PROGRAMME COMPLET – MERCREDI LE 10 DECEMBRE 2025

Amphithéâtre Ernest-Cormier (K-500) et hall d'honneur
Pavillon Roger-Gaudry, 2900 Boul. Édouard-Montpetit
Montréal, QC Canada, H3T 1J4, 4e étage

08h00 Accueil des participants

08h30 Mot de bienvenue
Alexandre Prat, directeur du département de neurosciences

08h40 Séance de présentations orales
Modérateur : Ossama Ghenissa

08h40 **Haritha Desu**, stagiaire postdoctorale (équipe Larochelle)
« CNS myeloid cell activation in chronic MS and EAE is sustained by ICAM-1 mediated interactions with T cells»

08h55 **Mathias Guayasamin**, étudiant au doctorat (équipe Murphy-Royal)
« Astrocytes integrate noradrenaline inputs to modulate fear memory specificity»

09h10 Conférencière d'honneur :
Marina Martinez, **professeure agrégée en neurosciences**
« Remarcher grâce à la neurostimulation: preuves de concept précliniques »

09h50 Pause et première séance de présentations par affiche (#A1 à A35)

11h15 Séance de présentations orales
Modératrice : Lucia Pizzoccaro

11h15 **Margaux Brin**, étudiante au doctorat (équipe Flamier)
« Les mutations du gène MECP2 perturbent les cils primaires et l'excitabilité neuronale dans le syndrome de Rett »

11h30 **Simon Alvado**, étudiant au doctorat (équipe Robitaille)
« Delayed neuromuscular junction reinnervation: a critical period in amyotrophic lateral sclerosis »

11h45 Conférencier d'honneur :

Éric Samarut, professeur adjoint en neurosciences
« Étude des bases moléculaires sous-jacentes aux troubles du mouvement reliés à RFC1 »

12h25 Lunch

13h45 Séance de présentations orales
Modératrice : Scanny Nzie

13h45 **Isaac Alejandro Vidal Paredes**, étudiant au doctorat (équipe Di Polo)
« Stress-induced mitochondrial fragmentation in endothelial cells disrupts blood-retinal barrier integrity causing neurodegeneration »

14h00 **Marie Filiatrault,** étudiante au doctorat (équipe Rahayel)
« Caractérisation de l'atrophie et des bases transcriptomiques des phénotypes de conversion dans le trouble comportemental en sommeil paradoxal isolé »

14h15 **Isabel Sarzo Wabi**, étudiante au doctorat (équipe Bou Assi)
« Seizure detection using miniaturized electromyography-accelerometry sensors »

14h30 **Lucia Pizzoccaro**, étudiante au doctorat (équipe Amilhon)
« Serotonergic inputs to the ventral hippocampus underlie sex differences in anxiety »

14h45 Pause et deuxième séance de présentations par affiche (#A36 à A76)

16h10 Conférencier d'honneur :

Anthony Flamier, professeur adjoint en neurosciences
« IPS-based modeling of neurodevelopment »

16h50 Remise des prix et honneurs

***** Événement soutenu financièrement par la Chaire Power Corporation du Canada en neurosciences de l'Université de Montréal *****

Liste de toutes les présentations orales et par affiche

Présentateurs/présentatrices	Type de présentation	Numéro	Séance d'évaluation
Haritha Desu	orale	O1	8h40 à 14h45
Mathias Guayasamin	orale	O2	8h40 à 14h45
Margaux Brin	orale	O3	8h40 à 14h45
Simon Alvado	orale	O4	8h40 à 14h45
Isaac Alejandro Vidal Paredes	orale	O5	8h40 à 14h45
Marie Filiatrault	orale	O6	8h40 à 14h45
Isabel Sarzo Wabi	orale	O7	8h40 à 14h45
Lucia Pizzoccaro	orale	O8	8h40 à 14h45
Odile Desaulniers	affiche	A1	matin
Scanny Chancelle Nzie	affiche	A2	matin
Loik Holdrinet	affiche	A3	matin
Jérémy Smili	affiche	A4	matin
Alex Rodrigue	affiche	A5	matin
Anais Rourre	affiche	A6	matin
Nathan Chochon	affiche	A7	matin
Nine Collomb	affiche	A8	matin
Maika Doré	affiche	A9	matin
Behiye Sanliturk-- ANNULATION	affiche	A10	matin
Sarra Chebaane	affiche	A11	matin
Emma Morgan	affiche	A12	matin
Marc-Antoine Gobeil	affiche	A13	matin
Louise Benhamou	affiche	A14	matin
Julie Le Tallec	affiche	A15	matin
Ala Ferdi	affiche	A16	matin
Quin Lagden	affiche	A17	matin
Farhan Jahan	affiche	A18	matin
Julia Price	affiche	A19	matin
Clara Vo-Dignard	affiche	A20	matin
Nour Eltaani	affiche	A21	matin
Adrien Rihoux	affiche	A22	matin
Candice Trouba	affiche	A23	matin
Anne-Catherine Chouinard	affiche	A24	matin
Justine Fortin-Houde	affiche	A25	matin
Marie-Josette De Medeiros	affiche	A26	matin
Willy Nguyen	affiche	A27	matin
Alessandra Ciancone	affiche	A28	matin
Soraya Rahimi	affiche	A29	matin
Perrine Coquelet	affiche	A30	matin
Daniel Alejandro Galindo Lazo	affiche	A31	matin

Présentateurs/présentatrices	Type de présentation	Numéro	Séance d'évaluation
Raphaëlle Denis	affiche	A32	matin
Margaux Asclipe	affiche	A33	matin
Marie Veziano	affiche	A34	matin
Nitya Khetarpal	affiche	A35	matin
Joseph Lefevre Lopez	affiche	A36	après-midi
Léa Bastien	affiche	A37	après-midi
Ayman Driouich	affiche	A38	après-midi
Yousra Lecheheb	affiche	A39	après-midi
Justine Gromaire	affiche	A40	après-midi
Alexis Doucet	affiche	A41	après-midi
Kathleen Ngo	affiche	A42	après-midi
Jessica Zevounou	affiche	A43	après-midi
Thomas Nicodemo Arrieta	affiche	A44	après-midi
Clara Ireland	affiche	A45	après-midi
Marilie Chalifoux	affiche	A46	après-midi
Salma Attebaa	affiche	A47	après-midi
Cederick Montplaisir	affiche	A48	après-midi
Alex Tchung	affiche	A49	après-midi
Tanya Leduc	affiche	A50	après-midi
Ali Gharbienne	affiche	A51	après-midi
Fanny Nobilleau	affiche	A52	après-midi
Mariam Chougharí	affiche	A53	après-midi
Marion Guillon	affiche	A54	après-midi
Soraya Paquereau-Gaboreau	affiche	A55	après-midi
Théo Rabin	affiche	A56	après-midi
Claudie Beaulieu	affiche	A57	après-midi
Chiara Bramati	affiche	A58	après-midi
Bryce Rampal	affiche	A59	après-midi
Diala El Masri	affiche	A60	après-midi
Corinne Leveau	affiche	A61	après-midi
Ossama Ghenissa	affiche	A62	après-midi
William Gauthier-Naud	affiche	A63	après-midi
Lovatiana Andriamboavonjy	affiche	A64	après-midi
Rishabh Singhal	affiche	A65	après-midi
Lisa Bianchin	affiche	A66	après-midi
Joaquim Streicher	affiche	A67	après-midi
Inoussa Balma	affiche	A68	après-midi
Maria-Isabel Carreno-Munoz	affiche	A69	après-midi
Amirhossein Jahani	affiche	A70	après-midi

Présentateurs/présentatrices	Type de présentation	Numéro	Séance d'évaluation
Vranda Garg	affiche	A71	après-midi
Amandine Even	affiche	A72	après-midi
Page Hayley	affiche	A73	après-midi
Ralph Saber	affiche	A74	après-midi
Daphné Citherlet	affiche	A75	après-midi
Camila Cabarcas Arrieta	affiche	A76	après-midi

RÉSUMÉS COMPLETS

O1 –

CNS myeloid cell activation in chronic MS and EAE is sustained by ICAM-1 mediated interactions with T cells

Haritha L. Desu (1,2), Jennifer Auvergnon (1,2), Megan Krysak (1,2), Renaud Balthazard (1,2), Victoria Mamane (1,2), Tayma S. Kabakibo (1,2), Qiao-Ling Cui (3), Bettina Zierfuss (1,2), Audrey Daigneault (1,2), Sandra Larouche (1,2), Clara Margarido (1,2), Vanessa Omana (3), Wendy Klement (1,2), Jack Antel (3), Jo Anne Stratton (3), Sami Obaid (1), Alexandre Prat (1,2), Nathalie Arbour (1,2), Catherine Larochelle (1,2)

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Chronic neuroinflammation causes neuroglial injury and disrupts repair in the central nervous system (CNS) of people with Multiple Sclerosis (pwMS). CNS myeloid cells and pro-inflammatory T cells accumulate at the edges of chronic active lesions; however, the contribution of their direct cell-cell interaction to CNS compartmentalized inflammation remains unclear. Cell adhesion molecules, such as intercellular adhesion molecule-1 (ICAM-1), mediate immune cell contact and signaling, but their role in T cell-CNS myeloid cell interactions during chronic MS is unknown. This study investigates how ICAM-1-dependent T cell-CNS myeloid cell interactions drive CNS myeloid activation in MS and its animal model, experimental autoimmune encephalomyelitis (EAE).

We observed T cells in direct contact with CNS myeloid cells in both MS and EAE CNS tissue by immunofluorescence. In vitro, using single cell RNA sequencing, we found that both human primary CNS myeloid cells shifted toward a pro-inflammatory profile after co-culture with autologous T cells. In silico analyses identified ICAM-1 as a candidate mediator of this interaction. Furthermore, circulating T cells from pwMS, especially in progressive MS, had elevated ICAM-1 expression compared to controls, with ICAM-1^{+} T cells further enriched in MS and EAE CNS tissue. Ablation of ICAM-1 on T cells in mice (CD4cre:ICAM-1fl/fl) led to improved clinical scores during chronic EAE in both sexes, accompanied by fewer immune cells in the CNS, limited CNS myeloid cell activation, lower serum neurofilament light chain levels, and reduced demyelination compared to littermate controls. Moreover, ICAM-1 blockade on human T cells reduced CNS myeloid activation in co-culture, downregulated cell cycle genes, and upregulated phagocytosis-related genes, indicating a shift toward a pro-repair phenotype. In conclusion, our results suggest that ICAM-1 on T cells mediates CNS myeloid cell activation and promotes deleterious neuroinflammatory processes associated with chronic EAE progression and CNS neuroglial injury.

O2 –

Astrocytes integrate noradrenaline inputs to modulate fear memory specificity

Mathias Guayasamin (1,2), Ossama Ghenissa (1,2), Lewis Depaauw-Holt (1,2), Sarah Peyrard (1), Ciaran Murphy-Royal (1,2)

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Astrocytes, the most abundant glial cell in the brain, play key roles in regulating neuronal circuits and behaviour. Through their complex morphologies, astrocytes integrate peripheral and central cues to directly influence a wide variety of behaviors including learning and memory. Importantly, we have previously found that genetic perturbation of amygdala astrocyte function is sufficient to replicate the effects of stress on both engram size and fear generalization. These findings suggest that astrocytes play a crucial role in tuning memory specificity. How precisely astrocytes integrate neural activity during learning and the mechanisms by which they regulate memory specificity remains unknown. Here, we highlight a role for the astrocytic integration of noradrenaline (NA) inputs in the lateral amygdala (LA) during the formation of specific fear memories. By using ex-vivo 2-photon calcium imaging in astrocytes expressing the calcium sensor GCaMP8, we found that out of a panel of neurotransmitters and neuromodulators, only NA triggers robust calcium responses in LA astrocytes by activating Gq-coupled α1-receptors. Next, we studied astrocyte calcium dynamics in the LA during fear conditioning in behaving animals through fiber-photometry. We report that astrocytes are activated during both fear memory learning and recall, suggesting a potential computational role for astrocytes during this task. To determine the role of astrocyte integration of NA signaling during fear memory formation, we used a novel specific α1-receptor knock down (KD) viral approach to block their responses to NA. We found that our KD abolished astrocyte calcium activity during learning and recall. Strikingly, we found that this manipulation is sufficient to induce a complete loss of discrimination between aversive and neutral cues compared to controls. These results highlight a central role for astrocytes in determining the specificity of fear memories and how astrocytes allow animals to discriminate between neutral and aversive stimuli.

O3 –

Les mutations du gène MECP2 perturbent les cils primaires et l'excitabilité neuronale dans le syndrome de Rett

Brin M, Guillon M, Gromaire J, Bianchin L, Rabin T, Veziano M, Laurent L, Flamier A

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Rett syndrome (RTT) is an X-linked neurodevelopmental disorder affecting approximately 1 in 10,000 births, predominantly in girls. It is characterized by severe intellectual disability, seizures, and motor impairments. In 95% of cases, RTT is caused by mutations in MECP2, which encodes a critical epigenetic transcriptional regulator essential for brain function. Our preliminary findings indicate that MeCP2 directly regulates the expression of primary cilia genes in human neurons. Primary cilia are sensory organelles in post-mitotic cells that play a fundamental role in neural excitability. We hypothesize that MECP2 deficiency disrupts ciliogenesis, contributing to RTT pathophysiology. To investigate this, we generated human embryonic stem cell (hESC) lines carrying three common RTT-associated MECP2 mutations using CRISPR/Cas9. Following differentiation into neurons, we observed a significant reduction in both the number and length of neuronal cilia. These findings were corroborated in four-month-old brain organoids derived from the same mutant lines. Given that RTT neurons exhibit hyperexcitability, we examined the role of primary cilia in this phenotype. Notably, treatment of wild-type neurons with ciliobrevin D, a ciliogenesis inhibitor, increased excitability, as measured by microelectrode arrays. This suggests a direct link between primary cilia dysfunction and neuronal hyperactivity in RTT. To identify potential therapeutic interventions, we are conducting a drug screen to identify compounds that rescue both ciliogenesis and neuronal excitability in RTT neurons. To date, we have identified four candidate molecules that restore neuronal excitability, which we hope could serve as the basis for future treatments.

O4 –

Delayed neuromuscular junction reinnervation: a critical period in amyotrophic lateral sclerosis

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While neuromuscular junction (NMJ) is a stable and robust synapse, it is can also undergo efficient reinnervation owing to reliable repair mechanisms. These repair processes appear deficient in disease such as Amyotrophic lateral sclerosis (ALS) where NMJs exhibit an abnormal dynamism with denervation-reinnervation cycles. However, the rapid response leading to functional repair remains unexplored, limiting our ability to understand the instability of NMJs in ALS. Hence, we developed a novel in-vivo approach to study reinnervation, allowing us to lesion a few axons and denervate downstream NMJs. Axonal photodamage was induced ~50 mm upstream from the NMJs. After a recovery phase (3-28 days), muscles and nerves were dissected, and electrophysiological recordings were performed to study synaptic functions of the reinnervated NMJs and of non-injured control neighbouring NMJs. Confocal imaging was used to assess NMJ innervation integrity. We observed that structural NMJ reinnervation is still ongoing in a majority of NMJs 3 days after injury, while all NMJs were reinnervated at 5 days postinjury where synaptic properties are consistent with weaker synaptic output. Surprisingly, at 11 days postinjury, NMJs were morphologically restablished but this weakness was physiologically maintained, and enhanced in ALS mice, indicative of a critical period of NMJ repair. Additionnally, this consolidation period was different between males and females, that may explain sex differences observed in ALS. NMJs showed synaptic properties like the ones observed in intact, uninjured NMJs only at 28 days postinjury. Hence, functional NMJ reinnervation is a relatively slow process that encompasses a critical period, before reaching functional maturity. Importantly, morphological reinnervation is an asynchrounous parameter of the quality of reinnervation that become unreliable in pathological context. We posit that the reinnervation process is implicated in the instability of the NMJs in disease such as ALS.

O5 –

Stress-induced mitochondrial fragmentation in endothelial cells disrupts blood-retinal barrier integrity causing neurodegeneration

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Introduction: The integrity of the inner blood-retinal barrier (iBRB) is crucial for maintaining an optimal microenvironment for neuronal function. However, the contribution of iBRB disruption to glaucomatous neurodegeneration remains poorly understood. Endothelial cells (ECs) rely on a finely tuned balance between fission and fusion to maintain healthy mitochondria. Here, we investigated whether altered mitochondrial dynamics in ECs contribute to the loss of vascular integrity and, if so, what mechanisms underlie mitochondria-related vascular leakage during ocular hypertension (OHT)-induced stress.

Methods: OHT was induced by magnetic microbead injection into Endo-MitoEGFP mice, which carry GFP-labeled mitochondria specifically in ECs. We examined vascular integrity using longitudinal fundus fluorescein angiography and Sulfo-NHS-Biotin (550 Da) tracer leakage, followed by stereological retinal sampling. We reconstructed the 3D volume of mitochondria in ECs using Imaris and quantified reactive oxygen species (ROS) levels using MitoSOX. To specifically inhibit mitochondrial fission, we used AAV-mediated expression of a dominant-negative DRP1 selectively in ECs. We increased Claudin-5 (CLDN5) expression in ECs via AAV. We quantified RGC density in RBPMS-stained retinas and assessed retinal-brain connectivity via optomotor reflex responses.

Results: We show that OHT induced mitochondrial fragmentation in retinal capillary ECs accompanied by increased oxidative stress and ultrastructural defects. Analysis of EC mitochondrial components revealed overactivation of dynamin-related protein 1 (DRP1), a central regulator of mitochondrial fission, during glaucomatous damage. Pharmacological DRP1 inhibition or EC-specific in vivo gene delivery of a dominant negative DRP1 mutant was sufficient to rescue mitochondrial volume, reduce vascular leakage, and increase expression of the tight junction claudin-5 (CLDN5). Remarkably, AAV-mediated CLDN5 supplementation improved iBRB integrity, promoted RGC survival, and rescued visual behaviours.

Conclusion: Our findings reveal that preserving mitochondrial homeostasis and EC function are valuable strategies to enhance neuroprotection and improve vision in glaucoma.

O6 –

Caractérisation de l'atrophie et des bases transcriptomiques des phénotypes de conversion dans le trouble comportemental en sommeil paradoxal isolé

Marie Filiatrault (1), Andrew Vo (1), Violette Ayral (1), Christina Tremblay (1), Celine Haddad (1), Joseph Lefevre (1), Véronique Daneault (1), Alexandre Pastor-Bernier (1), Jean-François Gagnon (1,2,3), Ronald B. Postuma (1,4,5), Petr Dusek (6), Stanislav Marecek (6), Zsoka Varga (6), Johannes C. Klein (7), Michele T. Hu (7), Isabelle Arnulf (8), Pauline Dodet (8), Marie Vidailhet (8), Jean-Christophe Corvol (8), Stéphane Lehéricy (8), ICEBERG Study Group (8), Simon Lewis (9), Elie Matar (10), Kaylena A. Ehgoetz Martens (10), Lachlan Churchill (10), Per Borghammer (11), Karoline Knudsen (1`1), Allan K. Hansen (11), Dario Arnaldi (12), Beatrice Orso (12), Pietro Mattioli (12), Luca Roccatagliata (12), Shady Rahayel (1)

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Le trouble comportemental en sommeil paradoxal isolé (TCSPi) est une parasomnie associée au développement des synucléinopathies : plus de 90% des personnes TCSPi développeront une démence à corps de Lewy (DCL), une maladie de Parkinson (MP) ou une atrophie multisystème (AMS). Les personnes TCSPi présentent déjà de l'atrophie dans le cerveau, mais notre compréhension des changements cérébraux associés à la transition du TCSPi vers ces conditions est limitée. Les scans IRM de 343 personnes TCSPi (suivi médian de 6 ans), dont 94 ayant converti, ont été analysés dans le cadre d'une étude multicentrique internationale. L'épaisseur corticale et les volumes sous-corticaux ont été extraits et standardisés pour le site, l'âge et le sexe. Des modèles linéaires généralisés ont permis de comparer les profils d'atrophie entre les phénotypes cliniques de TCSPi. Des analyses d'annotation spatiale et d'imagerie transcriptomique ont été effectuées pour chaque phénotype, afin d'examiner les caractéristiques biologiques des différents patrons d'atrophie. Les TCSPi-DCL présentaient un profil d'atrophie qui chevauchait la distribution spatiale de récepteurs sérotoninergiques, nicotiniques et dopaminergiques et qui était enrichi pour les gènes associés à la transmission cholinergique. Les TCSPi-MP avaient un profil d'atrophie enrichi pour les gènes liés à la fixation des métaux et au traitement des organophosphorés. Les TCSPi-AMS avaient peu de changements corticaux, mais une atrophie sous-corticale prononcée, enrichie pour des gènes inflammatoires et immunitaires. Notre étude montre que les trajectoires de conversion du TCSPi s'accompagnent de profils neurodégénératifs distincts, soulignant l'importance d'une stratification précoce lors du développement de biomarqueurs dans le TCSPi.

