Early-Career Researchers Symposium 2021

We are very proud to welcome you to the 3rd Annual Early-Career Researchers Symposium (ERS) 2021 hosted by the Young Swiss Society for Neuroscience (ySSN). In holding the ERS, the ySSN aims to provide a platform for young neuroscience researchers to present their work and gain insights into future career paths. This year we are fostering 13 talks and 23 poster presentations provided by researchers at multiple levels of training from Master's and PhD students to postdocs. They will present their work from various fields including basic molecular and cellular neuroscience, behavioural neuroscience with rodents and humans, and theoretical computational neuroscience.

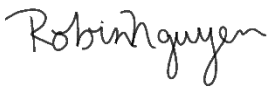
Additionally, we have invited two featured speakers at an advanced stage of their careers. In the morning, a keynote lecture will be provided by Dr. Sabine Krabbe. Dr. Krabbe completed her doctoral studies at Goethe University Frankfurt and Philipps University Marburg and moved then to Friedrich Miescher Institute for Biomedical Research in Basel for her postdoctoral studies. After being also a visiting scientist at HHMI Janelia Research Campus in Ashburn she has become the head of the DZNE Research Group called "Functional Diversity of Neural Circuits" in Bonn. She is focusing her research on associative learning and how it is influenced by emotions like fear, and physiological responses such as stress or hunger. In her talk she will be focusing on the inhibitory amygdala microcircuits and their role in associative learning. Being a young principle investigator, she will also give insights about her career trajectory and which challenges she had faced on her way to obtaining her current position.

In the afternoon we have invited Dr. Esther Schnapp. Dr. Schnapp did her doctoral studies at the Max Planck Institute for Molecular Cell Biology and Genetics, where she studied tail regeneration in the axolotl. Afterwards, she moved to the Stem Cell Research Institute of the San Raffaele Hospital in Milan where she worked on muscle development in zebrafish and on the characterisation of mesoangioblasts. In 2008 she joined EMBO reports, where she is now working as a senior editor. She will give insights into the publication process and internal workings at EMBO. Additionally, she will talk about her role as an editor and the steps which have led her to become a senior editor at EMBO reports.

At this point we would also like to mention all members of the ySSN which have been involved in initiating, planning and setting up this event and thank them for their ideas and support.

We are looking forward to an exciting and interesting event!

Your ERS 2021 organizing team



Dr. Robin Nguyen

Kristina Slabeva

Raquel Adaia Sandoval Ortega

Dr. Maria Reva

Dr. Norbert Hogrefe

Nagiua Haymour

Ed (Zhuoliang) Li

Pedro Espinosa

About the young Swiss Society of Neuroscience

The Young Swiss Society for Neuroscience is an organization run by a committee of dedicated PhD students and postdocs from universities throughout Switzerland.

We believe science communication is a fundamental part of the professional development of a researcher. Following this belief, we organize annual meetings and events to provide trainees the opportunity to share their research with the neuroscience community. The ySSN brings together early-career neuroscience researchers from institutes across Switzerland with the goal of fostering scientific exchange and networking in a vibrant and friendly environment.

Our Mission

The primary mission of the ySSN is to create a dynamic scientific network for the young neuroscience community in Switzerland.

To attain this goal, we organize events throughout the year which serve as a platform for young neuroscientists to increase their visibility and audience. We provide environments where early-career researchers can develop professional skills to aid their success in research. Specifically, we aim to:

- Increase knowledge transfer between trainees, laboratories, and institutions.
- Build effective communication skills to engage the audience in thinking and discussing the research of early-career neuroscientists.
- Create a diverse network that works together to train and promote outstanding future neuroscientists.

If you are interested to learn more about the ySSN or joining our group of motivated PhDs and Postdocs please write a mail to web.yssn@gmail.com or visit our website at https://www.yssn.ch/

We are looking forward to hearing from you!

ySSN
young Swiss Society for Neuroscience

The young swiss society of neuroscience

Program 3rd ERS 2021

08:45	Start
08:45-08:50	Opening Remarks
08:50-09:50	***Keynote Lecture*** Dr. Sabine Krabbe, Group Leader, DZNE *"Inhibitory amygdala microcircuits for associative Learning"* Chair: Kristina Slabeva
09:50-10:00	Break
10:00- 12:00	Plenary Talks
12:00-12:45	Lunch Break
12:45-14:15	Parallel Poster Sessions
14:15-15:15	Plenary Talks
15:15-15:25	Break
15:25- 16:05	**Featured Lecture** Dr. Esther Schnapp, Senior Editor, EMBO reports *"Publishing policies and initiatives at EMBO press"* Chair: Dr. Robin Nguyen
16:05- 17:05	Plenary Talks
17:15	Prize For Best Talk and Closing Remarks

Thank you to our sponsors

Timeline Talks

Morning Plenary Lecture Schedule: 10:00 - 12:10

10:00 - 10:20	**Benjamin Ehret, ETH Zurich** *"Stimulus-response mappings in prefrontal cortex population activity"*
10:20 - 10:40	**Nisheet Patel, University of Geneva** *"Dynamic allocation of limited memory resources in reinforcement learning"*
10:40 - 11:00	**Marie Labouesse, University of Zurich** *"New players in the basal ganglia: a second "collateral" direct pathway from the striatum to the GPe that supports motor control"*
11:00 - 11:30	**Kevin Thomas, University of Fribourg** *"Investigating the role of Nucleus Basalis of Meynert's Parvalbumin expressing neurons in Auditory Information Processing"*
11:00 - 11:30	**Hamid Azimi, University of Fribourg** *"Optogenetic activation of the posterior nucleus basalis parvalbumin neurons modulates local circuit activity as well as responses in the auditory pathway"*
11:30 - 12:00	**Jakub Kralik, University of Bern** *"Exploring the thresholds of bipolar-cell targeted optogenetic vision restoration in rd1 mice"*
11:30 - 12:00	**Giulia Schilardi, University of Bern** *"Electrophysiological Characterization of Retinal Bipolar Cells in Murine Retina: Optimize Restorative Approaches"*

Afternoon Plenary Lecture Schedule: 14:15-15:15

14:15 - 14:35	**Teresa Cramer, University of Zurich** *"Adamtsl3 is a novel extracellular synapse organizer that facilitates DCC function for GABAergic synapse formation and maintenance"*
14:35 - 14:55	**Stan Kerstjens, University of Zurich** *"Evidence for a Mitosis-induced Lineage Address Space in Mouse Brain"*
14:55 - 15:15	**Patricia Renz, University of Bern** *"Deciphering astrocyte polarization in perinatal white matter injury and its role in disease pathogenesis"*

Afternoon Plenary Lecture Schedule: 16:05- 17:05

16:05 - 16:25	**Karla Burelo, University of Zurich** *"Detecting High-frequency oscillations in scalp EEG recordings using a Spiking Neural Network"*
16:25 - 16:45	**Amelie Haugg, University of Zurich** *"Adaptive neurofeedback stimulation to support smoking cessation"*

16:45 - 17:05	**Vidmante Fuchs, University of Basel** *"Presence of SARS-CoV-2 Transcripts in the Choroid Plexus of MS and Non-MS Patients with COVID-19"*

Timeline Parallel Poster Sessions

GROUP A – NEURODEVELOPMENT	
12:45- 12:55	**Elkhan Yusifoc, University of Zürich** *"Investigating primary cilia in the development of the nervous system"*
12:55- 13:05	**Vera Tscherrig, University of Bern** *"What is the role of miRNAs in Wharton's Jelly-derived small extracellular vesicles (sEV) in neuro-regeneration?"*
13:05- 13:15	**Leslie Bargsted Friedrich Miescher Institute (FMI)** *"A Single Cell Approach to Study Transcriptional Heterogeneity of Precerebellar Neuron Subpopulations During Development"*
13:15- 13:25	**Teresa Cramer, University of Zürich** *"Adamtsl3 is a novel extracellular synapse organizer that facilitates DCC function for GABAergic synapse formation and maintenance"*
13:25- 13:35	**Stan Kerstjens, University of Zürich** *"Evidence for a Mitosis-induced Lineage Address Space in Mouse Brain"*
13:35- 13:45	**Patricia Renz, University of Bern** *"Deciphering astrocyte polarization in perinatal white matter injury and its role in disease pathogenesis"*
13:45- 14:15	**Open Discussion in group or Break out Rooms**

