNF signaling is required for behavioral and cognitive deficits in a rodent model of post-traumatic stress disorder

Houaria Adaidi[1], Maria Petryk[1], Joshua Wyrosdic[1], David Stellwagen[1]; [1]McGill University

Post-traumatic stress disorder (PTSD) is a debilitating mental illness that follows trauma and leads to persistent alterations in cognition and emotional regulation. Current treatments, including SSRIs, are slow and ineffective for many patients, highlighting the need for novel therapeutic strategies. Neuroinflammation has emerged as a promising avenue for PTSD treatment. Elevated levels of the pro-inflammatory cytokine tumor necrosis factor-alpha (TNF) have been reported in PTSD patients and rodent stress models. Our laboratory previously showed that acute stress induces a sustained increase in TNF in the ventral hippocampus, enhancing AMPA receptor–mediated glutamatergic transmission and driving anxiety-like behavior. The role of TNF in chronic stress, however, remains unclear. Using the single prolonged stress (SPS) paradigm, a rodent PTSD model, we found persistent anxiety-like behavior and cognitive impairments lasting at least 8 weeks, accompanied by elevated TNF in the hippocampus and frontal cortex. SPS failed to induce deficits in TNF knockout, TNF receptor 1 knockout, or microglial TNF–deficient mice. MDMA, a compound under clinical investigation for PTSD with reported anti-inflammatory effects, rescued anxiety-like behavior

when administered after SPS, suggesting that modulating inflammatory signaling contributes to its efficacy. These findings identify microglial TNF as a promising therapeutic target for PTSD.

Basolateral Amygdala Astrocytes Encode Anxiety States

Ossama Ghenissa[1], Guayasamin M[1], Ngo K.[1], Duquenne M[1], Peyrard S.[1], Amilhon B.[1], Murphy-Royal C.[1]; [1]Université de Montréal

The basolateral amygdala (BLA) has long been implicated in the regulation of emotional states, including anxiety. However, while previous experiments have demonstrated the important role of BLA principal neurons in driving anxiety-related behaviors, population-level recordings suggest that principal neurons encode broad exploratory states rather than anxiety per se. This discrepancy questions whether anxiety is indeed represented within the BLA, or if the BLA reflects a broader representation of behavioral states. Here, using simultaneous in vivo calcium (Ca2+) recordings in both astrocytes and principal neurons, we find that in contrast to neurons, astrocyte activity provides a stable and scalable representation of threat-induced anxiety across an array of behavioral tasks. We find that the magnitude of astrocyte response to anxiogenic stimuli is modulated by the individual anxiety levels of animals, and that exploration of anxiogenic environments can be decoded across multiple tasks using astrocyte activity alone. Through causal manipulation approaches combined with in vivo Ca2+ recordings, we then demonstrate a causal role for BLA astrocyte calcium in anxiety processing by showing that driving astrocytic Ca2+ effectively increases anxiety-related behavior. Finally, we uncover the signalling mechanisms underlying astrocytic anxiety coding. Using 2-photon imaging and pharmacological experiments in brain slices, we find that BLA astrocytes almost exclusively respond to norepinephrine. We then demonstrate in vivo that knocking down astrocytic alpha1 adrenergic receptors abolishes astrocyte anxiety coding and reduces anxiety-like behaviors. Altogether, our results establish a role for BLA astrocytes as key computational elements of anxiety circuits, and could pave the way for innovative astrocytes-targeting treatment for anxiety disorders.

When calcium fails to predict plasticity: Improving theta burst stimulation for vulnerable circuits

Angela Zolis[1], Angel Hsieh[1], Sridevi Venkatesan[1], Rachael Ingram[1], John Georgiou[1], Tarek K. Rajji[1], Graham L. Collingridge[1], Evelyn K. Lambe[1]; [1] University of Toronto

Intermittent theta burst stimulation (iTBS) applied to the prefrontal cortex is an emerging treatment for major depression. This complex treatment paradigm aims to improve synaptic connectivity in this brain region, which is decreased in depression. Despite the utility of preclinical work for mechanistic exploration, little investigation has been done into the clinically used iTBS treatment. Here, we use ex vivo calcium imaging in the mouse prefrontal cortex to investigate the impact and aspects of the mechanisms of this clinical paradigm (Clinical iTBS). We find that Clinical iTBS reliably induces synaptic potentiation in prefrontal slices from group-housed mice. However, depression modelled via prolonged social isolation compromises this reliability. Juvenile-onset isolation disrupts the predictive relationship between peak Clinical iTBS calcium levels and subsequent synaptic potentiation, with unexpected elevation of Clinical iTBS calcium after social isolation. Delivering fewer episodes of an iTBS protocol spaced minutes apart (Spaced iTBS) enhances synaptic potentiation of test pulse signals in the prefrontal cortex, but only in socially isolated mice, resulting in a significant interaction between induction protocol and housing condition. Spaced iTBS is also effective in

mice subjected to adult-onset social isolation. Together, these results suggest potential refinements in iTBS protocols to increase their efficacy in the vulnerable prefrontal cortex.

Monkeys choose to make mistakes

Meriam Zid[1], Veldon-James Laurie[1], Jorge Ramírez-Ruiz[1], Devin H. Kehoe[1], Hiba Kellil[1,2], Becket Ebitz[1]; [1]Department of Neuroscience, University of Montreal, [2]Department of Psychology, Concordia University

When engaged with a task, humans and other animals occasionally make seemingly irrational decisions known as “lapses”, even in static and well-learned environments. Because they deviate from reward-maximization, these suboptimal decisions are often attributed to disengagement, distraction or sensorimotor noise. However, a growing body of literature is supporting the idea that lapses could be caused by the same exploratory processes that help us learn in uncertain environments. Because there are multiple mechanisms for exploration, we do not know if exploratory lapses are truly intentional decisions that are related to the subject’s hidden objective, or else the result of some noise process involved in exploration. To tease these hypotheses apart, we used a novel reward learning task in which decisions are made serially rather than simultaneously. We found that 2 rhesus macaques sacrifice objective reward, withholding responses to rewarding options, to generate lapses, even in fully deterministic reward conditions. These results suggest that lapses can indeed be subjectively valuable, selective decisions in this species. However, these results also challenge current models of decision making, which do not allow for lapses after learning when there is no ambiguity in reward outcomes. We show that an ideal, reward-maximizing agent would always wait for the best option to appear once it has been identified in this task. To understand lapses, we developed a novel partially observable Markov decision process model that optimally trades off maximizing reward rate with a fixed drive for sampling information. The model can account for the occurrence of lapses, even when monkeys have learned the value of options and when there is no ambiguity in reward outcomes. These results suggest that lapses of task performance can be explained by an intrinsic and enduring motivation to seek information, both when it is useful and when it is not.

Closed loop synthetic image evolution for affective neuroscience

Darius Valevicius[1], Celine Haddad[1], Michelle Beaudoin[1], Rémi Buu Nyugen[1], Gurgen Soghoyan[1], Aurelio Cortese[1], and Vincent Taschereau-Dumouchel[1]; [1]Université de Montréal

The neural bases of the subjective experience of fear and other emotions remain poorly understood, despite playing a central role in our lives and in the burden of anxiety and mood disorders. This is partly due to a reliance on correlational methods, which may fail to distinguish patterns of brain activity underlying subjective emotional experience from related phenomena such as arousal or attention. Using a novel method, “Closed-loop Synthetic Image Evolution”, we can probe potential neural signatures of subjective fear. In this study, we evolve images generated by an AI model to maximize the activity of a target neural fear pattern, and we use self-reported responses to the images to measure the corresponding subjective state. In doing so, we can discover what features the neural patterns are selective for, and if targeting them is sufficient to produce fearful images. We scanned 40 healthy participants with high fear of animals in fMRI sessions in which we presented videos of animals and collected ratings of subjective fear. These data were used to compute candidate neural fear patterns: (1) A coarse whole-brain signature of fear, (2) an amygdala

pattern, and (3, 4) fine-grained patterns in the medial prefrontal cortex (mPFC) and fusiform gyrus (FG). These patterns were used as targets in synthetic image evolution fMRI sessions (n=16). The mPFC pattern was the only one that successfully predicted fear ratings in the closed-loop experiment, and produced the most fearful images. The FG pattern correlated with visual features of feared animals, but not with fear ratings themselves. Finally, the whole-brain pattern also struggled to generalize and showed strong habituation effects characteristic of arousal or attention. These results offer a deeper understanding of the neural bases of fear than correlational methods alone can provide.

Forecasting brain states in movie-watching with Dynamic Functional Connectivity

Tamires C. Marcal[1], Paule-Joanne Toussaint[1], Alan C. Evans[1]; [1]Department of Neurology & Neurosurgery, Montréal Neurological Institute, McGill University

INTRODUCTION: Movie-watching paradigms provide ecologically valid stimuli for understanding brain circuit dynamics, yet current studies lack agnostic, data-driven approaches to decompose brain signals during naturalistic viewing. We address this by decomposing Dynamic Functional Connectivity (dFC) to define brain states and develop a forecast model of future brain activity. METHODS: We analyzed data from 86 participants who watched 10 full-length movies (~117 minutes each) from the Naturalistic Neuroimaging Database. DFC was estimated using a sliding window approach (5-minute intervals with overlap). Dimensionality reduction and clustering identified brain states, groups of similar connectivity patterns. We validated our approach by training supervised models to classify latent components and forecasted brain activity 5–50 minutes ahead using prior states, latent variables, movie, age, and gender. RESULTS: From different preprocessing approaches, we selected the brain state set with the most stable state-to-state transitions. This achieved an F1 score of 70.0% (±1.7%) when forecasting 5–50 minutes into the future, with consistent performance across both near and far predictions. Moving averages of the first three latent variables from dFC decomposition were the strongest predictors. CONCLUSION & DISCUSSION: Our findings demonstrate that dFC captures both group-level and individual-specific brain dynamics. The framework successfully predicts brain states across extended periods, validating reliable temporal patterns in naturalistic viewing. This benchmark for modeling brain activity under naturalistic stimuli has implications for precision neuroimaging and investigating the neural basis of clinical symptoms and their temporal variability across individuals.

Echoing Tides: A Video Game for Psychosis Risk Screening

Kian Godhwani[1], Chris Drogaris[1], Philomené Labilloy[1], Jérôme Waldispühl[1], Deven Parekh[1], Al Powers[1], David Benrimoh[1]; [1]McGill University

Early treatment intervention for psychosis in schizophrenia helps reduce hospitalizations and relapse risk, improving long-term outcomes. Changes in how we process information involving cognitive domains such as perception often precede psychotic episodes. Developments in the field of computational psychiatry have facilitated the creation of novel paradigms that can identify the latent cognitive states linked to psychosis risk states. However, a major bottleneck has been implementing them in real-world settings as these paradigms have been tested in laboratory settings only. As a result, they are time-consuming, tedious to complete, and have limited ecological validity. To overcome these limitations, we are developing Echoing Tides, a modular

3D open-world video game designed to embed validated computational psychiatry paradigms and cognitive tasks into a naturalistic environment with narrative-driven gameplay. This will make the tasks more engaging, and feasible, facilitating monitoring of symptoms over time. Using artificial intelligence and custom computational psychiatry algorithms such as the hierarchical gaussian filter, player behaviour within the game is used to predict the risk of psychosis onset. Our project has two phases. First, already underway, we are co-designing the game with patient partners, clinicians, and game developers. Second, beginning June 2026, we will test the game in 30 individuals with psychosis risk and 30 healthy participants. This will help assess whether Echoing Tides is engaging, can measure cognitive changes over time, and predict symptom states accurately. Echoing Tides will help shift psychosis care from a reactive to preventative approach, enabling engaging, scalable screening and outcome monitoring. By translating complex cognitive assessments into immersive, real-world environments, this work lays the foundation for continuous, ecologically valid monitoring of mental health, bringing precision psychiatry closer to everyday clinical practice. Additionally, Echoing Tides is built as an open-source, modular platform, enabling researchers and clinicians to adapt, extend, and deploy it across diverse settings.

