NENA 2019

Celebrating 20 years of NeNa with our keynote lineup:

Birgit Derntl
Octavian Voiculescu
Simon Jacob

NOV 4-6 Schramberg

KEYNOTE LECTURES | STUDENT TALKS | POSTER SESSIONS | WORKSHOPS | EVENING FESTIVITIES | BLACK FOREST
NeNa Conference
2019

Neurowissenschaftliche Nachwuchskonferenz
(Conference of Junior Neuroscientists)

November 4 – 6, 2019
Schramberg, Black Forest
From the NeNa-Team

This year is the 20th annual NeNa conference! We are a group of driven doctoral students with a passion for neuroscience, and we are thrilled to have you on board. We hope that in this intimate and easygoing environment you will be able to meet new people, share your work, and inspire one another with your ideas.

Sincerely yours,

NeNa Organizing Committee 2019

Melanie Barth
Ian Chong
Lena Danyli
Jorge Garcia Morato
Marius Görner
Ann-Christin Kimmig
Anastasia Lado
Katrina Quinn
Florian Sandhäuser
Ramona Siebert
Betül Uysal
Monday, 4th November, 2019

12:00     Arrival in Schramberg
12:00 - 13:00 Lunch
13:00    Group Photo
13:15 - 14:30 Introduction Blitz
14:30 - 15:10 Nikhil Ranjan  
            Role of a tumor suppressor MTUS1/ATIP1 in gliomas: Association with epigenetics and DNA repair  
            Daria Ivanchenko  
            How correlated are drifts in both eyes during fixational eye movements
15:10 - 15:30 Drew Robson, Jennifer Li  
            A nonlinear oscillator coordinates brain-wide motivational state during foraging
15:30 - 16:00 Coffee
15:30 - 17:00 Poster Session I (P1 – P15)
17:00 - 18:00 Keynote Lecture I – Simon Jacob  
            Cellular and circuit dynamics of executive control: from mouse to man
18:00 - 19:00 Dinner
19:30    Social time
Tuesday, 5\textsuperscript{th} November, 2019

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Speakers

Octavian Voiculescu (Cambridge University)
Octavian Voiculescu investigates the principles of building and shaping the central nervous system in higher vertebrates, and the relationship between morphogenesis and patterning of embryos. At NeNa, he will talk about the growth and form of the neurulating embryo. He will explore the mechanism of shaping the embryo in amniotes (higher vertebrates), and how the main axis, including the neural plate, is generated by the action of stem zones.

Simon Jacob (Technical University of Munich)
Simon Jacob’s aim is to shed light on the cellular basis of neuropsychiatric diseases. To this end, his group studies complex cognitive functions at the level of individual neurons and on the network level in the prefrontal cortex, the parietal cortex and the basal ganglia, with particular focus on how subcortical neuromodulators like dopamine regulate these circuits and control how we subjectively experience our sensory environment, memorize behaviorally relevant information and make appropriate decisions. Jacob’s lab combines controlled behavioral tasks with several state-of-the-art techniques in mice, such as large-scale extracellular recordings, optogenetic manipulation of defined cell types and networks, fluorescent imaging and computational analysis. In a unique translational approach, they also record from single neurons in human neurosurgical patients.

Birgit Derntl (University of Tübingen)
To be female or male is one of the most important biological determinants of life with critical consequences on our health, our behavior and our brain. This interaction between gender, (endogenous and synthetic) sex hormones and health regarding socio-emotional competencies is the main focus of Birgit Derntl’s group. She is particularly interested in how different competencies ranging from basic emotional abilities to empathy, stress and motivation are influenced by these factors. Many patients suffering from mental disorders (e.g., schizophrenia, depression, bipolar, etc.) show severe deficits in these domains and here even less is known about the interaction of gender, sex hormone concentration and symptomatology. Her lab investigates behavioral performance, subjective ratings, psychophysiological responses, neuronal activation (fMRI) and connectivity patterns (resting-state fMRI), and multisensory imaging (e.g., olfactory + visual stimulation).
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Role of a tumor suppressor MTUS1/ATIP1 in gliomas: Association with epigenetics and DNA repair

Nikhil Ranjan\textsuperscript{*}, Vimal Pandey\textsuperscript{b}, Ulrike Naumann\textsuperscript{a}, Phanithi Prakash Babu\textsuperscript{b}

\textsuperscript{a}Hertie Institute for Clinical Brain Research, Department of Molecular Neurooncology
\textsuperscript{b}University of Hyderabad, Department of Biotechnology and Bioinformatics

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Glioblastoma (GBM) are highly ubiquitous, persistent and therapy-resistant primary brain tumors with an unfavourable prognosis and a median survival, even at optimal therapy, of less than 20 months. Glioma stem cell like cells (GSC) are an extremely resistant subpopulation of GBM cells supposed to be responsible for tumor initiation and recurrence. To develop novel therapeutic strategies, the understanding of the glioma biology and of the underlying mechanisms that lead to its high malignancy is of central importance. We investigated the role of the tumor suppressor gene MTUS1 (Microtubule-associated tumor suppressor) which encodes a family of angiotensin II (AT2) receptor-interacting proteins (ATIP). Using in vitro glioma cell lines, an orthotopic glioma rat model and clinical human glioma specimen we studied the expression and involvement of MTUS1/ATIP1 in glioma progression and malignancy. We observed a significant downregulation of MTUS1/ATIP1 in GSCs compared to established glioma cell lines or even brain epithelial cells. This observation correlated well with a diminished MTUS1/ATIP1 expression in clinical glioma samples compared to normal brain. To understand the role of methylation in MTUS1/ATIP1 downregulation we treated GSC’s and glioma cells with decitabine. In glioma cell lines stably expressing MTUS1/ATIP1 there was significant inhibition of cell growth, migration and invasion. Elevated expression of MTUS1/ATIP1 blocked the phosphorylation of PI3K/AKT and MEK/ERK. Both in vitro in glioma cells as well as in vivo using the rat-glioma model, we found a significant recovery of MTUS1/ATIP1 expression and depreciation of reactive astrocytes post temozolomide treatment. Further, survival analysis in transgenic mice represents that MTUS1/ATIP1 overexpression prolongs the median survival significantly. Overall, our findings suggest that MTUS1/ATIP1 dysregulation is involved in progression of GBM leading to a more malignant, cell death-resistant and invasively growing glioma cell.
How correlated are drifts in both eyes during fixational eye movements

Daria Ivanchenko*¹, Katharina Rifai², Ziad M. Hafed², Frank Schaeffel¹

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Even during stable fixation, our eyes make miniature movements called fixational eye movements. In most studies, such eye movements were measured in only one eye at a time. While a great deal can still be learned about the impacts of fixational eye movements on visual performance using monocular tracking, such tracking ignores the important integration of visual information from the two eyes that takes place in the visual brain. In this study, we used a custom-built video eye tracker to study intraocular correlations of slow fixational drifts. Importantly, since recent studies concluded that pupil-based eye trackers are not necessarily suitable to precisely measure vergence eye movements, we used additional software to correct position measurement artifacts caused by pupil size changes. We found that during sustained fixation, the eyes often drift in opposite directions, particularly in the horizontal direction. Since these movements are similar to those during convergent eye movements but with much smaller amplitude, they may be referred to as 'microvergence', in analogy to the commonly used term 'microsaccades' for small saccades. When we compared vertical eye positions between the two eyes, they were more positively correlated, again supporting the notion that the opposite motions in the horizontal direction were related to vergence eye movements. We hypothesize that a possible function of microvergence could be that it improves stereoaucuity. It is possible that small and low contrast disparities in the two eyes' retinal images can be better detected when microvergence is engaged.
**A nonlinear oscillator coordinates brain-wide motivational state during foraging**

João Marques†,a, Meng Li†,a,b, Diane Schaak,a, Drew Robson,a,b, Jennifer Li*a,b

*a Harvard University, Rowland Institute
Max Planck Institute for Biological Cybernetics, Systems Neuroscience (RoLi Lab)