GROUP B – DISORDERS	
12:45- 12:55	**Cristina Simon Martinez, University of Bern** *"The reorganization of the motor network after childhood stroke: A multimodal approach including resting state functional MRI and transcranial magnetic stimulation*
12:55- 13:05	**Luc Lagrace Nwamekang Belinga, University of Lausanne** *"Brain-secretases to predict presymptomatic (mild cognitive impairment) stage dementia"*
13:05- 13:15	**Gregory Lepeu, University of Bern** *"Cortical excitability as a marker of epileptic seizures susceptibility in the mouse hippocampus"*
13:15- 13:25	**Elena Konnova, University of Lausanne** *"Changes in excitability of afferent nociceptors after nerve injury"*
13:25- 13:35	**Dorottya Cserpan, University of Zürich** *"Sleep homeostasis affects scalp HFO rates in pediatric epilepsy"*
13:35- 13:45	**Karla Burelo, University of Zürich** *"Detecting High-frequency oscillations in scalp EEG recordings using a Spiking Neural Network"*
13:45- 14:15	**Open Discussion in group or Break out Rooms**

GROUP C – COGNITION	
12:45- 12:55	**Nina Sooter, University of Geneva** *"Probing Moral Resiliency: Do Protected Values Shield us from Stress-Induced Dishonesty?"*
12:55- 13:05	**Carlo Cerquetella, University of Bern** *"Neural circuits for emotional conflicts and decision making in the ventral CA1 hippocampus"*
13:05- 13:15	**Joana Duarte, University of Bern** *"Neural correlates for reward and aversive contextual memories in the ventral hippocampus"*
13:15- 13:25	**Emma Volitaki, University of Bern** *"Deciphering the role of parvalbumin interneurons in the ventral CA1 hippocampus during anxiety"*
13:25- 13:35	**Lotte Spierenburg, University of Bern** *"Dopaminergic neuromodulation of spike timing dependent plasticity in layer 5 pyramidal neurons of the anterior cingulate cortex"*
13:35- 13:45	**Nisheet Patel, University of Geneva** *"Dynamic allocation of limited memory resources in reinforcement learning"*
13:45- 14:15	**Open Discussion in group or Break out Rooms**

GROUP D – SENSORY SYSTEMS	
12:45- 12:55	**Marta Dimanico, University of Fribourg** *"Aspects of tree shrew consolidated sleep structure resemble human sleep"*
12:55- 13:05	**Newsha Ghasemi Nejad, University of Zürich** *"Deviant stimuli improve signal detection in the mouse somatosensory system"*
13:05- 13:15	**Raquel Adaia Sandoval Ortega, University of Bern** *"The Emotional and Physical Processing of Pain during Sleep"*
13:15- 13:25	**Jakub Králik, University of Bern** *"Exploring the thresholds of bipolar-cell targeted optogenetic vision restoration in rd1 mice"*
13:25- 13:35	**Giulia Schilardi, University of Bern** *"Electrophysiological Characterization of Retinal Bipolar Cells in Murine Retina: Optimize Restorative Approaches"*
13:35- 14:15	**Open Discussion in group or Break out Rooms**

Abstracts Talks

Morning Plenary Lecture Schedule: 10:00 - 12:10

STIMULUS-RESPONSE MAPPINGS IN PREFRONTAL CORTEX POPULATION ACTIVITY

10:00 - 10:20

Benjamin Ehret[1], Roman Boehringer[1], Christian Henning[1], Benjamin Grewe[1]

1) Institute of Neuroinformatics, University of Zürich and ETH Zürich

To survive in challenging environments, animals need to learn to perform adaptive behaviors in the presence of stimuli that predict threats or rewards. This type of learning depends on various interconnected brain regions that are involved in functions ranging from sensation to behavior execution, but how the mapping from a stimulus to an appropriate response is implemented and updated upon changing contingencies is poorly understood. The prefrontal cortex (PFC) has been shown to respond to behaviorally relevant stimuli, while also influencing behavior. Yet, it is unclear whether prefrontal activity implements specific stimulus response mappings, and how such mappings are learned and updated over time. Here we investigate the involvement of PFC in linking stimuli and behavior using novel aversive auditory conditioning paradigms with stimulus response mappings that change over the course of an experiment. During these conditioning paradigms, we use miniaturized fluorescence microscopes for calcium imaging to track the activity of prefrontal neurons for up to 11 days. We show that tone evoked responses in prefrontal cortex (1) are based on different subpopulations for different stimulus response mappings, (2) show a higher dependence on the associated response than on stimulus identity and (3) can be modulated by the execution of the associated behavior on a second to second basis. These results show that PFC links stimuli to behavioral responses by differential encoding of sensory information.

DYNAMIC ALLOCATION OF LIMITED MEMORY RESOURCES IN REINFORCEMENT LEARNING

10:20 - 10:40

Nisheet Patel[1], Luigi Acerbi[2], and Alexandre Pouget[1]

1) University of Geneva
2) University of Helsinki

Biological brains are inherently limited in their capacity to process and store information, but are nevertheless capable of solving complex tasks with apparent ease. Intelligent behavior is related to these limitations, since resource constraints drive the need to generalize and assign importance differentially to features in the environment or memories of past experiences. Recently, there have been parallel efforts in reinforcement learning and neuroscience to understand strategies adopted by artificial and biological agents to circumvent limitations in information storage. However, the two threads have been largely separate. In this article, we propose a dynamical framework to maximize expected reward under constraints of limited resources, which we implement with a cost function that penalizes precise representations of

action-values in memory, each of which may vary in its precision. We derive from first principles an algorithm, Dynamic Resource Allocator (DRA), which we apply to two standard tasks in reinforcement learning and a model-based planning task, and find that it allocates more resources to items in memory that have a higher impact on cumulative rewards. Moreover, DRA learns faster when starting with a higher resource budget than what it eventually allocates for performing well on tasks, which may explain why frontal cortical areas in biological brains appear more engaged in early stages of learning before settling to lower asymptotic levels of activity. Our work provides a normative solution to the problem of learning how to allocate costly resources to a collection of uncertain memories in a manner that is capable of adapting to changes in the environment.

NEW PLAYERS IN THE BASAL GANGLIA: A SECOND "COLLATERAL" DIRECT PATHWAY FROM THE STRIATUM TO THE GPE THAT SUPPORTS MOTOR CONTROL

10:40 - 11:00

Marie A. Labouesse[1,2,3], Joseph Villarin[1,2], Arturo Torres-Herraez [1,2], Xiaoxiao Sun[1], Sherry Lam[4], Jordi Bonaventura[4], Fernanda de Carvalho[1,2], Julia Greenwald[2], Alice Tang[1], Michael Michaelides[4], Savio Chan[5], Ofer Yizhar[6], Christoph Kellendonk[1,2]

1) Columbia University Medical Center, Departments of Psychiatry, Pharmacology and Biomedical Engineering
2) New York State Psychiatric Institute
3) University of Zurich, Institute of Pharmacology and Toxicology
4) NIH/NIDA and John Hopkins University School of Medicine
5) Northwestern University, Feinberg School of Medicine
6) Weizmann Institute of Science, Department of Neurobiology

The striatum is a well-established brain region within the basal ganglia that regulates motor behavior. Its neuronal projections are divided into two routes: a direct (dopamine 1 receptor expressing, D1) and an indirect pathway (D2), classically depicted as having opposite effects on movement and distinct target regions (midbrain vs. globus pallidus=GPe). Interestingly, several anatomical studies have described the existence of axonal collaterals ("bridging collaterals"): neuronal bridges arising from D1 neurons yet contacting the target region of D2 neurons: the GPe. Their relevance for behavior is, however, fully unknown, Here, we used a combination of genetic targeting, in vivo calcium imaging, chemogenetic/optogenetic manipulations and deep learning-based behavioral tracking (DeepLabCut) to determine the role of D1 bridging collaterals in motor function in mice. We found that bridging collaterals were activated during specific movements in a rotarod task. Bridging collateral inhibition also decreased locomotion and impaired rotarod performance. Recent physiology work shows that bridging collaterals preferentially target striatal-backprojecting, arkypallidal "stop neurons" expressing Npas1 in the GPe. We here found that stimulation of D1 neurons inhibited native Npas1 motor signals in awake behaving mice. Finally, we found that Npas1 stimulation recapitulated the effects of bridging collateral inhibition by decreasing locomotion and rotarod function. We propose a model by which bridging collaterals support motor function by inhibiting Npas1 neurons in the GPe. Thus, D1 terminals in the GPe act in concert with the canonical D1 terminals in the midbrain by inhibiting a potential stop signal going back to the striatum.