Human-specific gene SRGAP2C improves learning by promoting information-seeking

Chiara Bramati[1,2], Jorge Ramírez-Ruiz[2], Graziella Di Cristo[1,2], R.Becket Ebitz*[2], Roberto Araya*; *equal contribution, [1]Centre de recherche Azrieli du CHU Sainte-Justine, [2]Département de Neurosciences, Université de Montréal

Learning can arise through different behavioral strategies, from conservative trial-and-error to active, exploratory behaviors that favor information accumulation. We show that the human-specific gene SLIT-ROBO Rho GTPase activating protein 2C (SRGAP2C) modifies the learning strategy in mice performing a sensory detection task. SRGAP2C emerged from partial duplications of the ancestral gene SRGAP2A, a postsynaptic protein regulating synaptic development. In mouse cortical pyramidal neurons, SRGAP2C expression induces human-like features of synaptic development, increased cortio-cortical connectivity and improved sensory discrimination performance. To investigate SRGAP2C's role in learning, mice were trained to lick a water port to obtain a reward when a whisker stimulus was present and to withhold licking in its absence. We observed strikingly different learning strategies in SRGAP2C and control mice early in training. SRGAP2C mice displayed an enhanced drive to lick, an approach that accelerates the learning of stimulus-reward associations at the cost of more punishment timeouts. We show that SRGAP2C mice are able to gather more task information in the first sessions and exhibit higher mutual information – the information sensory input provides about behavior – later in training. These results reveal that SRGAP2C drives a shift in behavioral strategy, favoring information accumulation over punishment avoidance, leading to an improvement in use of perception to guide action. This suggests that evolutionary changes in synaptic development induced by human-specific gene duplications may have contributed to distinct features of human learning and decision-making.

An intrinsic evolving hippocampal scaffold guides the encoding of novel spatial memories

Javad Karimi[1]; [1]McGill University

Computational models suggest the hippocampus maintains an adaptive generative model of the world, where spontaneous offline activity reflects sampling from learned priors. New experiences update these priors, which subsequently influence future learning. This framework unifies two hippocampal phenomena: "preplay"—pre-experience sequential activity reflecting the prior—and "representational drift"—the continuous evolution of a spatial map, which is seen as a structured adaptation rather than noise. A key prediction is that the evolution of offline and online neural activity must be coordinated during learning. To test this, we used longitudinal miniscope calcium imaging and LFP recordings to track dorsal hippocampal CA1 neurons in mice for weeks before and during the learning of a novel environment. We found that offline hippocampal activity patterns around sharp-wave ripples (SWRs) evolve daily in a structured manner. Critically, the neural code during the first encounter with the novel environment was significantly more similar to the offline patterns from the immediately preceding sleep sessions than to those from days earlier. Furthermore, the similarity between offline activity on any two days was significantly correlated with the representational similarity of the encoding sessions that followed. Our results provide direct evidence that learning is guided by a slowly evolving intrinsic scaffold, revealing how the hippocampus balances stability and plasticity.

Telling Friends from Foes: Contributions of the Medial Amygdala to Social Memory

Sofiya Zbaranska[1,2], Alessandro Luchetti[1], Mohammed H. Sarikahya[1], Paul W. Frankland[1,2,3,4], Sheena A. Josselyn[1,2,3,4]; [1]Program in Neuroscience & Mental Health, Hospital for Sick Children, [2]Department of Physiology, University of Toronto, [3]Department of Psychology, University of Toronto, [4]Institute of Medical Science, University of Toronto

Social memory is our ability to remember and recognize others. It is critical to guide appropriate social interactions and is impaired in numerous neuropsychiatric disorders, including autism spectrum disorder and social anxiety disorder. While the hippocampus has traditionally been regarded as a major social memory hub, the role of other brain regions received less attention. Our study identifies the medial amygdala (MeA) as another critical site which houses engrams supporting social memory. The reactivation pattern of these engrams is social subject-specific, while the strength of engram reactivation positively scales with the success of social memory recall. Importantly, these engrams appear to be engaged in both neutral and emotionally salient types of social memory. We further show that blocking oxytocin receptors (OXTR) following initial social encounter impairs social memory recall via suppression of MeA engram reactivation. Using longitudinal calcium imaging, we observed that OXTR antagonism likely disrupts engram re-engagement during the late offline consolidation period, thus perturbing memory stabilization. Together, our findings accentuate the MeA as an important player in the engram network involved in different types of social memory.

Poster Abstracts

A1. Cognitive flexibility exacts a measurable neural energy cost in prefrontal cortex

[1]Erinn M. Grigsby, [1]Catherina Medeiros, [1]Erica Ozanick, [1]Noa Magen, [1]Meriem Zennouche, [1]R. Becket Ebitz; [1]Université de Montréal

Cognitive flexibility is both fundamental to intelligent behavior in dynamic environments and costly to initiate and sustain. While behavioral modeling suggests that cognitive flexibility is more energetically costly than rigid or consistent behavior, no study has directly linked the energetic costs of flexible behavior to cortical neural activity. Here, we developed an approach that assessed the dynamics of behavior in a rule-switching task and generated statistical inferences about the energy required to initiate and sustain flexible brain states. We then analyzed how these behavioral energy states related to population neural activity in the dorsolateral prefrontal cortex (dlPFC) of rhesus macaques (n=2) performing the rule-switching task. Using statistical models, we identified periods of flexible exploration and stable rule-following, quantified the energy landscape of behavior, and analyzed concurrent neural activity. We found flexible states were less frequent and associated with a distributed increase in spiking activity across neurons. By directly comparing state occupancy, state transitions, and neural activity, our results tested competing hypotheses about whether energetic costs arise from flexible states themselves, their initiation, or accompanying physiological processes. We found that neural activity peaked at precisely the times predicted by our statistical model: during flexible brain states and at transitions between flexible and inflexible brain states, regardless of direction. There was a striking correlation between the energy demand predicted from behavior and session-by-session variability in dlPFC spiking activity. These results provide a direct link between statistical measures of behavioral energetics and prefrontal spiking activity, establishing a mechanistic account of why cognitive flexibility is particularly energy-demanding.

A2. Exploration drives reward-dependent long-term memory

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In dynamic environments, we make decisions by balancing two latent states: exploiting options that maximize reward and exploring alternatives in order to learn about their value. Exploration is distinguished by an increase in reinforcement learning: the influence of rewards on future choices is enhanced during exploration (Ebitz et al, 2018). However, it remains unclear whether this happens because exploration generally improves memory encoding or specifically increases reward-dependent processing. To test these hypotheses, human participants (n=191) completed an uncertain decision-making task in which reward outcomes were paired with unique images from the Bank of Standardized Stimuli. A surprise recognition task was then used to assess how decision-making factors influenced image encoding. Consistent with prior reports, we found that reward-paired stimuli were better encoded than non-reward-paired stimuli (Miendlarzewska et al, 2016). However, images presented during exploration were no more likely to be recognized than other images, suggesting that exploration does not generally enhance encoding. Instead, we found that the increased recognition observed on rewarded trials was mostly driven by exploratory trials. Intriguingly, switches between states were linked to better recognition memory, independently of both state and reward, suggesting that state switching enhances mnemonic encoding while exploration enhances

reward processing. Together these results point to a new role for latent decision-making states in shaping how we encode information into long-term memory. Funding by NSERC Discovery Grant (RGPIN-2020-05577), Canada Research Chair in the Dynamics of Cognition.

A3. Effects of Optogenetic Stimulation of Central Amygdala Neurons on Sucrose Seeking Guided by Discriminative and Conditioned Stimuli

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Environmental cues associated with rewards strongly influence reward seeking. Discriminative stimuli (DSs) signal reward availability contingent on a seeking action, whereas conditioned stimuli (CSs) are paired with reward delivery as a consequence of a seeking action. The central amygdala mediates CS motivational value, but its role in DS-controlled behavior is unclear. We hypothesize that increasing central amygdala activity promotes incentive motivation elicited by reward-associated DSs and CSs. Female and male Sprague Dawley rats will learn to discriminate between DS+ trials, where lever pressing produces sucrose paired with a CS+, and DS− trials signaling no reward. Next, rats will receive tests of cue-evoked sucrose seeking, without sucrose, and conditioned reinforcement, where lever pressing produces the CS+ and DS+, without reward. Using optogenetics, we will increase central amygdala activity during testing. Control rats will receive into the central amygdala a viral vector containing eYFP alone, while experimental rats will receive a viral vector containing ChR2-eYFP, enabling optogenetic stimulation during cue presentation. If our hypothesis is correct, optogenetic stimulation will increase sucrose seeking (i.e., lever pressing) during DS+ presentation, and also increase lever pressing for CS+ and DS+ presentation, the latter indicating greater conditioned reinforcement. Regardless of outcome, our findings will clarify the central amygdala's role in incentive motivation and inform understanding of adaptive and maladaptive reward-seeking behaviour.

A4. The basal ganglia as a distributed reinforcement learning system computing general values

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Dopamine modulation of striatal circuitry is a key neural system for decision-making and motor control, where dopamine release onto striatal neurons serves as a learning signal that updates learned predictions encoded in the striatal neurons. While the reward prediction error hypothesis quantitatively predicts the activity of some dopamine neurons, many studies reveal a heterogeneous view, where dopamine-modulated striatal circuitry is involved in many computations, such as goal-directed behavior and habit formation. These functions are often associated with distinct striatal subregions that receive input from different midbrain dopaminergic populations, which have been independently manipulated using optogenetic stimulation across numerous rodent behavioral studies. However, these diverse observations lack a comprehensive computational framework that reconciles these sometimes conflicting experimental observations. To tackle this, we introduce VQH, a unified computational model for dopamine-modulated learning in the ventral striatum (VS), dorsomedial striatum (DMS), and dorsolateral striatum (DLS). We leverage the framework of general value functions to assign a distinct computational role to different striatal subregions and dopaminergic projections within the reinforcement learning framework. We show that our model can explain a range of experimental observations that separately manipulated the dopaminergic projections to VS, DMS, and DLS via optogenetic stimulation. More generally, the VQH model acts as a mechanistic,

anatomically referenced, and testable model that balances the three main axes of dopamine-modulated striatal computation. It can be used as an in-silico testbed to generate testable hypotheses to design future experiments that manipulate or record the activity of dopamine and striatal neurons in the basal ganglia.