O7 –

Seizure detection using miniaturized electromyography-accelerometry sensors

Isabel Sarzo Wabi (1,2,4), Daniel Alejandro Galindo Lazo (1,2,4), Amirhossein Jahani (3,4), Sarra Chebaane (3,4), Raphaëlle Hartwig (4), Carole Ruppli (4), Oumayma Gharbi (4), Manon Robert (4), Annie Perreault (4), Claudia Rodriguez (4), Juan Pablo Millan Sandoval (4), Gianluca D'Onofrio (4), Alexis Robin (4), Dang Khoa Nguyen (1,3,4,*), Elie Bou Assi (3,4,*)

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* Equally contributing principal investigators

Background: Epilepsy is a chronic neurological condition characterized by recurrent, spontaneous seizures due to abnormal synchronization of neuronal discharges. It affects ~65 million people worldwide, from which 30% continue to have uncontrolled seizures despite available treatment. Timely interventions during seizures are critical to reduce the risk of injuries and sudden unexpected death in epilepsy. Consequently, there is a need for seizure-detection wearables suitable for everyday use. In this study, a seizure-detection algorithm was developed using surface electromyography (sEMG) and accelerometry (ACC) signals recorded with miniaturized wearable sensors.

Methods: Continuous sEMG-ACC signals were acquired from patients in an epilepsy monitoring unit (EMU). Eight sensors were positioned bilaterally on the upper trapezius, anterior deltoid, biceps brachii, and tibialis anterior muscles. Temporal, spectral, and wavelet features were extracted in fixed-length epochs using overlapping sliding windows. An extreme gradient boosting classifier was trained to identify seizure epochs using setups with eight, two, and one sensor(s). Performance was evaluated via patient-wise nested cross-validation, and specificity was further assessed on an independent patient cohort without seizures.

Results: Eleven generalized tonic-clonic seizures (GTCS) and focal-to-bilateral tonic-clonic seizures (FBTCS) were recorded from nine patients over 1359.6h. With eight sensors, the algorithm achieved 90.9% sensitivity, 0.05 FAR/24h, and median detection latency of 22.5s. Single-sensor setups on the right biceps brachii and left tibialis anterior reached 100% sensitivity, 0.51 and 0.28 FAR/24h, and median latency of 32 and 26.5s, respectively. A dual-sensor setup with these muscles preserved 100% sensitivity, achieving 0.12 FAR/24h and median latency of 22s. On 1744.18h of continuous recordings from 19 patients without seizures, FARs/24h were 0.56 (eight sensors), 0.50-0.62 (one sensor), and 0.06 (two sensors).

Conclusion: The developed algorithm effectively detected GTCS and FBTCS in an EMU. Performance was preserved upon reducing the number of sensors, potentially leading to more practical and comfortable setups for patients.

O8 –

Serotonergic inputs to the ventral hippocampus underlie sex differences in anxiety

Pizzoccaro L (1,2), van der Veldt S (1,2,3), Henderson F (1,2), Simard AS (1,2), Pierrault F (1,2), Fortin-Houde J (1,2), Ducharme G (1), Amilhon B (1,2)

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Anxiety disorders are among the most common psychiatric conditions worldwide, with women being almost twice more likely than men to be diagnosed throughout their lifetime. Serotonergic (5-HT) neurons from the raphe nuclei are heavily involved in the regulation of mood and anxiety, yet the neural substrates underlying sex-related differences in anxiety remain largely unknown. The ventral hippocampus (vHP) acts as a major modulator of anxiety and receives dense 5-HT inputs. We hypothesize that serotonin release in the vHP is crucial in controlling anxiety, and that this process is influenced by sex. SERT-Cre mice were injected into the vHP with a retrograde virus carrying eYFP to target exclusively the raphe-vHP serotonergic neurons. vHP-projecting raphe neurons are located in the interfascicular part of the dorsal raphe (DRi), median raphe (MnR) and B9 subregions. Fiber photometry recordings of vHP-projecting MnR neurons during anxiety tests revealed sex differences in population activity levels. Pathway specific optogenetic activation of raphe-vHP 5-HT neurons was achieved using the excitatory opsin ChETA. Activating those neurons robustly increased anxiety levels in a sex-dependent manner, with female mice showing increased anxiety, increased grooming and decreased risk-assessment. Local field potential recordings in the vHP showed that this sex-dependent modulation of anxiety is accompanied by female-specific alterations of vHP theta rhythm. To investigate the cellular mechanism underlying the sex-differences in anxiety behavior, we performed whole-cell patch-clamp on raphe-vHP 5-HT neurons. Strikingly, no differences were found in passive membrane properties between regions or sexes, while significant sex differences were observed in excitability. Indeed, female MnR vHP-projecting neurons exhibited a more depolarized resting membrane potential and a higher firing frequency compared to their male counterparts, with firing frequency being the highest among all recorded regions. Together, these results provide a novel mechanistic insight into a previously under-investigated sexual dimorphism in the raphe-ventral hippocampus serotonergic pathway.

A1 –

Étude quantitative automatisée de la plasticité des filets périneuronaux dans le cortex visuel de souris lors d'un dommage rétinien de type DMLA et de la potentialisation cholinergique

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La potentialisation cholinergique via l'administration de donépézil (DPZ), un inhibiteur de l'acétylcholinestérase, montre des effets prometteurs sur la plasticité et l'apprentissage perceptuel lorsque couplé à un entraînement visuel. Toutefois, les mécanismes derrière ce phénomène demeurent mal compris. Dans cette étude, nous avons investigué les effets d'un traitement de DPZ suite à un déficit visuel sur les interneurones corticaux inhibiteurs exprimant la parvalbumine (PV) et sur les filets périneuronaux (PNNs) les entourant. Les PNNs sont des structures spécialisées de la matrice extracellulaire impliquées dans la plasticité corticale par leur régulation de l'activité des neurones PV+. Une néovascularisation choroïdienne (CNV) via photocoagulation a été induite dans l'œil droit de souris C57BL6 adultes. Les effets après deux et sept jours ont été examinés dans le cortex de ces animaux recevant ou non un traitement quotidien de DPZ (0.3mg/kg). La récupération visuelle a été évaluée à l'aide du test de la falaise visuelle. Les variations de densité des PNNs et des neurones PV+ ont été analysées par immunohistochimie et quantifiées à l'aide d'outils d'intelligence artificielle. Les résultats montrent une baisse significative de la densité des PNNs et des cellules doublement marquées (PV+/PNN+) deux jours après la CNV, qui est évitée par le DPZ. Cet effet est particulièrement marqué dans les couches 2/3 et 5 alors que la couche 4, thalamorécipiente, n'est pas affectée. Après sept jours, des résultats similaires sont observés, mais cette fois limités à la couche 2/3. Également, la densité des neurones PV+ diminue après sept jours, ce qui pourrait refléter un ajustement adaptatif de l'expression de cette protéine. Ces résultats suggèrent que la réduction des input visuels rétiniens entraîne un déséquilibre de la connectivité fonctionnelle interlaminaire du cortex visuel et que le DPZ pourrait protéger cette connectivité. Ces changements modifieraient la balance inhibition/excitation des couches supragranulaires et l'intégration corticale.

A2 –

Sleep/wake architecture and electrocorticographic activity after cofilin inactivation in mice

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Cofilin, a key regulator of actin dynamics, shapes dendritic spine and influences synaptic plasticity; its activity is altered by sleep deprivation (SD). Given the bidirectional links between plasticity and the sleep-wake cycle, we hypothesized that cofilin may shape cortical synchronization and hence electrocorticographic (ECoG) activity. Accordingly, we aimed to determine the involvement of cofilin in the regulation of ECoG activity in mice under undisturbed and SD conditions, while considering potential sex-related effect. To test this, adult male and female C57BL/6J mice received adeno-associated virus injections expressing inactive cofilin (AAV9-CaMKIIα-cofilinS3D-HA) or a control virus (AAV9-CaMKIIα-eGFP) in motor and visual cortices. ECoG electrodes were implanted during the same surgery. Recordings included a 24-hour baseline, a 6-hour SD, and 18 hours of recovery. Our results indicate that cofilin inactivation did not change time spent awake and asleep during baseline or after SD in either sex. For the motor cortex, absolute spectral power did not significantly differ between cofilin-S3D and GFP groups at baseline or after SD in males and females. Delta power in slow wave sleep (SWS) and theta/alpha power during wake also did not differ between groups or sexes. For the visual cortex, cofilin-S3D mice exhibited higher absolute spectral power than GFP controls at baseline across vigilance states in both sexes. During SD and recovery, this pattern persisted for wake and paradoxical sleep (not significant in SWS). During recovery, cofilin-S3D mice, especially males, showed higher delta power than GFP controls at specific times during the dark period, whereas alpha power increased transiently in the cofilin-S3D group near the end of the SD. These findings show that cortical cofilin inactivation increases ECoG power specifically for the visual cortex without altering sleep architecture, suggesting a region-dependent impact of actin stabilization on cortical synchrony and recovery from sleep loss.

A3 –

Mise en oeuvre d'une plate-forme supportant le développement de neuroprothèses flexibles

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Mon projet s'inscrit dans le développement de neuroprothèses flexibles destinées à restaurer les fonctions motrices des membres supérieurs après une lésion cérébrale. Les accidents vasculaires cérébrales entraînent fréquemment des déficits moteurs importants. Le cerveau possède une capacité de réorganisation, mais cette récupération demeure limitée. Les neuroprothèses, en stimulant directement le cortex, représentent une approche prometteuse pour soutenir cette récupération.

L'objectif principal de mon projet est de concevoir une tâche automatisée qui favorisera le développement d'une neuroprothèse capable de supporter des mouvements complexes et variés chez le primate non humain après une lésion corticale. Cette tâche permettra de quantifier les effets d'une stimulation intracorticale adaptative, fournie à l'aide d'un algorithme entraîné à partir de données électromyographiques et électrophysiologiques recueillies chez le même animal.La méthodologie comprend plusieurs volets : la conception d'un dispositif automatisé pour détecter et enregistrer les mouvements ; l'entraînement des primates à réaliser des tâches motrices précises de type atteinte-préhension ; la collecte d'activité neuronale et musculaire en condition éveillée; et l'application d'un protocole de stimulation intracorticale adaptative, déclenchée en temps réel en fonction des performances motrices.

La tâche nous permettra de mesurer la performance des primates lors d'une tâche de préhension et d'atteinte, de mesurer l'activité neuronale et musculaire chez les primates éveillés, trouver un paramètre de stimulation, observer l'amélioration des mouvements après stimulation et de mettre en place une infrastructure expérimentale pour tester différents protocoles neuromodulatoires. Nous prévoyons que l'utilisation de la neuroprothèse permettra une amélioration partielle des performances motrices chez les primates lésés. De plus, le dispositif automatisé permettra une collecte de données précise et continue, essentielle pour l'ajustement dynamique des paramètres de stimulation. Ce projet contribuera à l'avancement des interfaces cerveau-machine dans un cadre préclinique, tout en posant les bases nécessaires à leur transposition chez l'humain pour la réadaptation post-AVC.

A4 –

Analyse génétique chimique de la toxicité de la protéine tau dans la neurodégénérescence liée à l'âge

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La protéine Tau (MAPT, Microtubule-Associated Protein Tau) est une protéine intracellulaire qui se lie aux microtubules afin d'en assurer la stabilisation et le bon fonctionnement. Lorsqu'elle devient hyperphosphorylée, Tau perd sa capacité à stabiliser les microtubules et acquiert des propriétés toxiques, entraînant des dysfonctionnements cellulaires majeurs. Ce processus pathologique est à l'origine d'un groupe de maladies neurodégénératives, appelées tauopathies, dont la maladie d'Alzheimer et la paralysie supranucléaire progressive. À ce jour, aucun traitement curatif n'est disponible pour ces maladies et seules des approches symptomatiques permettent d'en atténuer temporairement les effets. Les mécanismes moléculaires précis responsables de la toxicité de Tau demeurent toutefois mal compris.

Le nématode Caenorhabditis elegans constitue un modèle expérimental particulièrement puissant pour l'étude des tauopathies, permettant de reproduire plusieurs aspects clés des pathologies humaines. Nous avons développé des souches transgéniques exprimant des formes hyper- ou hypophosphorylées de Tau, qui présentent des phénotypes caractéristiques tels qu'une dégénérescence des motoneurones, des altérations locomotrices, une réduction de la taille corporelle et une diminution de la descendance. Ces phénotypes reflètent la toxicité cellulaire induite par Tau et en font des modèles hautement pertinents pour le criblage de modulateurs génétiques et pharmacologiques.

Un criblage à grande échelle de plus de 4 000 composés a permis d'identifier une vingtaine de molécules capables d'atténuer la toxicité de Tau, dont certaines sont déjà approuvées par la FDA, telles que le bambutérol, PAC-1 et le chlorhydrate de mécamylamine. Le projet actuel vise à valider expérimentalement ces composés prometteurs et à évaluer leur potentiel neuroprotecteur à l'aide d'approches comportementales, physiologiques et génétiques. Ces travaux, à l'interface de la biologie moléculaire, de la pharmacologie et des neurosciences translationnelles, pourraient mener à l'identification de nouvelles cibles thérapeutiques pour les tauopathies.

A5 –

Développement d'un pipeline de vision par ordinateur pour l'analyse de la position du sommeil dans le cadre de la prévention de la mort subite inattendue dans l'épilepsie

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Introduction

La mort subite inexpliquée en épilepsie (SUDEP) représente un enjeu majeur de santé publique, avec un taux annuel estimé à 1 pour 1000 patients épileptiques. Cette condition, qui survient pendant les crises, présente une corrélation significative avec la position de sommeil : 73,3 % des cas se produisent lorsque le patient est couché sur le ventre. La surveillance nocturne des postures s'avère donc cruciale, mais elle est souvent entravée par la réticence des patients à utiliser des dispositifs corporels inconfortables. Ce projet vise à concevoir un système de classification des postures de sommeil basé sur l'analyse vidéo.

Méthodologie

Un ensemble de 5536 images a été constitué à partir de la base vidéo de l'unité de monitoring d'épilepsie du CHUM (UME), incluant 664 patients hospitalisés. Les images ont été annotées en 5 classes correspondant aux différentes postures, puis soumises à un prétraitement et à une augmentation de données. Un pipeline de vision par ordinateur utilisant des modèles d'apprentissage profond (réseaux de neurones convolutifs, CNN) a été conçu. Les modèles ont été entraînés et évalués par validation croisée sur 5 ensembles, avec optimisation d'hyperparamètres.

Résultats

Les résultats préliminaires pour la classification à 5 classes indiquent une précision de validation de 64,6 % avec une fonction de perte de 0,896. L'optimisation des modèles demeure en cours pour améliorer les performances prédictives.

Conclusion

Malgré la précision présentement modérée, les courbes de convergence démontrent une stabilisation appropriée du processus d'apprentissage, suggérant une architecture viable nécessitant des améliorations algorithmiques. Les développements futurs comprennent l'optimisation architecturale des modèles, l'enrichissement substantiel de la base de données d'entraînement, et l'implémentation d'algorithmes de post-traitement avancés pour améliorer la performance prédictive.

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A6 –

Le couplage neural dans les troubles de la conscience : un pont entre neuroscience clinique et IA

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Introduction: Les humains s'adaptent les uns aux autres lors d'interactions sociales, entraînant une synchronisation neuronale et comportementale. Après une lésion cérébrale, les patients présentant des troubles de la conscience (DoC) n'ont pas la capacité systématique d'entrer en interaction avec autrui, on ignore donc s'ils peuvent présenter une synchronisation neuronale avec leurs proches et si cela a une valeur clinique.

Objectifs: Cette étude pilote examinera si une synchronisation inter-cerveaux (IBS) peut survenir entre des patients cérébrolésés atteints de DoC et leurs proches, malgré l'absence de réactivité manifeste. Plus précisément, nous visons à déterminer si l'IBS : 1) est présente chez des patients DoC non réactifs et 2) peut contribuer à prédire le diagnostic et le rétablissement.

Méthodes: Nous recruterons 10 patients DoC non sédatés dans les unités de soins intensifs et de soins neurologiques de l'Hôpital du Sacré-Cœur de Montréal. Chaque patient formera des dyades avec un partenaire familier (proche) et un partenaire non familier (inconnu). Nous utiliserons l'hyperscanning en EEG haute densité (hd-EEG) afin d'évaluer l'IBS lors d'interactions verbales et physiques. Les patrons d'IBS seront analysés pour leur association avec le diagnostic de DoC et le pronostic à 3 et 6 mois. En parallèle, nous intégrerons un module de modélisation mécanistique par réseaux de neurones impulsionnels (SNN) bio-inspirés (neurones LIF, plasticité STDP/MSTDPET) afin de simuler des interactions dyadiques asymétriques (agent sain → agent lésé) et d'explorer comment des paramètres de stimulation peuvent moduler l'IBS résiduelle.

Résultats attendus: Nous anticipons une IBS plus forte dans les dyades familières, en particulier lors des interactions verbales, corrélée au rétablissement de la conscience. On s'attend à ce que la synchronie dans la bande de fréquences alpha-mu centro-pariétale droite présente les effets les plus marqués. Cette étude pourrait soutenir l'hyperscanning comme nouvel outil clinique pour l'évaluation et la pronostication des DoC.

A7 –

Phosphoinositide metabolism as a modulator of ageing and neurodegeneration

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Ageing is a major risk factor for neurodegenerative diseases such as amyotrophic lateral sclerosis. Yet, the molecular pathways linking cellular ageing to neurodegeneration remain poorly understood. Phosphoinositides (PIPs) are essential lipid messengers that regulate membrane dynamics, vesicular trafficking, axonal maintenance and stress responses. Their metabolism is tightly controlled by specific kinases and phosphatases, and growing evidence suggests that dysregulation of PIP signaling contributes to neuronal vulnerability.

In this project, we investigate how PIP levels and PIP-regulating enzymes are altered during ageing and in response to acute environmental stresses, including heat shock, cold shock, osmotic challenge and high-glucose exposure. Using C. elegans as a genetically tractable model, we combine fluorescent biosensors, genetic manipulation and stress paradigms to map dynamic changes in PIP metabolism across lifespan. We further assess how modifying key PIP kinases and phosphatases influences stress resilience and neurodegeneration-related phenotypes.

Our findings aim to identify age-dependent alterations in phosphoinositide signaling and uncover lipid-mediated mechanisms that could be targeted to protect neurons. Ultimately, this work contributes to a better understanding of how PIP metabolism integrates stress and ageing signals, paving the way for novel therapeutic strategies for ALS and related neurodegenerative diseases.

A8 –

Modulation de l’activité des transporteurs glycinergiques comme piste de thérapie de l’encéphalopathie glycinique

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L'encéphalopathie glycinique (EG) est une maladie métabolique génétique rare caractérisée par un niveau anormalement élevé de glycine dans le corps. Ses conséquences sont très graves (hypotonie, convulsions cérébrales, apnée et décès) et malheureusement, aucun traitement efficace n'est disponible. Le taux élevé de glycine observé dans les EG a été génétiquement lié à une défaillance du métabolisme de la glycine, et 75 % des cas sont dus à des mutations du gène de la glycine décarboxylase nommé GLDC. Un modèle de poisson zèbre de GE (gldc-/-), précédemment généré, récapitule de nombreux aspects pathologiques de la maladie, y compris la déficience motrice et les perturbations métaboliques. En utilisant ce modèle génétique, il a été montré que la diminution de l'expression et de l'activité des transporteurs à la glycine (GlyTs), exprimé majoritairement dans les astrocytes, joue un rôle essentiel dans la pathogénèse in vivo. Nous testons l'hypothèse que l'augmentation de l'activité des GlyTs peut inverser les phénotypes pathologiques associés à la GE chez le modèle de poisson zèbre.