INVESTIGATING THE ROLE OF NUCLEUS BASALIS OF MEYNERT'S PARVALBUMIN EXPRESSING

11:00 - 11:30

NEURONS IN AUDITORY INFORMATION PROCESSING

Kevin Thomas[1], Hamid Azimi[1], Michael Harvey[1], Gregor Rainer[1]

1) Univeristé de Fribourg

We are daily exposed to a multitude of sensory information, from which our brain must extract the most important ones based on context and relevance. Because of its direct projections to sensory areas, to the thalamus, and to Default Mode Network structures, the Basal Forebrain (BF) is known to play a major role in the modulation of information processing and attentional states. Its different nuclei are composed of entangled types of neurons, including the well-studied cholinergic cells, but also Parvalbumin expressing GABAergic (PV) neurons. How each of them contributes to the functional activity of the BF remains unclear. To answer this question, we designed an auditory detection paradigm coupled with optogenetics manipulation of the Nucleus Basalis of Meynert, a part of the BF known to interact with auditory processing areas, on PV-Cre rats. We use a behavioral task in which animals are trained to respond to a complex auditory signal in the context of noisy environment to understand how PV neurons of the NBM relate to fine auditory information detection, and back these observations with electrophysiological data.

OPTOGENETIC ACTIVATION OF THE POSTERIOR NUCLEUS BASALIS PARVALBUMIN NEURONS MODULATES LOCAL CIRCUIT ACTIVITY AS WELL AS RESPONSES IN THE AUDITORY PATHWAY

11:00 - 11:30

Hamid Azimi[1], Kevin Thomas[1], Michael Harvey[1], Gregor Rainer[1]

1) Department of Medicine, University of Fribourg

The basal forebrain powerfully modulates cortical and thalamic responses to sensory stimulation. These effects are notably mediated by BF cholinergic and parvalbumin (PV) GABAergic projections to primary sensory cortex, as well as to subcortical structures involved in sensory processing, including the thalamic reticular nucleus (TRN). Here we aimed to dissect the impact of these two classes of projection neurons on sensory processing. We utilized a PV-Cre rat line in order to optogenetically activate PV neurons in the auditory sector of the BF, whilst simultaneously recording single unit responses to band pass auditory noise stimuli in BF, TRN, the ventral medial geniculate nucleus (vMGN), and primary auditory cortex (A1). We found that while optogenetic activation reliably activated PV neurons and entrained spiking to the stimulation frequency, it also resulted in robust inhibition of other local BF neurons. BF PV projection neurons are thus capable of driving local inhibition in the BF, as well as affecting downstream targets. The results show that, when the receptive fields of BF and A1 neurons are overlapped, PV stimulation suppressed the auditory evoked response in A1, indicating a topographical BF to A1 projection. BF PV activation also modulated firing rate and response selectivity in both MGN and A1 neurons. Our results suggest that activity in BF PV neurons makes an important contribution to BF modulatory effects on sensory processing at both the cortical and subcortical levels, possibly assigning priority to behaviorally relevant stimuli in the environment. Furthermore, BF PV neurons provide local inhibition in the BF, thereby potentially downregulating other projection systems such as the cholinergic and glutamatergic projections."

EXPLORING THE THRESHOLDS OF BIPOLAR-CELL TARGETED OPTOGENETIC VISION RESTORATION IN RD1 MICE

11:30 - 12:00

Jakub Králik[1], Sonja Kleinlogel[1]

1) University of Bern, Department of Physiology

Retinitis pigmentosa (RP) represents a group of genetic disorders responsible for massive photoreceptor degeneration and gradual loss of vision in patients. Works by Kleinlogel lab and others showed possibility of restoration of light sensitivity and eventually vision in blind retinas using optogenetic gene therapy. In case of such approach retinal target cell type has to be considered. ON-bipolar cells are undoubtedly the most attractive target for maximizing receptive-field diversity and with that restoring high-quality vision.

Opto-mGluR6 is a designer chimeric protein that combines light sensitivity of melanopsin with intracellular signalling of the metabotropic glutamate receptor 6 (mGluR6). As mGluR6 is the direct transmitter of the light signalling cascade from rods and cones to ON-bipolar cells, Opto-mGluR6 represents a natural candidate for successful vision restoration in blindness. Employing a mouse model of RP treated with synthetic designer AAV vectors carrying Opto-mGluR6 under a highly specific synthetic ON-bipolar cell promoter, we were able to achieve robust reactivation of inner retinal signalling leading to differential RGC output.

Here we present multi-level functional evaluation and quantification of Opto-mGluR6-based optogenetic gene therapy in fully degenerated, blind mice. We performed electrophysiological recordings to assess the properties of artificially restored vision in response to variety of light stimuli – probing the functional boundaries and possibilities of Opto-mGluR6 vision restoration strategy. These insights will shine light on the quality of potentially restored vision by optogenetic manipulation of bipolar cells and elucidate retinal network adaptations during degeneration.

ELECTROPHYSIOLOGICAL CHARACTERIZATION OF RETINAL BIPOLAR CELLS IN MURINE RETINA: OPTIMIZE RESTORATIVE APPROACHES

11:30 - 12:10

Giulia Schilardi[1], Sonja Kleinlogel[1]

1) Institute of physiology, University of Bern

Bipolar cells, interneurons of the retina, are responsible for decoding the light signal captured by the photoreceptors. In photoreceptor degenerative diseases, the death of photoreceptors leaves behind a light-insensitive retina consisting of functional neurons, such as bipolar cells: making them good targets for optogenetic restoration. However, degeneration also causes changes in protein expression in bipolar cells, which may impact the quality of the synthetically restoration. By characterizing bipolar cells in healthy and degenerated mouse retinas, we aim at optimizing restorative approaches and improving functional output. We have recorded from WT rod bipolar cells (RBCs) and discovered the existence of two functional types of RBCs with different electrophysiological characteristics. We specifically activated and blocked BK

channels in healthy and degenerated retinas by using the specific agonist of NS1619 and the specific blocker paxilline. BK channel is an high conductance calcium- and voltage-dependent potassium channel. The voltage and calcium dependence are closely related and are responsible for oscillations of the membrane potential. The drugs did not execute any effect in the degenerated retina as in the healthy retina, suggesting a mal-function of BK channels or a loss or rewiring of BK-containing afferents. In combination with bipolar cell transcriptomics we hope to in the future be able to complement bipolar cells in the degenerated retina with proteins that re-establish natural signalling.

Afternoon Plenary Lecture Schedule: 14:15-15:15

ADAMTSL3 IS A NOVEL EXTRACELLULAR SYNAPSE ORGANIZER THAT FACILITATES DCC FUNCTION FOR GABAERGIC SYNAPSE FORMATION AND MAINTENANCE

14:15 - 14:35

Teresa Cramer[1], Lucie Pretre[1], Pinan-Lucarré Berangerie[2], Jean-Louis Bessereau[2], Shiva K. Tyagarajan[1]

1) Institute of Pharmacology and Toxicology, University of Zürich
2) Institut NeuroMyoGène, Université Claude Bernard Lyon 1

ECM proteins (eg. Orthodenticle homeobox 2, reelin, brevican, etc.) are central signaling components that are also known to influence synapse plasticity. In this study, we functionally characterize a novel ECM protein, namely Adamtsl3, a new member of the ADAMTSs (Disintegrin and Metalloproteinase with thrombospondin motifs) superfamily. The ortholog of Adamtsl3, ce-punctin/madd-4, was recently described in C.elegans and reported to be an essential organizer of the excitatory and inhibitory postsynapse through signaling downstream of the deleted in colorectal cancer (DCC) receptor (Pinan-Lucarré et al., 2014). Currently, the function of Adamtsl3 in the mammalian brain is unknown. Using a combination of in vitro assay systems, and Adamtsl3flox/flox mouse model, we report a role for Adamtsl3 at the DCC receptor at inhibitory synapses. Adamtsl3 facilitates GABAergic synapse formation and maintenance and further impairs hippocampal memory function in adult mice upon deletion. Overall, our data points to a critical role of Adamtsl3 in regulating DCC function for activity-dependent plasticity adaptations at DCC-containing synapses.

EVIDENCE FOR A MITOSIS-INDUCED LINEAGE ADDRESS SPACE IN MOUSE BRAIN

14:35 - 14:55

Stan Kerstjens[1], Gabriela Michel[1], Rodney Douglas[1]

1) Institute of Neuroinformatics, University of Zürich

The question of how developing brains are able to form stereotyped long-range conenctions remains unsolved. We argue that the successive mitoses of brain development induce an address space embedded in gene expression, that axonal growth cones could exploit for precise navigation toward remote targets. We analyzed gene expression data of developing and adult mouse brain, published by the Allen Institute for Brain Science, and found that the expressions of many sets of genes co-vary across the developing mouse brain on multiple spatial scales: the covariances have stable spatial patterns that bisect the brain into a hierarchy of nested regions resulting in a spatial partitioning of increasing resolution, consistent with an address space. We propose that this spatial organization reflects the lineage tree as can arises from two simple constraints on mitosis: that the post-mitotic daughter cells have, on average, similar

gene expression to their parent; and that on average they do not migrate too far from one another.