† These authors contributed equally to this work
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The motivational state of an animal sets its behavioral priorities and modulates its motor performance. In complex tasks such as foraging, internal state is dynamic, and behavior alternates between local search (exploitation) and global dispersal (exploration). It is unclear whether exploitation and exploration states are maintained by a specific set of master regulatory neurons or are emergent from large-scale population activity. Using tracking microscopy, we simultaneously imaged behavior and whole brain neural activity at cellular resolution in freely swimming zebrafish for hours during foraging behavior. We uncover a dorsal raphe subpopulation with persistent activity that encodes the exploitation state. The exploitation state-encoding neurons, together with a multimodal trigger network that is associated with state transitions, forms a stochastic nonlinear relaxation oscillator. The activity of this oscillatory network correlates with a global re-tuning of sensorimotor transformations during foraging that leads to dramatic changes in both the motivation to hunt for prey and the accuracy of motor sequences during hunting. This work reveals an important hidden variable that shapes the temporal structure of motivation and decision making.
Encoding of information – The role of a desynchronized brain state for information processing

Jan Weber*,a,b, Steffen Gaisa

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bUniversity of Tuebingen, IMPRS for Cognitive and Systems Neuroscience

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Human and animal research has demonstrated the central role of brain oscillations towards the perception, processing and finally consolidation and transformation of information into a new memory trace. From a mono-focused perspective on theta and gamma band synchronization as being beneficial for the processing of information, current literature suggests that also desynchronization of neuronal population firing determines the efficiency of stimulus processing. Under the assumption that the brain works as a predictive machine, it could be inferred that a synchronous brain state provides mere redundant information because the state of neuron X would predict the state of neuron Y, thus reducing state entropy whereas a desynchronized state would increase entropy and thus information coding. Although several studies nicely demonstrated the validity of this theory, a deeper understanding of whether desynchronization itself contains information on the stimulus or whether it just represents a network state in which information can be optimally processed, is still missing. In order to disentangle the role of neuronal desynchronization of either being essential for successful processing of a stimulus or simply enhancing stimulus processing by providing an optimal state for information coding, we assessed the encoding of information via EEG during the transition from wake to sleep meanwhile participants were continuously listening to an audiobook from which random sentences were taken for a later recall. First of all, our data is in line with previous research indicating that processing of a stimulus is associated with a desynchronization in the alpha (8 – 12 Hz) and beta frequency (12 – 30 Hz) band. Furthermore, comparing the subsequent memory effect for the different sleep stages during the wake-to-sleep transition our data provides a first hint that a desynchronized state is not causally linked to the successful encoding of a stimulus, but rather provides a brain state which facilitates information processing.
Modelling the CNS on a microfluidic/MEA integrated platform

Laura-Victoria Jentsch*,a, Beatriz Molina Martíneza, Paolo Cesarea, Peter Jonesb, Mathew McDonaldb, Peter Heutinkc

*a University of Tübingen, Natural and Medical Sciences Institute, Neuro-microphysiological Systems Group
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Central nervous system (CNS) disorders represent a dramatically growing condition in our society and an increasing burden for global health and primary care. Despite the significant efforts deployed by public and private stakeholders, advances in drug development and treatment of patients are limited. One of the main limitations is the lack of platforms with high physiological relevance to study the CNS and the effects of pharmacologic compounds. In order to have a better understanding of the CNS physiology and reduce the drug failure rate, many initiatives have focused on the development of in vitro systems. However, most of the researches are dependent on 2D in vitro experiments based on primary cells, which poorly represent the complexity of the human CNS and consequently have shown low predictive value in clinical studies. To fill this gap, the aim of this project is to mimic the architecture of the CNS based on human induced pluripotent stem cells (hiPSCs) by using a new high-throughput 3D in vitro platform integrating both microelectrode arrays and microfluidics. This may significantly improve predictability of a range of physiological, pharmacological and toxicological assays.
The effect of neurotransmitters on human neurogenesis

Shokoufeh Khakipoor*\textsuperscript{a}

\textsuperscript{a}Hertie Institute for Clinical Brain Research, Molecular Brain Development

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During evolution, the mammalian brain has changed significantly in size, structure, and cellular diversity. For example, the human brain is comprised of 1000 times more neurons than the mouse brain. However, rodents are one of the top model organisms used to study the human brain and its disorders because of their easy access and fast reproduction. According to a number of studies on rodents, neurotransmitters, such as serotonin, dopamine, and acetylcholine, play a role in embryonic and adult neurogenesis. For example, during embryonic neurogenesis, serotonin is essential for radial glial cells, the committed progenitor cells that give rise to neural cells. Interestingly, a recent study has shown that human radial glial cells express a unique serotonin receptor, which is not present in mouse radial glial cells. Therefore, we aim to determine the role of neurotransmitters during human neurogenesis and understand their effects on gene expression, cellular diversity, cellular behaviour and physiological activity. In our project, we will take advantage of a new model system called human cerebral organoids. In 2013, two organoids protocols with different approaches were introduced, which successfully recapitulate the formation of different types of neural progenitor cells and their morphologies. After a more extended growth period, organoid models also show deep and superficial cortical layers. The utility of organoid models has already been demonstrated for studying developmental brain disorders such as genetic microcephaly and prenatal Zika virus infection. The completion of this project will establish the molecular pathways through which neurotransmitters influence human embryonic neurogenesis. Future experiments aims to investigate aberrant neurotransmitter signalling during fetal brain development in various disorders such as maternal depression.
Emotional chemosignaling in autism-spectrum-disorder: A study protocol and preliminary results

Joana Grave*, a,b,c, Janina Nollc, Filipa Barrosa,b, Jonas Hornungc, Lydia Koglerc, Jessica Freiherrd,e, Dirk Wildgruberc, Andreas J. Fallgatterc,f, Sandra Soaresa,b, Birgit Derntlc,f,g

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d FAU Erlangen-Nürnberg, Department of Psychiatry and Psychotherapy, Neuroscience of Sensory Perception
e Fraunhofer Institute for Process Engineering and Packaging IVV, Department of Sensory Analytics
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Introduction: Autism spectrum disorders (ASD) are characterized by impairments in social cognition, often related to poor social functioning. There is growing evidence for chemosignaling in humans, with studies showing that body odors (BOs) can convey emotions and elicit subjective and physiological responses in others. However, little is known about emotional chemosignaling in ASD. We hypothesize that some of the social deficits in ASD could partially be due to abnormal responses to emotional BOs.

Aim: To explore the subjective and physiological responses to emotional BOs and non-social odors in ASD.

Methods: Within the first part of the study, BOs were collected based on a strict protocol. Twenty healthy individuals (10 women) donated their sweat while watching 30min of fearful, happy and neutral film-clips in three separated sessions. Cardiovascular and facial-muscle activity was assessed. Donors rated their emotions before and after film-clips. The second part is being implemented. Thirty ASD patients and 30 healthy controls will be recruited. Receivers will be exposed sweat samples (happy, fear, neutral) or non-social odors (positive, negative, neutral) for 5s. They will rate each odor (familiarity, intensity, arousal, pleasantness). Cardiovascular and facial-muscle activity will be measured.

