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ABSTRACT BOOK

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Akhavan, Sara

Pose Estimation Analysis of Interpersonal Motor Synchrony and Intrapersonal Movement Variability in Autism during Free-play

Sara Seyed Akhavan[1], Nada Kojovic[1], Marie Schaer[1], Thomas Maillart[1]

[1]University of Geneva

Non-verbal, motor aspects of social interaction, such as interpersonal motor synchrony (IMS), are broadly suggested to be atypical in autism, but remain mechanistically unclear and difficult to assess by the naked eye. Studies exploring IMS have predominantly required participants to be stationary, making them unsuitable for observing the full spectrum of autism phenotypes and behaviours in naturalistic settings. Our study analysed 60 autistic and 27 typically developing (TD) young children aged 1 - 4 years during free-play segments of ADOS-2 diagnostic sessions. To measure IMS between child-assessor dyads, we applied 2-D pose estimation technology, OpenPose, and dynamic time warping (DTW). Results showed that child-assessor dyads with autistic children exhibited significantly lower IMS compared to those with controls in both trunkregions and head regions. Additionally, autistic children had significantly higher levels of intrapersonal movement variability (IMV). IMS and IMV levels negatively correlated with each other. Both lower IMS and higher IMV in autistic children were significantly associated with higher autism severity, lower cognitive functioning skills, and lower adaptive functioning skills. Our findings demonstrate the strong potential of pose estimation and DTW as methods to effectively identify IMS and IMV atypicalities in autistic children, with their combination showing promise as an early behavioural marker. This study ultimately brings us closer to developing non-invasive digital methods for precise autism phenotyping in naturalistic settings.

Alem, Noor

Gait And Stair Ascent/Descent In Free-Living Conditions Present The Largest Limitations In Patients With Hip OA

Noor Alalem[1], Xavier Gasparutto[2], Kevin Rose-Dulcina[2], Didier Hannouche[2], Stéphane Armand[1]

[1]University of Geneva, [2]Geneva University Hospitals

Hip osteoarthritis (OA) is characterized by joint pain which leads to functional limitations [1]. The reduction of pain after total hip arthroplasty (THA) is well handled, but the functional improvement post-surgery remains limited [1]. Understanding patient functional change over time requires a good assessment of their pre-surgery status and has the potential to improve patient care and rehabilitation [2]. Specifically, understanding patient limitations during daily living activities is key since it is often cited among the most important expectations [3]. The aim of this study is to identify daily living activities where patients with end-stage hip OA face most difficulties when compared to a control group. 17 patients with end-stage hip OA (sex=59% F, age=63.7±4.8 years, BMI=25.0±2.9 kg/m^2) and 8 healthy controls (sex=75% F, age=67.9±7.8 years, BMI=23.8±3.6 kg/m^2) were selected for this study. Inclusion criteria for patients were: 1) scheduled for primary unilateral THA due to OA, 2) aged 30-85 years, 3) no prior lower-limb arthroplasty, 4) ability to walk 10m unaided. Inclusion criteria for controls were: 1) age- and weight-matched and 2) had no neurological or orthopaedic problems. Since free-living conditions offer no restriction on tasks, a compromise between controlled and free movement was chosen by asking participants to perform a 10 min tour in the hospital vicinity with daily life-like activities (gait on flat ground and ramps, turns, stair ascent/descent, sit-to-stand). Participants were equipped with 8 wearable inertial sensors (Physilog 6, MindMaze) and were video-recorded to ensure correct identification of activities performed. Sensor-derived spatiotemporal parameters (gait speed, cadence, gait cycle duration, gait cycle duration variability, stair ascent/descent speed, turn duration, step number per turn, thorax flexion range of motion in sit-to-stand and time to stand-up) were computed with an algorithm validated for elderly adults [4]. For statistical analysis, medians and interquartile ranges were calculated. Due to non-normal distribution of the data, Wilcoxon rank-sum test and Rank-Biserial correlation coefficient [5] were performed to compare patients to control groups ($p<0.05$). A median number of 316 and 339 cycles was obtained from patient and control gait, respectively. During gait, the median speed was 1.04±0.17 m/s and 1.25±0.07 m/s in patients and controls, respectively. As for stair ascent, median speed was 0.37±0.07 m/s and 0.48±0.08 m/s. Overall, gait and stair ascent and descent revealed the highest significant differences between patients and controls, particularly in speed yielding the following effect sizes per surface type: 1) Gait: effect size=-0.92 2) Gait up ramp: effect size=-0.90. 3) Gait down ramp: effect size=-0.56. The affected and dominant limbs were selected for patients and controls, respectively. Stair ascent and descent showed similar differences and effect sizes for speed, yielding -0.89 and -0.86, respectively. Finally, there were no significant differences for turns and sit-to-stands. Gait and stair ascent and descent were the activities with the greatest limitations before surgery, with speed being the most interesting parameter. These findings align with a previous study that found gait as the main limitation in THA patients before and after surgery [6]. This fast test of semi-standardized activities provided simple and complete biomechanical analysis of daily living activities. It could be a simple approach to evaluate hip OA patients' functional deficits before and after surgery.

ABSTRACT # 2

Asadi, Saina

Microstructure and Axon Radius Mapping using diffusion MRI at 7T: non-invasive prediction of conduction delays in the brain

Saina Asadi[1], Arthur Spencer[1], Yasser Aleman-Gomez[1], Helene Lajous[1], Erick J. Canales-Rodriguez[2], Emeline Mullier[3], Louise de Wouters[4], Isotta Rigoni[4], Maciej Jedynak[5], Michael Chan[6], Alexandre Cionca[6], Dimitri Van de Ville[7], Serge Vulliemoz[8], Olivier David[9], Patric Hagmann[1], Ileana Jelescu[1]

[1]Department of Radiology, Lausanne University Hospital (CHUV)|Faculty of Biology and Medicine, University of Lausanne, [2]Department of Radiology, Lausanne University Hospital (CHUV)|Signal Processing Laboratory 5 (LTS5), Ecole Polytechnique Fédérale de Lausanne (EPFL)|Center for Biomedical Imaging (CIBM), [3]Department of Radiology, Lausanne University Hospital (CHUV)|EEG and Epilepsy Unit, University Hospital and Faculty of Medicine of Geneva, University of Geneva, [4]EEG and Epilepsy Unit, University Hospital and Faculty of Medicine of Geneva, University of Geneva, [5]Institute de Neurosciences des Systèmes, Aix Marseille University Marseille, France, [6]Neuro-X Institute, École Polytechnique Fédérale de Lausanne (EPFL), [7]Neuro-X Institute, École Polytechnique Fédérale de Lausanne (EPFL)|Department of Radiology and Medical Informatics, University of Geneva, [8]Center for Biomedical Imaging (CIBM)|EEG and Epilepsy Unit, University Hospital and Faculty of Medicine of Geneva, University of Geneva, [9]Institute de Neurosciences des Systèmes, Aix Marseille University|Fondation Lenval, Department of Pediatric Neurosurgery Marseille, France|Nice, France

Conduction velocity (CV) of neuronal signals along axons is a key neurophysiological property that can be altered in various disease processes. Current invasive methods are limited to specific brain regions, preventing systematic whole-brain mapping of conduction delays (Lemaréchal, 2022). MRI-derived microstructural properties related to axon diameter and myelination (Drakesmith, 2019), enable comprehensive, non-invasive estimation of CV. To this end, we aim to develop an MRI-based model, validated against invasive EEG data, to predict CV and delays across the human brain white matter (WM) *in vivo*.

20 healthy participants were scanned on a clinical 7T Siemens Terra.X MRI system. A multi-shell dMRI protocol was acquired for Standard Model Imaging (SMI) microstructure estimation in WM (Coelho, 2022; Novikov, 2018). A multi-TE dMRI protocol was acquired for axon radius estimation using an intra-axonal T2 surface-based relaxation model (Barakovic, 2023) and group average microstructure properties were estimated for all WM bundles of the MultiConn atlas with 95 ROIs (Alemán-Gómez, 2022). Spearman's correlations assessed the relationship between CV (derived from electrophysiological delays and fiber lengths from the F-TRACT intracranial EEG database) and MRI microstructure metrics. Finally, multiple linear regression was performed to predict CV, model performance was evaluated through bootstrap resampling, and whole-brain velocity and delay matrices were generated.

Our results showed significant positive correlations between CV and radius (r=0.44), axonal water fraction (r=0.39) and fiber alignment (r=0.31), with negative correlations observed for perpendicular extra-axonal diffusivity (r=-0.28) and quantitative T1 (r=-0.21). The regression model explained 24% of CV variance, demonstrating the feasibility of MRI-based whole-brain conduction delay mapping *in vivo*.

Awada, Jade

A Longitudinal and Reproducible Anti-coactivation Pattern Between the Cerebellum and the Ventral Tegmental Area Relates to Apathy in Schizophrenia

Jade Awada[1], Farnaz Delavari [1], Thomas Bolton[1], Fares Alouf[1], Fabien Carruzzo[1], Noémie Kuenzi[1], Mariia Kaliuzhna[1], Tal Geffen[2], Terresa Katthagen[2], Florian Schlagenhauf[2], Dimitri Van de Ville[3], Stephen Eliez[1], Stefan Kaiser[4], Indrit Bègue[1]

[1]University of Geneva, [2]University of Berlin, Center Charité, [3]Ecole polytechnique de Lausanne, [4]Hopitaux Universitaires de Genève

Background : Negative symptoms of schizophrenia lack effective treatments. Anomalies in the reward system and cerebellum have been linked to these symptoms. The cerebellum modulates reward circuitry via the ventral tegmental area (VTA). The "cognitive dysmetria theory" posits that reduced cerebellar inhibition in schizophrenia may underlie striatal hyperdopaminergia. However, the role of cerebellum-VTA connectivity in negative symptoms remains unclear. Methods : From 427 individuals screened, 146 were recruited: 90 with schizophrenia (SZ) and 56 healthy controls (HC). At 3 months (T2), 65 individuals (36 SZ, 29 HC) completed follow-up. SZ participants were invited for clinical interviews at 9 months (T3; 33 SZ). After quality check, 105 participants were retained at T1, 41 at T2, and 21 at T3. A validation cohort included 53 individuals (28 SZ, 25 HC). The Brief Negative Symptom Scale quantified negative symptoms. Dynamic functional connectivity of the cerebellum and VTA was analyzed using coactivation patterns analysis. Results : A reproducible cerebellum-VTA anti-coactivation pattern was found across T1 and T2 ($r = 0.98$) in bilateral paravermal Crus I/II. Anti-coactivation emergence at T1 correlated negatively with apathy, particularly asociality and avolition. At T2, anti-coactivation persistence related negatively to apathy, especially anhedonia, and to anhedonia at T3. Similarly, reduced emergence at T2 was linked to worse asociality at T3. In the validation cohort, we replicated the pattern ($r = 0.93$), and its emergence negatively correlated with apathy, particularly asociality. Conclusion : Reduced cerebellum-VTA anti-coactivation is a reproducible neural marker of apathy in schizophrenia, highlighting its potential as a therapeutic target.

Badina, Aurélien M.

Spatial transcriptomics analysis of glial activation dynamics throughout the progression of Alzheimer's disease

Aurélien M. Badina[1], Kelly Ceyzériat[2], Laurene Abjean[1,3], Stergios Tsartsalis[1,3], Philippe Millet[1,3], Benjamin B. Tournier[1,3]

[1]Department of Psychiatry, Faculty of Medicine, University of Geneva, Geneva, Switzerland.
[2]CIBM Center for Biomedical Imaging, Geneva, Switzerland.
[3]Department of Psychiatry, University Hospitals of Geneva, Geneva, Switzerland.

Alzheimer's disease (AD) is the most prevalent neurodegenerative disorder, currently affecting 50 million people worldwide and projected to rise to 130 million by 2050. It is driven by the accumulation of amyloid-β (Aβ) and Tau, which form extracellular plaques and intracellular tangles. Astrocytes and microglia detect these deposits and adopt activated phenotypes. The role of activated glial cells is ambivalent, with studies pointing to damage control roles and other indicating pathological reactions. During their activation, they release pro-inflammatory mediators to recruit and activate further glial cells, potentially causing a vicious circle of neuroinflammation eventually contributing to damaging neurons.

We used spatial transcriptomics (10x Visium) to characterize the cellular microenvironment in amyloid-driven neurodegeneration and glial activation on human hippocampal slices. 16 subjects were distributed in three age-matched groups: controls, early stages AD and late stages AD. We then distributed spots in regions of interest depending on their distance to plaques, according to Aβ immunostaining. The goal is to create an atlas of existing glial states in the pathology and eventually understand the role of each cell subtype.

To do so, we started by computing homeostatic modules representative of each major cell type present in the hippocampus. The modules are based on single cell reference genes to build the most homeostatic cell types possible. We have eight modules: astrocytes, microglia, excitatory neurons, inhibitory neurons, oligodendrocytes, OPCs, endothelial cells and peripheral immune cells to study immune infiltration in later stages. The current step is the study of how these modules evolve with disease progression and proximity to Aβ plaques, how they morph and split into sub-modules corresponding to observed phenotypes in the pathology. Indeed, multiple activation and even more degenerative or dystrophic phenotypes have been reported. But it is unclear when or where they appear, and their role. Finally, once all these modules are identified, cellular communication will be quantified through ligand-receptor expression to determine how cell subtypes communicate together and their roles.

Mapping glial evolution through the pathology is essential to the understanding of inflammation and how it contributes to AD.

Bakhareva, Alisa

A role of prefrontal inputs to lateral hypothalamus and their modulation by catecholamines in stress response

Bakhareva Alisa (1, 2), Petzold Anne(1, 2, 3), Korotkova Tatiana (1, 2)

(1) Institute for Systems Physiology, University of Cologne, Cologne, Germany
(2) University Hospital Cologne, Cologne, Germany
(3) European Neuroscience Institute, A Joint Initiative of the University Medical Center Göttingen and the Max Plank Institute for Multidisciplinary Sciences, Göttingen, Germany

Animals experience various forms of stress - such as hunger, thirst, social isolation and aggression - throughout their lifetime. To successfully cope with such stressors, animals need to flexibly adapt behaviour. The impact of stress on behavioural adaptation depends on the type and duration of stress, as well as on the sex and age of the animal, and individual vulnerability.

The medial prefrontal cortex (mPFC) is involved in the stress response and in adapting behaviour to a certain context. One of the output targets of the mPFC is the lateral hypothalamus (LH), a brain region that regulates innate behaviours. Yet, little is known about whether and how the prefrontal-hypothalamic circuit mediates the influence of stress on innate behaviours. Both norepinephrine (NE) and dopamine (DA) dynamics respond to stressful experiences and strongly modulate neuronal activity in mPFC and LH. However, the dynamics of neuromodulator release in mPFC and LH during stress experiences is still elusive.

To address these questions, we first optogenetically stimulated mPFC inputs to LH and analysed innate behaviours of mice following physical, metabolic or social stress. We found that this circuit promotes behaviours that alleviate stress, such as food seeking following fasting or seeking out conspecifics following restraint. Further, we employed dual-site, dual-colour fibre photometry of neurotransmitter sensors for NE and DA in mPFC and LH of freely-moving mice. We identified the release patterns of these neuromodulators during innate and anxiety-related behaviours in response to different stressors.

Taken together, our data highlights the role of the mPFC-LH circuit and its neuromodulation in state- and context-dependent behavioural adaptation to stress.

Ballasch, Iván

Is IKZF3 a new theranostic marker for Schizophrenia?

Ballasch Iván 1,2,3, Wang Maoyu1,2,3, Laura López-Molina1,2,3, Kentaro Yomogida4, Joaquín Fernández-Irigoyen5, Enrique Santamaría5, Natalia Egri6, Manel Juan1,6,7, Carla Hernandez8, Jaume Solanas8, Belén Arranz8 and Albert Giralt1,2,3,9

1Departament de Biomedicina, Facultat de Medicina, Institut de Neurociències, Universitat de Barcelona, 08036, Barcelona, Spain.
2Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), 08036, Barcelona, Spain.
3Centro de Investigación Biomédica en Red Sobre Enfermedades Neurodegenerativas (CIBERNED), 28031, Madrid, Spain.
4University of Colorado School of Medicine BDC, M20-3201N (lab) M20-3309B (office), 1775 Aurora Ct, Aurora, CO 80045 Phone: 303-724-5667
5Proteomics Platform, Navarrabiomed, Hospital Universitario de Navarra (HUN), Universidad Pública de Navarra UPNA, IdiSNA, 31008, Pamplona, Spain.
6Servei d'Immunologia, Hospital Clinic Barcelona (HCB) - CDB, Fundació Clínic de Recerca Biomèdica - IDIBAPS, Barcelona, Spain.
7Plataforma d'Immunoteràpia HSJD-HCB, Barcelona, Spain.
8Parc Sanitari Sant Joan de Déu, CIBERSAM, Barcelona, Spain.
9Production and Validation Centre of Advanced Therapies (Creatio), Faculty of Medicine and Health Science, University of Barcelona, 08036, Barcelona, Spain.

IKZF3, a.k.a. Aiolos is a member of the Ikaros zinc finger protein (Ikzf) family. Aiolos together with other members of the Ikzf family are known to be essential for proper immune system development and function. Besides, some of the other members of the family, but not Aiolos, are known to be necessary for neural cells development and function and have been associated with psychiatric conditions such as schizophrenia. However, as far as we know, the potential implication of Aiolos in these contexts is still yet to be studied. Preliminary data of our lab indicates that the levels of Aiolos varies through development in several brain areas in mice. On the other hand, we have found dysregulations of Aiolos in immune and neural cells of schizophrenia patients. Overall, our results suggest that Aiolos is implicated in both contexts, brain development and schizophrenia neuro-immune pathology. As futures perspectives, we plan to deeper characterize the effect of Aiolos modulation in the brain of mice models. We hypothesize that the alteration of Aiolos will negatively impact on brain development and/or function. Likewise, we plan to evaluate possible alterations of Aiolos in other psychiatric conditions such as major depression disorder. We hypothesize that Aiolos is mainly dysregulated in schizophrenia and probably also in other psychiatric conditions.

Barcellini, Francesca

Infra-slow noradrenergic dynamics drive brain-wide coordination via mesoscale neurovascular waves

Francesca Barcellini[1], Georgios Foustoukos[2], Laura Fernandez[2], Anita Luthi[2], Valerio Zerbi[1]

[1]Department of Psychiatry, Faculty of Medicine, University of Geneva, Geneva, Switzerland, [2]Department of Fundamental Neurosciences, University of Lausanne, Lausanne, Switzerland

Infraslow neural oscillations (~0.01–0.05 Hz) have been increasingly recognized as a fundamental mechanism for large-scale brain coordination, yet their biological drivers and organizational principles remain poorly understood. Mechanistic theories posit that such rhythms arise from interactions between brainstem neuromodulatory nuclei and distributed cortical-thalamic circuits, supporting dynamic shifts in neural excitability and integrative processing. Here, we investigated the role of the locus coeruleus (LC)—a key noradrenergic arousal center—in orchestrating infraslow brain-wide dynamics. We developed a novel multimodal approach combining LC-targeted fiber photometry with resting-state fMRI in mice under urethane anesthesia, a condition we empirically validated as preserving LC infraslow oscillations that resemble those observed during natural NREM sleep. By recording calcium dynamics in LC neurons using GCaMP8, we identified two main states: one marked by coherent infraslow (~0.02 Hz) fluctuations and another characterized by low-amplitude, desynchronized activity. During infraslow LC states, brain-wide fMRI connectivity significantly increased, consistent with enhanced functional integration. Event-locked analysis of 156 LC infraslow peaks across 12 mice revealed consistent, traveling wave-like patterns of BOLD activation, with region-specific delays and trajectories. These spatiotemporal dynamics suggest that LC infraslow activity engages distributed brain systems through anatomically constrained propagation. To visualize whole-brain response dynamics, we used UMAP to project high-dimensional regional fMRI activity into a two-dimensional space. The resulting trajectories formed closed loops centered around LC peaks, but with distinct outbound and return paths—indicating that propagation and recovery follow asymmetric dynamics. These findings suggest that the LC functions not only as a phasic arousal modulator but also as a rhythm generator, whose infraslow dynamics organize intrinsic brain activity through structured, directional waves. This framework provides a biologically grounded model for understanding how slow neuromodulatory rhythms support large-scale communication and dynamic network regulation across the brain.

Beaux, Judith

Reln and serotonin in cortical development and neurodevelopmental disorders.

Beaux Judith (1)(2), Martina Riva (3), Alessandra Pierani (1)(2), Anne Teissier (1)(2)

(1) Department of Pathology and therapeutic Experimental, Institute of Neurosciences, University of Barcelona
(2) Department of Pharmacology, Ribeirao Preto Medical School, University of São Paulo, Brazil.

Reelin (Reln) is a large glycoprotein regulating multiple steps of mammalian cortical development and whose secretion appears to be sensitive to the environment. In humans, homozygous or compounds heterozygous reln mutations are associated with neuronal migration disorders as diverse as lissencephaly, pachygyria, polymicrogyria and heterotopia, while decreased Reln levels are associated with neurodevelopmental disorders (NDDs), such as autism spectrum disorders, schizophrenia and bipolar disorders. Similarly, rodent homozygous reln mutants (ie. Reeler) present dramatic alterations in cortical lamination, while heterozygous mutants display cognitive and behavioral abnormalities relevant to NDDs together with defects in neuronal cytoarchitecture and plasticity. Importantly, during development, Reln is secreted by sequential cellular sources from distinct origins and molecular profiles: Cajal-Retzius cells (CRs), the main Reln sources at embryonic stages, and cortical GABAergic interneurons (INs), the main Reln sources after birth, as CRs disappear by apoptosis during the first postnatal weeks. However, whether Reln produced by different sources plays distinct roles in cortical lamination and adult behavior remains unknown. Furthermore, Reln levels have been shown to be differentially modulated by serotonin (5-HT), a crucial neuromodulator of mood and behavior, throughout distinct developmental stages -prenatal versus postnatal- in both humans and rodents. This suggests differential sensitivities of Reln cellular sources to 5-HT, a hypothesis which remains to be verified.

Here, we first demonstrate specific and cooperative implications of Reln sources in cortical lamination, using conditional genetic models to specifically ablate reln in CRs and/or INs. In parallel, using similar genetic tools, we investigate their specific implications on behaviors relevant for NDDs. Finally, we want to assess the potentially distinct vulnerabilities of Reln+ population to 5-HT exposure during development, by performing bulk RNA sequencing on FACs enriched CRs or INs. These results will provide critical understanding on how Reln deficits are observed across the phenotypic spectrum of NDDs.

Beilmann, Viktor

Overactivation of astrocytes leads to dysregulation of prefrontal neuronal activity and impaired cognition via kynurenic acid.

Beilmann Viktor (1), J. Furrer (1), SM. Schalbetter (3), C. Glück (1), U. Weber-Stadlbauer (2,3), M. Wyss (1,2), A. Saab (1,2), B. Weber (1,2), U. Meyer (2,3), T. Notter (1,2)

1: Institute of Pharmacology and Toxicology, University of Zurich
2: Neuroscience Center Zurich
3: Institute of Pharmacology and Toxicology, University of Zurich, Vetsuisse

Astrocyte dysfunctions have long been implicated in psychiatric and cognitive disorders, yet the precise mechanisms underlying this association remain elusive. Here, we show that chemogenetic activation of prefrontal astrocytes in mice impairs short-term memory and sensorimotor gating and attenuates the activation of prefrontal parvalbumin (PV) interneurons. These alterations are accompanied by increases in prefrontal levels of kynurenic acid (KYNA), a neuroactive metabolite, which serves as an endogenous antagonist of NMDA receptors. Pharmacological inhibition of kynurenine aminotransferase II, the key enzyme mediating the transamination of kynurenine to KYNA, reinstates the short-term memory and sensorimotor gating impairments, and normalizes the deficits in prefrontal PV interneuron activation. These findings suggest that astrocyte-derived KYNA impairs cognitive functions by modifying prefrontal E/I balance. To test this hypothesis, in vivo 2-photon calcium imaging experiments in awake mice are being conducted, where the activity of prefrontal neurons and PV interneurons are simultaneously measured following astrocyte overactivation. Taken together, our study identified a mechanistic link between overactivation of prefrontal astrocytes, increased production of KYNA, and cognitive as well as cellular dysfunctions involved in major psychiatric disorders.

Bir, László

Structural convergence of excitatory and inhibitory inputs to the paraventricular thalamus supports its role in stress-induced social behavior alterations.

Biró László 1*, Zsolt Buday1,2, Kata Kóta1,2, Szabolcs Lőrincz1, László Acsády1*

1 Lendület Laboratory of Thalamus Research, HUN-REN Institute of Experimental Medicine; Budapest, Hungary

2 Neurosciences PhD School, Semmelweis University; Budapest, Hungary

The paraventricular nucleus of the thalamus (PVT) has emerged as a key integrative hub in the regulation of stress, arousal, emotion, and motivation. Recent findings suggest that the PVT also plays a central role in mediating stress-induced disruptions in social behavior, a core symptom domain across multiple psychiatric disorders. However, the structural organization of afferent inputs that enables the PVT to exert such broad behavioral influence—particularly over social domains—remains poorly understood.

Using viral tracing in transgenic mouse lines selective for GABAergic and glutamatergic neurons, as well as layer-specific cortical projections, we systematically mapped the excitatory and inhibitory afferents to the PVT. Our results reveal that the PVT receives a diverse array of subcortical inputs from hypothalamic and brainstem regions, many of which target the PVT in a transmitter-specific manner. Notably, both excitatory and inhibitory projections from areas such as the preoptic area and periaqueductal gray converge on the central "core" region of the PVT, which contains densely packed calretinin-positive (CR+) neurons. In parallel, medial prefrontal cortical input is layer-specific: layer 5 neurons preferentially target the CR+ core, while layer 6 projections dominate in the PVT–mediodorsal transition zone.

This precise anatomical convergence of cortical and subcortical signals onto the CR+ PVT core suggests a structural basis for the region’s role in integrating top-down and bottom-up information related to social context, threat processing, and affective state. These findings offer new insight into how stress alters social behavior via defined thalamic circuits and provide a foundation for future functional studies targeting this bottleneck region. Understanding the organization of these pathways is crucial for unraveling the neurobiology of social dysfunction in stress-related psychiatric disorders and may inform future therapeutic strategies.

Boehringer, Andrew

BOLD Variability and Cognitive Outcomes from Birth to School Age in Children Born Very Preterm

UNIGE

Premature birth has been linked to structural and functional brain alterations, increasing the risk of cognitive impairments later in life (Volpe, 2009). BOLD variability from resting-state fMRI correlates with cognitive performance in adults (Protzner et al., 2014; Garrett et al., 2010). However, little is known about its significance during childhood, particularly in children born very preterm (VPT; <32 weeks gestational age, GA). This study investigates changes in BOLD variability from the newborn period to school age in both VPT and full-term (FT) children, aiming to better understand how BOLD variability relates to brain functional maturation and cognitive performance, and how these processes are altered by very preterm birth. In the newborn group, 68 VPT and 35 FT infants underwent MRI at 40 weeks GA at the University Hospitals of Geneva. At school age, 23 VPT and 19 FT children were scanned at Campus Biotech, Geneva, and completed a battery of cognitive assessments. MRI at both timepoints included resting-state fMRI and anatomical T1- or T2-weighted images. BOLD variability was calculated as the standard deviation of the BOLD signal within each region of the AAL atlas. Two-sample t-tests were used to compare BOLD variability across groups and timepoints. A partial least squares correlation (PLSC) analysis was used to assess relationships between BOLD variability and cognitive performance at school age. Results show that mean BOLD variability was significantly higher in FT than in VPT newborns at 40 weeks GA ($p = 0.001$), but this difference was no longer significant at school age ($p = 0.09$). In both groups, mean BOLD variability was significantly higher at school age compared to the newborn period ($p < 0.001$). The PLSC analysis identified one significant latent component. In the FT group, higher BOLD variability across regions was associated with later GA at birth and better performance on the WISC Similarities subtest, emotional expressive suppression, and attentional flexibility tasks. In contrast, in the VPT group, higher BOLD variability was associated with poorer emotional expressive suppression and attentional performance. These findings suggest two key points: first, while early differences in BOLD variability between VPT and FT infants exist, they tend to normalize by school age. Second, despite similar group-level BOLD variability at school age, the functional implications differ—higher BOLD variability is associated with cognitive benefits in FT children but with deficits in VPT children. These results provide insight into the role of BOLD variability in early development and underscore the lasting impact of very preterm birth on brain function and cognition.

Bouhour, Camille

Power spectral analysis of resting-state EEG in cognitive decline and healthy aging

Camille Bouhour[1], Vincent Rochas[2], Denis Brunet[3], Konstantin Toussas[4], Paul G. Unschuld[5], Lucie Brechet[4]

[1]Univeristy of Geneva, [2]FCBG / University of Geneva, [3]CIBM / University of Geneva, [4]University of Geneva, [5]University Hospitals of Geneva (HUG) / University of Geneva

Mild cognitive impairment (MCI) is the transitory stage between normal aging and dementia, affecting 10-20% of adults aged 65 and older (1). Despite its prevalence, the mechanisms underlying the MCI stage of cognitive decline remain largely unclear (1). Resting-state electroencephalography (EEG) power spectral analysis is a widely used technique to investigate functional brain changes associated with cognitive decline and aging. Previous research indicates that Alzheimer's Disease (AD) is characterized by increased power in slow-wave (delta and theta) and decreased power in fast-wave (alpha and beta) frequencies (2-5). Similar, though less consistent, spectral patterns have been observed in individuals with MCI (2-5). In contrast, healthy aging is generally associated with reduced slow-wave and alpha activity, alongside increased beta power (3, 6-7). In this study, we performed a power spectrum analysis of resting-state EEG recordings from three groups: individuals with MCI, healthy older adults, and healthy younger adults. High-density EEG recordings (257 channels) were obtained from 149 participants in total (N = 58 Older adults; N = 58 Younger adults; N = 33 MCI adults) during a 5-minute resting-state with eyes closed. The EEG signal was preprocessed on Cartool (8) and the power spectrum analyzed using the Welch method across frequencies between 1 to 70 Hz. Independent samples t-tests were applied on each frequency band (delta: 1-4 Hz; theta: 4-8 Hz; alpha: 8-12 Hz; beta: 12-30 Hz; low gamma: 30-48 Hz; high gamma: 52-70 Hz) and FDR corrected between each pair of groups across all 204 kept channels. Results revealed a reduction in alpha power in both MCI and healthy older adults compared to younger adults over occipital and frontal regions, consistent with typical age-related neural changes (6, 9). MCI patients also showed increased theta power compared to healthy controls over frontal, parietal and right temporal regions, indicating EEG slowing. Interestingly, beta power increased in MCI patients compared to healthy younger adults over frontal and parietal regions, which may reflect age-related changes as older adults also had increased power compared to younger ones. These findings suggest that early cognitive decline in MCI may primarily involve increases in slow-wave activity, while decreases in fast-wave activity may occur later during progression toward AD.

Bouteldja, Farha

Neuronal Plasticity after Spinal Cord Injury: Unraveling extracellular matrix dynamics

Farha Bouteldja[1], Stacey Elshove[1], Ed Hasanovic[1], Quentin Amossé[1], Claudia Kathe[1]

[1]University of Lausanne

Spinal cord injury (SCI) leads to varying degrees of sensorimotor deficits in patients. However, spontaneous recovery usually occurs during acute phase after the injury, but plateaus in subacute phases. We have modeled this in a mouse model of SCI, and locomotor assessments show spontaneous motor improvements occur between 3 days and 21 days post-injury, but the recovery plateaus at 3 weeks with no further improvements, even tested at 3 months post-injury. Immune cells such as microglia and astrocytes are thought to play a crucial role in spontaneous recovery and anatomical alterations. This has been studied extensively at the lesion site but how immune cells regulate neuronal plasticity caudal to the injury site is poorly understood. This project is based on investigating how immune cells modulate extracellular matrix (ECM) components, which are involved in neuronal plasticity. Preliminary results show that after SCI, expression of ECM components and immune cells are highly perturbated in the spinal cord distal to lesion site. We hypothesized that by modulating the immune cells and extracellular matrix components, we could improve spontaneous recovery and furthermore trigger new spinal reorganization at a chronic stage, thus resulting in a better functional outcome.

Bouzourène, Narimane

Gut microbiota alterations and hypothalamic inflammation precede obseity in a rat model of binge eating

Narimane Bouzourène[1], Sedreh Nassirnia[1], Léa Aeschlimann[2], Gilbert Greub[1], Benjamin Boutrel[1], Claire Bertelli[1], Clara Rossetti[1]

[1]Lausanne University Hospital, [2]Lausanne University Hospital

Overconsumption of ultra-processed food and sedentary lifestyle are the main causes of obesity, which in turn, increases the risk of developing metabolic, cardiovascular, and psychiatric diseases. Loss of control over food intake and binge eating often worsen as obesity progresses. Many studies have shown the effect of obesity on gut-microbiota composition and inflammation. However, less is known about microbiota and central adaptations occurring during the initial phases of body weight gain. To address this question, we used a rat model of binge eating, in which, rats (C/P) were fed twice a week with homemade cheesecake, as palatable food, for two months. At the end of the feeding protocol, C/P rats developed cheesecake binge eating behavior compared to chow fed rats (C/C). Despite the lack of obesity and peripheral inflammation, C/P rats showed altered microbiota composition, increased Firmicutes/Bacteroidetes ratio (F/B ratio) and α-diversity. In the hypothalamus of C/P rats, using q-PCR, we observed impaired cytokine and leptin- signaling-related protein gene expression. Additionally, we performed immunofluorescence analysis of Iba1+ microglia cells in the hypothalamus consisting in microglia counting, branches analysis and fractal analysis. Cheesecake consumption in C/P rats led to increased number of Iba1+ cells and changes in their morphology. Microglia cells showed decreased complexity and increased density, known as typical features of a pro-inflammatory state. Taken together these data suggest that changes in microbiota composition and neuroinflammation precede obesity and could contribute to overeating. Therefore, strategies able to limit these gut-brain axis adaptations may be useful in preventing excessive body weight gain.

Bringaud, Audrey

The potential of circulating brain derived protein as a biomarker in infants at risk of autism spectrum disorder

Audrey Bringaud[1]

[1]Université de Lausanne

Aims: Autism Spectrum Disorder (ASD) is a complex neurodevelopmental condition with significant clinical and etiological heterogeneity, posing a major challenge for early detection and intervention. Emerging research suggests that microtubule-associated proteins, commonly implicated in neurodegenerative diseases, may also be relevant in neurodevelopmental processes associated to ASD. This study aims to explore whether circulating brain-derived protein can be reliably measured in pediatric biofluids —plasma, saliva, and urine— of children with ASD and typically developing controls. Methods: Plasma samples have been collected from children diagnosed with ASD and a control group of individuals with a copy number variant (CNV) at the 16p11.2 locus, previously associated with the risk to develop neurodevelopmental and psychiatric disorders. Brain-derived protein levels in their plasma have been measured using a set of appropriate biochemical techniques and Live Cell-based assay (size exclusion chromatography, immunoprecipitation magnetic). Results: We present preliminary findings supporting the feasibility of detection and quantification of brain-derived proteins in biofluid plasma, revealing significant differences as a function of diagnostic status. Brain-derived extracellular vesicles (BD-EVs) show distinct proteomic alterations: Autism Spectrum Disorders have no impact on the number of BD-EVs proteins, but affect the content. The study of signatures of circulating brain-derived extracellular vesicles suggests a promising tool to explore the relationship between neurobiology and behavioral characteristics of ASD. Conclusion: This research represents an innovative attempt to measure circulating brain-derived proteins in pediatric biofluids, potentially paving the way for the identification of new biomarkers of ASD. More specifically, tau-interacting proteins may serve as early biomarkers for stratifying children with ASD. Integrating clinical and biological markers to better understand the involvement of brain?derived proteins on neurodevelopment could provide crucial insights into the neurobiological mechanisms underlying ASD, and inform strategies for early intervention.

Çabas, Irmak

The Role of the Transcription Coactivator CRTC1 in Neuroinflammation and Depression

Irmak Çabas * (1), Laurent Fumeaux (1), Clara Rossetti (1) & Jean-René Cardinaux (1)

Center for Psychiatric Neuroscience, Lausanne University Hospital, University of Lausanne

CREB-regulated transcription coactivator 1 (CRTC1) plays a pivotal role in the brain by regulating the expression of genes involved in neuronal survival, synaptic plasticity, and long-term potentiation by interacting with cAMP response element-binding protein (CREB) (1). Our research utilizes a Crtc1 knockout (KO) mouse model, which exhibits increased aggressiveness, depressive-like behavior, and obesity in males (2).