B1. Modulation de la plasticité corticale par stimulation theta-burst

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Introduction : La stimulation theta-burst intermittente (iTBS) est une approche prometteuse pour induire une plasticité corticospinale, mais dont la variabilité des effets impacte la fiabilité. La répétition de blocs d'iTBS pourrait augmenter la persistance des effets, et potentiellement réduire cette variabilité. Toutefois, la durée interbloc influence fortement ses effets. À ce jour, aucun intervalle optimal n'a été identifié. Cette étude vise à comparer l'effet d'un intervalle de 2 et 15 minutes entre deux blocs d'iTBS. Matériel et méthodes : Trois rats ont été stimulés via une électrode épidurale corticale selon un protocole de deux blocs d'iTBS séparés de 2 ou 5 minutes, ou alors une stimulation a été simulée. Chaque condition a été testée deux fois par rat. Les potentiels évoqués moteurs (PEM) étaient enregistrés avant et pendant 1 heure suivant le protocole. Les PEM étaient ensuite normalisés sur leur amplitude préTBS. Les sessions ont aussi été classées comme facilitatrices, inhibitrices ou nulles selon l'amplitude post-TBS moyenne des PEM. Résultats et discussion : Les protocoles d'iTBS n'ont pas modifié l'amplitude des PEM ($p > 0,05$). Toutefois, une tendance différencie les groupes : l'iTBS-2min a diminué de 31% l'amplitude moyenne des PEM, alors que l'iTBS-15min l'a augmenté de 17%. Plus de sessions d'iTBS-15min ont été classées comme facilitatrices (50%) que celles d'iTBS-2min (16,7%), qui avait une majorité de sessions inhibitrices (66,7%). Ces tendances indiquent qu'un intervalle trop court serait inhibiteur, potentiellement à cause d'une métaplasticité. Conclusion : Si les tendances se confirment, un intervalle interbloc court (e.g. 2 minutes) favoriserait un renversement des effets attendus. L'intervalle de 15 minutes devrait être envisagé pour des protocoles de blocs répétés chez le rat.

B2. Multivariate Associations Between Resting State MEG Oscillatory and Aperiodic Spectral Features and PTSD Symptom Dimensions

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Posttraumatic stress disorder is increasingly understood to involve disruptions in memory-related neural systems rather than reflecting a single fear-based condition. However, most electrophysiological studies continue to rely on categorical diagnostic comparisons and univariate analyses that cannot capture how continuous symptom dimensions relate to distributed neural activity. Multivariate approaches that integrate oscillatory rhythms with the aperiodic structure of neural signals provide a principled framework for examining coordinated brain symptom relationships across the full spectrum of trauma-related symptom expression. The present study examined multivariate associations between resting state magnetoencephalography (MEG) spectral features and continuous dimensions of posttraumatic stress

symptoms (PTSS) using canonical correlation analysis (CCA). 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), with anxiety, depression, and concussion diagnosis included as covariates. Source-resolved oscillatory power across canonical frequency bands, together with parameterized aperiodic components of the neural power spectrum, were analyzed to capture complementary aspects of large-scale neural population dynamics.Significant multivariate relationships linked reexperiencing, avoidance or withdrawal, and hyperarousal symptom dimensions to coordinated variation in delta, theta, beta, and low gamma activity together with regional differences in aperiodic slope and offset, with statistically significant canonical functions observed across multiple spectral domains. These canonical functions revealed partially separable symptom-specific electrophysiological signatures rather than a single shared neural disturbance. These findings demonstrate that variability in PTSS maps onto coordinated oscillatory and aperiodic neural dynamics that support core memory processes, including encoding, contextual integration, retrieval, and regulatory control. Rather than reflecting a unitary fear-based neural disturbance, distinct canonical functions revealed symptom-specific alterations across distributed memory-related neural systems. Together, these results provide electrophysiological support for a dimensional memory systems framework of trauma-related symptom expression and highlight resting state MEG spectral features as candidate markers of symptom-specific alterations in large-scale memory system dynamics in trauma-exposed populations.

B3. Cerebellar Modulation of Motor Preparatory Dynamics Using Low-Intensity Focused Ultrasound Stimulation

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Hypothesis/Research Question: The cerebellum, particularly the dentate nucleus (DN), is recognized for its role in motor planning and execution. I hypothesized that low-intensity transcranial focused ultrasound (TUS) targeting the DN would modulate motor preparatory signals via dentato-thalamo-cortical (DTC) pathways, as indexed by the Bereitschaftspotential (BP). Materials and Methods: Ten healthy adults participated in EEG experiments across one session (active TUS and sham). Participants performed self-paced wrist extensions after offline TUS to the DN. EEG-derived BP was aligned to EMG onset and analyzed for peak negativity, slope, and area under the curve, each capturing a distinct aspect of the pre-movement preparatory buildup. Results: Dentate TUS altered BP dynamics: peak negativity was reduced by 6.07 μV, slope decreased by 2.44 μV/s, and area under the curve was reduced by 7.13 μV·s, indicating suppressed motor preparatory activity. Cortical effects extended across Cz, Fz, C4, and C3, suggesting network-level modulation. Conclusion: Cerebellar TUS targeting the DN can modulate motor preparatory potentials prior to voluntary movement. These findings support a causal role for the cerebellum in shaping cortical excitability through DTC pathways, with potential implications for conditions in which preparatory motor signaling is disrupted.

B4. A scalable EEG framework for monitoring anesthesia depth and nociceptive responses

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Accurately assessing consciousness under general anesthesia remains a critical clinical challenge. Inadequate anesthesia can lead to intraoperative awareness and severe psychological consequences, including post-traumatic stress disorder, while excessive anesthesia has been associated with increased morbidity, delayed neurocognitive recovery, and poorer clinical outcomes. These risks underscore the need for reliable, objective markers of anesthetic depth. Information-theoretic measures—particularly redundancy (shared information) and synergy (interaction-based information)—have been shown to track anesthesia depth using fMRI, but their clinical applicability is limited. Here, we extend this framework to EEG and evaluate its sensitivity to arousal fluctuations, including responses to noxious stimulation, under clinically realistic conditions. High-density EEG (128 channels) was recorded from eight surgical patients under propofol anesthesia (target effect-site concentration: 2.0 μg/mL, titrated to maintain BIS 45–55), including periods before and after noxious stimulation. Data were preprocessed and analyzed using the Integrated Information Decomposition (ΦID) framework, which quantifies unique, redundant, and synergistic information based on past–future signal relationships. Signals were aggregated into virtual sensors probing interhemispheric and anterior–posterior interactions. To assess clinical feasibility, analyses were repeated using reduced 24- and 2-electrode configurations. Under anesthesia, interhemispheric redundancy increased ($t = 2.92$, $p = 0.02$), while anterior–posterior unique information increased ($t = 4.07$, $p = 0.0048$), suggesting enhanced shared processing across hemispheres and increased functional segregation along the anterior–posterior axis. Following noxious stimulation, anterior–posterior redundancy decreased, indicating sensitivity to arousal perturbations. These effects were largely preserved in reduced electrode configurations, with meaningful patterns recovered even in a 2-electrode BIS-like setup. Together, these findings show that EEG-based information decomposition captures structured, arousal-sensitive changes in large-scale brain dynamics and remains robust under clinically realistic conditions. This approach provides a promising, scalable framework for anesthesia monitoring and the objective assessment of consciousness in the operating room.

C2. L'association du polymorphisme Val66Met du gène BDNF avec les caractéristiques des ondes lentes chez les personnes âgées avec et sans trouble cognitif léger.

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Le sommeil à ondes lentes (SOL) joue un rôle clé dans les fonctions restauratives impliquées dans la santé cognitive et la mémoire. Le facteur neurotrophique BDNF possède un polymorphisme commun, le Val66Met, associé à une altération de la plasticité synaptique, pouvant potentiellement influencer le SOL et contribuer au risque de la maladie d'Alzheimer. Cependant, peu d'études ont examiné l'association entre le Val66Met et

les caractéristiques des ondes lentes (OL) chez les personnes âgées sans démence. La présente étude visait à examiner la relation entre le Val66Met et les altérations d'OL (amplitude, densité, pente) et de la macroarchitecture du sommeil (incluant la durée totale [TST], %N3). L'étude incluait 133 participants âgés de ≥ 55 ans, cognitivement normaux (CN) ou ayant des troubles cognitifs légers (TCL), génotypés pour le gène BDNF (97 Val/Val, 36 porteurs Met). Une polysomnographie complète permis l'extraction des OL détectées principalement aux électrodes frontales (F3/F4) et de la macroarchitecture. Des ANCOVA ajustées pour l'âge, le sexe et l'index apnée-hypopnée (IAH) ont comparé les groupes. Des analyses stratifiées ont ensuite été faites selon le statut cognitif (CN vs TCL), puis de la présence d'apnée obstructive du sommeil (AOS, IAH ≥ 15). Les porteurs Met ne différaient pas des Val/Val pour les OL frontales ou la macroarchitecture, incluant la durée absolue de N3. Cependant, ils présentaient une densité d'OL pariétales plus élevée. Les porteurs Met-CN avaient une TST réduite comparativement aux Val/Val-CN. Puis, les porteurs Met sans AOS avaient une densité pariétale des OL et un %N3 plus élevés que les Val/Val. Le Val66Met n'était pas associé aux OL frontales, mais pourrait suggérer des mécanismes compensatoires chez les porteurs Met : (1) augmentation de la densité pariétale et (2) maintien de la durée de N3 malgré une TST réduite chez les CN, potentiellement modulés par le statut cognitif et l'AOS.

C3. Cannabis and alcohol show dissociable effects on adolescent functional brain network development and receptor architecture: A longitudinal study

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Introduction: Cannabis and alcohol are the most commonly co-used substances during adolescence, yet their effects on developing brain networks remain poorly understood and often conflated. A key methodological gap is the failure to distinguish session-to-session fluctuations in use from stable individual differences, two sources of variance that may exert fundamentally different effects on the developing connectome. Methods: We followed 151 high-risk adolescents (Neuroventure cohort) across three longitudinal resting-state fMRI sessions, parcellated into 200 nodes (Schaefer Atlas). Signed graph theory metrics like FC strength, clustering coefficient, and participation coefficient were modelled with multilevel mixed-effects models. Cannabis and alcohol were orthogonally decomposed into within-person and between-person components. Network-specific slopes were extracted via emtrends with FDR correction. Spatial correspondence with PET receptor maps (CB1, GABA-A, MU-opioid) was assessed using spin-test permutation via neuromaps. Results: Normative development showed widespread cortical FC strengthening with age which was most pronounced in somatomotor, default, and salience networks. Cannabis and alcohol showed a clean directional dissociation in within-person effects: cannabis was associated with reduced FC strength and disrupted network segregation, while alcohol produced widespread FC increases across all seven cortical networks. Strikingly, both substances reversed direction at the between-person level, suggesting habitual use recruits distinct neural dynamics from acute exposure. Between-person cannabis effects showed preferential spatial correspondence with CB1 receptor density; alcohol effects with GABA-A density, consistent with their primary pharmacological targets. Conclusion: Using a within/between decomposition, we demonstrate that cannabis and alcohol exert dissociable, directionally opposed effects on the adolescent functional connectome with effects grounded in receptor architecture and divergent across timescales of exposure.