Results: One donor (man) was excluded after checking for protocol compliance. Regarding BO collection, analysis yielded significant effects of emotion induction on happiness, stress, fear and anxiety. Furthermore, there were significant differences between pre and post emotion induction in all conditions. Further data is currently being analysed and will be presented.
Discussion: Studies have shown that humans are able to communicate their emotions to others via the sense of smell. The present study will provide evidence on whether this emotional chemosignaling is impaired in ASD, as usually observed for visuo-emotional cues. The results could drive novel paths of research and treatment, with implications on social cognition in ASD and psychiatric disorders.
Evidence for reciprocal modulation of EEG microstate sequence and vigilance level

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The momentary global functional state of brain is reflected in its electric field configuration. Cluster analytical approaches consistently show that four head-surface brain electric field configurations, referred to as EEG microstate classes A, B, C, and D, are common across subjects and explain the larger part of spontaneous EEG variance. Changes in microstate parameters, such as their mean duration, are associated with a number of neuropsychiatric disorders, task performance, and mental state. In this study we investigated how parameters of the EEG microstates change with loss of vigilance during typical eyes-closed rest. We analysed resting-state recordings from two data sets (39 and 19 healthy male subjects respectively) of simultaneous 3 Tesla fMRI and 64-channel EEG. Four microstates classes were identified using EEGLAB plugin for microstate analysis by Thomas Koenig. Time courses of duration, occurrence, contribution, and transition probabilities were estimated using non-overlapping six second windows. Vigilance time series were estimated as ratio of the root mean square (rms) amplitude in alpha (7-13 Hz) to the rms amplitudes in delta and theta (1-7 Hz) bands for the same windows. To test for the group level association between vigilance time series and time courses of the microstate parameters one-sample t-test on the Fisher z-transformed individual correlation coefficients was used. We also used support vector machine regression to predict vigilance time series based on the parameters of microstates. We found that microstate parameters have temporal dynamics that is strongly modulated by vigilance. We find that duration and contribution of the microstate class C, as well as transition probabilities towards microstate class C are positively, while occurrence and contribution of microstate classes A and B are negatively associated with vigilance. We also show that microstate parameters can be used for the prediction of the vigilance level (p<0.001).
Effects of cellular excitatory-inhibitory composition on dynamics of cultured hippocampal neurons

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Neural circuits in the brain have distinct and highly conserved ratios of excitatory and inhibitory neurons. However, it remains unclear whether unphysiological cellular excitatory/inhibitory ratios would affect collective neuronal dynamics and/or jeopardize the balance of excitation and inhibition at the synaptic level. To investigate this question, we developed an experimental framework that allowed us to reliably separate inhibitory and excitatory neurons from mice hippocampus. We cultured neurons with different prescribed excitatory/inhibitory ratios and recorded Ca-activity in developed networks. In experiments, all cultures developed spontaneous network bursting. Cultures with 10-80% of inhibitory neurons exhibited similar mean inter-burst intervals, whereas cultures with 0% and 100% of inhibitory neurons developed longer inter-burst intervals. In contrast, the coefficient of variation of inter-burst intervals linearly grew with the number of inhibitory neurons. To link the population dynamics and network properties, we designed a network of excitatory/inhibitory leaky integrate-and-fire neurons with spike-frequency adaptation. We reproduced the experimental results in the model with a balanced number of excitatory and inhibitory inputs to every neuron. The bursting dynamics, in this model, is the result of interacting inhibition and spike-frequency adaptation. We further probed this mechanism by blocking inhibition in vitro, which resulted in an increase of inter-burst intervals predicted by the model. Overall, our results show that hippocampal cultures tend to maintain the bursting dynamics and adapt to different numbers of inhibitory neurons by keeping the balance between excitatory and inhibitory connections.
Selective peri-saccadic suppression of low spatial frequencies is a visual phenomenon

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Visual sensitivity is strongly impaired around saccades, a phenomenon known as saccadic suppression. This robust phenomenon does not constitute a mere global suppression, but instead shows selectivity for low spatial frequencies, which has been used to suggest selective motor-driven suppression of magnocellular visual pathways (e.g. Burr et al., 1994). However, neural studies failed to reveal selective magnocellular pathway suppression. Moreover, Idrees et al. (VSS, 2018) recently described as surprisingly far-reaching contribution of visual image processing mechanisms to saccadic suppression, without the need to invoke explicit motor-based suppression commands. Here we show that this is also true for selective suppression of low spatial frequencies. Six participants localized a brief (12 ms) vertical Gabor grating flashed at one of four locations (4-AFC paradigm). The gratings had one of 6 spatial frequencies (0.41-6.83 cycles/deg), and they were presented over a uniform gray background in a dark room. At a radius of 10 deg from display center, the gray background was replaced by either a coarse or fine band-passed random texture (as in Idrees et al., VSS, 2018), in order to simulate a “virtual monitor” edge. In one condition, gratings were presented peri-saccadically with saccades directed towards display center; in another, gratings appeared during fixation after the “virtual monitor” and surrounding texture were translated in a saccade-like manner, again towards display center. With a coarse peripheral context, selective suppression of low spatial frequencies occurred with or without saccades, therefore due to saccade-like image translations. Even more surprisingly, when the surround was fine, both real and “simulated” saccades exhibited suppression that was not selective for spatial frequency, violating (Burr et al., 1994). Thus, selective or unselective suppression happens with or without saccades, as a function of saccade-induced image translations and peripheral visual contexts. Our results support the view that saccadic suppression is a primarily visual phenomenon.
T11

Default consciousness in high concentration meditative states

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This presentation describes an upcoming study on default consciousness in high concentration meditative states. High concentration mental states as stable plateaus are well-known and described in detail in several meditation traditions. Meditators typically report that they are experiencing being present and very alert when high concentration states occur. Interestingly, some papers on high concentration states report EEG data patterns similar to those of deep sleep. These papers also include reports of “spindle” activity and slow delta waves. This combination is controversial! These states deserve more thorough investigations which is what this study aims to do. A comprehensive data set combining nTMS-hdEEG with recording of biophysical parameters like heart- and respiration rates, MRI and detailed subject reports will be recorded. Data analysis will include comparisons with other studies of consciousness states performed at the Brain Signalling Group Laboratory. Among several parameters, we will investigate those used to measure consciousness level, for example Perturbational Complexity Index. We also have an interest in the Default Mode Network in the different states. The data from this study will be interpreted in context of current theoretical frameworks, and potentially the results will help us understand the neural correlates of consciousness.
Fractal and oscillatory components of resting state MEG functional connectivity are distinct

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Electrophysiological signals of cortical population activity contain oscillatory and fractal (1/frequency) components. However, the relationship between these components is unclear. To address this, we investigated human resting-state MEG recordings. We applied combined source-analysis, signal orthogonalization and irregular-resampling auto-spectral analysis (IRASA) to separate oscillatory and fractal components of the MEG signals at the cortical source-level. We then compared the spatial correlation structure of fractal and oscillatory components across the human cortex. We found that these correlation structures differed.
An Examination of the Neural Correlates of Interoceptive Processes in the Macaque Monkey

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Several well-established methods exist for recording and measuring the underlying signals of the brain. Methods such as electrophysiology and fMRI, when taken together, have the capacity to disclose local and global neuronal activity. Here, both techniques were employed to refine the working functional model of the insular cortex, a recipient of sensory afferents relaying information about the body’s physiological state. This dissertation serves to extend the current knowledge relating to the sensory afferent pathways relaying gustatory and interoceptive information to the brain, with special considerations of the role of the insular cortex. A series of fMRI experiments were conducted in the anesthetized macaque; whereby, responses to different types of interoceptive stimulation were measured (e.g. lower gastrointestinal distention, cutaneous thermal stimulation, auricular vagus nerve stimulation, and taste). The gross anatomical localization of these functions were mapped, providing a foundation for subsequent electrophysiological sampling across the insula. Using these methods, our results revealed a topographic organization of multi-modal interoceptive responses and the evidence garnered was analyzed within the context of insular cortex connectivity and its association with limbic and higher order cortical areas. Our results support previous evidence of a topographic representation of interoceptive afferents in the human insula and contribute to the working model of insular cortex function in non-human primates. The manner in which interoceptive information is organized may disclose how upstream regions integrate sensory information to form a conscious percept of the body’s physiological state, shaping cognition, and contribute to emotional embodiment. The present work serves as a basis for mapping functional responses with more involved paradigms designed to assess the emotional and cognitive responses to interoceptive sensations in the awake behaving state.
Flexible coding of social cues in the posterior superior temporal cortex