The bidirectional relationship between obesity and major depressive disorder is well-established, with both conditions linked to elevated neuroinflammatory markers in various brain regions (3). In the literature, CRTC1 overexpression has been associated with a protective effect against neuroinflammation in the hippocampus (4). Given the phenotype of our KO mice, we hypothesize that Crtc1 KO males may experience increased neuroinflammation, potentially serving as a triggering factor for depression symptoms and obesity in adulthood.

We initiated this project by performing in vitro experiments on primary glial cell cultures collected from wild-type (WT) and Crtc1 KO pups. Lipopolysaccharide (LPS) and interferon gamma (IFN□□ treatment revealed significant differences in the reactivity of WT and KO microglia and astrocytes in monocultures that diminished in the mixed cultures. Then, we proceeded with in vivo experiments consisting of immune system stimulation via acute or subchronic LPS injections. In all conditions, Crtc1 KO mice exhibited prolonged sickness behavior, with more severe hypothermia within the first 6 hours and higher weight loss on the following days. Additionally, KO mice refrained from voluntary running-wheel activity for a longer period compared to the WT. We are now investigating if this effect is due to higher or prolonged inflammatory response in the KO mice by performing multiplex protein immunoassays and qPCR. Future studies will investigate LPS-induced depressive-like behavior in WT and KO mice, focusing on serotonin/kynurenine pathway imbalances as well as glial cell activity. This project aims to deepen our understanding of CRTC1's role in emotional regulation, neuroinflammation, and metabolic disturbances.

Cannaerts, Lander

(A)periodic neurological differences between Substance Use Disorders (SUD's) and Eating Disorders (ED's)

Cannaerts L. (1), Baetens K (1) and Diercx E. (2,3)

(1) Brain, Body & Cognition, Vrije Universiteit Brussel ;

(2) Alexianen Zorggroep Tienen ;

(3) Personality and Psychopathology, Vrije Universiteit Brussel

Resting-state EEG is an important tool for investigating neural dynamics in psychiatry, as it captures both oscillatory (periodic) activity and more recently characterized nonoscillatory (aperiodic) components of the power spectrum. Whereas periodic measures such as band power have been widely used in clinical research for decades, aperiodic measures, including the spectral slope, represent a relatively novel approach that may provide additional sensitivity in differentiating between patient groups. Despite this promise, few studies have directly compared combined (a)periodic markers across distinct psychiatric populations.

In the present study, EEG recordings from 2,239 inpatients of a Belgian psychiatric hospital were analyzed, comprising 1,805 individuals with substance use disorders (67% male; mean age = 44.4 years, SD = 12.9) and 540 individuals with eating disorders (100% female; mean age = 21.4 years, SD = 6.0). Spectral decomposition was applied to extract both aperiodic slope estimates and relative band power across canonical frequency ranges. Group differences were evaluated using multivariate analyses of covariance, and predictive performance was assessed with DeLong tests and out-of-fold classification modelling.

Results indicated clear distinctions between groups: patients with eating disorders exhibited steeper aperiodic slopes compared to those with substance use disorders, alongside higher relative theta power and lower relative beta power. Classification accuracy was extremely high (AUC ≈ 0.99), with comparable performance when using slope, spectral bands, or both combined. Notably, slope alone explained nearly as much diagnostic variance as all four band power measures together, underscoring the discriminative strength of aperiodic markers.

These findings demonstrate that resting-state EEG provides meaningful signatures that distinguish between psychiatric populations when both periodic and aperiodic features are considered. The aperiodic slope, as a relatively new but robust metric, emerges as a particularly powerful discriminator. By integrating such measures into clinical research, EEG holds promise as a biomarker-based tool to support diagnostic decision-making and advance precision psychiatry.

Camelot, Léa

Perineuronal nets and synaptic transmission in the lateral habenula

Léa Camelot[1], Valentino Totaro [2], Tommaso Pizzorusso [2], Manuel Mameli[1]

[1]University of Lausanne , [2]Scuolar Normale Superiore, Pisa

Synaptic neurotransmission across the brain's lifespan is tightly regulated by various elements including the expression levels of perineuronal nets (PNNs), a form of extracellular matrix surrounding the somata and proximal dendrites of neurons. Proper regulation of synapses formation allows for the establishment of mature brain circuits, a process pivotal in the context of aversion related brain areas that, in turn, ensures appropriate behaviors for the survival of individuals in threatening contexts. The lateral habenula (LHb) is a key region for encoding negative stimuli, and synaptic plasticity occurring in adulthood while facing aversive context is key to trigger adaptive behavior. Additionally, PNNs are found in this structure throughout maturation and are disrupted when individuals experience negative events. However, whether glutamatergic and GABAergic neurotransmission properties change during the development of the LHb and whether PNNs regulate these properties influencing subsequent behaviors, remains unknown. Here, using in vitro electrophysiological recordings on acute brain slices, AMPA/NMDA ratios in the LHb were shown to differ between slices obtained from young (~P15) and adult mice (~P60). Additionally, we found PNNs expression in the LHb increasing from early ages to adulthood, and that disruption of the PNNs at the adult stage reduces AMPA/NMDA ratios indicative that glutamatergic synapses acquire a "rejuvenated state". At the behavioural level, disruption of PNN did not alter learning during active avoidance or encoding of an inescapable footshock. However, disrupting PNNs shifts behavioral strategy of mice in an anxiety-testing paradigm. In conclusion, excitatory synapses in the LHb change their properties between different periods across the lifespan and PNNs are important for stabilizing synaptic function in this structure. In addition, disrupting PNNs in the LHb leads to a "rejuvenated" synaptic phenotype and affects behavioural aspects.

Cataldo, Eugenie

A multi-technology approach to uncover the behavioral and neural mechanisms of object-based deficits

Eugénie Cataldo[1], Thibaud Delavy[1], Yvain Tisserand[1], Emmanuel Badier[1], Ilaria Sani[1]

[1]University of Geneva

Visuospatial neglect is a prevalent and debilitating cognitive deficit following stroke, where patients fail to attend to the side of space (egocentric) or objects-based (allocentric) opposite to their brain lesion. While egocentric neglect is well documented, object-based deficits remain poorly understood and likely underestimated clinically, yet crucial in daily life. This project investigates the behavioral and neural mechanisms of object-based deficits in subacute to chronic stroke patients to better understand its underlying processes and enhance the sensitivity and ecological validity of assessments and rehabilitation protocols. To address this issue, we designed an innovative cognitive battery integrated into a storyline to increase the motivation and engagement of patients. This battery assesses different behavioral components and includes immersive virtual reality and realistic touch-based dynamic tasks, objective quantitative measures such as eye and body motion tracking, as well as multimodal MRI to uncover structural and functional disconnections caused by the patients' lesions. Preliminary data from 10 stroke patients indicate that 20% of patients show signs of allocentric deficits. While presenting a minor deficit on traditional paper and pencil tests, patients with allocentric deficits consistently demonstrate deficits across multiple tasks in our experimental battery. This suggests that our paradigm is sensitive enough to detect object-based deficits (even the subtle ones) and may also help distinguish between different subtypes of these deficits. Importantly, patients reported high engagement with both the tasks and the storyline, supporting the ecological validity of our approach. These findings indicate that object-based deficits can persist in the subacute and chronic phases post-stroke, highlighting the need for more sensitive and ecologically grounded assessment tools. The use of quantitative, fine-grained behavioral metrics appears particularly promising for identifying nuanced deficits, predicting functional recovery trajectories and guiding personalized intervention strategies. Ongoing analyses aim to further delineate behavioral profiles, and map the neural mechanisms underlying these complex disorders, with the long-term goal of optimizing rehabilitation strategies.

Chauhan, Ishan-Singh

PeriPersonal Space-Time: temporal sensitivity of space dependent visuo-tactile integration

Ishan-Singh Chauhan[1], Anna Custo[2], Tommaso Bertoni[3], Andrea Serino[1]

[1]UNIL-CHUV, [2]CHUV, [3]EPFL

PeriPersonal Space (PPS)refers to the representation of the space surrounding the body, allowing physical interactions between the individual and the environment. PPS has often been described as an enhanced integration of tactile information with exteroceptive information in a distance dependent-manner, allowing contact prediction. Knowledge on how temporal features of body and external stimuli determines this distance-dependent integration is lacking. In the present study, healthy participants underwent a classical PPS paradigm during which a tactile stimulus was delivered to the hand while a visual stimulus was presented at different distances from the body. Crucially, various delays were applied between the tactile and visual stimuli, allowing to orthogonally manipulate contingencies between bodily and external stimuli both in time and space. For the different delay and distance combinations, PPS activation was measured through a validated EEG index based on spectral power desynchronization, capturing multisensory integration. Preliminary data show a trend indicating that PPS activation is modulated as a function of both spatial and temporal features of visuo-tactile stimulation, according to natural spatiotemporal regularities. That is, the PPS index appear stronger when stimuli are close, or far, in both space and time. Such results are encouraging and might support the idea that the concept of PPS should be reframed as PeriPersonal Space-Time (PPST), to account for both the spatial and the temporal dimensions.

Chauveau, Anna

A novel missense GRN variant: uncovering pathogenicity using patient-derived induced pluripotent stem cells.

Anna Chauveau[1], Paolo Salvioni Chiabotti[2], Dassine Berdous[1], Clara Gaillard[1], Gilles Allali[2], Olivier Rouaud[2], Sylvain Perriot[3]

[1]Lemanic Institute for Regenerative Medicine (LIRM), [2]Leenaards Memory Center - CHUV, [3]Lemanic Institute for Regenerative Medicine (LIRM), CNP - CHUV

State-of-the-art Mutations in the progranulin (GRN) gene are a major cause of Frontotemporal Lobar Degeneration (FTLD). To date, over 65 variants have been identified, mostly nonsense or splice-site mutations, resulting in a loss of function with progranulin (PGRN) haploinsufficiency and TDP-43 neuropathology. However, it has currently been not proven that missense mutations may also cause FTLD. Here, having diagnosed a patient with FTLD presenting borderline levels of PGRN and a novel missense GRN mutation, we aim to assess the pathogenicity of this novel variant using human induced pluripotent stem cells (hiPSCs) as a model. Methodology For this study, we reprogrammed hiPSCs from the aforementionned patient's cells. Then, we generated and phenotyped neurons and microglia derived from these hiPSCs. Last, using CRISPR Cas9 technology, we are correcting the GRN missense mutation in the patient-derived hiPSCs and introducing the mutation in control hiPSCs to firmly demonstrate its pathogenicity. Results Characterization of patient-derived neurons revealed several hallmarks of GRN-FTLD (cytoplasmic TDP-43, lysosomal dysregulation, and cell death). We are now characterizing patient-derived microglia and their role in neuroinflammation and neurotoxicity. These experiments demonstrate a disease-associated phenotype in hiPSC-derived brain cells from this patient. Last, characterization of CRISPR-edited cells will allow us to definitely uncover whether this missense mutation is the cause of the patient's pathology. Conclusion Our model provides for the first time biological insights into the pathogenic role of missense GRN mutations and offers a model to test potential treatments on patient-derived neurons and microglia.

Chibaatar, Enkmurun

Evaluating apelin as a potential biomarker in Major Depressive Disorder: Correlation with clinical symptomatology.

1, Rintaro Fujii 2, Atsuko Ikenouchi 1, Naomichi Okamoto 1, Tomoya Natsuyama 1, Gaku Hayasaki 1, Takahiro Shinkai 1 and Reiji Yoshimura 1*

1) Department of Psychiatry, University of Occupational and Environmental Health, Kitakyushu, Japan
2) Wakamatsu Hospital, University of Occupational and Environmental Health, Kitakyushu, Japan

To date, only a limited number of studies have investigated the potential effects of apelin on mood regulation and emotional behavior. Therefore, this study investigates apelin's role in major depressive disorder (MDD) by comparing serum and plasma apelin concentrations between 30 patients with MDD and 30 healthy controls (HCs) and correlated serum and plasma apelin levels and the severity of depressive symptoms using Montgomery–Åsberg Depression Rating Scale (MADRS). Blood samples were collected following 12 hours of fasting, and apelin levels were measured using an ELISA kit. Serum apelin concentrations showed no significant difference be-tween the MDD and HC groups, while plasma apelin levels were significantly lower in the MDD group ($p=0.002$). A positive moderate correlation was observed between total MADRS scores and apelin levels in plasma ($r = 0.439$), with statistical significance ($p < 0.05$). Additionally, MADRS subscales 5 (reduced appetite) and 6 (concentration difficulties) were positively correlated with both serum and plasma apelin levels ($p < 0.05$). These preliminary findings, although not definitive, suggest that apelin profiles may help to identify distinct subgroups within MDD patients, warranting further investigation into different apelin isoforms and their associations in different populations of MDD patients.

Chirich Barreira, Lara Mariel

Modulation of hippocampal fear memory circuits by orexin.

Chirich Barreira Lara Mariel (1), Hannah Gapp(1), Gina Marie Krause(1), Harini Srinivasan(2), Julia Henschke(3), Janelle Pakan(3,4,5), Oliver Stork(2,4,6), Anne Albrecht(1,4,6)

(1) Institute for Anatomy, Otto-von-Guericke-University Magdeburg, Germany; (2) Institute of Biology, Otto-von-Guericke-University Magdeburg, Germany; (3) Neural Circuits & Network Dynamics Group, Leibniz Institute for Neurobiology, Magdeburg, Germany; (4) Center for behavioral Brain Sciences (CBBS), Magdeburg, Germany; (5) Medical Faculty, Otto-von-Guericke-University Magdeburg, Germany; (6) German Center for Mental Health (DZPG), partner site Halle-Jena-Magdeburg

Circadian disturbances may lead to memory deficits and behavioral changes that are associated with a disrupted prefrontal cortex (PFC) to hippocampus (HIP) information flow in humans and in rodent models. Using a six-hour phase delay of the normal light-dark cycle to model an acute 'jet-lag' in mice resulted in a reduced contextual fear memory and a decrease in the RAM reactivation rate during retrieval. Neuronal activation, indicated by cFos immunohistochemistry, was increased in the hippocampal dentate gyrus (DG) and in the supramammillary nucleus (SUM), an important relay station for prefrontal-to-hippocampal information flow. The overactivation of SuM and DG by acute phase delay was the mimicked by a chemogenetic activation of the SuM or the DG before contextual fear memory retrieval using DREADD. Orexinergic neurons in the lateral hypothalamus were activated as well. Orexin is a wake-promoting neuropeptide targeting numerous brain regions relevant for memory and cognition. To investigate the potential modulation of the PFC-SUM-DG pathway by orexin, mRNA levels for orexin receptors were measured in laser microdissected neurons of the SUM, tagged by anterograde and retrograde viral tracers. SUM-to-DG projection neurons expressed low levels of the orexin receptor type 2 but not type 1 (OXR1). OXR1-positive PFC-to-DG relay cells in the SUM were then confirmed by a double tracing approach paired with immunohistochemistry. In the DG hilus, OXR1 was located in mossy cells, as demonstrated by RNAScope. Stimulating orexin receptors by intranasal application of orexin evoked a bimodal effect on contextual fear memory retrieval. Mice with different freezing levels showed differential in cFos activation signatures in the SUM, in DG mossy cells and in orexinergic neurons in the LH. Thus, orexinergic projections are well suited to modulate fear memory acting via the PFC-SUM-DG network, presumably on the internal state.

Cicciarelli, Felice

Unraveling the role of emotional memory in anxiety-related behaviors in rats.

Cicciarelli Felice [1], Giglio Camilla[1], Renna Annamaria[1], Milano Luisella[1], Sacchetti Benedetto[1]

[1]Department of Neuroscience, University of Turin, C.so Raffaello, 30, 10125, Turin, Italy

In the event of threatening stimuli, animals must pursue appropriate behaviors to overcome the threat. Normal fear and anxiety are emotional responses to these dangers. The first one induces an immediate defense behavior, the second one a lasting state of alert also in absence of threats. Brain areas involved in fear and anxiety neuronal circuits have been, at least in part, already established. Situations of acute or sustained stress can induce modifications in such brain areas, i.e prefrontal and cingulate cortex, through neuroplasticity mechanisms. This can lead to anxiety- and stress-related disorders often associated with generalized fear, for example post-traumatic stress disorders (PTSD). Anxiety-like behavior in rodents can be assessed through ethologically relevant assays designed to measure approach versus avoidance behavior and defensive responses. The mechanisms by which anxiety-related behaviors are maintained after a traumatic experience are still not fully understood.

Colombo, Giulia

Deficit of Parvalbumin-positive Interneurons and Overfunction of Somatostatinpositive Interneurons Are Involved in the Hippocampus-Dependent Cognitive Impairment of the Ts65Dn mouse model of Down Syndrome.

Colombo G. , A. Potenzieri, I. Colombi, A. Khan, A. Contestabile, L. Cancedda

[1]Department of Neuroscience, University of Turin, C.so Raffaello, 30, 10125, Turin, Italy

Dysfunction of GABAergic interneurons during sensitive time windows plays a crucial role in the etiopathogenesis of neurodevelopmental disorders. GABAergic transmission through Cl permeable GABA receptors (GABA R) is depolarizing in pyramidal neurons of the CA1 region of the hippocampus of the Ts65Dn mouse model of Down syndrome. This depends on the upregulation of the Cl-importer NKCC1 and leads to an impairment of synaptic plasticity and memory in Ts65Dn adult mice. Accordingly, inhibiting NKCC1 rescues the Ts65Dn phenotype. However, the contribution of specific interneuron subpopulations to the Ts65Dn mice deficits is largely unknown.

We characterized parvalbumin (PV) and somatostatin (SOM)-positive interneurons in the hippocampus of 3-months-old Ts65Dn mice versus control littermates by immunohistochemistry and electrophysiological recordings on brain slices. Ts65Dn mice showed fewer PV interneurons and lower expression of their perineuronal nets in the stratum pyramidale and dentate gyrus of hippocampus. Ts65Dn PV neurons showed higher membrane time constant, wider action potentials, lower action potential frequency, and their excitatory/inhibitory balance was shifted towards inhibition. Differently, Ts65Dn SOM interneurons were reduced in the CA1 region and showed lower membrane time constant, higher action potential threshold and higher action potential frequency. LTP experiments on hippocampal slices from Ts65Dn mice expressing excitatory DREADDs in PV interneurons showed that increasing their activity rescued synaptic plasticity, with no effect on controls. Conversely, inhibitory DREADDs in SOM interneurons showed that diminishing their activity rescued synaptic plasticity.

Our results suggest that PV neurons have a defective neurogenesis and maturation, whereas SOM neurons are hyperexcitable. This concurs to the defective hippocampal information-processing of Ts65Dn mice and interneuron manipulation holds promise as a future therapeutic strategy.

Comparini, Alessio

Late and Early Fusion Graph Neural Network Architectures for Integrative Modeling of Multimodal Brain Connectivity Graphs

Alessio Comparini[1], Lea Schmidt[2], Vanessa Siffredi[2], Damien Marie[3], Clara James[4], Jonas Richiardi[2]

[1]CHUV/UNUIL, [2]CHUV, [3]HES-SO, [4]CIBM

The integration of structural and functional brain connectivity provides a holistic view of the brain's organization, but its application in Graph Neural Network (GNN) models for predicting "brain age" is understudied, and a systematic benchmark of optimal data fusion strategies is currently lacking. We systematically benchmark the performances of early and late fusion multimodal architectures against single-modality models for brain age preddiction using structural and functional connectcomes, using five different GNN backbones on 747 healty partecipants (median age, 16.3 years; IQR 13.5-18.5 years) obtained from the Philadelphia Neurodevelopmental Cohort. The late fusion architecture improved performance over the structural-only baseline in three of five models, with the GCN model achieving the highest overall score in cross-validation (R^2=0.639 +- 0.05). The early fusion architecture showed inconsistent results and did not offer a reliable improvement over the single-modality baseline. Finally is observed that optimal model architecture depends on the data type: structural brain graphs favors deep, narrow models to capture their hierarchy, whereas functional brain graphs requires wider, shallower models.

Coquoz, Laure

CORTICAL RESPONSES TO EPIDURAL SPINAL CORD STIMULATION IN A COMPLETE SPINAL CORD INJURY PATIENT

Laure Coquoz[1], Simon Borgognon[2], Valeria Spagnolo[1], Sergio Hernandez Charpak[2], Guillaume Charvet[3], Jocelyne Bloch[4], Grégoire Courtine[2], Tomislav Milekovic[2], Henri Lorach[1]

[1]Université de Lausanne, [2]EPFL, [3]Univ. Grenoble Alpes, CEA, LETI, Clinatec, [4]Centre hospitalier universitaire Vaudois (CHUV)

This study investigates cortical responses to epidural electrical stimulation (EES) in a human with complete spinal cord injury (SCI). While EES elicits rapid cortical activity in healthy non-human primates, responses in the SCI patient were exclusively long-latency, suggesting the absence of fast, direct pathways. Cortical response latency increased with caudal electrode positioning, and decoding accuracy of stimulation sites improved with longer ECoG integration windows. These findings indicate that although fast spinal-cortical pathways are disrupted in complete SCI, residual long-latency cortical processing persists, which could inform future neuromodulation strategies.

Cosoli, Rita

Stress- Inducing Immersive 360° Video: An Effective Tool to Elicit Acute Physiological Stress in Professional Training

Rita Cosoli[1,2], Ulrike Rimmele[2], Alice Tela[1], Alberto Cattaneo[1]

[1] Swiss Federal University for Vocational Education and Training

[2] University of Geneva

Immersive 360° videos offer an ecologically valid method to expose participants to controlled, protected and repeatable professional simulations. Unlike VR, which is fully computer-generated, 360° videos are created from real-world recordings, ensuring the highest representational fidelity. Their realism has been demonstrated to elicit psychophysiological activation comparable to real-world professional situations (Schöne et al., 2023).

Building on research in immersive learning and stress induction, this study aims to validate a 360° video as a tool to induce stress, answering the following research question: *Can an immersive 360° video featuring an angry client induce higher acute stress responses in apprentices compared to a 360° video featuring neutral client consultation?*

This study employs a randomized, blinding, between-subjects design with 90 office clerk apprentices (mean age: 16.6 ± 1.39 years), who watched a first-person perspective video (angry vs. neutral condition) that dynamically adapts to verbal responses in real-time.

Stress responses were assessed through heart rate variability and salivary cortisol at three time points. Self-reported measures included the Positive and Negative Affect Schedule, the Subjective Units of Distress Scale, the Visual Analogue Scale, the eXtended Reality Presence Scale, and the ITC-Sense of Presence Inventory.

By integrating education, psychology, and physiology, this study bridges research and practice, providing a validated tool for emotional training in professional education, where its integration could align with psychological techniques such as VR exposure therapy.

Defferrard, Léa

Eye Tracking as a Biomarker of Cognitive Functioning

Léa Defferrard1,2, David Zeugin1,2, Loredana Catinari3, Caterina Bertini3, Patricia Poma4, Daniel Perez Marcos5, Julia Fellrath4, Andrea Serino2, Sonia Crottaz-Herbette1

1 Service Universitaire de Neuroréhabilitation, Centre Hospitalier Universitaire Vaudois (CHUV), Université de Lausanne, Suisse
2 MySpace Lab, Service Universitaire de Neuroréhabilitation, Centre Hospitalier Universitaire Vaudois (CHUV), Université de
Lausanne, Suisse
3 Centre for Studies and Research in Cognitive Neuroscience, University of Bologna, Cesena, Italy. Department of Psychology,
University of Bologna, Bologna, Italy
4 NeuroRehab Center, Hôpital de Lavigny, Suisse
5 MindMaze SA, Lausanne, Suisse

Introduction. Attentional capacity, notably spatial attention/neglect, serves as a cornerstone for cognitive functioning and meaningful interaction with the environment.
Traditional assessment methods rely on paper-and-pencil or computerized tools, which may lack ecological validity. Virtual Reality (VR) offers an alternative that could improve diagnosis through more ecologically valid measures. The integration of embedded eyetracking sensors further augments diagnostic capabilities by providing rapid, precise metrics. The focus of this study is on the use of a Free Viewing Exploration task (VRFVE) done in VR as a tool for understanding automatic orienting of attention in a manner akin to everyday behavior.
Methods. Data were collected from brain-injured patients with and without spatial attention deficits, as well as healthy subjects, enrolled in a newly developed VR-based cognitive rehabilitation program. Patients underwent standardized tests in the Test of Attentional Performance (TAP) battery as well as the novel VR-FVE task, both at baseline and post-completion of the rehabilitation protocol. The VR-FVE task integrated eye-tracking sensors to record various eye movement parameters. The eyetracking (ET) measures were compared against the TAP results and clinical diagnoses to ascertain their diagnostic accuracy.
Results. Significant correlations were found between several eye-tracking measures and clinical diagnoses. Clear differences emerged between healthy participants and patients with neglect, but not between healthy participants and patients with acquired brain injury (ABI) without neglect. This indicates that the eye-tracking metrics—such as gaze laterality, fixation duration on the left, and number of fixations on the right— are specifically sensitive to attentional deficits rather than to brain injury per se. Furthermore, deep learning algorithms were used to classify participants as healthy or having spatial attention deficits based on raw horizontal gaze patterns. The predictive models demonstrated a high degree of accuracy, affirming the utility of eye-tracking metrics as reliable indicators of attentional deficits.

Cuenca-Ortega, Javier

Cuenca-Ortega Javier (1,2), María Martínez (3,4), Leire Virto (3,5), Elena Figuero (3,4), Juan Carlos Leza (1,2), García-Bueno, B (1,2), Javier R Caso (1,2), David Martín-Hernández (1,2)

(1) Department of Pharmacology & Toxicology, Faculty of Medicine, Complutense University of Madrid, 28040 Madrid, Spain.
(2) Centro de Investigación Biomédica en Red de Salud Mental, Instituto de Salud Carlos III (CIBERSAM, ISCIII), 28029 Madrid, Spain.
(3) ETEP (Etiology and Therapy of Periodontal and Peri-Implant Diseases) Research Group, Complutense University of Madrid, Madrid, Spain
(4) Department of Dental Clinical Specialties, School of Dentistry, Faculty of Dentistry, Complutense University of Madrid, Pza. Ramón y Cajal s/n, Madrid 28040, Spain
(5) Department of Anatomy and Embryology, Faculty of Optics, Complutense University of Madrid, Madrid, Spain

Spherical Nucleic Acids (SNAs) represent a novel nanotechnology-based approach for delivering gene therapies to the brain, offering a promising solution for treating neurodevelopmental disorders. Unlike traditional linear oligonucleotide therapies, SNAs exhibit high cellular uptake, enhanced stability, and the unique ability to cross the blood-brain barrier (BBB) non-invasively. This study explores the potential of SNAs in targeting neurological conditions such as Angelman Syndrome (AS) and Huntington's Disease (HD) by delivering antisense oligonucleotides (ASOs) and microRNAs to selectively modulate disease-related genes. A gold nanoparticle core is utilized for its biocompatibility, providing stability and protection against degradation, while nucleic acids are engineered to suppress mutant gene expression. Current challenges in gene therapy, such as off-target effects and toxicity, are addressed by SNAs' precision targeting mechanisms. While previous ASO-based treatments have struggled with BBB penetration and adverse side effects, SNAs demonstrate superior efficacy, offering a potential breakthrough in the treatment of genetic brain disorders. Future research will focus on optimizing drug delivery, safety, and long-term therapeutic effects, with the goal of translating SNA-based therapies into clinical applications for neurodevelopmental and neurodegenerative diseases.

De Riedmatten, Ines

Interleaved TMS-fMRI using BOLD and diffusion functional contrasts to investigate inhibitory neural activity

Inès de Riedmatten[1], Arthur Spencer[2], Roberto Martuzzi[3], Vincent Rochas[3], Filip Szczepankiewicz[4], Ileana Jelescu[2]

[1]University of Lausanne (UNIL), [2]Centre hospitalier universitaire vaudois (CHUV), [3]Fondation Campus Biotech Genève, [4]Lund University

Brain activity has been extensively studied using blood oxygen level-dependent (BOLD) contrast, which captures both positive (excitatory activity) and negative (potentially reflecting inhibitory processes[1]) signals. More recently, the apparent diffusion coefficient (ADC)-fMRI (neuromorphological coupling) has shown promise for improved spatial and temporal specificity compared to BOLD[2-4]. While excitatory activity has been reported as negative ADC response, the ADC counterpart to negative BOLD remains to be investigated. Transcranial magnetic stimulation (TMS)-fMRI can be used to modulate brain activity during fMRI acquisition. Previous studies have shown that subthreshold 5 Hz TMS to primary motor cortex (M1) can induce contralateral M1 negative BOLD responses[5,6]. However, this approach remains highly experimental, with few prior studies[7]. Our study aims to replicate these BOLD findings and explore the corresponding diffusion fMRI (dfMRI) responses. We acquired isotropic dw-SE-EPI (iso-dfMRI, spherical b-tensor encoding[8]) and multi-echo GE-EPI (T2*-BOLD) data. During dfMRI scans, alternating volumes at b=200 and 1000 s mm-2 were acquired, from which ADC timeseries were calculated. We found expected positive and negative responses to TMS pulses not only in BOLD, but also for the first time in b200 and b1000 timecourses. The observed patterns are overall consistent with previous studies. However, a larger sample size is required for the ADC-fMRI analysis due to lower CNR.

de Wouters, Louise

Source-reconstructed EEG graph spectral decomposition and application to epilepsy surgery prognosis

de Wouters L 1, Roehri N 1, Lagarde S 1, Mullier E 1,2, Seeck M 1, Van De Ville D 3,4, Hagmann P 2, Rigoni I 1, Vulliémoz S 1,4

1 EEG and Epilepsy Unit, University Hospitals and Faculty of Medicine of Geneva, University of Geneva
2 Connectomics Lab, Department of Radiology, Lausanne University Hospital and University of Lausanne (CHUV-UNIL), Lausanne, Switzerland
3 Neuro-X Institute, Ecole polytechnique fédérale de Lausanne (EPFL), Geneva, Switzerland
4 Center for Biomedical Imaging (CIBM), Switzerland

Epilepsy is characterised by altered brain network organisation. This study uses graph spectral decomposition of source-reconstructed EEG on the structural connectome (SC) to assess structure-function (SF) coupling, while addressing the method's intrinsic biases. Applied to interictal epileptic discharges (IEDs), we use it to distinguish good vs poor surgical outcomes. IEDs during EEG recordings of 30 patients were source-reconstructed. Region of interest (ROI) time-series were obtained via the first component of the singular value decomposition (SVD), with an in-house SVD sign correction. Network harmonics were exacted from the SC and used to decompose the ROI time-series through the graph Fourier Transform. The transformed signal's energy spectrum was divided into low-frequency harmonics (LF, structure-coupled) and high-frequency ones (HF, structure-decoupled). Their energy distributions along the IED were compared with a cluster-based permutation test across patients. SF coupling at the IED peak was quantified as the ratio of coupled to decoupled signal norms and compared between outcome groups with a Wilcoxon rank-sum test. The leakage impact due to source reconstruction on the harmonic decomposition was further addressed with simulations. After SVD sign ambiguity bias correction and leakage impact analysis, we replicated previous findings of increased coupling at the IED peak ($p=0.0460$) and decoupling before ($p=0.0004$) and after ($p=0.0464$) it. Moreover, patients with poor surgical outcomes showed significantly lower SF coupling at the IED peak ($p=0.0213$). In conclusion, graph spectral decomposition of source-reconstructed EEG signals has biases that must be corrected but it could help identify optimal surgery candidates through SF coupling analysis.

Dimou, Maria

Inverse methods comparison using simultaneous EEG-iEEG dataset

Maria Dimou[1], Steven Beumer[1], Andrea Pigorini[2], Ezequiel Mikulan[3], Laurent Spinelli[1], Shahan Momjian[4], Margitta Seeck[1], Serge Vulliemoz[1], Nicolas Roehri[1]

[1]EEG and Epilepsy Unit, University Hospitals and Faculty of Medicine, University of Geneva, Geneva, Switzerland, [2]Department of Biomedical, Surgical and Dental Sciences. University of Milan, Milan, Italy, [3]Department of Health Sciences. University of Milan, Milan, Italy, [4]Department of Neurosurgery, University Hospitals and Faculty of Medicine, University of Geneva, Geneva, Switzerland

Background. EEG is essential for assessing brain activity and identifying seizure-prone regions in patients with epilepsy. Various inverse methods are applied to EEG to estimate the sources of neural activity. We aim to validate these EEG source-reconstructed signals by comparing them with the gold standard of simultaneous intracranial EEG (iEEG), using Exact and Standardized Low Resolution Brain Electromagnetic Tomography (eLORETA, sLORETA), and weighted minimum-norm estimate (wMNE). Methods. We obtained simultaneous high-density (hd)EEG-iEEG recordings of spontaneous activity from 33 patients of two centers (Geneva and Milan). After bandpass-filtering them (1-45 Hz), we used eLORETA to reconstruct source time-series, and projected them onto iEEG electrodes' positions, creating virtual iEEG electrodes. Reconstruction quality was assessed via the iEEG-virtual iEEG correlation matrix, from which we computed the center-of-gravity localization error (COFLE) and spatial deviation (SD), previously shown to relate negatively with correlation. The analysis was repeated with sLORETA and wMNE. Finally, we used three GLME models to compare the inverse methods, based on correlation, COFLE and SD, to determine the best method. Results. For reference, using eLORETA, we found a median iEEG-virtual iEEG correlation of 0.07 (range: 0 to 0.72). When comparing methods, sLORETA resulted in significantly higher correlation compared to eLORETA and wMNE. Furthermore, eLORETA had significantly lower COFLE, and SD than sLORETA and wMNE (all $p<.0001$). Conclusions. Our analysis revealed low iEEG-virtual iEEG correlations, likely due to localization errors and spurious activity spread. eLORETA appears to be the best option based on these two factors.

Elshove, Stacey

An Open-Source Pipeline for Unbiased Quantification of Gait in Preclinical Models of Neurological Disorders

Stacey Elshove1,2, Farha Bouteldja1, Ed Hasanovic1, Grégoire Bena1, Quentin Amossé1, Claudia Kathe1
1 Department of Fundamental Neurosciences, University of Lausanne (UNIL), Lausanne, Switzerland
2 Presenting author

Department of Fundamental Neurosciences, University of Lausanne,
Rue du Bugnon 9, 1005 Lausanne, Switzerland

Quantifying locomotor function remains a central challenge in neuroscience, particularly in preclinical models of neurological disorders. While recent advancements in marker-less, machine learning-based tracking software, such as DeepLabCut or Lightening pose, have enabled low-cost tracking of body parts across time, the analysis and interpretation of this data remain highly variable between laboratories. To address this, we are developing an open-source analysis pipeline for unbiased quantification of gait. This robust and adaptable pipeline first applies “locomotion sequencing” based on hindlimb trajectories to identify stereotyped movement patterns as clusters. It then extracts a broad set of interpretable and informative gait parameters (e.g. step height, joint angles, velocity) designed to capture a wide range of locomotor deficits, enabling clear and quantitative assessment of movement deficits across various neurological disease models. We demonstrate that this pipeline is sensitive to different phases of recovery after spinal cord injury and can also detect subtle gait abnormalities in rodent models of cerebral palsy. By providing a standardized and accessible Python-based toolbox, our pipeline can be broadly adopted across research laboratories and improve the reproducibility and depth of locomotor analyses in preclinical studies of neurological motor deficits.