C4. Multi-voxel pattern analysis for characterizing functional connectivity underlying grit in cognitively unimpaired older adults at-risk for Alzheimer's disease

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Introduction. Adherence to healthy lifestyle behaviours or to prescribed medication requires perseverance with stamina, and this is captured by Grit, a non-cognitive trait defined as perseverance and passion for long-term goals. Despite predicting cognitive decline and physical, emotional, and social functioning, Grit remains poorly understood and its neural substrates are unknown in cognitive aging. Methods. Sixty-six cognitively unimpaired older adults with a family history of Alzheimer's disease were recruited through the PREVENT-AD longitudinal cohort. Participants completed tests that assess grit and conscientiousness and underwent resting-state functional magnetic resonance imaging (fMRI). Multivariate pattern analyses (MVPA), a rigorous data-driven whole-brain approach, were used to examine if resting-state functional connectivity of connectome-wide voxels were associated with grit scores, controlling for age, sex, pTau217 levels, education years, perceived socioeconomic status, mean framewise displacement, and conscientiousness. Results. Our analyses identified two statistically significant (p-FDR <0.05) clusters in the right middle frontal gyrus and the left superior frontal gyrus underlying grit. Conclusion. Being the first to identify functional neural correlates supporting grit in the aging population while accounting for the variance of conscientiousness, our study provides unique insights into the construct which has important applications in adherence to clinical and empirical neurological interventions as well as in successful aging.

D1. Differential expression of neurotransmitter synthesis genes in aminergic neurons is associated with social roles in ants

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Introduction. Ants exhibit age-related task specialization, or temporal polyethism: young workers are prone to nurse inside the nest, while mature workers forage outside. Biogenic amines, particularly dopamine and octopamine, modulate neural circuits that underlie this behavioral transition. However, the anatomical distribution of aminergic neurons and the expression patterns of their biosynthetic genes remain poorly characterized. Methods. We used RNA fluorescent in situ hybridization to locate the dopaminergic and octopaminergic neurons in the brain, by labeling the transcripts for synthesis enzymes tyrosine hydroxylase and tyramine beta hydroxylase, respectively. Then, we quantified fluorescence intensity, and performed qPCR to compare these genes' expression between young (eclosion to 3 weeks) and mature (>1 month old) workers. Results. Both dopaminergic and octopaminergic neurons were present in the protocerebrum and subesophageal zone. Dopaminergic cells were also found in the optic lobes, whereas octopaminergic neurons were detected in the antennal lobes. Fluorescence intensity analysis revealed lower expression of both genes in mature workers. In contrast, qPCR showed significant age-related differences only in tyrosine hydroxylase expression. Discussion. Aminergic neurons are distributed in regions associated with sensory processing, integration, and social behavior. Octopamine-related transcripts might be transported from the soma to the

neurites in mature subjects. Dopaminergic transcript levels are elevated in young workers, which mainly perform tasks inside the nest.

D2. The ability to structure the world drives the developmental self-organization of behavioral and neural niches

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Brain and cognitive development are driven by a fundamental trade-off: organisms can invest expensive neural resources to adapt to a complex world, or they can actively structure the environment to match their neural representations. While this internalizing-constructing tradeoff is well-theorized, the developmental dynamics that commit organisms and their neural resources to one strategy over the other remain unclear. We present a computational model of cognitive development that optimizes a joint objective of sensory prediction error and environmental maintenance cost. We find that the interaction between prediction and action drives a spontaneous developmental bifurcation. Rather than a mix of strategies, an initially homogeneous population splits into two distinct, stable phenotypes: "internalizers" (high neural complexity, low structuring) and "constructors" (low neural complexity, high structuring). This mirrors phylogenetic divergences seen in nature (e.g., active hunting vs. web-building in spiders) and ontogenetic trade-offs in humans (e.g., complex cognitive maps for navigation vs. cognitive offloading via GPS). We also observe strong developmental canalization: early investment in complex models reduces adaptability when the environment changes. This canalization is alleviated by pruning neurons that are not used, demonstrating neural atrophy facilitates adaptability. These results demonstrate how active structuring creates a self-reinforcing loop between behavior and neural representation, driving the emergence of stable cognitive niches.

D3. Factorial Analysis of Ensemble Representation of Attention and Decision-making in Prefrontal Cortex of Macaque Monkeys

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Macaque monkeys were trained with positive reinforcement to perform a visual search task with separate interleaved 2x2 factorial manipulations of attention and of response decision operations. Attention was manipulated by varying the similarity between a singleton and distractors. Response decision was manipulated by varying the discriminability of a go/nogo cue. The organization and termination rule of the two operations were previously determined using System Factorial Technology (SFT; Lowe et al, 2019). Single-units were sampled in the frontal eye field (FEF) with linear electrode arrays. Here, results are reported from an ensemble level analysis using demixed Principal Component Analysis (dPCA). The ensemble of neurons in FEF embodied reliable representations of singleton location and response decision. The separate manipulations of attention and decision operations influenced the timing of these representations. The dPC for attention and for decision were not entirely orthogonal. The results indicate that attention and decision processes are embodied in overlapping neuronal subpopulations rather than in fully distinct groups. Future work will determine whether variation of the dPC accounts for systematic variation of response times and how single-neuron properties relate to the ensemble representations. We will also compare these representations across different processing architectures characterized by SFT. Supported by NIH RO1-EY08890, NIH P30-EY008126, NSERC RGPIN-2022-04592, and Canada Research Chair.

D4. Organization of neuropeptide systems in the human brain

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Neuropeptides are functionally diverse signaling molecules in the brain, regulating a wide range of basal bodily and cognitive processes. Despite their importance, the distribution and function of neuropeptides in the human brain remains underexplored. Here we comprehensively map the organization of human whole-brain neuropeptide receptors across multiple levels of description, including molecular and cellular embedding, mesoscale connectivity and macroscale cognitive specialization. Using gene transcription as a proxy, we reconstruct a topographical cortical and subcortical atlas of 38 neuropeptide receptors across 14 different neuropeptide families. We find that most neuropeptide receptors are highly expressed either in the cortex or subcortex, delineating an anatomical cortical–subcortical gradient. Mapping neuropeptide receptors onto hypothalamic nuclei, we demonstrate that their gene expression recapitulates fundamental anatomical divisions in the hypothalamus. Neuropeptides preferentially colocalize with metabotropic neurotransmitters, suggesting a system-wide correspondence between slow-acting molecular signaling mechanisms. To investigate the behavioral consequences of distributed neuropeptide systems, we apply meta-analytical decoding to neuropeptide maps and show a spectrum of functions, from sensory-cognitive to reward and bodily functions. Finally, using evolutionary analysis we find extended positive selection for neuropeptides in early mammals, suggesting that refinement of neuropeptides coincides with the emergence of neocortex and higher cognitive function. Collectively, these results show that neuropeptide receptors are highly organized across the human brain and closely intertwined with multiple features of brain structure and function.

E1. Cortical specificity matters: Targeted hindlimb cortical stimulation enhances locomotor recovery after spinal cord injury

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The motor cortex exhibits a somatotopic organization where specific territories modulate hindlimb kinematics. Our previous work showed that intracortical microstimulation (ICMS) delivered to hindlimb representations during locomotion immediately alleviates locomotor deficits associated with spinal cord injury and fosters recovery of voluntary locomotor control. However, the necessity of targeting specific cortical representations remains unclear. Here, we tested whether stimulating the hindlimb-specific cortical territory, compared to non-specific stimulation or no stimulation, differentially affects locomotor recovery in cats with severe thoracic spinal contusion (T10) producing long-term bilateral locomotor deficits. After regaining weight-supported stepping, cats underwent treadmill training (20 min/day) for 3 weeks across three experimental groups: no stimulation (n = 5); ICMS targeting the contralateral hindlimb representation (n = 2); and non-specific ICMS recruiting multiple cortical representations (n = 3). Locomotor recovery was assessed on a flat treadmill, ladder treadmill, and during obstacle avoidance until four weeks post- therapy. We demonstrated that only ICMS specifically targeting the hindlimb representation significantly enhances

voluntary locomotor control, particularly during complex tasks requiring precise paw placement. These results provide preclinical evidence that the functional specificity of cortical stimulation is essential for optimizing recovery, highlighting the importance of precise targeting in neuroprosthetic interventions.

E2. Prefrontal and Parietal Local Field Potentials Employ Different Visuospatial Codes for Reach: A Complex-Valued Network Classification Approach

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Understanding how cortical oscillations coordinate spatial memory and motor planning is a central challenge in systems neuroscience. We tested whether phase–amplitude dynamics in cortical local field potentials (LFPs) encode distributed versus region-specific signals for spatial memory and planning under varying visuospatial conditions. We developed a deep Complex-Valued Neural Network (CVNN; Benevenuto & Piazza, 1992; Georgiou & Koutsougeras, 1992) to decode landmark-dependent spatial states from LFPs recorded in the posterior ventrolateral prefrontal cortex (pVLPFC, 128 channels) and intraparietal sulcus (IPS, 32 channels) of a female rhesus monkey performing memory-guided reaching tasks in which visual landmarks were stable, shifted 8° in one of eight directions, or absent (Lin et al., SfN 2025; Sheldrick et al., SfN 2025). Preprocessed LFPs were transformed into complex-valued time series using the Hilbert transform to preserve phase and amplitude information. Separate CVNNs trained on IPS or pVLPFC signals classified the three landmark conditions with >90% training accuracy and ~51% validation accuracy, significantly above chance (33%). Validation revealed regional specialization: the IPS model performed best for no-landmark trials (82%), whereas the pVLPFC model showed superior performance for shifted-landmark trials (65%). Dual-stream models combining pVLPFC with different IPS recording sites confirmed these effects via region occlusion analysis: removing pVLPFC improved no-landmark classification, while removing IPS improved shifted-landmark classification, with IPS recording location modulating these effects. These findings suggest that IPS preferentially encodes egocentric spatial representations, whereas pVLPFC is more engaged during dynamic landmark conditions, with complementary but potentially competing spatial codes emerging during integration. This research was funded by the Connected Minds Program, supported by the Canada First Research Excellence Fund.

E3. Population structure of reward-induced remapping in the hippocampal CA1

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Hippocampal CA1 cells encode both task structure and environment to support a cognitive map. When task parameters change, place cells remap to support a goal-referenced representation. However, it remains unclear how single-unit remapping of non-place cells affects the population geometry. Here, we ask whether the larger population of non-place neurons remaps in a structured, behaviorally relevant way. To address this,

we re-analyze two-photon recordings of CA1 neurons recorded in virtual track with intra-session reward-zone switches. We isolate non-place cells via a Skaggs information criterion and study the population similarity kernel across space, which characterizes the representational geometry. We show that: 1) the population code exhibits a pronounced orthogonalization of peri-reward locations and remaps to maintain that orthogonalization when reward zone changes. 2) A cross-similarity kernel between pre- and post- reward-switch maps reveals strong shared structure, indicating a reward-relative code. 3) When both reward and environment change, reward-centric constraints persist at the population level but shared structure decreases at the single neuron level. 4) Tensor component analysis applied to trial-wise kernels quantifies the speed of remapping (<10 trials). 5) Finally, stronger peri-reward orthogonalization predicts higher lick ratio. Together, these findings identify a structured, reward-relative, and adaptable geometry of the population code in non-place CA1 neurons, emphasizing the need of a population geometry perspective to understand hippocampal coding.