DECIPHERING ASTROCYTE POLARIZATION IN PERINATAL WHITE MATTER INJURY AND ITS ROLE IN DISEASE PATHOGENESIS

14:55 - 15:15

Patricia Renz[1,2], Valérie Haesler[1], Vera Tscherrig[1,2], Shane Liddelow[3], Daniel Surbek[1], Andreina Schoeberlein[1], Amanda Brosius Lutz [1]

1) Department of Obstetrics and Gynecology, Inselspital, Bern University Hospital and Department for BioMedical Research (DBMR), University of Bern, Switzerland
2)Graduate School for Cellular and Biomedical Sciences (GCB), University of Bern, Switzerland
3)Neuroscience Institute, Department of Neuroscience and Physiology, New York University (NYU), New York City, New York, USA

White matter injury (WMI) is the most common form of brain injury in preterm infants. It is characterized by reactive microgliosis and astrocytosis and defective oligodendrocyte maturation. Recent studies in the mature brain show the formation of diverse reactive astrocyte subtypes after injury, some favoring brain repair and other «inflammatory» astrocytes contributing to neurodegeneration. The specific nature of astrocyte reactivity after WMI remains obscure. Here we report the results of experiments investigating inflammatory astrocyte formation in WMI.
WMI was induced in rats at postnatal day (P)2 using a combination of hypoxic-ischemic and inflammatory insults. To confirm successful WMI, myelin deficits were evaluated using immunohistochemistry for myelin basic protein at P11. Inflammatory astrocyte formation was investigated through in situ hybridization (ISH) using a complement protein 3 (C3)-specific probe. We further characterized astrocyte reactivity by performing microfluidic qRT-PCR analysis of a panel of reactive astrocyte transcripts on mRNA isolated from astrocytes purified by immunopanning from injured and healthy brains. ISH shows a significant increase of C3-positive inflammatory astrocytes in subcortical white matter tracts across multiple rodent WMI models. Supporting this finding, preliminary qRT-PCR results suggest that purified primary astrocytes from injured brains exhibit a multi-gene inflammatory astrocyte signature at the transcriptome level.
We demonstrate the formation of inflammatory astrocytes in rodent models of WMI. This result is an important step towards understanding astrocyte polarization in WMI and opens the door to experiments investigating whether prevention the formation of this astrocyte subtype ameliorates WMI disease outcomes.

Afternoon Plenary Lecture Schedule: 16:05- 17:05

DETECTING HIGH-FREQUENCY OSCILLATIONS IN SCALP EEG RECORDINGS USING A SPIKING NEURAL NETWORK

16:05 - 16:25

Karla Burelo[1, 2], Mohammadali Sharifshazileh[1,2], Giacomo Indiveri[1, 3], Johannes Sarnthein[2, 3]

1) Institute of Neuroinformatics, University of Zurich and ETH Zürich
2) Department of Neurosurgery, University Hospital Zurich, University of Zurich
3) Neuroscience Center Zurich, ETH Zurich

Introduction:
There is recent evidence that the HFOs, biomarkers for epileptogenic zone detected in invasive EEG recordings, are also detected in non-invasive scalp EEG recordings in young

patients. The automatic detection of this biomarker is promising for long-term monitoring of the disease as well as pre-surgical studies. This kind of application can therefore benefit from an embedded system able to detect HFOs in real-time, without the need to process large amounts of data off-line, with external computers or cloud servers.

Methods:
In this study, we use an artificial Spiking Neural Network (SNN) for detecting clinically relevant HFOs found in pre-and postsurgical scalp EEG recordings, measured from eleven children with drug-resistant focal epilepsy that underwent epilepsy surgery.
The proposed SNN consists of a core HFO detection part, already validated with intraoperative ECoG data, extended with a new artifact rejection part used to eliminate false positive HFOs caused by sharp transients. Here we show that the HFO rates found by this novel SNN architecture compare favorably to those detected in the same dataset by a clinically validated automatic HFO detector (mean 2.13 HFO/min vs 2.82 HFO/min in 16 pre-resection recordings).

Conclusions:
The SNN proposed was designed using elements and parameters fully compatible with mixed-signal neuromorphic circuits. This therefore represents an important step towards the construction of a low-power embedded neuromorphic signal processing system for continuous-time on-line detection of HFOs and long-term non-invasive assessment of disease severity in patients with epilepsy.

ADAPTIVE NEUROFEEDBACK STIMULATION TO SUPPORT SMOKING CESSATION

16:25 - 16:45

Amelie Haugg [1,2], Mirjam Habegger [1], Anna Speckert [3], Sarah Meier [4], Ronald Sladky [2], Philipp Staempfli [1], Cindy Lor 2, Ellen van Maren [4], Apurva Watve [1], Andrei Manoliu [5], Erich Seifritz [1], Matthias Kirschner [6], Marcus Herdener [1], Boris B. Quednow [1], Frank Scharnowski [1,2]

1) University of Zurich, Zurich Switzerland
2) University of Vienna, Vienna, Austria
3) Université de Fribourg, Fribourg, Switzerland
4) Swiss Federal Institute of Technology, Zurich, Switzerland
5) University College London, London, United Kingdom
6) McGill University, Montreal, Canada

Controlling cigarette craving is a key factor to quit smoking. To help smokers tolerate cigarette craving better and to support their smoking cessation, we used a novel adaptive neurofeedback (NF) stimulation paradigm for downregulating cue-induced craving activation in the anterior cingulate cortex (ACC).

64 nicotine dependent subjects participated in the study. They were randomly assigned to either the experimental group (EG, N=32, age=25.94±5.29, 18m) or a control group (CG, N=32, age=27.62±5.29, 16m). Subjects in the EG were trained to downregulate their ACC activity, an area responsive to craving-related cues. During training runs, they were presented with images whose craving intensity was dynamically coupled to ongoing brain activity in the ACC). The better subjects were at down-regulating their ACC activity, the more intense got the presented smoking cues (i.e., the downregulation task became more difficult). In the CG, subjects received the same instructions, but intensity of the presented cues was linked to activity in the angular gyrus, which is not associated with nicotine craving.

All subjects were trained for 10 NF training runs. Before and after training, clinical and behavioral assessments were performed, including a follow-up session six weeks after the last NF session.

At the follow-up session, subjects in the EG showed a greater reduction in cigarette consumption ($p<0.05$) and Fagerström dependence scores ($p<0.01$) as compared to subjects in the CG. Both groups showed a reduction in cue-induced cigarette craving (as assessed by image ratings).

Our results suggest that brain-controlled adaptive nicotine cue exposure stimulation might be promising novel therapeutic tool in addiction."

Presence of SARS-CoV-2 Transcripts in the Choroid Plexus of MS and Non-MS Patients with COVID-19

16:45 - 17:05

Vidmante Fuchs[1], Michael Kutza[2], Sven Wischnewski[2], Nikolaus Deigendesch[3], Luc Lutz1, Laila Kulsvehagen[1], Gerda Ricken[4], Ludwig Kappos[1], Alexandar Tzankov[3], Simon Hametner[4], Stephan Frank[3], Lucas Schirmer[2,5,6], Anne-Katrin Pröbstel[1]

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"Although primarily targeting the respiratory system, coronavirus disease 2019 (COVID-19) also manifests with central nervous system (CNS)-related symptoms. Little is known about the clinical course of pre-existing CNS autoimmune disease and concurrent SARS-CoV-2-infection. Multiple sclerosis (MS) is the most frequent autoimmune disease of the CNS with inflammatory demyelination and blood-brain barrier (BBB) disruption being typical pathological hallmarks. Whether multiple sclerosis (MS) renders patients more susceptible to CNS involvement and/or infection during COVID-19 and the impact of SARS-CoV-2 infection on disease activity remains elusive.
We combined histopathological assessment with multiplex in situ hybridization analysis for SARS-CoV-2 and ACE2 transcripts in autoptic brain tissue of an MS patient, who died from COVID-19-associated respiratory failure, compared to other non-MS COVID-19 cases and inflammatory controls.
Despite a general microglia activation in MS and non-MS COVID-19 brain parenchyma and minor BBB leakage in MS COVID-19 brain, we found neither evidence for active demyelinating activity nor presence of SARS-CoV-2 transcripts in MS lesions. SARS-CoV-2 and ACE2 transcripts were consistently detected in epithelial cells of the choroid plexus (CP) and ependymal cells of the CSF-brain interface in both MS and non-MS COVID-19 cases.
Our findings provide no evidence for MS disease exacerbation or presence of viral transcripts in MS lesions. Notably, presence of viral transcripts in CP suggests the CP being a key restraint of SARS-CoV-2 entry into the CNS. Future studies will need to shed light on SARS-CoV-2-associated pathology in COVID-19 patients with a more active MS course and other autoimmune comorbidities."