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Intelligent social behavior requires flexibly attending to different aspects of the social information provided by the others. For instance, in one moment we may assess the other’s eye direction in order to identify her/ his focus of attention, whereas, in the next moment, we may focus on the other’s facial expression in order to gauge her/ his emotional state or her/ his facial identity. And in order to arrive at a complete interpretation of the given social context, we need to switch between features and concatenate the information collected. Although many studies have tried to explain how different facial features are independently encoded by the primate brain, the neurophysiological principles that orchestrate ensembles of neurons to flexibly switch between distinct facial features are largely unknown. Here we tried to quantify the ability of neurons in the posterior superior temporal sulcus (pSTS) of two rhesus monkeys to flexibly encode two distinct features of faces, gaze direction and facial identity, each relevant for specific behaviors probed by the experiment: Monkeys were trained to use two distinct rules, called up by the color of the central fixation dot, to shift their focus of attention either by following the central portrait’s gaze towards one out of four eccentric targets, or alternatively, by using previously learned associations between the same portraits and the four targets while ignoring gaze direction. Task-selective neurons recorded from the right pSTS exhibited a clear topographical organization characterized by a distinct patch of neurons, the gaze following patch (GFP), activated by the processing of gaze direction, surrounded by neurons, mostly driven by the facial information on identity. Time-resolved principle component analysis of the activity of all neurons recorded revealed a trajectory in neural state space characterized by a series of state transitions between gaze and identity cues. Dissecting the neural state space into two sub-spaces considering the aforementioned topography of types of neurons showed that neurons in the GFP are responsible for the early gaze selectivity of the trajectory, whereas the later identity selectivity is contributed by the population of neurons surrounding the GFP. All results together suggest that the pSTS is able to flexibly switch between social cues by generating different temporal patterns of selectivity by recruiting distinct sub-population of neurons.
Posters
The human Retina-on-a-Chip provides a novel multi-tissue screening platform

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Visual disorders such as retinitis pigmentosa or age-related macular degeneration are major health issues of global population. The lack of curative treatment options demands the establishment of adequate models of the human retina for improved development and testing of new treatment strategies. Existing models are often poorly transferable to the human patient due to the lack of the human physiology (animal models) or complexity (in vitro models). In that course, the discovery of human induced pluripotent stem cells (hiPSC) and their differentiation into 3-dimensional (3D) retinal organoids (ROs) opened up new venues for creating accurate human in vitro models. ROs feature all major retinal cell types as well as a layering comparable to the retina in vivo and are light sensitive. Nevertheless, ROs are still limited in their maturation capability and an insufficient interaction of photoreceptors with retinal pigment epithelium (RPE). To overcome these issues, we developed the Retina-on-a-Chip (RoC), which facilitates the co-cultivation of ROs with RPE and other cell types to create a physiological microenvironment enabling optimized and reproducible culture conditions. We could show successful integration and viability of RO and RPE as well as long-term cultivation for several weeks in the Retina-on-a-Chip. Furthermore, we could establish several endpoint and live cell methods, such as fluorophore-driven promoter constructs, immunohistochemistry, electron microscopy and qPCR. The versatility of the Retina-on-a-Chip with multiple analysis options allow the implementation of the RoC in developmental studies, disease modeling and drug testing.
Concurrent TMS-fMRI: a proof-of-principle MVPA experiment

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Functional magnetic resonance imaging (fMRI) reveals neural activity correlating with specific cognitive processes. In contrast, transcranial magnetic stimulation (TMS) interferes causally with activity of brain regions and thus affect cognitive processes. Combining both methods in a concurrent TMS-fMRI setup allows to measure the neural effects of TMS interventions across the whole brain and to correlate them with behavioral consequences. We built up a concurrent TMS-fMRI setup in our lab using state-of-the-art devices. To show the feasibility of this concurrent TMS-fMRI setup, we present here first results of a proof-of-principle single subject multivariate pattern analysis (MVPA). In this fMRI-only experiment we decoded the content of visual working memory. In our task, one of four visual stimuli had to be held in working memory during a maintenance period. Using support vector machines, we could significantly decode the different patterns for each of our four visual stimuli during the retention interval in several different brain areas. Specifically, we found high decoding accuracies in parietal and early visual areas in accord with previous studies. In future experimental sessions, we plan to investigate, using our TMS-fMRI setup, how the whole-brain encoding of working memory is affected by TMS stimulation in different target areas, such as the prefrontal, parietal and early visual cortex.
Behaving systematically towards different classes of input is fundamental to a successful interaction with the world and acquired through the learning of categories. Semi-supervised categorisation is concerned with contexts where explicit feedback on the target response is only partially available. Many natural learning problems that humans encounter are more accurately reflected by this than either supervised or unsupervised conditions alone. Despite its relevance, research on the topic is surprisingly sparse and inconclusive. We hypothesise that the a priori match between task and mental representations of the inputs determines whether feedback is necessary to acquire a novel categorisation. To put this to test, we present a behavioural experiment aiming to explain the source of incoherence across experiments.
Anticipating Every Turn: Learning About Learning in Mice

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Animal intelligence is thought to rely on powerful mental models as representations of knowledge. Particularly in the initial phases of learning about a new environment, decision-making is considered to be usefully informed by a developing internal model of the environment. Nevertheless there have been few attempts to study in a formally rigorous way the process of learning a model of a moderately complex animal behavioural task from scratch. We take some first steps in this direction, by building a computational modelling framework with the necessary capacities, feeding it observations from a behavioural decision-making task, and then analysing the models that result. To compare this with the capacities of animals, we can later rely on an existing large data set of mice performing the same task. The structure we use to capture a generative model of the observations is a hierarchical Dirichlet process, hidden semi Markov model. This non-parametric Bayesian model can encompass a potentially infinite number of states, which is exactly what we need to capture the flexibility of actual mental models. Further, the model can be exploited by a reinforcement learning agent to underpin control. We describe the elements of the decision-making task and our modelling framework, and exhibit some of the facets of this framework in action. We also compare both real and artificial agents with a classical inference algorithm for our behavioural task, namely the drift-diffusion model.
Contraception allows women to exercise autonomy over their reproductive health. But what are the behavioural, and on a larger scale the societal effects of contraception? Are there differences between different methods of contraception? While hormonal contraception is becoming more and more widespread, there is still a lack of studies on their behavioural effects. Studies mainly focus on the bodily effects of oral contraceptives (OCs), though evidence is accumulating that OC-intake also affects brain and behaviour. For intra-uterine devices (IUDs), similar effects can potentially be assumed; however direct investigations of the effect on socio-emotional behaviour are scarce and limited. Even though both methods of contraception are of hormonal nature, serum levels and effects are not the same: Ewies (2009) reported that the serum and tissue levels of exogenous hormones were much higher in IUD-women compared to OC-women, despite IUDs having lower dosage than OCs. So far several studies reported a blunted cortisol response to stress tests in OC-taking women, while very recently cortisol response in IUD-women showed a potentiated reaction to a laboratory stressor. This study clearly demonstrates that IUDs have different effects than OCs. The question rises in what other areas those contraceptive methods differ – the main aim of this contribution. Understanding the differential effects of OCs and IUDs on behaviour could be of immense importance to better understand relevant mechanisms of hormones on brain, behaviour and mental health as well as to allow women to make a more informed choice of contraception.
Electrical microstimulation establishes a causal role of the superior temporal gaze-following patch (GFP) in controlling gaze-following and its context dependent modulation

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In order to identify an object a conspecific is looking at, one must be able to determine his/her eyes and head directions and redirect one’s own attention towards said object, thereby establishing joint attention. This process is known as gaze-following, and work in our group has previously shown that a cortical patch in the posterior superior temporal sulcus (pSTS), which we have designated the GFP, is recruited for this behavior. Characterization of the GFP has revealed that it contains a variety of neurons responding to the spatial location of an object of interest under the gaze of another individual, as well as providing information needed to suppress gaze-following when the latter is not required. To investigate the role that the GFP plays in gaze-following, we trained two male rhesus macaque monkeys in a gaze-following and identity-mapping paradigm, and deployed electrical microstimulation in the GFP to disrupt normal information processing in the patch in order to establish causality. We demonstrate that the GFP is causally involved in gaze-following; specifically stimulating this part of the pSTS during presentation of spatial cue and targets significantly impaired gaze-following. The errors induced by microstimulation also do not reflect any spatial target or task bias. However, when we shifted the perturbations to the instruction period of the paradigm, the suppression on gaze-following was abolished, and instead identity-mapping became compromised. All in all, our results support a causal role of the GFP in gaze-following. Moreover, they indicate that the GFP is also involved in the executive control of gaze-following, i.e. suppressing gaze-following if inappropriate, by integrating expedient signals contributed by other cortical areas.
Generation of isogenic controls from Retinitis Pigmentosa derived iPSCs