E4. Early functional immaturity of the reinnervated neuromuscular junction

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While neuromuscular junction (NMJ) is a stable and robust synapse, it can also undergo efficient reinnervation owing to reliable repair mechanisms. This repair appears deficient in Amyotrophic lateral sclerosis (ALS) where NMJs exhibit abnormal denervation-reinnervation cycles. However, the rapid response leading to functional repair remains unexplored, limiting our understanding of the ALS NMJ instability. We posit that an inadequate functional reinnervation contributes to the instability of NMJs in ALS. We developed the Single Axon In-vivo Injury (SAIVI), a method that allows us to damage few axons and denervate 50µm downstream NMJs to precisely monitor in time and space the reinnervation. After a recovery time (3-28 days), muscles and nerves were dissected, and synaptic electrophysiological recordings were performed on reinnervated NMJs and non-injured control nearby NMJs. Confocal imaging assessed structural NMJ innervation. We observed in WT mice that all NMJs were reinnervated at 5 days postinjury (DPI). However, we noticed a maintained synaptic immaturity until 11 DPI while NMJ structure was restored and robust. We interpret this delay of the function gain over the NMJ morphology as a consolidation period. Surprisingly, it was shorter in females. Furthermore, in our ALS mouse model, this period became critical with a worsening of the synaptic function from 5 to 11 DPI. Hence, while morphological NMJ reinnervation is efficient, it depends on a slower process of functional stabilisation that encompasses a critical period, before reaching functional maturity.

F1. Unravelling Non-Canonical Subicular Circuits: Projecting Somatostatin Cells Anatomy and Function in Memory.

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Connectomic studies of hippocampal circuits have traditionally focused on excitatory long-range projections, with inhibitory neurons often assumed to act locally. While most inhibitory neurons in this structure are indeed interneurons, here we uncover a dense, long-range projection from subicular somatostatin (Sst)

expressing neurons to CA1. Using the Synaptag system to label presynaptic sites of Cre-expressing neurons. We found that Sst neurons with soma in the dorsal subiculum heavily innervate the stratum lacunosum-moleculare of CA1, with projection density increasing toward rostral dorsal CA1. To map monosynaptic inputs to subicular Sst neurons, we performed cell-type–specific rabies tracing in Sst-Cre mice. This revealed that the primary input to subicular Sst neurons arises from CA1 pyramidal cells at rostro-caudal levels matching their projection targets. To assess functional connectivity, we combined high-density silicon probe recordings across the subiculum and CA1 with optogenetic manipulation using the bidirectional opsin BiPOLE. Activation of subicular Sst cells strongly inhibited CA1 pyramidal cells and putative inhibitory neurons in the stratum oriens. Together, these findings reveal a reciprocal inhibitory–excitatory loop between CA1 and the subiculum, mediated by Sst neuron projections. Ongoing work leverages this experimental framework to investigate the activity patterns of projecting subicular Sst neurons and their influence on CA1 oscillations and pyramidal cell representations during learning in virtual navigation and trace-fear conditioning tasks.

F2. Traumatic brain injury activates vasopressin and oxytocin neurons of the supraoptic nucleus, causing hyponatremia

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After a traumatic brain injury (TBI), one in three people experience hyponatremia. This electrolyte disorder characterized by low serum sodium causes water to move into tissues, leading to swelling that is particularly dangerous for the brain. However, the mechanisms by which TBI leads to hyponatremia are unknown. Because supraoptic vasopressin (VP) neurons lie in a mechanically vulnerable area, we investigated the hypothesis that TBI inappropriately excites VP neurons, causing excessive VP release, renal water retention and hyponatremia. We also tested if excessive oxytocin (OT) release participates in TBI-induced hyponatremia. Using a preclinical closed head model, we found that TBI lowered serum sodium in male and female mice versus sham injury. This effect was mimicked by pharmacologically activating peripheral VP or OT receptors, and partially rescued by antagonists. c-Fos analysis showed that TBI activates VP and OT neurons of the supraoptic nucleus. Accordingly, patch clamp recordings revealed an increased firing rate in supraoptic VP neurons from TBI mice, with increased intrinsic excitability and facilitated excitatory inputs. We are currently investigating the mechanisms leading to inappropriate activation of supraoptic neurons. Our c-Fos data indicated that supraoptic astrocytes are also acutely activated by TBI, and ex vivo calcium imaging showed that TBI increases astrocytic calcium event duration. We propose that TBI acutely activates supraoptic astrocytes, causing neuronal excitation and inappropriate VP and OT release, which results in hyponatremia.

F3. Spontaneous and miniature excitatory postsynaptic currents in medium spiny neurons of the dorsomedial striatum in Bmal1 knock-out mice.

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Disruption of circadian rhythms has been consistently associated with altered alcohol consumption and increased susceptibility to alcohol abuse. Emerging evidence implicates core clock genes such as Bmal1 as key regulators of alcohol-drinking behavior in both humans and animal models. Our behavioral results indicate that conditional deletion of Bmal1 from medium spiny neurons (MSNs) in the dorsomedial striatum (DMS) significantly decreases voluntary alcohol consumption in female mice versus controls, but not in male

mice. Bmal1 expression in the DMS therefore influences alcohol consumption in a sex-specific manner. To study the underlying mechanisms, we investigated the electrophysiological characteristics of MSNs in the DMS of female Bmal1-knockout mice using whole-cell recordings. Effects of intermittent alcohol exposure on recordings were assessed because long-term alcohol intake can increase mEPSC amplitude and frequency in MSNs. Chronic alcohol exposure alone did not significantly alter the amplitude, frequency, or decay time of spontaneous EPSCs, but it selectively reduced the amplitude and frequency of miniature EPSCs. Notably, the effects of Bmal1 deletion on spontaneous EPSCs were dependent on prior alcohol exposure, and Bmal1 knockout increased the decay time of spontaneous EPSCs in alcohol-naïve animals, but decreased decay time in animals with a history of intermittent alcohol consumption. Results point to synaptic alterations in the DSM associated with disruption of the striatal circadian clock which may be associated with alterations in alcohol consumption.

F4. Role of Astrocytes in Regulation of CRH Neurons and the HPA Axis.

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Neuron-glia interactions are essential to regulate synaptic transmission and plasticity throughout the brain. Astrocytes are active participants in central stress responses across multiple regions, including the cortex, hippocampus, amygdala, and hypothalamus; however, their direct contribution to the modulation of stress-responsive neuronal circuits remains poorly defined. Here, we investigated astrocyte–neuron interactions in the paraventricular nucleus of the hypothalamus (PVN), a key stress-regulatory center containing corticotropin-releasing hormone (CRH) neurons that drive glucocorticoid release. Our study aims to understand the influence of astrocyte activity specifically on CRH neurons in the PVN. To address this knowledge gap, we generated a transgenic mouse line to remove glucocorticoid receptors (GR) in astrocytes by crossing GLAST-creERT with GR-flox mice. CRH^+ neurons were identified using a TdTomato-expressing viral construct, and neuronal excitability, synaptic transmission, and intrinsic membrane properties were assessed using whole-cell patch-clamp recordings in both male and female mice. Preliminary results reveal sex-dependent effects following astrocytic GR deletion. Male CRH^+ neurons exhibit a reduction in excitability, whereas female CRH^+ neurons display a distinct electrophysiological phenotype that is still under investigation. Atypical activity patterns were observed in CRH^+ neurons lacking conventional action potentials, suggesting alternative forms of neuronal activity. Future perspective will be exploring lactate as a potential factor.

G1. Cognitive Trajectories During Cannabis Abstinence in Individuals With Attention-Deficit/Hyperactivity Disorder Symptoms

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Attention-deficit/hyperactivity disorder (ADHD) is a common neurodevelopmental disorder characterized by inattention, impulsivity, hyperactivity, and associated cognitive impairments. Individuals with ADHD are more likely to use cannabis, initiate use earlier, and progress to problematic use compared to those without ADHD. Cross-sectional studies examining effects of cannabis use on ADHD symptoms report mixed findings, with evidence of improvements and impairments on hyperactivity, attention and impulsivity, potentially reflecting effects on underlying cognitive processes. These inconsistencies may reflect methodological limitations, including reliance on unsupervised online self-reports and forum data. Additionally, most studies are cross-

sectional, restricting causal inference, and often fail to account for recency of cannabis use, making it difficult to disentangle acute intoxication, withdrawal, and chronic effects. The current study addresses these limitations using a 28-day cannabis abstinence paradigm, enabling characterization of within-person changes in ADHD symptoms over time. Males and females aged 18–55, with subclinical or clinical ADHD (as defined by the Adult ADHD Self-report Scale) who met criteria for a cannabis use disorder or use cannabis ≥4 times/week and without current psychiatric comorbidities, were assigned to a cannabis abstinence arm (CAN-) or a cannabis as-usual (CAN+) arm. CAN- underwent 28 days of abstinence supported by contingency management, weekly behavioral sessions and biochemically confirmed with urine samples collected twice weekly. Cognitive outcomes were assessed with the Cogstate battery or an open cognitive battery and included measures of attention, executive function, and working memory at baseline and day 28. Linear mixed-effects models will examine within-subject changes over time and between-group differences (Can- vs. -CAN+), including group × time interactions, while controlling for relevant covariates. To date, 28 participants (CAN-, n=20 abstinent; CAN+, n=8 as-usual) have completed the study, with recruitment ongoing. Findings will help clarify the direction of the association between cannabis use and cognition, informing clinical management and public health policy.

G2. Unlocking Antidepressant Response: Early Insights from Astrocyte-Derived Extracellular Vesicle microRNAs

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Major depressive disorder (MDD) exhibits substantial heterogeneity in response to antidepressant treatment, with many patients failing to respond to multiple antidepressants trials or experiencing relapse. This variability highlights the critical need to better understand the biological mechanisms underlying treatment response, and to identify accessible biomarkers for predicting and monitoring treatment outcomes. Astrocytes are active regulators of synaptic, metabolic, and inflammatory processes. Evidence from postmortem and experimental studies show that astrocyte dysfunction contributes to depressive-like

behaviors and antidepressants may act in part through astrocytic signaling pathways. However, directly assessing astrocyte activity in living patients remains challenging. Astrocytes release extracellular vesicles (EVs), which are nanocarriers of molecular cargo as a form of dynamic intercellular communication. These astrocyte-derived EVs (ADEVs) are detectable in peripheral blood, providing a unique minimally invasive window into astrocytic involvement in antidepressant response. To explore whether ADEV miRNAs reflect treatment-related changes, we profiled ADEV miRNAs from plasma samples collected at baseline and after 8 weeks from psychiatrically healthy individuals (n=73) and MDD patients (n=142) undergoing escitalopram treatment. Patients were classified as responders (n=71) or non-responders (n=71) based on symptom improvement. EVs were isolated using size exclusion chromatography followed by immunoprecipitation with antibody against, GLAST, a highly specific marker of astrocytes, to enrich for ADEVs. Small RNA sequencing was performed on miRNA from these ADEVs. After preprocessing and filtering, we identified 39 miRNAs confidently expressed in ADEVs. Longitudinal analyses showed 3 miRNAs: miR-100-5p, miR-125b-5p and miR-222-3p, with differential trajectories between responders and non-responders. Notably, by week 8, expression levels of these miRNAs in responders shifted towards those observed in healthy controls at baseline. Functional enrichment analyses suggest involvement in apoptosis and stress-related pathways. Astrocyte-derived EV miRNAs may capture the biological processes in the brain that underly MDD treatment response and may serve as promising biomarkers for monitoring therapeutic effects.