Faggella, Melissa

Inter-individual variability in event-related potentials is not noise

Melissa Faggella[1], Maya Roinishvili[2], Eka Chkonia[3], Michael Herzog[1]

[1]Laboratory of Psychophysics, Brain Mind Institute, EPFL, Switzerland, [2]Laboratory of Vision Physiology, Beritashvili Centre of Experimental Biomedicine, Georgia, [3]Department of Psychiatry, Tbilisi State Medical University, Georgia

While EEG is highly effective for detecting high signal-to-noise brain events (e.g., epileptic discharges) and widespread changes in brain state (e.g., sleep phases, coma), its impact in other fields of research, such as psychiatry or cognitive neuroscience, remains otherwise mitigated. We argue that one key reason is the substantial inter-individual variability inherent to EEG. In particular, population heterogeneity complicates the standardization of pre-processing and analysis procedures and reduces the effect size and generalizability (predictive power) of group-level results. In the present work, we use within-subject experimental designs to demonstrate that individual differences are not noise, but a major stable source of EEG variance. First, in a longitudinal visual evoked potential (VEP) study, we found that individual-level EEG as measured using diverse methods (single electrode potentials, global field power, microstates…) remained remarkably stable over periods of 5 and 10 years (N5y = 90, N10y = 35). This long-term stability was observed across all recorded electrodes and even persisted in individuals with a chronic psychiatric condition (schizophrenia). Such consistency suggests that incidental state-related (e.g., fatigue, stress) and technical (e.g., electrode placement, impedance, pre-processing) factors exert minimal influence on EEG reliability. Moreover, while analyzing data from batteries of visual tasks, we found that individuals had highly similar VEPs across experimental conditions (e.g. same range of amplitude, landmarks…) but also to some extent across completely distinct tasks, such as for example between coherent motion and backward masking. Our results suggest that a dominant portion of the EEG signal variance is explained by individual variability rather than by the effect of a disease or experimental manipulation of interest. In conclusion, individual differences in task-related EEG appear to capture highly stable and generalizable information about the subjects, possibly reflecting variations in anatomy such as in cortical folding pattern.

Ferreira Morais, João Pedro

The role of sleep in the learning of a Go/No-Go sensorimotor task

João Morais[1], Lila Banterle[1], Georgios Foustoukos[1], Paola Milanese[1], Laura Fernandez[1], Anita Lüthi[1]

[1]University of Lausanne

Introduction: Memory consolidation during sleep is traditionally assessed in rodents through single-session overnight learning experience, such as fear conditioning or novel object recognition. Here, we instead aim to address the adaptive sleep-dependent processes by which memory and learning evolve across days. Therefore, we ask how sleep architecture and spectral composition evolve during progressive learning and whether we can identify learning-specific alterations in cortical activity. Material and Methods: We used a Go/No-Go sensorimotor learning task in which head-fixed mice had to discriminate between two auditory stimuli to collect rewards. Behavioral sessions happened daily at Zeitgeber times ZT2-6. Mice became experts in the forward learning task over 7-12 days and were then exposed to a 10-day reversal-learning in which the tone contingencies were reversed. Control animals underwent the same protocol but had freely available reward during behavioral sessions. Using polysomnography, we recorded the spontaneous sleep-wake cycle at the end of the task (ZT6-12) and in the following dark phase (ZT12-24). We recorded EEG, EMG signals, as well as local field potentials (LFP) from stereotaxically defined sites in medial prefrontal cortex (mPFC), orbitofrontal cortex (OFC), tongue-jaw primary motor (tjM1), primary sensory (S1) and auditory (A1) cortices. All recording sites were verified histologically. Results: As the animals progressed through the experimental protocol, we observed changes in their sleep architecture with an overall increase in the time spent in both NREM and REM sleep, suggesting that sleep need adapts in response to the daily sensorimotor learning experience. Furthermore, LFP recordings suggest region-specific alterations in NREM sleep dynamics and interareal cross-correlations that follow the learning phases, suggesting that post-task sleep periods differentially recruit cortical areas in response to the learning experience. Conclusion: The identification of cortical areal activity modulated during sleep in different stages of progressive learning opens an opportunity to pursue regional-specific roles of NREM sleep functions in memory consolidation.

Fonteneau, Mathieu

Pharmacological modulation of D2 dopamine receptor-expressing striatal projection neurons activity to alleviate autistic-like symptoms in Rett syndrome.

Florian Bolot, Agathe Brugoux, Julie Le Merrer, Jérôme A.J. Becker, Mathieu Fonteneau

Université de Tours, INSERM, Imaging Brain & Neuropsychiatry iBraiN U1253, 37032, Tours, France

Rett syndrome (RTT) is a rare neurodevelopmental disorder that primarily affects girls, leading to severe motor deficits, intellectual disability, and autistic-like symptoms such as impaired social interaction, communication difficulties, and stereotyped behaviors. In most cases (95%), RTT is caused by a de novo mutation in the MECP2 gene. To better understand the disease, genetically modified mouse models have been developed, including female Mecp2+/- mice, which reproduce key aspects of the disorder and help in researching potential therapeutic approaches.

Trofinetide (Daybue®) has demonstrated efficacy in alleviating symptoms in a subpopulation of subjects with RTT. Beyond this, no pharmacological treatments are available to specifically improve autistic symptoms in RTT or other autism spectrum disorders (ASDs). Previously, we highlighted the crucial role of balancing activity between D1- and D2-expressing striatal projection neurons (D1- and D2-SPNs) in the nucleus accumbens (NAc) in regulating social behavior, showing how excessive D2-SPN activity compromises social interactions.

In this study, we investigated whether modulating D2-SPN activity could help alleviate ASD-like symptoms and motor deficits in RTT. Using a pharmacological approach, we reduced D2-SPN activity either with VU0155041, a positive allosteric modulator (PAM) of the mGlu4 metabotropic glutamate receptor, or with istradefylline, an adenosine A2a receptor (A2a) antagonist. Chronic administration of mGlu4 PAM normalized social interaction and reduced motor stereotypies in Mecp2+/- mice. It also restored skilled motor learning in the rotarod task and alleviated cognitive deficits. Similarly, blocking A2a activity improved autism-like symptoms in Mecp2 mutant mice, while its effects on motor and cognitive abilities remain under investigation. Finally, we used RNAscope® in situ hybridization to assess Fos expression in D1- and D2-SPNs within the NAc following social interaction in Mecp2+/- mice. This study will allow us evaluating a potential contribution of the NAc D1/D2-SPNs activity balance to the autistic-like behaviors observed in Mecp2+/- mice.

Forrer, Silas

Longitudinal Fingerprinting reveals Disrupted Sensory-Default Mode Remodelling and Divergent Network Maturation Trajectories in 22q11DS Psychosis High-Risk

Silas Forrer[1], Farnaz Delavari[1], Corrado Sandini[1], Dimitri Van De Ville[2], Stephan Eliez[1]

[1]University of Geneva, [2]EPFL

BACKGROUND Psychosis risk is increasingly linked to disrupted brain network maturation, yet the dynamics of these developmental deviations remain unclear. We used longitudinal connectome fingerprinting to investigate age-dependent changes in network stability and distinctiveness in 22q11.2 deletion syndrome (22q11DS), a high-risk model for psychosis, compared to healthy controls.

METHODS Resting-state fMRI from 56 individuals with 22q11DS and 55 controls (ages 8–30, 2–5 visits) were analyzed using a moving-window approach. Patients were stratified into those with and without psychotic symptoms (PPS+, PPS-). Connectome fingerprinting metrics (Iself, Iothers, PredAcc) quantified individual-specificity, and longitudinal intraclass correlation (ICC) assessed temporal network stability.

RESULTS Controls showed low prediction accuracy in adolescence, followed by a steady increase into adulthood. 22q11DS individuals began with high accuracy but diverged: PPS(-) showed a drop into early adulthood then increased, whereas PPS(+) declined steadily into adulthood. ICC reflected this pattern for controls and PPS(-), but not for PPS(+). Temporal ICC analysis revealed that controls underwent a transient adolescence network reorganization, primarily in default-sensorimotor/visual connectivity. PPS(-) showed delayed entry into this pattern, remained longer than controls, but eventually progressed beyond it, while PPS(+) exhibited diffuse, disorganized patterns throughout and lacked adolescent reorganization.

CONCLUSION Our findings highlight two deviant trajectories in 22q11DS: delayed, partial reorganization in PPS(-), predominantely in sensory-default mode connectivity, and early, disorganized stabilization in PPS(+). These results suggest that disrupted remodeling during adolescence between sensory-driven and internalizing structures contributes towards the increased risk of positive psychotic symptoms. Developmental fingerprinting trajectories may thus serve as sensitive early markers of neuropsychiatric vulnerability.

Frayssinhes, Camille

Optimal timing for EES-augmented rehabilitation to enhance the recovery of mobility in people with spinal cord injury

Camille Frayssinhes[1,2,*], Gaia Carparelli[1,2], Léonie Asboth[1,2], Jocelyne Bloch[1,2,3,4,*], and Grégoire Courtine[1,2,3,4,*].

[1] Defitech Center for Interventional Neurotherapies (.NeuroRestore), CHUV/UNIL/EPFL, Lausanne, Switzerland
[2] NeuroX Institute, School of Life Sciences, Swiss Federal Institute of Technology (EPFL), Lausanne, Switzerland
[3] Department of Neurosurgery, Lausanne University Hospital (CHUV) and University of Lausanne (UNIL), Lausanne, Switzerland
[4] Department of Clinical Neuroscience, Lausanne University Hospital (CHUV) and University of Lausanne (UNIL), Lausanne, Switzerland

Spinal cord injury (SCI) disrupts connections from the brain to spinal motor neurons below the lesion, leading to permanent paralysis. Globally, SCI affects between 250,000 and 500,000 individuals annually, causing severe emotional, economic and social impact on affected people, their families, and society. For affected individuals, restoring mobility remains a top priority.
Over the past decade, considerable progress has been made in restoring functional movement following chronic SCI. We developed a neuroprosthesis that uses spatiotemporal epidural electrical stimulation (EES) of the lumbosacral spinal cord to reactivate spinal motor neurons by recruiting dorsal root axons. This neuroprosthesis, combined with rehabilitation, enabled standing, walking, biking, and swimming in individuals with chronic SCI. Remarkably, long-term use restored voluntary leg movement even when the device is turned off. These results indicate that EES can leverage neural plasticity to reorganize motor control circuits and restore mobility functions.
SCI patients usually undergo rehabilitation 12 to 18 months after the injury, when it is in chronic state. However, while motor function in chronic SCI patients typically plateaus, acute and subacute patients are still undergoing a phase of natural recovery, with significant neurological reorganization occurring within the first 3 months[7]. Early rehabilitation interventions are therefore expected to be more effective during this critical phase. Additionally, early therapy may mitigate long-term complications associated with delayed treatment, such as maladaptive compensations and muscle atrophy. Preliminary results in rodents indicate that early intervention leads to faster and more natural walking compared to delayed intervention. These findings suggest that similar outcomes could be achievable in humans. The EIGER clinical trial aims to define the optimal timing for EES-augmented rehabilitation to enhance the recovery of mobility in people with SCI.

Galli, Riccardo Mattia

Biasing dominance of the visual system via fMRI-based neurofeedback

Riccardo Galli[1], Patrik Vuilleumier[1]

[1]University of Geneva

Attention is a crucial cognitive function allowing us to select pertinent sensory information while ignoring irrelevant stimuli in the environment. This capacity emerges from top-down mechanisms involving bilateral fronto-parietal networks that interact with early visual areas. Following frontal or parietal brain lesions and therefore disruption in this system, peculiar conditions may emerge, such as unilateral spatial neglect (USN): a syndrome denoted by impaired awareness of stimuli presented in the visual field contralateral to the lesion site, in absence of pure sensorial or motor losses. One functional explanation of this condition might rely on abnormal biases in top-down regulation of sensory pathways from higher-level attentional networks towards early visual areas. Neuromodulation and up-regulation of such preserved sensory areas have proved to account for partial restoration of this balance and improvement in clinical symptoms. In particular, functional MRI (fMRI) based real-time neurofeedback (NFB) represents a promising and effective neuromodulation tool. However, specific mechanisms underlying successful modulation of visual areas via fMRI NFB are still unclear. For this reason, we couple the spatial precision of fMRI with the temporal resolution of EEG in EEG-MRI multimodal imaging fashion during NFB training to unravel structural and functional correlates of such learning process in the brain. Results from this study will further help develop an informed EEG-NFB based protocol to apply in clinical context for USN rehabilitation.

Gallo, Maria Teresa

Perinatal fluoxetine and brain development: sex-dependent behavioral outcomes and disrupted sensitive periods

Gallo Maria Teresa (1), Anaïs Virenque (2), Alessia Golinelli (1), Fabio Fumagalli (1), Eero Castrén (2), Paola Brivio (1) Francesca Calabrese (1).

1 Institute for Cognitive Neuroscience, HSE University
2 AI and Computer Science Institute, HSE University

Sensitive periods (SP) are windows of heightened neuroplasticity that occur during early development and extend into adolescence. SP opening is driven by the maturation of GABAergic parvalbumin-positive (PV+) interneurons and the activation of "trigger" genes, while closure is regulated by the aggregation of perineuronal nets (PNNs) around PV+ interneurons and the expression of "brake" genes. Interestingly, alterations in SP markers have been identified in neuropsychiatric disorders, suggesting their involvement in the emergence of these conditions.

In previous studies, we demonstrated that perinatal exposure to fluoxetine (FLX) in rats leads to distinct pathological-like phenotypes depending on sex and timing of exposure. Males were more sensible to prenatal-FLX (gestational day 0 - postnatal-day (PND) 0), developing an anhedonic-like phenotype, whereas females more affected by postnatal-FLX (PND0 to 21) exhibiting cognitive deficits. Of note, these behaviors emerged only at adulthood and not during adolescence.

Here, based on the delayed onset of symptoms, we hypothesized that FLX exposure alters brain developmental trajectories, altering SP dynamics, and leading to long-term behavioral consequences

In line with the pathological-like adult phenotypes observed, the molecular results revealed clear sex differences, including significant changes in the density of PV+ cells, the proportion of PV+ cells surrounded by PNNs, as well as in the expression of trigger and brake genes across the lifespan, in the prefrontal cortex and dorsal hippocampus. Notably, we observed the most pronounced effect in the dentate gyrus (DG) of the dorsal hippocampus with prenatal-FLX males showing an early SP opening and postnatal-FLX females displaying a delayed SP opening.

We suggest that the molecular targets herein described may serve as potential biomarkers for individuals at increased vulnerability. Accordingly, we can propose that targeted interventions aimed at correcting these abnormalities could help prevent the emergence of pathological symptoms.

Gay, Ayla

Upper limb perceptual and motor errors

Ayla Gay[1], Gaia Risso[1], Michel Akselrod[1], Eugenio Scaliti[2], Francesco Crottini[3], Jacopo Evi[4], Cristina Becchio[5], Andrea Serino[6], Michela Bassolino[1]

[1]HES-SO Valais-Wallis, [2]Italian Institute of Technology, [3]University of Pavia, [4]Università Vita-Salute San Raffaele, [5]Universitätsklinikum Hamburg-Eppendorf, [6]CHUV, Unil

Even in healthy individuals, representations of our own body are not entirely accurate. A well-documented phenomenon is the presence of metric distortions in hand perception: people typically perceiving their hands as shorter and wider than they actually are (Longo & Haggard, 2010; Peviani & Bottini, 2018). However, while the biased estimation of size and shape has been well studied, less is known about how people perceive the location of their body parts in space, especially without visual guidance. Furthermore, the relationship between such perceptual distortions and motor execution remains poorly understood. In this new experiment, we investigated upper-limb representation in healthy right-handed adults using a body landmarks localization task. Participants verbally indicated when a moving stick aligned with specific landmarks on their hidden right arm. The task was performed across four spatial positions forming a square around the body midline allowing us to assess how space affects both metric distortions (segment length perception) and localization biases (misplacement of perceived landmark positions). As expected, participants showed a consistent metric bias, underestimating arm length by approximately 20% across all spatial positions and overtime. Additionally, their estimated landmark positions deviated by an average of ~10 cm from the real position, typically biased toward the midline and closer to the body, with increasing mislocalization across trials. Participants then performed a pointing task from the same four spatial positions, reaching straight ahead with the right hand from near to far (right-close to right-far, or left-close to left-far), without visual feedback or online correction. We observed systematic overshooting of targets (~5 cm) in both trajectories assessed, with direction-specific errors: greater along the proximodistal axis for rightward trajectories and along the mediolateral axis for leftward ones. Importantly, perceived arm length (right trajectory: $R^2=0.70$, $\beta=-0.46$, $t(19)=-2.85$, $p=0.01$; left trajectory: $R^2=0.72$, $\beta=-0.42$, $t(19)=-3.07$, $p=0.006$), and not real arm length (right trajectory: $R^2=0.51$, $\beta=-0.34$, $t(19)=-0.86$, $p=0.40$; left trajectory: $R^2=0.48$, $\beta=0.35$, $t(19)=-0.27$, $p=0.79$), significantly predict the pointing trajectory length, suggesting that participants used their internal distorted body dimensions rather than veridical ones when executing the movement. These findings broaden our understanding of upper-limb representation by showing how perceptual distortions shape motor behavior.

Goossens, Amelien

Behavioural and Molecular Convergence of ASD Mutations Using Drosophila melanogaster

Amelien Goossens[1], Kyriaki Foka[1], Vittoria Mariano[2], Alexandros Kanellopoulos[3], Carlo Fusco[1], Mathieu Quinodoz[4], Tilmann Achsel[1], Carlos Rivolta[4], Claudia Bagni[1]

[1]University of Lausanne, [2]Institute of Science and Technology Austria, [3]Dsm-firmenich, [4]Institute of Molecular and Clinical Ophthalmology Basel

Autism spectrum disorder (ASD) is a neurodevelopmental condition with increasing prevalence, estimated to affect 1 in 31 children aged 4-8 in the United States (CDC, 2022). It is clinically heterogeneous, with core features including social impairments and repetitive behaviours, often accompanied by deficits in cognition and language. Comorbid conditions, such as ADHD, epilepsy and sleep disorders are also frequently observed. More than 1,200 genes have been linked to ASD, reflecting extensive genetic heterogeneity that likely contributes to its broad phenotypic variability. This complexity remains a major barrier to the development of effective treatments, as curative interventions have yet to be identified. It has been proposed that this genetic heterogeneity may converge on shared molecular pathways underlying specific behavioural traits. To test this, we used Drosophila melanogaster to model 26 ASD-associated mutations. Behaviour was assessed across five paradigms reflecting ASD-like symptoms, and molecular changes were analysed by mass spectrometry. We observed that the ASD mutants under study exhibited distinct combinations and severities of behavioural deficits. In addition, preliminary proteomic data revealed convergence on specific molecular pathways. Based on these findings, we aim to link genetic variation to behavioural phenotypes and molecular mechanisms, with the goal of identifying targeted treatments to reverse the phenotypes.

Granja, Daniel

Eyes Wide Shut: The Impact of Eye Visibility on Facial Emotional Recognition

Daniel Granja[1], Nicolas Burra[1]

[1]ESCLab, FPSE, Université de Genève

Interpreting emotional facial expressions (EFE) is fundamental in social cognition. In Western cultures, the eyes are a primary source of information for decoding emotions. However, when the eyes are inaccessible, whether obscured by dark glasses or closed, the perception and interpretation of EFE changes. While occluded eyes in both cases prevent direct visual access, closed eyes signal disengagement, whereas dark glasses introduce ambiguity regarding the person's capacity to see. This raises the question: does the interpretation of EFE remain stable regardless of eye occlusion, or is there another level of appraisal? In this study, participants (N=34) viewed faces displaying anger, fear, happiness, and neutral expressions under three eye conditions: open, closed, and obscured by dark glasses. They rated the emotions on scales, and eye-tracking recorded eye fixation to assess attentional allocation to the eye region. Results showed that eye occlusion reduced emotion recognition, particularly for fear and anger, confirming that these emotions recognition rely on eye cues. Crucially, different occlusion types produced distinct effects: closed eyes led to a greater shift in emotion categorization than glasses (e.g. fearful faces being misinterpreted as expressions of pleasure). Fixation data showed reduction in time spent looking at the eye region when the eyes were occluded. These findings provide evidence that eye perception plays a critical role in emotion recognition and attentional processing. They highlight how the perceived accessibility of another's gaze influences social cognition, with implications for both models of emotion recognition and real-world interactions.

Grouvel, Gautier

Impact of chronic bilateral and unilateral vestibulopathy on head mobility during daily living tasks

Gautier Grouvel[1], Julie Corre[1], Maurizio Ranieri[1], Samuel Cavuscens[1], Anissa Boutabla[1], Jean-François Cugnot[2], Raymond van de Berg[3], Nils Guinand[1], Stéphane Armand[4], Angélica Pérez Fornos[1]

[1]Division of Otorhinolaryngology Head and Neck Surgery, Geneva University Hospitals and University of Geneva, Geneva, Switzerland, [2]Clinical Neurosciences Department, Neurorehabilitation Department, Geneva University Hospitals, Geneva, Switzerland, [3]Division of Balance Disorders, Department of Otorhinolaryngology and Head and Neck Surgery, Maastricht University Medical Center+, Masuastricht, The Netherlands, [4]Kinesiology Laboratory, Geneva University Hospitals and University of Geneva, Geneva, Switzerland

Introduction It is well established that the daily lives of patients with bilateral or unilateral vestibulopathy are significantly altered, notably due to imbalance and oscillopsia. However, their ability to perform everyday tasks in realistic environments remains largely unexplored, in particular the specific head movement strategies that patients employ to compensate for their deficit. This is particularly relevant for the establishment of efficient rehabilitation strategies and to design effective stimulation strategies for vestibular implants. Like the audiogram in audiology, this study aims to better understand the head movement strategies used by these patients in functional tasks close to daily life, and to build a «vestibulogram» based on head movement velocities and accelerations during these tasks. Methods The study included three groups of participants: a group with 19 chronic bilateral vestibulopathy (BV), a group with 20 chronic unilateral vestibulopathy (UV), and a group of 20 healthy subjects (HS). Angular velocities of the head were measured using an inertial sensor, specifically a gyroscope, and angular accelerations were obtained by deriving angular velocities. Data analysis focused on 11 daily living tasks, reflecting a wide range of reported difficulties encountered by patients. For statistical analyses, data distributions were plotted, and the mode of angular velocities and accelerations was extracted to visualize each task by participant group on a 2D graph, representing angular velocities as a function of angular accelerations. Results The results showed a general trend towards a reduction in angular head velocities in patients, particularly in the BV group (around 10 deg/s for the majority of the tasks for the BV and UV groups, between 10 deg/s and 25 deg/s for the HS group). Angular accelerations showed little variation between the pathological groups but was task dependent. Healthy subjects, on the other hand, showed higher overall head angular velocities and angular accelerations than patients. For example, for the Uneven ground task, angular velocities were 12 deg/s for the BV and UV groups, and 14 deg/s for HS group, and angular accelerations were 130 deg/s2 for the BV and UV groups, compared with 180deg/s2 for the HS group. Differences between groups were particularly pronounced in dynamic and complex tasks such as walking, walking on unstable ground, head rotations while walking, stair climbing, and half-turning. Discussion This reduction in angular head velocities in patients seems to reflect the stiffening of the head and trunk, probably adopted as a compensatory strategy to limit the absence of vestibular input. In contrast, the angular velocity and angular acceleration profiles of healthy subjects showed an ability to adapt to the demands of each task, reflecting greater freedom of movement. These results may provide a better understanding of patients' movement patterns and limitations. They could also contribute to the development and implementation of rehabilitation therapies, such as the development of vestibular implant stimulation strategies.

Hankov, Nicolas

The implantable system that restores hemodynamic stability after spinal cord injury

Nicolas Hankov[1], Aasta Gandhi[1], Sergio D. Hernandez[1], Nadine Intering[1], Marina D'Ercole[2], Jordan Squair[1], Robin Demesmaeker[1], Léonie Asboth[1], Jocelyne Bloch[1], Grégoire Courtine[1]

[1]UNIL/CHUV/EPFL, [2]ONWARD

Spinal cord injury (SCI) disconnects brainstem cardiovascular regulatory centers from the sympathetic circuits that regulate blood pressure. Affected individuals have daily debilitating episodes of orthostatic hypotension that restrict participation in rehabilitation, and engagement in social activities, exacerbate cardiovascular risk, and dramatically reduce quality of life. Here, we developed the ARCIM Therapy, which comprises epidural electrical stimulation (EES) applied over the lower thoracic spinal cord to alleviate hemodynamic instability and is the first purpose-built implantable neuromodulation technology for people living with SCI. As we previously demonstrated in rats, non-human primates, and in one human with SCI, the location of the hemodynamic hotspot was confirmed to be at the lower thoracic level with a direct human intra-subjects comparison. In total, we applied the ARCIM Therapy in 14 participants across multiple clinical studies, wherein all participants presented with severe orthostatic hypotension. Immediately after turning ARCIM Therapy on, the severity of orthostatic hypotension was robustly reduced in 14 out of 14 participants. We quantified this as a reduction in the drop in arterial blood pressure as well as an increased tolerance during formal tilt tests. By modulating and increasing arterial pressure, cerebral blood flow was also enhanced to healthy levels in the seated position, thereby preventing the occurrence of syncope. All participants use the stimulation multiple hours a day and reported multi-faceted benefits of this novel therapy. Moreover, ARCIM Therapy also enables the prosthetic recruitment of trunk musculature, leading to enhanced trunk stability, rehabilitation, and recovery. These results demonstrate that ARCIM Therapy has the potential to reduce the severity of orthostatic hypotension, increase trunk stability, and significantly improve participants' rehabilitation, social involvement, and quality of life.

Harput, Elif

Comparison of two preprocessing methods for 18F-flortaucipir PET quantification in Alzheimer's disease

Elif Harput[1], Debora Elisa Peretti[1], Max Scheffler[2], Nicholas J. Ashton[3], Kaj Blennow[3], Henrik Zetterberg[3], Ruben Smith[4], Giovanni Frisoni[1], Valentina Garibotto[1], Cecilia Boccalini[1]

[1]University of Geneva, [2]Division of Radiology, Geneva University Hospitals, [3]University of Gothenburg, Mölndal, Sweden, [4]Skåne University Hospital, Malmö, Sweden

Background: Abnormal tau protein accumulation is a key pathophysiological feature of Alzheimer's disease (AD) that can be visualized in vivo using tau-PET imaging. However, variations in image processing, especially whether data are analysed in a participant's native space or normalized to a standard template, may influence the quantification of tau pathology and its utility as a biomarker for disease staging and progression. Our study aims to assess the comparability of two commonly used PET preprocessing methods, respectively in native and standard spaces, in quantifying tau deposition and in their ability to identify discriminating AD patients. Methods: 209 subjects from the memory clinic of Geneva University Hospitals including 62 cognitively unimpaired (CU) individuals, 113 mild cognitive impairment (MCI) and 34 dementia patients were included. Images were processed in native space and in standard space using inferior cerebellar grey matter as reference region. Standardized uptake value ratios (SUVRs) were extracted from AD regions of interests and regions used for Braak staging. Pearson correlations were performed to evaluate SUVRs obtained by native and standard space approaches and for comparison with plasma biomarkers for external validation. ROC analyses were applied to compare the discriminative power of SUVRs obtained with the two methods in discriminating visually assessed tau status, amyloid-positive cognitively impaired from amyloid-negative CU, and subjects with declining cognition over time. Results: Strong positive correlations were observed between SUVR obtained by the two methods across all regions. However, SUVR obtained by both processing methods showed systematic differences, with higher values obtained with processing in standard space. Processing in native space provided a higher accuracy in all target regions to discriminate visually positive from negative scans, and SUVR in the medial temporal lobe obtained with native space processing performed better to identify declining subjects. For all other analyses the two methods performed equally well. The correlation with plasma biomarkers was comparably high with both methods. Conclusion: While preprocessing in native and standard space is adequate for quantifying 18F-flortaucipir PET and for discriminating AD patients, a higher accuracy can be obtained in the mesial temporal regions and to predict cognitive decline using processing in native space. These findings highlight reference space selection in quantification of tau can impact biomarker sensitivity and may enhance future standardization methods for tau-PET in research and clinical practice.

Hasanovic, Ed

Exploring spinal network maturation in Cerebral palsy

Ed Hasanovic[1]

[1]University of Lausanne

Cerebral palsy (CP) is a neurodevelopmental disorder which affects up to 2 out of 1000 children. Characterised by spasticity, the disease is caused by an insult to the central nervous system during the perinatal stage. While most research has been focusing on the brain, recent evidence from our laboratory indicates that spinal circuits in rat models of CP are altered. However, the role of these spinal circuits in CP remains poorly understood. Therefore, we performed kinematic recordings of basic locomotion tasks and extracted gait parameters using machine learning to describe the progression of gait development post-natally in healthy and CP rats. To uncover the changes on the anatomical level, we are performing multiplexed immunohistochemistry at various timepoints during development. Furthermore, we are developing new viral vector strategies to perform anatomical studies of specific neuronal populations within the spinal cord. Leveraging RNA-sensing, we will express fluorescent markers in neuronal populations to study the role of these neurons in motor deficits in CP. This research will elucidate how spinal circuits are altered in CP and how these differences lead to motor impairments.

Herve, Nino

Connectome-Guided EEG Source Imaging Remains Accurate Despite Incomplete or Erroneous Brain Graphs

Nino Herve[1], Patric Hagmann[1]

[1]Connectomics Lab, Department of Radiology, Lausanne University Hospital and University of Lausanne (CHUV-UNIL)

Electrical source imaging (ESI) is a computational technique used to estimate the locations of neural activity within the brain from non-invasive EEG recordings. A recently developed method, Connectome Spectrum Electromagnetic Tomography (CSET), integrates structural information from brain connectomics—where white matter pathways are modeled as a graph—to improve the accuracy of these reconstructions. Traditional ESI methods, such as sLORETA, typically do not incorporate information about structural connectivity and may struggle to accurately reconstruct activity that is spatially distributed across brain regions. In contrast, CSET leverages the brain's structural connectome to guide the reconstruction process. In simulations where activity propagates through the brain's network, CSET outperforms sLORETA in recovering the underlying source activities. We further investigate two key practical challenges: (1) How robust is CSET to inaccuracies in the structural connectome? and (2) Can it still perform well without access to subject-specific diffusion MRI? Our results show that CSET maintains superior performance even when over 50% of the graph connections are corrupted. Moreover, using a simplified model based solely on cortical geometry—connecting neighboring regions without white matter tractography—still yields reliable reconstructions. These findings suggest that CSET is a robust and biologically informed source imaging approach, with strong potential even when detailed diffusion MRI data are unavailable.

Hillier, Daniel

Seeing the Whole: Fine-Grained 3D Reconstruction of Functional Mesoscale Domains in Cat Visual Cortex.

Abel Petik1,2, Klaudia Csikos1,3, Domonkos Horvath1,2, Michael Sternbach5, Attila B. Dobos1, Alan Urban3, Fred Wolf5, Botond Roska6, Daniel Hillier 1,2

1. Institute of Cognitive Neuroscience and Psychology, HUN-REN Research Centre for Natural Sciences, Budapest, Hungary
2. Faculty of Information Technology and Bionics, Pázmány Péter Catholic University, Budapest, Hungary
3. János Szentágothai Neuroscience Doctoral School, Semmelweis University, Budapest, Hungary
4. Neuro-Electronics Research Flanders, VIB, Department of Neuroscience KU Leuven, Imec, Leuven, Belgium
5. University of Göttingen, Göttingen Campus Institute for Dynamics of Biological Networks, Department Physics of Biological Systems, Göttingen, Germany
6. Institute for Molecular and Clinical Ophthalmology Basel, Basel, Switzerland

In large animals like cats, the visual cortex consists of feature-processing circuits organized into mesoscale patterns critical for sensory integration. Capturing the function of these intricate structures remains challenging due to trade-offs between spatial coverage and resolution in traditional techniques. We developed a novel 3D functional ultrasound imaging (fUSI) method that reconstructs the functional architecture of the visual cortex with unprecedented spatial (150 µm) and temporal (5 Hz) resolution across a 2560 mm^3 volume spanning multiple cortical areas.

Our findings include detailed 3D reconstructions of cortical retinotopy and orientation preference maps across primary and higher visual cortical areas. Notably, we identified distinct organizational patterns within orientation preference maps—such as orientation pinwheels—and tracked their dynamics within functional space.

This fUSI pipeline offers transformative potential not only for studying sensory processing but also for extending investigations into higher-order brain regions implicated in cognition and psychiatric disorders. By bridging mesoscale functional mapping with translational applications in large-brained models like cats, our work lays the foundation for understanding complex neural circuits relevant to both health and disease.

Hinnen, Gabriel

Improving cognition and stress in adolescents: a sleep workshop-based intervention

Gabriel Hinnen[1], Paola Soulié[1], Kevin Mammeri[2], Camille Piguet[2], Sophie Schwartz[1], Virginie Sterpenich[1]

[1]UNIGE, [2]UNIGE, HUG

Adolescents are an extremely vulnerable population, prone to many changes. In parallel, sleep is an essential parameter that plays a fundamental role in cognitive and emotional functioning. Unfortunately, a major health issue nowadays is that adolescents sleep less and less even though they need more sleep than adults. This critical public health issue needs to be adressed as bad sleep can lead to impaired concentration, mood disturbances and an increased risk for chronic health conditions. This project aims at reaching out to adolescents that sleep poorly, but have not sought out help from dedicated therapists. We propose a 4-week workshop-based intervention, directly in schools or at the hospital. These workshops, inspired by cognitive-behavioural therapy for insomnia (CBT-I), have been adapted for teenagers in a group setting. In parellel, adolescents measure their sleep at home using a sleep diary and an actiwatch. The primary goal is to enhance the quality and quantity of sleep in adolscents. In addition, a test session including memory, vigilance and emotional regulation tasks is performed before and after the 4-week intervention to demonstrate that improved sleep has positive effects on these key everyday life parameters. Results from 101 participants who already went through the sleep intervention show sleep, cognitive and emotional functioning improvements. This further emphasizes the importance of a good sleep in adolescence, but also of giving adolescents more access to practical solutions for a better sleep.

Hong, Dou

Investigating the Post-Acute Effects of Psychedelics on Behavioural Flexibility Across Multiple Time Points Using a Maze Task.

Hong D, Alam T, Walton M

University of Oxford

Cognitive flexibility, the ability to adapt to new situations and changes, is an important skill for survival and is often studied in rodents using a task called probabilistic reversal learning (PRL). In PRL, animals must learn to adjust their behavior when reward rules change. Faster adaptation is seen as a sign of better cognitive flexibility. However, over time, rodents become more familiar with the task, and their decision-making may become stable without needing significant brain changes, making PRL less effective for measuring long-term cognitive flexibility. This stability can occur through the medial prefrontal cortex (mPFC), which may reduce the ability of tasks like PRL to detect changes driven by interventions such as psychedelics.

To overcome this, we will use a new 7x7 tower maze, developed by Dr. Thomas Akam from the Walton lab, which requires rodents to make dynamic decisions based on both the layout of the maze and the most direct path to the goal. The maze will be altered every three days to continuously challenge the animals, requiring them to update their strategies, providing a strong and continuous measure of cognitive flexibility.

In our study, rodents will receive either psilocybin or a placebo (saline) every 2–4 weeks. We will measure how well they adapt to changes in the maze after each modification. This within-subjects design allows us to track the effects of psilocybin on cognitive flexibility over time and reduces variability between animals. By examining how the animals learn after each drug administration, we hope to understand if psilocybin enhances the brain's ability to adapt to new environments. This research could offer insights into how psychedelics might help treat psychiatric disorders, such as obsessive-compulsive disorder and depression, which involve difficulty in adapting to new or changing situations.

Ichim, Ana-Maria

D-Serine Modulation of Network Dynamics in GluN2D-KO Mice.

Ichim Ana-Maria, Harald Barzan, Adriana Nagy-Dabacan, Vlad-Vasile Moca & Raul Cristian Muresan.

Transylvanian Institute of Neuroscience

N-methyl-D-aspartate receptor (NMDAR) hypofunction represents a critical mechanism underlying schizophrenia's complex neurophysiological disruptions. Specifically, the GluN2D subunit plays a pivotal role in regulating excitatory-inhibitory circuit dynamics and network oscillations. Our study explores the potential therapeutic modulation of these circuit-level disturbances through D-serine, a critical NMDAR co-agonist, in a genetically modified mouse model.

Employing in vivo electrophysiological techniques, we systematically examined spontaneous and evoked gamma-band oscillations in the visual cortex of wild-type and GluN2D knockout (KO) mice. Our experimental design incorporated comprehensive assessments of neural network activity before and after systemic D-serine administration, revealing nuanced genotype-specific responses.

Preliminary findings demonstrate differential gamma oscillatory power modulation, with particularly pronounced effects observed in the GluN2D-KO mice. These results suggest a potential compensatory mechanism by which D-serine may rescue impaired NMDAR-mediated signaling, offering novel insights into circuit-level interventions for neuropsychiatric disorders.

