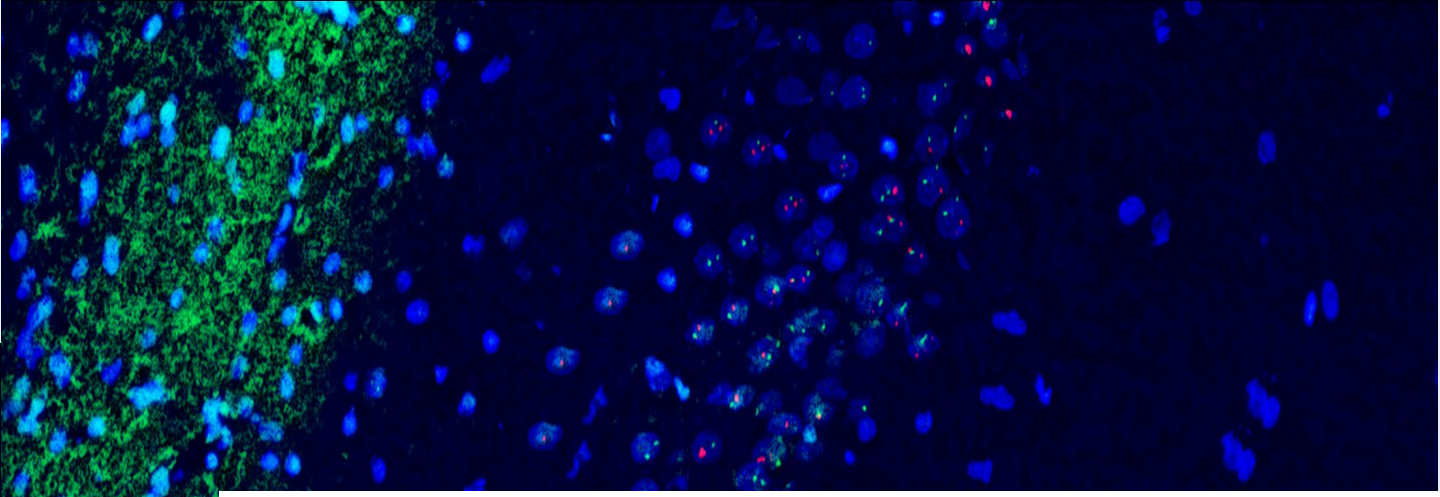

Fifth International Conference on the
FUNCTIONAL ARCHITECTURE OF MEMORY
18th -20th May 2022

SPEAKERS

John Disterhoft (Feinberg School of Med., NWU, USA)
Emrah Duezel (DZNE Magdeburg, DE)
Loren Frank (Howard Hughes Medical Institute/Kavli Inst. for Fundamental Neuroscience, USA)
Steffen Gais (Univ. Tübingen, DE)
Sheena Josselyn (SickKids, CA)
James Knierim (The Zanvyl Krieger Mind/Brain Institute, USA)
Jill Leutgeb (Univ. of California San Diego, USA)
Liset Menendez de la Prida (Inst. Cajal – CSIC, ES)
Hannah Monyer (Heidelberg Univ./Deutsches Krebsforschungszentrum, DE)
Charan Ranganath (UC Davis, USA)
Stefan Remy (LIN Magdeburg, DE)
Magdalena Sauvage (LIN/OvGU Magdeburg, DE)
Menno Witter (Kavli Institute for Systems Neuroscience/ NTNU, NO)
Thomas Wolbers (DZNE Magdeburg, DE)
Motoharu Yoshida (LIN / DZNE Magdeburg, DE)

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LIN LEIBNIZ INSTITUTE FOR NEUROBIOLOGY MAGDEBURG

General information

1. Venue

Address:
Leibniz Institute for Neurobiology (LIN)
Brenneckestr. 6
39118 Magdeburg

Coming by car:

Coming from Berlin or Hannover via A2 use exit *Magdeburg-Zentrum* and follow the city highway. Use the exit *Leipziger Straße*, choose left lane and then follow the road for around 600m.

Coming from Halle/Leipzig via A14 exit at *Magdeburg-Sudenburg/ Magdeburg-Zentrum* and follow the city highway. Use the exit *Leipziger Straße*, choose right lane and then follow the road for around 600m.

Public transport from the main station:

From Magdeburg main station use the tram station *Hauptbahnhof Ost* and take the tram line 9 (direction: *Leipziger Chaussee*). Get off the tram at stop *Brenneckestraße* (12 min drive). Turn right and take a 10 min walk along *Brenneckestraße* to the institute's yellow brick building. Tram routes and tickets are available via the app EasyGO.

2. Wifi

Eduroam
LIN-Conference (Access Code: meet@LIN)

3. Lunch

During the breaks, snacks and coffee will be provided. There is also a vending machine in the Atrium of the LIN where you can purchase snacks, coffee etc. Alternative options are either on the campus of the University Hospital or in walking distance (10min).

4. Students/speakers sessions 1pm (50 min)

Each day after lunch students and postdocs (no PIs) have the opportunity to get feedback from the speakers of the day. We strongly encourage students to take advantage of this unique opportunity to ask the questions they never ‚dared' to.

5. Conference Dinner (Thursday May 19th)

www.restaurant-die-kirche.de

For participants who registered for the conference dinner, a transfer from the LIN to the restaurant *Die Kirche* is available.
Departure from the LIN: at 5:30 p.m. sharp.
Return: pick-up at the drop off point at 9 p.m. sharp. 2 stops: Motel One (city centre) and the LIN.
If you miss the transfer to the restaurant, you can go by tramline 3 or 9 from the stop *Brenneckestraße* to the main station, switch to line 4 in direction Cracau, and get off at final destination *Cracau/Pechauer Platz*. This takes approximately 20 minutes. From there, walk along the main road towards the town exit Magdeburg-Pechau. After an 8-minute walk, you will reach the restaurant.
Alternatively, you can call a cab (0049 391 73737).

In case you miss your return transfer from the restaurant, walk along the main road from *Die Kirche* into town until you reach the tram station *Cracau/Pechauer Platz*. Line 4 goes directly to the city centre. For final

destination Motel One use the stop *main station*. If you wish to go back to the LIN, switch to tram line 3 with direction *Leipziger Straße* and get off at *Brennecke Sraße* (see map under 1.)

No specific events are organized for Wednesday 18th or Friday 20th.
Please refer to the map in the "Recreational Information" chapter of this booklet for restaurant recommendations (page 57).

Emergency numbers

Police 110
Fire Department 112
Medical on-call service 116117
Taxi 0049 391 73737

Useful websites and apps

Train connections https://www.bahn.com/en
Tram connections in Magdeburg https://www.mvbnet.de/

Tram routes and tickets https://mvb.myeasygo.de/en/home-mvb.html
(available on the AppStore and Google play)

Program

Time	Wednesday May 18th	Time	Thursday May 19th	Time	Friday May 20th
09:30 - 09:40	"Welcome" Prof. Dr. Sauvage	09:30 - 10:10	**Menno Witter (Kavli Institute/NTNU, Norway)** The entorhinal cortex as integrative gatekeeper in the hippocampal memory system	09:30 - 10:10	**Charan Ranganath (Univ. of CA, USA)** The importance of setting boundaries: How cortico-hippocampal interactions at event boundaries support memory and prediction
09:40 - 10:10	Data Blitz Session Part I				
10:10 - 10:50	Data Blitz Session Part II	10:10 - 10:50	**Magdalena Sauvage (LIN/ OvGU)** 'Spatial' and 'non-spatial' medial temporal lobe memory subnetworks: information processing and coordination	10:10 - 10:50	**Emrah Duezel (DZNE Magdeburg)** Episodic memory in preclinical and prodromal Alzheimer's disease
10:50 - 11:00	Coffee	10:50 - 11:20	Coffee	10:50 - 11:20	Coffee
11:00 - 12:00	Data Blitz Session Part III	11:20 - 12:00	**Liset Menendez de la Prida (Instituto Cajal - CSIC)** Two hippocampal axes: a proximodistal and radial perspective of entorhinal-hippocampal function	11:20 - 12:00	**Jill Leutgeb (Univ. of CA San Diego, USA)** Dentate network computations for memory and decisions
12:00 - 13:00	Lunch Break	12:00 - 13:00	Lunch Break	12:00 - 13:00	Lunch Break
13:00 - 13:50	Students/ Speakers Round Table	13:00 - 13:50	Students/ Speakers Round Table	13:00 - 13:50	Students/ Speakers Round Table
14:00 - 14:40	**Loren Frank (Kavli Institute, USA)** Memories and Mental Simulation: Multiplexing the Past, Present and Future	14:00 - 14:40	**Thomas Wolbers (DZNE Magdeburg)** Mechanisms and consequences of altered entorhinal/hippocampal coding in human aging	14:00 - 14:40	**Motoharu Yoshida (DZNE)** Mechanism of working memory in individual hippocampal CA1 cells
14:40 - 15:20	**Steffen Gais (Univ. Tübingen)** Multiple systems for declarative memory	14:40 - 15:20	**Hannah Monyer (Heidelberg Univ./DKFZ, DE)** Medial Entorhinal Cortex Commissural Input Regulates the Activity of Spatially Tuned Cells and Episodic Memory	14:40 - 15:20	**James Knierim (Johns Hopkins Univ., USA)** Loss of functional heterogeneity along the CA3 transverse axis in aging
		15:20 - 15:25	Group picture (in front of the LIN)		
15:20 - 15:40	Coffee	15:25 - 15:40	Coffee	15:20 - 15:40	Coffee
15:40 - 16:20	**Sheena Josselyn (Univ. of Toronto, CA)** Excitability mediates allocation of pre-configured ensembles to hippocampal engram supporting contextual conditioned fear in mice	15:40 - 16:20	**Stefan Remy (LIN/ DZNE)** Subcortical control of hippocampal activity and behaviour	15:40 - 16:20	**John Aggleton (Cardiff University, UK)** The anterior thalamic nuclei: A hub for space, attention, and memory
16:20 - 17:00	Open Discussion	16:20 - 17:00	Open Discussion	16:20 - 17:00	Open Discussion