G3. A Canadian guidance framework for integrating social determinants of health in aging and Alzheimer's disease research

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Dementia risk and outcomes are unevenly distributed across populations in Canada, reflecting inequities driven by social and structural determinants of health (SSDH). Despite their importance across the lifecourse, SSDH are inconsistently measured in aging and dementia research, and no Canadian guidance exists for their systematic integration into research practice. We used a multi-pronged approach combining: (1) participatory engagement with community partners; (2) a review of current SSDH data collection practice across 23 Canadian longitudinal studies of aging; (3) a national public survey (N = 600) to understand the factors that matter most to Canadians; and (4) a Delphi consensus study with experts (n = 27) to prioritize SSDH indicators. Findings from these diverse sources are being triangulated with community partners and knowledge users to co-develop a guidance framework that will be disseminated through an open-access toolkit. Community engagement informed the project from inception, identifying determinants of brain health that were incorporated into later phases. The environmental scan revealed substantial variability in SSDH collection: demographic variables were commonly assessed, whereas economic, environmental, and psychosocial factors were infrequently or only partially captured. Public survey respondents identified income, financial security, and stress as major influences on health — factors that remain inconsistently measured in cohort studies. Experts prioritized a core set of SSDH indicators that only partially overlapped with community and public priorities, revealing important gaps between lived experience and research practice. By identifying misalignment between what matters to communities, the public, and experts and

what is currently measured, this work provides an empirical foundation for a national SSDH guidance framework to support equity-driven dementia research. This project is part of a broader Healthy Brains Healthy Lives (HBHL)-funded initiative aimed at improving the integration of SSDH into Canadian neuroscience research, with the goal of building a more equitable evidence base for brain health across the lifecourse.

G4. Toward parity in brain health: Characterizing neuroprognostication practices after drug-associated cardiac arrest

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Objective: Patients with drug-associated cardiac arrest (DA-CA) are often admitted to the intensive care unit (ICU) and most die after the withdrawal of life-sustaining treatments (WLST) based on predictions of poor prognosis[1]. Neuroprognostication guidelines aim to inform WLST decisions after CA but are used variably in practice[2–4], posing a risk of disparity and inequity in brain injury treatment and health outcomes among critically ill patients. We sought to compare neuroprognostication practices (as guideline adherence) between patients with and without DA-CA, as patients with DA-CA have social vulnerabilities that could influence clinical care. Methods: We identified out-of-hospital cardiac arrests via the British Columbia Cardiac Arrest Registry (Jan. 1, 2023 – Dec. 31, 2024) who: 1) survived to ICU admission; and 2) died after WLST. We classified patients as DA if diagnosed as such by ICU clinicians and otherwise as non-DA. We defined guideline adherence based on the 2023 Canadian Cardiovascular Society Position Statement[5]: 1) the presence of ≥2 poor prognostic findings; and 2) ≥72 hours between return of spontaneous circulation and WLST (approx. time of death). We compared between-groups differences and performed the Chi-squared test for association. Results: We included 171 patients: among DA- and non-DA patients, ≥2 prognostic findings were present in 51/75 (68%) and 53/96 (55%), respectively; and WLST occurred after ≥72 hours in 54 (72%) and 55 (57%), respectively. Overall, prognostication was guideline-adherent for 45 (60%) OD- and 44 (46%) non-DA patients (difference -14%; 95% CI -0.29, 0.007; p=0.066). Conclusion: Adherence to neuroprognostication guidelines prior to WLST is low in both DA- and non-DA-CA, but we did not detect a difference between groups. The heterogeneous practices underscore the opacity in clinical decisions to preform early WLST, especially in the absence of clinical testing per existing recommendations. Standardized approaches to neuroprognostication may promote parity in brain health and outcomes.

H1. Title: Role of neuronal projections from the prelimbic cortex to the nucleus accumbens in cocaine seeking triggered by discriminative cues

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Relapse is the greatest challenge in treating individuals with addiction, with most people returning to drug use within a year of abstinence. Environmental cues play a critical role in promoting relapse. Two classes of environmental drug cues contribute to relapse. First, conditioned stimuli (CS) signal drug delivery after drug-seeking actions (e.g., the throat-numbing sensation after snorting cocaine). Second, discriminative stimuli (DS) signal drug availability before any seeking action is initiated (e.g., accidentally encountering a drug-use partner). Because DSs are present before, during and after drug-seeking responses, they contribute in unique ways to drug use and relapse. Projections from the prelimbic cortex (PrL) to the nucleus accumbens core (NAcc) mediate CS-induced relapse, but their role in DS effects has not been determined. We addressed this here. First, we trained rats to self-administer intravenous cocaine injections under the control of discrete cues indicating cocaine availability (DS+) or unavailability (DS-) and also in the presence of a drug CS. We then examined the extent to which these cues triggered cocaine-seeking behaviour during abstinence, with or without chemogenetic inhibition of the PrL- NAcc pathway. Preliminary results suggest that inhibition of PrL-NAcc neurons accelerated extinction of (DS+)-induced cocaine-seeking behaviour. Should these findings be confirmed in an ongoing study, they would suggest that the PrL-NAcc circuit contributes to DS-triggered cocaine seeking after abstinence, potentially providing new avenues for reducing cue-induced drug craving and relapse in cocaine addiction.

H2. Investigating the anxiolytic effect of exercise on neuronal stress circuits in people with Parkinson's Disease

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Anxiety is often an overlooked and understudied symptom of Parkinson's Disease (PD), a neurodegenerative disorder primarily characterised by motor deficits. Previous research by Zhang et al. (2024) has shown reduced functional activation between the dentate nucleus and the basolateral amygdala in patients with co-morbid anxiety. Their research also showed increased activation and anxiolysis after exercise observed in rats. This study will analyze longitudinal diffusion tensor imaging (DTI) and resting-state fMRI imaging of people with PD who engage in regular exercise to look for increased functional connectivity between the dentate nucleus and the amygdala compared to sedentary individuals with PD. Reduction of anxiety will be tracked through behavioural assessments and correlated with imaging to look for evidence of anxiolysis over time as participants engage in long-term exercise habits. This study is the first to look for exercise-induced activation between the dentate nucleus and the amygdala as a vehicle for anxiety-relief and has the potential to provide evidence for the use of physical activity as a rehabilitation method beyond motor dysfunction.

H3. Loosening the Nets: Psychedelics Unlock Hidden Plasticity

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Introduction: Astrocyte dysfunction has been linked to stress-related psychiatric disorders such as anxiety and depression in both human post-mortem studies and rodent models. Work from the Murphy-Royal laboratory using early-life stress (ELS) paradigms has directly demonstrated astrocyte dysfunction in the amygdala and hypothalamus, establishing astrocytes as promising therapeutic targets. Traditional antidepressants like SSRIs act on neuronal deficits but show limited efficacy and little progress in decades. However, psychedelics provide rapid and durable relief in treatment-resistant depression, though their

mechanisms remain unclear. Our limited understanding suggests that antidepressant effects are elicited via modulation of perineuronal nets (PNN) around parvalbumin (PV) interneurons. As astrocytes are major PNN producers, we hypothesize that psychedelics reopen critical period by enabling plasticity in stress circuits through astrocytic regulation of PNNs. This project sets out to 1) investigate whether psychedelics such as 5-MeO-DMT reverses depression-like behavior in mice and 2) reveal the underlying cellular mechanisms. Methods: We examined the effects of 5-MeO-DMT on PV interneurons and PNN structure in the lateral amygdala. Using a maternal separation-based ELS model, C57BL/6J mice received either 5-MeO-DMT or saline injections, and brains were collected 24 hours later. Tissues were then immunostained for PV and PNNs and then imaged by confocal microscopy. Quantitative analyses included PV cell density, the proportion of PV surrounded by PNN, and the relative surface coverage of PV by PNN. Results: 5-MeO-DMT significantly reduced the proportion of PV surrounded by PNNs and decreased overall PNN coverage, indicating a loosening of extracellular matrix constraints and enhanced structural plasticity. Furthermore, this effect was more pronounced in females, suggesting sex-specific mechanisms. Conclusion: These findings demonstrate that 5-MeO-DMT modulates inhibitory circuits in the amygdala by remodeling PNNs. This supports the hypothesis that psychedelics can reopen critical periods and highlights sex-specific mechanisms that may be leveraged for therapeutic strategies against stress-related disorders.

H4. Imaging Endocannabinoid Signalling in Individuals with Nicotine Dependence

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Nicotine addiction remains a major public health concern, with individuals requiring multiple quit attempts before achieving sustained abstinence. Existing treatments have high relapse rates, underscoring the need for more effective interventions. Advancing our understanding of the neurobiology underlying nicotine addiction may facilitate the development of novel pharmacotherapies. Emerging evidence implicates the endocannabinoid system in the modulation of reward, reinforcement, and withdrawal processes associated with nicotine use. Fatty acid amide hydrolase (FAAH), the enzyme that breaks down the endocannabinoid anandamide, may influence nicotine behaviours, such as seeking, relapse, and withdrawal, as suggested by preclinical evidence showing that its inhibition reduces these effects. However, the relationship between nicotine addiction and FAAH has not yet been examined in the human brain. We hypothesize that FAAH activity will be elevated in individuals with nicotine addiction relative to healthy controls, particularly in brain regions implicated in reward and addiction including the prefrontal cortex and striatum. This study uses positron emission tomography (PET) imaging to examine differences in FAAH activity between individuals with nicotine addiction and healthy controls. Participants undergo PET scans with a selective radiotracer for FAAH, enabling its measurement across the brain. Time–activity curves (TACs), representing tracer concentration over time, are extracted from regions of interest, including the prefrontal cortex and striatum using automated anatomical templates. A kinetic modeling approach is then applied to estimate FAAH activity, indexed by a parameter reflecting irreversible tracer trapping. In parallel, voxel-wise analyses are conducted to identify regional differences between groups. Eleven participants meeting inclusion criteria (moderate nicotine dependence) have completed the study, with recruitment ongoing. This project will be the first exploration of FAAH in the human brain with nicotine addiction. Results may elucidate novel molecular mechanisms implicated in tobacco addiction which can guide the development of more efficacious treatments for this prevalent and deadly disorder.

I1. Title: Optimization of SEEG electrodes implantation guided by MEG source imaging and anatomical constraints: a simulation study

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Approximately one-third of epilepsy patients do not respond to anti-seizure medications, leaving surgical resection of the epileptogenic zone as the only effective option to achieve seizure freedom. In complex cases, Stereoelectroencephalography (SEEG) is used to localize the seizure onset zone (SOZ) through the implantation of electrodes in the brain. Planning SEEG implantation relies on comprehensive presurgical evaluation integrating clinical hypotheses, seizure semiology, video-EEG monitoring, multimodal imaging, and neuropsychological assessment. Despite these advances, SEEG implantation remains a challenging procedure requiring precise multimodal and multidisciplinary coordination. Previous approaches have mainly focused on quantitative implantation strategies that aim to maximize gray matter coverage while avoiding vascular structures when targeting mesio-temporal structure. In this work, we propose incorporating functional constraints derived from magnetoencephalography (MEG) source imaging to enhance coverage of the presumed epileptogenic zone and its spatial extent. Our approach is based on reconstructing MEG sources from epileptic spikes and estimating virtual SEEG potentials from these sources. To validate this method, we analyzed 30 seizure-free patients from a multicentric study, for whom SEEG electrode locations were available and the SOZ had been identified and reconstructed as a three-dimensional volume. After projecting all SOZ volumes onto a common anatomical template, we generated realistic simulations of MEG epileptic spikes for each SOZ localization. This framework enabled us to evaluate how MEG-derived source information could guide optimal SEEG implantation strategies, compared with the clinically implanted electrodes considered as ground truth.