Ilaridou, Iliana

Heterogeneity of response to Early Start Denver Model: Identifying developmental trajectories and predicting cognitive outcome

Iliana Ilaridou[1], Nada Kojovic[1], Thibaut Chataing[1], Kenza Latreche[1], Fiona Journal[1], Corrado Sandini[1], Marie Schaer[1]

[1]UNIGE

Background: Autism Spectrum Disorder (ASD) is a complex neurodevelopmental disorder, characterized by social impairments as well as restrictive and/or repetitive behaviors. ASD is significantly impacting the quality of life of the individuals. However, diagnosis at a young age gives the opportunity to intervene early by applying Early intensive interventions such as Early Start Denver Model (ESDM) that can improve the developmental trajectories of these children. ESDM, is a naturalistic method known to enhance communication, cognitive, social and motor skills in autistic children, using natural environments and rewards. Precisely, findings of previous studies support the effectiveness of ESDM, with children achieving 20 points of cognitive gain. However, prior research has also shown that there is a wide heterogeneity of responses in ESDM intervention with some children benefiting more than others. Methods: In this study, we evaluated the cognitive skills, adaptive behavior and severity of autistic symptoms, of 107 children (1.74-3.5 y.o.) receiving 1.5 to 2 years of ESDM intervention. We tried to identify significant changes during this intervention and compare our findings with current literature. Furthermore, we conducted a latent class regression analysis (LCR) to recognize the different trajectories that these children follow and used stepwise repression to understand which baseline factors influence the evolution of each trajectory. Finally, we attempted to predict the cognitive outcome of these children by using these factors and building specific regression equations for each class. Results: Throughout this intervention the children gained on average 19 points of cognitive score and 5 points of adaptive skills. LCR identified 3 classes: the Progressive Group A (PrGA) which achieved the highest cognitive scores, the Progressive Group B (PrGb) with baseline scores in the range of intellectual deficiency that reached the lower normal DQ range by the end, and the Stable Group (StG) that showed minimal improvement and remained relatively stable throughout the intervention. Furthermore, stepwise regression detected the baseline factors that were most strongly associated with the developmental outcome of each group. Precisely, for PrGA Age, Daily Living Skills, Motor and Communication skills were chosen as the most important ones. For PrGB the selected factors were Social Affect and Age, and for StG the variables of Age and Restrictive and Repetitive behaviors were chosen as the most significant variables for prediction. Finally, these factors were used in different regression equations for each group, enabling the prediction of the final cognitive outcomes of these children based on information available at baseline. Conclusions: Our results support previous findings about the efficacy of ESDM and the heterogeneity of responses in this intervention, this time replicated in a relatively larger sample of 107 children. Predicting the developmental trajectory of children receiving ESDM with information available at baseline provides the chance to propose more personalized interventions and further support to participants that don't benefit as much from this intervention. Although our model requires external validation, it offers a step toward customizing interventions to maximize each child's developmental gains.

Illeperuma, Mindula

EEG-Based Signal Processing Framework for Self-Organized Criticality Detection.

Illeperuma, M. (1), De Silva, V. (2), Pina, R. (3)

Loughborough University London, UK

Advancements in digital signal processing have enabled cost-effective brain state observation through electroencephalography (EEG). This has contributed to fields such as well-being assessment in healthcare, driver state monitoring, and Neurofeedback training for high-performance athletes. An emerging focus in brain analysis is self-organized criticality (SOC), a hallmark of brain activity, which can be studied through spontaneous cascades of neuronal activity known as neural avalanches. While SOC has been examined in resting-state conditions, little is known about its role in active visual recognition tasks. In this study, we apply signal processing and unsupervised learning to analyze critical brain dynamics during a target detection task. We propose a signal processing framework integrated with unsupervised learning for SOC detection; application of this method revealed five components accounting for 99\% of pre-stimulus and 94\% of post-stimulus variance. Using our framework we then demonstrate how post-stimulus SOC features can be predicted using just three pre-stimulus features with a multiple R score of 0.84. Our methods may help to inform the design of brain-computer interface based feedback mechanisms to be used in emerging applications such as driver engagement assessment and neural state prediction.

Jayaram, Spatika

Contrasting profiles of metabolism in the Subgenual Anterior Cingulate and Dorsolateral Prefrontal Cortices during critical developmental periods: insights from spectroscopy in marmosets.

Jayaram S (1) (2), Stasiak A (1) (2), Gould S (1) (2), Cockcroft G (1) (2), Lynn-Jones T (1) (2), Roberts A.C. (1) (2), Sawiak S.J. (2) (3)

(1) Department of Physiology, Development and Neuroscience, University of Cambridge, Downing Street, Cambridge, UK
(2) Behavioural and Clinical Neuroscience Institute, University of Cambridge, Downing Site, UK
(3) Wolfson Brain Imaging Centre, University of Cambridge, Box 65 Addenbrooke's Hospital, Cambridge, UK

Mood disorders are commonly diagnosed in adolescence, a period of significant prefrontal cortical development. Two regions implicated in depression are the subgenual anterior cingulate cortex (sgACC-25) and the dorsolateral prefrontal cortex (dlPFC-46). Both are targets for treatment, with success related to the extent of their anti-correlated activity. Earlier studies in marmoset monkeys outlined distinct trajectories of morphological development for these subregions. In this study, we examined the potential metabolic mechanisms underlying these differences by analysing magnetic resonance spectroscopy data from 77 monkeys, imaged 1-5 times from infancy to adulthood (3-30 months, 202 scans). Inositol, creatine, n-Acetylaspartate (NAA) and choline showed significant differences between both regions. Inositol and creatine (involved in membrane turnover and energy metabolism) were significantly higher in sgACC-25 and increased across development, reflective of an actively developing region. Development in dlPFC-46 was marked by a decrease in choline, likely reflective of earlier myelination here since decreasing choline levels are linked to its incorporation into the myelin sheath. As myelination is one of the last developmental processes, this highlights the earlier metabolic maturation of dlPFC-46. Comparison of metabolic and structural trajectories suggested that metabolic changes in dlPFC-46 overlapped considerably with the window of structural maturation, while the extended profile of metabolic change in sgACC-25 appeared displaced later in development, following the onset of structural maturation in this region. We hypothesise that the prolonged and elevated metabolic demands in sgACC-25 may be driven by its extended structural development, potentially increasing its susceptibility to dysregulation across adolescence and into adulthood. This may, in turn, disrupt circuit development, including its interaction with dlPFC-46, contributing to heightened vulnerability to mood disorders.

Jobard, Morgane

Interindividual molecular and behavioral differences in a chronic mild stress model at adolescence.

Jobard M (1,2), Demaille B (3), Jay T (1), Krebs MO (1,2), Chaumette B (1,2,3), Marzo A (1), Le Pen G (1,4)

(1) Université Paris Cité, Institute of Psychiatry and Neuroscience of Paris (IPNP), INSERM U1266, Physiopathology of Psychiatric Disorders : Vulnerability and Development, 75014 Paris, France;
(2) GHU-Paris Psychiatrie et Neurosciences, Hôpital Sainte Anne, Pôle PEPIT, F-75014 Paris, France;
(3) Université Paris Cité, Institute of Psychiatry and Neuroscience of Paris (IPNP), INSERM U1266, Bioinformatic platform, 75014 Paris, France;
(4) Université Paris Cité, Institute of Psychiatry and Neuroscience of Paris (IPNP), INSERM U1266, PhenoBrain platform, 75014 Paris, France

Schizophrenia is a severe chronic mental disorder that typically appears during adolescence and patients present a constellation of symptoms like psychosis and impairment of sensorimotor filtering. Its development is thought to result from an interaction between genes and environment, suggesting a genetic vulnerability accelerated by environmental factors such as stress particularly during adolescence, a critical developmental period. The gene x environment interaction also reveals interindividual variability, which can translate into the vulnerability of certain individuals. The biological mechanisms underlying resilience and/or vulnerability remain poorly understood, and a better understanding of these mechanisms could help identify biomarkers of the transition and propose new therapeutic avenues for the different stages of the disease. In this regard, the animal model is a very informative tool. The objective is to identify molecular biomarkers for stress vulnerability in a chronic mild stress (CMS) model on adolescent rats.

Rats were exposed to a 3-week CMS protocol during adolescence and long-term behaviours were evaluated 3 weeks after the end of CMS. We used a composite score, based on behavioral data, to identify vulnerable and resilient rats to stress. PFC was dissected for methylomic and transcriptomic analyses.

We succeeded in distinguishing vulnerable and resilient rats. Vulnerable rats showed alteration in locomotion activity, anxiety-like behavior and sensorimotor information filtering, whereas resilient rats showed no deficit. We found some differentially methylated genes and differentially expressed transcripts in the prefrontal cortex of vulnerable rats compared to resilient and control (not exposed to stress) rats.

This study reveals long-term inter-individual behavioral and molecular differences after chronic stress in adolescence, highlighting vulnerability and resilience statuses. In the future, we plan to manipulate targets related to genes identified in our study to understand molecular mechanisms of entry into schizophrenia.

Kim, Yuri

Epigenetic dysregulation in developing neocortical neurons associated with neurodevelopmental disorders.

Kim Yuri (1), Kawaguchi Daichi (1), Goto Takahiro (1), Watanabe Takaki (2), Fujino Shuhei (3), Sugaya Yuki (3), Kano Masanobu (2), Watanabe Takamitsu (4), Gotoh Yukiko(1,4)

(1) Graduate School of Pharmaceutical Sciences, The University of Tokyo,
(2) Advanced Comprehensive Research Organization, Teikyo University,
(3) Graduate School of Medicine, The University of Tokyo,
(4) International Research Center for Neurointelligence (WPI-IRCN), The University of Tokyo

Epigenetic regulation plays a critical role in gene expression dynamics during brain development, and its dysregulation has been implicated in neurodevelopmental disorders (NDDs). Mutations at the Kdm6b (also known as Jmjd3), an H3K27me3 specific demethylase, locus have been commonly found in NDDs such as autism spectrum disorder and schizophrenia. However, its role in cortical development and pathogenesis of NDDs remains poorly understood. We, therefore, generated Kdm6b conditional knockout (cKO) mice using a Nex-Cre line, in which Cre recombinase was expressed in postmitotic excitatory neurons in the developing neocortex and hippocampus. Behavioral results indicated that dysfunction of Kdm6b in excitatory neurons leads to behavioral abnormalities associated with NDDs, such as hyperactivity and impaired sociability in the adult stage. Furthermore, Kdm6b cKO reduced the size of rostral areas containing the prefrontal cortex (PFC) and led to physiological excitation/inhibition imbalance within the medial PFC (mPFC), which may underlie behavioral deficits associated with NDDs. RNA-seq analysis revealed dynamic molecular changes in Kdm6b cKO mice. In particular, serotonin-related genes including serotonin transporter Slc6a4, transiently expressed in the deep layer of the mPFC during the early postnatal period, were significantly downregulated in the Kdm6b cKO brains. Furthermore, pharmacological manipulation of serotonin levels tended to rescue the part of behavioral abnormalities in Kdm6b cKO mice. Taken together, our data indicate that KDM6B in postmitotic excitatory neurons plays a pivotal role in cortical organization and prefrontal circuit formation through the developmental time-dependent regulation of gene expression, which may be necessary for suppressing NDDs.

Koh, Isabel

Modelling of Schizophrenia In Vitro Using Cortical and Thalamic Organoids.

Koh Isabel (1), Mitsuru Ishikawa (2), Yuko Arioka (3), Hiroki Okumura (3), Norio Ozaki (3), Akiko Hayashi-Takagi (1)

(1) RIKEN Centre for Brain Science, Saitama, Japan
(2) Fujita Health University, Aichi, Japan
(3) Nagoya University, Aichi, Japan

Despite symptoms mainly appearing during adolescence, psychiatric disorders are thought to have neurodevelopmental origins, and it has been postulated that abnormal connectivity between the cerebral cortex - responsible for cognitive processes – and the thalamus – responsible for sensory integration – play a role in these disorders. Several genetic factors have also been implicated in psychiatric disorders, one of which is the SETD1A loss-of-function (LoF) variant that has been linked to a high risk of schizophrenia. However, it is difficult to study neurodevelopment of the brain in humans due to ethical reasons. Advances made in CRISPR technology, as well as human induced pluripotent stem cells (hiPSCs) and their differentiation to organoids have made it possible to recapitulate some aspects of the human brain in vitro. In this work, the effect of SETD1A knockout in iPSCs by CRISPR on organoid formation and differentiation will be investigated by generating cortical and thalamic organoids and comparing their differences in proliferation and differentiation to brain region-specific neural cells. I will also discuss the pathomechanism of schizophrenia, considering differences between species (mouse vs. human), brain regions (cortex vs. thalamus) and developmental stages (developing vs. adult) by making comparisons between hiPSCs, SETD1A KO mice, and human post-mortem brain tissues. In the future, we expect to expand the outcomes of this research to integrate studying how the connectivity between cortical and thalamic brain regions is affected in psychiatric disorders.

Konik, Stéphanie

Body representations after stroke: characterising distortions in upper limb perception

Stéphanie Konik[1], Isabella Martinelli[2], David Zeugin[3], Michela Pelosin[3], Sonia Crottaz-Herbette[3], Jean-Baptiste Ledoux[3], Samanta Simioni[4], Eleonora Guanziroli[5], Franco Molteni[5], Michela Bassolino[2], Andrea Serino[6]

[1]CHUV UNIL et HES-SO Valais-Wallis, [2]HES-SO Valais-Wallis, [3]CHUV, [4]Institution de Lavigny, [5]Villa Beretta Rehabilitation Center, [6]CHUV UNIL

Following stroke, patients may experience altered perceptions of their body, which may affect both their recovery and quality of life. Despite their potential clinical significance, such disturbances are rarely assessed in routine practice, likely due to limited understanding of their characteristics and a lack of appropriate tools. This study aimed to characterize disturbances in perception of the most affected upper limb (aUL) after stroke, by estimating their rate, severity, evolution over time, associations with sensorimotor deficits, functional recovery, and neural correlates. We developed a structured, digitalized questionnaire to quantitively evaluate a broad range of disturbances in aUL perception (e.g., disownership, illusory movements, perceived temperature, etc.). One hundred and twelve sub-acute stroke patients were assessed at rehabilitation admission (T1) and at discharge (T2). At T1, a large proportion (69%) of patients reported at least one altered perception of their aUL, irrespective of lesion laterality. These alterations were frequently associated with sensorimotor deficits, but interestingly also occurred in their absence. Predictive modelling showed that motor and sensory impairments significantly contributed to the severity of these perceptual disturbances. VLSM analysis revealed associations with brain regions involved in body structural representation and motor planning. Importantly, the severity of aUL perception alterations at T1 was predictive of motor function both at admission and discharge. While the rate of these disturbances is reduced following rehabilitation, a substantial number of patients continued to report them at T2. These findings challenge prevailing assumptions that altered body perceptions are rare, limited to the acute phase, or specific to right hemisphere lesions and motor deficits. They underscore the need for systematic assessment in clinical practice and contribute to a deeper theoretical understanding of post-stroke body representation disorders and recovery.

Kyprou, Marios

Ventral Hippocampus Activity in the PV-Cre; ErbB4F/F Mouse Model and the Effect of Psychedelic Treatments.

Kyprou, M. (1), Li, K. (1), Ciocchi S. (1)

(1) Department of Physiology, University of Bern

Schizophrenia is a severe psychiatric illness that affects approximately 1% of the general population. Its negative and cognitive symptoms seem to be more persistent throughout life with a greater toll on functioning and quality of life, compared to the positive symptoms. Previous research has shown that multiple brain areas and cell types may be affected in schizophrenia, resulting to its observable symptoms. In recent years, rodent models show a characteristic disruption of the connectivity between the hippocampus and brain areas such as the prefrontal cortex, as well as early onset endophenotypes in the ventral/anterior hippocampus. Such biomarkers may mediate behavioral abnormalities of the disease, including negative and cognitive symptoms. Here, we wish to examine a genetic mouse model with schizophrenia-like phenotypes and biomarkers, based on mutations found in human patients to better mimic neural and behavioral features of the disease. We will use calcium imaging techniques in a battery of cognitive and emotional tests in mice to describe cell-specific abnormalities of the ventral hippocampus, and test the hypothesis that psychedelic treatment may alleviate abnormal neural activity patterns and behavior.

Labancová, Katarína

Neural mechanisms of online information integration and compression in working memory

UNIGE

During language comprehension, the brain needs to integrate incoming information according to rules of syntax to compose a coherent meaning. Crucially, this unfolds over time: earlier words need to be maintained in working memory until they can be integrated with later ones. Although working memory is typically described to have a span of 7-+2 items (Miller, 1956), we are able to understand sentences much longer than that. This implies that working memory is equipped with a mechanism that can manipulate its contents - through syntactic integration, representations are effectively compressed to free up resources and can be decompressed when needed (Desbordes et al., 2024). This necessitates a dynamic working memory system that is able to dynamically encode, maintain, compress, update, and retrieve structured information (Miller, Lundqvist & Bastos, 2018). This PhD project investigates the neural mechanisms - particularly the role of neural oscillations and oscillatory coupling (Lisman & Jensen, 2013) - that support information integration and compression in working memory during online language comprehension. The focus is on how the brain transforms incoming input into structured hierarchical representations (Whittington et al., 2022), effectively reducing their representational load, and how these compressed representations can be reliably decompressed and reactivated when required. Decoding and oscillatory analyses will be employed at high temporal resolution (Desbordes et al., 2024; Lundqvist et al., 2016) to examine the precise timing of neural activity underlying these working memory computations.

Ka Chung Lam, Thomas

Neural Control of Reaching in Drosophila

Pavan Ramdya[1], Jasper Phelps[1], Thomas Ka Chung Lam[1]

[1]EPFL

Reaching movements are a fundamental class of goal-directed motor actions that animals use to interact with their environment and with conspecifics. While reaching has been extensively studied in vertebrates such as primates and rodents, we use the fruit fly as a model system because its genetic accessibility and fully mapped brain connectome provide a unique opportunity to dissect complete reaching circuits with mechanistic precision. Here, we characterize a previously understudied behavior in flies: a socially evoked "fending" response in which the middle leg reaches toward a nearby conspecific, potentially to maintain social distance. These movements are goal-directed, with the reach direction continuously tracking the position of the other fly. To quantify this behavior, we developed a multi-view imaging setup that captures high-speed, high-resolution recordings of interacting flies and reconstructs the 3D kinematics of the legs during reaching. This system also allows for precise experimental control by replacing the conspecific with a magnetically actuated dummy fly, enabling us to probe the sensory requirements of the behavior and the relationship between stimulus trajectory and leg movement. To investigate the underlying neural mechanisms, we built a setup for simultaneous functional imaging of the central nervous system and behavioral recording of reaching movements. This approach allows us to examine how reaching is encoded in descending neurons, a small population comprising approximately 1% of all neurons, which form the bottleneck in the pathway for transmitting motor commands from the brain to the ventral nerve cord (the functional equivalent of the vertebrate spinal cord). Finally, we use the adult fly connectomes to guide the identification of specific neurons involved in controlling reaching.

Latreche, Kenza

Unraveling Language Development Trajectories in Autism Spectrum Disorder: Electrophysiological Evidence

Kenza Latrèche[1], Michel Godel[1], Ana Flò[2], Valentina Borghesani[3], Marie Schaer[1]

[1]Autism Brain and Behavior Lab, Faculty of Medicine, University of Geneva, Geneva, Switzerland, [2]Cognitive Neuroimaging Unit, Université Paris Saclay, NeuroSpin center, Gif-sur-Yvette, France, [3]Neurobiology of Concepts Expression Laboratory, Faculty of Psychology and Educational Sciences, University of Geneva, Switzerland

Language development in autism spectrum disorder (ASD) is heterogeneous, ranging from subtle differences to significant delays. In previous work, we identified three autistic language profiles in early childhood: Language Unimpaired (LU), Language Impaired (LI), and Minimally Verbal (MV). While these profiles show distinct vocabulary, grammar, and pragmatic development, understanding their underlying neural correlates is essential to predict outcomes and develop targeted interventions. Here, we examined whole-brain resting-state EEG (RS-EEG) power across five canonical frequency bands in a longitudinal sample comprising 66 typically-developing children and 122 autistic children (ages 1.56-6.01 years), yielding 358 time points. Within the ASD group, 61 children belonged to the LU profile, 44 children to LI, and 17 children to MV. Compared to TD peers, autistic children showed increased power in low-frequency (delta, theta) and high-frequency bands (beta, gamma). Gamma power varied by autistic language profile, with the highest levels in MV children. Gamma power within ASD followed a quadratic trajectory in relation to word combination acquisition, peaking around the time of acquisition and decreasing afterward. This pattern suggests a dynamic, compensatory mechanism supporting the transition to phrase speech – a critical milestone toward functional speech that may predict language outcomes in ASD .

Law, Man Hoi Rachel

Enhancing Stem Cell Therapy for Parkinson's Disease with Non-Invasive Deep Brain Stimulation and Functional Imaging

Rachel Man Hoi Law[1], Sofia Peressotti[1], Christina Grimm[2], Valerio Zerbi[1]

[1]University of Geneva, [2]École Polytechnique Fédérale de Lausanne

Parkinson's Disease (PD) is one of the most prevalent neurodegenerative diseases worldwide. While current treatments can partially manage symptoms, patients often develop medication resistance or side effects, and therapeutic outcomes are highly inconsistent. Cell replacement therapy harnessing human stem cell-derived neurons offers a promising approach for restoring the impaired dopaminergic system (Sawamoto et al., 2025; Tabar et al., 2025). However, the integration of transplanted cell grafts into the host brain is a slow and variable process, which can delay behavioral improvements for up to two years after transplantation. Therefore, there is a clear need for strategies that can both accelerate and reliably monitor the functional integration of these cells. This project investigates the use of Temporal Interference Stimulation (TIS), an electrical stimulation technique, to enhance the functional integration of transplanted human iPSC-derived mesencephalic dopaminergic (mesDA) neurons (Grossman et al., 2017). TIS has gained growing interest clinically and preclinically for its ability to deliver focal, non-invasive deep brain stimulation via temporally interfering electrical fields. Recent in vitro evidence suggests that TIS can promote neural differentiation and maturation in primary embryonic neuroprogenitor cells (Peressotti et al., in progress). Here, we aim to systematically assess the functional integration of cell grafts in vivo and investigate the potential of TIS towards improving PD cell replacement therapy. To enable precise, long-term control of transplanted neuronal activity, we have generated an iPSC line stably expressing the optogenetic actuator Chrimson-Red. This allows for selective activation of grafted neurons following transplantation. To monitor the functional responses of these cells, we employ both fiber photometry and functional ultrasound (fUS) during simultaneous optogenetic stimulation, enabling assessment of functional integration at both the cellular and network levels. Chrimson-Red–tagged mesencephalic dopaminergic (mesDA) neurons are unilaterally transplanted into the striatum of Crl:NU(NCr)-Foxn1nu athymic mice. Temporal Interference Stimulation (TIS) is applied starting one-two week after transplantation, with various patterns, intensities, and frequencies delivered for up to three consecutive weeks (1 hour per day). To detect local dopamine dynamics in response to graft activation, striatal host cells are transduced with the dopamine-specific fluorescent sensor dLight, and fiber photometry is used to record dopamine release during optogenetic stimulation of the transplant. The Iconeus One fUS system is used to detect neural activity–coupled hemodynamic changes during optogenetic activation of mesDA neurons, providing insight into the broader network-level connectivity established between the graft and host brain. Preliminary results will be presented on the characterization of Chrimson-Red iPSC-derived mesDA neurons, as well as on the optimization of the transplantation protocol. Ongoing work includes detailed characterization of TIS focal targeting within the mouse striatum using both electrophysiological recordings and photometry. This work aims to establish a non-invasive, translatable strategy to enhance cell therapy outcomes in Parkinson's Disease using TIS, advancing both fields of regenerative medicine and neuromodulation.

Liyanagoonawardena, Sandali

Rethinking Individual Differences in Children's Vision

Sandali Liyanagoonawardena[1], Simona Garobbio[1], Michael Herzog[1]

[1]École Polytechnique Fédérale de Lausanne (EPFL)

Longitudinal behavioural studies are a key method for assessing neural mechanisms underlying perception, which offer insights into both momentary performance and developmental trajectories that reflect plasticity and evolving perceptual abilities. Children provide a valuable window for longitudinal research, both due to their heightened brain plasticity and due to being unaffected by factors such as development and extensive life experiences. This study examines the longitudinal trajectories of children's vision perception to explore common latent factors underlying visual abilities and inter-individual differences in perceptual development. We evaluated the visual abilities of 52 children in a longitudinal study spanning three visits, each spaced six months apart. During each visit, participants completed a battery of assessments that included 8 visual tasks and 10 visual illusions, with each test repeated twice to assess test–retest reliability. Our analysis began with examining correlations among visual tests to understand inter-individual differences at a single time point. We then explored how individual performance changed over time to assess whether developmental or declining patterns in visual abilities were correlated. Finally, we evaluated the stability of these individual differences across the three visits. Among all the test pairs, only one showed a correlation that reached at least the moderate threshold in Spearman's normative values, indicating greater-than-expected differences between individuals in children's visual perception. Although these individual differences remained stable over time, the correlations between the slopes of performance change across tests, as well as the changes in performance themselves, were weak. This points to considerable variability between individuals even in how their visual abilities develop over time.

Mammeri, Kevin

Pages from an insomnia diary: Mental imagery to calm the heart and reduce hyperarousal

Kevin Mammeri[1], Saskia Czura[1], Karissa Humailo[1], Nahema Leone[1], Vincent Rochas[1], Laurence Bayer[1], Lampros Perogamvros[1]

[1]University of Geneva

Insomnia disorder (ID) is the most prevalent sleep disorder and is associated with significant daytime impairment. According to the hyperarousal model of insomnia, a central mechanism of the disorder is a persistent elevation of cognitive, emotional, physiological, and cortical arousal, collectively referred to as hyperarousal. The present study specifically targets this mechanism using imagery rescripting (IR), a cognitive technique in which individuals transform pre-sleep intrusive negative images into positive and relaxing scenario. This preliminary analysis includes data from 13 adults with insomnia, aged 18 to 45, enrolled in an ongoing randomized controlled trial designed to evaluate the efficacy of IR in reducing physiological and cognitive hyperarousal. All participants completed a structured inclusion process followed by four weekly IR intervention sessions. Throughout the intervention, heart rate was continuously monitored, and subjective hyperarousal was assessed both within each session and after the intervention. Preliminary findings indicate that IR leads to reductions in both subjective and objective measures of hyperarousal, observed both within sessions and across the intervention period. These initial results suggest that IR may be an effective non-pharmacological approach for targeting hyperarousal, one of the core factors of insomnia. The final outcomes from the full sample will further clarify IR's impact on insomnia severity and its underlying therapeutic mechanisms.

Mansour, Solène

Validation of a Neurodevelopmental Screening Scale for Psychiatric Disorders in Adults: Insights from the Diagnostic of Developmental Disorders Questionnaire

Sophie Boubet, Solène Mansour, Anton Iftimovici, Marie-Odile Krebs

IPNP, France

Adult psychiatric disorders such as schizophrenia, bipolar disorder, and autism spectrum disorder display high clinical heterogeneity, suggesting that current diagnostic boundaries may not fully capture underlying vulnerability mechanisms. Increasing evidence points toward a shared neurodevelopmental origin, with early developmental anomalies acting as vulnerability markers.

In this study, we aimed to construct a composite neurodevelopmental score that integrates multiple developmental variables, including childhood history, neurological soft signs, learning difficulties, and obstetrical complications, using data from the Psycare 4.0 cohort. Two complementary approaches were tested: Principal Component Analysis (PCA), a linear and interpretable method, and autoencoders (AE), a non-linear deep learning model. Both methods allowed us to reduce multidimensional developmental information into a single continuous score per individual.

The neurodevelopmental score was then used for transdiagnostic clustering, enabling the identification of subgroups with distinct developmental profiles. This approach supports patient stratification beyond categorical diagnoses and provides a framework for linking developmental trajectories with clinical, cognitive, and biological outcomes.

Our findings highlight the potential of data-driven composite scores to capture shared neurodevelopmental vulnerability across psychiatric disorders. Such tools may pave the way for more personalized and dimensional approaches to understanding and treating mental illness.

Marchessaux, Florian

Midbrain D2-autoreceptor function in impulsivity and susceptibility to amphetamine sensitization

Florian Marchessaux[1]

[1]Université de Genèse

Impulsivity is a multidimensional trait closely linked to vulnerability to drug abuse, but these underlying mechanisms remain unclear. One possibility may involve the D2 receptors (D2Rs), as their deficit in the midbrain has been associated with impulsivity. Notably, D2Rs act as an autoreceptor on dopamine (DA) neurons and play a key role in controlling both DA release and neuronal firing. Given their regulatory role in DA neuron excitability and their link to impulsivity, we hypothesized that repeated drug exposure induces distinct D2-autoR adaptations in impulsive compared to non-impulsive individuals, contributing to heightened drug abuse vulnerability. Psychostimulant sensitization is a well-established preclinical model of drug abuse, marked by increased locomotor activity and DA release in the nucleus accumbens (NAc), reflecting early neuroadaptations linked to drug vulnerability. In this study, we used Roman High- (RHA) and Low-Avoidance (RLA) rats, which differ in impulsivity and sensitivity to amphetamine (AMPH). We also included Wistar rats, the original strain from which RHAs and RLAs were derived, to evaluate whether these lines exhibit behavioral or neurobiological traits that make them more prone or resistant to AMPH sensitization. In the first experiment, impulsivity was assessed using the 3-Choice Serial Reaction Time Task, followed by a three-week AMPH sensitization protocol. Locomotor activity and DA release were measured at baseline (saline), on the first day of AMPH exposure, and ten days after the last dose with a challenge AMPH injection. In the second experiment, rats received either the same AMPH regimen or chronic saline. D2-auroR function was assessed ten days after the last injection using ex vivo electrophysiology. RHAs and Wistars exhibited higher impulsivity and greater behavioral and neurochemical sensitization to AMPH compared to RLAs. The magnitude of these sensitization indices was positively correlated with impulsivity. At baseline, no innate differences in D2-autoR function or VTA DA neuron activity were observed across strains. However, AMPH exposure led to differential neuroadaptations in high-impulsivity lines only. Indeed, AMPH-treated RHAs and Wistars showed reduced D2-autoR current and function, as reflected by increased basal firing rates and neuronal excitability in VTA DA neurons. These findings suggest that impulsivity predicts the magnitude of AMPH-induced sensitization and is linked to drug-induced adaptations on D2-autoRs. Such neuroadaptations result in diminished inhibitory feedback on VTA DA neurons, potentially contributing to increased vulnerability to drug abuse in highly impulsive individuals.

Marchetti, Claudia

Glutamate Receptor Plasticity in the Nucleus Accumbens Core After Social Choice-Induced Voluntary Abstinence: Implications for Synaptic Adaptations in Addiction.

Marchetti Claudia 1,2,3, Soami F. Zenoni 1,2, Sara Pezza 1,2, Maria Chiara Ruano 2, Jacopo Modoni 2, Ingrid Reverte 4, Davide Ragozzino 1,2, Daniele Caprioli 1,2.

1 Department of Physiology and Pharmacology, Sapienza University of Rome, Rome, Italy.
2 Santa Lucia Foundation (IRCCS Fondazione Santa Lucia), Rome, Italy.
3 Department of Neuroscience, Università Cattolica, Rome, Italy.
4 Department of Life Sciences, Link Campus University, Rome, Italy.

Pre-clinical studies on drug addiction and relapse often overlooked volitional social interactions despite their critical importance in human addiction. Recently, it has been demonstrated that social choice-based voluntary abstinence (SVA) prevents the incubation of methamphetamine craving in rats, yet the underlying neurobiological mechanisms remain poorly understood. Here, we interrogated excitatory synaptic transmission onto medium spiny neurons (MSN) of NAc core of rats, to understand how it is differentially shaped by SVA compared to forced abstinence (FA). Our findings reveal that SVA restores basal glutamatergic activity, renormalizes synaptic strength, and prevents the increase in excitatory drive observed in FA. A key mechanism driving cue-induced drug craving is the accumulation of calcium-permeable AMPAR (CP-AMPARS) in the Nac during abstinence. However, while SVA blocks the incubation of methamphetamine craving, our findings suggest that this mechanism is independent from CP-AMPAR accumulation, suggesting the involvement of alternative mechanisms at glutamatergic synapses onto MSN. Finally, our findings highlight the therapeutic potential of positive social interactions as a non-pharmacological intervention to reduce relapse vulnerability in methamphetamine use disorder, suggesting that SVA counteracts maladaptive synaptic plasticity and exerts a positive effect by preserving neurophysiological homeostasis in the NAc.

These findings support the DDD as a valid tool for assessing neurodevelopmental deviations in psychiatric disorders, particularly in distinguishing ASD from SCZ, emphasizing the importance of early neurodevelopmental assessment.

Mauriello, Cheyenne

Investigating relative temporal order memory in Down syndrome, Williams syndrome, and typical development using a novel behavioral task

Cheyenne Mauriello1, Lucia-Manuela Cantonas1, Pierre Lavenex2 and Pamela Banta Lavenex1

1Laboratory of Neurocognitive Development, Faculty of Psychology, UniDistance Suisse, Brig, Switzerland
2Laboratory of Brain and Cognitive Development, Institute of Psychology, University of Lausanne, Lausanne, Switzerland

Relative temporal order memory is the memory for the order of the events that make up our lives, specifically in relation to other events or sub-events. Relative temporal order memory relies on the hippocampus, and constitutes a fundamental component of episodic memory.

I will investigate relative temporal order memory in individuals with atypical hippocampus development, specifically Down syndrome (DS) and Williams syndrome (WS), and in typically developing (TD) children from 4–9 years of age. TD children will serve both as a mental-age matched comparison group for individuals with DS or WS, as well as an experimental group in which to describe the typical development of hippocampus-dependent temporal order memory abilities, since the hippocampus exhibits delayed postnatal development. I will use a novel behavioral paradigm designed to assess object memory (“what”), spatial memory (“where”), and their interactions (“what-where”; “what-when”; “where-when”; and “what-where-when”).

Menoud, Pauline

Impact on everyday cognition, fatigue and quality of life of a novel cognitive neurorehabilitation protocol using a real-time adaptive exergame in multiple sclerosis: a randomized controlled trial

Pauline Menoud[1], Etienne Sallard[2], Giulia Binarelli[2], Petr Grivaz[2], Elia L. Fischer[3], Charlene Moser[2], Camille A. Pestiaux[2], Florian W. Sander[2], Grégoire Eberlé[2], Philippe Ryvlin[2], Marie Théaudin[2], Caroline Pot[2], Renaud A. Du Pasquier[2], Joaquin A. Anguera[4], Adam Gazzaley[4], Riley Bove[4], Arseny A. Sokolov[2]

[1]CHUV (Centre hospitalier universitaire vaudois) / UNIL (Université de Lausanne), [2]CHUV (Centre hospitalier universitaire vaudois), [3]CHUV (Centre hospitalier universitaire vaudois), Inselspital (Bern University Hospital), [4]UCSF (University of California, San Francisco)

Aims. This pilot two-arms RCT assessed the feasibility (adherence, safety and satisfaction) and provided preliminary insights into the clinical efficacy of the cognitive exergame Body-Brain Trainer (BBT) for cognitive neurorehabilitation of people with multiple sclerosis (pwMS). Methods. Twenty-four pwMS (18-65 years) with cognitive complaints and objective cognitive deficits were randomly allocated to the BBT intervention (n=12) or to an expectancy-matched active control group Mind-Body Trainer (MBT; n=12). Both groups attended 12 supervised in-lab sessions over four weeks. Cognitive and physical assessments were conducted at baseline and post-training. The primary outcome was the change in processing speed from baseline to post-training, measured with the Symbol Digit Modalities Test (SDMT). Secondary measures included patient-reported outcomes (PROMs) assessing everyday cognition (Multiple Sclerosis Neuropsychological Screening Questionnaire; MSNQ-s, Rating Scale of Attentional Behaviour; RSAB), fatigue (Modified Fatigue Impact Scale; MFIS) and quality of life (Multiple Sclerosis Quality of Life; MSQoL-54). Results. Adherence was high (91.67%) and no Serious Adverse Events (SAEs) were reported during the protocol. Participants in both groups reported high enjoyment (BBT: 7.2 ± 1.99; MBT: 6.58 ± 1.83) on a custom-made experience questionnaire (fun; 1 = not at all, 9 = extremely). Both the BBT and MBT groups improved on the SDMT, with mean increases of 2.5 (SD = 7.35, n = 10) and of 4.92 points (SD = 8.21, n = 12), respectively. Between-group analyses revealed no statistically significant differences (B = -2.48 [-8.25, 3.28], p = 0.42). Within-group analyses showed improvements for the BBT group in everyday cognition (MSNQ-s: B = -4.95, 95% CI [-8.42, -1.49], p = 0.006; RSAB: B = -5.68, 95% CI [-9.82, -1.54], p = 0.009), fatigue (MFIS total score: B = -10.92, 95% CI [-20.94, -0.89], p = 0.034) and quality of life (MSQoL-54, mental composite: B = 10.2, 95% CI [0.75, 19.65], p = 0.035). No statistically significant between-group differences were observed. Conclusion. This study confirms the feasibility of the BBT intervention among pwMS and shows promising preliminary results supporting the development of a larger confirmatory RCT. Moreover, these results highlight the value of PROMs as meaningful outcomes that, alongside objective measures, contribute to a more patient-centered assessment of improvements following cognitive neurorehabilitation.