Abstracts Posters

Group A – Neurodevelopment

INVESTIGATING PRIMARY CILIA IN THE DEVELOPMENT OF THE NERVOUS SYSTEM	**Group A**

Elkhan Yusifov[1]

1) University of Zürich

Primary cilia are microtubule based cell surface structures that play an important role in vertebrate development by serving as signaling hubs for signals, such as Sonic hedgehog. C5orf42 is the most frequently mutated gene in Joubert syndrome, a ciliopathy subtype. Patients with mutated C5orf42 showed craniofacial abnormalities, polydactyly and intellectual disabilities. C5orf42 is essential in the formation of primary cilia but a link to neural development was not known. Knocking down C5orf42 in an animal model revealed defects in neural circuit formation.

As a first step towards a better understanding of ciliary function in neural circuit formation in the PNS, it was necessary to analyze the presence of primary cilia during development. By studying chicken embryos between E3 and E7, we have demonstrated the presence of primary cilia in migrating NCC but also in their derivatives. In addition, primary cilia were present in all Dorsal Root Ganglion (DRG) neurons in vivo, as well as in DRG explants, but not in dissociated neurons. Furthermore, we found primary cilia on Schwann cell precursors and on sympathetic neurons. Future studies will focus on the role of cilia in neural circuit formation, by knocking down candidate genes.

WHAT IS THE ROLE OF miRNAS IN WHARTON'S JELLY-DERIVED SMALL EXTRACELLULAR VESICLES (SEV) IN NEURO-REGENERATION?	**Group A**

Vera Tscherrig[1,2], Sophie Cottagnoud[1], Valérie Haesler[1], Patricia Renz[1,2], Daniel Surbek[1], Andreina Schoeberlein[1], Marianne Jörger-Messerli[1]

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Perinatal white matter injury (WMI) is one of the most common neurological complications of preterm birth and it is a global health problem resulting in long-term neurodevelopmental and neurobehavioral disabilities. WMI results from hypoxia-ischemia and inflammatory insults to the developing brain during a vulnerable period of the brain's myelinating cells. Failed myelination during white matter development occurs. Until now, there is no cure for perinatal WMI. Recently, our lab and others have shown promising results towards the use of mesenchymal stromal cell derived small extracellular vesicles (MSC-sEV) as therapeutic

approach for neuronal injuries. MSC-sEV carry small non-coding RNA such as microRNAs (miRNAs). MicroRNAs might interfere with signaling pathways involved in premature WMI. Thus, we hypothesize that miRNAs, released by sEV upon uptake in their target cells, have a key function in the observed beneficial effects of MSC-sEV.
MSC were isolated from the connective tissue of human umbilical cords, the so-called Wharton's jelly. sEV were purified from the cells using ultracentrifugation, followed by size-exclusion chromatography (SEC). The fractions were characterized by the expression of sEV markers using western blot analysis and miRNAs by quantitative PCR.
The SEC fractions with the highest protein content showed positive signals for the sEV markers CD81 and CD63. No cellular contamination was observed (no signal for GM130 or Grp94). These fractions contained high amounts of miRNAs, such as miRNA 22-5p, miRNA 27b-3p or let7b-5p.
The targets of the highly abundant miRNAs in the sEV fractions play a role in apoptotic or inflammatory pathways and drive oligodendrocyte differentiation. Therefore, these miRNAs might influence WMI outcomes.

A SINGLE CELL APPROACH TO STUDY TRANSCRIPTIONAL HETEROGENEITY OF PRECEREBELLAR NEURON SUBPOPULATIONS DURING DEVELOPMENT

Group A

Leslie Bargsted[1,2], Upasana Maheshwari[1,2], Charlotte Soneson[1], Nathalie Vilain[1], Hubertus Kohler[1], Sirisha Aluri[1], Sebastien Smallwood[1], Filippo M. Rijli[1,2].

1) Friedrich Miescher Institute for Biomedical Research
2) University of Basel

The projection neurons of the pontine nuclei (PN) constitute the main mossy fiber input to the cerebellum transmitting signals from the cerebral cortex. The connectivity pattern between cortical areas and PN and the complex organization of ponto-cerebellar connectivity have been extensively investigated. At the cellular level, an internal-external lamellar organization of cortical axon fields might topographically match an inside-out organization of PN neurons based on their birthdate (Altman and Bayer, 1987; Leergard et al.,1995). Moreover, our laboratory recently discovered an intrinsic organization of PN neurons according to their rostro-caudal origin in the precerebellar rhombic lip which is topographically maintained through migration and nucleogenesis (Di Meglio et al., 2013). However, little is still known about the establishment of molecular diversity of PN neuron subpopulations during development, underlying such a complex cellular organization and cortico-pontine-cerebellar circuit connectivity. Here, we used single cell RNA- seq to characterize PN neuron subtype identities and transcriptional heterogeneity during nucleus assembly and connectivity. Preliminary results will be presented.

ADAMTSL3 IS A NOVEL EXTRACELLULAR SYNAPSE ORGANIZER THAT FACILITATES DCC FUNCTION FOR GABAERGIC SYNAPSE FORMATION AND MAINTENANCE

Group A

Teresa Cramer[1], Lucie Pretre[1], Pinan-Lucarré Berangerie[2], Jean-Louis Bessereau[2], Shiva K. Tyagarajan[1]

1) Institute of Pharmacology and Toxicology, University of Zürich
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ECM proteins (eg. Orthodenticle homeobox 2, reelin, brevican, etc.) are central signaling components that are also known to influence synapse plasticity. In this study, we functionally characterize a novel ECM protein, namely Adamtsl3, a new member of the ADAMTSs (Disintegrin and Metalloproteinase with thrombospondin motifs) superfamily. The ortholog of Adamtsl3, ce-punctin/madd-4, was recently described in C.elegans and reported to be an essential organizer of the excitatory and inhibitory postsynapse through signaling downstream of the deleted in colorectal cancer (DCC) receptor (Pinan-Lucarré et al., 2014). Currently, the function of Adamtsl3 in the mammalian brain is unknown. Using a combination of in vitro assay systems, and Adamtsl3flox/flox mouse model, we report a role for Adamtsl3 at the DCC receptor at inhibitory synapses. Adamtsl3 facilitates GABAergic synapse formation and maintenance and further impairs hippocampal memory function in adult mice upon deletion. Overall, our data points to a critical role of Adamtsl3 in regulating DCC function for activity-dependent plasticity adaptations at DCC-containing synapses.

EVIDENCE FOR A MITOSIS-INDUCED LINEAGE ADDRESS SPACE IN MOUSE BRAIN

Group A

Stan Kerstjens[1], Gabriela Michel[1], Rodney Douglas[1]

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The question of how developing brains are able to form stereotyped long-range conenctions remains unsolved. We argue that the successive mitoses of brain development induce an address space embedded in gene expression, that axonal growth cones could exploit for precise navigation toward remote targets. We analyzed gene expression data of developing and adult mouse brain, published by the Allen Institute for Brain Science, and found that the expressions of many sets of genes co-vary across the developing mouse brain on multiple spatial scales: the covariances have stable spatial patterns that bisect the brain into a hierarchy of nested regions resulting in a spatial partitioning of increasing resolution, consistent with an address space. We propose that this spatial organization reflects the lineage tree as can arises from two simple constraints on mitosis: that the post-mitotic daughter cells have, on average, similar gene expression to their parent; and that on average they do not migrate too far from one another.

DECIPHERING ASTROCYTE POLARIZATION IN PERINATAL WHITE MATTER INJURY AND ITS ROLE IN DISEASE PATHOGENESIS

Group A

Patricia Renz[1,2], Valérie Haesler[1], Vera Tscherrig[1,2], Shane Liddelow[3], Daniel Surbek[1], Andreina Schoeberlein[1], Amanda Brosius Lutz [1]

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3)Neuroscience Institute, Department of Neuroscience and Physiology, New York University (NYU), New York City, New York, USA

White matter injury (WMI) is the most common form of brain injury in preterm infants. It is characterized by reactive microgliosis and astrocytosis and defective oligodendrocyte maturation. Recent studies in the mature brain show the formation of diverse reactive astrocyte subtypes after injury, some favoring brain repair and other «inflammatory» astrocytes contributing to neurodegeneration. The specific nature of astrocyte reactivity after WMI

remains obscure. Here we report the results of experiments investigating inflammatory astrocyte formation in WMI.
WMI was induced in rats at postnatal day (P)2 using a combination of hypoxic-ischemic and inflammatory insults. To confirm successful WMI, myelin deficits were evaluated using immunohistochemistry for myelin basic protein at P11. Inflammatory astrocyte formation was investigated through in situ hybridization (ISH) using a complement protein 3 (C3)-specific probe. We further characterized astrocyte reactivity by performing microfluidic qRT-PCR analysis of a panel of reactive astrocyte transcripts on mRNA isolated from astrocytes purified by immunopanning from injured and healthy brains. ISH shows a significant increase of C3-positive inflammatory astrocytes in subcortical white matter tracts across multiple rodent WMI models. Supporting this finding, preliminary qRT-PCR results suggest that purified primary astrocytes from injured brains exhibit a multi-gene inflammatory astrocyte signature at the transcriptome level.
We demonstrate the formation of inflammatory astrocytes in rodent models of WMI. This result is an important step towards understanding astrocyte polarization in WMI and opens the door to experiments investigating whether prevention the formation of this astrocyte subtype ameliorates WMI disease outcomes.