Le premier axe de ce projet consiste à tester l'effet d'une surexpression stable de GlyTs dans les cellules gliales (promoteur gfap), en utilisant le double système d’expression GAL4/UAS. La modulation pharmacologique des GlyTs permettrait d’identifier des molécules capables de stimuler l’expression endogène des GlyT1s. Pour ce faire, nous tirerons profit d’une lignée cellulaire d’astrocytes immortalisés sur laquelle nous réaliserons un criblage à haut débit de plus de 50,000 petites molécules (plateforme IRIC).

Nos données préliminaires ont montré que la micro-injection de l'ARNm codant pour GlyT1, exprimé au niveau des cellules gliales, dans des embryons gldc-/- était suffisante pour sauver leurs défauts de motilité précoces. Ces résultats confirment que les GlyT1s sont une cible potentielle dans le contexte de cette maladie.

A9 –

Le dynamisme de la jonction neuromusculaire, une cible pour l'identification de nouveaux biomarqueurs pour la SLA

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La sclérose latérale amyotrophique (SLA) est une maladie neurodégénérative fatale affectant les neurones moteurs. L'absence de biomarqueurs spécifiques demeure un obstacle majeur au diagnostic, au suivi et à l'évaluation de l'efficacité des traitements en développement. Un évènement précoce et universel dans la SLA est la dénervation des jonctions neuromusculaires (JNM), survenant plusieurs mois avant la rétraction complète de l'axone. Ce processus, marqué par des cycles répétés de dénervation et de réinnervation, s'accompagne de la libération de protéines neuromusculaires dans la circulation, suggérant que la dynamique de la JNM représente une cible prometteuse pour l'identification de nouveaux biomarqueurs sanguins. Une étude protéomique comparative menée chez des souris SOD1G37R entre muscles résistants et vulnérables à la maladie a permis de sélectionner trois protéines candidates. Nous avons ciblé la laminine β2 (LAMB2) comme première candidate, une protéine localisée exclusivement à la JNM et essentielle à son organisation. Les analyses par buvardage Western ont révélé une diminution significative de LAMB2 dans les muscles Extensor Digitorum Longus (EDL) et soléaire (SOL) de souris SOD1G37R symptomatiques comparativement aux souris sauvages. Cette diminution, déjà présente au stade pré-symptomatique et non corrélée à l'état d'innervation, demeure stable au cours de la maladie et n'est pas observée après lésion nerveuse, confirmant sa spécificité à la SLA. De façon cohérente avec les observations tissulaires, les niveaux sériques de LAMB2 sont significativement réduits chez les souris SOD1G37R dès le stade pré-symptomatique, alors qu'aucun changement n'est observé après une lésion nerveuse, contrairement aux niveaux de NfL qui augmentent, confirmant la spécificité de la baisse de LAMB2 à la physiopathologie de la SLA. Cette diminution, détectable dès le jour postnatal 100, soit environ 300 jours avant la manifestation clinique, précède de plusieurs mois l'apparition des symptômes et positionne LAMB2 comme un biomarqueur précoce sensible, ouvrant une fenêtre diagnostique exploitable avant la phase symptomatique.

A10 – AFFICHE NON PRÉSENTÉE

Effets de la cécité sur les déficits induits par un accident cérébro vasculaire chez la souris

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La neuroplasticité permet à des régions du cerveau de prendre le contrôle de nouvelles fonctions après une lésion. Chez les personnes aveugles, le cortex visuel peut régir des fonctions tactiles et motrices. Étant donné que chez les aveugles, une plus grande proportion du cerveau est consacrée à des fonctions non visuelles nous nous attendons à ce qu'une lésion dans le cortex moteur, comme un accident vasculaire cérébral (AVC), puisse avoir un impact dévastateur limité sur les déficiences motrices. Inversement, étant donné que le cortex visuel des aveugles contribue maintenant aux fonctions non visuelles, une lésion dans ce cortex a pour conséquence des dysfonctions motrices.

L'objectif est de mesurer les fonctions motrices de souris aveugles, suite à un AVC ischémique du cortex visuel ou moteur.32 souris âgées de 3 mois ont été utilisées. 14 souris énucléées et 18 voyantes étaient divisées en trois groupes : Sham, avec un AVC moteur, et avec un AVC visuel. Les fonctions motrices ont été évaluées quotidiennement à l'aide de tests comportementaux moteurs, incluant le score de déficit neurologique (NDS), le test du rotarod, le faisceau d'équilibre et le placement des pattes. Des lésions photothrombotiques ont ensuite été induites dans le cortex moteur ou visuel à l'aide d'une injection de Rose Bengal et d'un laser vert, et les fonctions motrices ont été évaluées pendant 10 jours supplémentaires. A la fin de l'expérience, les cerveaux des souris sont analysés à la microscopie Lightsheet afin de quantifier et mesurer la taille des AVC.

A11 –

Automated epilepsy diagnosis using cross-frequency coupling and machine learning

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Introduction: Epilepsy diagnosis largely depends on identifying interictal epileptiform discharges (IEDs) in electroencephalogram (EEG) recordings, yet 29% to 55% of routine 30-minute EEGs contain no IEDs, leading to diagnostic uncertainty and delayed treatment. Recent work has explored computational biomarkers extracted from EEG. Most methods have focused on spectral band power within isolated frequency ranges. Cross-frequency coupling (CFC) is particularly relevant because it quantifies interactions between frequency components and may reveal abnormal network coordination even when no IED is visible. This study presents a machine-learning framework that leverages CFC as a novel computational biomarker of epilepsy, aiming to enable automated and objective diagnosis.

Methods: We analyzed 555 EEG recordings from 465 patients, including 228 with epilepsy, collected at the Centre hospitalier de l'Université de Montréal between 2018 and 2021, all without visually identifiable IEDs. Data were divided into independent training, validation, and test cohorts using a patient-wise split. All preprocessing, feature selection, and model tuning were performed on the training set, with learned transformations applied to validation and test data to prevent leakage. CFC features were computed across standard EEG bands, and the 100 most informative were selected using the minimum redundancy maximum relevance method. Support Vector Machine (SVM), Random Forest (RF), and LightGBM classifiers were optimized via cross-validation. Patient-level predictions were obtained by majority voting across epoch-level outputs.

Results: The Random Forest model achieved the best generalization, with a Receiver Operating Characteristic Area Under the Curve (ROC AUC) of 0.704 and accuracy of 0.641 at patient-level, and a ROC AUC of 0.698 with accuracy of 0.650 at epoch-level on the held-out test set.

Conclusion: These results support the feasibility of CFC-based biomarkers for automated epilepsy screening using a leakage-resistant pipeline. Future work will focus on confirming these findings in larger, multicenter, and prospective cohorts to assess generalizability before clinical integration.

A12 –

Functional characterization of median raphe VGLUT3-positive projections to the dorsal and ventral hippocampus

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The hippocampus (HP) is critical for episodic memory. Along its dorsoventral axis, the HP can be segregated in distinct functional compartments: the dorsal hippocampus (dHP) essential for spatial memory and navigation, and the ventral hippocampus (vHP) involved in emotional processing. Both regions receive inputs from the median raphe nucleus (MnR). These inputs include two anatomically distinct glutamatergic populations of neurons expressing the type 3 vesicular glutamate transporter (VGLUT3) that project to either hippocampal pole (VGLUT3 MnR→dHP and VGLUT3 MnR→vHP). However, the activity pattern of these two VGLUT3MnR→HP pathways is still unknown. Studies have shown that activating VGLUT3MnR→HP neurons powerfully modulate hippocampal activity. These results suggest that VGLUT3MnR→dHP and VGLUT3MnR→vHP neurons could independently modulate the activity and functions associated with dorsal and ventral hippocampal poles.

In this study, we aim to investigate the activity of both VGLUT3 pathways during behavioural tasks predominantly involving the dHP or the vHP. We hypothesize an increase in activity in VGLUT3MRN→dHP neurons preferentially during spatial-memory-related behaviour while VGLUT3MRN→vHP neurons are expected to show an increase in activity during emotionally salient epochs.

To accomplish this, we use dual-colour fibre photometry, in which both pathways express a different calcium sensor and their activity is recorded simultaneously during different behavioural tasks. The behavioral assays include a social memory test, quinine/sucrose presentation assay, fear-conditioning test, and tail suspension test. Overall levels of activity, frequency and amplitude of the calcium events are measured during the different phases of the tests. This project reveals the activity of novel pathways involved in differential modulation of memory and sheds more light on the role of the MnR-HP projections.

A13 –

Topographie des oscillations neuronales du noyau sous-thalamique dans la maladie de Parkinson

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Introduction : Dans la maladie de Parkinson, l'utilisation des potentiels de champ locaux (LFP) pour optimiser la stimulation intracérébrale (SIC) du noyau sous-thalamique (NST) constitue un domaine de recherche important. Une activité LFP élevée dans les fréquences bêta est associée à la sévérité des symptômes moteurs. Cependant, la topographie précise des LFP au sein du NST reste mal définie. Une meilleure compréhension de cette organisation pourrait guider l'optimisation des stratégies de stimulation, notamment avec des électrodes directionnelles. Cette étude vise à caractériser l'organisation spatiale de l'activité électrophysiologique du NST.Méthode : Les LFP de 20 NST ont été mesurés au moyen du neurostimulateur Percept PC (Medtronic) avec la SIC désactivée, puis activée. Les contacts d'enregistrement ont été reconstruits dans un espace standardisé (MNI) via Lead DBS. Une interpolation spatiale et un lissage gaussien ont permis de générer des cartes de puissance du NST pour différentes fréquences d'oscillations neuronales. Leur distribution spatiale a été caractérisée par modèle linéaire généralisé et par leur centroïde de puissance.

Résultats : Sans stimulation, l'activité bêta est significativement plus élevée en position latérale ($p = 0,006$), avec un centroïde de puissance bien délimité. Sous stimulation, elle diminue de manière plus marquée latéralement ($p = 0,0015$). La position de l'électrode selon l'axe antéro-postérieur influence significativement la modulation de l'activité alpha : la stimulation postérieure l'augmente, tandis qu'une stimulation antérieure la réduit ($p < 0,001$).

Discussion et Conclusion : Cette étude révèle la topographie des oscillations neuronales dans le NST, ainsi que l'effet de la stimulation sur cette organisation. L'intégration de la dimension spatiale des biomarqueurs électrophysiologiques pourrait permettre d'optimiser la programmation des électrodes directionnelles en SIC.

A14 –

Investigating the mitochondrial functions regulated by THAP12

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Background: Mitochondrial dysfunction has been shown to be involved in many neurodevelopmental disorders (NDDs) such as Leigh and Dravet syndrome. Recently, our lab has shown that compound heterozygous variants in the gene THAP12 are pathogenic and contribute to a severe NDD. The mechanisms behind which a loss of THAP12 contributes to NDDs currently remains unknown. In our preliminary work, through chromatin immunoprecipitation followed by deep sequencing (ChIP-seq), we have shown that THAP12 is binding genes involved in essential mitochondrial processes. Using RNA-seq, we have confirmed that THAP12 is acting as a transcriptional activator of these bound genes. Furthermore, using co-immunoprecipitation (Co-IP) followed by liquid chromatography mass spectrometry (LC-MS) we revealed several protein interactors, many of which are involved in mitochondrial translation. Hypothesis: In line with this preliminary data, we believe that THAP12 regulates genes essential to mitochondrial function. Methods: Objective 1. Pinpoint localization of THAP12 through subcellular fractionation and immunofluorescence on HEK293FT cells, using our THAP12-KO HEK293FT cells as a negative control. Objective 2. Assess mitochondrial function by conducting a Mito Stress Test using a Seahorse Bioanalyzer on our THAP12-KO HEK293FT cells. Objective 3. Use MitoTracker staining followed by flow cytometry (FACS) to assess mitochondrial mass in HEK293T and THAP12-KO HEK293T cells. Objective 4. Investigate how the assembly of key oxidative phosphorylation (OXPHOS) complexes are impacted by a loss of THAP12 using a Blue-Native Page followed by immunoblotting with antibodies specific for complexes I-V. Results: Through a Mito Stress Test we have shown that a loss of THAP12 leads to a severe impairment in oxidative phosphorylation with significant reductions in ATP production, basal respiration and proton leak.Conclusion: By understanding how a loss of THAP12 can impact mitochondrial function, we aim to uncover a previously unknown function of this protein, which may contribute to its pathogenicity.

A15 –

Epileptic seizure onset zone localization from iEEG signals based on graph neural networks

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Background: Accurate localization of the seizure onset zone (SOZ) is a key step in the presurgical evaluation of patients with drug-resistant focal epilepsy. Current identification methods, which rely on expert visual inspection of intracranial EEG (iEEG) recordings, are subjective, time-consuming, and fail to adequately capture the network-level organization that characterizes epileptic dynamics. Recent machine learning approaches have attempted to automate this process, yet most remain constrained by small patient cohorts and simplified models that overlook key aspects of brain's network-level organization and connectivity.

Methods: We propose a 2-stage pipeline for automated SOZ localization. The framework estimates, for each electrode, the probability of belonging to the SOZ by learning spatiotemporal activation patterns across seizure segments aligned to the onset time. A patient-specific Graph Neural Network - Gated Recurrent Unit (GNN-GRU) module first identifies local ictal propagation by capturing spatial dependencies between electrodes and temporal seizure dynamics. A patient-agnostic post-hoc classifier then interprets temporal activation profiles to produce a calibrated SOZ probability map. Model performance is assessed using a leave-one-patient-out cross-validation strategy to ensure patient-level generalization. Our dataset includes 178 seizures from 40 patients collected at the Epilepsy Monitoring Unit of the Centre hospitalier de l'Université de Montréal (CHUM) and a complementary open-source repository with iEEG recordings from the Hospital of the University of Pennsylvania.

Expected outcomes: Model training and evaluation are currently ongoing. We expect the proposed framework to reveal stable, localized network activation clusters around clinically identified SOZs, and to maintain uniformly low probabilities when the implantation fails to cover the true onset region, thereby providing clinicians with indirect cues about suboptimal electrode coverage.

Conclusion: This ongoing work aims to illustrate the potential of graph-based spatiotemporal modelling to move beyond electrode-level features toward a network-centred and interpretable approach for quantitative SOZ localization in epilepsy surgery planning.

A16 –

Characterizing stress granule formation in ALS TDP-43 mouse models

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One of the hallmarks of amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD), two diseases on the same spectrum, is the abnormal translocation of TAR DNA binding protein 43 (TDP-43) from the nucleus to the cytoplasm, where it aggregates. TDP-43 is primarily a nuclear protein that plays essential roles in RNA splicing and RNA metabolism. In our previous publication, we showed that TDP-43 stabilizes G3BP1 mRNA. G3BP1 is a core component of stress granules, which form through liquid-liquid phase separation when cells are exposed to external stress. This stress response, which is thought to be impaired in ALS patients, is critical for maintaining cell viability. Consistent with this, we also found that G3BP1 transcript levels are reduced in ALS/FTD neurons exhibiting TDP-43 pathology. Our lab has further demonstrated that stress granule (SG) formation is impaired in a mouse model expressing the ALS-causing TDP-43 M337V mutation. We next sought to determine whether this defect is also present in other ALS models, such as rNLS8 and TDP-43 Q331K mice. To evaluate SG formation in vivo, we developed a whole-body hyperthermia protocol that subjects mice to heat stress. This paradigm activates the integrated stress response (ISR) and promotes SG formation, which can be tracked using poly(A) labelling by FiSH, an obligate component of stress granules. SG protein levels will be measured by western blot, while TDP-43 translocation and aggregation will be assessed by immunofluorescence. Together, this work will provide valuable insight into stress granule dynamics in vivo in the context of TDP-43 proteinopathies.

A17 –

Thérapie cognitivo-comportementale en ligne et rythmes veille-sommeil : étude chez des personnes âgées souffrant d'insomnie chronique

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Chez les personnes âgées, l'insomnie chronique constitue le trouble du sommeil le plus répandu. Cela s'explique notamment par les altérations du sommeil liées au vieillissement, incluant des perturbations du rythme circadien. Une altération de marqueurs circadiens a récemment été associée à un sommeil moins réparateur chez des personnes souffrant d'insomnie. Dans cet essai randomisé contrôlé, nous avons investigué l'effet d'une thérapie cognitivo-comportementale en ligne (eTCC+) pour l'insomnie sur les rythmes veille-sommeil chez des personnes âgées souffrant d'insomnie chronique. Comme la eTCC+ régularise les horaires de sommeil et est efficace, nous faisons l'hypothèse d'une amélioration de l'organisation temporelle des périodes de sommeil et d'éveil après l'intervention. 26 participants souffrant d'insomnie ont été randomisés dans le groupe eTCC+ (67,0±4,9 ans, 21 femmes) et 27 (67,2±5,3 ans, 22 femmes) dans le groupe contrôle actif (intervention ciblant la santé générale, CTRL). Les participants ont porté un actimètre pendant deux semaines lors de l'évaluation initiale (V1) et après 10 semaines (V2). Deux indices d'actimétrie ont été dérivés: la variabilité intrajournalière (VI), qui reflète la fragmentation des rythmes de veille-sommeil au cours d'une journée, et la stabilité interjournalière (SI) qui indique la régularité des rythmes d'un jour à l'autre. Des analyses ANCOVA mixtes ont été effectuées avec les facteurs temps et groupe en ajustant pour l'âge et le sexe. La VI (p=.005) et la SI (p=.033) ont augmenté de V1 à V2 dans les deux groupes. Aucun effet significatif de l'interaction groupe×temps n'a été trouvé (VI:p=.462;SI p=.300). Ces augmentations correspondent à un rythme veille-sommeil moins fragmenté et plus régulier au suivi en comparaison à l'évaluation initiale. La eTCC+ n'a pas démontré d'effet spécifique sur le rythme veille-sommeil chez les aînés souffrant d'insomnie chronique. La tenue d'un journal de sommeil pourrait favoriser un horaire de sommeil plus régulier et pourrait expliquer les augmentations observées, indépendamment du groupe.

A18 –

Tracking early neural markers of developmental language disorder in bilingual children: a longitudinal fNIRS study

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Developmental Language Disorder (DLD) affects approximately 7-8% of preschool-aged children and has lasting consequences on cognitive and social development. Early detection is crucial to optimize intervention outcomes; however, current diagnostic tools remain limited, particularly for bilingual children. This longitudinal study investigates the neural patterns underlying DLD in French-English bilingual preschoolers using functional near-infrared spectroscopy (fNIRS).

The main goal is to identify early neural biomarkers of DLD and examine how the disorder impacts language processing, working memory, and brain activity. Thirty bilingual children aged 36-60 months will be recruited and divided into two groups: typically developing (TD) and diagnosed with DLD. The experimental tasks include language measures (nonword repetition, vocabulary, and language-switching tasks) and memory assessments (digit span and picture recall).

Brain activity will be recorded with fNIRS and analyzed using mixed-effects modeling, parametric tests, and growth curve modeling. Although data collection is ongoing, we hypothesize that children with DLD will show distinct activation patterns, particularly in regions associated with language and working memory. By identifying early neural biomarkers, this research aims to enhance screening tools, inform clinical interventions, and strengthen educational practices. Ultimately, the findings could support more equitable access to neurodevelopmental assessments and guide future research on targeted interventions in bilingual populations.