Data Blitz Sessions Overview

09:40 - 10:10	**Data Blitz Session Part I (talk: 5 mins; questions: 1 min)**
	Alessio Attardo (LIN Magdeburg, Germany) Structural synaptic instability, a bug or a feature for hippocampal memory?
	Alessandro F. Ulivi (LIN Magdeburg, Germany) Imaging *in vivo* of individual hippocampal synaptic sub-groups
	Matthias Prigge (LIN Magdeburg, Germany) Can Engram Ensemble Size Predict Performance in an Object-in-Place Task?
	Niklas Vockert (DZNE Magdeburg, Germany) Hippocampal vascularization patterns and their effect on cognitive abilities and brain structure in old age
	Alberto Arboit (DZNE Magdeburg, Germany) Combining fMRI and in vivo electrophysiology to study how the cholinergic system controls neuronal activity in the hippocampus and prefrontal cortex
10:10 - 10:50	**Data Blitz Session Part II (talk: 5 mins; questions: 1 min)**
	Liv Mahnke (LIN Magdeburg, Germany) Bridging animal and human memory function: fMRI in awake rats
	Erika Atucha (LIN Magdeburg, Germany) Imaging memories in MTL and PFC subareas over half a life-time: uncovering a fundamental principle for memory consolidation?
	Gürsel Çalışkan (OvGU & CBBS Magdeburg, Germany) Lateralization of pattern completion function in the hippocampal mossy fiber synapses
	Jacob Bellmund (MPI Leipzig, Germany) Structuring time: The hippocampus constructs sequence memories that generalize temporal relations across experiences
	Fatima Amin (LIN Magdeburg, Germany) Moonwalking punishment and what dopamine has to do with it
	Sanja Mikulovic (LIN Magdeburg, Germany) Functionally distinct hippocampal rhythms and circuits predict valence of the subsequent locomotion
	Maria P. Contreras (Tübingen University, Germany) Prior experiences strengthen the temporal coordination of SO, spindles, and ripples during memory consolidation in developing rats

Data Blitz Sessions Overview

11:00 - 12:00	Data Blitz Session Part III (talk: 5 mins; questions: 1 min)
	Deetje Iggena (Charité Berlin), Germany Multisensory input modulates memory-guided spatial navigation
	Yee Lee Shing (Goethe University Frankfurt, Germany) Age-related differences in memory consolidation: Comparing children and young adults
	Svenja Klinkowski (University of Tübingen, Germany) Formation of conceptual representations in visual processing areas
	Anuck Sawangjit (University of Tübingen, Germany) Two distinct ways to form long-term object-recognition memory during sleep and wakefulness
	Yaroslav Sych (Center for Experimental Neurology, Switzerland) The role of noradrenaline in sleep-dependent memory consolidation
	Svenja Brodt (University of Tübingen, Germany) Sleep strenghtens early neocortical traces and thalamic and striatal contributions to declarative memory recall
	Alexander Dityatev (DZNE Magdeburg, Germany) Mental retardation-related protease neurotrypsin regulates spinogenesis, learning, and sociability
	Javier Ortiz-Tudela (Goethe University Frankfurt, Germany) Episodic memory content as feedback signals in the early visual cortex
	Panagiotis Iliopoulos (DZNE Magdeburg & IKND, Germany) Successful mnemonic discrimination is linked to decreased functional connectivity between hubs in the frontoparietal and default mode network
	David Berron (DZNE Magdeburg, Germany) Hippocampal subregional thinning related to tau pathology in early stages of Alzheimer's disease

Data Blitz Session Abstracts

Synaptic instability, a bug or a feature for hippocampal memory?

Tim Castello-Waldow [1], Ghabiba Weston [1,2], Alireza Chenani [1] Alessandro F. Ulivi [1,3] Yonatan Loewenstein [4], Alon Chen [1,5] and Alessio Attardo [1,2,3]

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[2] Graduate School for Systemic Neuroscience
[3] Leibniz Institute for Neurobiology
[4] Hebrew University of Jerusalem
[5] Weizmann Institute of Science

Mammalian hippocampus is crucial for episodic memory formation. It is widely believed that neural synapses and their structural counterparts – dendritic spines - are elemental sites of information storage. However, there is no direct evidence of the causal role of hippocampal dendritic spines in learning and recalling information. We previously tested the prediction that the lifetimes of hippocampal synapses match the longevity of hippocampal memory and found that CA1 spines were transient with a mean lifetime of ~1–2 weeks. This was in striking contrast to neocortical spines and quantitatively supported the idea that the turnover dynamics of hippocampal synapses directly reflects the transience of hippocampal-dependent memory. We have recently shown that the density and the survival of hippocampal dendritic spines predict hippocampal-dependent recall (freezing to the context) but not hippocampal-independent recall (freezing to the tone). This suggests that also in the hippocampus - as in the neocortex - structural synaptic dynamics support brain area-specific cognitive functions. Interestingly, animals with higher baseline density or stability of CA1 dendritic spines showed lower levels of freezing. This might seem counterintuitive based on the notion of dendritic spines as cellular correlates of permanently recorded information. However, the hippocampus might not store information for the long-term but rather provide a large synaptic space to quickly represent new information and hold it for a limited amount of time as it progressively transits to neocortical long-term storage sites. In this framework fast structural turnover of synapses might reset the synaptic space to allow for new information to be encoded. Thus, faster structural turnover - i.e., shorter survival time - would make synaptic space available faster, which might benefit encoding and thus result in better recall.

Imaging *in vivo* of individual hippocampal synaptic sub-groups

Alessandro F. Ulivi [1]; Hannah Klimmt [1]; Bhargavi Murthy [1]; Rosa Eva Hüttl [2]; Stefanos Somatakis [2]; Jinhuyn Kim [3]; Alon Chen [4] and Alessio Attardo [1]

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[2] Max Planck Institute of Psychiatry
[3] Korean Institute of Science and Technology
[4] Max Planck Institute of Psychiatry and Weizmann Institute of Science

The two cornerstones of the investigation of the neurobiology of memory are the assumptions that memory formation is corresponded by a biochemical change of brain parenchyma, a trace called *engram*; and that synaptic plasticity is at the core of this process. Recently it became possible to label and directly manipulate engrams, by exploiting the expression of molecular markers as c-Fos, Arc and CREB. These studies proved that various hippocampal neuronal sub-populations have critical roles in memory allocation, encoding and expression. They also suggest that synaptic plasticity differs among different neuronal sub-groups when memory is formed and retrieved. Still, how hippocampal synaptic dynamics relate to hippocampus -dependent learning remains elusive.

To fill this gap, I have extended longitudinal deep brain *in vivo* imaging of CA1 dendritic spines – used as proxies for excitatory synapses – to imaging of synaptic contacts, labelled by means of the **m**ammalian **G**FP **R**econstitution **A**cross **S**ynaptic **P**artners (mGRASP) system. mGRASP exploits the expression of two GFP fragments, respectively delivered to the pre- and post- synaptic compartments, to visualize synapses after the full protein is reconstituted across the synaptic cleft. This technique offers several advantages over imaging of dendritic spines: 1) it labels true structural synapses. 2) It extends the imaging to aspiny synapses. 3) It labels synapses sparsely, thus ameliorating the limitations due to optical resolution. Finally, 4) it enables tracking the dynamics of distinct synaptic sub-groups, as pre- and post- mGRASP markers can be targeted to selective neuronal sub-populations.