Miftari, Arben

Idiopathic normal pressure hydrocephalus: A sulcal morphometry approach to brain phenotype and clinical response

Arben Miftari[1], Fabrizio Pizzagalli [2], Giulia Bommarito[1], Stéphane Armand[3], Frédéric Assal[3], Dimitri Van de Ville[4], Alessandra Griffa[5], Gilles Allali[1]

[1]Lausanne University Hospital and University of Lausanne, [2]University of Turin, [3]Geneva University Hospitals and University of Geneva, [4]EPFL, [5]Lausanne University Hospital, University of Lausanne, and EPFL

Introduction Idiopathic normal pressure hydrocephalus (iNPH), the leading cause of reversible dementia in the elderly, is characterized mainly by gait disturbances along with ventricular enlargement, and can be treated with shunting procedure. Neuroradiological features rely on visual assessment, including sulcal characteristics. This study applies automatic sulcal-based morphometry to characterize the iNPH sulcal phenotype and to distinguish iNPH patients who respond or not to the cerebrospinal fluid tap test (CSF-TT), a prognostic test to predict response to shunting. Methods The study included 32 patients (mean age: 78.9y / Females: 14) diagnosed with iNPH and 41 healthy controls (HC) (mean age: 74.9y / Females: 30). Quantitative gait assessments were performed before and after the CSF-TT to identify responders (Resp) and non-responders (nResp). Sulcal morphology was evaluated using MRI, focusing on depth, width, length, and surface area. A generalized linear model (GLM) identified the iNPH sulcal phenotype, and a Support Vector Machine (SVM) classifier was applied to distinguish iNPH patients from controls, as well as Resp from nResp. Results The GLM analysis identified sulcal depth and opening as the main features characterizing the iNPH phenotype, with respect to HC. Eight core sulci contributed the most, including compressed central, superior frontal, and frontal intraparietal bilateral sulci, as well as flattened left calcarine and posterior lateral fissures. An SVM classifier trained on these features effectively differentiated iNPH patients from HC (area under the curve (AUC): 0.933) but had limited accuracy for Resp vs. nResp (AUC: 0.556). Discussion/Conclusion This study identified an iNPH neuroradiological phenotype based on sulcal morphology, emphasizing depth and opening as key markers. An SVM classifier trained on these features accurately distinguished iNPH patients from HCs but was less effective for Resp vs. nResp. Further studies are needed to explore more advanced sulcal landmarks in iNPH.

Mijsters, Yannick

Loss of Sense of Agency Leads to Increased Apathy - Online and EEG Studies using the Effort-Based Decision Making Paradigm

Yannick Mijsters[1], Juan Carlos Farah[1], Fosco Bernasconi[1], Levi Goldberg[2], Serena Girard Nguetsop[1], Jevita Potheegadoo[1], Halima Rafi[1], Caroline Rouge[1], Pierre Vassiliadis[1], Friedhelm Hummel[1], Olaf Blanke[1]

[1]EPFL, [2]Middlebury College

Sense of agency, the feeling of controlling one's actions and their outcomes, is distorted in several neurodegenerative disorders. In this study, we explore the effects of loss of sense of agency on apathy, a transdiagnostic syndrome of amotivation linked to decreased reward sensitivity and resulting in a reduced acceptance rate during effort-based decision-making (EBDM) tasks. We hypothesize that loss of sense of agency decreases willingness to act, reflecting a state of increased apathy. To test this hypothesis, we ran an online study (n=81) and an EEG pilot study (n=4) in a healthy young sample using a validated EBDM task, where participants received offers to perform physical effort (i.e., keyboard tapping) for a reward, which they could accept or reject. We modified this task to manipulate sense of agency by adding a visuomotor conflict to the visual tapping feedback. Our study found a significant reduction in trial acceptance for the visuomotor conflict condition. This was confirmed in self-report results from participants, who indicated being in a state of increased apathy after blocks with visuomotor conflict. Additionally, subject who scored high on the self-initiation apathy trait (DAS) were more affected by the visuomotor conflict. No significant results were found in the EEG pilot, however, an increase in mu activity during visuomotor conflict was visible. Broadly, our results highlight the role of sense of agency disruptions in altering decision-making and motivation. This offers a new path for studying apathy in diseases like Parkinson's that have been linked to a reduced sense of agency.

Milanese, Paola Esther

Exploring noradrenergic signaling and sleep patterns in prodromal stages of Alzheimer's disease mouse models

Paola Milanese[1], Georgios Foustoukos[1], Lila Banterle[1], Laura M.J. Fernandez[1], Anita Lüthi[1]

[1]University of Lausanne

The onset of Alzheimer disease (AD) and the onset of abnormal sleep patterns are both signaled by initially minute but ultimately disastrous physiological malfunctions of the brain. Among these, the Locus Coeruleus (LC) is a key brain region affected in the initial stages of AD. The LC generates noradrenaline (NA) signals crucial for wake cognition and sleep architecture in mice. Understanding how sleep disturbances in AD relate to LC malfunctions could provide sensitive signatures to recognize the earliest stages of AD. We explore the real-time noradrenergic system functionality during AD's prodromal phase in APP/PS1 and AppNL-F/Mapt double knock-in (dKI) mice using two-site fiber photometric measurements in freely moving animals expressing biosensors neuronal CA2+ fluctuations in LC neurons projecting either to the thalamus or to CA1, and for free NA levels in respective projection areas. Combined with polysomnography (EEG/EMG), we record local field potentials (LFP) in the somatosensory cortex (S1) and CA1 to assess vigilance states in carrier and non-carrier mice spanning early and late disease stages. Preliminary findings suggest that during the late prodromal phase, EEG spectral properties during non-rapid eye movement sleep (NREMS) differ between genotypes. Additionally, APP/PS1 mice in late stages of the disease show a shortening of rapid-eye movement sleep (REMS) bouts accompanied by a heightened LC activity, suggesting disruption of the typical LC silencing occurring during REMS. In contrast, dKI mice over 1 year old do not show any sign of LC or sleep dysfunction nor signs of memory impairment, implying that this is too early a timepoint in the course of the disease for this model. Ongoing work will refine our AD models, and link findings to spatial memory performance and histological markers of AD. Decoding LC dysfunction patterns during AD's prodromal phase and their effects on sleep could prove essential to early diagnosis of AD and for potential interventions.

Molinuevo Gomez, Daniel

A brain-machine-interface approach for interrogating neural memory dynamics: mechanisms of directed memory recall during behavior

Daniel Molinuevo Gomez[1], James Priestley[1]

[1]EPFL

The hippocampus is a key brain region for the formation and consolidation of episodic memories. Place cells in the hippocampus are thought to provide a neural framework for the spatial and contextual organization of memories. Remarkably, neural activity dur- ing periods of rest often recapitulates the patterns of place cell activity recorded during behavior, and this “neural replay” is widely believed to be a biomarker of memory reacti- vation. Nevertheless, it remains largely unknown if replay is driven by intentional access of memory by the subject. We aim to bridge this knowledge gap by linking neural replay and volitional memory recall. We aim to test whether mice can actively control hippocampal replay events and use these dynamics to optimize memory-guided behavior. We will combine 2-photon calcium imaging and closed-loop, real-time analysis to develop a brain-computer interface, which will allow us to test whether replay can be used by mice to control a virtual reality system. This innovative approach has the potential to link neural replay and directed memory recall for the first time, and can transform our understanding of how hippocampal dynamics are engaged and controlled during memory recall and decision making.

Monney, Jonathan

The hidden patterns of single unit activity during IEDs

Jonathan Monney[1], Lora Fanda[1], Jules Veber[1], Laurent Spinelli[2], Shahan Momjian[2], Fiorenzo Artoni[3], Pierre Mégevand[4]

[1]Unige, [2]HUG, [3]UNIGE, [4]Unige, HUG

The neural dynamics of epilepsy, a condition which is estimated to affect over 50M people worldwide, remain in large part a mystery. While modern neurophysiological techniques allow for single unit recording in humans the elusive and unpredictable nature of seizures makes their repeated monitoring challenging at best. Interictal epileptiform discharges (IEDs), more frequent and regular, offer an alternative perspective in neuronal activity which may be linked to the activity observed at seizure onset. This research focused on data collected during continuous recording of iEEG signals in a single patient. Single unit activity was recorded by microelectrodes on a Utah Array placed beneath an electrocorticography grid in the vicinity of the seizure onset zone. Spike sorting was performed to identify single units and extract their continuous activity during IEDs using Kilosort 4.0. Our current findings display repeated and reliable changes in single unit spiking activity during IEDs. These results, when combined with those obtained from seizure onsets, could lead us to finding reproducible patterns of neuronal activation which in turn may become reliable biomarkers for seizure detection.

Moro, Andrea Stefano

The Contribution of the Right Inferior Frontal Gyrus to Inhibitory Control and Delay Discounting: Evidence from a Pilot Transcranial Direct Current Stimulation Experiment.

Moro AS (1), Saccenti D (1), Lamanna J (2), Ferro M(1)

1-Department of Psychology, Sigmund Freud University, Milan, Italy

2-Center for Behavioral Neuroscience and Communication (BNC), Vita-Salute San Raffaele University, Milan, Italy

Inhibitory control (IC) is a fundamental component of executive functioning, enabling the suppression of one's own cognitive and behavioral responses. Although IC exerts substantial effects on both everyday life and clinical settings, its neural underpinnings and relationship with other higher-order cognitive functions remain poorly understood. The right inferior frontal gyrus (rIFG) has been proposed as a potential target for neuromodulation, given its putative role in the inhibition of premature or maladaptive motor responses. In this study, we applied transcranial direct current stimulation (tDCS) over the rIFG in healthy participants, each undergoing two experimental sessions — one with active stimulation and one with sham stimulation. Prior to stimulation, participants completed the Metacognitions Questionnaire-30 and a Monetary Intertemporal Choice Task (MICT) to assess delay discounting (DD). During stimulation, subjects performed the Go/No-Go task (GNGT) and the Stop-Signal Task (SST) to evaluate IC. Following stimulation, they repeated the MICT. Linear mixed-effects models showed that anodal tDCS over the rIFG enhances IC when assessed using the SST but not when measured with the GNGT. Furthermore, active tDCS reduced DD compared to sham stimulation. Although a negative correlation has been detected between positive beliefs about thinking and IC, no significant associations were observed between IC and DD. These findings not only suggest that both IC and DD engage the rIFG but also pave the way for future research on the efficacy of tDCS in reducing DD and enhancing IC in psychological conditions where these higher-order cognitive functions are impaired, such as mood disorders and substance addiction.

Mota Caseiro, David Alexandre

Oxytocinergic modulation of central lateral amygdala network dynamics underlying social buffering of fear

David Alexandre Mota Caseiro, Ruifang Niu, Erwin van den Burg, Ron Stoop

UNIL/CHUV

The neuropeptide oxytocin is a key mediator of fear reduction in the presence of a companion. This is known as social buffering of fear (SBF). We found that oxytocin in the central lateral amygdala (CeL) activates buffer and inhibits fear neurons suggesting that oxytocin alters local network dynamics to induce SBF. Furthermore, oxytocin is necessary for SBF memory, so that SBF remains effective even in the absence of the companion. However, the precise CeL microcircuit underlying SBF is not known. Here we aim to determine how oxytocin brings about SBF and its memory in the CeL network by using transgenic rats expressing CRE in oxytocin receptor (OTR)-expressing cells. We found that the highly specific OTR agonist TGOT indeed excites fluorescently labelled OTR cells by patch clamp electrophysiology, demonstrating the validity of the transgenic rat line. Next, we retrogradely labelled CeL neurons that project to the parabrachial nucleus (PBN) and found that OTR cells in majority do not project to the PBN directly, and may thus contact the PBN indirectly through PBN projectors. Indeed, TGOT had either excitatory or inhibitory effects on PBN projectors, as evidenced by decreased or increased inhibitory postsynaptic currents (IPSCs), respectively. As OTRs are expressed in GABAergic cells, this suggests that OTR cells directly inhibit or indirectly disinhibit PBN projectors. The opposite effects of TGOT on PBN projectors indicate a complex local microcircuitry that may be involved in SBF. Future optogenetic and molecular experiments will test this and also address the role of CeL-PBN connections in SBF. This research project aims to investigate how oxytocin modulates the circuitry of the central lateral amygdala (CeL) to reduce fear in the presence of a companion. We hypothesize that oxytocin acts on specific neuronal populations within the CeL to alter the balance of excitatory and inhibitory signalling, thereby attenuating fear responses. Using a combination of electrophysiological, chemogenetic and optogenetic techniques, we will explore how oxytocin modulates CeL neuronal circuits and their downstream effects to other brain regions important for the expression of fear such as the parabrachial nucleus (PBN). Up to now, we have seen a modulation in activity of OTR+ cells and projecting cells to PBN within the CeL under TGOT administration. Understanding these interactions could provide insights into novel therapeutic approaches for anxiety and pain disorders, emphasizing the role of social and neurochemical factors in emotional regulation. This project will contribute to the broader understanding of how neuropeptides like oxytocin can modulate complex brain networks involved in fear and pain, highlighting the CeL-PBN pathway as a potential target for intervention.

Mousavi, Maryam

Investigating the effects of gut microbiota-derived metabolite administration in a mouse MCAO stroke model

Maryam Mousavi [1,2], Lara Buscemi [1,2], Julia Castillo González [1,2], Melanie Price [1,2], Lorenz Hirt [1,2*]
[1]Department of Clinical Neurosciences, Lausanne University Hospital (CHUV),1011 Lausanne, Switzerland;
[2]Department of Fundamental Neurosciences, University of Lausanne, 1005 Lausanne, Switzerland

The complex bidirectional crosstalk between the gut microbiota and brain, referred to as the microbiota-gut-brain (MGB) axis, plays a critical role in regulating the host's immune and circulatory systems, as well as metabolism. Emerging studies have highlighted the significant impact of the gut-brain axis and gut microbiota-derived metabolites in modulating neurological disorders, including stroke. In this study, we investigated the therapeutic potential of pre- and post-treatment with Tauroursodeoxycholic acid (TUDCA), a secondary bile acid conjugated with taurine, on the progression of stroke outcome in a rodent model of middle cerebral artery occlusion (MCAO). Furthermore, we evaluated the effects of D-lactate, a lactate isomer mainly produced by gut bacteria, following the same experimental approach. For both compounds, we conducted different sets of experiments where mice received either the metabolite candidates (TUDCA or D-lactate) or vehicle (PBS) via the tail vein either before or after MCAO. Lesion volume was measured using cresyl violet staining, and neurological function was evaluated using the 28-point neuroscore in treated animals. In addition, the integrity of the blood-brain barrier was determined by immunofluorescence staining. Our data showed no significant differences in infarct volume and behavioural outcome assessments between the TUDCA- and PBS-treated groups. Similarly, no significant differences were detected in the D-lactate experiments. Our present data suggest that treatment with TUDCA or D-lactate did not exert neuroprotective effects in the mouse MCAO model. We are currently testing another promising gut bacteria metabolite in our model.

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Nadav, Tehila

The ADHD Emotion Trap: Is It Reactivity or Attention?

Nadav T (1), Henik A (1)

1-Department of Psychology, Sigmund Freud University, Milan, Italy

2-Center for Behavioral Neuroscience and Communication (BNC), Vita-Salute San Raffaele University, Milan, Italy

Emotional dysregulation (ED), is a core feature of ADHD, affecting functioning and well-being. Individuals with ADHD exhibit enhanced reactivity to emotional stimuli, which may make it harder for them to flexibly transition between emotional states in daily situations. These difficulties likely stem from deficits in emotional and attentional processing, making emotional regulation more effortful. To examine these processes, we conducted two studies using a Picture-Picture Priming Task. Study 1 included 30 adults with ADHD and 30 neurotypical controls who evaluated the valence of a target picture preceded by a prime (100 ms). Primes varied in valence (positive/negative/neutral), creating congruent, incongruent, and neutral conditions. Results showed that ADHD participants had greater difficulty transitioning between emotions, particularly when a negative prime preceded a positive target. Study 2 (N=70, 35 ADHD) replicated these findings and examined the role of attentional functioning. Attentional abilities were assessed via self-reports and an attention task. Our findings highlight the interplay between emotional and attentional processes in ADHD and the need to consider both domains when developing interventions for ED.

Neugebauer, Simon

Developing Biomarkers of Negativity Bias: An RDoC-Informed Study Integrating Electrophysiology, Neuroendocrine, and Neuroplasticity Markers.

Neugebauer S (1), Schreiber R (1), Kox J (1), Vrijsen J (2, 3, 4)

(1) Section of Psychopharmacology, Neuropsychology and Psychopharmacology, Faculty of Psychology and Neuroscience, Maastricht University, Maastricht, The Netherlands
(2) Department of Psychiatry, Radboud University Medical Centre, Nijmegen, The Netherlands
(3) Donders Institute for Brain, Cognition, and Behaviour, Nijmegen, The Netherlands
(4) Depression Expertise Centre, Pro Persona Mental Health Care, Nijmegen, The Netherlands

Background: Negativity bias, a pervasive tendency to prioritize negative information and transdiagnostic symptom across emotional disorders, involves aberrant corticolimbic connectivity and cognitive rigidity. An RDoC-informed understanding of its neurobiology is vital for targeted interventions. Hypothesized mechanisms include altered prediction error processing, reduced prefrontal and hippocampal neuroplasticity, and dysregulated corticolimbic dynamics involving excessive amygdalohippocampal signaling and impaired prefrontal control. This study seeks reliable neurocognitive, physiological, and molecular markers of negativity bias in healthy individuals, examining modulation by acute stress.

Methods: We will conduct an RDoC-informed study in healthy volunteers stratified by high trait negativity bias (Negative Cognitive Processing Bias Questionnaire; NCPBQ). To examine state-dependent changes, negativity bias will be induced using the Maastricht Acute Stress Test (iMAST). Pre- and post-iMAST assessments will include EEG event related potential components (ERPs) (RewP and FRN) elicited during a probabilistic reinforcement learning task, salivary cortisol levels measured repeatedly to index HPA axis reactivity, the NCPB scale, state mood/stress measures (VAS), and plasma Brain-Derived Neurotrophic Factor (BDNF) levels.

Expected Results: We hypothesize that: 1) Individuals with high trait negativity bias will exhibit blunted RewP, potentiated FRN and behavioral learning biases. 2) Cortisol reactivity will correlate with baseline negativity bias scores and stress-induced changes in EEG and behavioral markers. 3) Baseline plasma BDNF levels will correlate inversely with trait negativity bias and potentially show modulation following acute stress.

Conclusion: By examining specific ERP components linked to prediction error processing alongside HPA axis reactivity and a peripheral marker of neuroplasticity (BDNF), this study employs a multi-level RDoC approach to identify robust biomarkers of negativity bias. These findings will provide a mechanistic foundation for future studies investigating targeted interventions.

Nguyen-Duc, Jasmine

Exploring functional connectivity and resting-state networks within isotropic ADC-fMRI

Jasmine Nguyen-Duc[1], Arthur Spencer[1], Jean-Baptiste Perot[1], Inès de Riedmatten[1], Filip Szczepankiewicz[2], Ileana Jelescu[1]

[1]CHUV, UNIL, [2]Lund University

Resting-state (RS) fMRI [1] captures coherent spatial patterns known as Resting State Networks (RSNs) [2], characterised by synchronous Blood Oxygen Level-Dependent (BOLD) fluctuations [3]. Functional connectivity (FC) analysis typically shows strong correlations among grey matter (GM) regions within RSNs. Some studies have extended FC analysis to include white matter (WM) [4–6], although this remains challenging with BOLD-fMRI due to limited WM vasculature and delayed hemodynamic response functions (HRFs) [5]. To address these limitations, recent works have explored Apparent Diffusion Coefficient (ADC)-fMRI, which is independent of vascular signals and equally sensitive to neural activity in GM and WM [7–9].

In this work, we study ADC-fMRI in RS and compare the results with BOLD-fMRI. We investigate RSNs using Independent Component Analysis (ICA) and FC within both modalities. For this, we used diffusion spherical tensor encoding [11] with full brain coverage. The data was acquired from 13 subjects. Preprocessing followed [10], and FC matrices were computed using Pearson correlations between and accross GM [Desikan-Killiany] and WM [Juelich] ROIs, retaining only positive values.

Among the strongest connections, BOLD exhibited a greater number of GM-GM interactions whereas ADC-fMRI showed more WM-GM interactions. RSNs identified by ICA largely overlapped across modalities, though ADC components appeared more fragmented, possibly due to lower SNR.

Despite weaker overall correlations, ADC-fMRI captured consistent RS patterns and showed more WM-GM links than BOLD. These findings support ADC-fMRI as a promising tool for RS studies with enhanced sensitivity to WM involvement.

Nickl, Peter

Robust and Adaptive Planning Through Uncertainty Decomposition

Alexandre Pouget[1], Peter Nickl[1]

[1]University of Geneva

Planning in stochastic environments poses a significant challenge in reinforcement learning, particularly when relying on imperfect world models and limited data. Such settings require solutions that are robust to uncertainty and sample-efficient.

We propose a planning agent that evaluates actions through probabilistic rollouts from a learned world model. Our approach explicitly decomposes predictive world model uncertainty into aleatoric (inherent data noise) and epistemic (model uncertainty) components. Empirical results show that optimal frequency of planning and the length of rollouts depend on these uncertainties. We suggest leveraging this insight to adaptively adjust planning frequency and planning horizon at decision time, enabling robust decision-making under resource constraints.

This computational framework offers a normative account of robust and adaptive planning under uncertainty, with potential links to hippocampal preplay phenomena observed in navigating mice. We hypothesize that natural agents may similarly use dual uncertainty to guide resource-efficient, flexible planning.

Nonni, Martina

Emotion components and fMRI: validating a VR video game paradigm testing Expectation and Uncertainty

Martina Nonni[1], Emmanuel Badier[1], Yvain Tisserand[1], Patrik Vuilleumier[1]

[1]University of Geneva

The generation and nature of emotions and emotional episodes continue to be subjects of active debate in the literature, but prevailing theories seem to suggest their multicomponent nature. This project aims to establish links between the multiple components of emotions and functional brain systems by developing and validating a novel procedure that actively elicits emotions in a naturalistic and dynamic manner. Drawing inspiration from appraisal models of emotion causation, we designed an interactive, first-person perspective video game task to be experienced in virtual reality to acquire fMRI data. The task was newly integrated for an fMRI study, with the current focus of manipulating expectation, uncertainty and goal congruence appraisals to link in-game events with specific emotional responses (physiological measures such as respiration, heart rate, skin conductance, and brain activity). Here, behavioral validation results show that manipulating expectation and uncertainty appraisals significantly influences self-reported emotion ratings, indicating that emotional preferences are condition-dependent. Preliminary imaging data will be presented.

Notario Reinoso, Anais

Long-term effects of adolescent cannabinoid receptor activation on adult prefrontal cortex function and behaviour.

Notario Reinoso A. (1), Z.Smit (1), H.W.Kessels (1), P.J.P. Chameau (1)

(1) Swammerdam Institute for Life Sciences, University of Amsterdam

Cannabis consumption, particularly among adolescents, has increased significantly over the past decades. Adolescence is a critical period for brain development, during which the prefrontal cortex (PFC) undergoes maturation. Strong evidence suggests that the endocannabinoid system plays a key role in regulating brain development and the maturation of the PFC during this stage. However, the long-term consequences of chronic cannabinoid receptor activation during adolescence on PFC function and associated behaviors remain largely unexplored. Here, we show that repeated administration of the cannabinoid receptor agonist WIN55,212-2 during adolescence induces sex-specific long-term alterations in synaptic transmission, cellular properties, and network activity of layer 5 neurons in the infralimbic and prelimbic areas. However, PFC-dependent behaviors, such as social hierarchy and reversal learning, remained unaffected. In conclusion, our findings demonstrate that repeated cannabinoid receptor activation during adolescence disrupts normal PFC development in a sex-specific manner. These results underscore the long-term, sex-dependent risks of adolescent cannabis use and provide insights into neural adaptations to cannabinoid exposure during this critical developmental period.

Orban Szigeti, Boglarka

Theta-burst TMS in schizophrenia to ameliorate negative and cognitive symptoms: a double-blind, sham-controlled, randomized clinical trial.

Orban Szigeti Boglarka, Janos Rethelyi, Gabor Csukly

Semmelweis University Budapest

Schizophrenia is a major mental disorder that affects approximately 1% of the population worldwide. Social cognition impairments and negative symptoms such as blunted affect or emotional withdrawal strongly contribute to the psychosocial functioning deficits and long-term disability in schizophrenia. The state-like and trait-like components of social cognition are impaired in schizophrenia

Objectives: Treatment effects of conventional approaches with antipsychotics or psychosocial interventions are limited when it comes to reducing negative and cognitive symptoms in schizophrenia. While there is emerging clinical evidence that new, augmented protocols based on theta-burst stimulation can increase rTMS efficacy dramatically in depression, data on similar augmented therapies are very limited in schizophrenia. The different patterns of network impairments in subjects may underlie that some but not all patients responded to given stimulation locations.

We propose an augmented theta-burst stimulation protocol in schizophrenia by stimulating both locations connected to negative symptoms, namely the vermis of the cerebellum and the left Dorsolateral Prefrontal Cortex (DLPFC). Ninety subjects with schizophrenia presenting negative symptoms and aging between 18-50 years will be randomized to active and sham stimulation in a 1:1 ratio. The TBS parameters we adopted follow the standard TBS protocols, with 3-pulse 50-Hz bursts given every 200 ms (at 5 Hz) and an intensity of 100% active motor threshold. We plan to deliver 1800 stimuli to the vermis and 1800 stimuli to the left DLPFC daily in two 9.5-minute blocks for four weeks. Results: The primary endpoint is the change in negative symptom severity measured by the Positive and Negative Syndrome Scale (PANSS). The safety outcome is the number serious adverse events.

Pajot, Clémentine

Role of Ephrinb3 in POMC neurons in the control of energy balance

Clémentine Pajot[1], Gwenaël Labouèbe[1], Léa Camelot[1], Angélique Vaucher[1], Esther Landaluce Iturriria[1], Isabel Lopez-Mejia[1], Manuel Mameli[1], Bernard Thorens[1], Sophie Croizier[1]

[1]University of Lausanne

Today, one in eight people in the world is obese, which can result in comorbidities such as diabetes or pre-diabetes, characterized by insulin resistance and glucose intolerance. However, the mechanisms leading to this onset remain to be elucidated. In the brain, proopiomelanocortin (POMC) neurons have been primarily described as regulating feeding behaviour. Nevertheless, mounting accumulating evidence also highlights the pivotal role of these neurons in the control of glucose homeostasis. The present project aims to elucidate novel mechanisms underlying the control of energy and glucose homeostasis through the synaptic plasticity of POMC neurons, and subsequently their activity. A recent study conducted within our research group demonstrated that modulation of EphrinBs (EphrinB1, B2, B3) proteins, which are well-known actors in the formation and plasticity of glutamatergic synapses, resulted in a reduced number of glutamatergic inputs into POMC neurons. This, in turn, led to impaired glutamatergic-dependent activity and insulin secretion in response to hyperglycemia. In order to ascertain the role of EphrinB3 in the control of synaptic plasticity of POMC neurons, we silenced (Pomc-Efnb3-KD) Efnb3 (gene encoding EphrinB3) in POMC neurons of adult male mice by means of stereotactic viral infusion and exposed the animals to a high-fat high-sucrose diet (HFHS), a potent modulator of synaptic plasticity of POMC neurons. Interestingly, Pomc-Efnb3-KD male mice showed decreased glial coverage surrounding POMC neurons associated with greater body weight gain and fat mass accumulation compared to control mice. Ultimately, this project identified a novel role of EphrinB3 in the regulation of POMC neurons adaptability to metabolic disorders.

Panzeri, Alessandra

Cardiac interoception and insular cortex: a pathway to understanding social deficits in Autism

Alessandra Panzeri[1], Camilla Bellone [1]

[1]University of Geneva

Interoception, the brain's ability to process internal bodily signals, plays a crucial role in regulating physiological states and adaptive behavior. The insular cortex, particularly its posterior region (pIC), is a key hub for integrating interoceptive and sensory information. Disruptions in these processes have been implicated in neurodevelopmental conditions, including autism spectrum disorder (ASD), where altered sensory integration and autonomic regulation are observed. This study investigates how neuronal populations within the pIC encode interoceptive signals and their role in shaping behavior. Using a combination of in vivo imaging, behavioral paradigms, and physiological recordings in a mouse model, we examine the relationship between neural activity and cardiac dynamics in both typical and altered conditions. By identifying the circuits involved in interoceptive processing, this research may provide insights into mechanisms underlying sensory and social deficits in ASD and related disorders.

Pascarella, Silvia

How early life adversity reshapes the cerebellum

Pascarella Silvia (1), Pellegrino Lippiello(1), Floriana Volpicelli(1), Luisa Speranza(1), Maria Grazia Ferraro(2), Claudia Cristiano(1), Maria Concetta Miniaci(1)

(1)Department of Pharmacy, School of Medicine and Surgery, University of Naples Federico II, Italy

(2)Department of Molecular Medicine and Medical Biotechnology, School of Medicine and Surgery, University of Naples Federico II, Italy

Exposure to early life stress (ELS), can negatively influence brain development and functions, increasing vulnerability to neuropsychiatric disorders in adulthood, such as anxiety, depression, and attention-deficit/hyperactivity disorder, as well as increased reactivity to stress, drug abuse vulnerability, and personality disorders. A particularly vulnerable brain region to ELA is the cerebellum (Cb) since it exhibits a high density of glucocorticoid receptors during early development and a prolonged developmental timeline, wherein neurogenesis and synaptogenesis occur extensively after birth. Using a multidisciplinary approach, we have examined the effects of maternal separation (MS), a model of ELS, on the Cb at functional, structural, and molecular levels in juvenile, adolescent, and adult offspring. Behavioral tests were performed to assess the neuropsychiatric phenotypes of MS mice. Structural analysis of Purkinje cells in cerebellar slices, through biocytin labeling, revealed that MS causes significant alteration of dendritic arborization. Patch-clamp recordings from cerebellar slices demonstrated that MS affects long-term synaptic plasticity, i.e., long-term potentiation and depression, at parallel fiber-Purkinje cell (PC) synapses.

Using quantitative PCR and western blot analysis, we investigated the molecular alterations induced by MS. Specifically, we examined BDNF, a neurotrophic factor essential for neuronal growth and plasticity, ERK, a key component of the BDNF signaling pathway, and on CREB, a transcription factor involved in synaptic plasticity.

These results provide new insights into the cellular and molecular mechanisms suggesting that early life stress may alter the proper development of the cerebellar neural circuits during a critical and sensitive period.

Pascucci, Alessandro

Atypical Glymphatic Development and Excitation/Inhibition Imbalance in 22q11.2 Deletion Syndrome: A Pathway to Psychosis Risk

UNIGE

Background: Emerging evidence suggests that impairment of the glymphatic system and brain clearance may contribute to altered brain development and increased vulnerability to psychiatric conditions such as psychosis. In particular, altered glymphatic efficiency may disrupt neurochemical homeostasis during critical periods of brain maturation, resulting in brain structural and circuit alterations and elevating risk for psychosis. However, the relevance of glymphatic function to early neurodevelopmental risk trajectories remains largely unexplored. Methods: We combined longitudinal diffusion tensor imaging (DTI) and magnetic resonance spectroscopy (MRS) in individuals with 22q11.2 deletion syndrome (22q11DS), a neurodevelopmental condition associated with elevated psychosis risk. Glymphatic function was estimated using the diffusion tensor image analysis along the perivascular space (DTI-ALPS) index, based on both manual and automated ROI placement methods. Excitation/inhibition (E/I) balance was assessed in the right hippocampus via CSF-corrected GABA and Glx levels. Linear mixed-effects models tested group and age effects on ALPS trajectories, and linear regressions examined associations between ALPS and Glx/GABA ratio. Results: Glymphatic efficiency was significantly reduced in 22q11DS compared to matched controls, particularly in the right hemisphere ($p = 0.022$). These group-level differences were replicated using an atlas-based automated ROI placement pipeline, supporting the robustness and reproducibility of the finding. Individuals with positive psychotic symptoms (PPS+) showed a divergent developmental trajectory, failing to exhibit the age-related ALPS increase observed in PPS− participants (group × age interaction: $p = 0.009$ for the average index). In a subset with spectroscopy data ($n = 39$), lower ALPS index predicted higher Glx/GABA ratio in the right hippocampus ($p = 0.002$ for average index). Conclusions: These findings provide initial in vivo evidence that glymphatic dysfunction emerges early in neurodevelopment and follows atypical developmental trajectories in those at risk for psychosis. Moreover impaired clearance is associated with excitatory/inhibitory imbalance. The glymphatic system dysfunction may represent an additional pathway contributing to psychosis vulnerability and could serve as a potential target for early intervention.

Patsourakos, Vasileios

Optogenetic therapy to treat spasticity in a mouse model of spinal cord injury

Vasileios Patsourakos [1], Steven Ceto [2], Kangling Wu[3], Sriparma Ghosal [2], Ivana Gantar[4], Jocelyne Bloch[1], Gregoire Courtine[3], Stephanie Lacour [3], Thomas H. Hutson[5]

[1]University of Lausanne , [2]Wyss Center for Bio and Neuroengineering, [3]École Polytechnique Fédérale de Lausanne, [4]Wyss Center for Bio and Neuroenigneering , [5]Wyss Center for Bio and Neuroengineering

Spasticity is a sensorimotor condition that presents a unmet clinical need and affects more than 12 million people world-wide. It is highly prevalent in a number of neurological conditions, affecting 79% after spinal cord injury, 85% with cerebral palsy, 35% after stroke and 80% of patients with multiple sclerosis. Current treatments are often ineffective due slow pharmacokinetics, increased tolerance or unspecific side effects. Consequently, novel treatments with higher spatiotemporal precision are urgently needed. To achieve this we are developing an optogenetic therapy for spasticity. This therapy involves two components, firstly, a motor neuron targeted gene therapy to deliver light-sensitive inhibitory opsins to spinal motor neurons. We have achieved retrograde transduction of motor neurons that innervate spastic muscles via intramuscular injections and targeted expression of opsins in spinal motor neurons. Secondly, an implantable optoelectronic nerve cuff, which is soft and stretchable and contains micro-LEDs for optical stimulation of the sciatic nerve. Optical stimulation is triggered in closed-loop using muscle activity recordings to detect spasms which are then mitigated by optical-stimulation. We demonstrate efficient optogenetic inhibition of muscle activity in uninjured mice and are now characterising a spinal cord injury model of spontaneous hindlimb spasticity using chronic muscle activity recordings to assess hyperreflexia. Successfully treating spasticity and hyperreflexia in a spinal cord injury model will validate the efficacy of the optogenetic strategy, providing a first step towards clinical translation. Harnessing the power of cell-targeted gene therapies coupled with implantable, bio-compatible optoelectronic devices holds the promise of transforming lives of individuals with a range of neurological disorders. By modifying the gene therapy component, the same optoelectronic strategy has the potential to manage other peripheral nervous system conditions, including the control of micturition, alleviation of pain, and the facilitation of motor function.