Group B – Neurological Disorders

THE REORGANIZATION OF THE MOTOR NETWORK AFTER CHILDHOOD STROKE: A MULTIMODAL APPROACH INCLUDING RESTING STATE FUNCTIONAL MRI AND TRANSCRANIAL MAGNETIC STIMULATION

GROUP B

Cristina Simon-Martinez[1], Juan Antonio Delgado Rodríguez[1], Sandeep Kamal[1], Alain Kaelin-Lang[2,3], Leonie Steiner[1,4], Nedelina Slavova[5,6], Andrea Federspiel[7,8], Stephanie Homan[9], Roland Wiest[5], Regula Everts[1], Maja Steinlin[1], Sebastian Grunt[1]

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To develop tailored rehabilitation, insights of the neuroplastic processes after childhood arterial ischemic stroke (AIS) is crucial. To this purpose, resting-state functional MRI (rsfMRI) and Transcranial Magnetic Stimulation (TMS) have been used. While rsfMRI depicts functional connectivity between cortical networks at rest, their function can be determined with TMS. Combining both methods may help to understand the motor network reorganization after childhood AIS.
Thirteen participants (mean age 15y 3m) diagnosed with AIS underwent rsfMRI to study motor network functional connectivity at rest. Single-pulse TMS evaluated cortical excitability of each hemisphere. Paired pulse TMS assessed interhemispheric inhibition/facilitation. Hand-

strength asymmetry was measured with a dynamometer. We investigated the relationship between interhemispheric connectivity and interhemispheric inhibition/facilitation; intrahemispheric connectivity and cortical excitability; and motor network measures and motor function. Partial correlations (controlling for lesion size) were interpreted as absent (<0.25), fair (0.25-0.50), moderate (0.50-0.75) or excellent (>0.75) and performed in jamovi 1.6.1.
Higher interhemispheric connectivity fairly correlated to interhemispheric facilitation in the stroke-to-nonstroke direction and moderately related to inhibition in the nonstroke-to-stroke direction. Higher intrahemispheric connectivity was moderately related to cortical excitability in the non-lesioned hemisphere. Larger hand strength asymmetry was fairly associated to poor excitability of the lesioned hemisphere.
This multimodal neuroplasticity model of the motor network illustrates how interhemispheric interactions and cortical excitability may affect cortical networks and motor function.

BRAIN-SECRETASES TO PREDICT PRESYMPTOMATIC (MILD COGNITIVE IMPAIRMENT) STAGE DEMENTIA

Group B

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Mild cognitive impairment (MCI) refers to cognitive decline that does not interfere with the person's daily function. MCI can progress to dementia in 8% to 27% of affected persons. Alzheimer's disease is the most common form of dementia, 20 million cases in the world and projections of 55 million cases by 2050. The most frequent histopathological lesion in neurodegenerative dementia is the accumulation of the beta amyloid peptide, mediated by enzymes known as secretases. In the absence of a curative treatment for dementia and the diagnostic difficulty using non-invasive techniques, we resort to investigating the role of β and γ secretases to assess cognitive impairment in its early phase. For this purpose, we will conduct a longitudinal cohort study If possible at the Lausanne university hospital and research center for psychiatric neuroscience from 20 September 2021 to 20 February 2024. We will recruit participants in two groups namely: Group 1 (Persons with mild cognitive impairment, with Montreal cognitive assessment (MOCA) score between 18-25 and mini-mental state examination (MMSE) score between 20-25; Group 2 (persons without mild cognitive impairment, with MOCA score between 25-30 and MMSE score between 26-30. Participants will be paired by age, sex, socio economic status and cerebrovascular risk factors. They will be characterised at baseline and followed-up for at least 3 years. Secretases from blood samples obtained from the two populations will be studied in detail and the outcomes used to correlate this biological signature with the clinical profile of patients.

CORTICAL EXCITABILITY AS A MARKER OF EPILEPTIC SEIZURES SUSCEPTIBILITY IN THE MOUSE HIPPOCAMPUS

Group B

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Background:
Epileptic seizures are characterized by paroxysmal pathological activity of neurons. The episodic nature of seizures indicates fluctuation of seizure susceptibility across time. However, the exact nature of this fluctuation, and the methods to measure it, remain to be determined.
Aim:

Using optogenetic stimulation of In Vivo mice entorhinal neurons, we aim at characterizing the correlation between cortical response to short perturbations and seizure threshold.
Methods:
We developed a circuit-specific model of optogenetically induced “on-demand” seizures.
We measured the EEG response of theses neurons to single and paired optogenetic pulses as a biomarker of cortical excitability, and compared its variations with seizure threshold, measure as the duration of optogenetic stimulation needed to elicit a seizure (“time-to seizure”). We then explored how these markers varied in the presence of drugs modifying cortical excitability: Diazepam and Pentylenetetrazol (PTZ).
Results:
In this preliminary study we found a decrease time-to-seizure in the presence of Diazepam, which confirms that this method can be used to quantify the seizure threshold. Moreover, it was correlated with weaker cortical responses to single and paired pulses. We did not find any major effect of PTZ on these metrics.

Conclusion:
Probing cortical excitability using very short perturbation of ongoing activity may be a good indicator of the current cortical excitability state, at least towards inhibition.

CHANGES IN EXCITABILITY OF AFFERENT NOCICEPTORS AFTER NERVE INJURY

Group B

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Peripheral nerve injury causes damage to the axons of afferent primary sensory neurons and leads to neuropathic pain. The injured neurons undergo gene expression change in an attempt to regenerate. Neighbouring non-injured fibres become sensitised due to ongoing neuroinflammation. Increase in activity of afferent neurons is thought to drive subsequent central sensitisation to establish chronic pain. We aim to distinguish the excitability of injured and non-injured nociceptors after nerve injury.
The spared nerve injury (SNI) model of neuropathic pain involves the lesion of the peroneal and tibial branches, leaving the sural branch of the sciatic nerve intact. The cell bodies of the injured and non- injured sciatic sensory neurons are found mixed in the lumbar L3 and L4 dorsal root ganglia (DRG). Using ATF3-GFP transgenic mice, we are able to identify the labelled injured from the other non-injured neurons. Whole-cell patch clamp recordings of small DRG neurons in primary culture revealed different current-evoked excitability profiles.
The current clamp recordings illustrated various features of hyperexcitability and changes in action potential shape. Injured neurons have a reduced ability to elicit multiple action potentials during sustained current stimulation, and have lower amplitude action potentials. The population of non- injured neurons fire action potentials at higher frequency. Thus, after SNI, injured nociceptive neurons have overall a weaker current-evoked response, but many non-injured nociceptive neurons become hyperexcitable.

SLEEP HOMEOSTASIS AFFECTS SCALP HFO RATES IN PEDIATRIC EPILEPSY

Group B

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Scalp HFO is a new and promising non-invasive epilepsy biomarker that appears to have a particularly high added value for the pediatric population. Further than their implementation in the delineation of the epileptogenic zone for surgical resection, HFO are currently investigated as potential biomarkers of epileptogenesis, disease severity, and treatment response. However, the issue of sufficient data selection for HFO analysis is still under debate: the choice of the appropriate sample size and of the most suitable time window to ensure data quality and representativity is essential for the validity of results. HFO analysis is routinely performed in sleep to avoid contamination by muscle artifacts but considerable fluctuations of HFO characteristics have been observed across sleep stages and cycles. HFO rates have recently been shown to decrease with accumulated time in sleep in invasive recordings, rendering the first sleep cycle best suitable for studying HFOs in epilepsy. However, it is unclear if these findings that derive from invasive EEG in mainly adult cohorts with drug-resistant focal epilepsy are applicable on unselected scalp EEG recordings across different age groups and epilepsy syndromes. The impact of sleep on scalp HFO rates and spatio-temporal characteristics in pediatric epilepsy, potentially of crucial importance for further analysis, is therefore still under debate. The goal of our project is to delineate the changes occurring in pathological HFO features across the different sleep stages and cycles and determine the selection of representative data intervals for valid and accurate HFO analysis. We hypothesize that scalp HFO rates change on various timescales: HFO rates decrease with time spent in sleep as well as with age.