Can Engram Ensemble Size Predict Performance in an Object-in-Place Task?

Julia Büscher[1], Ceylan Steinecke[2], Erika Atutxa[2], Magdalena Sauvage[2] &, Matthias Prigge[1]

[1] Research Group Neuromodulatory Networks Leibniz Institute for Neurobiology, Magdeburg, Germany
[2] Department Functional Architecture of Memory, Leibniz Institute for Neurobiology, Magdeburg, Germany

How well we perform in given memory task depends on many capriciously factors; yet throughout animal kingdom variability seen in performance levels between subjects are larger and stable when compared to averaged subject trial performance. We thought to set-out to identify neuronal correlates that can predict such inter-individual differences. Here, we aimed to label neurons that are active in the prefrontal cortex and hippocampus during object recognition task with high temporal resolution using the activity-dependent photoconvertible protein CaMPari2. Therefore, we develop an object-in-place task for mice that allows us to score animals during their habituation phase to various degrees of their explorative drive, anxiety and arousal levels and motor parameters. These categorizations enable us to investigate and potentially rule-out any predictive-power of such behavioural traits, that could bias our identification of differences in neuronal correlates between subject in our OiP task.
During the testing phase, photoconversion of active neurons in the PFC and HIP were triggered in a close-loop fashion, when animals explore a specific object. After testing phase, animal's brain were extracted and brain areas were cleared to quantify number and position of neurons that were active during object recognition, and exposed to sufficient photons for an efficient conversion.
Preliminary results indicate a weak predictive-power for behavioural traits after removing animals with clear non-engaging behaviour.
Efficiency of photoconversion exhibit a strong dependence to light power attenuation from the tip of the optical fiber; yet cell ensembles at normalized distances from the tip of the optical fiber show a trend to stronger degrees of photoconversion with performance. Early analysis did not identify a consistent cell ensemble size dependence in PFC or HIP with memory performance.
As our results still have to be taken with caution, we established a close-loop behaviour-triggered labelling strategy for active and task-relevant neurons to investigate inter-individual differences in mice.

Hippocampal vascularization patterns and their effect on cognitive abilities and brain structure in old age

Niklas Vockert[1], Valentina Perosa[2,3], Gabriel Ziegler[1,4], Frank Schreiber[1,2], Anastasia Priester[5], Marco Spallazzi[6], Merita Aruci[1], Hendrik Mattern[7], Aiden Haghikia[1,2], Emrah Düzel[1,2,4,8,9], Stefanie Schreiber[1,2,9], Anne Maass[1]

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[9] Center for Behavioral Brain Sciences (CBBS), Magdeburg, Germany

The hippocampus within the medial temporal lobe is highly vulnerable to age-related pathology such as vascular disease. Vascular supply of the hippocampus can be broadly distinguished into two categories: a single supply that is solely dependent on the posterior cerebral artery versus a dual supply with an additional contribution of the anterior choroidal artery. In a cohort of older adults, a dual vascular supply was positively associated with measures of cognition and brain structure. Hence, an augmented hippocampal vascularization might contribute to maintaining structural integrity in the brain and preserving cognition despite age-related degeneration.

Combining fMRI and in vivo electrophysiology to study how the cholinergic system controls neuronal activity in the hippocampus and prefrontal cortex

Alberto Arboit[1], Karla Krautwald[1], Frank Angenstein [1,2,3]

[1] Functional Imaging Group, Deutsches Zentrum für Neurodegenerative Erkrankungen (DZNE), Magdeburg, Germany.
[2] Leibniz Institute for Neurobiology (LIN), Magdeburg, Germany.
[3] Medical Faculty, Otto von Guericke University, Magdeburg, Germany

Acetylcholine is a fast-acting neurotransmitter in the peripheral nervous system, however, in the central nervous system; it acts mainly as a modulator. It regulates neuronal excitability, alters neurotransmitters release, and coordinates the firing of groups of neurons. Furthermore, the central cholinergic system is involved in many cognitive functions (memory, learning, attention) as well as in various neurological disorders (epilepsy, schizophrenia, Alzheimer's disease).

Nowadays fMRI is widely used in cognitive science to investigate neuronal processes involved in memory formation and/or retrieval. However, the specific impact of cholinergic system modulation on fMRI signals, such as BOLD (blood oxygen level-dependent) responses, is not yet well understood.

Therefore, we investigate how modulation of the cholinergic system alters BOLD and neuronal responses in the hippocampus and in one of its targets region, the prefrontal cortex (PFC), during electrical stimulation of the perforant pathway (PP). To this end, we coupled fMRI measurements with concurrent local field potential recordings in the dentate gyrus and PFC. Our data indicate that stimulation of the PP with high-frequency pulse bursts already activates the endogenous cholinergic system. In addition, our results show that the cholinergic system modifies stimulus-induced fMRI BOLD responses mainly only indirectly, by modulating signal processing in local neuronal circuits and GABAergic as well as glutamatergic transmission.

Bridging animal and human memory function: fMRI in awake rats

Liv Mahnke[1], Caroline Chwiesko[1], Mathias Hoehn[4], Frank Angenstein[2], Magdalena Sauvage[1,5]

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Memory function and its neural substrates are typically investigated with fMRI in humans. The Medial Temporal Lobe of the brain (MTL) is crucial for episodic memory as damage to this area leads to severe memory deficits. This damage is however rarely circumscribed to a specific MTL subarea, for example the hippocampus. Also, the use of high resolution fMRI imaging is still scarce, which constitutes a major challenge to disentangle the role of the different MTL subareas in memory function. Invasive approaches, that allow for subareas to be targeted in a selective manner (for example, lesions, transient optogenetic inactivation or electrophysiological recordings), combined to fMRI could circumvent such a short-coming. This type of approaches are possible in rodents under controlled conditions. However, most small rodent fMRI studies are performed under sedation, which does not allow for a direct investigation of memory function. A handful of fMRI studies have however been conducted with awake mice, albeit without performing contrasts relevant to memory function. Here, we proposed to contribute to bridging the gap between species by establishing a protocol and pipelines for the study of memory function in awake rats. In an attempt to render findings more easily transferable to humans, we established the first fMRI-compatible memory paradigm for awake rats, imaged brain activity with a 9.4T fMRI scanner and performed analyses under conditions similar to those used in humans (SPM software, group analyses, 'old vs new' contrasts). We report patterns of activity comparable to those observed in humans under similar conditions, including a higher BOLD signal in the hippocampus and cognitively -related areas for the presentation of stimuli for which a memory could be formed ('old' stimuli) as opposed to the presentation of 'new' stimuli. These results constitute a first promising step towards bridging human and animal memory function and paves the way for future investigations including the combination of fMRI in awake rats and invasive approaches to achieve a broader understanding of memory function, but also for investigations that would require fMRI in awake small rodents in general.

Imaging memories in MTL and PFC subareas over half a life-time: uncovering a fundamental principle for memory consolidation?

Erika Atucha[1], Celia Fürst[1] and Magdalena Sauvage[1,2]

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[2] Medical Faculty, Otto von Guericke University, Magdeburg, Germany.

The consolidation of memory has mainly been investigated in emotionally arousing tasks like fear conditioning, with the hippocampus and the prefrontal cortex (PFC) as foci and without systematically dissociating the role of their subareas. We showed in a previous study that the contribution of the hippocampal subfield CA3 is restricted to the retrieval of recent and early remote fear memories in mice (i.e. up to 1 month-old) while CA1's contribution persists up to 1-year (comparable to 40 years in humans based on life expectancy; Lux et al., elife, 2016). In addition, we reported that MTL cortical areas (MEC, LEC, PER and POR) were maximally engaged for recalling the most remote memories (6 months and 1 year-old). Here, we tested whether this overtime network switch could constitute a general mechanism for memory consolidation, i.e. whether it would also be at play for memories devoid of fear content. In addition, we studied the kinetics of the recruitment of PFC areas (ACC, PL, IL) over the same time-window. To do so, we adapted an object-in place recognition task to study up to 6 month-old memories and imaged MTL and PFC subareas activity upon memory retrieval. This was done using a high resolution imaging technique based on the detection of the RNA of the gene Arc, tightly linked to synaptic plasticity and memory function. We report that, as was the case for fear motivated memories, CA3's contribution was restricted to retrieving the most recent memories and that the LEC, MEC, PER, POR were maximally engaged for recalling the most remote memories. Within the PFC, this latter pattern was mirrored exclusively in the ACC while PL and IL's recruitment was low independently of the age of the memory. These results suggest that a shift from the engagement of CA1 and CA3 to the recruitment of CA1, the MTL cortical areas and the ACC for the recall of memory as it ages might constitute a fundamental principle of memory consolidation.