Pavan, Tommaso

Voxel-Based Normative Modelling of Brain Microstructure with GAMLSS

UNIL

Introduction: In the normative modelling framework, individual differences are mapped to a reference level defined as the “norm” (Rutherford, 2022). The normative reference is estimated on a large cohort of healthy participants to predict a response variable (metric of interest) from a set of explanatory variables (e.g. age, sex), to which the observed empirical value of any individual (e.g. early psychosis (EP) patient) is compared.Generalized Additive Models for Location Scale and Shape (GAMLSS) is a univariate distributional regression framework that allows modelling any non-Gaussian distribution, accounting for location, scale, skewness and kurtosis (Dinga, 2021). GAMLSS has long been used for normative modelling of brain volumes (Bethlehem, 2022) and by the World Health Organization for growth charts (Onis, 2007). Here, we present an optimized R package: “VBGAMLSS” to flexibly apply GAMLSS to voxel- or vertex-wise neuroimaging data for individual level-analysis, and we demonstrate an application to diffusion MRI data from the Human Connectome Project (HCP, Van Essen, 2013) and our psychosis cohort (LSP). Methods: VBGAMLSS builds on the gamlss2 R package (Rigby, 2005), parallelizing and optimizing it for voxel/vertex computations, also featuring cross-validation (CV), segmentation-aware modelling, and an integrated high-performance computing cluster submission/monitoring system. As demonstration of our package, MRI data from 2033 healthy participants from 6 datasets (304 HCPdevelopment, 512 HCPaging, 1032 HCPyoung-adults, 56 HCPearly-psychosis, 59 LSPPrisma, and 70 LSPTrio) aged 15 to 70 years old, were used to generate 55 age-specific multimodal templates using ANTs. Template generation uses T1w, fractional anisotropy (FA), and white and gray matter segmentation maps. Age-specific templates were used to form a final template across ages, where every healthy subject white matter (WM) mean diffusivity and kurtosis maps (MD, MK; Jensen, 2010) were projected to. This approach allows the prediction of expected values in template space and computation of z-scores in native space. To model MD and MK as a function of age, sex, dataset, and brain volume for each WM voxel, we used SHASH distribution (Jones & Pewsey, 2009). Fourteen models were considered, from which we selected the best across folds and WM voxels by running a 5-fold CV, and ranking models based on best model frequency, minimum global deviance (GD=-2log(L)) and Akaike Weights (Wagenmakers & Farrell, 2004). Finally, we estimated the z-scores for MD and MK maps in EP patients from the HCPearly-psychosis dataset (N=112) in both native and template space. Results: The CV model selection settled on a model including three smooth effects, one for age per sex and one for the brain volume, while dataset/study effects were corrected via a random intercept for dataset). In our application, at individual EP patient level, the genu of the corpus callosum and anterior corona radiata showed elevated MD ($z>0$) and reduced MK ($z<0$). At group level, the pattern was more pronounced, though with high variability across patients. Finally, a highly negative z-score rim can be noticed around the ventricles in the average-patient MK z-score map, possibly indicating ventricular enlargement.

Paź, Marta

Aging enhances self-referential processing

Paź Marta and Anna Nowicka

Laboratory of Language Neurobiology, Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland

Adaptive behavior in social interactions requires the effective processing of conflicting emotional information. The impact of expectancy on conflict processing remains a relevant research question. This EEG/ERP study investigated the influence of primed expectancy on conflict processing using the Emotional Stroop paradigm and variants where expectancy was introduced. Neurophysiological and behavioral data were collected from 20 healthy participants who completed three variations of a Classical Emotional Stroop neural responses were compared to those based on the same paradigm but in the presence of prior expectancy cues derived from facial expression or emotional letter labels. N400 and Slow Potential neural responses were consistent with previous findings during the classical Emotional Stroop condition. However, significant changes in conflict processing were observed under expectancy conditions, differing between face and letter emotion cues. Parietal alpha and beta power decreases occurred specifically for face expectancy cues, which were attenuated by conflict processing. Behaviorally, expectancy conditions produced higher hit rates compared to the classical Emotional Stroop. These findings suggest that attentional resources are differently prioritized by face versus letter emotion expectancy cues, with face driven expectancy generating distinctive neurophysiological patterns and facilitating subsequent conflict resolution.

Peithi, Amalia

Neuroanatomical investigation of hippocampal structure in a mouse model of Williams syndrome

Amalia Peithi[1], Stéphanie Dijkhuizen[2], Laurens W.J. Bosman[2], Chris I. De Zeeuw[2], Pamela Banta Lavenex[3], Pierre Lavenex[1]

[1]University of Lausanne, [2]Erasmus MC Rotterdam, [3]UniDistance Switzerland

Williams syndrome (WS) is a rare neurodevelopmental disorder of genetic origin with a unique cognitive and behavioral profile. It has an incidence of 1 in 7,500 – 20,000 live births and is due to a hemizygous deletion of about 26 genes on chromosome 7. Individuals with WS exhibit severe visuospatial and allocentric spatial learning deficits. These hallmark characteristics raise questions about the neurobiological substrates of cognition in WS. Behavioral and neuroimaging studies indicate functional alterations in the hippocampus of individuals with WS, a critical region for episodic memory and spatial navigation. Here, in order to gain deeper insight on the impact of the WS hemideletion on hippocampal structure, we provide quantitative data on the cellular organization of the hippocampus in a mouse model replicating the hemideletion found in more than 90% of individuals with WS. We implemented design-based stereological techniques on 50-µm thick Nissl-stained brain sections to provide estimates of the volume, neuronal number and soma size of the main hippocampal regions of mutant and wild type mice. Initial findings show that mutant mice exhibit a lower number of granule cells in the dentate gyrus and an overall smaller volume of the dentate gyrus, mainly due to a smaller molecular layer. These findings reveal that the WS hemideletion impacts the structural integrity of the hippocampus, and contributes to elucidating the genotype-phenotype relationship in individuals with WS.

Pereira Da Silva, Sayonara

Implications of cognitive reserve for APOE-related Alzheimer's risk: A systematic review

Sayonara Pereira da Silva[1], Charikleia Lampraki[1], Tainá dos Santos Rêgo[2], Paolo Ghisletta[1], Matthias Kliegel[1], Jürgen Maurer[3], Matthias Studer[1], Élvio Rúbio Gouveia[4], Marcelo de Maio Nascimento[5], Andreas Ihle[1]

[1]University of Geneva, [2]University Hospital Zurich / ETH Zurich, [3]Universtiy of Lausanne, [4]University of Madeira, [5]University of Vale do São Francisco

Alzheimer's disease (AD) is marked by progressive neuropathological changes in the brain, resulting in a gradual decline in cognitive functioning. AD etiology is multifaceted, encompassing genetic factors, aging, lifestyle, environmental exposures, and other factors that may interact to influence disease progression. Modifiable life experiences, such as educational attainment, occupational complexity, and engagement in leisure activities, are known proxies for cognitive reserve (CR) and may modulate the APOE genetic predisposition to AD. This study systematically investigated the literature on the interplay between APOE-related AD risk and CR, synthesizing evidence on their combined impact on AD development. Comprehensive online searches in PubMed and Web of Science databases yielded 33,861 references, of which 15 studies involving human participants with AD diagnoses met all predefined criteria. The included studies exhibited considerable heterogeneity in methodological design, operationalization of CR proxies, and outcome measures. The publications presented mixed results: seven studies supported a protective effect of CR in mitigating genetic risk, four reported adverse interactions, and four detected no significant relationship. Discrepancies among results can be partly attributed to the methodological limitations of relying on single proxy measures, which may not sufficiently represent the multifaceted nature of CR. Overall, the evidence suggests that interventions aimed at enhancing CR may be especially beneficial for individuals with genetic vulnerability to AD. The implications of these findings for CR and aging research as well as for public health policies are discussed in detail in the published study: https://doi.org/10.1016/j.arr.2025.102809.

Perrin, Florian

Intracerebral EEG investigation of the Heartbeat Evoked Response across vigilance states in human

Florian Perrin 1,2, Marzia De Lucia 2, Philippe Ryvlin 1

1 : NeuroDigital@NeuroTech, Clinical Neuroscience Department, University Hospital (CHUV).
2 : Brain-Body and consciousness laboratory, University Hospital (CHUV) and University of Lausanne (UNIL), Lausanne, Switzerland

Over recent years, the critical role of body-brain interactions in the emergence of consciousness has gained increasing recognition. In this context, brain-heart interactions have been proposed as potential biomarkers of consciousness levels, with Heartbeat-Evoked Responses (HERs)—neural responses to heartbeat—being linked to perceptual consciousness, bodily self-awareness, and the presence of residual consciousness in brain-injured patients. HERs have been primarily studied using scalp EEG during wakefulness, where they have been associated with a widespread network of cortical regions. However, their neural mechanisms during altered states of consciousness, such as sleep, remain largely unexplored. Additionally, the lack of standardized methodologies to distinguish HERs from cardiac-related artifacts has hindered our understanding of their underlying network. Here, we investigate HERs across vigilance states using intracranial EEG (SEEG). This approach offers unmatched temporal and spatial resolution, enabling a more precise characterization of the neuronal response to heartbeat and its underlying network. We analyzed intracranial recordings from N = 10 epileptic patients undergoing SEEG for presurgical evaluation. HERs were extracted during wakefulness and sleep stages (N2, N3, and REM) by averaging peristimulus epochs time-locked to the R-peak of the heartbeat. Our results reveal that HERs are consistently present across all vigilance states, with the insula emerging as a key neural source of this evoked potential. These findings highlight the critical role of the insula in cardiac signal processing across sleep and wakefulness and advance our understanding of brain-heart interactions across different states of consciousness.

Petrova, Teya

Brain dysconnectivity and cognitive impairment in early psychosis: interplay between nature and nurture

Teya Petrova[1], Federico Luchetti[2], Edgar Céléreau[1], Yasser Alemán-Gómez[1], Giorgio Pistis[1], Pascal Steullet[1], Raoul Jenni[1], Lilith Abrahamayan-Empson[1], Philippe Conus[1], Luis Alameda[3], Paul Klauser[1]

[1]CHUV, [2]CHU, [3]King's College London

Processing speed (PS) impairment is one of the most common and severe cognitive deficits in schizophrenia, related to poor clinical outcome and impacting other cognitive domains. Previous research has reported correlations between PS and white matter diffusion properties, particularly generalized fractional anisotropy (gFA), suggesting that white matter alterations could underlie decreased PS. Schizophrenia is known to arise from a complex interaction of genetic and environmental factors. Among environmental factors, childhood adversities, including subtypes of abuse (sexual/physical/emotional) and neglect (physical/emotional), have been linked to a higher risk for psychosis, increased symptom severity and greater functional impairment. Genetically, schizophrenia is highly heritable and has a polygenic basis. Genome-wide association studies have provided novel insights into the etiology of schizophrenia capturing the combined effects of many genetic variants through polygenic risk score (PRS) calculation. More recently, pathway-specific PRSs, related to the pathophysiology of psychosis, have improved predictive accuracy in distinguishing patient status. Participants included early psychosis patients from the Treatment and Early Intervention in Psychosis (TIPP) program in CHUV (n = 168) and healthy controls from the general population (n = 179). All participants underwent a comprehensive set of clinical, cognitive, genetic and neuroimaging evaluations. Logistic regression analyses were conducted to study the predictive power of pathway-specific PRS and of the presence of childhood adversities. Voxel-based analysis was used to examine correlations between gFA and processing speed performance. Pathway-specific PRS related to neuroinflammation (OR = 1.33; p = 0.006) and GABAergic interneurons (OR = 1.17; p = 0.009) significantly predicted patient status. Childhood trauma was associated with psychosis, especially neglect (OR = 1.31; p > 0.001) along with its subtypes. Patients showed reduced gFA compared to controls (t = -4.13; p > 0.001); however, no significant correlation was found between gFA and processing speed.

Petruccioli, Giulia

Behavioral profiling predicts vulnerability and resilience to stress.

Petruccioli Giulia (1) (2), Silvia Poggini (1), Gloria Matte Bon (1) (3), Aurelia Viglione (1), Claudia Delli Colli (1), Alessandro Giuliani (4), Igor Branchi (1)

(1) Italian National Institute of Health, Center for Behavioral Sciences and Mental Health, Rome, Italy;
(2) Department oh Human Neuroscience, Sapienza University of Rome
(3) Department of Psychiatry and Psychotherapy, Tübingen Center for Mental Health, University of Tübingen, Tübingen, Germany" e "Department of Women's and Children's Health, Science for Life Laboratory, Uppsala University, Uppsala, Sweden;
(4) Italian National Institute of Health, Department of Environment and Health, Rome, Italy.

Stress exposure represents the primary risk factor for developing psychopathologies, such as major depressive disorder, though individual susceptibility varies. Understanding this individual variability and identifying predictors of vulnerability and resilience are key biomedical research goals. Longitudinal data on individual behaviors and emotions are increasingly used to profile patients by psychological and physiological features. Here, we evaluated whether individual behavioral differences predict stress vulnerability since behavior has been hypothesized to represent a critical factor in the organization of brain functioning.

We monitored the behavior of 90 C57BL/6J adult female mice for three days to identify behavioral profiles. Then, the mice went through 14 days of chronic unpredictable mild stress and we assessed depressive-like responses, as liking-type and wanting-type anhedonia. We evaluated the hypothalamus-pituitary-adrenal (HPA)-axis activity by measuring blood levels of corticosterone before and after stress exposure. Data were analyzed with one-way ANOVA, Principal Component Analysis (PCA) for dimensionality reduction, K-means algorithm for unsupervised machine learning data clustering, and Canonical Correlation Analysis (CCA) to assess correlations.

Results showed that differences in behavior significantly identify mice that will display a depressive-like phenotype, predicting vulnerability to stress. We identified significantly distinct behavioral profiles associated with different vulnerabilities to stress, both in the anhedonic responses and corticosterone levels: mice that showed a proactive behavioral profile were more affected by stress exposure, with significantly higher liking-type anhedonia, wanting-type anhedonia, as well as a higher increase in corticosterone levels compared to the animals showing a reactive behavioral profile.

Our study confirms the relevance of monitoring individual variations in behavior for predicting vulnerability and resilience to stress and the risk of developing psychopathologies as depression. These findings hold translational significance as the identification of specific phenotypes linked to vulnerability can contribute to the expanding realm of medical models, such as personalized psychiatry and lifestyle medicine.

Piron, Nicolas

Exploring the Theta-Gamma Code in MEG Data

Nicolas Piron[1], Théo Desbordes[1], Nina Kazanina[1], Sophie Schwartz[1]

[1]University of Geneva

Episodic memory, the capacity to remember events in the order they unfolded, depends critically on representing when each element occurred. Associative learning on its own cannot explain sequence learning, because it does not represent the position of items in time. A dedicated temporal (or positional) code is required to (i) bind elements in the correct order during encoding, (ii) preserve that serial structure during consolidation, and (iii) permit flexible retrieval and manipulation of the resulting memory trace. One prominent candidate for such a code is cross-frequency coupling between theta (4–8 Hz) and gamma (30–90 Hz) oscillations, which may provide a rhythmic time-stamp for human memory. Although the theta-gamma framework was largely theoretical only a few years ago, recent empirical studies have produced conflicting results. Two critical questions therefore remain: Does theta-gamma coupling truly support sequence memory, and, if so, can it be detected with magnetoencephalography (MEG)? Here we review two recent papers that addressed these issues and present new simulations aimed at resolving them.

Policet—Bétend, Héloïse Salomé

The translational functional architecture of cardiovascular interoceptors

Heloise POLICET-BETEND[1], Christophe LAMY[1]

[1]UNIGE

Cardiovascular interoception plays a key role in emotional behavior. Its alteration has been linked to emotional dysregulation and anxiety. Cardiovascular states and blood composition are monitored by specialized receptors located in large vessels and the heart. However, it is unclear whether those receptors are altered in disease states linked to interoceptive dysregulation. In addition, their cellular and molecular structure is poorly characterized in humans. In this work we leveraged large scale human tissue clearing and multiplexed immunostaining to provide a detailed mapping of human cardiovascular interoceptors. We showed that they are more widely distributed and heterogeneous than presented in previous descriptions. We also traced their innervation to better understand the pathways linking them to the brain. Eventually, we studied with a similar approach equivalent structures in mice. Altogether, our data provides a detailed, functionally-relevant 3D cellular map of cardiovascular interoceptors in mice and humans which can serve as a base for mechanistic and translational research on interoception and interoceptive pathology.

Souza, Adriana

Dopaminergic modulation and social deficits: effects of prenatal valproic acid exposure in male mice

Adriana Souza (1,2) ; Rizzo, A 1; Gomes F.V. 2; Bonaventura J.1

(1) Department of Pathology and therapeutic Experimental, Institute of Neurosciences, University of Barcelona
(2) Department of Pharmacology, Ribeirao Preto Medical School, University of São Paulo, Brazil.

Autism Spectrum Disorders (ASD) are neurodevelopmental disorders characterized by deficits in social interaction, communication impairments, and repetitive behaviors. Although the etiology of ASD is multifactorial, increasing evidence suggests a role for dopaminergic dysfunction in the pathophysiology of social deficits. The mesocorticolimbic (MCL) pathway, particularly the projection from the Ventral Tegmental Area (VTA) to the Nucleus Accumbens (NAc), plays a crucial role in processing social reward and motivation. Dysregulation in this circuit has been implicated in ASD-related social impairments. The present study investigates the correlation between dopaminergic alterations and social deficits in a valproic acid (VPA)-induced mouse model of ASD. To assess these alterations, dopaminergic release in the NAc was evaluated during a sociability test in mice exposed to VPA in utero using fiber photometry with the dopamine sensor dLight. Additionally, the impact of dopaminergic modulation was examined by selectively inhibiting or enhancing the VTA-NAc pathway using designer receptors exclusively activated by designer drugs(DREADDs). The findings revealed an increased frequency of transient dopamine events in the NAc of VPA-exposed mice, accompanied by a reduction in social interaction time. Additionally, the duration of dopamine transients was reduced during habituation, suggesting an alteration in dopaminergic signaling dynamics. Inhibition of the VTA-NAc pathway in VPA exposed animals alleviated social deficits without affecting locomotion. Conversely, increasing dopaminergic activity within this circuit in control animals led to a significant reduction in social interaction, mirroring the behavioral phenotype observed in VPA-exposed mice, while locomotor activity remained unaffected. These findings provide evidence that hyperdopaminergic activity in the MCL pathway contributes to ASD-like social impairments and suggest that targeting this circuit could represent a potential therapeutic strategy for ameliorating social deficits in ASD. The results highlight the importance of balanced dopaminergic signaling in social behavior.

Reich, Natacha

From Impulsivity to Psychosis: The Role of Obesity and Cerebellar Maturation in 22q11.2DS

Natacha Reich[1], Corrado Sandini[1], Farnaz Delavari[1], Lara Pajic[1], Andrea Escelsior[2], Silas Forrer[1], Andrea Imperato[1], Nada Kojovic[1], Caren Latrèche[1], Valeria Parlatini[3], Samuele Cortese[4], Maude Schneider[1], Stephan Eliez[1]

[1]University of Geneva, [2]University of Genoa, [3]University of Southampton | King's College London , [4]University of Southampton | New York University | University "Aldo Moro"

Background: Early-life obesity and metabolic dysregulation have been associated with increased risk for adult psychosis, but causal mechanisms remain unclear—particularly in the context of genetic vulnerability. Understanding these mechanisms requires: (1) identifying early-life metabolic mediators of genetic risk, (2) characterizing the behavioral origins of early obesity, and (3) clarifying neurodevelopmental pathways linking obesity to psychosis symptoms. Methods: We studied 184 individuals with 22q11.2 Deletion Syndrome (22q11DS), a population at high genetic risk for psychosis, and 182 healthy controls, followed longitudinally since childhood. We integrated repeated BMI measurements with clinical, neurocognitive, and neuroimaging data. Analyses examined whether childhood impulsivity predicted BMI trajectories, how these related to later psychosis risk, and whether cortical or cerebellar development mediated these associations. Results: Childhood behavioral impulsivity predicted early and persistent increases in BMI, mediating the effect of 22q11DS on early-life obesity. Chronic BMI elevations during childhood, in turn, predicted the emergence of psychosis in adolescence and early adulthood. The duration of elevated BMI was associated with worsening motor and cognitive disorganization—a key symptom domain in schizophrenia—mediated by progressive gray matter reductions in the posterior-inferior cerebellum. Conclusions: Our findings suggest that in 22q11DS, early-life behavioral impulsivity increases psychosis risk through a pathway involving chronic obesity and cerebellar dysmaturation. These results underscore the importance of targeting metabolic health in childhood as a potential early intervention strategy for individuals genetically at risk for psychosis.

Renard, Margot

Single-Cell Profiling of Migrating GnRH Neurons

Margot Renard[1], Ismael Torres-Romero[2], Maude Muriset[2], Andrea Messina[1]

[1]EDM CHUV, Université de Lausanne, [2]EDM CHUV

Gonadotropin-releasing hormone (GnRH) neurons are a small hypothalamic cell population essential to mammalian reproduction. They migrate from nose to brain tissue during embryonic development, then integrate signals from their surrounding network, shaping activity patterns that regulate puberty onset and adult fertility. However, the precise molecular mechanisms governing these processes remain largely unknown. Our study aims to characterize the transcriptomic landscape of the migrating and maturing GnRH neurons and identify critical gene expression trajectories necessary to their development and to reproductive function. Using Gnrh1::GFP mouse embryos, we captured GnRH neurons and surrounding cells by fluorescence-activated cell sorting throughout the course of their migration. After single-cell RNA sequencing and quality control, the dataset comprised 50,000 cells, including 1,376 GnRH neurons. Using unsupervised clustering and cell annotation based on spatially-validated markers, we identified cell populations from both the developing forebrain and the nasal region including the olfactory epithelium and GnRH neurons. We were able to isolate the olfactory/GnRH neurogenic niche and identify the molecular determinant of two main trajectories leading to GnRH and olfactory sensory neurons. Focusing on GnRH neurons, we investigated their gene expression heterogeneity under the influence of spatial, temporal, sex-related, and other factors. Our analysis revealed developmental time and localisation along the migratory route as the main drivers with high expression of genes associated with neuronal migration and cell adhesion (e.g. Cdh22, Gpc5) at early stages, and genes involved in neural circuit formation (e.g. Homer1), and neuropeptide maturation (e.g. Pcsk1) in cells that have reached their destination. Finally, we evaluated how gene expression dynamics influences cell–cell communication and observed that GnRH neuron molecular repertoire adapts to the surrounding environment. The axon-guidance cue Netrin-1 is expressed by specific populations in both nasal and brain regions, while its receptors show distinct spatial patterns within the GnRH population. Dcc is enriched in nasal GnRH neurons, coinciding with its known role in olfactory axon guidance—an indirect prerequisite for GnRH migration. In contrast, in brain-resident GnRH neurons, Dcc is downregulated but heterogeneously present across the population, while Unc5c, a receptor associated with chemorepulsion, is upregulated. This suggests that at stages when Netrin/Dcc signaling may guide GnRH neurite extension toward their target region—the median eminence—the response to Netrin-1 is modulated according to the maturation stage of individual GnRH neurons. Altogether, this study advances our understanding of the molecular mechanisms underlying GnRH neuron migration and may help identify novel diagnostic targets for infertility-related disorders.

Ribeiro, Joana

Astrocytic CB1–EAAT Crosstalk Shapes LTD and Mood

Joana Gonçalves-Ribeiro1,2, Leandro Rodrigues-Freitas1,2, Carmen Nanclares3, Mariana Sottomayor1,2, Sara Pinto1,2, Madalena Gualdino1,2, Daniela Magalhaes1,2, Ana M. Sebastião1,2, Alfonso Araque3, Sandra H. Vaz1,2

1 Instituto de Farmacologia e Neurociências, Faculdade de Medicina, Universidade de Lisboa, Lisbon, Portugal

2 Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina, Universidade de Lisboa, Lisbon, Portugal

3 Department of Neuroscience, University of Minnesota, Minneapolis, Minnesota, USA

Excitatory amino acid transporters (EAATs), predominantly expressed in astrocytes, are dynamic regulators of synaptic function and plasticity. Yet, how glutamate uptake adapts during endocannabinoid-mediated long-term depression (eCB-LTD) remains unclear. In the infralimbic cortex (IL), eCB signaling is a central modulator of synaptic plasticity, influencing both memory and mood regulation. We hypothesized that astroglial cannabinoid type 1 receptors (CB1Rs) shape eCB-LTD by modulating EAAT activity, thereby impacting depressive behaviors. Using ex vivo calcium imaging, electrophysiology, and behavioral assessments in IP3R2 knockout mice (which lack astroglial Ca^{2+} signaling) we found that IL eCB-LTD is astroglial Ca^{2+}-dependent and relies on CB1R-mediated inhibition of EAATs. Strikingly, absent LTD in IP3R2KO mice was restored by EAAT manipulation. Furthermore, eCB-LTD was associated with antidepressant-like behavior. These findings reveal a previously unrecognized mechanism in which astroglial CB1Rs reduce EAAT activity via Ca^{2+}-dependent signaling, a process essential for LTD maintenance and potentially relevant to mood regulation.

Richard, Jeanne

Modulating food ratings with gamified inhibitory control training

Jeanne Richard[1], Anais Quossi[2], Marion Chatelain[2], Zoltan Pataky[3], David Sander[4], Lucas Spierer[5], Geraldine Coppin[2]

[1]University of Geneva & UniDistance Switzerland, [2]UniDistance Switzerland, [3]Geneva University Hospitals, [4]Unniversity of Geneva, [5]University of Fribourg

High Body Mass Index (BMI) is a risk factor for several diseases, such as diabetes and cardiovascular conditions. On a behavioral level, higher BMI is associated with low inhibitory control and high "wanting" for food rewards. This project investigates how food "wanting" can be modulated through inhibitory control training (ICT) in individuals with various BMIs. We hypothesized a larger decrease in "wanting" for food after training in the experimental group compared to the control group. The ICT was gamified and personalized, reinforcing intrinsic motivation, engagement, and adherence to the intervention. Unlike most studies in the field that only provide a single training session, we trained participants for 200 minutes over 4 weeks, at home. We compared an experimental training group in which high-calorie foods were associated with motoric inhibition to an active control group in which both high- and low-calorie foods are linked with motoric inhibition. As the difference between the experimental and control training conditions lay only in the stimulus-response (SR) mapping proportions, both groups did the same task and had similar expectations. This control of participants' expectations is another major asset of our approach. Results show a significant interaction between intervention (experimental vs control training) and time (pre- vs post-intervention), $F(1, Inf) = 4.3$, $p < .04$. The two intervention groups are currently still under a double-blind procedure. If we demonstrate that ICT can effectively reduce the valuation of high-calorie foods, it could provide easily implementable tools for weight management.

Rodriguez Peris, Laura

Impulsivity, sensation seeking, anxiety, and mGluR5 in a rat model of cocaine addiction

Laura Rodriguez Peris, Florian Marchessaux, Raphaël Goutaudier, Nathalie Ginovart

Department of Psychiatry, Faculty of Medicine, University of Geneva, Switzerland; Department of Basic Neuroscience, Faculty of Medicine, University of Geneva, Switzerland

Drug addiction is a chronically relapsing disorder, characterized by compulsion to seek and take the drug, loss of control in limiting intake, and emergence of a negative emotional state when access to the drug is prevented. The transition from recreational to compulsive use occurs in only 15% of the individuals, highlighting the need to identify vulnerability factors. Behavioral traits such as impulsivity, sensation-seeking and anxiety are suspected risk factors due to their high prevalence in drug addiction. Notably, most studies in this field have been conducted on males, highlighting the need for research to evaluate whether there are sex differences in the risk factors that predict drug abuse and progression to addiction. From a neurobiological perspective, emerging evidence suggests that reduced metabotropic glutamate receptor 5 (mGluR5) density in the medial prefrontal cortex (mPFC) may underlie impulsivity and contribute to addictiLon vulnerability. Indeed, recent data from the lab showed that impulsivity in rodents is linked to mPFC deficits in mGluR5. Moreover, neuroimaging studies in patients with substance use disorders revealed lower brain levels of mGluR5 (Milella et al., 2014). However, it remains unclear if these changes in mGluR5 density predate or are a consequence of chronic drug exposure.

This study investigates the predictive roles of sensation-seeking, anxiety and impulsivity as risk factors for the development of addiction-like behaviors in female rats. It also aims to determine whether mGluR5 dysregulation observed in cocaine addiction is a predisposing factor or a result of chronic cocaine exposure.

We used two different rat lines, the Roman High Avoidance (RHA) and Low Avoidance (RLA) rats, exhibiting different phenotypes in terms of impulsivity and addiction-like behaviors. Female and male animals were first tested at baseline to assess sensation-seeking, anxiety and impulsivity, and were scanned with positron emission tomography (PET) to index mGluR5 levels in brain. Subsequently, female rats were exposed to an intermittent schedule of cocaine self-administration (SA) for 6 weeks and re-scanned with PET. Lastly, animals were tested for three criteria of addiction-like behaviors (persistence of drug-seeking in the absence of drug, motivation for the drug, and compulsivity).

At baseline, data indicate no between-line differences in sensation-seeking but overall higher levels of sensation-seeking in females when compared to males. Anxiety levels did not differ across lines or sexes. Notably, RHAs displayed higher impulsivity levels compared to RLAs, irrespective of the sex. In the 3-criteria model of drug addiction, female RHA rats showed a higher propensity to self-administer cocaine, meet more addiction-like criteria, and exhibited a higher addiction score (based on the individual performances across the three criteria) than RLA females. Data collection is ongoing, and additional analysis will focus on the impact of cocaine SA on the density of mGluR5 receptors. These findings will enhance our understanding of the behavioral and neurobiological mechanisms underlying addiction vulnerability and the neuroadaptations associated with cocaine addiction.

Roque, João

Addressing cerebellum defects in a mouse model of schizophrenia harbouring a human mutation in the CACNG2 gene encoding stargazin

Roque João 1,2, Ângela Inácio1, Nuno Beltrão1,3,4, Ana Luísa Carvalho 1,2

1 CNC – Center for Neuroscience and Cell Biology, University of Coimbra, Portugal

2 Department of Life Sciences, University of Coimbra, Portugal

3 Doctoral Program in Experimental Biology and Biomedicine, University of Coimbra, Portugal

4 Dominick P. Purpura Department of Neuroscience, Albert Einstein College of Medicine, New York, USA

Cerebellar dysfunction has been implicated in several neuropsychiatric disorders. Both connectivity impairments and structural alterations in this brain region have been found in schizophrenia patients, suggesting a potential role for the cerebellum in the expression of schizophrenia-related phenotypes. However, despite these findings, the precise cerebellar defects that result in cognitive impairment and social behaviour abnormalities remain poorly understood.

This project aimed to study cerebellar defects in a mouse model harbouring a human mutation in the CACNG2 gene, which was identified in association with schizophrenia. Stargazin, the CACNG2-encoded protein, is a synaptic protein highly expressed in the cerebellum, where it plays non-redundant functions in targeting AMPAR to the synapse. Knock-in mice harbouring a stargazin mutation associated with intellectual disability show abnormal cognitive and social behaviours, as well as impaired motor learning. Therefore, we aimed to assess social behaviour and sensorimotor gating in knock-in mice expressing a schizophrenia-associated variant of stargazin (STGSN-KI mice), as well as to evaluate cerebellar neuronal excitability.

Behavioural characterization revealed that STGSN-KI mice show depressive-like behaviour, deficits in prepulse inhibition of the acoustic startle response and in social behaviour. Overall, these results indicate that STGSN-KI mice recapitulate phenotypes observed in schizophrenia patients and other animal models of schizophrenia. Expression of mutant stargazin led to aberrant intrisic pattern of firing and higher excitability of Purkinje cells in the Crus I region of the cerebellum of STGSN-KI mice, compared to wild-type animals. Altogether, this work unveiled specific behavioural features altered in STGSN-KI mice, shedding light into the excitability deficits in Crus I Purkinje cells that might contribute to the behavioural abnormalities observed in this animal model.

Russell, Rosie

Mapping a timeline of synaptic maturation from adolescence to adulthood in the neocortex.

Russell Rosie (1), Paul Anastasiades (2)

Bristol Medical School, University of Bristol, United Kingdom.

Childhood is extremely influential in forming world perception, social climate, and identity as an adult. However, it is poorly understood how and when neurodevelopmental biology contributes towards these essential processes. As a result, it is important to characterise how the brain matures across development. This was achieved with whole brain high-throughput imaging using mice with knock-in fluorescent reporters for postsynaptic scaffolding proteins postsynaptic density 95 (PSD95)-eGFP and synapse-associated protein (SAP102)-mKO2 (Zhu et al., 2018). These are membrane associated guanylate kinases (MAGUKs) which colocalise with NMDAR GluN2A/B subunits at excitatory synapses. As SAP102 is expressed in immature synapses and PSD95 expression increases as synapses mature, this produced a timeline of how each brain area matures over the transition from adolescence (P25) to adulthood (P55). Fluorescence profiles from this timeline were extracted from cortical hierarchical regions using Fiji. My results highlighted how different regions and layers of the neocortex develop from adolescence to adulthood. In the future I aim to utilise AI deep learning tools to examine other brain areas as well as how these maturation patterns may differ in models of psychosis.

Rutz, Dionys

Enhancement of Prediction Accuracy for Motor Recovery from Acquired Brain Injury with Minimal Use of Wearable Devices: Protocol for an Observational Study

Dionys Rutz[1], Antoine Zaczyk[2], Arseny Sokolov[3], Jean-Michel Pignat[3], Andrea Serino[1], Traian Popa[1]

[1]NeuroRehab Research Center, Department of Clinical Neurosciences, Lausanne University Hospital, 1011 Lausanne, Switzerland., [2]University NeuroRehabiltation Unit (SUN), Lavigny Institute, 1175 Lavigny, Switzerland., [3]University NeuroRehabiltation Unit (SUN), Department of Clinical Neurosciences, Lausanne University Hospital, 1011 Lausanne, Switzerland.

Background Early functional abilities after acquired brain injury (ABI) play a critical role in shaping long-term outcomes, including quality of life, discharge destination, and rehabilitation planning. Trunk stability and limb strength are known to influence motor recovery and the functional abilities of both upper and lower limbs. Understanding how these motor components relate to the evolution of spontaneous daily functional performance can support more personalized and effective interventions. This study investigates the relationship between motor recovery biomarkers and the evolution of spontaneous functional performance in individuals with ABI. Method Adults with acquired brain injury (ABI) will be recruited in the acute phase (<7 days post-injury) within the Clinical Neurosciences Department of Lausanne University Hospital. Motor recovery markers—trunk control (TCT), limb strength (SAFE, Motricity Index) and motor evoked potential from TMS-—will be assessed from the acute phase through rehabilitation and up to 12 months. Functional capacity (FAC, FM-UE, ARAT, gait evaluation) and spontaneous performance (48-hour IMU-based activity monitoring) will be measured at key time points: acute phase, admission to rehabilitation, 3–9 weeks during rehabilitation, discharge, and at 6- and 12-month follow-ups. Secondary measures include cognitive status, socioeconomic factors, PROMs, body perception (ALPQ), and response to a high-dose motor gaming program. Discussion This study aims to improve understanding of motor recovery and spontaneous functional performance after acquired brain injury by combining longitudinal assessments of trunk stability, limb strength, and real-life movement over 12 months. Importantly, it seeks to develop a clinically applicable predictive model to inform individualized rehabilitation planning and enhance patient outcomes. The findings are expected to provide clinicians with robust tools to better anticipate recovery trajectories and optimize therapeutic interventions throughout the continuum of care.

Sanchez Lopez, Paula

Purpose-built spinal cord neuroprothesis to alleviate gait deficits in individuals with advanced Parkinson's disease

Paula Sanchez Lopez[1], Camille Varescon[1], Elsa Mauguin[1], Celine Deschenaux[1], Lea Bole-Feyson[1], Sergio Hernandez-Charpak[1], Gaia Carparelli[1], Anne Watrin[2], Fabio Becce[3], Viviana Aureli[1], Jocelyne Bloch[1], Eduardo Martin Moraud[1], Gregoire Courtine[1]

[1].NeuroRestore, EPFL, CHUV, UNIL, [2]Onward Medical SA, [3]CHUV

Despite advances in neuromodulation therapies for Parkinson's disease (PD), a large number of patients with advanced PD develop disturbances of gait and balance, including postural instability, festination, or freezing of gait, that are often refractory to existing treatments. These deficits lead to frequent falls and increase comorbid conditions. We previously reported that epidural electrical stimulation (EES) of the lumbosacral spinal cord improved gait asymmetry, shuffling steps, imbalance, and freezing of gait in one patient with advanced PD (STIMO-PARKINSON clinical trial, NCT04956770). This proof-of-concept trial used re-purposed technology originally developed to treat chronic pain and is therefore suboptimal for this application. To confirm our preliminary results, we are now conducting a clinical trial in 6 individuals with PD who present severe gait and balance deficits (SparkL, NCT06295614). We also aim to resolve technological limitations of repurposed technologies with the evaluation of a purpose-built implantable platform designed for precise stimulation of the spinal cord and enhanced usability to support daily mobility. Our first participant so far demonstrated improved gait quality, extended walking capacities, decreased freezing of gait, and increased confidence during daily mobility. At-home monitoring confirmed these improvements, which translated into a reported increase in his quality of life. These results will have to be confirmed in the next participants.