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Retinitis Pigmentosa (RP) belongs to the group of pigmentary retinopathies and it is characterized by a progressive degeneration of photoreceptors cells leading to a gradual visual loss that can ultimately cause blindness. RP is a highly heterogeneous genetic disease caused by a variety of mutations in several genes. So far, mutations that can cause RP have been found in 77 genes, among these mutations in the Crumbs Homologous 1 (CRB1) gene are responsible for 3-9 autosomal recessive RP forms. Since for patients carrying mutations in CRB1 a clear genotype-phenotype correlation is still lacking, it has been hypothesised that the genetic background plays a crucial role in the severity of the disease. The discovery that human induced pluripotent stem cells (iPSCs) can be derived from somatic cells combined with the development of iPSC-derived optic cup like structure called retinal organoids (ROs) opened up the possibility to firstly thoroughly study the role of CRB1 in the developing retina and secondly to analyse retinal cells from patient suffering from Retinitis Pigmentosa. In that endeavour, we generated iPSC lines from two affected RP brothers harbouring the same homozygous point mutation in the CRB1 gene (C948Y) but showing different disease phenotypes. Subsequently, we designed a strategy to correct the mutation in both iPSC lines using CRISPR/Cas9 technology and therefore to check for effects of the mutation and additionally identifying disease modifier explaining patient-to-patient variations. In the future, a thorough study of these modifiers could help to contribute to the understanding of the disease mechanisms as well as to identify future therapeutic intervention targets.
The Effects of Mood on Effort During Uncertainty

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Although mood and emotion are thought to be linked to motivation, the mechanisms behind this are still being explored. Recent work exploring the idea of “mood as momentum” has indicated that positive mood and emotion are associated with increased willingness to pursue rewards (Eldar, Rutledge, Dolan, & Niv, 2016). Although studies have shown that positive mood increases willingness to take risks, it is not known if such effects extend to the related area of willingness to exert physical effort. Here, we used monetary gains and losses via a lottery to manipulate mood in a sample of N = 21 healthy participants and examined how this affected effort exerted to earn monetary and food rewards, including when the amount of effort necessary was uncertain. Lottery outcomes affected happiness ratings (p = .003) but not scores on the Positive and Negative Affect Schedule (PANAS). When working for larger rewards, effort invigoration increased after winning lottery trials and in response to happiness, consistent with the mood as momentum idea (p = .011). However, when working for small magnitude rewards, the effect was opposite, such that winning at lottery trials and happiness both predicted lower invigoration of effort (p = .011). This implies that the “mood as momentum” idea is an over generalization and that when actually working for rewards, cost-benefit trade-offs are combined with consideration of how many larger rewards were already obtained to guide behavior, consistent with ideas about optimal foraging behavior.
Using diffusion MRI – which is sensitive to tissue microstructure – recent studies have challenged the idea that systems memory consolidation is an inherently slow process. Regions in a parietal memory network, encompassing among others the precuneus, show rapid signatures of online (measured with fMRI as well as offline (measured with dMRI) memory representations diffusion parameter changes after learning of spatial layouts or object-location pairings. These regions could abstract general information from multiple instances to create a schema, or form category knowledge. To test this prediction, in this study we present participants with visual stimuli of abstract 3D-shapes. These were created from different prototypes, and hence grouped into separate non-overlapping categories. In a ‘category learner’ condition participants need to focus on similarities between stimuli and acquire the underlying category structure for successful task completion. In an ‘exemplar learner’ condition the categories are irrelevant to the task and participants must carefully consider details of each stimulus to make a correct response. These manipulations should bias memory representations to be built either in the parietal medial cortex (‘category learners’) or in the hippocampus (‘exemplar learners’). An active control group engaged in a task with a similar set of stimuli but without learning will be tested to ensure specificity of diffusion related changes in the experimental groups. We expect to replicate findings of parietal cortex activation and plasticity during learning also using a new set of stimuli. Furthermore, the aim is to asses how fast after learning structural changes can be detected and how long these changes last. To this means, pre-post diffusion measurements, functional MRI during the task, and interspersed short sequences of diffusion MRI will be acquired among other measures not discussed in the following. This poster will explain the design of the study and show preliminary behavioral and – potentially – neuroimaging data.
Maternal Depressive Symptoms Trajectories and Impact on Toddler Behavior

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Maternal perinatal depression is a common public health problem affecting mothers and children worldwide. This study aimed to increase the knowledge regarding maternal depression trajectories and early child behavioral difficulties, and assessing the impact of child gender and maternal bonding. Data were drawn from a population-based Swedish mother-infant study (n=1353). Linear regression models were utilized for the association between maternal depression trajectory; antenatal depression, postpartum depression, both antenatal and postnatal depression/persistent perinatal depression and non-depressed, based on longitudinal ratings on the Edinburgh Postnatal Depression Scale (EPDS) and child behavioral problems assessed with the Child Behavior Checklist (CBCL) at 18 months. The analyses were repeated after stratification for gender. A path analysis was applied to assess the mediating role of maternal bonding. Children with mothers following antenatal and persistent depression trajectories had higher scores (Total, Internalizing and Externalizing problems) on the CBCL, after adjusting for confounding factors. The stratified regression modeling, showed that girls were affected at a greater degree. Postpartum bonding mediated most of the negative effects of postpartum and persistent but not antenatal depression on child behavior. The results indicate an effect of antenatal depression on fetal programming but also a substantial mediating effect of maternal bonding postpartum.
Harmonic signatures dissociate cortical alpha waveforms

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Non-sinusoidal waveform shapes of neuronal oscillations may reflect- and provide a novel window into specific neuronal circuit interactions. However, little is known about non-sinusoidal waveform shapes in the human brain. To address this, we investigated region-specific harmonic structures of alpha-oscillations in human resting-state MEG (human connectome project data: 89 subjects). Specifically, we focussed on the following waveform-shape characteristics, that conjoinly allow the precise reconstruction of a waveform shape: Peak-Frequency of consistent alpha oscillations, relative amplitude of the higher harmonics to the fundamental alpha oscillation and the harmonic phase-relation between alpha and its higher harmonics. As well as, furthermore, the coupling strength as an indicator for waveform-shape consistency over time. We found that Alpha waveform-shape characteristics differ significantly across the cortex. We could dissociate four region-specific alpha modes (sensory-motor, superior parietal/ medial postcentral, occipital and temporal); with inferior parietal cortex as a potential fifth mode. While waveform-shape characteristics are variable across subjects, these characteristics are stable within subjects across recording sessions.
Establishing methods to study internally generated predictive signals in the mouse vibrissal system

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Sensorimotor interactions in the mouse vibrissa system include complex neural processing. A movement comes with the generation of internal predictive signals i.e. efference copies or corollary discharges, that predict the sensory consequences of the act to dissociate self-generated sensory information (reafferent) from external sensory information (exafferent). We aim to check the existence of such predictive signals, by recording the motor command to the whiskers in the facial motor nucleus at brainstem level and the sensory signal in S1 somatosensory cortex in head fixed, water restricted mice, which generate large amplitude protraction whisker movements in air to get water reward. For this purpose, an immobile single electrode is implanted in brainstem facial nucleus using micro-stimulation-guided mapping, and a mobile four electrode array in S1 somatosensory cortex guided by intrinsic imaging. After habituation for head-fixation, the mice are trained using monitoring of the movement of one whisker. The reafferent loop is opened by surgically severing the distal facial motor nerve innervating whisker muscles. Triggering on the movement-predicting FN activity we apply experimentally controlled (artificial) sensory consequences of the motor command by deflecting the whisker using a Piezo actuator. Our hypothesis is that predictive signals reduce the amplitude of the fully predicted whisker flicks. Therefore, we expect that omitting the whisker flick will generate a timed inhibition in S1 sensory signals.
Implementing dynamic time warping algorithm for estimation training performance in fMRI neurofeedback