Lateralization of pattern completion function in the hippocampal mossy fiber synapses

Gürsel Çalışkan[1, 2, *], Syed Ahsan Raza[1, 2, *], Miguel del Àngel[1], Guilherme M. Gomes[2, 3], Michael R. Kreutz[2, 3, 4] & Oliver Stork[1, 2*]

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In everyday life, presence of a resembling contextual feature (e.g., an odour, colour) of a past experience can trigger the recall of that particular episodic memory ("pattern completion"). Such associations between a particular event and the contextual background of its experience allows for categorization, generalization and novelty detection. Of note, accumulating evidence suggests that even a minor maladjustment in circuits that mediate background context memory can trigger inappropriate recall of the contextual information representing one of the core features of post-traumatic stress disorder (PTSD). In this study, in C57BL/6 mice, we investigated cellular mechanisms of dentate gyrus (DG)-to-Cornu Ammonis (CA)3 communication involved in pattern completion during recall of a previously acquired background contextual fear memory. We considered a potential lateralization since evidence has accumulated that functional and structural asymmetry do exist in the rodent hippocampus. Via employing a pattern completion task based on a background contextual fear conditioning paradigm, synaptic physiology, network activity read-outs, engram labelling (RAM: robust activity marking), chemogenetics (DREADDs: Designer Receptors Exclusively Activated by Designer Drugs (DREADD) and dual-eGRASP (green fluorescent protein reconstitution across synaptic partners), we show a profound left-right asymmetry in the DG-CA3 communication and preferential involvement of mossy fibre synapses of the right hippocampus in the pattern completion of background context memory.

Structuring time: The hippocampus constructs sequence memories that generalize temporal relations across experiences

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[4] Kavli Institute for Systems Neuroscience, Centre for Neural Computation, The Egil and Pauline Braathen and Fred Kavli Centre for Cortical Microcircuits, Jebsen Centre for Alzheimer's Disease, Norwegian University of Science and Technology, Trondheim, Norway
[5] Institute of Psychology – Wilhelm Wundt, Leipzig University, Leipzig, Germany

The hippocampal-entorhinal region supports memory for episodic details, such as temporal relations of sequential events, and mnemonic constructions combining experiences for inferential reasoning. However, it is unclear whether hippocampal event memories reflect temporal relations derived from mnemonic constructions, event order, or elapsing time, and whether these sequence representations generalize temporal relations across similar sequences. Here, participants mnemonically constructed times of events from multiple sequences using infrequent cues and their experience of passing time. After learning, event representations in the anterior hippocampus reflected temporal relations based on constructed times. Temporal relations were generalized across sequences, revealing distinct representational formats for events from the same or different sequences. Structural knowledge about time patterns, abstracted from different sequences, biased the construction of specific event times. These findings demonstrate that mnemonic construction and the generalization of relational knowledge combine in the hippocampus, consistent with the simulation of scenarios from episodic details and structural knowledge.

Moonwalking punishment and what dopamine has to do with it

Fatima Amin[1], Christian König[1], & Bertram Gerber[1]

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Conventional wisdom has it that we learn to avoid what we dislike. We reasoned that the reverse can also be true, that avoiding things can make us dislike them. Here, we exploit Drosophila melanogaster as a powerful insect model system to study these processes. Specifically, when during training an odour is presented together with optogenetic activation of a set of descending brain neurons that induce backward locomotion (the 'moonwalker' neurons: Bidaye et al. 2014, Science) learned avoidance towards this odour is observed in a later test. We will present data with respect to the valence conferred by avoidance, the role of movement-induced sensory feedback and the role of dopaminergic reinforcement systems in this paradigm. This may well shed light on processes of generality across species.

Functionally distinct hippocampal rhythms and circuits predict valence of the subsequent locomotion

Sanja Mikulovic

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Humans, as animals, move for different reasons: we move to accomplish a motor task, reach a specific place, receive a reward, flee from a dangerous situation, or help an individual in need. Theta oscillations (4-12 Hz) is one of the most extensively investigated rhythms of the brain, closely linked to locomotion and diverse types of learning and memory. Previous studies (Whishaw et al, 1973; Bland et al, 2006) have reported that theta frequency predicts different heights in a jump avoidance test. The widely accepted view, in accordance to the "sensorimotor integration model" is that theta frequency predicts the subsequent movement. However, the jump avoidance test involves a strong fear component, leading to an elusive conclusion whether theta activity predicts solely movement or fear of the subsequent jump. To address this conundrum, we designed an experiment in which we performed 2 Photon imaging in combination with oscillations recordings in mice running on a treadmill. To investigate the predictive coding of a motor- and fear-related stimuli, we first introduced a brake, and subsequently an air puff stimulus at specific locations. Analysis of oscillatory activity revealed that theta rhythm was differentially affected by learning the position of the two stimuli, while Calcium imaging data revealed that brake- and puff- related cells form largely non-overlapping populations. These results indicate that distinct hippocampal rhythms and circuits predict valence of the subsequent locomotion rather than movement per se. In the final part of the talk, I will show preliminary data from my newly established laboratory addressing the role of hippocampal circuits in the "move to help".

Prior experiences strengthen the temporal coordination of SO, spindles, and ripples during memory consolidation in developing rats

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Sleep supports the consolidation of memories that rely on the cortico-hippocampal system. Recent research has shown that prior experiences improve cortico-hippocampal memory capabilities during development and that the coupling of the cortical sleep oscillations indexes the maturation of these memories. Here, we wondered whether prior experiences enhance memory capabilities during development by shaping the temporal coordination of the cortico-hippocampal sleep oscillations. To answer this question, we exposed juvenile rats to either a spatial experience condition or a control condition. In the former, rats were challenged to recognize new object locations on three occasions, (each occasion on every second day). In the control condition, rats were exposed to stationary objects. At the test phase, the spatial memory capability of both groups was evaluated with the classical object-place recognition (OPR) task. The task consisted of an encoding and retrieval phase separated by 3 hours of consolidation period during which frontal and parietal EEGs and hippocampal local field potentials (LFP) were recorded while the rats were sleeping. Behavioral results showed that rats with prior spatial experiences formed a robust spatial memory compared to controls. In parallel, the rats of the Spatial experience group displayed an increased percentage of ripples coupled to a SO-spindle complex. Interestingly, this increase in the triple-coupling of ripples was restricted to SO-spindle events occurring in the parietal cortex. Also, rats of the Spatial experience group, unlike the Controls, showed significant ripple-spindle phase-locking, in conjunction with an increased ripple activity triggered by the parietal spindle onset, suggesting a cortico-to-hippocampal modulation of hippocampal sleep oscillations. We provide the first evidence for an experience-induced strengthened of cortico-hippocampal temporal coordination during sleep in developing rats.

Multisensory input modulates memory-guided spatial navigation

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Successful spatial navigation relies on the integration of multisensory input with spatial memory representations. However, studies of spatial navigation in humans typically use stationary experimental setups that neglect multisensory information and have limited ecological validity. Here, we investigate the effects of multisensory input on memory-guided spatial navigation in patients with hippocampal lesions. Eleven patients and 22 age-, sex- and education-matched control participants performed a virtual water maze task, once in a stationary desktop setup in which the experiment was presented on a flat screen, and once in a mobile setup (MoBI) using head-mounted virtual reality goggles allowing the participant to move around freely. While the general spatial layout was mantained, the virtual scene differed between the two setups and the setup as well as the virtual scene was counterbalanced. In both experimental setups, the participants learned the location of six objects and had to navigate back to that location from four alternating starting positions.
Multisensory input modulated spatial navigation in both patients with hippocampal lesions and their healthy controls. Both groups showed a more goal-directed behavior and increased use of environmental cues, as evidenced by less surface coverage, and an increase in initial head rotations in the mobile setup. Remarkably, patients benefited more from multisensory information than the control group. The patients showed a decrease in path error already during learning and eventually an increase in spatial precision for a memorized location in probe trials. The increase in spatial precision can be attributed to a greater replication of a trajectory previously learned in the learning trials.
In conclusion, multisensory input modulates navigational behavior and compensates for deficits in spatial navigation due to hippocampal lesions.