Sanders, Bryan

Electrophysiological signature of loud speech and articulatory complexity in patients with motor speech disorders

Bryan Sanders[1], Monica Lancheros[1], Marina Laganaro[1]

[1]University of Geneva

Apraxia of speech and Dysarthria are two types of Motor speech disorders (MSD) caused by various etiologies resulting in impairment of speech production (SP) (Kent, 2000). It is well known that impaired SP significantly impact the quality of life of patients on multiple levels. However, scientists interested in those MSD still cannot provide a clear differential diagnostic potentially resulting in inappropriate behavioral treatments. Therefore, additional empirical evidence is needed to support the characterization of the behavioral and the neural mechanisms that are disrupted in MSD. The present study, still in data collection, will compare scalp electroencephalography (EEG)/event related potentials (ERPs) generated during a delayed production task (Laganaro & Alario, 2006) in a 2x2 design with speech modes as one condition (i.e., speaking normally and speaking louder than usual) and articulatory complexity as the other condition (i.e., cluster [CCV] in the first syllable or no cluster [CV]). Regarding results, we assume that pseudowords starting with a cluster will entail more errors and higher latency of production in patients diagnosed with Apraxia of speech (Aichert & Ziegler, 2004). In this regard, we expect an EEG signature of articulatory complexity in a time window far from the vocal onset. Moreover, we presume that speaking louder than usual will impair the performance of patients with Dysarthria (Bourqui et al., 2025). Again, this behavioral outcome should be observable on the EEG analyses with modulation of brain activity in a time window likely closer to the vocal onset in comparison to the other condition.

Saneei, Sarah

Investigating Lexico-semantic Representations in Artificial and Biological NeuralNetworks: an Optimization Loop

Sarah Saneei[1], Valentina Borghesani[1], Timothée Proix[2]

[1]Faculty of Psychology and Educational Sciences, University of Geneva, [2]Department of Basic Neurosciences, Faculty of Medicine, University of Geneva

A core question in cognitive neuroscience is how and where lexico-semantic representations are encoded in the brain. Neuropsychological and lesion-based studies have identified the anterior temporal lobe and posterior middle temporal gyrus as critical hubs for semantic processing [1, 2]. In contrast, recent correlational studies using natural speech and embeddings from large language models (LLMs) suggest that semantic information is represented across a broader network of cortical areas [3]. To reconcile these perspectives, inspired by Walker et al. [4], we developed a closed-loop optimization approach that uses in vivo neural recordings and regression-based embedding manipulations to causally test how specific semantic dimensions influence neural responses across cortical regions. We recruited six participants with drug-resistant focal epilepsy undergoing intracranial EEG (iEEG) monitoring. Participants first listened to the audiobook of "Le Petit Prince" while we recorded their neural activity. We then used regression analysis to correlate brain activity with LLM-derived sentence embeddings. Based on this, we identified words predicted to maximally activate specific neural sites and embedded them into short narratives. In a subsequent session, participants listened to these customized stories. We hypothesized that brain regions causally involved in processing specific semantic features would show significantly stronger responses to these optimized words compared to control words. To date, the experimental protocol has been implemented (with minor variations) in six participants and encouraging preliminary findings suggest that some electrodes exhibit selective sensitivity to specific semantic embedding dimensions. Analysis of the full sample is currently ongoing.

Sayin, Ozge

The evolving potential for dementia prevention in Switzerland: population attributable fractions of risk factors over time

Ozge Sayin[1], Federica Ribaldi[1], Augusto J. Mendes[1], Giovanni B. Frisoni[1]

[1]University of Geneva

It is estimated that modifiable risk factors (RFs) account for approximately 45% of dementia cases worldwide. While several studies have examined the extent to which these RFs contribute to dementia incidence in other regions, such as Brazil, Denmark, China, and the USA, Switzerland has not yet been investigated. This gap is particularly relevant given recent evidence of a declining dementia incidence in high-income countries, with the corresponding evolution of population attributable fraction (PAF) remaining poorly understood. Therefore, we aimed to calculate the PAF for dementia in the Swiss population over time. We used data from the Swiss National Health Survey collected over two waves (2007, 2022) covering 25141 participants aged between 45 to 100 years old. We adjusted for the communality between 14 modifiable RFs of dementia identified by the Lancet Commission on dementia prevention and calculated the overall weighted PAF. We investigated the temporal trends to understand the changes that occurred in 15 years. The current PAF of Switzerland is lower when compared to worldwide estimates. In specific, the overall PAF for potentially modifiable RFs decreased from 44% in 2007 to 40% in 2022. Over this 15-year period, social isolation and depression consistently remained as the primary determinant of dementia. This study illustrates the contribution of potentially modifiable RFs to dementia risk in Switzerland since 2007. The comparatively lower PAF estimates may reflect healthier lifestyle and high-quality health care system, which likely contribute to the observed decline in PAF over time. By identifying the evolving impact of individual RFs, these findings can help refine dementia prevention strategies and ultimately contribute to reducing the national burden of dementia.

Schipper, Kate

Motor Cortical Beta Burst Dynamics Reorganize With Extended Training Under Adaptive and Non-Adaptive Conditions

Kate Schipper[1], Paolo Ruggeri[1], Bogdan Draganski[2], Jérôme Barral[1]

[1]Université de Lausanne, [2]Université de Bern

Motor skill learning unfolds over time through repeated attempts, feedback, and refinement. Adaptive training—where task difficulty increases with performance—is thought to sustain this refinement by promoting continued exploration and error correction. However, the neural mechanisms supporting learning under adaptive versus fixed training conditions remain unclear, particularly in relation to motor cortical beta dynamics. While event-related desynchronization/synchronization (ERD/ERS) have traditionally indexed motor-related engagement, growing evidence suggests that these averaged signals are driven by transient, high-amplitude beta bursts that offer a more precise window into the dynamics of neural adaptation. In this study, 32 participants trained on a complex bimanual coordination task over nine sessions. EEG was recorded at early, middle, and late stages of training, and source-level analyses focused on bilateral primary motor cortex (M1). Half of the participants trained under adaptive conditions, with task difficulty adjusted based on performance; the other half trained at constant difficulty. Across all participants, motor performance improved with training. At the neural level, beta burst dynamics reorganized systematically over time. Burst probability became more distinctly modulated, with greater suppression during movement and increased occurrence after movement. In right M1, post-movement burst timing became more consistent across trials, suggesting enhanced temporal precision. Critically, post-movement burst amplitude increased significantly only in the adaptive group, consistent with strengthened confidence in internal model predictions under sustained performance demands. These findings indicate that beta burst dynamics reorganize across multiple dimensions with extended training and highlight their sensitivity to training context. Burst-resolved EEG offers a powerful tool for tracking motor cortical plasticity beyond conventional time–frequency measures.

Schoenfeldt-Reichmann, Eva Tabea

Effects of physiotherapy on mood disorders in patients with MSA, PSP, and PD.

Eva Tabea Schoenfeldt-Reichmann[1,2], Victoria Sidoroff[3], Hamid Moradi[4], Gaëlle Prigent[5], Stefano Sapienza[6], Frank Jagusch[3], Isabelle Teckenburg[7], Marzieh Asalian[4], Nina Hergenroeder-Lenzner[7], Marijus Giraitis[6], Jean-Pierre Ndayisaba[3], Georg Goebel[3], Klaus Seppi[3], Anisoara Ionescu[5], Florian Krismer[3], Juergen Winkler[7,9], Bjoern M. Eskofier[4,10], Jochen Klucken[6], Kamiar Aminian[5], Gregor Wenning[3†], Heiko Gassner[7,11], Cecilia Raccagni[3,12], David Benninger[1-2,8], Mobility_APP Study Group

1 Université de Lausanne, Lausanne, Switzerland
2 Neurology, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland
3 Department of Neurology, Medical University of Innsbruck, Austria
4 Machine Learning and Data Analytics Lab, Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Erlangen, Germany
5 Laboratory of Movement Analysis and Measurement, École Polytechnique Fédérale de Lausanne, Switzerland
6 University of Luxembourg, Luxembourg
7 Department of Molecular Neurology, University Hospital Erlangen, Germany
8 Neurology, Reha Rheinfelden-University of Basel, Switzerland
9 Center for Rare Diseases Erlangen (ZSEER), University Hospital Erlangen, Germany
10 Institute of AI for Health, Helmholtz Zentrum München-German Research Center for Environmental Health, 21 Neuherberg, Germany
11 Fraunhofer IIS, Fraunhofer Institute for Integrated Circuits IIS, Erlangen, Germany
12 Department of Neurology, Provincial Hospital of Bolzano, Italy; Paracelsus Private Medical University, Austria

Objective: To investigate the impact of physiotherapy on mood disorders such as apathy, anxiety, and depression in patients with Parkinson's disease (PD), multiple system atrophy (MSA), and progressive supranuclear palsy (PSP), and whether mood improvement correlates with increased physical activity and better motor function.

Background: PD, MSA, and PSP are neurodegenerative diseases primarily marked by motor symptoms. However, mood disorders, like apathy, depression and anxiety, are prevalent and associated with increased frailty and disability, rapid functional decline and increased mortality[1–4]. Increasing evidence supports the efficacy of physiotherapy and exercise in improving motor and cognitive function which complement the pharmacological therapy[5–8].

Methods: This project is part of the Mobility_APP-Study, a multicenter, randomized, controlled, double-blind interventional study, comparing two approaches of physiotherapy. The intervention consists of a 2-week daily in-patient physiotherapy session followed by 5 weeks of home-based training. The assessment includes motor and cognitive testing, questionnaires, an Instrumented Gait Analysis (IGA) and a 1-week sensor-based monitoring of physical activity at baseline and study end.

Results: We enrolled 72 PD patients, 51 patients with PSP and 44 with MSA. Compared to PD, atypical PD (PSP&MSA) patients show worse cognition, mood and motor performance at baseline, and throughout the study. All patients globally improve in mood with the in-patient physiotherapy, but then stabilize during the home-training phase. Only in PSP patients can we see a long-term, significant improvement of anxiety.

All groups show consistent significant improvement in UPDRS-II scores, with slight balance improvement (BBS) in MSA patients and better postural stability and gait (PIGD) in patients with APD. PD patients show an improvement in self-assessed disease severity. Globally, better mood correlates with better motor function. There is a particular correlation between moods and the mobility at home (UPDRS-II score) as well as between the sense of disability (PGI-S) and clinical motor scores (UPDRS-III).

Conclusions: Physiotherapy improves both motor symptoms and mood including apathy, anxiety and depression, which appear to be interlinked. This underlines the efficacy of non-pharmacological interventions in the treatment of patients with PD and APD.

Shen, Changlin

Hierarchical goal and subgoal representations across prefrontal regions in navigation

Changlin Shen[1], Hiroshi Ito[1]

[1]University of Lausanne

Navigating to a distant goal in a complex environment can be facilitated by dividing the journey into shorter subgoal-directed segments. Several lines of behavioral evidence suggest that both humans and rodents employ such subgoal-based strategies for navigation (McNamara et al., 2008; Shamash et al., 2021). While this ability requires the brain to maintain information about both the final goal and intermediate subgoals concurrently during navigation, the underlying neural circuit mechanisms remain poorly understood. To address this question, we developed a novel navigation task in which rats alternated between two final goals by passing through a common subgoal. Crucially, the available directions of travel from the subgoal were determined randomly by door openings, requiring trial-by-trial de novo route planning and preventing fixed action-goal association. Given previous evidence that prefrontal cortex subregions play distinct roles in representing goals and task progress, we performed recordings from neurons in the orbitofrontal cortex (OFC) and medial prefrontal cortex (mPFC) to compare goal-relevant activity between these two regions. We found that OFC neurons dynamically represented the subgoal of each navigational segment, consistent with their previously described role in representing the immediately succeeding destination (Basu et al., 2021). In contrast, mPFC neurons maintained one of the two task states corresponding to the final goals throughout the entire journey. Dimensionality reduction of mPFC population activity revealed a continuous ring-shaped manifold, capturing the neural dynamics of the entire journey progress, whereas OFC activity was organized into distinct ring manifolds, each corresponding to a separate subgoal-directed segment. We further confirmed the functional relevance of the specializations in mPFC and OFC using optogenetic perturbations. Perturbing OFC activity during navigation segments involving route choices led to an increase in the animal's erroneous decisions that end up in incorrect final destinations, whereas perturbation during non-choice segments had no effect. In contrast, perturbing mPFC activity impaired the animal's navigation performance regardless of the timing of the disruption, consistent with its role in maintaining a goal-corresponding state throughout the entire journey. Together, these findings reveal a hierarchical organization in the prefrontal cortex, where mPFC sustains long-term goal state representations and OFC encodes subgoals and guides immediate action planning within subgoal-directed segments. This division of labor may enable the brain to solve complex problems by maintaining an overarching objective in mPFC while guiding intermediate subproblems via OFC, thereby supporting efficient problem solving.

Shi, Chunyan

The temporal dynamics of reappraisal

Chunyan Shi[1], Jonathan Wirsich[2], Zile Chen[1], Patrik Vuilleumier[1]

1 Department of Fundamental Neuroscience, Faculty of Medicine, University of Geneva, Switzerland

2 Brain and Behaviour Laboratory, CIBM MRI UNIGE Cognitive and Affective Neuroimaging Section , University of Geneva, Switzerland

Reappraisal is an intentional attempt to change emotion through reconstrual or repurposing. In our study, we want to reveal the differences between more positive reappraisal (reinterpret the cause, outcome and consequence in a more positive way) and less negative reappraisal (reinterpret in a less negative way). Thirty participants with healthy mental states were recruited to perform an emotion regulation task, in which they need to watch or reappraise the emotion that are triggered by the pictures (40 neutral and 120 negative, from the Nencki Affective Picture System) according to the instructions. After each picture, they rated on positive emotion, negative emotion and arousal scales. At the same time, brain oscillations were measured using a 64-channel electroencephalography system and skin conductance level was measured with Biopack system. Results indicated that more positive reappraisal was more specialized in regulating emotions, while less negative reappraisal worked well in regulating both arousal level and emotions. More importantly, less negative reappraisal is more effective in reducing arousal level and negative emotion than more positive reappraisal. The amplitude of early late positive potential (300-1000 ms) is smaller in less negative reappraisal condition than more positive reappraisal, implying less cognitive resources attributed to the conflict monitoring process in the early stage of emotion processing, which may explain why less negative reappraisal is more effective in reducing arousal level and negative emotion.

Sinanaj, Lorina

Mapping Symptom-General and Symptom-Specific Targets for Transcranial Magnetic Stimulation in Schizophrenia: An Electrical Modeling Meta-Analysis

Lorina Sinanaj[1], Konstantinos Pallis[2], Anahita Fazel Dehkordi[1], Philippe Huguelet[2], Stefan Kaiser[2], Indrit Bègue[1]

[1]University of Geneva, [2]Hopitaux Universitaires de Geneve

Negative, positive, and cognitive symptoms of schizophrenia relate to disruptions in partially distinct brain circuits. Although promising, transcranial magnetic stimulation (TMS) strategies across and within symptom domains remain to be established due to TMS protocol heterogeneity. For this, we combined standard meta-analysis with electric field (E-field) modeling to identify stimulation sites where E-field strength was associated most significantly with clinical improvement. Standard meta-analysis of randomized, sham-controlled studies in 4,283 patients demonstrated the benefit of TMS across symptom domains, regardless of target or protocol. TMS significantly improved negative and cognitive symptoms with high-frequency stimulation applied to the left prefrontal cortex, whereas positive symptoms improved with low-frequency TMS applied to the left temporoparietal cortex. In-depth examination of these results with E-field modeling identified stimulation to left dorsomedial prefrontal cortex (L-DMPFC), left orbitofrontal cortex (L-OFC), and left cerebellar crus II and right lobule IX to be significantly associated with improvement across all symptom domains. Greater overlap of studies' stimulation sites with L-DMPFC and L-OFC related to improved outcomes. For negative symptoms, E-field distribution in L-DMPFC and L-OFC related most significantly to clinical improvement. Greater proximity to L-DMPFC stimulation site indicated better outcomes, with at-trend significance for L-OFC. In the cognitive domain, E-field distribution in the left dorsolateral prefrontal cortex was related to clinical improvement. Finally, strongest E-field association with clinical improvement was found in the right cerebellar lobules VIIIA, VIIIB, and IX for positive symptoms. These results support symptom-general and symptom-specific TMS approaches for distinct therapeutic goals towards personalized neuromodulation in schizophrenia.

Song, Jie

Dynamic neural transformation between egocentric and allocentric reference frames in VR-based spatial navigation

Jie Song[1], Kishen Senziani[1], Emmanuel Badier[1], Ilaria Sani[1], Patrik Vuilleumier[1]

[1]University of Geneva

Navigating a complex 3D environment is a challenging yet fundamental cognitive skill. In daily life, the brain integrates past experiences with current environmental cues to plan future navigation. Moreover, we are capable of combining and flexibly switching between these strategies to determine our location and navigate effectively. Previous studies have shown distinct brain mechanisms underlying two common navigation strategies: egocentric and allocentric reference frames. However, how the brain organizes spatial information, prepares for future actions, and flexibly utilizes different reference frames remains unclear. To address these questions, we designed two complementary and innovative virtual reality (VR) experiments—a plus-maze task and a three-intersection task—conducted inside a 3T MRI scanner using a 3D screen. We recruited participants who performed well, yielding a final sample of 32 individuals for the plus-maze task (aged 23.8 ± 3.1; 18-33; 15 females) and 38 individuals for the three-intersection task (aged 24.3 ± 3.3; 18-33; 20 females). In the plus-maze task, participants learned spatial routes at a plus-shaped intersection with distinct landmarks. Then, they either retraced a previously experienced path to locate a phone box, or identified their original approach direction based on a memorized car location and the landmark configuration. In the three-intersection task, participants learned a route through three sequential intersections, each defined by a unique set of landmark houses. During imagination and retrieval phases, they mentally simulated and recalled the route either from the original start or end point (black car or red phone box, engaging more egocentric navigation) or from one of the intermediate intersections (involving more allocentric navigation and allo-ego transformation). Behaviorally, allocentric navigation was associated with longer reaction times and lower accuracy compared to egocentric navigation. Using a combination of general linear models (GLM), representational similarity analysis (RSA), and multi-voxel pattern analysis (MVPA) on fMRI data, we found that both imagined and actual egocentric navigation engaged the superior parietal cortex, precentral gyrus, and motor-related networks. In contrast, allocentric navigation relied on the hippocampus, parahippocampal gyrus, and lingual cortex. Notably, the retrosplenial cortex (RSC) and posterior cingulate cortex (PCC) emerged as key regions supporting the transformation between egocentric and allocentric representations. In conclusion, our findings reveal two distinct neural pathways for spatial navigation: egocentric navigation primarily involves the dorsal visual stream, while allocentric navigation relies more on the ventral visual stream. This flexible transformation is mediated by the PCC and RSC, highlighting their central role in spatial cognition.

Spagnolo, Valeria

An implantable brain-spine interface restoring lower limb movements in patients with complete spinal cord injury

Valeria Spagnolo[1], Laure Coquoz[1], Gaia Carparelli[1], Nadine Intering[1], Celine Deschenaux[1], Sergio Hernandez Charpak[1], Nicolas Hankov[1], Thibault Collin[1], Icare Sakr[1], Simon Dehane[1], Vincent Rouanne[1], Andrea Galvez[1], Felix Martel[2], Pedro Abranches[1], Malo Simodin[1], Zakarya Souid[1], Charles David sasportes[1], Marina D'Ercole[3], Lea Bole-Feysot[1], Anne Watrin[3], Charlotte Jaquet[3], Serpil Karakas[2], Matthieu Bosquet[2], Olivier Faivre[2], Tetiana Aksenova[2], Pierre Bessot[3], Vincent Delattre[3], Julien Deddeley[3], Jean-Baptiste Ledoux[4], Camille Haxaire[1], Fabio Becce[4], Viviana Aureli[1], Robin Demesmaeker[1], Jordan Squair[1], Leonie Asboth[1], Guilleume Charvet[2], Jocelyne Bloch[1], Gregoire Courtine[1], Henri Lorach[1]

[1]NeuroRestore, Swiss Federal Institute of Technology (EPFL), Lausanne University Hospital (CHUV) and University of Lausanne (UNIL), Lausanne, Switzerland, [2]Univ. Grenoble Alpes, CEA, LETI, Clinatec, Grenoble, France, [3]ONWARD Medical, Lausanne, Switzerland, [4]Department of Radiology, CHUV, Lausanne, Switzerland

A spinal cord injury (SCI) interrupts the communication between the brain and the spinal cord, resulting in sensory, autonomic and motor deficits below the level of the lesion. Applying electrical epidural stimulation (EES) over the lumbosacral region of the spinal cord can reactivate the dormant, yet functional, motor neurons that control lower limb muscles and produce walking. In order to restore voluntary motor control, EES can be controlled by the motor intentions of the patients. We designed an implantable digital bridge linking the motor intentions recorded at the level of the motor cortex and EES to restore voluntary motor control after complete paralysis. The system is composed of an epidural electrocorticographic array (WIMAGINE®, CEA, France) implanted over the leg sensorimotor cortical area to decode motor intentions, connected to a purpose-built EES system (ARCIM, Onward Medical). The system was approved for preliminary safety and efficacy testing in the Think2Go clinical study ("Brain Controlled Spinal Cord Stimulation In Participants With Spinal Cord Injury For Lower Limb Rehabilitation", clinicaltrials.gov, NCT06243952, Swissethics CER-VD2023-D0102, Swissmedic 10001282, EUDAMED CIV-23-11-044654). Two participants with chronic motor complete paralysis were recruited in the study. Pre-operative planning with anatomical and functional MRI enables a precise and personalized implantation of the recording and stimulating device. In a single surgery, the full system (ARCBSI Lumbar System) is implanted. Raw brain signals are wirelessly streamed and decoded in real-time through classification algorithms, which generates online predictions of motor intentions. These intentions are translated into electrical stimulation commands that are wirelessly delivered to the neurostimulator targeting the dorsal roots of the spinal cord. The system is calibrated during two weeks to optimize the spinal cord stimulation and decoding models, sequentially as well as in combination. Within 3 days of calibration, it is possible to calibrate a 3-states decoding model and connect it to primitive movements, producing brain-controlled stepping with assistance. Further calibration enables the restoration of up to 6 different lower limb joints movements with high accuracy. The digital bridge is then used during 14 weeks of neurorehabilitation and finally packaged for home-use. In conclusion, the digital bridge strategy can restore lower limb motor function after motor complete spinal cord injury.

Sprenger, Thibault

Stimulation of astrocytes in the neurogenic niche of the dentate gyrus

Thibault Sprenger[1], Nicolas Toni[1]

[1]University of Lausanne

Adult neurogenesis is a process by which hippocampal neural stem cells (NSCs) proliferate and produce new and functional neurons. This process is observed in two regions of the mammalian brain, the subventricular zone and the dentate gyrus of the hippocampus. In the hippocampus, adult neurogenesis is involved in learning and memory. Interestingly, the direct cellular environment of NSCs, the neurogenic niche, provides major neurogenic cues. In particular, astrocytes play a crucial role in several steps of adult neurogenesis including NSC proliferation, new neurons' survival, and synaptic integration. In order to further investigate the role of astrocytes on the regulation of adult neurogenesis, we used a novel viral approach to target the expression of activating Designer Receptor Exclusively Activated by Designer Drugs (DREADD) specifically in astrocytes. Using calcium imaging, we verified the appropriate targeting of astrocytes and DREADD functional expression in these cells. We then used this approach in vivo to control the activity of astrocytes in the dentate gyrus and examine their role in the regulation of adult hippocampal neurogenesis. The goal of this study is to test the possibility that artificially activating astrocytes may increase adult neurogenesis and hippocampal function. These investigations will enable a better understanding of the regulation mechanisms of adult neurogenesis in the hippocampus by the neurogenic niche. These mechanisms are relevant to hippocampal function and diseases, such as Alzheimer's disease and mood disorders.

Stamate, Matei-Alexandru

The Biological Predisposition For Cooperative Behavior Through The Lenses Of Event Related Potentials

Stamate M (1), Vasile A(2), Petrescu L(1)

(1) Department of Anatomy, Animal Physiology and Biophysics, Faculty of Biology, Bucharest, Romania

(2) Re-Design Association

Understanding what the triggers are for and how the brain generates cooperative behavior is a crucial step in the development of better education systems and behavioral therapies. In this study, we've developed a version of a socio-economic game (Prisoner's Dilemma), with the purpose of measuring event related potentials (ERPs) during the result presenting phase and correlating them with behavioral data and theta rhythms. The components of time-locked ERPS that we have analyzed were the N200, P300, Late Positivity Potential (LPP) and Late Negativity Potential (LNP), mainly to observe if we could predict the subject's intention to reciprocate the result they received from their opponent, a strategy known as "tit-for-tat". This opponent was represented by a computer algorithm for both groups, while one group was led to believe that its opponent was human. For this latter group, we have observed a pronounced early negative response as well as a late negative spike in amplitude, which may imply a strong emotional valence encoding by the brain, and which were elicited before a reciprocal “defect” response. We have also uncovered theta waves patterns over the frontal medial-lateral areas of the brain after a “defect” response, a possible intervention of the limbic system in the case of the simulated social encounter. The brain generated predominantly positive responses in cases where the result matched the previous choice and more notably in the group that knew played against a computer. We concluded that certain ERP components and brain waves correlations can describe the cooperative behavior or its absence.

Stimpfling, Victor

FlyTrack, simultaneously measuring 3D poses and muscle activity in freely behaving Drosophila

EPFL

Animal behavior arises from coordinated neural signals. However, these behaviors are first filtered by nonlinearities arising from passive viscoelastic properties of the musculoskeletal system and physical interactions with the environment. Thus, a direct mapping from neural activity to observed behaviors requires an understanding of the intermediate transformation imparted by the body's muscles and skeleton. Although tethering has facilitated the discovery of neural and muscle activity underlying behavior, it is even more crucial (and difficult) to unravel this transformation in an unrestrained setting in which the full capacity of postural and kinematic muscles are engaged. To address this challenge, we have built an optical setup capable of recording accurate 3D poses and underlying muscle activity in untethered flies at high framerates. To achieve this, we are leveraging the genetic toolkit available for studying the fly, _Drosophila melanogaster_. Specifically, we are using muscle driver lines to express genetically encoded calcium sensors. In our setup, flies walk freely in a linear corridor with prism mirrors as walls. This enables the capture of three views (two side and one ventral) using a single infrared-sensitive high-speed camera. This camera is mounted on a translating stage to follow the animal as it locomotes. These three camera views are then used to obtain triangulated 3D poses. Simultaneously we leverage an epifluorescence module to record muscles activity readout as changes in GCaMP-related fluorescence. We use a muscle map derived from an X-ray based reconstruction of the fly to align muscle signals with the animal's 3D pose, allowing us to measure the activity of individual muscles. Ultimately, we plan to combine these data with existing fly morphology datasets to model muscle-based actuation in our detailed neuromechanical model of the adult fly, NeuroMechFly. In summary, FlyTrack opens up the possibility of uncovering the contribution of muscle activity in fly behavior toward the ultimate goal of obtaining a complete understanding of how neural signals give rise to actions in a physically complex world.

Tapparel, Malika

From craving to consumption: the role of Pavlovian bias in food behaviour

Malika Tapparel[1], Hugo Najberg[1], Lucas Spierer[1]

[1]University of Fribourg

Cravings contribute to eating behaviours and health, yet how they emerge and translate into consumption remains unclear. Learning bias in Pavlovian conditioning (sign-tracking and goal-tracking) provides a framework for exploring how food cues drive cravings and consumption. Cravings, emerging from associations between environmental cues and physiological responses, may be amplified by sign-tracking bias, enhancing the cues' salience. This bias may also moderate the relationship between cravings and consumption by intensifying automatic and habitual processes. To test these hypotheses, a two-week longitudinal study will use Ecological Momentary Assessments through a smartphone-based app to measure high-calorie food cravings and intake in real-world contexts. The learning bias will be measured using a Pavlovian learning task coupled with eye-tracking. Findings could inform personalised strategies to manage unhealthy eating behaviours. We expect that stronger sign-tracking bias will be significantly associated with elevated cravings and increased consumption for high-calorie foods.

Teixeira de Almeida, Mélanie

Neurohormonal markers of stress in Borderline Personality Disorder: interplay between oxytocin and cortisol

Mélanie Teixeira de Almeida[1], Lara Quattrocchi[1], Tatiana Aboulafia-Brakha[2], Nader Perroud[2]

[1]Université de Genève, [2]HUG

Borderline personality disorder (BPD) is characterized by important emotion dysregulation, particularly in response to psychosocial stressors. Individuals with BPD often experience and express emotions—especially anger and sadness—with greater intensity. The physiological stress response involves the release of cortisol and oxytocin, secreted by the adrenal glands and the pituitary gland, respectively. Our study aims to better understand the interplay between hormonal markers (cortisol and oxytocin). We recruited 46 patients with BPD and 47 healthy controls. Each participant completed three sessions, which included: a psychological assessment, collection of endogenous salivary cortisol and oxytocin samples in a naturalistic setting, and exposure to a standardized psychological stressor (the Trier Social Stress Test, TSST). Our findings revealed significant circadian variations in both cortisol and oxytocin levels, as well as marked hormonal reactivity to the stress task. The hormonal response was influenced by several factors, including contraceptive use, symptom severity, relationship duration, and history of childhood trauma. This study contributes to a better understanding of the neurobiological mechanisms underlying BPD and may inform the development of novel psychotherapeutic and pharmacological interventions.

Thakar, Darshit

Encoding of taste valence and interoception in the Insula

Thakar Darshit1, David Manor2, Shaked Rosenblum3, Ahmad Abu-Akel3, Kobi Rosenblum1

1 Sagol Department of Neurobiology, University of Haifa

2 MRI Unit, RAMBAM Health Care Campus, Haifa

3 School of Psychological Sciences, University of Haifa

The Insular cortex (IC) is involved in taste perception and interoception. IC plays in associating taste stimuli with their after-effects, known as taste valence encoding. The anterior IC receives taste inputs, whereas the posterior IC receives interoceptive information. Taste imparts insights into potential dangers or benefits, contributing to survival. Taste is influenced by learned experiences, which assists in the evaluation of safety and the metabolic impact of food. Currently our lab has shown immune learning through taste a process called Conditioned Immune response (CIR). The exploration of the brain's role in storing taste along with interoceptive information and its impact on physiology is an underexplored field in neuroscience. To address it, we recently found connectivity from anterior to posterior insula subserves conditioned immune response in mice. To extend the findings to humans and to elucidate the functional similarities and differences in IC between the humans and mice, we utilize functional magnetic resonance imaging (fMRI) in young healthy humans. Our preliminary results in humans confirm the involvement of left anterior IC during imagination of taste and right anterior IC in perception of disgust. We further aim to explore functional connectivity within IC and with other regions during encoding of interoception to understand the IC's involvement in the encoding of taste, and in storing and modulating interoceptive information.

Tomà, Romain

Oxytocin mediates social collaboration in a cortical-amygdala network

R. Tomà [1, 2], J. van Honk [3], E. van den Burg [1, 2], C.T. Li [4], R. Stoop [1, 2]

[1]Centre for Psychiatric Neuroscience, Lausanne University Hospital Center, Department of Psychiatry, Prilly, Switzerland, [2]University of Lausanne, Lausanne, Switzerland, [3]University of Cape Town, Department of Psychiatry and Mental Health, Rondebosch, Cape Town, South Africa, [4]Lingang Laboratory, Shanghai, China

Social interaction is a fundamental pillar of our society. It has made possible extraordinary achievements such as going to the moon. In humans, a rare autosomal disease characterized by calcification of the basolateral amygdala (BLA) has revealed the importance of the BLA and its connections to the medial prefrontal cortex (mPFC) in generous and prosocial behavior. However, the neural mechanisms underlying social interactions that lead to fruitful cooperation remain largely unknown. In this project, I investigated the connectivity between the mPFC and BLA in rats, focusing on how oxytocin modulates this circuit. Using a transgenic rat line expressing CRE under the control of the OTR promoter, combined with viral tracing techniques, I mapped OTR-expressing neurons in the mPFC. These cells are predominantly found in the ACC, PL, and IL subregions, with strong expression in layers II/III and fewer in layer V. To identify neurons projecting from the mPFC to the BLA, I injected a retrograde viral tracer into the BLA. These projection neurons are also located in layers II/III and V, overlapping with the distribution of OTR expressing cells, but do not themselves express OTRs. This suggests that oxytocin modulates the mPFC to BLA pathway indirectly, likely through local interneurons. Consistently, immunostaining with GAD67 showed that most OTR-positive cells in the mPFC are GABAergic interneurons. Patch-clamp recordings revealed that OTR-expressing neurons increase their firing rate in response to oxytocin agonists, whereas BLA-projecting neurons showed more variable responses. Ongoing optogenetic experiments aim to determine whether activation of OTR-positive interneurons modulates the excitability of BLA-projecting neurons. Finally, I developed a cooperative behavioral task where rats pull a platform to deliver food to themselves or a partner. I am currently investigating how oxytocin shapes cooperative success and social communication in this task.

Toussas, Konstantin

Individual MRI-based EEG Source Localization Accuracy in Mild Cognitive Impairment

Konstantin Toussas[1], Denis Brunet[1], Camille Bouhour[1], Serge Vulliemoz[1], Paul Unschuld[1], Lucie Bréchet[1]

[1]University of Geneva

The purpose of Electromagnetic Source Imaging (ESI) is to localize brain regions generating scalp-recorded electrical activity. While template head models have facilitated the widespread use of ESI, age and disease-related structural changes, such as neuronal loss, cortical thinning, and ventricular enlargement, can alter tissue conductivities and compromise source localization accuracy. We hypothesized that individual MRI-based head models would yield more precise localization than templates, particularly in mild cognitively impaired (MCI) patients. As part of the MemStim randomized clinical trial, 33 MCI, 35 age-matched healthy older (HO) and 35 healthy younger (HY) participants underwent high-density EEG and T1-weighted MRI. Resting-state EEG microstates A-D are brief periods of stable scalp electrical activity topographies reflecting transient brain-states. EEG microstates were source-localized using personalized and template head models. We observed distinct activity patterns between individual MRI- and template-based activity maps across all four microstates. Microstate A exhibited predominantly frontal-temporal activity in HY and HO subjects, but more temporal-parietal activity in MCI patients. Microstate B showed frontal-temporal activity in all groups, with MCI subjects showing primary activity in the temporal lobe. Microstate C indicates dominant activity in the parahippocampal gyrus bilaterally, except in MCI patients with only left-hemispheric activity. Microstate D was localized primarily in bilateral temporal-parietal regions, whereas for MCI patients, activity was in right temporal and bilateral occipital regions. The individual-based head model showed less spread activity to other areas, such as the cerebellum, and more focal activity than template-based head models. Although both ESI approaches show similar activation patterns, individual MRI-based ESI is more homogenous across groups with less widespread and more specific activity in each microstate. Microstate C was consistently localized in the medial temporal lobe, reflecting the advantages of individual MRI- over template-based ESI. All groups showed generally similar microstate localization, except for microstate A, where MCI patients showed more temporal-parietal activity and microstate D where activity was more right lateralized than in HY and HO subjects. These findings highlight the importance of personalized head models in EEG source localization for aging and neurodegeneration research.

Touya, Maylis

Estimation and prediction of fatigue in patients with glioblastoma

Maylis Touya, Stéphanie Viguet-Carrin, Pauline Ducouret, Nicolas Desbaillet, Philippe Rylvin & Andreas Hottinger

CHUV

Introduction: Fatigue is a subjective and significantly under-researched symptom, particularly impactful in glioblastoma (GBM) patients, who face intensive treatment regimens and limited prognoses. Contributing factors may include, treatment modalities, depressive symptoms due to rapidly declining health and autonomic nervous system dysregulation. Reliable prediction of fatigue is essential for optimizing the standard of care. We hypothesize that integrating physical and autonomic activity data from wearable devices can provide objective biomarkers for fatigue, seizure frequency, clinical progression, and possibly, survival.