I2. Combined cortical and peripheral stimulation alleviates locomotor deficits in a feline model of incomplete spinal cord injury

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After a spinal cord injury (SCI), disrupted interactions between supraspinal, sensory, and spinal circuits result in persistent locomotor deficits, such as paw dragging. To restore these interactions, we employed electrical

stimulation to engage neural circuits in real time, with the aim to assist movement. We recently demonstrated that motor cortex stimulation increases step height and reduces paw dragging in rodent and feline models of incomplete SCI. Our preliminary findings also suggest that peripheral stimulation similarly alleviates locomotor deficits. Here, we hypothesized that combining cortical and peripheral sensory stimulation would synergistically engage residual motor circuits to maximize motor efforts. In a feline model, we implanted electrode arrays in the hindlimb motor cortices, cuff electrodes around the superficial peroneal nerves innervating the foot dorsum, and electromyographic electrodes in hindlimb muscles. Cats then received a spinal contusion at T10, paralyzing both legs. Prior to and after SCI, we assessed the ability of cortical and/or peripheral stimulation to modulate locomotion on a treadmill and facilitate motor evoked potentials. We further characterized how the precise timing and amplitude of these stimulations influenced kinematic parameters and EMG activity. Our preliminary data show that combined stimulation enhances step height, reduces dragging, and increases motor evoked potentials more effectively than either approach alone. These findings highlight the potential of multi-level stimulation strategies for assisting movement after SCI.

I3. Exploring neural signatures for the development of chronic postsurgical pain using electroencephalography

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ABSTRACT: Chronic postsurgical pain (CPSP) impacts millions of patients worldwide, and particularly up to 50% of patients undergoing thoracic surgery. Current preventative efforts and pain management strategies remain ineffective due to an incomplete understanding of the risk factors and maladaptive neurophysiological mechanisms underlying its development. To address this gap, we aimed to investigate potential neuromarkers associated with the development of CPSP using electroencephalography (EEG), a valuable tool that has shown predictive and diagnostic value for other chronic pain conditions. Patients undergoing thoracic surgery completed EEG assessments 2-3 weeks pre-surgery and 3 months post-surgery. Each assessment included resting-state EEG recordings under eyes-open and eyes-closed conditions. Preliminary analyses will present baseline differences in resting-state power across various frequency bands between patients who developed CPSP versus those who did not. Such an investigation is an important step towards informing preventative approaches and targeted therapies to reduce the burden of CPSP. Additionally, this investigation offers a unique opportunity to study the transition from a pain-free to a chronic pain state, which holds value for understanding the underlying neurophysiology that may increase susceptibility to chronic pain, a condition that impacts nearly 20% of adults worldwide.

I4. Cortical switching dynamics shape delta activity under propofol anesthesia

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Delta-frequency activity is a defining feature of brain states associated with reduced or absent consciousness, like NREM sleep and general anesthesia. In sleep, delta activity shows slow oscillations (SOs, <1Hz) and slow waves (SWs, 1-4Hz). Recent work introduced transition frequency (speed of negative-to-positive deflection) as an amplitude-independent marker of cortical state switching, revealing slow and fast switching SWs during sleep. Whether similar dynamics are equally present under general anesthesia remains unclear. High-density EEG (128-channel) was recorded for ≥5 min during stable propofol anesthesia in eight adults before surgical incision. Propofol was administered via target-controlled infusion, targeting 2.0μg·mL^{-1} and adjusted to maintain a BIS of 45–55 (increments of 0.2mcg/ml). Delta events were detected per channel, classified as SOs/SWs, and transition frequency was computed. Transition frequency distributions differed importantly between wave types: SOs exhibited a largely unimodal distribution with limited variability (IQR=0.252 Hz), mostly concentrated under 1Hz, whereas SWs showed a broad, bimodal distribution (IQR=1.467 Hz), with a separation around 1.7Hz. These findings indicate that anesthetic delta activity is structured by distinct transition-dynamic regimes with slow and fast switching SWs clearly present under propofol anesthesia. This suggests that switcher dynamics are not exclusive to sleep homeostasis, but may reflect intrinsic modes of cortical switching that persist during pharmacologically induced unconsciousness.

J1. From synaptic instability to serum biomarkers: NMJ-derived protein change in ALS

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The lack of reliable biomarkers has hampered therapeutic development in amyotrophic lateral sclerosis (ALS), a fatal neurodegenerative disease affecting motor neurons. Common in all ALS cases, the denervation of neuromuscular junctions (NMJs) is a process that begins long before symptoms onset and characterized by prolonged cycles of denervation and reinnervation. We therefore hypothesized that this NMJ dynamism represents a valuable source of biomarkers that closely reflect disease state and progression. Proteomic analysis comparing resistant and vulnerable muscles and disease progression in SOD1^{G37R} mouse model led to the identification of many NMJ-associated candidate proteins. We first focused on laminin β2 (LAMβ2), an NMJ-specific protein essential for structural organization. Serum LAMβ2 levels were significantly reduced at the pre-onset stage. In contrast to neurofilament-light chain (NfL), a widely used biomarker of axonal damage, LAMβ2 levels were unchanged following nerve injury, indicating disease specificity. Notably, LAMβ2 reduction was detectable as early as postnatal day 100, more than 300 days before symptom onset, where

NfL was unchanged, making LAMβ2 as the earliest potential measurable biomarker. We next investigated synapse-associated protein 1 (SYAP1), involved in synaptic plasticity. Serum SYAP1 levels were significantly reduced at disease onset compared with both wild-type and pre-onset mice. Together, these findings identify LAMβ2 and SYAP1 as novel potential NMJ-biomarkers that could improve early diagnosis and disease monitoring in ALS.

J2. Investigating tumour-oligodendrocyte lineage cell interactions in invasive melanoma brain metastases

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Approximately 20-40% of metastatic cancer patients develop brain metastases (BrM). Unfortunately, these patients suffer from poor outcomes, diminished quality of life and approximately 60% of patients that undergo BrM resection recur within 1 year. Our group described histological growth patterns associated with recurrence, where highly invasive (HI) BrM are more likely to recur, compared to minimally invasive (MI) BrM. Cancer cell invasiveness can be driven by crosstalk with the microenvironment, through secreted factors from brain cells or from cancer cells that colonize the brain. We have profiled the secretome of HI and MI patient-derived xenograft BrM using human- and mouse-specific multiplex ELISA. This screen revealed high levels of platelet-derived growth factor A (PDGF-AA) in HI melanoma BrM. Importantly, overexpression of PDGF-AA in MI melanoma cells accelerated intracranial tumour growth and shortened survival in vivo. Conversely, PDGF-AA knockout in HI melanoma cells diminishes intracranial tumour growth and extends survival in vivo. Despite several studies reporting autocrine PDGFRα signaling downstream of PDGF-AA in aggressive glioblastomas, we demonstrate that such a mechanism is not operative in our models. Consistent with reports of PDGF-AA's role as a chemoattractant and pro-proliferative factor for oligodendrocyte precursor cells, we observe the accumulation of olig2-positive cells at the brain-tumor interface of PDGF-AA-expressing melanoma brain tumours. Considering these results, we are now investigating the mechanisms through which oligodendrocyte lineage cells may impact aggressive melanoma BrM growth. Brain microenvironmental remodeling factors such as PDGF-AA are important to investigate as potential druggable targets in BrM. Should PDGF-AA be involved, clinically available PDGFRα inhibitors could be a potential treatment option to disrupt such crosstalk in individuals with recurring BrM.

J3. Development of a neuro-immune co-culture model to better understand the mechanisms involved in the neuronal death in Parkinson's disease

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The main motor symptoms of Parkinson's disease (PD) are caused by the loss of dopaminergic neurons (nDA) in the substantia nigra. It has also been observed that PD patients present signs of inflammation, with

lymphocyte infiltration into the brain and activation of the microglia. Even growing evidence links inflammation to the onset of the disease, the underlying mechanisms are unclear. Loss-of-function mutations of the Parkin gene are associated with early-onset forms of PD. This protein act as key regulators of innate immune responses, suppressing antigen presentation by major histocompatibility complex class I (MHC-I) on peripheral antigen-presenting cells (APCs). The loss of Parkin consequently leads to the activation of $CD8^+$ T cells, which may contribute to the impairment of nDA. In the brain, microglia function as APCs. We hypothesize that, like their peripheral counterparts, microglia have an exacerbated pro-inflammatory profile in the absence of Parkin and in response to pathogen-derived signals. Furthermore, we suggest that this increased activation impacts nDA, possibly through interactions with cytotoxic T cells. Our preliminary results from co-culture experiments show that $CD8^+$ T cells are sufficient to induce around 40% nDA loss when cells received an inflammatory stimulus. Interestingly, activated microglia accentuates this loss to around 50% in WT and 80% in Parkin KO. So far, our results suggest that only some of the physiological properties of Parkin-deficient microglia are altered under inflammatory conditions. Indeed, while a similar elevation of MHC-I and a comparable capacity to phagocytose latex beads were observed between the two genotypes, Parkin-deficient microglia secrete more pro-inflammatory cytokines and chemokines. In current experiments, we are investigating the specific mechanism(s) leading to neuronal loss, particularly by live microscopy. The results of this study will allow us to better understand the implication of microglia in regulating the vulnerability of nDA in genetic forms of PD.

J4. Neuroprotective Effects of Remote Ischemic Conditioning in a Mouse Model of Repetitive Mild Traumatic Brain Injury

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Traumatic brain injury (TBI) is a leading global cause of disability. Repetitive mild TBI (r-mTBI) is associated with persistent neuroinflammation and neurodegeneration, yet no treatments exist. Remote ischemic conditioning (RIC) is a non-invasive intervention shown to reduce neuroinflammation and blood–brain barrier disruption, but its effects in r-mTBI are unknown. This study evaluated the effects of RIC on r-mTBI-induced motor and cognitive dysfunction, neuroinflammation, and molecular changes. Thirty-two male C57BL/6 mice were randomized into four groups: sham/no RIC, sham/RIC, r-mTBI/no RIC, and r-mTBI/RIC. RIC consisted of four cycles of 5-min ischemia and reperfusion applied daily to the hindlimbs for 14 days. r-mTBI was induced using a Lateral Impact Model, with one mTBI administered daily for 5 consecutive days. Neurobehavioral testing was performed 1-3 days post-injury. Neuroinflammation was assessed by immunohistochemistry for astrocytic and microglial markers in the motor cortex and hippocampus. Cytokine/chemokine levels were quantified from whole-brain homogenates, and proteomic profiling was performed using liquid chromatography-tandem mass spectrometry. r-mTBI increased foot slips on the beam walk compared to controls ($p<0.05$), an effect reduced by RIC ($p<0.05$). RIC also decreased microglial density and Iba1 mean fluorescent intensity in the motor cortex ($p<0.05$). Cytokine analyses showed significant changes in IL-1α, IL-

2, IP-10, and MIP-2. Proteomic analyses are ongoing. These findings identify RIC as a potential promising prophylactic strategy for r-mTBI.