Age-related differences in memory consolidation: Comparing children and young adults

Yee Lee Shing

LISCO Lab, Developmental Psychology, Goethe University Frankfurt

Episodic memory (EM) consolidation has its ontogenetic roots in early childhood. It sets the basis for autobiographical memory and future imagination. We investigate the functional neural correlates of EM consolidation in middle childhood (age five to seven) in comparison to young adulthood (age 21 to 30). In a micro-longitudinal design, participants learned and retrieved object-location associations over two weeks. After a short delay (one night of sleep), we observed lower retention rates for children compared to adults. In the fMRI retrieval task after short delay, children recruited ventromedial PFC, temporal and parietal areas for remote versus recent items. Compared to adults, children showed lower activations in lateral PFC for remote items, which may point to a lower level of strategic retrieval operations (Shing et al. 2010). After long delay (two weeks), retention rates decreased in both groups, with a steeper decline in children. Here, children recruited right temporal occipital fusiform cortex more for remote than for recent items. In young adults, we detected a higher BOLD-response for remote items in areas within the Posterior Medial Episodic Network (Ritchey & Cooper, 2020), namely parahippocampal gyrus (PHG) and precuneus. Over time, adults increasingly recruit PHG, precuneus and lateral prefrontal cortex (PFC) for remote EM retrieval. In contrast, hippocampal involvement remained stable across sessions for both groups, supporting the multiple trace theory (Nadel & Moscovitch, 1997). Taken together, our findings demonstrated that short- and long-term EM consolidation in children functions on a lower level than in adults. We propose that this evolves due to an ongoing structural and functional maturation of the prefrontal and parietal areas and their connectivity with the hippocampus.

Formation of conceptual representations in visual processing areas

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The presented study investigates the idea of concurrent memory encoding in the hippocampal-neocortical memory network, and specialized subsystems coding for different aspects of the memory. The newly developed paradigm includes two experimental groups that encoded the same abstract visual stimuli during fMRI scanning and were instructed to either remember the detailed item-context combinations (DET) or to identify conceptual categories (CEP). 24h later performance was tested in a categorization and an item-context recognition task, where CEP perform better at categorization and DET at context recognition. The behavioral differences were complemented by differential activation during encoding between the two groups including a stronger increase in visual processing areas over category repetitions in CEP compared to DET which might indicate the formation of conceptual representations.

Two distinct ways to form long-term object-recognition memory during sleep and wakefulness

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Sleep is considered as the brain state that is optimal for long-term memory formation. However, some observations suggest that long-term memory can also be formed in the waking state. Here, we compared the effects of 2-h post-encoding periods of sleep and wakefulness on the formation of long-term memory for objects and their associated environmental contexts. We employed a novel-object recognition (NOR) task in rats, using object exploration and exploratory rearing on hind limbs, respectively, as behavioral indicators of these memories.
Rats in both post-encoding wake and sleep conditions showed significant long-term NOR memory at remote recall testing (1-week), with NOR memory after sleep predicted by the occurrence EEG spindle-slow oscillation coupling during sleep. Importantly, rats in the sleep group exhibited a decrease in exploratory rearing at recall testing, revealing successful recall of environmental context. In contrast, the wake rats showed no change in rearing behaviors, suggesting that although NOR memory was present, context memory was lost. Disruption of hippocampal function during the post-encoding interval suppressed long-term NOR memory together with context memory formation, when the rats had slept in this interval, but enhanced NOR memory when they were awake. Also, we show that, under certain conditions (e.g., recognition of objects in a context other than learning), NOR memory in the wake rats was superior to that after sleep.
Our findings indicate two distinct and competing modes of long-term memory formation. Sleep consolidation is hippocampus-dependent and implicates event-context binding, whereas wake consolidation is impaired by hippocampal activation and strengthens context-independent representations.

The role of noradrenaline in sleep-dependent memory consolidation

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Noradrenaline release in the brain is controlled by the midbrain neurons residing in the locus coeruleus (LC). LC projects widely throughout the neocortex and subcortical brain regions. It is known that noradrenaline dynamics on the short time scale can modulate task performance. On the longer time scale, noradrenaline can modulate sleep state transitions. However, little is known about the role of noradrenaline in sleep-dependent memory consolidation. Here we used the genetically encoded fluorescent noradrenaline sensor GRABNE and multi-fiber photometry to examine how salient experiences during wakefulness, such as learning a reward-based auditory discrimination task, relate to noradrenergic modulation of frontal cortical circuits. We identified region-specific noradrenaline changes on the short time scale of behavioral trials during task engagement, corresponding to memory encoding, as well as on the longer time scale of task learning, corresponding to memory consolidation. During task execution, sustained elevated levels of noradrenaline were present in lateral orbitofrontal cortex (lOFC) and anterolateral motor cortex (ALM). During the first episodes of NREM sleep, after reaching the expert criterion of task proficiency, noradrenaline levels in ALM increased as compared to the NREM sleep in the pre-learning phase. Conversely, noradrenaline levels decreased during NREM sleep for lOFC and prefrontal cortex as compared to the pre-learning state. Furthermore, we identified a fraction of sleep spindles that was coupled to the noradrenaline dynamics during NREM sleep. This coupling of sleep spindles and noradrenaline was also strengthened by task learning in the medial orbitofrontal cortex and ALM. Bilateral optogenetic silencing of LC neurons with ArchT slowed task learning and decreased the coupling between sleep spindles and noradrenaline. Our results underscore the region-specific role of noradrenaline at multiple time-scales for memory encoding and consolidation.

Sleep strenghtens early neocortical traces and thalamic and striatal contributions to declarative memory recall

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Sleep benefits declarative memory via a process of offline reactivation that consolidates hippocampus dependent memory traces into neocortical networks for stable memory storage. Based on recent evidence suggesting that awake rehearsal can also lead to rapid systems consolidation, in this study we investigated how sleep influences the consolidation of rehearsal-induced early neocortical memory traces. Participants encoded and recalled object-place associations across multiple rehearsal rounds either in the morning (wake group, n=19) or in the evening (sleep group, n=20) and twelve hours later after a day of wakefulness or a night of sleep. During the task, functional brain activity was measured with fMRI. In addition to a behavioral benefit of sleep for memory retention, we observed differential changes between the groups in functional brain activity during memory recall across a network spanning the precuneus, thalamus and striatum when controlling for potentially confounding effects of time spent awake. The effect was characterized by a robust increase in activation levels from session 1 to session 2 in the sleep group, and a transient decrease during the first recall repetition of session 2 in the wake group. Upregulation of activity in the thalamus and striatum was associated with behavioral benefits. Importantly, all three regions decreased their functional connectivity with the hippocampus more strongly across sleep. Altogether, our data indicate that early neocortical memory traces undergo additional sleep-dependent memory consolidation. In addition to further promoting consolidation mechanisms within the declarative memory subsystems, sleep seems to specifically benefit the integration of early neocortical traces across different memory systems.

Mental retardation-related protease neurotrypsin regulates spinogenesis, learning, and sociability

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Neurotrypsin is a neuronal trypsin-like serine protease whose mutations cause severe mental retardation in humans. Neurotrypsin activity is controlled by neuronal activity and promotes the formation of dendritic filopodia in a process dependent on proteolytic cleavage of the proteoglycan agrin. Here, we investigated the functional importance of this mechanism ex vivo and in vivo. We report that juvenile neurotrypsin-deficient (NT-/-) mice exhibit impaired long-term potentiation induced by a protocol designed to probe the generation of new filopodia and the conversion of these filopodia into functional synapses. Behaviorally, juvenile NT-/- mice exhibit impaired contextual fear memory and have a significant deficit in sociability. Impaired sociability persisted in aged NT-/- mice, which, unlike juvenile mice, showed normal recall but impaired extinction of contextual fear memories; these mice also failed in the novel object recognition task. Morphologically, juvenile mutants showed significantly reduced spine density in the CA1 region compared to wild-type littermates (NT+/+); naïve NT-/- mice exhibited fewer thin spines/filopodia and no alterations in spine parameters following fear conditioning and extinction in contrast to NT+/+ mice. Spine loss in NT-/- mice was abrogated by injecting an adeno-associated virus expressing an NT-generated fragment of agrin, agrin-22, but not a shorter fragment, agrin-15, showing a specific effect of agrin-22 in promoting spine formation in vivo. Moreover, we demonstrate that agrin-22 coaggregates with multiple pre- and postsynaptic terminals immunopositive for vesicular glutamate transporter 1 and postsynaptic density protein PSD-95, suggesting that agrin-22 may support the clustering of excitatory synapses. Indeed, reanalysis of spine location in mice after fear conditioning and extinction revealed a paradigm-dependent modulation of spatial distribution of spines along secondary dendrites in NT+/+ but not in NT-/- mice.