A19 –

Optimisation des paramètres de stimulation magnétique transcrânienne basée sur l'apprentissage-machine pour réduire la variabilité et augmenter l'efficacité

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La stimulation magnétique transcrânienne (SMT) est une technique non-invasive sécuritaire qui permet de moduler l'activité corticale à l'aide d'impulsions électromagnétiques appliquées sur le crâne. Il s'agit d'une approche prometteuse pour étudier le cerveau et pour favoriser la réadaptation motrice après des lésions telles que causées par l'accident vasculocérébral (AVC). Toutefois, les études rapportent que les effets de la SMT varient considérablement d'une personne à l'autre, notamment parce que les protocoles actuels utilisent des paramètres de stimulation fixes appliqués uniformément à tous les participants. Cette variabilité limite la reproductibilité des effets et l'efficacité de la thérapie. Notre hypothèse principale est que l'individualisation des paramètres de stimulation pourrait maximiser les effets modulateurs induits par la SMT. À ces fins, nos groupes de recherche ont développé un algorithme d'apprentissage-machine capable d'optimiser les paramètres de stimulation selon chaque individu. Les réponses musculaires de la main et du bras à différentes stimulations sont enregistrées et utilisées pour entraîner l'algorithme, qui apprend ensuite à modéliser la relation entre les paramètres et les réponses observées. Il peut ainsi prédire et ajuster en temps réel les combinaisons paramétriques produisant les effets les plus marqués. Cette approche constitue la première application de notre algorithme à une technique de neurostimulation non-invasive chez l'humain. À long terme, elle pourrait transformer l'usage clinique de la SMT en rendant les traitements de réadaptation motrice plus efficaces, personnalisés et accessibles aux personnes vivant avec des déficits moteurs dus à un AVC.

A20 –

Un déséquilibre du GABA dans le cortex cingulaire antérieur est associé à des perturbations du sommeil dans l'insomnie chronique

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L'insomnie chronique est un trouble du sommeil affectant la santé et la qualité de vie de nombreuses personnes. Elle a été associée à plusieurs altérations cérébrales suggérant notamment un surplus d'activité et un défaut d'inhibition neuronale. Le GABA, comme principal neurotransmetteur inhibiteur, est clé dans le fonctionnement cérébral et le sommeil. Certaines études pointent vers un déséquilibre de l'inhibition GABAergique, particulièrement dans le cortex cingulaire antérieur (CCA), chez les personnes souffrant d'insomnie, mais les résultats demeurent hétérogènes. Cette étude cherche donc à évaluer les relations entre les niveaux de GABA, mesurés par spectroscopie à résonance magnétique du proton (1H-MRS), et les perturbations du sommeil en insomnie.

Dans le cadre d'un essai clinique randomisé contrôlé, des évaluations pré-traitement, incluant une séance d'IRM avec acquisition 1H-MRS, ont été administrées chez 57 adultes avec insomnie chronique (38 femmes, 44,0±11,1 ans) et 20 contrôles bons dormeurs (10 femmes, 36,8±11,5 ans). Nous avons quantifié les niveaux de GABA auCCA, qui ont été comparés entre personnes avec insomnie et contrôles, et corrélés avec différents paramètres extraits de journaux de sommeil.

Aucune différence significative n'a été constatée dans les concentrations de GABA avec ou sans insomnie ($p>0,05$). Nos résultats confirment toutefois, chez les personnes avec insomnie, une association entre moins de GABA et des paramètres indicatifs d'un moins bon sommeil, soit plus d'éveils nocturnes ($t=-0,2$, $p=0,025$) et une plus faible efficacité de sommeil ($t=0.18$, $p=0,039$). Surprenamment, nos résultats montrent une corrélation positive entre le ratio GABA/glutamate, reflétant l'équilibre entre inhibition et excitation, et la latence d'endormissement ($t=0.26$, $p=0,015$).

Nos résultats initiaux supportent une implication du GABA dans les perturbations du sommeil en insomnie chronique. Pour mieux comprendre le rôle de l'inhibition GABAergique dans la neurobiologie de l'insomnie et son traitement, nous évaluerons ensuite l'effet d'une thérapie cognitivo-comportementale sur le GABA et ses relations avec le sommeil.

A21 –

Segmentation automatique de gliome de bas grade pédiatrique

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Mon projet de maîtrise porte sur le développement d'un système de segmentation automatique des gliomes de bas grade pédiatriques à partir d'images d'IRM, dans le cadre de l'essai clinique TRAM-01 évaluant l'efficacité du trametinib, un inhibiteur de la voie MAPK. L'objectif principal est d'automatiser et d'optimiser la détection et la délimitation des tumeurs cérébrales afin d'améliorer le suivi clinique et la mesure de la réponse au traitement. Pour ce faire, j'utilise le cadre d'apprentissage profond nnU-Net, un modèle auto-adaptatif basé sur la U-Net, qui ajuste automatiquement son architecture et ses hyperparamètres en fonction des caractéristiques des données médicales. Les performances de ce modèle sont comparées à celles de méthodes classiques, telles que les U-Net standards, les approches atlas-based et semi-supervisées. Les données d'entrée proviennent d'IRM multimodales (T1, T2, FLAIR) prétraitées et anonymisées. La segmentation manuelle réalisée sous 3D Slicer par des experts sert de référence pour l'entraînement et la validation du modèle. L'évaluation repose sur plusieurs indicateurs de performance, dont le Dice Similarity Coefficient et la robustesse intersujet. Le but ultime est de réduire le temps d'analyse, de minimiser la variabilité interobservateur et d'accroître la précision du suivi longitudinal des volumes tumoraux.

Ce projet s'inscrit dans une démarche translationnelle visant à intégrer l'intelligence artificielle dans la pratique clinique en neuro-oncologie pédiatrique. En facilitant la quantification objective de la réponse au trametinib, il pourrait contribuer à une meilleure personnalisation du traitement et à l'amélioration de la qualité de vie des enfants atteints de gliome.

A22 –

Compound heterozygous inheritance with tissue-specific imbalance in IARS1 causes congenital myopathy

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Congenital myopathies are diagnostically challenging and genetically heterogeneous disorders. We investigated a familial case comprising of three affected siblings born to unaffected parents. Clinical features included generalized hypotonia, while muscle biopsies revealed fiber atrophy with centralized nuclei.

A combination of whole-exome and muscle RNA sequencing enabled the identification of a tissue-specific allelic imbalance of the isoleucyl-tRNA synthetase (IARS1) gene. Variant analysis revealed a compound heterozygous inheritance pattern in IARS1, whereas the mother carried a heterozygous missense variant (p.R661H) while an intronic variant near exon 25, a known methylation region, was uncovered in the father through whole-genome sequencing. In the affected children, transcriptomic data revealed a near-exclusive expression of the maternal pathogenic allele in muscles, suggesting a tissue-specific silencing of the paternal allele. The resulting pseudo-homozygous state explains the congenital myopathy in the children despite the asymptomatic carrier status of the mother and the absence of additional de novo variants.

To validate IARS1's role in muscle function, we showed that muscle-specific knockdown of its ortholog in C. elegans causes progressive sarcomeric disorganization. To dissect the cellular consequences of the variants, we established human cell models of IARS1-knockout myoblasts and myotubes transdifferentiated from patient fibroblasts for mechanistic studies. We performed functional assays to determine the downstream effects of impaired IARS1 function, including cellular metabolism (WST-1), proliferation (IncuCyte), and enzyme kinetics (aminoacylation).

This work highlights a novel muscle-specific, epigenetically modulated compound heterozygous inheritance mechanism for an AARS-related myopathy and provides insights into how disruptions in protein synthesis lead to a specific muscle pathology.

A23 –

Co-expression profiles of cell adhesion molecules (CAMs) across leukocyte sub-populations in the context of multiple sclerosis (MS)

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Introduction: Multiple sclerosis (MS) is an immune-mediated neurological disease characterized by leukocyte infiltrations into the central nervous system (CNS), leading to demyelination and neurological disabilities. The transendothelial migration of leukocytes depends on the expression of cell adhesion molecules (CAMs). Recently, DICAM was described as a key mediator of pathogenic Th17 CNS infiltration. However, anti-DICAM blockade has shown partial efficacy in vitro and in vivo, probably due to functional redundancy, as other CAMs exist and promote CNS infiltration in MS. In this study, I will establish the distinct CAMs co-expression profiles underlying the various leukocyte subsets.

Methods: The co-expression of CAMs is studied by flow cytometry using peripheral blood. People with MS (PwMS) and healthy controls (HC) are compared. Our flow cytometry panel discriminates between five subsets of cells known to contribute to MS (NK, CD4 and CD8 T cells, B cells, monocytes). This panel is complemented by DICAM, ALCAM, MCAM and JAML antibodies.

Results: Preliminary data (12 MS, 12 HC) revealed four CAMs monocyte subsets dominated by a double positive DICAM+ JAML+ subpopulation (30%). The DICAM+ JAML+ MCAM+ monocyte subset was increased in PwMS. In B, T and NK cells, CAMs patterns were more homogenous with 1 or 2 profiles, with not difference between PwMS and HC. Preliminary migration assays conducted in modified Boyden chambers (n=2) suggest an enrichment of CAMs in migrated cells, consistent with their role in CNS infiltration.

Conclusion: Monocytes harbour a complex pattern of CAMs co-expression dominated by DICAM+JAML+ subset. PwMS displayed more CAMs co-expression. In vitro assays will be performed to verify if these distinct profiles affect the monocyte's capacity to migrate across endothelial cells and their sensitivity to an anti-DICAM blockade. These findings may support the relevance of combinatory CAM blockades as a strategy for better preventing CNS infiltration in MS.

Subvention: MS Canada

A24 –

Peripheral stimulation immediately alleviates walking deficits in a feline model of incomplete spinal cord injury

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Physical rehabilitation following spinal cord injury facilitates the recovery of locomotion, albeit with persisting deficits such as foot dragging. Peripheral nerve stimulation has shown potential to modify locomotor patterns, but this strategy has not yet been tested in preclinical models of motor paralysis. To address this unmeet need, we developed an approach that allows peripheral stimulation to be applied in synchrony with walking. We used a feline model of thoracic spinal cord contusion (T10) which induces a transient paralysis of both hindlimbs and long-term locomotor impairments, such as foot drag. In three cats, we bilaterally implanted cuffs around the superficial peroneal cutaneous nerves of the two hindlimbs. Before and after a spinal cord contusion, we enhanced the evoked motor response by optimizing the amplitude, timing, frequency, and duration of nerve stimulation.

In n=3 cats, peripheral stimulation efficiently modulated foot trajectory during treadmill locomotion, resulting in an increase in step height and a reduction of paw dragging. The stimulation exhibited maximum efficacy when applied at the onset of the swing phase, particularly at a frequency of 120 Hz with a burst duration of 150 ms. Notably, the stimulation amplitude demonstrated a linear modulation of step height within a functional range. This study holds significant potential for clinical translation, particularly due to the accessibility of targeting the cutaneous nerve in spinal cord injured patients. Comparable stimulation protocols could be implemented to aid in rehabilitation efforts and foster gait recovery.

A25 –

Modulation des rythmes de l'hippocampe par les neurones glutamatergiques du raphé median

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Le raphé médian contient une population glutamatergique caractérisée par l'expression du transporteur vésiculaire du glutamate de type 3 (VGLUT3) qui projette à l'hippocampe. Deux rythmes de l'hippocampe soit les « sharp-wave ripples » (SWR, ~50 ms, 150-250 Hz), présents majoritairement durant le sommeil NREM, et le rythme thêta (5 à 12 Hz), présent durant le sommeil REM et l'éveil, sont modulés par l'activité du raphé médian. Ces rythmes sont essentiels à la consolidation de la mémoire, une fonction clé de l'hippocampe. Toutefois, la contribution spécifique des neurones VGLUT3+ du raphé médian à la modulation de ces rythmes n'a pas été décrite. Les objectifs de notre étude sont de 1) mesurer l'activité des neurones VGLUT3+ pendant les états de vigilance en relation avec les rythmes de l'hippocampe, et 2) d'évaluer l'impact de la manipulation de l'activité des neurones VGLUT3+ sur les SWR et le rythme thêta. Pour cibler les neurones VGLUT3+, nous injectons des virus Cre-dépendants dans le raphé médian de souris VGLUT3-Cre. D'abord, l'activité des neurones VGLUT3+ a été mesurée à l'aide de la photométrie de fibre avec l'enregistrement simultané de l'hippocampe. Les neurones VGLUT3+ sont très actifs à l'éveil et en sommeil REM. Leur activité covarie avec la fréquence et la puissance du rythme thêta. Pendant le sommeil NREM, ils sont actifs par bouffées anticorrélées à l'occurrence des SWR. Ensuite, les neurones VGLUT3+ ont été activés ou inhibés à l'aide de l'optogénétique. L'activation des neurones VGLUT3+ pendant le sommeil NREM réduit drastiquement les SWR. Pendant le sommeil REM, les manipulations optogénétiques perturbent le rythme thêta. Nos résultats montrent un patron d'activité contrasté des neurones VGLUT3+ du raphé médian à travers les états de vigilance et révèlent une importante modulation des SWR et du rythme thêta. Cela suggère une contribution potentielle aux fonctions de l'hippocampe tel que la consolidation de la mémoire.

A26 –

In vivo investigation of the effect of early-life stress on the calcium dynamics of astrocytes and behaviors during the dark/active phase in mice

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Early-Life Stress (ELS) is a major factor in vulnerability to emotional and motivational disorders in adulthood. This study aims to explore the impact of ELS on the calcium dynamics of astrocytes of the lateral hypothalamus (LH), a key region in the regulation of wakefulness, motivation, and behavioral homeostasis. Using in vivo calcium fiber photometry, we recorded the activity of LH astrocytes in naive and ELS mice in different contexts: exploration and locomotion (open field), anxiety (elevated plus maze), and motivation (voluntary wheel running). Recordings were made during the dark phase, a period of natural activity for rodents. Our results show that ELS has heterogeneous effects depending on the context. Behaviorally, the most marked changes concern anxiety-related behaviors: ELS males exhibit a significant increase in freezing, while naive females explore the environment more, a behavior that is reduced after ELS. Conversely, motivated behaviors in a familiar environment, such as voluntary running, appear to be generally preserved. At the cellular level, the calcium activity of LH astrocytes seems strongly modulated by the behavioral context and altered by ELS. Under basal conditions, astrocytes activate during exploration of open areas or transition to motor behavior. After ELS, hypo-responsiveness is observed in anxiogenic contexts and an exaggerated or disorganized response in locomotor transitions. These data suggest that ELS alters the balance of glial responses, with increased sensitivity in some contexts and disengagement in others.

A27 –

Neurovascular dynamics underlying intermittent theta burst stimulation

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Les techniques de neuromodulation sont des outils essentiels à la compréhension et à la promotion des mécanismes de plasticité neuronale. La stimulation theta burst intermittente (iTBS) est une technique prometteuse car applicable de manière non invasive. Cependant la variabilité de ses résultats limite son utilisation. La plasticité neuronale repose sur des schémas spécifiques d'activité neuronale en étroite relation avec le système vasculaire. Caractériser cette relation offrirait une fenêtre unique pour mieux appréhender ses mécanismes et ainsi optimiser son utilisation.

Mon projet se décompose en deux étapes. Dans un premier temps, il s'agit d'identifier les dynamiques neurovasculaires du cortex moteur autour de l'iTBS. Dans un second temps, l'objectif est d'évaluer à quel point les paramètres neurovasculaires les plus informatifs permettent de prédire le résultat de la neuromodulation. L'hypothèse générale est qu'il est possible d'extraire des signatures neurovasculaires et d'en faire des prédicteurs du résultat de l'iTBS.Le plan expérimental combine des enregistrements électromyographiques évoqués, reflets de changements d'excitabilité corticospinale, et des mesures de débit sanguin cérébral chez un modèle de rat anesthésié à travers un protocole iTBS. (Objectif 1) Nous évoquons des changements neurovasculaires avant, pendant et après l'iTBS sur lesquels nous extrayons des paramètres temporels. Ces derniers sont compressés pour fournir une visualisation de l'évolution neurovasculaire au cours du temps. (Objectif 2) L'apprentissage automatique est utilisé pour classifier les différents résultats de l'iTBS puis ces données servent à entrainer un nouveau classifieur capable de prédire un résultat à partir des représentations neurovasculaires calculées précédemment.

Cette approche combine l'expertise des laboratoires Martinez et Girouard et permettra une caractérisation unique des relations neurovasculaires dans le cadre de la plasticité neuronale. En plus de contribuer à la fiabilité de l'iTBS, notre étude impactera aussi directement les procédures largement utilisées chez l'Homme, reposant sur la mesure du débit sanguin pour inférer l'activité neuronale.

A28 –

Sub-anesthetic ketamine impairs auditory deviance detection across cellular, population, and mesoscale levels

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Detecting unexpected sensory events is crucial for adaptive behavior. In the neocortex, repetitive stimuli elicit reduced responses, whereas deviant stimuli trigger enhanced activity. This phenomenon is reflected in the mismatch negativity (MMN), an EEG biomarker of deviance detection that depends on NMDA receptor function. Despite its importance, the cellular and network mechanisms involved remain poorly understood. We used multi-electrode array recordings in awake mice to investigate how sub-anesthetic ketamine, a partial NMDA receptor antagonist, affects auditory deviance detection. In primary auditory cortex (A1), a subset of neurons exhibited a biphasic spiking response to deviant sounds. The second peak of this response was abolished after ketamine administration, highlighting NMDA receptor-dependent signaling. We also recorded from the posterior parietal cortex (PPC), a key hub for multisensory integration. PPC neurons responded selectively to deviant, but not repetitive, sounds, and this response required intact NMDA receptor function. Functional connectivity analyses using Granger causality and Weighted Phase Lag Index revealed directed signaling from A1 to PPC during deviant detection. Ketamine disrupted this inter-regional communication, indicating impaired propagation of prediction error signals. Together, these results show that sub-anesthetic ketamine weakens both local neuronal responses and long-range cortical coordination during auditory deviance detection. Our findings provide new insights into how NMDA receptor hypofunction alters predictive processing in the auditory system. This work is currently under review for publication in the European Journal of Neuroscience.

Impact: This work identifies ketamine-sensitive cortical circuits that support novelty detection, offering a mechanistic understanding of NMDA receptor-dependent predictive processing. These insights are relevant for interpreting sensory and cognitive deficits in neuropsychiatric disorders and may inform future therapeutic strategies targeting impaired cortical communication.

A29 –

Functional connectivity between the primary and premotor cortices during ipsilateral and contralateral reaching-to-grasp movements in macaque monkeys

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Hand movements rely on coordinated activity across multiple cortical areas, including primary motor cortex (M1) and the dorsal (PMd) and ventral (PMv) premotor cortices. While these regions have distinct roles in motor control, the nature of their intra-hemispheric connectivity is still not well understood. Gaining insight into their neural dynamics is essential for understanding how motor information is coded and processed. We simultaneously recorded neural activity from M1, PMd and PMv of three macaques as they did a precision grip (PG) task with either the contralateral or ipsilateral hand. Connectivity was analyzed using a time-resolved cross-correlation approach between well-isolated neurons, examining temporal alignment with behavioral markers and lag-dependent connectivity within cortical networks during the PG task. We then compared connectivity patterns between M1-PMv, M1-PMd, and PMv-PMd using Z-scores by measuring coupling strength as a function of task performance, which was defined by the incidence and magnitude of Z-scores. Coupling strength was analyzed separately for each monkey, followed by pooling the results across three monkeys for group-level analysis. Marked changes in connectivity pattern were observed across different task phases. At the population level for M1-PMv and M1-PMd, coupling strength was highest during reaching when data were aligned was relative to the go-cue event as well as at the end of grasp when the alignment was with the start of grasp for both arms. However, it was consistently stronger and more defined for the contralateral arm. For PMv-PMd, coupling strength followed a similar trend but was generally lower than M1-related connections, with stronger interactions for the contralateral arm and weaker for the ipsilateral arm. The analysis shows that premotor areas initially lead M1 during strong coupling periods, indicating a shifting direction of influence that later reverses. High-resolution recordings reveal motor network dynamics, advancing understanding of neurological disorders and treatments.