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Neurofeedback (NF) is a promising technique of improving mental states or processes of the participant through operant conditioning learning to self-control brain activity. This technique has a potential clinical application as an alternative or supplementary treatment option for neuropsychiatric disorders, including Major Depressive Disorder (MDD). The recent development of computational efficacy allowed to implement real-time processing of functional MR data, which allowed to implement real-time fMRI neurofeedback to provide direct feedback to participants about the ongoing activity level in the specific brain areas (Scharnowski et al., 2012). Despite the promising results of real-time fMRI neurofeedback, reports on neurofeedback efficacy are inconsistent. One critical factor contributing to this inconsistency of results is the challenge of account for inter-subject variability and the sluggish nature of the BOLD signal. There is still no consensus on how to determine training performance based on the analysis of the BOLD signals, exacerbating the true efficacy and specificity of neurofeedback. To tackle this issue, we developed a novel approach to determine Neurofeedback training performance, by applying dynamic time warping (DTW). In this method we determine a within-subject reference level of optimal learning performance within the BOLD signal and compute the Euclidian distance between the Reference signal and subject’s BOLD signal with DTW. This distance is used in permutation analysis to calculate the performance score of neurofeedback training. We do control for inter-subject variability and thereby gain more accurate performance measures. We show that our novel approach outperformed conventional performance measures in fMRI Neurofeedback. Our algorithm is fully data driven and does not assume any particular hemodynamics response. We apply our metric on a data set consisting of 20 healthy male subjects (mean age 26.8 ± 7.6) that participated in a one-day NF session of 3 Neurofeedback and 2 Transfer (before and after NF training) runs. Subjects were asked to up- or downregulate their dorsal Anterior Cingulate Cortex (dACC) activity. Critically, we show that this novel
approach provides new ways to measure the specificity and efficacy in neurofeedback, since behavioral performance was positively associated with the DTW measure and significant improvements after NF training were observed in EEG resting state.
Set-up neuron-glia co-cultures for functional studies on MEA platforms

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Neuropathic Pain (NP) is frequently associated with peripheral nerve injury or disease. Experimental models of neuropathic pain showed that non-neuronal cells play a very active role in the development of sensory abnormalities, but the exact mechanisms haven’t been clarified yet. By using a high-density multiple electrode arrays (MEA) system, we are able to record the electrical activity of both pure sensory neurons and non-purified neurons with relative glial cells after different culturing conditions. Surprisingly, cultures of pure neurons show no electrical activity in response to capsaicin application, furtherly suggesting a role for non-neuronal cells in the development of pain abnormalities. The implementation of neurons-glia co-cultures and the functional characterization of their interaction mechanisms could then lead to the identification of novel targets and biomarkers involved in NP.
Single men vs couple scenes - The influence of endogenous as well as synthetic ovarian hormones on female’s sexual responsiveness

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The few existing studies on potential psychological and neurobiological side-effects of oral contraceptives (OCs) implicate significant alterations in psychological well-being and social behaviour: mood and sexual desire as well as sexual arousal are affected. It is unknown whether OC intake could, next to sexual desire, also alter sexual responsiveness including approach avoidance tendencies. To test differences in sexual responsiveness, 58 women (OC-use: n=22; early follicular: n=19 and ovulation: n=17) rated images of 1) males only and 2) couples depicted in a) erotic, b) positive non-erotic and c) aversive scenes for sexual appeal and sexual approach towards the depicted male (scale: 1-4). A mixed ANOVA with within-factors image type (erotic, positive and aversive) and male type (male, couple) and the between-factor group (OC, fNC and oNC) was run. For the sexual appeal, the fNC group, when viewing erotic images, rated males in couple scenes significantly more sexually appealing than the single males. There was no such difference for the remaining groups. Whilst both NC groups would be more likely to sexually approach a male within an erotic couple image, there was no difference for the OC group. Only women taking OCs showed a higher sexual approach rating for males in positive non-erotic images than for males in erotic images. Overall erotic pictures appear to evoke more sexual responsiveness when depicting couples, especially for naturally cycling women. The different findings regarding the approach behaviour towards positive non-erotic males in women using OCs could point towards somewhat altered social approach behaviour.
More than nothing: Neuronal correlates of numerosity zero in the avian endbrain

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Numerical competence is ubiquitous across the animal kingdom, yet, very few species have been shown to possess a quantitative understanding of empty sets. Apart from this, neurophysiological investigations thereof have only been conducted in one species of non-human primates. Recently, it was thus demonstrated how empty set representations are attached with quantitative meaning along the hierarchy of the primate neocortex. Carrion crows (Corvus corone), members of the corvid songbird family, exhibit numerical abilities on par with higher primates despite lacking a layered neocortex. Instead, an associative endbrain area called the nidopallium caudolaterale (NCL) has been repeatedly shown to be implicated in these excellent numerical abilities. We therefore asked whether carrion crows would treat empty sets as having null value and, if so, how the NCL gives rise to this behaviour. To this end, we trained two crows on a computerized, delayed match-to-numerosity task. The used stimulus set comprised random dot arrays with 0 – 4 dots and controls for low-level visual features, such as background shape or luminance, leaving the animals with only numerical cues to solve the task. Along with overall high task performance, the behaviour of the crows indicates handling of empty sets as part of the numerical continuum. Electrophysiological recordings revealed that empty set preferring single units were the most abundant class of numerosity-tuned neurons in the NCL, with both, categorical as well as numerical response profiles. On a population level, numerosities including the empty sets were encoded in a behaviourally relevant manner. These results mark the first account of neuronal mechanisms behind the understanding of numerosity zero outside the mammalian taxon. Thereby, they underline the central role of the avian NCL not only in numerical cognition, but also cognition in general.
Internal state dynamics shape brain-wide activity and foraging behavior

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The brain has persistent internal states that can modulate every aspect of an animal’s mental experience. In complex tasks such as foraging, internal state is dynamic. C. elegans alternate between local search and global dispersal. Rodents and primates exhibit trade-offs between exploitation and exploration. However, fundamental questions remain about how persistent states are maintained in the brain, which upstream networks drive state transitions, and how state-encoding neurons exert neuromodulatory effects on sensory perception and decision making to govern appropriate behavior. Using tracking microscopy in larval zebrafish, we can monitor whole brain neuronal activity at cellular resolution in a freely moving animal across spontaneous internal state transitions. We show that larval zebrafish alternate between two persistent behavioral states during foraging for live prey (paramecia). In the exploitation state, the animal inhibits locomotion and promotes hunting, generating small localized trajectories. In the exploration state, the animal promotes locomotion and suppresses hunting, generating long ranging trajectories that enhance spatial dispersion. We uncover a dorsal raphe subpopulation with persistent activity that robustly encodes the exploitation state. The exploitation state-encoding neurons, together with a multimodal trigger network that is associated with state transitions, form a stochastically activated nonlinear dynamical system. The activity of this oscillatory network correlates with a global re-tuning of sensorimotor transformations during foraging that leads to dramatic changes in both the motivation to hunt for prey and the accuracy of motor sequences during hunting. This work reveals an important hidden variable that shapes the temporal structure of motivation and decision making.
Time is of the essence: Modeling the temporal dynamics of effort allocation