Episodic memory content as feedback signals in the early visual cortex

Javier Ortiz-Tudela

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Predictive Processing models assume that predictions stem from some form of high-order representations. These representations can range from learned perceptual regularities to rich semantic memories. In this study we aimed at characterizing the nature of visual predictions by targeting episodic and semantic memories as candidate sources for content. Our participants studied images depicting objects embedded in indoor scenes; on the following day, they performed a retrieval task from partially occluded images while we recorded brain activity. Critically, we used functional retinotopy and visual field mapping to isolate brain voxels that did not receive any meaningful stimulation from the environment. Then, using Representational Similarity Analysis, we quantified the amount of contextual and mnemonic information present in the occluded portions of V1 and V2 during episodic and semantic retrievals. Our results reveal that both types of information are constituents of prediction signals but that the extent to which mnemonic content is represented in V1 and V2 depends on whether memories are retrieved through an episodic or a semantic route (but not in the object-selective cortex). Moreover, functional connectivity analyses show that the coupling between visual areas and other brain networks changed from dorsal to ventral as a function of retrieval route. These results highlight the crucial role that memory plays in informing visual predictions as a main contributor to our active perception.

Successful mnemonic discrimination is linked to decreased functional connectivity between hubs in the frontoparietal and default mode network

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Successful memory depends on the process of mnemonic discrimination to establish discrete memory representations of similar episodes. Although previous neuroimaging research has focused on the well-known role of hippocampus, less is known about how brain areas belonging to the frontoparietal (FPN) and default-mode network (DMN) interact during this process. The present study investigated the functional connectivity between the hubs of these networks during a mnemonic discrimination task. Our sample consisted of 55 young adults (age: M = 23.67 years, SD = 3.38, 61.8% female), who had to discriminate similar objects and scenes ('lures') from identically repeated items ('repeats'). Stimuli were presented in sequences of 12 items. The first six stimuli were always new images, while each of following six stimuli could be either a lure or a repeat trial. During the task, 3T functional magnetic resonance imaging data were collected (resolution 2 mm, TR = 2.2 s). The imaging data were preprocessed using the standard 'fmriprep' pipeline (MNI152 normalization) and statistically modelled using generalized psychophysiological interaction (gPPI). We performed region of interest (ROI) to-ROI analyses. During successful mnemonic discrimination (lures versus repeats contrast), we found decreased functional connectivity between the lateral prefrontal cortex (LPFC; FPN hub) and the lateral parietal cortex (DMN hub). Our results implicate a role of functional communication between DMN and FPN hubs for mnemonic discrimination during task, extending previous findings in the literature. In future studies, we will examine its relationship to behavioral mnemonic discrimination measures and how cognitive training may affect such functional communication between brain areas involved in memory.

Hippocampal subregional thinning related to tau pathology in early stages of Alzheimer's disease

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Subregions in the medial temporal lobe (MTL) are affected early by Alzheimer's disease (AD) pathology and subject to grey matter atrophy. Measuring the earliest AD-related atrophy in the hippocampus is challenging as region-of-interest (ROI) analyses of hippocampal subregional volumes collapse across voxels within anatomical subregions. PET imaging studies, however, report accumulation of tau pathology between anatomical subregions in the earliest disease stages (Berron et al., 2021) fitting reports from the neuropathological literature (Lace et al., 2019; Ravikumar et al., 2021). Thus, sensitive in vivo methods of point-wise structural measures are needed in order to detect the earliest hippocampal thinning in AD along the anterior-posterior as well as the medial-lateral hippocampal axis.

Here we analyzed data from amyloid-beta negative (Aβ-) cognitively normal (CN), Aβ+ CN individuals and Aβ+ patients with mild cognitive impairment (MCI) from the BioFINDER-2 study, who underwent 7 Tesla T2-weighted structural magnetic resonance imaging, tau positron emission tomography imaging (using 18F-RO-948) and cognitive assessments. First, we segmented hippocampal subfields and extrahippocampal subregions. Second, we calculated point-wise hippocampal thickness estimates (Diers et al.) of hippocampal subfields subiculum, cornu ammonis (CA)1, CA2 and CA3 on the level of the

hippocampal body. Thirdly, we extracted local tau-PET SUVR from Area 35 (A35), entorhinal cortex and amygdala. Finally, we assessed relationships between hippocampal local thickness and tau accumulation as well as cognitive performance.

Our analyses revealed earliest hippocampal thinning associated with tau accumulation in an area spanning the boundary of subiculum and CA1 at the level of the anterior hippocampal body. Aβ+ MCI patients showed more posterior thinning in comparison to Aβ- CU participants. Median thickness in an ROI comprising vertices with A35 tau-related thinning (A35-TauThinning-ROI) was significantly lower in MCI Aβ+ and tended to be lower in CU Aβ+ compared to CU Aβ-. Higher median thickness in the hippocampal A35-TauThinning-ROI, but not whole CA1 nor subiculum thickness, was associated with better 10-Word-Delayed-Recall and higher PACC scores.

Our results suggest that tau-related thinning of hippocampal subregions can be observed already in early disease stages. Tau-related point-wise thickness measures were more sensitive compared to volumetric measures of anatomical subregions.

Invited Talks
Day 1

Memories and Mental Simulation: Multiplexing the Past, Present and Future

Loren Frank

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As an animal explores an environment it creates memories of its experiences. These memories are useful because they can be retrieved to help animal make to predictions about future events. Adaptive behavior engages both memory formation and memory-based prediction, but how these two functions are expressed and coordinated remains unclear. In this talk I will discuss work from our laboratory that is helping us understand the structure of representations of past, present, and potential future in the hippocampus and how these representations are coordinated with activity elsewhere in the brain.

Multiple systems for declarative memory

Steffen Gais

Institute of Medical Psychology and Behavioural Neurobiology, University of Tübingen, Germany

The classical view of declarative memory sees the hippocampus and the prefrontal cortex as complementary storage systems, which are thought to differ predominantly in their temporal dynamics during encoding and consolidation of memories. Recent evidence, especially from human functional imaging studies, has raised some questions regarding the specific contribution of the hippocampus to declarative memory and added a number of new players to the memory game, especially areas in the parietal cortex. These regions have been found to contribute early and enduringly to memory recall, and some experimental evidence and theoretical considerations speak for a role in the actual storage of the memory engram. I will discuss potential implications of these recent developments for our view on memory systems. A topic of particular interest is whether memory systems are involved consecutively as proposed by the systems consolidation idea or whether encoding occurs in parallel in different systems. Another central question is whether there are redundant systems for declarative memory that store the same type of information or whether different systems always store distinct aspects of a memory.

Excitability mediates allocation of pre-configured ensembles to hippocampal engram supporting contextual conditioned fear in mice

Sheena Josselyn

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Engrams are sparse groups of neurons that store memories. Although much progress has been made on understanding how engrams are formed using a variety of molecular and optogenetic manipulations, little is understood about how engrams are formed endogenously. Using in vivo calcium imaging, we examined activity dynamics of mouse CA1 hippocampal neurons before, during, and after contextual fear conditioning. Engram neurons (high activity during memory recall) were more active than Non-Engram neurons during training, and 3h (but not 24h) in homecage before training, indicating neurons with higher pre-training excitability tended to be allocated to the engram. We also observed stable pre-configured functionally connected sub-ensembles of neurons. Sub-ensembles containing Engram neurons pre-training were preferentially allocated and training further stabilized their pattern of functional connectivity. The activity patterns of Engram sub-ensembles during training were recapitulated during testing, in a context-dependent manner. These findings indicate neuronal excitability in the hours before training and pre-configured functional connectivity mediate allocation to an engram and that training selectively stabilizes the functional connectivity among engram ensembles to support a stable, context-specific memory.

Invited Talks
Day 2

The entorhinal cortex as integrative gatekeeper in the hippocampal memory system

Menno Witter

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Laboratory of Systems Neuroscience & Department of Developmental Neuroscience, Graduate School of Medicine, Tohoku University, Sendai, Japan,

There are several fundamental, almost canonical architectural features of the entorhinal cortex (EC) that need re-appraisal. In my presentation, I aim to assess the concept of parallel pathways mediated by lateral and medial domains of EC, with the hippocampus acting as the site of convergence of these parallel pathways. In contrast, I will argue that they might be less parallel than currently perceived based on connectional data supporting extensive interactions at the level of EC. Though the functional relevance of this intrinsic entorhinal convergence is as yet unclear, two principles are emerging. First, that lateral EC is best considered a high-order multimodal cortex, appropriately positioned to integrate sensory representations of the external world, modulated by information originating from amygdala, orbitofrontal, medial prefrontal and insular cortex. Second, that allocentric spatial information from medial EC might be mixed in and that this controls transmission from lateral EC to different domains in the hippocampus.
I will also revisit the concept of layer V, acting as the main output layer initiating two output loops, one sending hippocampally processed information to telencephalic cortical and subcortical structures, and another, feeding into a recurrent input loop to the hippocampus via neurons in layers II and III. This circuit is considered to be stable along the dorsoventral extent of the entorhinal-hippocampal system. Although true for lateral EC, I will show that in dorsal parts of medial EC, ventral hippocampal output is able to directly and selectively influence the output to telencephalic structures, but less so the second recurrent loop.