A30 –

Contribution of inflammation to the underlying pathobiological mechanisms of back pain

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Degeneration of the intervertebral discs (IDD) contributes to back pain and is characterized by extracellular matrix (ECM) degradation, neovascularization, and immune cells infiltration. Inflammation is increasingly recognized as a key factor in IDD pathobiology, both locally in disc and systemically. Matrix metalloproteinases (MMP) participate in ECM degradation, but the inflammatory triggers driving their activation remain unclear. Altered plasma levels of growth factors, cytokines, and chemokines have been reported in IDD patients compared to controls. Our group recently identified plasma biomarkers predictive of post-surgical recovery, showing that high CRP and low CCL22 levels, combined with age, predict incomplete recovery, whereas the opposite profile indicates full recovery. We hypothesize that peripheral inflammatory molecules can penetrate the disc and contribute to its degeneration.

Clinical data (age, sex, pain, and recovery at two months post-surgery) were collected. Peripheral blood mononuclear cells (PBMCs) were isolated from IDD patients pre-surgery and age/sex-matched healthy controls (HC). RNA sequencing was performed on PBMCs. Resected disc tissues were digested to isolate disc cells, which were cultured and exposed to inflammatory molecules (IFNγ, IL-1β, TNF, CRP, leptin, IL-18) for 48h. Supernatants and lysates were analyzed by multiplex ELISA, and surface markers by flow cytometry.PBMCs from IDD patients exhibited a distinct transcriptional profile, with upregulation of P2RY1, SLC1A3, and TLR2 compared to HC, suggesting increased immune activation. Human disc cells exposed to inflammatory stimuli secreted higher levels of MMP-1, 2, 3, 7, 10, and 13, while TIMPs remained unchanged, indicating an imbalance favoring ECM degradation. Moreover, CRP, leptin and IL-18 treatments enhanced the expression of adhesion molecules CD24 and CD54, while CRP and IL-18 also upregulated CD155 and HLA-ABC, supporting enhanced immunogenic potential.IDD patients exhibit distinct immune signatures. Inflammatory mediators promote ECM degradation and disc cell activation, highlighting potential therapeutic targets in IDD-associated inflammation.

A31 –

Deep learning of motor biomarkers: video-based detection of epileptic seizures

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Introduction: Epilepsy affects over 50 million people worldwide. One-third continue to experience drug-resistant, unpredictable seizures that can lead to injury and, in rare cases, sudden unexpected death. Automated video monitoring of patient motion offers a non-invasive approach to seizure detection, particularly where electroencephalography is not feasible. However, existing models are trained on short clips, leading to inflated performance estimates and high false-alarm rates when applied to continuous recordings. To address this, we aim to develop a real-time deep-learning model trained on long-term video recordings that relies solely on motion cues to detect bilateral tonic-clonic seizures.

Methods: We used the CHUM epilepsy monitoring unit database (9,350 hours, 41 patients, 74 bilateral tonic-clonic seizures) for model development. An object detection model was fine-tuned to localize patients, and a Recurrent All-Pairs Field Transforms (RAFT) model was optimized to quantify motion within patient subframes. Next, 3D convolutional neural networks will be trained on continuous, patient-only motion streams. Models will be validated using patient-wise nested cross-validation (85% training/validation, 15% held-out testing) and integrated into a real-time seizure detection pipeline. Performance will be assessed in terms of precision and recall for the patient detector module, and sensitivity, false alarms rate and detection latency for the seizure detection.

Preliminary Results and Expected Outcomes: The patient detector achieved 97.6% recall and 96.8% precision, remaining robust under occlusion and low-visibility conditions. Motion extraction was computed at 150 frames per second, capturing pixel-level displacement between consecutive frames. It is expected that our deep learning model will learn from these motion fields to distinguish daily activities from seizure activity, enabling accurate and real-time video-based seizure detection.

Conclusion: A patient-focused model trained on motion data from continuous recordings enable real-time seizure detection. By overcoming the bias of clip-trained systems, this method shows potential for scalable monitoring in outpatient settings.

A32 –

Why do substantia nigra dopamine neurons grow such a complex axonal arbor? An in vitro exploration

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Dopamine (DA) neurons of the substantia nigra pars compacta (SNc) are known to establish a distinctly arborized axonal domain, with a much larger number of axonal neurotransmitter release sites compared to most other types of neurons. Ventral tegmental area (VTA) DA neurons show a more modest axonal arbor. This characteristic has been suggested to contribute to the elevated vulnerability of SNc DA neurons and other affected neuromodulatory neurons in Parkinson's disease. Very little is presently known about the cellular and molecular developmental mechanisms that underlie such axonal complexity. Our global hypothesis is that a unique cell-autonomous mechanism drives axonal branching in DA neurons, but that glial and neuronal-derived signals also contribute. To tackle this question, primary postnatal neurons obtained from transgenic mice expressing the red fluorescent protein tdTomato selectively in DA neurons were examined using immunocytochemistry and confocal imaging. Our results reveal that the rate of growth over 3 days in vitro (DIV) is almost twice as fast for SNc neurons compared to VTA DA neurons. This suggests that a key stage of axonal development occurs before 3 DIV in our model.

Activity-dependent mechanisms also seem to be already at play at this early stage because blocking firing with tetrodotoxin reduces axonal development. In line with this, we find that DA neurons at this early stage already fire at a rate of approximately 2 Hz. We are presently exploring the contribution of glial-derived secreted factors to this initial axonal development. This project will provide a better understanding of the development of DA neurons, which could ultimately help to identify new strategies to reduce their vulnerability in Parkinson's disease.

A33 –

Preservation of neural dynamics across species

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Over evolutionary timescales, natural selection guides changes in ancestral brain circuits to produce behaviors that are advantageously adapted to each species' environment. Nevertheless, aspects of the resulting neural circuitry, such as brain regions, are conserved across species even with distant evolutionary ancestors. The motor cortex, for example, first emerged over 125 million years ago and performs similar functions in many modern mammals including rodents and primates. However, it remains unclear whether these ancestral regions operate by similar neural processes in these divergent species. Here, we hypothesized that despite their phylogenetic distance, the motor cortex of mice, monkeys, and humans should produce behavior by conserved functional processes, captured here through neural population dynamics. We tested this empirically using a dataset of neural population activity recorded intracortically from the motor cortex of three species (mice, monkeys, and a human) performing reaching, grasping, and object manipulation tasks with their forelimbs/ arms. We compared the neural dynamics within- and across-species using Dynamical Similarity Analysis (DSA), an analytical approach to compare the underlying rules governing the state transitions of two different dynamical systems. Remarkably, we found that neural dynamics were as similar across all species as any two individuals within a species, indicating evolutionarily preserved functional processes for movement in the motor cortex. Indeed, neural dynamics were more similar across species than those across brain regions even in the same human (motor cortex vs. somatosensory cortex) and across distinct behavioral contexts in the same monkeys (covert planning vs. overt movement). Altogether, these findings suggest strong conservation of motor cortical dynamical processes across species. We thus assert that evolution maintains effective functional processes across the phylogenetic tree even as behavioral repertoires expand.

A34 –

Human iPSC models reveal a protective role for NEUROD6 against Alzheimer's-related pathology

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Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by cognitive decline, synaptic dysfunction, and neuronal loss. Although numerous genetic and epigenetic alterations have been associated with AD, the molecular mechanisms through which they contribute to disease progression remain incompletely understood.

Recent single-nucleus RNA sequencing (snRNA-seq) across seven brain regions from 48 individuals, including AD patients and healthy controls, revealed a specific and consistent downregulation of NEUROD6 in excitatory neurons of AD brains. NEUROD6 encodes a transcription factor critical for neuronal differentiation, plasticity, and survival.

To explore its functional role in AD, we mapped NEUROD6 genomic binding sites in neurons derived from wild-type human induced pluripotent stem cells (iPSCs). This analysis revealed that NEUROD6 directly regulates several AD-associated genes, including DLG4 and GSK3B. Furthermore, overexpression of NEUROD6 in iPSC-derived neurons from AD patients significantly decreased β-amyloid42 peptide levels, indicating a potential protective effect against AD-related pathology.

Together, these findings suggest that the loss of NEUROD6 expression in AD may disrupt transcriptional programs essential for neuronal function and resilience. Our results position NEUROD6 as a novel modulator of AD pathophysiology and a potential therapeutic target. Restoring NEUROD6 activity could represent a promising strategy to counteract key molecular drivers of AD and promote neuronal health.

This study also highlights the value of iPSC-based human neuronal models in uncovering disease-relevant mechanisms and opens new perspectives on the role of transcriptional regulation in neurodegenerative disorders.

A35 –

Distinguishing primary progressive multiple sclerosis via peripheral immune cell transcriptomic profiles

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Introduction. Multiple sclerosis (MS) is a central nervous system (CNS) autoimmune disorder, characterized by neuroinflammation, demyelination, and neurodegeneration. Peripheral immune cell infiltrates are observed in MS brain tissue. In Canada, ~10% of patients are diagnosed a posteriori with primary progressive MS (PPMS), defined by steady neurological decline. Current disease-modifying therapies (DMT) are less effective in PPMS, highlighting the need to explore their immune specificities and alterations. I aim to identify disease-defining immunological signatures that can discriminate PPMS from other treatable relapse-remitting MS (RRMS) and healthy controls, define disease severity, and are refractory to DMT.

Methods. I have selected an age- and sex-matched cohort (N=56) from single-cell RNA sequencing (scRNAseq) samples collected for the CANadian PROspective COhort Study for People Living with MS (CanProCo): selected PPMS patients show higher disease duration (measured as time since first symptoms to study enrollment) and severity via Expanded Disability Status Scale (EDSS) than RRMS. As scRNAseq enables characterization of heterogenous immune cell identity and function, I can compare the transcriptional profiles of PPMS to RRMS and healthy donors using R and python packages.

Results. I generated a scalable preprocessing pipeline with six samples and 37844 single cells. Upon integration, I identified 16 clusters, each ranging 13-7400 cells, ~2800 genes/cell, and ~9600 UMIs/cell. Cluster resolution assessment, annotation, and scaling from six to 56 samples is underway.

Conclusion. Next, I will compare cluster composition and differentially expressed genes in PPMS, then validate discriminating cell subpopulations to define transcriptional signatures indicative of PPMS, generating a deep scRNAseq profiling of peripheral signatures in MS. As PPMS is poorly understood and inadequately treated by current DMT, identifying cell-specific transcriptional programs linked to disease severity and treatment response can drive potential biomarker discovery and inform targeted therapeutic strategies.

A36 –

Quantification neurodégénérative du putamen dans le trouble comportemental en sommeil paradoxal et ses impactes sur l'architecture de connectivité cérébrale

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Le trouble comportemental en sommeil paradoxal isolé (TCSPi) se caractérise par une perte d'atonie musculaire pendant le sommeil paradoxal. C'est un précurseur aux synucléinopathies, avec ~90% des patients développant la maladie de Parkinson (MP) ou la démence à corps de Lewy (DLB) après 15 ans. Des études IRM ont identifié une atrophie du putamen dans le TCSPi, structure centrale à la régulation des mouvements. On ignore encore si son atrophie suit un schéma topographique et si ses patrons de connectivité sont affectés. Notre objectif est d'étudier comment l'atrophie affecte la morphologie du putamen dans le TCSPi et son impact sur les patrons de connectivité afin d'identifier un marqueur prédictif de conversion. L'étude porte sur 198 patients TCSPi suivis longitudinalement et 121 contrôles appariés en âge et sexe. Tous ont reçu des scans IRM T1 et de diffusion dans le cadre d'une initiative internationale multicentrique. Les scans T1 sont analysés par morphométrie basée sur la déformation pour déterminer le degré d'atrophie. Puis, le putamen est segmenté le long des axes anatomiques pour examiner son schéma spatial d'atrophie. Une régression Cox évalue si le schéma identifié dans le TCSPi prédit la conversion en MP ou DLB. À partir des IRM de diffusion, la tractographie reconstruit les fibres de matière blanche pour dériver les matrices de connectivité structurelle. Ensuite, BrainSpace dérive les gradients de connectivité individuellement, une mesure d'affinité aux patrons de connectivité. Les gradients sont comparés pour déterminer si le putamen est anormalement pondéré sur ceux-ci. Dans le TCSPi, la section latérale du putamen à l'hémisphère gauche est plus atrophiée, et cette atrophie prédit la conversion en MP. Trois gradients de connectivité ont été identifiés pour tous les participants, avec une altération du premier gradient du putamen et une préservation des autres dans le TCSPi, indiquant une connectivité altérée mais pas ségrégée.

A37 –

Signature de déformation cérébrale qui prédit la demence à corps de Lewy dans le trouble comportemental en sommeil paradoxal

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Introduction : Le trouble du comportement en sommeil paradoxal isolé (TCSPi) constitue un stade précoce des synucléinopathies : plus de 90 % des patients développent une démence à corps de Lewy (DCL), une maladie de Parkinson (MP) ou une atrophie multisystématisée (AMS). Aucun biomarqueur cérébral ne permet de prédire le type de phénoconversion. Des travaux préliminaires ont suggéré qu'une signature cérébrale issue de l'IRM pouvait anticiper la conversion vers la DCL, mais elle n'a été testée que sur 70 patients et nécessite une validation à grande échelle.

Méthodes : Nous avons réuni 1450 IRM cérébrales issues de 11 sites : 456 patients avec TCSPi confirmé par polysomnographie, 332 avec une synucléinopathie manifeste (DCL, MP), et 662 contrôles. Les patients TCSPi ont été suivis en moyenne 7 ans, dont 101 ont évolué vers une synucléinopathie. Les IRM T1 ont été analysées par morphométrie basée sur la déformation, générant des cartes jacobiennes. La signature initialement identifiée a été répliquée et appliquée à ces cartes pour obtenir un score individuel, harmonisé selon site, âge et sexe. Un test t a été réalisé pour voir si les scores d'expression différaient entre les iRBD et les contrôles. Des analyses de survie ont été mené pour prédire le risque spécifique d'évolution vers la DCL.

Résultats : La signature retrouvait le profil d'atrophie initial, expliquant 28 % de la variance clinique. Elle est surexprimer chez les patients iRBD comparé au contrôles ($p < 0.001$; Cohen = 33%). Aussi, un score élevé prédisait une conversion vers la DCL chez les iRBD (HR = 2,14 ; p = 0,0016).

Discussion : Nous validons une signature IRM, capable de prédire spécifiquement la conversion vers la DCL. Ce biomarqueur ouvre la voie à la stratification des patients, à un suivi objectif de la neurodégénérescence et à de nouvelles stratégies de prévention et d'essais cliniques ciblés.

A38 –

Neuronal dynamics in the cortex of a mouse engaged in a virtual reality environment

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Fluorescent calcium (Ca2+) imaging is the gold standard in neuroscience used to unveil the intricacies of neuronal activity, such as how attention affects the brain. Combined with virtual reality (VR), it allows the investigation of complex information processing in a well-controlled ecological environment. This work showcases the spatiotemporal neuronal dynamics in head-fixed Thy1-gCaMP6s mice exposed to a moving VR scene. Ca2+ activity was recorded using mesoscopic fluorescence imaging, while 20-second videos simulating a journey in the mouse cage with different shelters and stimuli were displayed on 2 monitors in front of the animal. A salient stimulus (20 deg. horizontal sinusoidal grating at the top of the binocular visual field) was displayed for 7 sec during a stationary phase. Four simulations were presented: with or without the salient stimulus in a normal background (stim and sham, respectively), and with or without the salient stimulus in a dimmed background (grey filter application, stim/fg and sham/fg). Using the umIToolbox on MATLAB, the variation of fluorescence (ΔF/F) was extracted for different areas across the cortex and analyzed using a 1-way repeated measure ANOVA, i.e. in the primary visual cortex, extrastriate AM, LM, PM, AL visual areas, posterior parietal cortex (RL), retrosplenial, and anterior cingulate cortical areas. Our analysis showed a significant increase in Ca2+ activity upon the appearance of big or contrasted objects when the cage environment was moving, compared to the stationary phase, in the videos stim and sham for most cortical areas. The salient stimulus, although small, was powerful enough to evoke neuronal activity in the visual cortices, which were absent in the sham group. For stim/fg and sham/fg, the calcium response was increased only by the salient stimulus in the RL cortex. These results suggest that a dynamic VR simulation can elicit distinct neuronal activity in different cortical areas.

A39 –

Cartographie fonctionnelle peropératoire des faisceaux de matière blanche: une revue de la portée et méta-analyse

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Introduction : La stimulation électrique directe (SED), typiquement réalisée durant des chirurgies éveillées, consiste à appliquer un courant sur le cerveau afin de provoquer des déficits transitoires, mettant en évidence le lien entre une fonction et la région stimulée. Cette approche optimise la résection tout en préservant les structures critiques. Au-delà de son intérêt clinique, la SED fournit un aperçu unique du fonctionnement cérébral. Toutefois, si le cortex a été largement étudié par cette méthode, la matière blanche a reçu moins d'attention.

Méthodes : Nous avons synthétisé la littérature rapportant les fonctions de matière blanche obtenues par SED dans PubMed et EMBASE en suivant la méthodologie PRISMA.

Résultats : À partir de 2 681 sites de stimulation rapportés dans 200 articles, deux groupes de faisceaux de matière blanche ont été distingués. Le premier regroupait ceux associés à des fonctions principales primaires et non latéralisées : le faisceau corticospinal (motricité), les radiations optiques (perception visuelle) et les radiations thalamo-corticales (traitement somatosensoriel). Le second concernait des fonctions principales plus complexes et généralement latéralisées : le faisceau fronto-occipital inférieur (traitement sémantique bilatéral), le faisceau longitudinal supérieur et le faisceau arqué (traitement phonologique à gauche, mentalisation à droite), le faisceau longitudinal inférieur (lecture à gauche, reconnaissance visuelle à droite), le faisceau frontal oblique (production de la parole à gauche, boucle phonologique à droite) et le faisceau fronto-striatal (contrôle moteur bilatéral). Plusieurs faisceaux présentaient aussi des rôles moins fréquents. Une redondance fonctionnelle a également été observée pour certains faisceaux, suggérant l'existence de circuits communs sous-jacents.

Conclusion : Ce travail contribue à consolider les connaissances fonctionnelles sur la matière blanche, enrichissant ainsi notre compréhension globale du cerveau. Nous anticipons que ces résultats complémenteront les avancées en neuronavigation et orienteront la prise de décision neurochirurgicale, afin d'améliorer la qualité de vie des patients subissant une résection sous-corticale.

A40 –

Functional modeling of human epilepsy using neurons generated from patient-specific induced pluripotent stem cells

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Epilepsies affect over 50 million people worldwide, and approximately 50 % of the cases have an unknown etiology. As a result, the underlying mechanisms of the disease remain poorly understood. This lack of insight contributes to the fact that nearly one-third of patients are pharmacoresistant, failing to achieve seizure control despite treatment with at least two antiepileptic drugs (AEDs). While alternative treatments such as surgical resection of the epileptogenic focus exist, they often carry substantial risks and long-term consequences, which can significantly impact the patients' daily lives. The interindividual variability in response to AEDs underscores the need for personalized models to optimize therapeutic strategies. This research project aims to model the functional phenotypes of patient-specific epilepsies to support the development of individualized treatment approaches. We hypothesize that neurons differentiated from patient-derived induced pluripotent stem cells (iPSCs) represent a valid model for studying neuronal responses to AEDs, and may thus help predict pharmacological treatments efficacy for each individual patient. We obtained 12 epileptic patients' fibroblasts cell lines, which we reprogrammed into iPSCs and differentiated into functional neurons. We then assessed neuronal network activity through extracellular electrophysiology (multi-electrode array, MEA) in response to various AEDs. The neurons showed spontaneous activity patterns that varied between cell lines, with each presenting features resembling an epileptic phenotype. By enabling more personalized treatment approaches, this project could pave the way for precision medicine in epilepsy and meaningfully improve the quality of life for patients affected by these complex neurological disorders.

A41 –

Towards a better understanding of factors influencing regular cannabis use in persons living with psychosis: a qualitative collaborative research study

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Introduction : Selon l'enquête québécoise sur le cannabis (EQC), environ 12% des 18-35 ans consomment du cannabis de façon régulière. Pour les jeunes adultes admis dans un programme pour premiers épisodes psychotiques (PPEP), c'est près de la moitié d'entre eux. Les motifs de la consommation et les impacts, tant bénéfiques qu'indésirables, varient d'une personne à l'autre. L'objectif du projet est de caractériser les facteurs personnels et sociaux influençant l'utilisation de cannabis chez les personnes vivant avec un trouble psychotique.