DETECTING HIGH-FREQUENCY OSCILLATIONS IN SCALP EEG RECORDINGS USING A SPIKING NEURAL NETWORK

Group B

Karla Burelo[1, 2], Mohammadali Sharifshazileh[1,2], Giacomo Indiveri[1, 3], Johannes Sarnthein[2, 3]

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Introduction:
There is recent evidence that the HFOs, biomarkers for epileptogenic zone detected in invasive EEG recordings, are also detected in non-invasive scalp EEG recordings in young patients. The automatic detection of this biomarker is promising for long-term monitoring of the disease as well as pre-surgical studies. This kind of application can therefore benefit from an embedded system able to detect HFOs in real-time, without the need to process large amounts of data off-line, with external computers or cloud servers.

Methods:
In this study, we use an artificial Spiking Neural Network (SNN) for detecting clinically relevant HFOs found in pre-and postsurgical scalp EEG recordings, measured from eleven children with drug-resistant focal epilepsy that underwent epilepsy surgery.
The proposed SNN consists of a core HFO detection part, already validated with intraoperative ECoG data, extended with a new artifact rejection part used to eliminate false positive HFOs caused by sharp transients. Here we show that the HFO rates found by this novel SNN architecture compare favorably to those detected in the same dataset by a clinically validated

automatic HFO detector (mean 2.13 HFO/min vs 2.82 HFO/min in 16 pre-resection recordings).

Conclusions:
The SNN proposed was designed using elements and parameters fully compatible with mixed-signal neuromorphic circuits. This therefore represents an important step towards the construction of a low-power embedded neuromorphic signal processing system for continuous-time on-line detection of HFOs and long-term non-invasive assessment of disease severity in patients with epilepsy.

Group C – Cognition

PROBING MORAL RESILIENCY: DO PROTECTED VALUES SHIELD US FROM STRESS-INDUCED DISHONESTY?

Group C

Nina Sooter[1], Rajna Gibson[1], Giuseppe Ugazio[1]

1) University of Geneva

Do people adapt their honesty decision-making when under acute stress? Honesty is vital for proper institutional and societal functioning, however, compliance with this norm often depends on trade-offs between acting morally and increasing personal gain. Previous experimental studies have demonstrated that individuals who hold honesty as a protected value are less inclined to give in to selfish temptations. These decisions frequently take place in highly stressful situations, yet we have very little knowledge on how stress impacts decisions to comply with honesty. Stress is known to alter behavior by enhancing neural sensitivity to immediate rewards and decreasing activity in brain areas involved in response inhibition and goal selection. Thus, stress could affect honesty by: 1) making monetary rewards more attractive and 2) inducing habitual behavior by reducing self-control. In the present study, we explore these potential mechanisms by acutely stressing participants and asking them to make decisions in three tasks measuring honesty. We posit that subjects' protected values for honesty may act as a buffer against stress, mediating the relevance of the increased saliency of rewards on their choices. We will test four main hypotheses disentangling the specific ways in which individuals' protected values for honesty, reward values, and self -control interact under acute stress.

NEURAL CIRCUITS FOR EMOTIONAL CONFLICTS AND DECISION MAKING IN THE VENTRAL CA1 HIPPOCAMPUS

Group C

Carlo Cerquetella[1], Stéphane Ciocchi[1]

1) University of Bern

The ventral part of the hippocampus (vHC) is a key brain structure involved in a large-scale network mediating anxiety. However, its role in arbitrating approach-avoidance behaviour during emotional conflicts is still unclear. To test whether there is an involvement of the ventral CA1 hippocampus (vCA1 HC) in decision-making processes during emotional conflicts, I have characterized the neural activity of vCA1 HC cells in mice facing emotional conflicts using novel behavioural tasks and single-unit recordings.

We have obtained preliminary results revealing a scaling in neural activity in the overall population recorded and a remapping of firing-rate spatial fields in anxiogenic situations. These results are selective for the conflict level the animals face and are novelty-independent.
Moreover, an important target of the vCA1 HC thought to be crucial for the coordination of decision-making behaviour is the medial prefrontal cortex (mPFC). The neural activity of the subgroup of vCA1 HC to mPFC projection cells exhibits the same decision-making related activity as the overall population recorded and their optogenetic inhibition performed at the terminals level influenced the decision-making processes during emotion conflict.
Taken together, these results further reinforce the idea of a strong involvement of the vCA1 HC in anxiogenic situations and support the hypothesis that pyramidal cell assemblies within the vCA1 HC represent different emotional conflicts assigning them a role in decision-making processes during different emotional conflicts.

NEURAL CORRELATES FOR REWARD AND AVERSIVE CONTEXTUAL MEMORIES IN THE VENTRAL HIPPOCAMPUS

Group C

Joana Mendes Duarte[1], Stéphane Ciocchi[1]

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Assessing and exploiting on memories of rewarding and aversive events is critical for animal survival. This behavior relies on the brain ability to simultaneously construct salient emotional experiences and internal representations of the spatial environment in which they occur. The ventral hippocampus (vHip) is a high-order cortical area implicated in emotional behaviors associated with positive and negative stimuli. However, the neural dynamics of the vCA1 that underlie memory for emotional spaces remain poorly understood.
To address this knowledge gap, we developed a two-stage behavioral task that allowed for the assessment of both contextual fear and reward learning, while monitoring vHip CA1 single-unit electrophysiological activity. The behavioral protocol starts with the social place preference (SPP) task, a paradigm in which mice were trained to associate one of the two distinctive compartments with a social reward odor, in this case female odors found in bedding. In second part of the behavioral protocol, the animals were subjected to a contextual fear conditioning (CFC) task that was performed in two different novel contexts, in which one of the context will be associated with an aversive stimulus.
We observed vCA1 neurons that discriminated their activity between emotional learning contexts. Furthermore, this selective activity detected differed significantly from those observed in the habituation session, showing their emotional context-selective expression. Taken together, these results suggest a tuning of the vCA1 in representing rewarding and aversive stimuli with contexts to form emotional maps of the environment. Additional experiments will determine which inputs are necessary for the emergence of these emotional-related patterns.

DECIPHERING THE ROLE OF PARVALBUMIN INTERNEURONS IN THE VENTRAL CA1 HIPPOCAMPUS DURING ANXIETY

Group C

Emmanouela Volitaki[1], Stéphane Ciocchi[1]

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Anxiety is the emotional response elicited upon the perception of potential threats. The ventral hippocampus is a high-order cortical area implicated in emotional behaviours. Neuronal populations of the CA1 region (vCA1 HC) demonstrate enhanced neural activity in the open (anxiogenic) arms of the elevated-plus-maze (EPM) in rodents. However, the mechanisms underlying this selective activation remain unknown. We hypothesise that parvalbumin (PV+) interneurons are involved in the approach-avoidance aspect of anxiety and control the formation of anxiety-related pyramidal cell assemblies through their GABAergic synaptic interactions. Using single-unit recordings and optogenetics in freely-moving mice, we showed that subsets of putative pyramidal cells and interneurons have anxiety-related firing patterns during EPM navigation. Importantly, the majority of optogenetically-identified PV+ interneurons increased their activity at the centre and/or open arms of the EPM. Additionally, the inhibition of PV+ interneurons during center and open arm exploration resulted in fewer entries in the open arms. These results indicate an involvement of PV+ interneurons during the confrontation to anxiogenic situations and risk assessment. Additional experiments will determine whether the activity of PV+ interneurons is necessary for the emergence of anxiety-related pyramidal cell assemblies and anxiety behaviour.

DOPAMINERGIC NEUROMODULATION OF SPIKE TIMING DEPENDENT PLASTICITY IN LAYER 5 PYRAMIDAL NEURONS OF THE ANTERIOR CINGULATE CORTEX

Group C

Lotte Spierenburg[1], Thomas Nevian[1]

1) Physiology Department, University of Bern

The anterior cingulate cortex (ACC) is a brain region involved in higher cognitive function, like error detection and pain processing. Moreover, the ACC is highly regulated by neuromodulatory inputs, like dopamine. Synaptic plasticity is instrumental for cortical processing and plasticity rules can be influenced by neuromodulatory inputs. However, synaptic plasticity mechanisms and the role of neuromodulators in the ACC are still elusive. Our research therefore focuses on dopaminergic neuromodulation of spike-timing-dependent plasticity in in the ACC.

We study LTP using whole-cell patch-clamp recordings of L5 pyramidal neurons in the ACC, using an EPSP-3AP pairing protocol. EPSPs are evoked at proximal or distal inputs to the apical dendrite by electrical stimulation. Additionally we study input-specific activation of identified afferents transfected with Channelrhodopsin.