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Interoceptive feedback via the vagus nerve plays a vital role in motivation by tuning actions according to physiological needs. Whereas vagus nerve stimulation (VNS) reinforces actions and enhances dopamine transmission in animals, the time course of the motivational effects of VNS in humans is yet to be characterized. To assess this, 81 healthy, overnight-fasting participants (MBMI = 23.1 ± 3.0 kg/m\(^2\)) participated in an effort allocation task (EAT) in which participants worked to earn food and monetary rewards by exceeding required levels of relative button-press frequency. Participants completed the EAT twice, once during sham and once during transcutaneous VNS. Linear mixed-effects models were run for each of the 30 one-second bins of the trial. The t-values over time revealed early effects of stimulus condition and reward magnitude and late effects of stimulus condition, reward magnitude, and task difficulty. An interaction between reward magnitude and task difficulty only showed an effect in the mid-stages of the trial. The random effects suggested diverging behavior for reward magnitude and task difficulty. Behavior for the interaction between reward magnitude and task difficulty, however, diverged by the middle of the trial only to reconverge in later stages. The intraclass correlation (ICC) revealed a low ICC early in the trial and increased to fluctuate between 0.4 and 0.5, indicating indistinguishable behavior at the beginning that became slightly more predictable as the trial progressed. To model this behavior, autoregressive integrated moving average forecasting and machine learning using Gaussian process predictions of the relative frequency of button press will be done to understand the temporal dynamics of effort allocation. Results from these time series analyses could potentially be used in diagnostics to identify changes in effort as an indicator of potential depressive symptoms and other psychiatric disorders.
Acute effects of ketamine on cortico-striatal connectivity and gene co-expression associations

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The NMDA-antagonist ketamine is increasingly studied for its rapid antidepressant effects. After 24 hours, ketamine administration reduces functional connectivity (FC) in the default mode network of the brain, a functional network that is hyperconnected in depressed patients. In addition, increases in prefrontal synaptogenesis have been reported. Acute effects of ketamine (1h) that may underly these putative mechanisms of action have been understudied. The cortico-striatal circuitry is a prime target for study, as ketamine, like all psychomimetic substances, ultimately affects striatal dopamine release. FC changes in this circuit after ketamine infusion have not yet been characterized in detail. In a sample of 80 healthy individuals measured at ultra-high field (7 Tesla), we will investigate the acute effects of ketamine administration (0.5 mg/kg body weight) compared to saline on voxel-wise FC within the cortico-striatal circuit. As a first step, we will investigate the relationship between acute FC changes in this circuit and coupling to canonical co-expression of genes that code for key neurotransmitters in this pathway, including dopaminergic and glutamatergic genes. Increasing evidence suggests that gene (co-)expression and functional connectivity within networks are tightly linked. Gene expression data will be obtained from the Allen Human Brain Atlas. Associations between FC and gene co-expression within the same circuit could put functional changes in the context of potential changes in neurotransmitter activity in humans within the cortico-striatal pathway. Results will be presented at NeNa.
Brain states across continuous emotional stimulation and their correspondence to behavioral and psychological labels

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Background: The human experience and expression resultant from its interaction with the environment is complex and multimodal, specially when emotions are involved. We investigated the correspondent neural, behavioral and physiological signals of a continuous emotional natural stimulus. The study of continuous signals can appeal untraveled process Its complexity lead to the question whether there is a consensus across subjects regarding responses and whether these correspond to specific events on the stimulus.

Methods: 22 female healthy subjects were scanned with MRI 3T while they watched a video, with negative emotional content ($t(21) = -6.67, p < 0.001$). Continuous arousal response was measured for the same videos outside the scanner, as well as electrocardiogram (ECG) which was recorded via an electrode placed at the base of the back, this position is recommended to maximize the signal to noise of the R-peak in the ECG trace. HRV was derived from ECG data during the videos. A video with neutral content was used as a control.

Results: We observed a coupling across different modalities corresponding with events in the natural stimulus, as well as a pairing of main neural networks whose activity synchronize in certain periods of time for all subjects. These periods correspond with the changes in arousal and HRV.

Conclusions: We were able to observed the way brain activity couples with the rest of the body signals when we are perceiving a complex emotional natural stimulus, as well as the synchronization of different neural networks.
Vascularization of human retinal organoids using iPSC-derived endothelial cells

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The inner blood-retinal barrier (iBRB) is crucial for the normal function of retina by providing a barrier for freely circulating substances in the blood and neural retina. This barrier is mainly implemented by tight junctions forming between the endothelial cells of the retinal capillaries that are covered with pericytes, Müller glia and astrocytes. In diabetic retinopathy, the iBRB is disrupted due to pericyte dropout and consequent endothelial cell dysfunction. In later stages of the disease, hypoxia-induced neovascularization occurs, which can lead to vision loss if left untreated. Current therapies for diabetic retinopathy only target VEGF, which inhibits neovascularization. A comprehensive understanding of the disease progression and therapeutic targets are still lacking.

Retinal organoids (ROs) can be derived from human induced pluripotent stem cells (hiPSCs) and harbor all major neuronal cell types of human retina. However, they lack a vasculature which is hampering the study of vasculature-related disorders. Recently, it has been discovered that vascular organoids (VOs) can be generated from hiPSCs. VOs include endothelial cells as well as mural cells and can form a functional vasculature when transplanted into animal models. In this study, we aim to generate a fusion spheroid model of vascular and retinal organoids from the same source of hiPSCs creating a so-called assembloid. First results of our study demonstrate that endothelial cells fused with ROs mainly interact with retinal pigment epithelium (RPE) and Müller glia. This model has the potential to shed light on the formation of the human iBRB in vitro and a subsequent use as disease model, for drug testing and toxicity studies.
My Body/ Your Body: Neural correlates of body processing in women with binge eating disorder

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Individuals suffering from binge eating disorder (BED) experience recurrent episodes of binge eating in the absence of compensatory behavior such as purging or misuse of laxatives. Body dissatisfaction plays a central role in the etiology and maintenance of BED. However, the neural correlates to body image disturbances in BED remain unclear. An early fMRI-study suggested that patients with anorexia nervosa and bulimia nervosa exhibit reduced responses towards body images in the extrastriate body area (EBA), possibly reflecting body image difficulties. Following studies however did not consistently support these results. In addition, the validity of these results remain limited, because visual attendance of the stimuli was not ensured. We performed functional magnetic resonance imaging (fMRI) and eye-tracking while confronting 20 women with BED and 17 control subjects with 16 standardized pictures of their own body and another person’s body dressed in a set of underwear, as well as two types of control stimuli (a vase and morphed body images). Stimuli were presented in a block-wise fashion, and participants had to perform a one-back task. Contrary to our hypotheses, when controlling for visual attendance, participants with BED demonstrated higher responses in the EBA than control subjects. However, this EBA over-activation was not specific to body stimuli. This result suggests a lower threshold for the activation of body-related schemata in BED, which might play a role in maintaining body image disturbances. Because we have not reached our full sample yet, these preliminary results should be treated cautiously.
Video capture and analysis of the mouse’s natural visual environment

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To ensure that an animal survives and procreates, it needs to interact with its environment in an optimal manner. Each species’ early visual system is adapted to the statistics of the species-specific environment. Thus, to understand how the visual system works, it is crucial to probe it with scenes taken from the species’ habitat. Mice have become an important model in vision research, but it is still rarely considered that, compared to primates, they live in a different environment and therefore have different visual needs. For example, mice are dichromatic and perceive UV (peak at 360 nm) and “green” (peak at 510 nm) light. Moreover, the mouse retina is subdivided into a mostly “green” sensitive dorsal and UV sensitive ventral retina. Under the assumption that a substantial fraction of mouse eye movements serves to stabilize the retinal image, we built a gimbal-stabilized, spectrally-calibrated hand-held camera to explore the natural habitat of mice in the relevant spectral bands. We intensity-calibrated the camera with LEDs of defined wavelengths and brightness using a power meter / spectrometer combination. The camera was moved close to the ground along mouse tracks and UV/green movies of the mouse habitat were recorded for different representative scenes at different times of the day and different seasons. By analysing contrast statistics of the movies, we found that contrast distribution between UV and green channel differ greatly in the upper but not in the lower visual field. This resonates with reports of a higher fraction of colour-opponent retinal ganglion cells in the ventral mouse retina and superior behavioural colour discrimination in the upper visual field. In addition, we found that during dusk, a black drone (“predator”) coming from the sky was more easily detectable in the UV than the green channel, which may emphasize the UV’s role for mouse vision.
The Adaptive Brain – Influence of Estradiol on Hippocampal and Amygdalar Volume