Méthodes : Suivant une méthode qualitative, 33 entrevues semi-dirigées ont été menés chez des personnes vivant avec un trouble psychotique et consommant du cannabis régulièrement (≥3j/sem), ainsi que chez des proches. 22 entrevues individuelles et 11 groupes de discussion ont été réalisés à l'échelle de la province du Québec. Selon une méthodologie participative, les personnes avec expérience vécue (PAEV) et des proches de PAEV furent inclus à chaque étape du projet, notamment lors de la construction du guide d'entrevue et l'animation des groupes de discussion. Une approche hybride a servi à l'analyse : d'abord déductive, s'appuyant sur de thèmes inspirés du modèle socio-écologique, et ensuite inductive, découlant d'un processus itératif de révision des données.

Résultats : À ce jour, l'ensemble des entrevues sont codées, et l'analyse thématique est en cours. Les données ont entre autres été classées selon les catégories individuelles, relationnelles, communautaires et sociétales, et en fonction d'une synthèse narrative des similarités et différences entre PAEV et proches. Nos résultats préliminaires touchent les codes du niveau individuel du modèle socio-écologique, tel que psychose, santé mentale et trajectoire de consommation.

Conclusion : Ce projet aidera à mieux comprendre la diversité des facteurs qui agissent sur la consommation de cannabis chez les personnes vivant avec un trouble psychotique, et ainsi adapter les soins et les messages de santé publique à leur réalité.

A42 –

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.

A43 –

Mécanismes responsables de l'augmentation du rythme respiratoire lors du mouvement

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La respiration est une activité fondamentale pour la survie des animaux. Elle doit s'adapter aux différentes conditions dans lesquelles les animaux évoluent. Par exemple, lors de la production de mouvement, la fréquence et l'intensité respiratoires augmentent de façon importante. Nous savons maintenant que cette augmentation dépend grandement de mécanismes centraux avec, entre autres, la région locomotrice mésencéphalique (RLM) qui projette directement aux centres nerveux du tronc cérébral contrôlant la respiration. La RLM est une structure du système nerveux central située à la frontière entre le mésencéphale et le rhombencéphale des vertébrés. Elle est d'une extrême importance dans le contrôle de la locomotion. Le laboratoire de Réjean Dubuc a montré que chez la lamproie, un vertébré basal, la RLM est impliquée également dans les ajustements respiratoires liés à la locomotion. Par exemple, la substance P et l'acétylcholine ont des effets d'accélération sur le rythme respiratoire (Mutolo et al., 2010, 2011). Or, la RLM de la lamproie contient une petite population de neurones utilisant la substance P et de très nombreux neurones utilisant l'acétylcholine.

Nous proposons de définir, à l'échelle cellulaire, les mécanismes responsables de l'augmentation du rythme respiratoire suite à l'activation de la RLM. L'hypothèse de recherche est que les neurones de la RLM utilisant la substance P collaborent avec ceux utilisant l'acétylcholine pour moduler le rythme respiratoire durant la locomotion. Nous réaliserons des expériences anatomiques et physiologiques chez la lamproie, un modèle animal qui, depuis plusieurs décennies, a démontré son utilité dans l'étude des mécanismes cellulaires responsables de l'intégration sensorimotrice.

A44 –

Characterization of ischemic white matter strokes following insulectomy for epilepsy

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Background: Insular cortex resection for drug-resistant epilepsy achieves complete seizure control in 60-80% of patients but carries significant morbidity, with approximately 40% experiencing postoperative deficits. Among the mechanisms involved, white matter ischemic strokes (WMIS) affecting subcortical bundles remain often overlooked and understudied. This study evaluates the relationship between cortical resection volume/location and WMIS occurrence, and their association with the presence/severity of neurological/neuropsychological deficits after surgery.
Methods: Retrospective analysis of 15 patients who underwent insular corticectomy for drug-resistant focal epilepsy between 2006-2018. WMIS lesions were manually segmented on postoperative imaging and registered to preoperative T1 space using nonlinear diffeomorphic registration. White matter bundles from the normative BundleSeg atlas were registered to each patient, with white matter damage quantified as percentage of fibers intersecting the ischemic lesion. Neurological and neuropsychological evaluations were analyzed and correlated with surgical characteristics, including resection zone/volume and WMIS presence.
Results: Postoperative WMIS occurred in 10 patients. Neurological deficits affected 8/15 patients: 3 aphasias, 3 hemipareses, and 2 quadrantanopias, with only visual deficits remaining permanent. Neuropsychological deficits were observed in 8/11 evaluated patients. Resection volume did not differ significantly between patients with and without WMIS (median 16.52 cm^3 vs 36.58 cm^3, p=1.00). Ventral dysgranular and granular insular cortex resection was most associated with WMIS occurrence, without reaching significance (p=0.242). Patients with WMIS had significantly more neuropsychological deficits than those without (p=0.02).
Conclusions: This preliminary analysis demonstrates functional dissociation between cortical and subcortical lesional mechanisms after insular resection. WMIS significantly increases neuropsychological but not neurological deficit risk, suggesting complex cognitive functions depend more on white matter connectivity integrity. The lack of correlation between resection volume and WMIS occurrence indicates ischemic complications likely involve anatomical vascular factors rather than surgical extent. These findings highlight the need for surgical techniques minimizing white matter ischemic risk while achieving adequate seizure control.

A45 –

Role of astrocytes in regulating CRH neurons and the HPA axis

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Neuron-glia interactions are essential to regulate synaptic transmission and plasticity across the entire brain. While astrocytes have been shown to be active participants in the central response to stress across the cortex, hippocampus, amygdala, and lateral hypothalamus, whether these cells are directly implicated in driving or attenuating stress responses remains poorly understood.

Here, we focused on understanding astrocyte-neuron interactions in the paraventricular nucleus of the hypothalamus (PVN). As the PVN is home to a dense population of corticotropin-releasing hormone (CRH) neurons, which drive glucocorticoid production, 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 signalling in astrocytes by crossing GLAST-creERT with GR-flox mice before carrying out patch-clamp recordings in both male and female mice in the PVN.

We analyzed excitatory postsynaptic currents (EPSCs), action potentials, current-clamp recordings and performed immunohistochemistry to compare CRH neurons with other PVN neurons. Our findings demonstrate the impact of astrocytes on CRH neuron activity and their role in the HPA axis and stress response.

A46 –

Monitoring adherence to antiseizure medication using an electronic pill bottle in home-based patients

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INTRODUCTION: Nonadherence to antiseizure medication (ASM) is known to be associated with poor seizure control and reduced quality of life in individuals with epilepsy. Poor seizure control is also associated with an increased risk of morbidity and mortality. Considering the limitations associated with self-reported adherence measurements, the MEMS 8 Smart Cap was designed to objectively measure medication adherence. The primary objective of this work is to measure ASM adherence in people with epilepsy using the MEMS Cap. Secondary objectives include evaluating the correlation between adherence and seizures, exploring the potential existence of an adherence cycle linked to seizure occurrence, and assessing the feasibility and reliability of monitoring people with epilepsy in their home environment using the MEMS Cap.

METHODS: The study will include 100 adults (≥18 years) with ≥3 seizures per year, recruited at the CHUM epilepsy clinic and followed for one year. Bottle openings, occurring when patients take their prescribed ASM, will be recorded in real time by the electronic cap.

RESULTS AND DISCUSSION: From July 25 to August 4, 2025, five participants simulated medication regimens in the context of a preliminary study. MEMS adherence statistics were calculated for all participants and compared with Apple Health self-reported adherence for two of them. The MEMS Cap enabled passive data collection. In our upcoming study, descriptive statistics will be computed to assess adherence variations over time, and correlation analyses will assess adherence in relation to seizure frequency and physical activity. The temporal relationship between adherence fluctuations and seizure occurrence will be modeled in cycles to evaluate the potential existence of an adherence cycle.

CONCLUSION: Despite preliminary findings supporting the feasibility of using the MEMS Cap to monitor medication adherence, its applicability in the context of at-home antiseizure medication use remains to be demonstrated.

A47 –

Impact d’un traitement ciblant le métabolisme lipidique sur la récupération après privation de sommeil chez la souris 3xTg

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Les modèles murins de la maladie d'Alzheimer (MA) présentent des perturbations du sommeil, qui constituent un facteur de risque pour le développement de la MA, et des altérations lipidiques. L'hypothèse est qu'un traitement modulant le métabolisme lipidique améliorera la qualité du sommeil dans un modèle animal de la MA. Les souris triple transgéniques (3xTg), porteuses de mutations dans trois gènes liés à la MA (App, Mapt, Psen1), et les contrôles sans mutation ont été implantées d'électrodes pour l'électrocortico-graphie (ECoG) et d'une pompe permettant l'infusion intracérébroventriculaire d'un inhibiteur de l'enzyme stéaroyle-coenzyme A désaturase (SCDi) ou d’un véhicule. Cette enzyme convertit les acides gras saturés en monoinsaturés, et son inhibition améliore la cognition et la pathologie lipidique dans le modèle 3xTg. Après 28 jours de traitement, l’enregistrement ECoG a eu lieu pendant une privation de sommeil de 6 heures et lors de la récupération. Les résultats préliminaires ne montrent aucun effet significatif du traitement ou du génotype sur le temps passé en éveil/sommeil lors de l’analyse sur 24 heures. Toutefois, le traitement augmente le temps en éveil et réduit le sommeil (lent et paradoxal) en période de lumière, tandis qu’il produit un effet inverse en période d’obscurité. Les souris 3xTg présentent une augmentation du temps en éveil et une diminution du sommeil (lent et paradoxal) comparativement aux contrôles en période de lumière, et un effet opposé est observé en période d’obscurité. Le projet déterminera si le modèle animal présente une récupération altérée après une privation de sommeil, ainsi que l’effet du traitement ciblant les lipides sur le sommeil de récupération et le profil des gouttelettes lipidiques dans le cortex moteur. Ces travaux contribueront à mieux comprendre les liens entre le métabolisme lipidique et la régulation du sommeil dans la MA, et pourraient orienter le développement de nouvelles approches thérapeutiques ciblant ces interactions.

A48 –

The connectome analysis for pediatric epilepsy surgery (CAPES) study: leveraging normative disconnectome mapping to predict seizure outcomes

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Introduction: Surgical treatment for drug resistant epilepsy (DRE) achieves seizure freedom in ~60% of temporal lobe epilepsy (TLE) and ~25-40% of extratemporal cases. Pediatric epilepsy differs markedly from adult disease, with higher rates of cortical malformations and extratemporal foci, complicating outcome prediction. Normative disconnectome analysis maps a patient's resection onto a population based tractography atlas to estimate likely white matter disconnections.

Methods: We conducted a multicenter retrospective study of children undergoing frontal or temporal resective surgery. Pre and postoperative T1 weighted MRI were used to manually segment resection cavities in ITK SNAP, then nonlinearly registered to an age specific MNI template with ANTs. A pediatric normative connectome was built from HCP Development diffusion data using constrained spherical deconvolution in MRtrix3. Each patient's lesion mask was projected onto this connectome to estimate tract disconnections. Associations between specific disconnections and postoperative seizure outcome were tested with rank based statistics and regularized logistic models using nested cross validation.

Results: In a preliminary cohort (n=9), disconnection of the entorhinal cortex was associated with postoperative seizure recurrence. Parcellation based lesion symptom mapping with the Desikan Killiany atlas and tract based analyses using TractSeg/CSD did not yield significant associations in frontal or temporal subgroups. Model performance was limited by small sample size and overfitting.

Conclusion: Seizure outcome prediction remains a critical yet unresolved challenge in pediatric DRE. Normative disconnectome analysis is feasible and biologically informative, highlighting temporal pathways potentially linked to recurrence, and may complement presurgical evaluation when high resolution diffusion MRI is unavailable. An expanded multicenter cohort across six participating sites will increase statistical power, reduce overfitting from the initial sample, and permit rigorous external validation of these preliminary observations. If confirmed, this strategy could enable individualized prognostic modeling and refine future surgical planning by identifying white matter pathways whose preservation or transection influences outcomes.

A49 –

Différents modes de stress cellulaire affectent les sites de libération axonale des neurones dopaminergiques de manière différentielle

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Le stress oxydatif et la dysfonction mitochondriale sont souvent considérés comme une voie commune menant à la maladie de Parkinson (MP). Alors que plusieurs molécules induisant un stress cellulaire sont couramment utilisées pour étudier la dégénérescence neuronale et axonale, il n'est pas clairement établi si ces agents agissent par le stress oxydatif. Il n'est pas non plus clair s'ils agissent préférentiellement sur le domaine axonal. Notre étude vise donc à tester l'hypothèse que seulement certaines de ces molécules agissent par le stress oxydatif et à identifier de nouveaux agents neuroprotecteurs.

À cette fin, nous avons exposé des neurones dopaminergiques de souris en culture primaire à un panel de molécules fréquemment utilisées dans les études sur la MP, incluant le MPP+, la 6-OHDA, la lactacystine et le peroxyde d'hydrogène. Nos résultats montrent que seule la toxicité neuronale induite par la 6-OHDA est atténuée par le prétraitement des cultures avec l'antioxydant N-acétyl-cystéine, indiquant un lien direct avec le stress oxydatif. Par ailleurs, nous avons observé que toutes les toxines ont un impact négatif sur l'intégrité axonale, incluant une réduction de la densité mitochondriale axonale et de la quantité de terminaisons axonales capables de relâcher des neurotransmetteurs de manière calcium-dépendant. Finalement, nous montrons que des molécules connues pour améliorer l'efficacité de la mitochondrie, telles que l'honokiol et le dexpramipexole, protègent partiellement contre les effets du 6-OHDA ou du MPP+.

Cette étude met en lumière les mécanismes distincts par lesquels les stresseurs cellulaires agissent sur la viabilité des neurones dopaminergiques, révélant des mécanismes au-delà du stress oxydatif et ouvrant la voie à des stratégies neuroprotectrices ciblant la mitochondrie.

A50 –

Neuronal rescue of Nlgn2 splice isoforms in adult knockout mice mitigates behavioral and sleep impairments

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Neurodevelopmental disorders (NDDs) often present with sleep disturbances which potentiate symptomatology. Synaptic adhesion molecules (SAMs) such as Neuroligins (NLGNs) modulate vigilance states through their regulation of neurotransmission, and NLGN mutations were found in patients with NDDs. Clarifying how NLGNs shape sleep-wake duration and quality could thus have tangible outcomes in the treatment of NDDs. NLGN2 mainly regulates inhibitory transmission, yet exists in two isoforms that are differentially expressed between glutamatergic and GABAergic synapses. Nlgn2 knockout (KO) mice exhibit anxiety-like behavior and abnormal social interactions, spend more time awake, and show massive changes in electrocorticographic (ECoG) activity. However, it remains unclear whether adult manipulation of NLGN2 can affect behavior and sleep phenotypes, and whether the different NLGN2 isoforms have similar roles.

Adult Nlgn2 KO mice and wild-type (WT) littermates were injected in the motor and visual cortices with a virus encoding either of the NLGN2 isoforms, or the green fluorescent protein (GFP) control, all under a neuronal promoter. Mice underwent ECoG electrode implantation, and signal was recorded for 24 hours of baseline, 6 hours of sleep deprivation, and 18 hours of recovery. Anxiety-like and social behaviors were explored using the open field, elevated plus maze, and 3-chamber tests. Nesting ability was also evaluated.

Preliminary data suggest that manipulating NLGN2 expression in adult mice reverses the increased time spent awake, some of the changes in ECoG activity, and the impaired preference for social novelty found in KO mice, but not the anxiety-like and abnormal nesting behaviors. The differential isoform effects however remain to be clarified. Additionally, gene and protein expression analyses indicate altered expression of chloride channels and other SAMs under NLGN2 manipulations.

Overall, this work will increase the understanding of the mechanisms by which NLGN2 shapes behavior and vigilance states, and potentially uncover a druggable target for sleep-wake modulation in NDDs.

A51 –

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

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Following a spinal cord injury (SCI), though locomotor training can promote some recovery, persistent deficits, such as paw dragging, remain due to disrupted interactions between supraspinal, sensory, and spinal circuits. To restore these interactions, our lab employs electrical stimulation to engage neural circuits in real time, with the aim to assist movement. We recently demonstrated that cortical stimulation, when delivered in synchrony with paw lift, enhances step height and decreases paw dragging in both rat and cat models of incomplete SCI. Additionally, our preliminary findings suggest that peripheral stimulation may also alleviate locomotor deficits in a feline model of incomplete paraplegia. Combining these approaches has the potential to act synergistically to engage residual motor circuits and maximize motor efforts, which is the primary goal of this study. In a cat model, we implanted stimulation electrode arrays in the hindlimb motor cortices, cuff electrodes around the superficial peroneal nerve that innervates the foot dorsum, and intramuscular electrodes within both hindlimbs. Cats then received a contusion SCI at thoracic level 10 that initially paralyzed both legs. Prior to, and after SCI, we assessed the ability of cortical and/or peripheral stimulation to modulate walking during treadmill locomotion. We characterized the impact of timing and amplitude of each stimulation source, alone and combined, on kinematic parameters. Preliminary data shows that combined cortical and peripheral stimulation more efficiently enhances step height and reduces dragging than either approach alone. These findings highlight the potential of multi-level stimulation strategies for assisting movement after SCI.

A52 –

RFC1, a gene involved in late-onset ataxia, regulates cerebellar neurogenesis in zebrafish

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The Cerebellar Ataxia, Neuropathy, Vestibular Areflexia Syndrome (CANVAS) is a rare adult-onset ataxia with a prevalence of less than 1 in a million, characterized mainly by imbalance and sensory neuropathy. Although CANVAS remained only clinically defined, recent findings identified a biallelic repeat expansion (AAGGGexp) in the second intron of the RFC1 gene as a major cause of CANVAS. RFC1 encodes the largest subunit of the replication factor C required for DNA replication and repair. Whereas the reference allele contains eleven repeats of the pentanucleotide AAAAG11, the pathogenic expansion usually comprises hundreds of AAGGG repeats. However, the mechanisms by which this intronic repeat expansion in RFC1 gene is causing this neurological disorder are unknown. Recent papers also identified frameshift mutations in RFC1, suggesting that a loss of function could drive pathogenicity. Interestingly, we showed that rfc1 is expressed in the developing cerebellum, indicating that it might play a role in its development. Since knocking-out RFC1 in mammals leads to embryonic lethality, we generated a zebrafish loss-of-function (KO) model of rfc1 using CRISPR/Cas9. We found that rfc1-/- larvae survive until 10 dpf and depict a severe morphological phenotype from 2 dpf onwards. More importantly, we showed that the development of the cerebellum is severely affected, with disorganized Purkinje cell organization and a severe reduction in the number of granule cells at 5 dpf. Using scRNAseq, we demonstrated that rfc1 is expressed in early neural progenitors and that its loss-of-function leads to defects in DNA replication processes. Ultimately, defective RFC1 signalling leads to massive apoptosis among this cell population, affecting subsequent neurogenesis, particularly of cerebellar neurons. This work is the first to investigate the function of RFC1 in vivo. By showing its role in the development of the cerebellum, this suggests that CANVAS could be, at least partially, caused by RFC1 loss-of-function mechanisms.

A53 –

Competitive binding between TDP-43 and miRNAs regulates G3BP1 mRNA stability

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G3BP1 is a key RNA-binding protein that nucleates stress granules-cytoplasmic foci that assemble under stress as part of the integrated stress response, promoting cell survival. In amyotrophic lateral sclerosis (ALS), stress granule (SG) dynamics are disrupted, in part due to the pathological mislocalization of TDP-43 from the nucleus to the cytoplasm. This mislocalization results in a loss of TDP-43 nuclear functions, including its role in stabilizing G3BP1 mRNA through binding to its 3′ untranslated region (3′UTR).