Our results show that when electrically stimulated at proximal or distal dendritic sites, synapses onto L5 ACC pyramidal neurons do not appear plastic. However, STDP is facilitated by dopamine at proximal, but not at distal synapses. Specifically, in presence of dopamine pairing at proximal synapses led to LTP. Furthermore, input-specific pairing showed that plasticity is not only dependent on available neuromodulators, but also on the ACC afferent.

These results indicate that dopaminergic neuromodulation can selectively differentiate specific inputs at different synaptic sites, potentially acting as a plasticity switch mechanism. Here we show a mechanism which could explain how the ACC can process the vast and often contradictory inputs it receives.

DYNAMIC ALLOCATION OF LIMITED MEMORY RESOURCES IN REINFORCEMENT LEARNING

Group C

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Biological brains are inherently limited in their capacity to process and store information, but are nevertheless capable of solving complex tasks with apparent ease. Intelligent behavior is related to these limitations, since resource constraints drive the need to generalize and assign importance differentially to features in the environment or memories of past experiences. Recently, there have been parallel efforts in reinforcement learning and neuroscience to understand strategies adopted by artificial and biological agents to circumvent limitations in information storage. However, the two threads have been largely separate. In this article, we propose a dynamical framework to maximize expected reward under constraints of limited resources, which we implement with a cost function that penalizes precise representations of action-values in memory, each of which may vary in its precision. We derive from first principles an algorithm, Dynamic Resource Allocator (DRA), which we apply to two standard tasks in reinforcement learning and a model-based planning task, and find that it allocates more resources to items in memory that have a higher impact on cumulative rewards. Moreover, DRA learns faster when starting with a higher resource budget than what it eventually allocates for performing well on tasks, which may explain why frontal cortical areas in biological brains appear more engaged in early stages of learning before settling to lower asymptotic levels of activity. Our work provides a normative solution to the problem of learning how to allocate costly resources to a collection of uncertain memories in a manner that is capable of adapting to changes in the environment.

Group D – Sensory Systems

ASPECTS OF TREE SHREW CONSOLIDATED SLEEP STRUCTURE RESEMBLE HUMAN SLEEP

Group D

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Understanding human sleep requires appropriate animal models. Sleep has been extensively studied in rodents, despite substantial differences from human sleep like, for example, sleep fragmentation and number of discernible stages. This lead researcher to study sleep in a variety of animal models. Here we investigate sleep in tree shrews, small diurnal mammals phylogenetically close to primates and humans. We provide detailed information about tree shrew sleep structure, cycles, transitions and spindle occurrence. Tree shrews exhibited a consolidated sleep structure, with few interruptions by wake episodes, unlike the fragmented sleep structure in rodents that is often punctuated by extended wakefulness. The sleep bout duration parameter, which we estimated for tree shrews, was uncharacteristically high for a small mammal, and was similar to the parameter describing human sleep. We observed two distinct NREM sleep stages in tree shrews: a mixed NREM2 and NREM3 stage characterized by high delta waves and sleep spindles as well as a transitory NREM1 stage that occurred on NREM2/3 to REM transitions and consisted of intermediate delta waves with concomitant pronounced transient theta-alpha activity. Transition analyses confirmed that NREM1 to REM transitions reliably occurred in tree shrews, were undetectable in rats and interestingly appeared to occur also in humans, albeit on only a minority of stage transitions. Finally, coupling events between sleep spindles and slow waves tended to cluster near the beginning of the sleep period,

paralleling findings in humans. Our results suggest a close homology of sleep structure between humans and tree shrews in spite of the large difference in body mass between these species.

DEVIANT STIMULI IMPROVE SIGNAL DETECTION IN THE MOUSE SOMATOSENSORY SYSTEM

Group D

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Automatic detection of a sudden change (deviant) in the sensory input is a core element of exogenous attentional control which is reflected in an additional negative wave in the event-related potentials, called Mismatch Negativity (MMN).
Stimulus-specific adaptation (SSA) has been proposed as a single neuron correlate of MMN. SSA describes the property of neurons to adapt to frequent stimuli while remaining highly responsive to deviating stimuli. However, little is known about the relationship between SSA and perception, specifically how it relates to exogenous attentional processes. The aim of this study is to assess whether deviant stimuli trigger attentional reallocation and facilitate signal processing at the single neuron level in the primary sensory cortex. In our new behavioral paradigm combined with extracellular recordings, animals performed a simple visual detection task. The visual target stimulus was preceded by a spatial somatosensory deviant stimulus embedded in a sequence of repetitive stimuli ('standard') without carrying any information about the upcoming location of the visual target. Statistical analysis revealed a significant deviant effect on the animals' performance: better detection and faster reaction times were achieved in the presence of a deviant stimulus compared to no-deviant control trials which coincided with enhanced neural responses to deviant stimuli compared to standard stimuli. However, this behavioral effect diminished over time (days) potentially as a result of neural adaptation to the irrelevance of an uninformative deviant. Further neural analysis is needed to clarify the link between this attentional effect and its behavioral relevance to the amplitude of SSA.

THE EMOTIONAL AND PHYSICAL PROCESSING OF PAIN DURING SLEEP

Group D

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Pain is a complex experience based on a physical, an emotional and a cognitive component. When we are awake, all these three components are part of our processing of pain. But, what about when we are asleep?
When we are asleep, there is a sensory disconnection from the environment and hence, we are not aware of our surroundings. This phenomenon occurs because during sleep, the thalamic nuclei gating information to the cortex highly increase the sensory threshold. Consequently, the amount of information reaching cortical areas is severely reduced. Nonetheless, both visual and auditory signals have been shown to reach the cortex and be processed during sleep. Yet, little is known about the thalamic gating of pain during sleep.
Here we show that both touch and pain reach the cortex during sleep. In addition, our data suggests that in sleep, not only the physical component of pain is processed, but also the emotional one.

EXPLORING THE THRESHOLDS OF BIPOLAR-CELL TARGETED OPTOGENETIC VISION RESTORATION IN RD1 MICE

Group D

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Retinitis pigmentosa (RP) represents a group of genetic disorders responsible for massive photoreceptor degeneration and gradual loss of vision in patients. Works by Kleinlogel lab and others showed possibility of restoration of light sensitivity and eventually vision in blind retinas using optogenetic gene therapy. In case of such approach retinal target cell type has to be considered. ON-bipolar cells are undoubtedly the most attractive target for maximizing receptive-field diversity and with that restoring high-quality vision.

Opto-mGluR6 is a designer chimeric protein that combines light sensitivity of melanopsin with intracellular signalling of the metabotropic glutamate receptor 6 (mGluR6). As mGluR6 is the direct transmitter of the light signalling cascade from rods and cones to ON-bipolar cells, Opto-mGluR6 represents a natural candidate for successful vision restoration in blindness. Employing a mouse model of RP treated with synthetic designer AAV vectors carrying Opto-mGluR6 under a highly specific synthetic ON-bipolar cell promoter, we were able to achieve robust reactivation of inner retinal signalling leading to differential RGC output.

Here we present multi-level functional evaluation and quantification of Opto-mGluR6-based optogenetic gene therapy in fully degenerated, blind mice. We performed electrophysiological recordings to assess the properties of artificially restored vision in response to variety of light stimuli – probing the functional boundaries and possibilities of Opto-mGluR6 vision restoration strategy. These insights will shine light on the quality of potentially restored vision by optogenetic manipulation of bipolar cells and elucidate retinal network adaptations during degeneration.

ELECTROPHYSIOLOGICAL CHARACTERIZATION OF RETINAL BIPOLAR CELLS IN MURINE RETINA: OPTIMIZE RESTORATIVE APPROACHES

Group D

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Bipolar cells, interneurons of the retina, are responsible for decoding the light signal captured by the photoreceptors. In photoreceptor degenerative diseases, the death of photoreceptors leaves behind a light-insensitive retina consisting of functional neurons, such as bipolar cells: making them good targets for optogenetic restoration. However, degeneration also causes changes in protein expression in bipolar cells, which may impact the quality of the synthetically restoration. By characterizing bipolar cells in healthy and degenerated mouse retinas, we aim at optimizing restorative approaches and improving functional output. We have recorded from WT rod bipolar cells (RBCs) and discovered the existence of two functional types of RBCs with different electrophysiological characteristics. We specifically activated and blocked BK channels in healthy and degenerated retinas by using the specific agonist of NS1619 and the specific blocker paxilline. BK channel is an high conductance calcium- and voltage-dependent potassium channel. The voltage and calcium dependence are closely related and are responsible for oscillations of the membrane potential. The drugs did not execute any effect in the degenerated retina as in the healthy retina, suggesting a mal-function of BK channels or a loss

or rewiring of BK-containing afferents. In combination with bipolar cell transcriptomics we hope to in the future be able to complement bipolar cells in the degenerated retina with proteins that re-establish natural signalling.