Methods: GBM patients were monitored daily using a wearable device and electronic diaries, which recorded daily fatigue levels via a Visual Analog Scale (VAS) and seizure occurrences. Routine clinical assessments—including MRI and validated instruments such as the Multidimensional Fatigue Inventory (MFI-20)—were conducted every 2 to 3 months.

Results: As of August 2025, 11 of 20 patients have been enrolled. Daily VAS fatigue scores showed a positive correlation with the "Reduced Motivation" subscale of the MFI-20. Lower physical activity levels were consistently observed on days with higher reported fatigue. Ongoing analyses are exploring relationships with mood, treatment responses, and survival outcomes.

Conclusion: Preliminary data suggest that daily VAS fatigue assessments, combined with continuous wearable monitoring, may serve as early and objective indicators of fatigue. This approach offers a feasible and scalable method for enhancing fatigue monitoring and prognostication in GBM patients.

Uhl, Quentin

Reduced NEXI protocol for the quantification of human gray matter microstructure on the CONNECTOM 2.0 scanner

Quentin Uhl[1], Tommaso Pavan[1], Julianna Gerold[2], Kwok-Shing Chan[2], Yohan Jun[2], Shohei Fujita[2], Aneri Bhatt[2], Yixin Ma[2], Qiaochu Wang[2], Hong-Hsi Lee[2], Susie Y. Huang[2], Berkin Bilgic[2,*], Ileana Jelescu[1,*]

[1] Department of Radiology, Lausanne University Hospital (CHUV) and University of Lausanne, Lausanne, Switzerland

[2] Department of Radiology, Massachusetts General Hospital, Athinoula A. Martinos Center for Biomedical Imaging, Boston, MA, USA

* Joint last authorship

Purpose: Neurite Exchange Imaging (NEXI) provides a promising framework for probing gray matter microstructure by estimating compartment sizes, diffusivities, and inter-compartmental water exchange time (t_{ex}). However, existing protocols require long scan times, limiting their clinical utility. This study proposes a reduced acquisition scheme for the Connectome 2.0 scanner that preserves model accuracy while substantially shortening scan duration.

Methods: We combined Fisher Information Matrix (FIM)-based optimization with a SHAP-guided recursive feature elimination framework using XGBoost models trained on synthetic NEXI signals. From an initial 15-feature protocol, a reduced 8-feature protocol was selected to ensure that NEXI parameters could be estimated with high accuracy and precision under realistic conditions. Performance was validated in vivo across seven healthy participants, with full and reduced protocols processed independently. The consistency of parameter estimates, the preservation of anatomical contrast, and test-retest reproducibility were assessed.

Results: The reduced protocol yielded parameter estimates comparable to the full 15-feature protocol, including tex distributions in cortical gray matter. Estimation errors in synthetic data remained low across the physiological range. Cortical maps of f, D_i, D_e, and t_{ex} retained anatomical specificity, and test-retest variability was minimally impacted. Compared to FIM-derived and naive reduced protocols, the XAI-optimized scheme showed superior robustness and spatial agreement with the reference.

Conclusion: A hybrid optimization framework enables clinically viable NEXI imaging in 14 minutes without loss of parameter fidelity. This approach supports the broader application of exchange-sensitive dMRI in neuroscience and clinical research, and offers a generalizable method for designing efficient acquisition protocols in biophysical imaging.

Ulrich, Olivier

Hippocampal sequences are governed by the rapid integration of ongoing sensory experience

Olivier Ulrich[1], James Priestley[1]

[1]EPFL

Neural activity in the hippocampus is organized by highly reliable sequential dynamics. The neural sequence progresses in response to changes in physical, sensory, or cognitive variables, typified by place cells during active exploration. A prominent theory proposes that these sequences arise and persist through the internal dynamics of hippocampal networks, and that these pre-configured sequences are allocated to specific experiences during learning. Rather than represent sensory content directly, hippocampal activity serves as a pointer or index to sensory sequences encoded elsewhere in the brain. Here we used procedurally generated virtual reality in mice to test the robustness of ongoing hippocampal dynamics to perturbations in sensory content. Novel sensory information always and immediately interrupted the existing neural sequence, triggering the formation of a divergent sequence. These bifurcating representations occurred regardless of whether the absolute position of reward or animals' action plan changed or remained the same in the altered virtual environments. Further, the original sequence could be interrupted and later recombined through the injection of novel segments at intermediate positions within the environment, indicating the activity reflected mainly the current visual experience of the animal, with limited history dependence. These results demonstrate that place cell sequences are strongly yoked to changes in the sensory content of experience, which is compatible with its role as a more general, task-agnostic memory system.

Urwicz, Leah

Enhancing Word Learning with Non-Invasive Brain Stimulation

Leah Urwicz[1], Adrian Guggisberg[2]

[1]University of Geneva, [2]HUG

Learning new vocabulary is key for language development and rehabilitation. While traditional non-invasive brain stimulation techniques like transcranial direct current stimulation (tDCS) have shown some promise, recent evidence suggests that their effects are limited — for example, tDCS tends to improve verb learning but shows inconsistent effects for nouns. To overcome these limitations and to promote broader network engagement, we investigated whether newer stimulation methods, transcranial random noise stimulation (tRNS) and transcranial alternating current stimulation (tACS), could produce stronger and more general effects on rare word learning in healthy young adults. Thirty-six adults (18–36 years old) completed a three-day protocol with pre- and post-tests, a learning session under active or sham stimulation, and resting-state and task-related EEG. Stimulation targeted the left Inferior Frontal Gyrus (IFG) using a 4×1 HD montage. We found that tRNS significantly improved rare word learning for both verbs and nouns compared to sham ($p = .0029$), whereas tACS did not produce significant behavioral effects. Resting-state EEG showed that tRNS increased beta-band connectivity, particularly involving the precuneus and occipital regions, suggesting broader network engagement. These results highlight the potential of tRNS to boost word learning and could support its future use in language rehabilitation interventions.

Verda, Nicola

The role of astrocytes in ASD related neuronal dysfunctions

Nicola Verda[1,2], Erwin Van den Burg[1,2], Sumantra Chattarji[3], Ron Stoop[1,2]

[1]Centre for Psychiatric Neuroscience, Department of Psychiatry, Lausanne University Hospital Center,
[2]University of Lausanne, CH-1015 Lausanne, Switzerland
[3]Centre for High Impact Neuroscience and Translational Applications (CHINTA), TCG-CREST, Kolkata 700091, India

Autism Spectrum Disorder (ASD) is a neurodevelopmental condition characterized by intellectual disabilities, sensory processing dysfunctions, repetitive behaviors, and a high comorbidity with epilepsy. Despite its prevalence and clinical burden, there are currently no treatments that target the underlying cellular mechanisms driving these symptoms. One widely identified feature of ASD is neuronal hyperexcitability, thought to result from an imbalance between excitation and inhibition at the neuronal level. While most studies have focused on neuronal dysfunction, growing evidence suggests that astrocytes, through their roles in potassium buffering and modulation of synaptic activity, may critically influence network excitability. In this project, I am investigating the hypothesis that astrocytic dysfunction, specifically impaired potassium clearance via the Kir4.1 channel, contributes to neuronal hyperexcitability in ASD. Failure to clear extracellular potassium can lead to increased astrocyte depolarization, altered calcium signaling, and release of soluble factors which may disrupt neuronal inhibition through multiple pathways. These cascading effects may amplify excitability and contribute to ASD phenotypes. To test this hypothesis, I will use the Fragile X Syndrome (FXS) rat model and an in-vitro systems. First, astrocytic calcium dynamics was monitored by expressing GCaMP6f under the GFAP promoter using an AAV vector. Imaging was performed in acute medial prefrontal cortex (mPFC) slices and primary astrocyte cultures to quantify spontaneous calcium transients and responses to increased extracellular potassium. Moreover, in brain slices, I will perform whole-cell patch-clamp recordings from nearby neurons to assess excitability and firing rates. Then, to determine causality, I will selectively inhibit astrocyte activity using chemogenetics. An inhibitory DREADD receptor will be expressed in astrocytes via a GFAP-driven AAV. Upon application of clozapine-N-oxide (CNO), I will assess whether modulating astrocytic activity can normalize neuronal excitability. I will extend this approach in vivo by injecting the same DREADD construct into the mPFC of FXS rats. Animals will undergo behavioral testing, including social interaction and marble burying tasks, before and after CNO administration, to evaluate whether acute astrocyte inhibition can alleviate ASD-like behaviors. This will allow me to link astrocyte dysfunction to both neural and behavioral phenotypes. Finally, I will try to validate my findings in human iPSC-derived co-cultures of astrocytes and neurons from FXS patients. Using the same AAV tools, I will assess whether abnormal calcium dynamics and astrocyte-driven hyperexcitability are conserved in the human context, and whether chemogenetic suppression of astrocyte activity can rescue neuronal function. In conclusion, this project will investigate the contribution of astrocytic dysregulations to neuronal hyperexcitability in ASD and evaluate astrocytes as a potential therapeutic target in both rodent and human systems.

Veres, Judit

Cell type-specific rearrangement of perisomatic inhibition in the valproate model of autism

Veres Judit M. 1, Anita Varga2,3, Zsófia Reéb1,3, Viktor Román2,6, Norbert Hájos1,4,5

1 HUN-REN Institute of Experimental Medicine, 'Lendület' Laboratory of Network Neurophysiology, Budapest, Hungary;
2 Gedeon Richter Plc., Laboratory of in vivo Pharmacodynamics, Budapest, Hungary;
3 ELTE Eötvös Loránd University, Institute of Biology, Doctoral School of Biology, Budapest, Hungary;
4 The Linda and Jack Gill Center for Neuroscience, Indiana University Bloomington, 47405, Indiana, USA;
5 Program in Neuroscience, Department of Psychological and Brain Sciences, Indiana University Bloomington, 47405, Indiana, USA;
6 Semmelweis University, Richter Department, Budapest, Hungary.

Autism spectrum disorder (ASD) is characterized by disrupted excitatory/inhibitory balance, with evidence suggesting interneuron dysfunction across cortical networks. This study investigated the cell type-specific changes in perisomatic inhibition in the valproate (VPA) mouse model of autism, focusing on two major interneuron populations: parvalbumin-positive basket cells (PVBCs) and cholecystokinin-positive basket cells (CCKBCs). Pregnant mice received VPA at embryonic day 12.5, and male offspring demonstrated core ASD-like behavioral phenotypes, including decreased ultrasonic vocalizations, increased tactile sensitivity, and reduced sociability. Using immunohistochemistry and confocal microscopy, we observed an increased density of total neurons but a specific decrease in PV-expressing interneurons in the basolateral amygdala of VPA-treated mice. Analysis of perisomatic inhibitory terminals revealed a significant reduction in PV-positive bouton density around principal neurons, while CB1 receptor-positive boutons (representing CCK interneuron terminals) showed no change. Functional validation through optogenetic stimulation of PV cells and whole-cell recordings from BLA principal neurons confirmed decreased PV-mediated inhibitory input with steeper input-output relationships in VPA-treated mice. The ratio of CB1-sensitive GABAergic inputs remained unchanged when tested with a CB1 agonist. These findings indicate a cell type-specific rearrangement of perisomatic inhibition in the BLA of VPA-treated mice, with specific weakening of PV-mediated inhibition that may contribute to amygdala hyperreactivity in autism. This interneuron-specific dysfunction may represent a potential target for therapeutic

Vilademunt Alcaide, Marta

Restoring the Neurogenic Niche: Astrocytic Modulation of Microglial Reactivity in Alzheimer's Disease

Marta Vilademunt Alcaide[1], Luana Piano Vieira[2], Fabio Grieco[1], Irmak Cabas[1], Nicolas Toni[1]

[1]University of Lausanne and Lausanne University Hospital, [2]University of Lausanne

Alzheimer's disease (AD) is a progressive neurodegenerative disorder marked by cognitive decline, memory loss, and behavioral changes. A key pathological feature of AD is the disruption of adult hippocampal neurogenesis (AHN), a process essential for learning, memory, and emotional regulation. The neurogenic niche, where AHN occurs, is tightly regulated by glial cells—particularly microglia and astrocytes. Microglia influence neurogenesis through immune surveillance and cytokine secretion, while astrocytes support neuronal development and synaptic integration. Although both cell types are essential for maintaining niche homeostasis, their interactions in the context of AD remain poorly understood. Our research aims to elucidate the glial crosstalk within the neurogenic niche and explore therapeutic strategies to restore its function in AD. Previous findings from our lab demonstrated that astrocyte-secreted molecules attenuate microglial activation, reduce pro-inflammatory cytokine release, and enhance neurogenesis. In the APP/PS1 mouse model of AD, we observed early impairments in AHN, with a more pronounced and earlier onset in females (4 months) compared to males (6 months). This was characterized by a decrease in doublecortin-positive (DCX+) immature neurons, despite increased proliferation. Building on this, we compared the effect of astrocyte-derived molecules and Toll-like receptor inhibition on APP/PS1 mice, on the neurogenic niche, adult neurogenesis and cognitive function. Out preliminary data suggest that targeting astrocyte-microglia interactions can rebalance the neurogenic niche, promote neurogenesis, and potencially alleviate cognitive deficits in AD. This study highlights the therapeutic potential of modulating glial communication to combat neurodegenerative diseases.

von der Weid, Laure

When Breath Guides Action: Altered Coupling in Functional Neurological Disorder

Laure von der Weid[1], Cristina Concetti[1], Michaël Mouthon[1], Selma Aybek[1]

[1]University of Fribourg

Introduction: Functional Neurological Disorders (FND) are characterized by neurological symptoms in the absence of organic lesion. The origin of this disease is still unclear but may involve disruptions in the Sense of Agency i.e the ability to feel in control of one's own action. This concept includes the ability to perform and recognize a voluntary action. In healthy controls, spontaneous action has been shown to be linked with the breathing cycle, occurring significantly more often during the expiration phase than the inspiration. This study aimed to investigate this relationship in healthy participants and FND patients. Methods: 27 FND patients and 28 age- and gender-matched healthy controls (HC) took part in a task involving a spontaneous button press while their respiration was recorded with a breathing belt and their brain activity with an EEG device. The timing of the voluntary action, i.e. the button press, was recorded while participants had to focus either on the position of their button press (Movement condition) or the position of their initial intention to press (Wanting condition) and subsequently indicate it (M-Judgement and W-Judgement, respectively). The actual button presses were then compared to the participant's breathing cycle using a permutation test for inequality of distribution in both conditions. Results: In healthy participants, a link between button pressing and the expiration phase was observed in the Movement condition ($p = .0002$) but not in the Wanting condition ($p = .473$). In contrast, FND patients exhibited this link in both conditions ($p = .0004$ in Movement, $p = .0024$ in Wanting),. The W-Judgment isn't delayed in our sample and, consequently, the interval between the W and M-judgment isn't reduced as expected in patients. However, the FND group showed a higher variability in the reported position of the wanting to press ($p < .001$) and not in the reported position of the actual pressing ($p= .802$). Discussion: These results show that FND patients exhibit a stronger binding of their action to their breathing cycle compared to HC, even when shifting their attention to their own mental processes. This suggests a reduced flexibility in adapting their action-breathing coupling strategy. Our sample shows that patients are less precise in rating their voluntary movement, although the W-Judgment isn't delayed, as found in previous reports in FND. However, both ours and previous results suggest deficits in their Sense of Agency.

Watt, Lisa

Molecular Mechanisms of Remote Fear Memory Attenuation within Engram Cells

Lisa Watt[1], Marion Leleu[1], Davide Coda[1], Liliane Glauser[1], Johannes Gräff[1]

[1]EPFL

Understanding the factors that facilitate the attenuation of remote memories is key to developing targeted therapeutic interventions aimed at addressing maladaptive memory persistence. Despite the extensive body of research on memory processes, there is a significant gap of literature focusing on the diminution of long-standing memory traces. Recently, our lab has identified a hippocampal recall engram that is a key player in remote memory attenuation (Khalaf et al., 2018, Science), opening an avenue for memory-relevant cell type-specific molecular investigations. In this study, we aim to elucidate the processes at work within these engram cells. Utilising the cFos-tTA transgenic mouse model in conjunction with contextual fear conditioning and extinction training, we have labelled engrams activated at recall and post-extinction for subsequent molecular analysis. Employing single-nucleus RNA sequencing, we have pinpointed several candidate genes to be differentially expressed in these cells, including BDNF and the lysine demethylase KDM6B, an enzyme of the epigenetic machinery. The latter is of particular interest given its known role in cocaine-induced reconsolidation and behavioural reinstatement (Zhang et al., 2018, Neuropharmacology). Accordingly, when we over-expressed KDM6B in remote fear memory engram cells, we observed enhanced remote fear attenuation. Currently, we aim to further understand KDM6B-related molecular pathways alongside associated epigenetic alterations. Ultimately, this will aid in the understanding remote fear memory attenuation from an engram-centred perspective, as well as provide insight into potential pharmacological targets.

Wirk, Eesha

Influence of the contralateral hippocampus for ictogenesis in temporal lobe epilepsy

Eesha Wirk, Fabien Friscourt, Karl Schaller and Charles Quairiaux

HUG & UNIGE

Temporal lobe epilepsy (TLE) is the most common form of focal epilepsy, characterized by unpredictable seizures, disabling cognitive and mood disorders, and a high rate of pharmacoresistance. The hippocampal epileptic focus (EF) alone cannot fully explain the widespread pathology of TLE. Growing evidence suggests that distributed networks are involved in ictogenesis. Several studies using the kainate mouse model have demonstrated that regions distant from the EF can influence epileptiform activity (EA) within the focus. Recently, we showed that acute pharmacological TTX inactivation of the contralateral hippocampus completely abolishes ictal but not interictal activity in the EF. We hypothesize that the contralateral hippocampus functions not only as an irritative zone but also as an ictogenic node. This suggests that seizures involve not only EF microcircuits but also interactions between the hippocampal circuits of both hemispheres. In this project, we aim to further investigate this mechanistic hypothesis by utilizing freely moving bi-hippocampal recordings in the kainate mouse model of TLE, combined with chemogenetic manipulation of specific neuronal populations. Specifically, we will study the dynamics of bihippocampal ictal and interictal EAs, as well as the local and interregional neuronal circuits involved in interactions between the EF and the contralateral hippocampus. Here, we present data illustrating the effects of inhibiting glutamatergic neurons in the contralateral hippocampus on epileptic activity in the EF, displaying significant reduction in interictal spike trains and even stronger suppression of ictal hippocampal paroxysmal discharges, along with a significant rebound effect on the day after CNO administration.

Wittmann, Adrien

The integration of prosody and semantics in non-literal speech comprehension: A voxel-wise encoding model approach using LLMs

Adrien Wittmann[1], Didier Grandjean[1]

[1]Geneva University

Irony and sarcasm are complex forms of non-literal language that hinge on a misalignment between the surface meaning and the speaker's intent, requiring listeners to integrate contextual, semantic, and prosodic cues. While prior neuroimaging studies have implicated a broad network—including the temporal cortex, inferior frontal gyrus (IFG), and medial prefrontal cortex (mPFC)—in the comprehension of ironic and sarcastic speech, the precise neural mechanisms underlying the integration of semantic and prosodic information remain unclear. In the present study, we addressed this gap by employing voxel-wise encoding models to systematically identify brain regions specifically involved in combining prosodic and semantic cues during non-literal language comprehension. Participants listened to naturalistic auditory dialogues in which discourse context, target utterance semantics, and prosody were systematically manipulated. We derived custom text embeddings using transformer-based models to capture context-sensitive semantic representations of ironic statements, alongside extracted prosodic features characterizing affective intonation. Ridge regression models were fitted to predict BOLD responses at the voxel level using semantic, prosodic, and combined features. We systematically examined voxels best predicted by the combination of both modalities rather than either alone, to identify regions likely involved in integrating semantic and prosodic information. We present preliminary results highlighting key regions involved in this integrative process.

Wu, Cheng-Hsi

Lateral Habenula neuronal activity and adult-newborn interactions in virgin mice

Cheng-Hsi Wu[1], Salvatore Lecca[1], Manuel Mameli[1]

[1]UNIL

Interaction between adults and newborns is essential for ensuring offspring survival, a behavior observed not only in humans but across animal kingdom. Mice display a variety of interactions such as nesting, pup grooming, and pup retrieval. Virgin mice exhibit distinct behaviors toward pups compare to parental mice: females take care of newborns while males tend to attack them. Among the brain regions involved in these interactions, recent data suggest a contribution of aversion-processing hub, the Lateral Habenula (LHb). LHb neurons are excited by distress pup calls, and their activity is necessary for pup retrieval in virgin female mice. Additionally, the LHb exhibits sexual differentiation in various aspects. Anatomical innervation and gene expression differ between virgin female and male mice. Therefore, we aim to tackle two questions: First, does sexual dimorphism define cellular properties of LHb neurons? Second, do adult-newborn interactions alter LHb neuronal activity? To investigate this, we ex vivo electrophysiology recording to reveal the cellular properties underlying adult-newborn interactions in LHb.

Yu, Ina Bianca

Interfacing brain-decoded motor intentions with cervical epidural electrical stimulation to restore arm and hand movement after spinal cord injury

Ina Bianca Yu, Thibault Collin, Icare Sakr, Valeria Spagnolo, Sergio Hernandez, Nadine Intering, Julie Hervé, Céline Deschenaux, Gaia Carparelli, Félix Martel, Rémi Souriau, Alice Bruel, Pedro Abranches, Nicolas Hankov, Grégory Dumont, Pierre Bessot, Charlotte Jacquet, Anne Watrin, Léa Bole-Feysot, Charles David Sasportes, Malo Simondin, Serpil Karakas, Laure Coquoz, Vincent Rouanne, Federico Ciotti, Simon Dahan, Philippe Forrero, Remy Tang, Andrea Galvez, Yu Zhang, Jean-Baptiste Ledoux, CamilleHaxaire, Carole Poulin, Fabio Becce, Stefano Carda, Viviana Aureli, Matthieu Bosquet, Marina D'Ercole, Julien Dedelley, Erika Ross, Léonie Asboth, Robin Demesmaeker, Fabien Sauter, Olivier Faivre, Tetiana Aksenova, Guillaume Charvet, Jocelyne Bloch, Grégoire Courtine, Henri Lorach

CHUV-NeuroRestore

Cervical spinal cord injury (SCI) disrupts the communication between the brain and the regions of the spinal cord that produce upper limb movements, resulting in permanent deficits in arm and hand functions. Epidural Electrical Stimulation (EES) has proven to promote recovery as well as improve capabilities in humans both for lower and upper limb functions by targeting the large diameter afferent fibers entering the spinal cord. Moreover, a recent study has shown that enhanced lower limb neurological recovery could be observed when EES is synchronized with a patient's intentions through an artificial, digital bridge between the brain and the spinal cord. Here, we implemented for the first time a similar technological framework to restore voluntary control of arm and hand motor activity. We implanted two participants suffering from incomplete C3/C4 spinal cord injury, each with two spinal cord electrode arrays (from C4 to T1) connected to two implanted pulse generators (ONWARD IPGs) and an electrocorticographic (WIMAGINE ECoG) device placed over the sensory-motor cortex. We optimized electromyographic activity and induced kinematics with various stimulation parameters, building a heuristic myotome with frequential preferences for motor neurons activation. From the ECoG signals, we built algorithms to decode each participant’s motor intention to extract up to 6 states. We then modulated optimized EES parameters based on the state probabilities during 2 months of rehabilitation to promote recovery. In these first participants, we demonstrated 1) the safety and feasibility of using the system, and 2) that extended use of brain-controlled cervical EES rehabilitation supports neurological recovery in the arm and hand motor functions of patients suffering from incomplete SCI.

Zhou, Jiafeng

Dual lineage origins contribute to neocortical astrocyte diversity

Jiafeng Zhou[1], Ilaria Vitali[2], Sergi Roig-Puiggros[1], Awais Javed[1], Iva Cantando[2], Matteo Puglisi[3], Paola Bezzi[2], Denis Jabaudon[1], Christian Mayer[4], Riccardo Bocchi[1]

[1]university of geneva, [2]university of lausanne, [3]Ludwig-Maximilians-Universität München, [4]Max Planck Institute for Biological Intelligence

Recent studies reveal that astrocytes are not a uniform population but exhibit diverse morphological, molecular, and functional characteristics. However, how this diversity originates and establishes during development, remains largely unknown. Using single-cell RNA sequencing and spatial transcriptomics, we identified five astrocyte subtypes with unique molecular features, spatial distributions and functions in the mouse neocortex and discovered essential regulators for their formation. Using TrackerSeq to track clonally related astrocytes, we identified two distinct lineages that give rise to the five astrocyte subtypes. The first lineage derives from Emx1+ radial glial cells that initially generate neurons and later switch to astrocyte production. The second lineage, with minimal neuronal output, predominantly produces a distinct subset of astrocytes marked by Olig2. Knocking out Olig2 disrupted lineage specification, leading to changes at molecular, morphological and functional level. These findings offer novel insights into the cellular mechanisms underlying astrocyte diversity, highlighting the presence of multiple radial glial cell subtypes, responsible for generating cortical astrocyte subtypes.

Zlatkova, Despina

Neurofeedback Targeting Global Alpha-band Connectivity Of Visual Areas To Improve Visual Perception

Despina Zlatkova[1], Marija Uscumlic[1], Adrian G Guggisberg[1]

[1]Division of Neurorehabilitation, Department of Clinical Neurosciences, University Hospital of Geneva, Av. de Beau-Séjour 26, Geneva 1211, Switzerland

Alpha-band (8–12 Hz) functional connectivity (FC) between visual regions and the rest of the brain was found to positively correlate with perceptual performance in neurotypical individuals and with deficit severity in patients with affected visual field. Building on this evidence, the present study investigated whether neurotypical participants could enhance global alpha-band connectivity of visual areas through auditory neurofeedback, and whether this modulation relates to improvements in visual perception. Twenty-six participants were randomly assigned to either an active group or a control group. Both groups received real-time auditory neurofeedback based on their alpha-band FC, enabling them to learn to modulate their brain activity. Each participant completed two neurofeedback sessions, with 24 minutes of effective training per session. The active group aimed to increase global alpha-band FC of visual areas (V1-3), whereas the control group targeted ipsilateral dorsal and frontal gyri regions. We hypothesized that participants in the active group would enhance alpha-band FC in visual brain regions, leading to improved visual perception. This improvement was expected to be region-specific, meaning that such effects would not be observed in the control group. Visual perception was assessed on separate days, prior to and following the neurofeedback sessions, using six fixed low-contrast stimuli. Neurophysiologically, the results suggest that the active group sustained higher FC in the targeted visual region following neurofeedback training, whereas the control group exhibited a decline over time. This difference between groups became more pronounced during the second day of training. Behaviorally, both groups showed reduced perceptual contrast thresholds following neurofeedback training. The improvements were more notable in males from the active group, suggesting a sex-related difference in neurofeedback effects. In conclusion, neurofeedback can help sustain high alpha-band FC in visual areas; however, extended neurofeedback training may be necessary to enhance this connectivity and induce perceptual improvements. This study is an important step in exploring the potential of neurofeedback to enhance global alpha-band FC in visual areas, potentially leading to new approaches to rehabilitate visual field deficits.

Zufferey, Valentin

Mitochondrial Biosensors in Astrocytes: A Cellular Platform for Detecting Neurological Pathology in Biofluids

Valentin Zufferey[1], Jeanne Espourteille[1], Enea Parietti[1], Héloïse Guénon[1], Nicolas Preitner[2], Morvane Colin[3], Kevin Richetin[4]

[1]Centre de neurosciences psychiatriques (CNP), CHUV – Université de Lausanne (UNIL), 1015 Lausanne, Suisse, [2]AC Immune SA, 1015 Lausanne, Suisse, [3]Univ. Lille, Inserm, CHU Lille, LilNCog—Lille Neuroscience & Cognition, 59000 Lille, France, [4]Centre de neurosciences psychiatriques (CNP), CHUV – Université de Lausanne (UNIL), 1015 Lausanne, Suisse ; Centre Leenaards de la Mémoire, CHUV – UNIL, 1011 Lausanne, Suisse

Astrocytes, integral to brain homeostasis and pathology, exhibit mitochondrial sensitivity to extracellular pathological material, positioning them as ideal biosensors for neurological disorders. Richetin et al. (2020) demonstrated that tau accumulation in astrocytes disrupts mitochondrial dynamics, correlating with synaptic dysfunction and cognitive decline in Alzheimer's disease models. Building on this, Perbet et al. (2023) revealed that extracellular vesicles (EVs) transfer neuron-derived tau isoforms (3R/4R) to astrocytes, inducing isoform-specific mitochondrial responses: 3R-tau fragments mitochondria, while 4R-tau increases branching. Leveraging lentiviral-delivered MitoTimer biosensors, our lab established a live-imaging platform to monitor mitochondrial turnover and redox states in astrocytes, thus enabling real-time detection of pathology-induced changes. Using this approach, we detected pathological EVs in human biofluids (plasma, cerebrospinal fluid), with mitochondrial signatures distinguishing Pick's disease (3R-tau) from progressive supranuclear palsy (4R-tau). Furthermore, synthetic tau extracellular paired-helical filaments (ePHF-tau) were detected by astrocytes in a 3D neuron-astrocyte co-culture, where glial cells displayed a much stronger response compared to neurons. The phagocytic activity of astrocytes, their anatomical positioning at blood-brain interfaces, and their mitochondrial plasticity make them sensitive "sniffer cells" for brain-derived pathological material, which can be specifically and non-invasively isolated from biofluids like plasma or saliva. While current limitations include temporal data complexity and intercellular variability, scalability improvements could enable high-throughput screening for diagnostics and therapeutic monitoring in the future.

Chippalkatti, Vaibhav

Investigating the role of long-range corticocortical and thalamocortical projections in sensory perception

Vaibhav Vinod Chippalkatti1,2, Foivos Markopoulos1, Ronan Ch´ereau1, Anthony Holtmaat1
1Department of Basic Neurosciences, University of Geneva
2Lemanic Neuroscience Doctoral School

(Introduction) Mice rely on their whiskers to explore their environment. In the brain, tactile information from the whiskers is conveyed via the thalamus to a subdivision of the primary somatosensory cortex (wS1). Sensory-evoked activity in wS1 is shaped by direct thalamic input from the ventral posteromedial nucleus (VPM) of the thalamus as well as, among others, long-range glutamatergic projections from the higher-order posteromedial thalamic nucleus (POm) and from contralateral S1 (cS1). These long-range projections both excite and inhibit cortical pyramidal neurons (PNs) in wS1, but how these dual functions affect cortical activity during sensory perception remain poorly understood.
(Methods and Results) Here, we investigated how wS1 afferents from cS1 and the Pom influence the detection of varying whisker deflection amplitudes. After confirming that wS1 is essential for proper perception, we found that activating wS1 in the opposite hemisphere significantly impaired sensory detection compared with control trials. Using electrophysiology in brain slices neurogliaformcells (NGCs) were identified as synaptic targets of cS1 projections, and thus as potential key cellular mediators of this interhemispheric inhibition. Indeed, the optogenetic activation of NGCs reproduced the suppression of sensory perception that had been observed with ipsilateral stimulation. To investigate the role of POm afferents, we applied either a rhythmic whisker stimulation protocol – which has been shown to activate POm and recruit its disinhibition of PNs, or the chemogenetic inhibition of POm. Both procedures failed to alter sensory perception. Together, these results reveal distinct contributions of transcallosal and the higher order thalamocortical pathways to sensory processing in wS1.
Ongoing experiments include calcium imaging of PNs across cortical layers (L2/3 and L5), as well as dendritic activity in layer 1, combined with targeted modulation of thalamic and corticocortical inputs to determine how these pathways regulate sensory perception and learning.

van Oorschot, David

Spatiotemporal integration of dendritic potentials in the somatosensory cortex

van Oorschot, D. J.1,2, Chereau, R.1, Brandalise, F.1, a, Holtmaat, A.1

1Department of Fundamental Neuroscience, Faculty of Medicine, University of Geneva. 2Lemanic Neuroscience Doctoral School, University of Geneva. a Current address : Department of Biomedical Sciences; University of Cagliari.

In the mouse primary somatosensory cortex (S1), feedforward tactile whisker information is dynamically integrated with various sources of feedback information. This generates context-dependent neuronal activity that lies at the basis of behaviourally relevant sensory perception. In our recent work, we have shown that synaptic inputs from POm feedback projections to distal tuft dendrites selectively enhances dendritic excitability in broad-tufted pyramidal cells in layer (L) 2 of S1. We found that POm afferents activate group-1 metabotropic glutamate receptor (mGluR)-dependent mechanisms, promoting the closing of two-pore domain potassium leak-channels (K2P) and thereby increasing membrane resistance. Moreover, when their activation was combined with other synaptic inputs to this cell type – such as from the primary motor cortex (M1), POm projections promoted their supralinear integration. Taken together, the facilitating drive of POm projections, as well as their specific spatial arrangement on the distal tuft dendrites, brought us to investigate whether the integration of POm- with other feedback inputs is sensitive to temporal sequences in their respective arrival. We tested the effects of small delays (Δ10 and Δ50ms) between optogenetically activated POm- and M1 inputs in either direction on the postsynaptic dendritic potentials, as compared to simultaneous or single input stimulation. Preliminary results indicate that the Δ50ms delays drove responses mostly as if inputs were activated independently, whereas Δ10ms delays enhanced the responses to variable degrees. This suggests that small temporal delays in these synaptic inputs have no enhancing effect on their dendritic integration compared to simultaneous activation, but a short temporal window for integration may be facilitated. Work is currently in progress to pharmacologically dissect the potential GABAergic influences on these postsynaptic responses, as well as to characterise their individual and combined recruitment of AMPA/NMDA receptors. In parallel, a second research line has been started to investigate the role of POm feedback projections on the excitability and synaptic integration of apical dendritic trunks from L5a/b pyramidal cells.

Born, Maren

Disgust Sensitivity Modulates Immune and Neural Responses to Virtual Infection Threats

Maren Born [1], Tommaso Bertoni [1], Michel Akselrod [1], Sara Trabanelli [2,3], Camilla Jandus [2,3], Andrea Serino [1]
[1] MySpace Lab, Department Clinical Neurosciences, University Hospital Lausanne (CHUV), Lausanne.
[2] Departement of Oncology, UNIL-CHUV, University of Lausanne, Epalinges.
[3] Targeting of cytokine secreting lymphocyte (TCSL) laboratory, Department of Pathology and Immunology, Faculty of Medicine, University of Geneva.

Recent research suggests that approaching infectious avatars and entering the peripersonal space (PPS) in virtual reality (VR) modulates innate lymphoid cell (ILC) activation. Here, we investigate how individual disgust sensitivity influences neuroimmune responses to virtual infections. Disgust sensitivity, a key component of the behavioral immune system (BIS), aids pathogen avoidance and may pre-activate immune defenses.
Using a bio-behavioral approach combining VR exposure, behavioral assessments, questionnaires, and pre- and post-exposure blood sampling, we assessed the interplay between disgust, immune signaling, and brain activity. Higher disgust susceptibility was associated with reduced ILC activation in response to infectious avatars, suggesting that individuals prone to disgust may have had reduced real-world pathogen exposure, potentially contributing to weaker immune activation.
We then analyzed eicosanoids, neuroinflammatory markers, and hormones from blood samples collected after VR exposure, identifying linear relationships between disgust sensitivity and these metabolomic profiles. This allowed us to predict metabolite levels from disgust scores. Additionally, a neural network trained on these metabolomic markers accurately predicted ILC activation, demonstrating a potential mechanistic link between metabolomic markers and immune response profiles. When predicting immune responses solely from disgust scores, via the intermediate metabolomic predictions, the same negative correlation between disgust scores and immune responses was observed, reinforcing the link between disgust sensitivity and immune modulation.
In a separate cohort, fMRI analysis revealed that hypothalamic connectivity with visual and sensorimotor areas was modulated by disgust levels, with high-susceptibility individuals showing increased connectivity after, compared to before, virtual pathogen exposure.
These findings highlight a complex interaction between disgust sensitivity, neural processing, and immune signaling, suggesting that disgust modulates immune preparedness through neuroimmune pathways triggered by virtual pathogen exposure.