We previously showed that depletion of nuclear TDP-43 leads to reduced G3BP1 expression, though the underlying mechanism remained unresolved. Here, we identify a brain-enriched microRNA whose binding site overlaps with a conserved UG-rich element within the G3BP1 3′UTR, a known TDP-43 binding region. Our data reveal that loss of TDP-43 exposes this miRNA seed sequence, allowing miRNA-mediated degradation of G3BP1 transcripts.

Using a combination of qPCR, Western blot, microRNA mimic strategies, electrophoretic mobility shift assays (EMSAs), and RNA stability analyses in neuronal cell lines, we demonstrate that TDP-43 directly competes with this miRNA for binding to G3BP1 mRNA. Overexpression of a miRNA mimic significantly decreases G3BP1 mRNA and protein levels, while TDP-43 overexpression or restoration stabilizes the transcript in both murine and human neurons. Furthermore, miRNA-mediated G3BP1 depletion sensitizes cells to stress, resulting in increased cell death and impaired SG formation. To counteract this effect, we developed antisense oligonucleotides (ASOs) targeting the miRNA binding site to prevent G3BP1 degradation and assessed their efficacy in human cells and mice using stereotaxic injections, in the perspective of developing a therapeutic strategy to modulate G3BP1 levels in ALS.

Together, our findings uncover a competitive post-transcriptional regulatory mechanism between TDP-43 and a brain-specific miRNA that controls G3BP1 mRNA stability, providing new insight into SG dysregulation in ALS and identifying a potential RNA-based therapeutic strategy for disease intervention.

A54 –

MECP2 Mutations disrupt early human neurodevelopment and cortical lineage specification

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Rett syndrome is a severe neurodevelopmental disorder that affects approximately 1 in 10 000 live births. It results from loss-of-function mutations in the X-linked chromatin regulator MECP2. Although the genetic cause has been well-established, the earliest molecular derailments occurring during human development remain incompletely understood. To investigate this, we used isogenic human embryonic stem cell (hESC) models carrying three common different MECP2 mutations. We systematically tracked transcriptional changes from the pluripotent stage through successive developmental milestones, including the neuroectodermal, neural stem cell, and neural progenitor stages, culminating in four-month-old cerebral organoids. Our analyses revealed that while transcriptional variance was predominantly driven by developmental stage, a shared secondary transcriptional program emerged across all mutants. This program was notably enriched for genes associated with the synaptic membrane and the extracellular matrix. Single-cell RNA sequencing further identified a naïve-like and hyper-proliferative state at the hESC stage, characterized by a striking upregulation of ZFP42, a marker of early pluripotency. Remarkably, we also observed consistent suppression of EMX1, a key determinant of cortical radial glia, starting from the earliest stages of differentiation. This repression persisted and manifested in cerebral organoids that produced fewer excitatory neurons, instead favoring the differentiation of inhibitory neuronal and glial lineages. Altogether, these data outline a continuous and altered developmental trajectory in MECP2-mutant human cells and identify ZFP42 and EMX1 dysregulation as potentially tractable entry points to better understand the early pathogenic mechanisms underlying Rett syndrome.

A55 –

Compensatory exocytotic pathways preserve dopamine release and function in Syt1KO mice

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The motor symptoms of Parkinson's disease result from the degeneration of dopaminergic neurons (DAn) in the substantia nigra, greatly reducing the release of dopamine (DA) in the striatum. In response to an action potential, this release is thought to be controlled by the synaptic vesicle calcium sensor synaptotagmin-1 (Syt1). Indeed, in Syt1KO mice, DA release induced by acute stimulation falls by 90%. However, the motor behavior and extracellular DA levels of these mice remain normal.Given that DAn are spontaneously active (1-5Hz) and can also discharge in bursts (10-50Hz), we hypothesize that these discharge patterns could maintain part of the DA release in KO mice.To test this hypothesis, we performed cyclic voltammetry recordings on striatal slices from Syt1WT and KO mice following acute stimulation or trains (burst activity at 6Hz/10Hz/50Hz). The impact of applying continuous stimulation (spontaneous activity at 1Hz/2Hz/5Hz) prior to release measurements was also evaluated. As described above, acute stimulation induced a 90% decrease in DA release in KO mice. However, during ongoing stimulation, this decrease was less pronounced in KO mice. Spontaneous activity reduced DA release induced by acute stimulation in both WT and KO mice, but this reduction was twofold less pronounced in KO mice. These results demonstrate that both discharge patterns significantly reduce the difference in dopamine release initially observed during acute stimulation in Syt1KO and WT mice. It is therefore highly likely that the release observed in Syt1KO mice occurs through an alternative exocytotic mechanism, which is sufficient to sustain dopamine levels and normal behavior in vivo.

A56 –

Développement de modèles 2D et 3D dérivés de cellules souches pluripotentes induites (iPSCs) pour l'étude de l'ataxie cérébelleuse héréditaire

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L'ataxie cérébelleuse héréditaire est une maladie neurodégénérative rare, d'origine génétique, touchant environ une personne sur 10 000. Elle se manifeste par des troubles sévères de la coordination motrice, de la parole et de la posture, auxquels s'ajoutent souvent des complications systémiques. À ce jour, aucun traitement curatif n'existe, et les mécanismes cellulaires et moléculaires responsables demeurent mal compris.

Ce projet vise à développer des modèles in vitro de l'ataxie cérébelleuse à partir de cellules souches pluripotentes induites (iPSCs) humaines, afin de reproduire la complexité du tissu cérébelleux et d'en explorer les mécanismes pathologiques. Deux approches complémentaires sont employées : la génération de co-cultures neuronales (modèles 2D) et la production d'organoïdes cérébelleux (modèles 3D). Pour les modèles 2D, nous utilisons des stratégies d'induction rapide basées sur la surexpression de facteurs de transcription spécifiques : NGN2 pour les neurones excitateurs, ASCL1 et DLX2 pour les interneurones inhibiteurs, et NFIA avec SOX9 pour les astrocytes. Les cassettes d'expression sont intégrées de manière ciblée dans le locus AAVS1 via CRISPR/Cas9, assurant une expression stable et contrôlable par la doxycycline. Les différenciations seront validées par RT-qPCR, immunomarquage et analyses fonctionnelles (MEA et imagerie calcique).

En parallèle, des organoïdes cérébelleux seront générés selon un protocole établi (Nature Protocols, Atamian et al., 2024). Ces structures tridimensionnelles permettront d'étudier l'impact de mutations spécifiques sur la différenciation neuronale et l'organisation tissulaire. Des analyses d'immunofluorescence, de séquençage unicellulaire (scRNA-seq) et d'imagerie 3D permettront de caractériser les populations cellulaires et d'identifier des signatures pathologiques.

En combinant ces approches, notre projet établira une plateforme de modélisation innovante et transposable à d'autres pathologies neurologiques, telles que l'épilepsie.

A57 –

Time to revise the dogma? Involvement of axonal collaterals in dopamine release in the midbrain

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Parkinson's disease (PD) is associated with the age-dependent, gradual death of dopamine neurons in the substantia nigra (SNc), leading to severely reduced dopamine (DA) levels in the striatum. Although the main focus in PD has been to find strategies to restore DA levels in the striatum, it is perhaps important to consider that DA neurons can also release DA within the ventral midbrain, where their cell bodies are located. This release is typically referred to as somatodendritic (STD) DA release because it has been hypothesized that such DA secretion arises exclusively from the cell bodies and dendrites of these neurons. Interestingly, some evidence suggests that DA release in the midbrain is more resilient in PD. The cellular and molecular mechanisms of DA release in the midbrain are still controversial to this day. Notably, while some work suggested that loss of the exocytosis calcium sensor synaptotagmin-1 (Syt1) leads to reduced STD DA release, other work suggests that STD DA release is reliant on Syt4 and Syt7 but not Syt1. Here we will present work testing the hypothesis that this controversy is mainly due to the presence of dopaminergic axonal collaterals within the midbrain. Using a combination of viral tracing, confocal microscopy, electron microscopy, STED super-resolution imaging and cyclic voltammetry, we find that the midbrain contains Syt1-positive axonal-like varicosities, but that Syt1 is absent from the cell body and dendrites of DA neurons. We also find that in a partial intra-striatal 6-OHDA DA depletion model, DA release in the midbrain is resilient compared to striatal DA release and that Syt1 levels in the midbrain are upregulated. These results suggest that a reconsideration of our models of DA release in the midbrain is warranted and that release in this brain region may arise from a combination of STD and axonal sources.

A58 –

Human-specific gene SRGAP2C drives information-seeking strategy in mice

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Learning can arise through different behavioral strategies, from a conservative trial-and-error approach to more active engagement. Here, we show that the human-specific gene SRGAP2C modifies the learning strategy of mice in a sensory reward-based Go/No-Go detection task. SRGAP2C emerged from a partial duplication of the ancestral gene SRGAP2A, which regulates synaptic development. When expressed in mouse cortical pyramidal neurons, SRGAP2C induces human-like characteristics including a delayed dendritic spine maturation and increased spine density, characteristics likely associated with altered synaptic plasticity thresholds. However, SRGAP2C's role in learning had remained unclear.

In this study, mice were trained to lick a water port to obtain a reward when a whisker stimulus was present (Go) and to withhold licking in its absence (NoGo). Although both SRGAP2C and control mice reach similar sensitivity levels, their early learning strategies were strikingly different. SRGAP2C mice displayed an enhanced drive to lick in all trial types, an information-seeking approach that accelerates the learning of stimulus-reward associations at the cost of more punishment timeouts. We show that with this strategy, SRGAP2C mice are able to gather more task information early in training and overall exhibit higher mutual information between sensory input and behavioral output - in other words SRGAP2C mice used sensory cues more effectively to guide their actions.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.

A59 –

Investigating the molecular function of THAP12

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Problem. Lennox-Gastaut Syndrome (LGS) is a very severe form of epileptic encephalopathy, where the cause remains unknown in nearly 30% of cases. Recently, our lab identified two siblings diagnosed with LGS who share novel compound heterozygous variants in the zinc finger protein THAP12. THAP12 has never been previously associated with any neurological disorder and its function in neurodevelopment remains unknown. Our preliminary results have shown that a loss of Thap12 leads to embryonic lethality in mice, whereas a loss of thap12 in zebrafish results in severe neurodevelopmental defects including reductions in brain size, deficits of neural progenitor pools, and seizure-like activity (Ochenkowska et al., in preparation).
Hypothesis. Based on our preliminary data, we posit that THAP12 is a transcriptional regulator of genes essential for neural progenitor cell (NPC) proliferation.
Methods. Objective 1. Identify the molecular function of THAP12. Perform a molecular characterization of THAP12 in HEK293FT and iPSC-derived neural progenitor cells to identify genes regulated by THAP12 (ChIP-seq coupled with RNA-seq) and potential co-activators or interacting partners (Co-IP and LC-MS) involved in its function. Objective 2. Determine how a loss of THAP12 impacts differentiation outcomes. We will generate brain organoids following an unguided differentiation of reprogrammed patient iPSCs. Immunostaining with neuronal markers alongside scRNA-seq will be employed to determine how a loss of THAP12 impacts differentiation outcomes. We will also perform microelectrode array (MEA) analysis to assess how functional maturation of synapses may be impaired.
Results. We have confirmed the role of THAP12 as a transcriptional activator of genes involved in essential cell processes, including cell cycle progression and mitochondrial function. We have also revealed several novel interacting partners of THAP12 involved in mitochondrial translation.
Conclusion. Throughout this project we will establish the networks governed by THAP12 across development, laying the groundwork for the development of future targeted therapies.

A60 –

Glial derived-MULT1 drives early immune activation in experimental autoimmune encephalomyelitis, animal model of multiple sclerosis

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Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system (CNS) characterized by demyelination, axonal injury, and progressive neurodegeneration. Increasing evidence implicates glial-immune interactions as key drivers of disease initiation and progression. Among these, the NKG2D signaling pathway has emerged as a central mediator of crosstalk between stressed glial cells and infiltrating immune cells in MS and in its animal model, experimental autoimmune encephalomyelitis (EAE). NKG2D is expressed by cytotoxic lymphocytes, including $CD8^+$ and $CD4^+$ T cells and natural killer cells, whereas its ligands (NKG2DL) are typically absent under physiological conditions but upregulated during cellular stress and inflammation. $NKG2D^+$ T cells accumulate in MS lesions, and our group previously demonstrated that the human ligand ULBP4 is highly expressed by astrocytes surrounding blood vessels in post-mortem MS brain tissue. In mice, the homologous ligand MULT1 is markedly upregulated in the CNS during EAE. We hypothesize that glial-derived MULT1 enhances local immune activation and exacerbates disease severity. To test this, we modulated MULT1 expression in the MOG_{35-55} EAE model using serotype 9 adeno-associated viruses (AAV9). NKG2D wild-type and knockout mice received intrathecal injections of AAV9-MULT1 or control AAV9-GFP either before or at disease onset to dissect phase-specific effects. AAV9-MULT1 delivery increased CNS-restricted MULT1 expression, particularly in astrocytes and oligodendrocytes, without affecting peripheral tissues. Mice injected before disease onset exhibited worsened clinical scores and increased IFN-γ production by CNS-infiltrating T cells, while peripheral responses remained unchanged. These findings identify glial-derived MULT1 as an amplifier of immune activation specifically during the early inflammatory phase of EAE, emphasizing the importance of temporally defining immune-glial mechanisms across disease stages. Ongoing experiments targeting MULT1 knockdown aim to validate its potential as a therapeutic target in MS. Altogether, our results highlight the NKG2D-NKG2DL axis as a stress-induced pathway driving phase-specific neuroimmune interactions in MS.

A61 –

Le brouillard cérébral post-COVID : une étude pilote pour comprendre les séquelles cognitives de la COVID longue

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Introduction
Il est estimé que plus de 15% de Canadiennes et Canadiens ayant eu la COVID-19 ont eu des symptômes durant plus de trois mois, voire plus d'un an dans la moitié des cas. Ces symptômes persistants portent plusieurs noms, dont celui de COVID longue (LC). L'éventail de symptômes rapporté est très large, incluant souvent douleurs, troubles de sommeil, difficultés cognitives ainsi que l'exacerbation des symptômes suite à un effort, suggérant un chevauchement avec l'encéphalomyélite myalgique (EM). L'objectif cette étude pilote était de suivre des personnes atteintes de COVID longue pendant un an afin d'évaluer les l'évolution des difficultés cognitives des patients.

Méthodologie
Une cohorte de 60 LC et 25 témoins sains (SC) a été recrutée. Les LC devaient avoir des symptômes depuis plus de six mois post-infection, alors que les SC devaient avoir été guéris en deux semaines. En une année, les participants ont été vus trois fois par une infirmière de recherche. À chaque visite, les participants ont fait un test cognitif (BrainCheckTM) mesurant l'attention, la flexibilité mentale, les fonctions exécutives et la mémoire. À la première visite, les participants ont également été soumis à un test à l'effort afin d'évaluer les conséquences sur les fonctions cognitives.

Résultats
À la visite 1, il n'y avait pas de différence entre les groupes, mais après le test à l'effort, le groupe SC s'est beaucoup amélioré ($p<0,0001$). Au cours de l'année, les SC se sont progressivement améliorés ($adj.p<0,05$), ce qui est cohérent avec le biais d'apprentissage, mais pas les LC suggérant d'important troubles cognitifs. Après un an, plusieurs situations ont été observées : amélioration, constance, ou détérioration des symptômes. Les participants LC-amélioré n'étant plus significativement différents des contrôles ($p>0,05$), cela suggère un rétablissement partiel, mais incomplet étant donné la présence d'autres symptômes. Ceci met l'emphase sur l'aspect débilitant de la condition.

A62 –

Astrocytic encoding of anxiety states in the basolateral amygdala

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The basolateral amygdala 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 recordings in both astrocytes and principal neurons, we find that in contrast to neurons, astrocytic 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 threatening 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 population recordings, we then demonstrate a causal role for BLA astrocyte calcium in anxiety processing by showing that driving astrocytic Ca2+ increases anxiety-related behavior, while silencing astrocytes dampens anxious phenotypes. Finally, we uncover the signalling mechanisms underlying astrocytic anxiety coding. Using 2-photon imaging and pharmacological experiments in slice preparations, 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 for the first time 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.

A63 –

MicroRNA regulation of alpha-synuclein, a key protein in Parkinson's disease

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MicroRNAs (miRs) are small non-coding RNAs that are critical post-transcriptional regulators of gene expression. In the nervous system, miRs are particularly enriched among neuronal cells and are essential for maintaining neuronal identity, function, and resilience. In both animal models and human samples, dysregulation of miRs expression and processing has been implicated in neurodegenerative diseases, including Parkinson's disease (PD). More specifically, aberrant miRs activity is hypothesized to contribute to the pathological accumulation of α-synuclein, a key player in PD.

Recent evidence suggests that miRs targeting α-synuclein mRNA are themselves regulated by RNA-binding proteins (RBPs), which modulate their maturation and processing. We hypothesize that specific RBPs interact with immature forms of α-synuclein targeting miRs, such as miR-153, modulating their maturation and controlling α-synuclein expression in neurons.To test this hypothesis, we are currently pursuing three specific aims: (1) validating the regulation of α-synuclein levels by miRs in human and murine models, (2) identifying RBPs that associate with α-synuclein-targeting miRs using riboproteomics, bioinformatic approaches, and (3) characterizing the role of specific RBPs using cell-based assays. Our findings are uncovering a regulatory axis involving RBPs and miRs that modulates α-synuclein expression, offering novel insights into RNA-based mechanisms and pointing to potential biomarkers and therapeutic targets for PD.

A64 –

Comparative gene-based burden and variant analysis of Parkinson's disease across Montreal and Guadeloupe cohort

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Human genetics research lacks diversity, a gap especially evident in Parkinson's disease (PD), where Black individuals represented only 4% of studies on underrepresented populations. Across all populations, despite extensive research, the genetic causes of about 90% of PD cases remain unknown, suggesting that multiple biological processes are involved and may differ across diverse groups.We aimed to (i) characterize the rare variant landscape and gene-based burden of PD in cohorts from Montreal and Guadeloupe, (ii) identify biological pathways associated with genes carrying burdened variants, and (iii) explore the genomic context of burdened variants through linkage disequilibrium (LD) with PD-associated, proxy, or population-specific variants.We recruited PD patients and matched controls from Montreal (8 PD, 8 controls) and Guadeloupe (9 PD, 8 controls). RNA-sequencing of PBMCs identified disease-related variants, filtered for pathogenicity and allele frequency, and curated in Franklin according to ACMG guidelines. Gene-based burden analysis with SKAT-C was performed across population-specific comparisons, and LD was assessed with PLINK using 1000 Genomes European (EUR) and Admixed American-African (AMR-AFR) panels. Burden analysis revealed networks involving IL-17, NF-κB, TNF, MAPK, NOD-like, and B-cell receptor signaling in PD-all vs CTRL-all. PD-Montreal vs CTRL-Montreal highlighted IL-17 signaling, whereas PD-Guadeloupe vs CTRL-Guadeloupe showed immune response, viral infection, and MHCI/II pathways. PD-Montreal vs PD-Guadeloupe emphasized alternative splicing and nervous system disease. LD analysis found no SKAT-C variants in linkage with known PD GWAS variants, though 61 EUR and 87 AMR-AFR variants emerged as likely proxies. Our findings highlight population-specific burdened gene networks in PD, suggestion distinct biological mechanisms across cohorts. While SKAT-C variants were not in LD with established PD GWAS variants, population-matched proxies suggest novel contributors. These results underscore the importance of multi-population studies for unraveling PD pathophysiology and informing targeted therapies.