'Spatial' and 'non-spatial' medial temporal lobe memory subnetworks: information processing and coordination

Magdalena Sauvage

Leibniz Institute for Neurobiology (LIN), Magdeburg, Germany

The spatial and non-spatial information forming a memory has long been thought to be funneled to the medial temporal lobe (MTL) by distinct perceptual streams, to be ultimately integrated at the level of the hippocampus. Since a decade, we have however accumulated evidence that spatial and non-spatial information might remain segregated along the proximodistal axis of the hippocampus, especially when only one of the dimensions of the memory is salient (Nakamura et al, J. Neurosc. 2013; Flasbeck et al, 2018; Beer and Vavra, Plos Biol. 2018). This led us to suggest the existence of MTL subnetworks preferentially processing spatial or non-spatial information: a 'spatial' subnetwork including the MEC, proximal CA1, distal CA3 and the enclosed blade of the dentate gyrus and a 'non-spatial' subnetwork including the LEC, distal CA1, proximal CA3 and the exposed blade of the dentate gyrus (Nakamura et al, J. Neurosc. 2013). In this talk, I will present studies from our laboratory that leverage rat versions of human memory tasks, optogenetics and single cell/LFP electrophysiological recordings to further characterize these subnetworks and to investigate the coordination of the activity of these areas as memory is recalled.

Two hippocampal axes: a proximodistal and radial perspective of entorhinal-hippocampal function

Liset Menendez de la Prida

Instituto Cajal – CSIC, Madrid, Spain

The temporal lobe is crucial for navigation and memory. Yet, understanding how hippocampal representations emerge from basic microcircuits remains elusive. In this talk, I will review recent data on the role of entorhinal inputs which activate specific types of hippocampal neurons by direct and indirect pathways. We will discuss how an entorhinal dialogue with a diversity of hippocampal cells provides substrates for a wealth of hippocampal representations.

Mechanisms and consequences of altered entorhinal/hippocampal coding in human aging

Thomas Wolbers

Deutsches Zentrum für Neurodegenerative Erkrankungen (DZNE), Magdeburg, Germany

While decades of research into cognitive aging have focused on functions such as memory and attention, spatial navigation has been understudied. This is surprising because key structures of the brain's navigation circuit are particularly vulnerable to the deleterious consequences of aging. In addition, deficits with spatial orientation are often among the first noticeable symptoms in patients with Alzheimer's Disease.
In this talk, I will discuss recent studies that have begun to elucidate age-related changes in navigational processing, using novel paradigms that target specific spatial computations. Importantly, these studies also offer novel insights into general mechanisms of brain ageing that could affect processes beyond the spatial domain. Finally, I will conclude with a discussion on how navigational indicators could aid early detection of neuropathological conditions and be sensitive markers of treatment-related improvement or disease-related decline.

Medial Entorhinal Cortex Commissural Input Regulates the Activity of Spatially Tuned Cells and Episodic Memory

Hannah Monyer

Heidelberg University, Germany
Deutsches Krebsforschungszentrum (DKFZ), Heidelberg, Germany

Extensive interhemispheric projections connect many homotopic brain regions, including the hippocampal formation, but little is known as to how information transfer affects functions supported by the target area. I will present a recent study in which we asked whether commissural projections connecting the medial entorhinal cortices (MEC) contribute to spatial coding and memory. We demonstrate that input from the contralateral MEC targets all major cell types in the superficial MEC modulating their firing rate. Notably, a subpopulation of spatially tuned cells exhibits remapping in the presence or upon translocation of an object. Commensurate with this finding are behavioral results that, upon inhibiting commissural projections selectively, revealed their contribution to episodic memory retrieval.

Subcortical control of hippocampal activity and behaviour

Stefan Remy

Leibniz Institute for Neurobiology (LIN), Magdeburg, Germany

Before the onset of locomotion, the hippocampus undergoes a transition into an activity-state specialized for the processing of spatially related input. This brain-state transition is associated with increased firing rates of hippocampal pyramidal neurons and the occurrence of theta oscillations, which both correlate with locomotion velocity. Subcortical circuits modulate and select the appropriate behavioral response, including locomotion, based on the external demands and the internal state of the animal. Here, I will present comprehensive data on how a basal forebrain region, the medial septum, contributes to the control of hippocampal theta oscillations, hippocampal neuronal activity and behavioural selection with a focus on the circuitry underlying the control of the onset and vigour of locomotor-related behaviours.

Invited Talks
Day 3

The importance of setting boundaries: How cortico-hippocampal interactions at event boundaries support memory and prediction

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In neuroscience, episodic memory is depicted as a process of activating "engrams" in the hippocampus that provide a static and faithful record of the past. This view stems from the longstanding tradition going back to the work of Ebbinghaus (1885), and subsequent work in the "behaviorist" tradition over the 20th century that characterized memory in terms of simple stimulus-response associations. In reality, a half century of research has shown that human memory is dynamic and constructive, such that we do not replay the past, but rather, we rely on prior knowledge about events, along with a small amount of retrieved information to imagine how the past could have been. Drawing from this work, my colleagues and I have embraced a radical alternative to the dominant view in systems neuroscience: Rather than recording every moment of experience, the brain might reconstruct past events from information gathered at moments of high uncertainty or prediction error, or "event boundaries". Our data are consistent with the view that the hippocampus and neocortex serve as complementary learning systems, with the former playing a role in recording snapshots of cortical activity at event boundaries, and the latter involved in using prior knowledge to understand and reconstruct past events. Beyond episodic memory, this division of labor might be computationally optimal for prediction of upcoming experiences, decision-making, and goal directed behavior such as spatial navigation.

Episodic memory in preclinical and prodromal Alzheimer's disease

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Brain regions that support episodic memory functions belong to those that are preferentially targeted by tau and amyloid pathology in Alzheimer's disease. Consequently, episodic memory impairment is an early clinical sign of Alzheimer's disease. I will discuss how amyloid and tau-pathology impair episodic memory in preclinical and prodromal phases of Alzheimer's disease. I will touch upon mechanisms of brain reserve and cognitive reserve that alleviate the impact of pathology on episodic memory. Finally, I will provide an outlook on open issues and future research directions in this area.

Dentate Network Computations for Memory and Decisions

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While computational models and experimental evidence point to the hippocampal dentate gyrus (DG)-CA3 network as the key hippocampal circuit for memory-related computations such as pattern separation and pattern completion, the physiology of the DG-CA3 network is vastly understudied compared to the CA1 network. We have recently described a novel role of dentate cells in organizing CA3 neuronal activity patterns. In a dentate-dependent working memory task with multiple reward locations, the majority of active DG cells were not found to be active during exploration as typical place cells, but were selectively active when rewards were consumed. During this phase, DG activity was necessary for biasing CA3 activity towards reactivating neurons during sharp wave ripples that point to sites with future available reward. I will present additional data in support of a necessary role for the DG in organizing CA3 activity across different brain states. By observing the selective effect of removing either medial entorhinal cortex or DG inputs to the downstream CA3 network during working memory, we found that during theta states the DG preferentially contributes to spiking during the late phase of the theta cycle when neural activity is predictive of future behavior. Moreover, DG input, but not MEC input, is required for maintaining the temporal order of CA3 cell sequences. Our results demonstrate a unique role for the DG in support of sequence coding in the downstream CA3 network across brain states.

Mechanism of working memory in individual hippocampal CA1 cells

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The hippocampus has been known to contribute to working memory and temporal bridging tasks. Persistent firing is believed to support working memory and temporal bridging tasks by retaining necessary information during these tasks. However, it still remains unclear which molecular mechanisms are supporting this persistent firing, and whether the same mechanisms support working memory and persistent firing in vivo. Here, I will demonstrate that transient receptor potential canonical (TRPC) channels are necessary for persistent firing in individual neurons in the hippocampus, and a deletion of these channels in vivo impairs working memory performance in mice. In addition, in vivo electrophysiological recordings indicate altered activity both in LFP and single cell levels in these mice. These results suggest that hippocampal TRPC channels control persistent firing in individual cells and are necessary for working memory.