K1. The Effects of D-amphetamine Maintenance Treatment During IntA Cocaine on Discriminative Stimulus- and Conditioned Stimulus-Induced Cocaine Seeking Behaviour

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Drug addiction is a global public health problem. For cocaine addiction, there are currently no approved medications to reduce drug use and relapse. One promising strategy is d-amphetamine maintenance, which can reduce cocaine use in both laboratory animals and humans. However, its effects on cue-induced cocaine cravings and relapse are unknown. This is an important question to address, as drug cues are amongst the most effective triggers of drug cravings and use. Here, we will test whether d-amphetamine treatment reduces cue-triggered cocaine seeking. Female rats learned to press a lever to self-administer intravenous cocaine during 4-h intermittent-access sessions, alternating between 5-min cocaine ON periods signaled by a discriminative stimulus (DS+) and 25-min cocaine OFF periods (25 min) signaled by a DS-. Each self-administered infusion was also paired with a 5-second conditioned stimulus (CS) presentation. Thus, the DSs and CS became cocaine-associated cues. During this period, half the rats received d-amphetamine maintenance treatment via sub cutaneous osmotic minipump. After D-amphetamine treatment cessation and two weeks of forced abstinence, rats will receive a cue-induced cocaine-seeking with response-independent cue presentations. Lever presses (producing no cocaine or cues) indexed cocaine seeking. If d-amphetamine reduces cue-triggered cocaine-seeking, d-amphetamine rats should show suppressed lever-pressing behaviour on the test day compared to controls. Whatever the outcome, the results will inform about the potential for d-amphetamine maintenance in reducing cue-induced craving and relapse in cocaine addiction.

K2. Machine Learning-Enhanced Surface-Enhanced Raman Spectroscopy for Neurotransmitter Detection and Quantification

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Understanding neurotransmitter dynamics is essential for advancing neuroscience and developing real-time sensing tools. In this work, we present a machine learning-assisted surface-enhanced Raman spectroscopy (SERS) platform for the detection and quantification of key neurotransmitters in complex environments. The approach combines plasmonic nanostructures with advanced data-driven models to improve sensitivity, specificity, and quantitative accuracy. High-dimensional Raman spectral data were acquired for multiple neurotransmitters, including dopamine, glutamate, and gamma-aminobutyric acid (GABA), under varying concentrations and experimental conditions. Preprocessing techniques were applied to reduce background

interference and enhance spectral features. Supervised machine learning models, including convolutional neural networks and regression algorithms, were developed to classify and quantify analytes from spectral signatures. The proposed framework enables simultaneous identification and concentration prediction with high accuracy, even in the presence of overlapping spectral features. Additionally, model performance was evaluated using cross-validation and independent test datasets to ensure robustness and generalizability. The integration of SERS with machine learning provides a scalable approach for analyzing complex biochemical systems. This work highlights the potential of combining spectroscopy and artificial intelligence for neuroscience applications, including chemical sensing and optophysiology. The developed platform offers a step toward real-time, label-free monitoring of neurotransmitters, which may contribute to improved understanding of neural activity and the development of next-generation biosensing technologies.

K3. Re-examining ATP and Norepinephrine Signalling in Sympathetic Neurotransmission

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Adenosine triphosphate (ATP) and norepinephrine are co-released by sympathetic nerves to modulate signalling in tissues like blood vessels, but how they are differentially released at synaptic sites remains unclear. The vesicular nucleotide transporter (VNUT) and the vesicular monoamine transporter 1 (VMAT1) load vesicles with adenosine triphosphate (ATP) and norepinephrine (NE), and identifying their vesicle localization is key to understanding co-transmission. Understanding these mechanisms may reveal new strategies to selectively tune sympathetic signalling, with potential therapeutic relevance for drug-resistant hypertension, diabetes-related vascular disease, chronic stress, and autonomic disorders. While sympathetic neurons present difficulties in culture, pheochromocytoma cells (PC12) provide a genetically modifiable model for studying sympathetic co-transmission. Immunofluorescence was used to examine ATP and NE transporter localization in two PC12 lines (adherent and non-adherent) differentiated with nerve growth factor. Relevant genes for catecholamine and ATP signalling were quantified by droplet digital PCR (ddPCR). Novel GRAB fluorescent sensors, which bind agonists, were used to monitor real-time transmitter release from individual vesicles. In both PC12 lines, imaging showed that the ATP and norepinephrine vesicle transporters exhibited minimal colocalization. The ATP vesicle transporter also showed minimal colocalization with the vesicle marker synaptotagmin-1. ddPCR revealed low expression of dopamine-ß hydroxylase (DBH), the vesicular enzyme that converts dopamine to norepinephrine, in both PC12 lines. Live imaging with GRAB sensors showed that PC12 cells exhibited vesicular ATP release, while vesicular norepinephrine release was not detected, consistent with the low DBH expression observed. These findings suggest that ATP and catecholamines are packaged into distinct vesicle populations in PC12 cells. Additionally, limited DBH expression and norepinephrine release suggest that dopamine may be a more informative measure of vesicular catecholamine release in this model. Together, this work provides a framework for using GRAB sensors to identify drugs that selectively reduce ATP and dopamine release in diseases associated with sympathetic overactivity.

K4. Phasic axonal dopamine release appears to involve mechanisms beyond synaptotagmin-1

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Parkinson's disease (PD) is characterized by the degeneration of dopaminergic neurons (DAn), resulting in motor deficits. Dopamine (DA) release in the striatum is tightly regulated by vesicular calcium sensors, such as synaptotagmin-1 (Syt1). Previous studies in mice have shown that Syt1 knockout (Syt1KO) significantly reduces DA release after a single stimulation, without altering observable motor behaviors or the level of DA in the striatum. Given that DAns display spontaneous firing (1–5 Hz) and burst activity (10–50 Hz), we hypothesized that these firing modes could sustain residual phasic DA release in Syt1KO mice. To test this hypothesis, we performed cyclic voltammetry recordings on striatal slices from WT and Syt1KO mice following single stimuli or trains (burst activity at 6Hz/10Hz/50Hz). The impact of applying continuous, pacemaker-like stimulation (1Hz/2Hz/5Hz) prior to release measurements was also evaluated. DA release induced by acute stimulation was reduced by 90% in Syt1KO mice. However, DA release evoked by burst firing was reduced much less extensively. Pacemaker-like activity attenuated acutely evoked DA release in both WT and KO mice, with a twofold smaller effect in KO mice. These results are globally compatible with the hypothesis that while DA release evoked by single stimuli is dependent mainly on Syt1, release evoked by higher frequencies of stimulation also implicates other exocytosis calcium sensors. We further hypothesize that DA-dependent behaviors are sustained by multiple modes of DA secretion.

L1. Health-related quality-of-life in patients with pediatric low-grade glioma: Findings from the initial phase of the TRAM-01 Study

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Background: Patients with pediatric low-grade gliomas (PLGG) are living longer at the expense of a compromised health-related quality of life (HRQoL). These patients frequently report poorer physical and psychosocial health compared with their healthy peers, and parent proxy reports similarly indicate reduced HRQoL in this population. As such, HRQoL is recognized as a critical survivorship outcome, but it remains insufficiently explored in phase II clinical trials. To address this gap, the TRAM-01 study prospectively evaluates the impact of trametinib on HRQoL in patients with PLGG. Methods: Patients (N=114) completed HRQOL assessments in the pre-treatment phase of the TRAM-01 study using the PedsQL generic core scales and brain tumor module. Child self-reports were obtained for patients aged ≥5 years, and parent proxy-reports for children aged ≥2 years. HRQOL was examined across four clinical groups: (1) NF1-associated progressive or refractory glioma; (2) NF1-associated plexiform neurofibroma; (3) progressive or refractory glioma with KIAA1549–BRAF fusion; and (4) progressive or refractory glioma with MAPK/ERK pathway activation. Results: HRQoL was impaired across all subgroups, with overall PedsQL scores ranging from 70.0 to 82.7, reflecting moderate but clinically meaningful reductions prior to treatment. Generic Core scores (74.4±5.9) were similar to Brain Tumor Module HRQOL scores (76.1±2.7), highlighting the specific burden of their neurological disease. Patients with NF1, particularly those with plexiform neurofibromas, demonstrated

lower baseline HRQoL compared with non-NF1 PLGG patients, notably in physical functioning and pain-related domains. Across all groups, parent proxy-reports systematically yielded lower HRQoL scores compared with the child self-reports, with mean differences ranging from 3 to 8 points. Conclusion: Patients with PLGG have impaired HRQoL at baseline, before starting their treatments. Discrepancies between child self-reported and parent proxy-reported HRQoL were identified, consistent with existing literature. These findings highlight the importance of HRQoL assessment in pediatric neuro-oncology clinical trials to provide supportive care.

L2. Scalable 3D longitudinal tumor monitoring in pediatric low-grade glioma using a Slicer-embedded nnU-Net

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Background: Pediatric low-grade glioma (PLGG) responses are typically measured using 2D assessments, but irregular lesion morphology presents a significant clinical challenge. 3D volumetric analysis could improve monitoring, but manual segmentation is labor-intensive and limits scalability. Methods: We analyzed MRIs from a clinical trial (TRAM-01-NCT03363217) of patients with refractory or recurrent PLGG treated with trametinib for 18 months. We developed a 3D Slicer extension utilizing a 3D full-resolution nnU-Net architecture. The model was trained on 132 expert-confirmed T2-FLAIR studies of PLGG with BRAF fusion. To evaluate clinical utility, we tested a personalized longitudinal strategy: for a patient's timeline, n scans were used for training and m reserved for testing. This approach allows the model to learn patient-specific anatomical baselines to ensure consistent longitudinal tracking. Results: A total of 445 MRIs were annotated. For a representative patient, training on a subset of the available scans and testing on the rest yielded high predictive value (Dice score 0.95–0.98), indicating strong intra-patient utility. Preliminary testing on an unseen PLGG subgroup (n=17) not included in training showed strong generalization (mean Dice ≈ 0.78; IQR 0.66–0.88). Automation significantly improved workflow, reducing median processing time from around 25 minutes per scan manually to 1–2 minutes with the tool. Conclusion: A Slicer-integrated nnU-Net provides a practical, expert-supervised solution for scalable 3D longitudinal volumetry. This demonstrates that full-resolution models effectively capture patient-specific progression. Future work will extend training to all TRAM-01 groups and implement a longitudinal strategy using prior segmentations as a reference to improve predictions for a follow-up study and inference time.

L3. Bio-imaging strategy to follow the infectious pathway of adeno-associated viruses inside neurons

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Adeno-associated viruses (AAVs) are indispensable viral vectors **for** fundamental and clinical research. In fact, AAVs are composed of a single-stranded DNA contained in a 25 nm capsid. These two components can

be modified to create recombinant AAVs (rAAVs), which can then be designed for a specific use. For example, some rAAVs allow the delivery of optogenetic tools and render the study of in vivo mechanisms possible. Other rAAVs can cross the blood brain barrier and represent an interesting avenue for central nervous system gene therapy. However, while rAAVs enable a panoply of applications, the transduction of the viral particle itself remains very intricate and underknown. There is a critical need to further our understanding of this tool to optimize its use and therefore lead to the development of highly efficient viral vectors. Thus, the goal of this project is to develop a bio-imaging and analysis method to follow the journey of rAAVs throughout cells in real time. First, AAV capsids are labelled with a fluorophore via click chemistry. This unique AAV labelling strategy was optimized to minimize the impacts on the viral capsid integrity and its transduction properties. Second, subcellular regions like the cell membrane and the nuclear envelope are tagged to create checkpoints during the rAAV transduction. Neurons will be the main cells of interest considering AAVs' central nervous system gene therapy perspective. Third, the monitoring of the fluorescently labelled rAAVs infection process is made using real-time videorate fluorescence microscopy. Fourth, analysis and quantification of the AAV transduction will then be realized to obtain unprecedented data on this pathway. Furthermore, a wide variety of cellular models and AAV serotypes are compatible with the developed labelling methods, which will open the door to further studies on this viral vector and contribute to its widespread and optimized use.