A65 –

dACC stimulation disrupts onset of exploration

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Balancing exploration and exploitation is crucial for navigating unpredictable, ever-changing environments. Exploitation stabilizes decision-making to maximize rewards while exploration introduces variability, destabilizing behavior to search for new opportunities. Previous studies have implicated the dorsal anterior cingulate cortex (dACC) in exploratory decision-making, but also in tracking important decision-making variables like reward. Critically, the relationship between dACC and these variables remains ambiguous because neither link has been tested causally. Here, we stimulated dACC during multiple tasks that allowed us to differentiate the effects of dACC microstimulation on exploration and reward processing. First, two rhesus macaques performed a decision-making task—a multi-arm bandit—where they selected one of three targets by making a saccade towards it. Although the targets were visually identical, each was associated with a dynamic reward probability. This encouraged monkeys to use reward information to choose between exploiting good targets and exploring alternatives that could offer greater long-term gains. We then stimulated dACC and a control region, dorsolateral prefrontal cortex (dlPFC), during inter-trial intervals on random trials. Stimulating dACC but not dlPFC stabilized the behavior by reducing the likelihood of starting to explore. This was not due to a change in reward processing: stimulation stabilized behavior regardless of reward history. To assess whether dACC stimulation stabilized behavior because it was itself hedonically rewarding, the monkeys completed another task, choosing between reward cues that were either paired or unpaired with dACC stimulation. dACC stimulation did not systematically influence subjective target value. These findings causally and selectively implicate dACC stimulation in regulating exploration.

A66 –

Détermination du rôle de l'extrémité N-terminal de TMEM106B dans la reconnaissance de l'amyloïde la maladie d'Alzheimer

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La maladie d'Alzheimer (MA) est une maladie neurodégénérative caractérisée par un déclin cognitif causé par une accumulation de plaque amyloïde entrainant la mort neuronale. Actuellement, aucun traitement n'est disponible pour stopper ou ralentir la maladie. Notre étude porte sur le rôle de TMEM106B, une protéine lysosomale transmembranaire, dans l'élimination de l'amyloïde en condition pathologique. La littérature a montré la présence d'agrégats de TMEM106B colocalisées avec des plaques amyloïdes dans les cerveaux de patients ainsi que l'implication de TMEM106B dans plusieurs démences. Nos études préliminaires ont montré une modification d'expression de TMEM106B chez les patients MA. D'un point de vue structurale, TMEM106B possède région intrinsèquement désordonnée (RID) à son extrémité N-terminale. Notre étude se focalise sur la RID de TMEM106B qui lui confère la capacité de former des condensés biomoléculaires par séparation de phase liquide-liquide. Nous avons observé que les condensées de la RID de TMEM106B avaient la capacité d'interagir avec l'amyloïde-beta (Aß42) lorsqu'elles sont en contact. Ses résultats renforcent notre hypothèse que TMEM106B, reconnait l'amyloïde pour faciliter son élimination. Pour mettre en relation nos observations et la MA, nous utilisons des cellules souches pluripotentes induites (iPSC), TMEM106B-KO ou de la MA (APPV717I et sporadique) possédant un HaloTag à l'extimité C-terminale de TMEM106B afin de suivre sa dynamique en live-imaging. Les iPSC sont différenciées en neurones dans le but d'étudier l'impact de TMEM106B sur la production et sécrétion d'Aß42. Nos premiers résultats supportent l'hypothèse que la RID de TMEM106B joue un rôle essentiel dans la reconnaissance de l'amyloïde, afin de limiter son accumulation et en influençant la pathologie liée à l'amyloïde. Cependant, aucune preuve directe ne supporte encore la formation de condensés biomoléculaires de TMEM106B ni son rôle fonctionnel dans la MA. Ce projet vise à explorer le potentiel de TMEM106B à former des condensés et leurs contributions dans la MA.

A67 –

Toward a multimetric bedside EEG assessment of consciousness after brain injury

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Up to 40% of unresponsive patients with disorders of consciousness (DoC) are misclassified as unconscious because they cannot produce reliable behavioral responses, underscoring the need for objective, accessible neural markers to inform diagnosis, prognosis, and care decisions. Signal complexity—reflecting lower predictability and richer structure—has been linked to the presence of consciousness and better recovery. Likewise, healthy conscious brains are hypothesized to operate near criticality, a balance between order and chaos that optimizes information processing; deviations from this regime appear in altered states, including anesthesia and DoC. Information decomposition approaches that quantify synergistic (emergent) versus redundant (shared) information between brain regions have also tracked changes in consciousness. We applied these three families of metrics to 128-channel EEG from 57 unresponsive DoC patients under continuous sedation during routine clinical sedation interruption. Complexity was assessed with Lempel-Ziv complexity, Approximate and Permutation Entropy; criticality with Pair Correlation Function and Chaoticity indices; and synergy-redundancy via Integrated Information Decomposition (φID). In this etiologically heterogeneous cohort, these metrics alone—whether during sedation or when sedation was interrupted—did not reliably separate clinically conscious from unconscious patients nor predict recovery three-month post injury based on Glasgow Outcome Scale-Extended (GOS-E) scores.Though our preliminary results suggest that these families of markers may limited standalone utility in this population and context, next steps include integrating metrics through latent-space models (e.g., Linear Discriminant Analysis, Partial Least Squares) and expanding the feature set with additional candidates such as EEG microstates to improve diagnostic and prognostic performance.

A68 –

BK hypoactivity alters synaptic integration of excitatory inputs onto the basal dendrites of layer 5 pyramidal neurons in a mouse model of Phelan-McDermid syndrome

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Rationale: Atypical sensory responses are a core symptom of Phelan-McDermid syndrome (PMS). PMS is due to a 22q13 macrodeletion, involving SHANK3; a gene which encodes a scaffolding protein enriched in dendritic spines. Integration of excitatory inputs onto the basal dendrites of layer 5 pyramidal neurons (L5PNs) is a key component of sensory perception. While Shank3 deletion is believed to be the main contributor to the neuropsychiatric phenotype of PMS, its impact on synaptic integration at the level of individual spines remains to be elucidated.
Objective: to determine the integration algorithm of excitatory inputs onto the basal dendrites of Shank3-deficient L5PNs.
Methods: We photoactivated multiple dendritic spines separately and near-simultaneously while recording their somatic voltage responses in wild-type (WT), Shank3 heterozygous (Shank3 Het), and homozygous (Shank3 KO) knockout mice. Comparing the voltage responses from the two activation regimes allowed us to determine the integration algorithm.
Results: while subthreshold excitatory inputs integrate linearly in WT and Shank3 KO L5PNs, they summate supralinearly in those from Shank3 Het mice. Bath application of the BK channel activator, NS1619, restores normal synaptic integration in Shank3 Het L5PNs. We also observed a reduction in the NMDA-to-AMPA ratio due to a decreased NMDA expression in Shank3 Het L5PNs. Biophysical simulations reproduced the experimental data and showed that, with reduced NMDA currents in Shank3 Het spines, only two-thirds of BK channels were open during the near-simultaneous activation of neighboring spines. This resulted in the supralinear summation of synaptic inputs. Finally, BK channel hypoactivity amplifies NMDA-mediated dendritic spikes in Shank3 Het L5PNs.
Conclusion: Our study suggests that sensory inputs are overrepresented in the basal dendrites of Shank3 Het L5PNs because of BK channel hypoactivity. Therefore, pharmacological interventions designed to enhance BK channel activity could be a potential therapeutic approach for addressing sensory hypersensitivity in PMS.

A69 –

Estrous cycle modulates cortical auditory responses across species

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Introduction. Female mammals experience cyclical physiological and behavioral changes driven by hormonal fluctuations. However, whether and how the estrous cycle modulates different aspects of auditory sensory processing and the activity of distinct neuronal populations remain unclear. Here, we investigated brain responses to auditory stimulation in mice and humans across reproductive phases.

Method. We recorded EEG activity from men and women and intracortical local field potential (LFP) from male and female mice. Female participants and mice were recorded during two specific phases of their reproductive cycle characterized by low estradiol (E2) concentration (first day of the ovarian cycle in women and late estrus phase in mice) and high E2 concentration (10th day of the ovarian cycle in women and early proestrus in mice). To probe estradiol's causal role, female mice also received systemic injections of estradiol or saline during the late estrus phase.

Results. During the high E2 phase females of both species exhibited decreased baseline gamma power and weaker auditory entrainment (AE), stimulus-specific adaptation (SSA) and response to deviant sounds. In mice at low E2 phases, acute E2 administration increased baseline gamma power, AE, and SSA, suggesting a causal relationship between estradiol levels and these auditory cortical responses. Tetrode recordings in mice further revealed that baseline firing rates of a specific neuron population neurons were selectively reduced during late estrus. Additionally, evoked spiking activity was modulated depending on the estrous cycles. Finally spiking to LFP coherence was also significantly increased during late estrus.

Conclusions. These findings indicate that auditory processing is modulated by estrous cycle across species, suggesting that hormonal status should be kept in account when evaluating auditory perception in mouse models or women with psychiatric disorders. Further experiments will address whether distinct neuronal populations are differentially modulated by estrous cycle and estradiol.

A70 –

Localizing the epileptic seizure onset zone through perturbation sensitivity of intracranial EEG networks

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Background: Identifying the epileptogenic zone is a key challenge in presurgical evaluation of drug-resistant epilepsy, with seizure-onset zone (SOZ) providing crucial clues to its localization. Conventional methods based on visual inspection or static connectivity often miss the dynamic network changes driving seizures. We propose a perturbation-based network framework that quantifies how local connectivity alterations affect global dynamics, revealing nodes critical for ictogenesis.Objective:To evaluate whether perturbation-based graph metrics can reliably identify the SOZ and predict postoperative seizure freedom.Methods:We analyzed intracranial EEG data from 74 patients (264 seizures; mean age 34.7 ± 10.6 years; 32 F/42 M; mean 92 ± 34 channels) collected at the Centre Hospitalier de l'Université de Montréal and two public NIH-UMMC and Johns Hopkins datasets. Phase-locking values were computed for each 1-s ictal window and averaged across the 5-125 Hz band. Three network metrics—spectral radius (ρ), global efficiency (E), and node-strength entropy (H)—were computed before and after simulated perturbations. Standardized change (Δρ, ΔE, ΔH) were combined into a concordance score ($C = z(\Delta\rho) + z(\Delta E) - z(\Delta H)$), representing each node's contribution to network fragility. Channels were ranked by, and discrimination between SOZ and non-SOZ nodes was quantified using AUROC and enrichment factor (EF), defined as the ratio of SOZ channels in the top 10% to their overall proportion.

Results: Across all seizures, the median AUROC for SOZ identification was 0.61 [IQR 0.50-0.71]. Fifty patients with good surgical outcome exhibited significantly higher AUROC (0.66 [IQR 0.54-0.74]) than 24 patients with poor-outcome (0.55 [IQR 0.41-0.65], Mann-Whitney U test: $p = 0.016$). EF was higher in good-outcome (1.46) than poor-outcome patients (0.58), showing stronger SOZ concentration among top-ranked nodes.

Conclusion: Perturbation-based network measures could capture clinically relevant network fragility, showing better performance in patients with good postsurgical outcomes and may complement existing methods for surgical planning.

A71 –

Functional role of Depdc5 in GABAergic synaptogenesis in zebrafish

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Epilepsy, one of the most common brain disorders worldwide, affects over 70 million people. 30% of the patients fail to respond to available anti-epileptic drugs. Such cases bring an urgent need to understand all possible functions of epilepsy-associated genes so that novel therapeutics can be developed for the patients. Loss of function mutations of DEPDC5 account for 12-37% cases of focal seizures. DEPDC5 inhibits mTOR, and some disease-causing mutations are located within the protein domain related to its mTOR function. However, other mutations are located in domains of unknown functions, which are highly conserved in vertebrates and do not regulate mTOR signaling. Our lab previously found decrease in the number of GABAergic synapses in 6 days old zebrafish mutants, thereby, established novel functions of depdc5 in the development of inhibitory synapses in brain that are independent of its mTOR functions. In my post-doctoral studies, I have found an increase in number of GABAergic synapses in 5 days mutant larvae, and currently evaluating 4 days old fish. However, I did not find any changes in the number of Glutamatergic synapses in mutant fish, indicating that depdc5 specifically regulates GABAergic synapse development. I am also determining which domain of Depdc5 is mediating non-canonical functions by developing zebrafish lines with in-frame deletion of a few conserved amino acids in each domain. I am also understanding which interaction partner of DEPDC5 is involved in mediating non-canonical functions and Dihydropyrimidinase Like 2 (DPYSL2), a key player in synaptogenesis, emerges as a strong candidate. I have found a significant decrease in the expression of dpysl2 in depdc5 mutants. I am using CRISPANT approach to knock out dpysl2 in zebrafish and check if dpysl2 mutants have the GABAergic synapse and other defects. Altogether, our study will enhance understanding about functioning of DEPDC5 and ultimately pave the way for development of novel therapeutics for patients.

A72 –

Evaluation of the implication of microglia and CD8+ T cells in neuronal vulnerability in Parkin knockout mice

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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. PD patients also present signs of inflammation in the brain, as lymphocytes infiltration or microglial activation. Even growing evidence links inflammation to the onset of the disease, the underlying mechanisms are unclear. Parkin mutation is associated with early-onset forms of PD. This protein act as key regulators of innate immune responses, suppressing antigen presentation by MHC-I on peripheral antigen-presenting cells (APCs). The loss of function of Parkin consequently leads to the activation of CD8+ T cells, which may contribute to the impairment of nDA. Microglia are the primary brain resident immune cells and function as APCs. We hypothesize that, like their peripheral counterparts, microglia have an exacerbated pro-inflammatory response to pathogen-derived signals in the absence of Parkin. We suggest that this increased activation impacts nDA, possibly through interactions with cytotoxic CD8+ 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, the presence of activated microglia accentuates this loss to around 60% in WT and 80% in Parkin KO. Parkin-deficient microglia show similar elevation of MHC-I compared to WT after an inflammatory stimulus but higher secretion of pro-inflammatory cytokines and chemokines. We also observed in vitro a comparable ability of Parkin KO microglia to phagocytize latex beads relative to WT controls. In current experiments, we are investigating the specific mechanism(s) leading to neuronal loss. Our results suggest that only a subset of the physiological properties of microglia are altered in the absence of Parkin. 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.

A73 –

Unraveling neurocomputational principles of sensorimotor integration in spinal neural ensembles

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Motor function requires the coordination of multiple areas in the brain including information on motor planning from premotor cortex and sensory feedback from the somatosensory cortex. This integration is primarily attributed to upper motor neurons and has been the focus of past research with results that range from the encoding of movement direction to the generation of force; however, there is also significant involvement of spinal cord circuits, made up of other descending projections, sensory afferents, and spinal interneurons, which modulate the output. To better understand their participation in motor control, we explored the integration of descending cortical neuron activity into ongoing peripheral processes at the spinal cord by stimulating the motor cortex and recording spiking activity from the cervical spinal cord of female rats using a Neuropixel probe during an anesthetized procedure. Cortical stimulation was combined with electrical stimulation of nerves within the forelimb using a broad coverage of parameters including stimulation intensity and frequency to uncover the contribution of activity originating at each level of the motor system. As a result of our investigation, we were able to build the pipeline required for collecting data and get early insights into the layers of sensorimotor processing that are a part of the translation of central commands for movement execution.

A74 –

Développement, déploiement et validation d'un modèle d'apprentissage profond appliqué à l'électroencéphalogramme pour la pronostication de l'épilepsie

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L'épilepsie est une maladie neurologique chronique touchant des millions de personnes, avec des crises récurrentes dont la prédiction demeure un défi central en clinique. L'électroencéphalogramme (EEG) est l'outil de référence pour le diagnostic et l'évaluation du risque de récidive des crises. L'interprétation des EEG repose principalement sur la détection des décharges épileptiformes intericales (DEI), considérées comme le biomarqueur électrophysiologique le plus spécifique de l'épilepsie. Toutefois, les DEI ne sont pas toujours présentes dans les enregistrements de routine, et leur interprétation peut être sujette à des erreurs humaines. Les modèles d'apprentissage profond (DL) offrent un potentiel prometteur pour extraire des biomarqueurs subtils dans les EEG, mais leur validation reste insuffisante, et les applications cliniques sont limitées.

Ce projet s'appuie sur un modèle DL, DeepEpilepsy, récemment développé par notre équipe, pour prédire le risque et le délai de récidive des crises à partir de données EEG de routine. Une base de données multicentrique de 18 400 EEGs, incluant des données du CHUM, de Harvard et de l'Université de Pennsylvanie, sera utilisée pour entraîner et valider le modèle. Le projet intègre une approche d'auto-apprentissage afin d'améliorer la performance du modèle en générant des pseudo-étiquettes sur des cas non annotés.

Nous anticipons que le modèle, une fois validé, permettra une meilleure prédiction du risque de récidive, y compris pour les patients sans DEI. L'objectif est d'atteindre un indice de concordance supérieur à 0,75, validant ainsi l'outil comme complément efficace au diagnostic clinique.

Ce projet vise à rendre l'EEG de routine plus fiable et informatif, en fournissant un outil de prédiction pour améliorer la gestion de l'épilepsie. Si validé prospectivement, ce modèle pourrait standardiser l'interprétation des EEG et améliorer les soins pour les patients à haut risque, notamment dans des régions dépourvues de spécialistes en épileptologie.

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A75 –

Non-medical cannabis use in epilepsy: prevalence, motivations, and mental health impact

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Rationale: Surveys suggest that nearly half of people with epilepsy (PWE) use non-medical cannabis (NMC; without medical supervision), often motivated by its purported anti-seizure properties. This rationale is concerning as NMC, typically high in THC and low in CBD, has not proven effective for seizure control and has been associated with deleterious health effects. Given the potentially harmful effects of cannabis on health, it is necessary to describe and evaluate its impact on mental health and quality of life (QoL).

Method: A total of 251 PWE completed an online questionnaire addressing their cannabis use habits and motivations, as well as QoL and symptoms of depression (BDI) and anxiety (BAI).

Results: Cannabis use was reported by 23% of PWE in the past three months (30% of men and 18% of women), and by 28% in the past 12 months. Among recent users, 54% reported recreational use and 27% both recreational and self-medication purposes. The most frequent reasons to use cannabis were anxiety/nervousness (24%), sleep disorders (21%), and seizure control (20%). Among NMC users, 30% of women and 54% of men consumed cannabis that was higher in THC than CBD, equal in THC and CBD, or exclusively high in THC. There were no significant differences in BDI, BAI, and QoL scores between users and non-users, although non-users tended to have higher QoL score ($p = .051$). However, NMC use was associated with higher levels of pessimism and feelings of choking ($p < .001$). Sex-stratified analyses showed that men who used cannabis reported a higher level of self-criticism.

Conclusion: NMC use is common among PWE. While depression, anxiety, and QoL scores were similar, specific symptoms were elevated among users, including pessimism, self-criticism, and feelings of choking. These findings highlight the need to inform PWE about the implications of NMC use in mental health.

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Astrocytic morphological alterations in the basolateral amygdala following early-life stress

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Early-life stress (ELS) has been recognized for having long-term negative effects on neuronal circuits, affecting behavior, cognition, and emotional regulation. The amygdala is particularly susceptible to structural and functional changes following both acute and chronic stress however, these observations have been mostly studied through a neuron-centric lens leaving the impact of stress on non-neuronal brain cells relatively understudied. Recent work has shown that astrocyte dysfunction following early-life stress has also been associated with behavioral deficits. Astrocytes are highly plastic cells, with perturbations in their morphology forming a key hallmark of many neurological diseases. Although studies in distinct brain regions has demonstrated stress-induced changes in astrocyte volume and process complexity, little is known about the morphological changes that occur in the basolateral amygdala. To explore this question, female and male mice were subjected to an early-life stress paradigm comprising maternal separation and reduction of bedding for four hours a day over a total of seven days (P10-P17). Around P30, they were injected with a blood-brain barrier permeable adeno-associated virus (AAV.PhP.eB-GfaABC1D-eGFP) into the retro-orbital sinus to target astrocytes throughout the brain. Three weeks later, immunohistochemistry was used to stain for the glial fibrillary acidic protein (GFAP), cell nuclei using DAPI, and to amplify the eGFP signal. Confocal microscopy was used to capture images, then analyzed using the IMARIS software to create 3D reconstructions of surfaces and filaments. In female mice, astrocytes in the ELS group have similar volume and process complexity to those in the naïve group, whereas in male mice, volume and total filament length were significantly decreased in the ELS group compared to the naïve group. These data highlight persistent sex-specific structural changes in astrocytes following early-life stress, which may contribute to cellular, synaptic and behavioural maladaptation following stress.