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Sex hormones play an important role in organizing the brain prenatally, but also in structuring the brain due to hormonal fluctuations. In women, already short-term fluctuations of estradiol and progesterone during the menstrual cycle can lead to structural changes in several brain regions, including the hippocampus, the amygdala and the fusiform gyrus. As the different sex hormones constantly interact, it becomes difficult to disentangle hormone-specific effects. Therefore, the aim of this study was to systematically elevate estradiol levels in young naturally cycling women in their early follicular phase by administering estradiol valerate (E2) over 24 hours. Thirty women received 12mg E2 and placebo in a double-blinded fashion and in alternating order. All underwent two MRI T1 brain scans with measurements scheduled 2-3 months apart. Blood samples were taken at both time points to ensure compliance of hormone intake. For the MRI analysis, the Freesurfer standard segmentation pipeline as well as subfield segmentation of the hippocampus and the amygdala were performed. The administration of E2 led to a significant increase in estradiol levels (p <.001) comparable to levels during ovulation. Significant volumetric differences in the hippocampal subfields included the left presubiculum head, p <.001, left parasubiculum p <.037, and right molecular layer HPhead, p <.001. Differences in the amygdala nuclei volume were observed for the cortical nucleus, p <.001, and left paralamic nucleus, p <.001. Several significant correlations between estradiol levels and structural volume occurred. As expected, estradiol administration led to increases in grey matter volume compared to the placebo condition. The results demonstrate the high plasticity of the female brain due to hormonal fluctuations.
Abstract Choice Representations Generalize Between Task Contexts

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Humans can make abstract choices independent of motor actions. It is unclear under which conditions, where and when in the brain abstract choices are represented, and whether these representations generalize to contexts in which choices are linked to actions. To disentangle sensory, decision, and motor stages, we measured MEG signals in 33 participants during variants of a sensorimotor decision-making task with known and unknown choice-response mapping. Using multivariate decoding, we found reliable stimulus, choice and response information with distinct cortical source distributions. Choice representations were invariant to whether the response mapping was known at the time of stimulus presentation. Our results suggest the presence of widespread abstract choice representations, independent of sensory and motor representations.
Dissecting the visual processing hierarchy using degraded natural stimuli in MEG

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Object recognition takes place in interconnected hierarchical areas in the ventral visual stream. In this hierarchy, higher areas have larger receptive fields and become increasingly specific for more complex visual features. These areas receive visual input by bottom up signals from lower areas and provide information to higher brain areas, as well as top down feedback signals to previous processing stages. However, the precise role of these feedback signals is not fully understood. To look into this, we designed a diverse set of stimuli based on natural images, by keeping their lower-level statistical properties identical while removing global object context. Theoretically, these stimuli generate similar feedforward signals up to a certain stage, but different feedback signaling. We recorded MEG from human subjects and analyzed changes in neural representations for different manipulations. Here, we present preliminary results using multivariate decoding. We found varying amounts of neuronal information about image and category identity depending on the specific image modification. Thus, the disruption of global context decreased the decodability of natural images. Moreover, local image statistics alone were not sufficient to explain category-selective signals. Further decoding and cross-decoding analyses aim to reveal the role played by both lower-level statistics and global context in neural representations of objects and categories. This may enable us to investigate how modifications of visual features disrupt processing stages, how information is passed through the hierarchy and thereby to uncover signatures of feedforward and feedback communication.
Beyond the uncanny valley: naturalistic dynamic monkey head avatar elicits behavioral reactions comparable to videos of real monkeys

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Natural faces and especially facial expressions provide crucial social information not only for humans, but also for monkeys. In humans, the likability of computer avatars or robots increases the more human-like they are. However, the uncanny valley hypothesis predicts that this trend is limited by the experience of eeriness if the synthetic entities become very realistic. Previous work on monkeys has argued that also they exhibit an uncanny reaction if exposed to sufficiently realistic monkey avatars. We aimed at generating a standardized monkey head avatar capable of producing natural facial expressions (fear grin, lip smacking, threat and neutral) that does not elicit an expression of uncanniness, but instead natural species-typical reactions. To this end we developed a highly naturalistic rhesus monkey face avatar, animated by motion capture data of real monkeys, and, in addition, degraded variants of decreasing degrees of realism (furless, grayscale and wireframe avatar heads). We exposed eight adult male rhesus macaques to dynamic and static clips of all different avatars as well as to videos of a real monkey and recorded their oculomotor behavior, their facial reactions and various physiological parameters. The avatars’ facial expression modulated how long the monkeys looked at the faces, how detailed they explored it and which parts of the faces they focused on. We show that two less realistic avatar variants, but not the most naturalistic or the most unrealistic ones, elicited clear signs of an uncanny avoidance reaction. Moreover, only the most naturalistic avatar elicited facial reactions comparable to those towards the real monkey video. Hence, our findings confirm the existence of an uncanniness reaction in monkeys and support the notion of an evolutionary conserved behavior shared by monkeys and man. As this reaction can be overcome, it is not a simple reflection of the degree of realism.
Role of microglial HIF-1α in Aβ pathology

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Microglial cells play an elemental role in the development of neurodegenerative diseases. Previous analyses of murine microglia have shown an enrichment of the mTOR and HIF-1α signalling pathways in a cerebral β-amyloidosis model compared to wildtype mice (Wendeln & Degenhardt et al., Nature 2018). Furthermore, HIF-1α was specifically enriched in plaque-associated microglia. In the experiments presented here, we characterize two models with an induced HIF-1α knockout (KO) in microglia cells. Preliminary results show increased microglia clustering around β-amyloid plaques in HIF-1α KO mice and decreased neuronal damage, as well as an altered microglial phenotype. Nevertheless, no changes could be observed in plaque load. Our preliminary data indicates that HIF-1α inhibition might lead to an increased microglial barrier function around plaques, thereby protecting neurons.
Workshops
W1

Causality in neuroscience

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We believe at the core scientists want a causal answer to their question. It is indeed true that for some systems - due to their enormous complexity - it is extremely hard to get to a causal answer. But our literature survey showed that sometimes scientists end up settling for correlation-based results. In the workshop, we will go over “Ten Simple Rules for doing Causal Research”. Here, we will equip you with simple mathematical tools (shown programmatically with python notebooks distributed to students) that you can use in your research especially, while designing experiments, to ensure you can make a causal claim. For example, what are the observations you will need, what are things you must control for, how can you randomize to remove the effects of certain confounders, and so on. In addition, we also go over some empirical tools developed and used by economists, who also work with a complex dynamically changing the system, while making policies and how we can borrow some of them to do causal neuroscience research.
The ability to present your ideas in an accessible way is a must-have nowadays. We all have something to say but due to lack of practice don’t really know where to start from, so stay silent. It’s really hard sometimes just to stand up in the audience and ask a question, not to mention giving a public talk. During the workshop we’ll cover the following topics: preparing your speech, making slides, tips on delivering it and how to deal with questions.
The workshop will focus on topics like what Public Relation tools scientists can benefit from, how to get in contact with media and how to choose the right media outlet/journalist to contact, and what university/MPI public relation teams could help the labs with. I will share my experience from the years I have spent working in PR, as well as include some information that university/MPI PR teams will provide me with.
Organization and documentation of data, scripts and your own tasks is tremendously important, not only for good scientific practice but also to prevent life as a researcher from becoming more stressful than necessary. This self organization is often assumed to just work out of the box, although there is a rich pool of tools available to support you as a researcher. Thus, in this workshop I want to give an overview of available tools, how to use them to benefit your work and which tools specifically could improve the workflow in your project.
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