Persistent Firing in LEC III and DG in Aging and Young During Temporal Associative Learning

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The role of persistent firing in different neurons within the interconnected temporal lobe sites, lateral entorhinal cortex (LEC III) and dentate gyrus of the hippocampus (DG), that are involved in temporal associative learning will be discussed. First, persistent firing was evoked in vitro from LEC III neurons from young and aged rats that were behaviorally naïve or trace eyeblink conditioned. Persistent firing ability of neurons from behaviorally naïve aged rats was lower compared to neurons from young naïve rats. Neurons from learning impaired aged animals also exhibited reduced persistent firing capacity, contributing to aging-related learning impairments. Successful acquisition of the trace eyeblink task, however, was associated with increased persistent firing ability in both young and aged rats. These changes in persistent firing ability are due to changes to the afterdepolarization, which is modulated by the postburst afterhyperpolarization. How these alterations in persistent firing capacity in LEC III neurons may support temporal associative learning via their interactions with CA1 hippocampus neurons will be discussed. Second, the dentate gyrus serves as the first site for information processing in the hippocampal trisynaptic circuit and is an important structure for the formation of associative memories. We investigated the functional role of granule cells, mossy cells and interneurons in dentate gyrus during trace eyeblink conditioning by conducting in vivo single-neuron recording in conjunction with physiological determination of cell types in head fixed mice. In the conditioned group, granule cells tended to show an increase in firing rate during conditioned stimulus presentation while mossy cells showed a decrease in firing rate during the trace interval and the unconditioned stimulus. Interestingly, populations of interneurons demonstrated learning-related increases and decreases in activity that began at onset of the conditioned stimulus and persisted through the trace interval. Our recent findings from two adjacent cortical sites strongly suggest that persistent firing is a key cellular mechanism recruited for successful temporal lobe-dependent temporal associative learning.

Loss of functional heterogeneity along the CA3 transverse axis in aging

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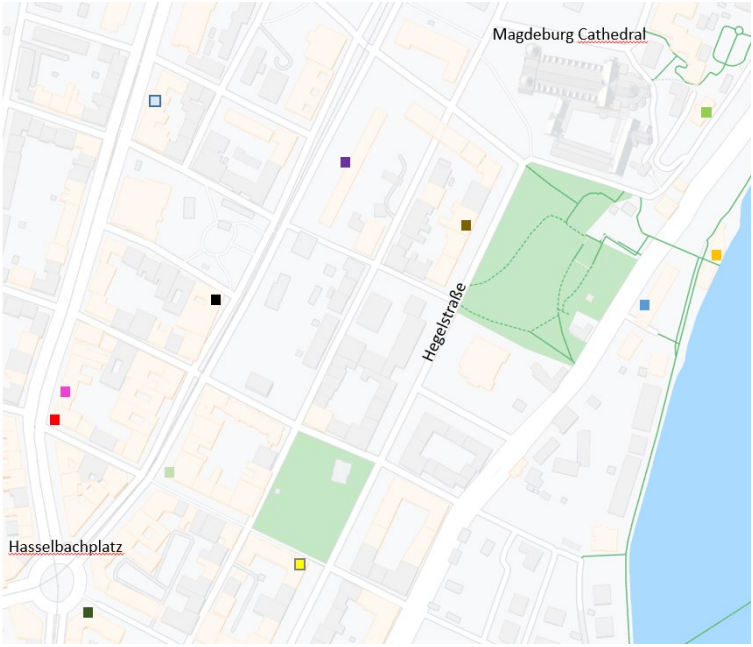
Age-related deficits in pattern separation have been postulated to bias the output of hippocampal memory processing toward pattern completion, which can cause deficits in accurate memory retrieval. While the CA3 region of the hippocampus is often conceptualized as a homogeneous network involved in pattern completion, growing evidence demonstrates a functional gradient in CA3 along the transverse axis, as pattern-separated outputs (dominant in the more proximal CA3) transition to pattern-completed outputs (dominant in the more distal CA3). We examined the neural representations along the CA3 transverse axis in young (Y), aged memory-unimpaired (AU), and aged memory-impaired (AI) rats when different changes were made to the environment. Functional heterogeneity in CA3 was observed in Y and AU rats when the environmental similarity was high (altered cues or altered environment shapes in the same room), with more orthogonalized representations in proximal CA3 than in distal CA3. In contrast, AI rats showed reduced orthogonalization in proximal CA3 but showed normal (i.e., generalized) representations in distal CA3, with little evidence of a functional gradient. Under experimental conditions when the environmental similarity was low (different rooms), representations in proximal and distal CA3 remapped in all rats, showing that CA3 of AI rats is capable to encoding distinctive representations for inputs with greater dissimilarity. These experiments support the hypotheses that the aged-related bias towards pattern completion is due to the loss in AI rats of the normal transition from pattern separation to pattern completion along the CA3 transverse axis.

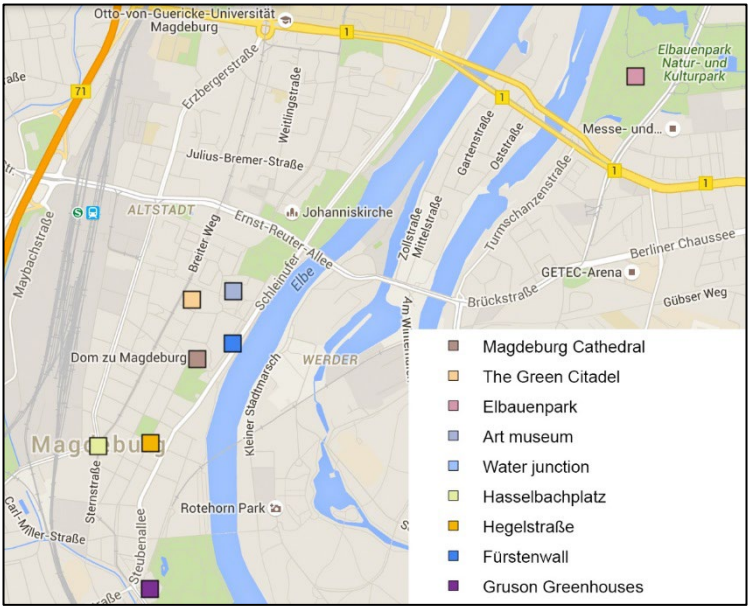
Recreational Information

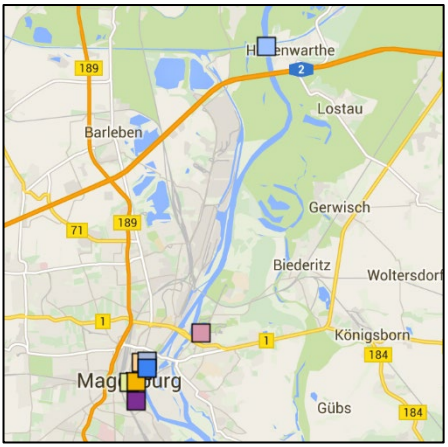
Restaurants



Berner & Brown Tapas Bar	€€	Restaurant Balkan	€€
Toro Grosso	€€€	Indian Palace	€€
Culinaria	€€€	Thai Sawadee Restaurant	€€
Sakura	€€	Restaurant Kroatien	€€
Kazoku Izakaya	€€	BOTANICA (vegan)	€€
Sen Viet BBQ & Soup	€€	HOFLIEFERANT	€€

Sightseeing





The water junction cannot be reached via public transport. Taxi Magdeburg: +49 391 737373

The Green Citadel of Magdeburg

One of Magdeburg's most eye-catching attractions for visitors is also one of the last architectural masterpieces designed by the artist Friedensreich Hundert-wasser. The Hundertwasser Building is located among a mixture of Baroque facades and examples of modern design.

Magdeburg Cathedral

Magdeburg Cathedral is the first Gothic-style cathedral to be constructed on German soil, one of the largest church buildings in Germany and the most famous attraction in Magdeburg, the capital city of the federal state of Saxony-Anhalt.

Art Museum in the Monastery of Our Lady

The Art Museum in the Monastery of Our Lady is the most important venue for contemporary art and sculpture in the German Land of Saxony-Anhalt and is one of the most popular tourist attractions in the region.

Fürstenwall

The Fürstenwall area dates back to the Middle Ages and contains city fortifications facing the river Elbe and the two preserved fortified towers. Built in 1725, this was the first public promenade in Germany. The adjacent Möllenvogteigarten is the oldest preserved garden design in the city of Magdeburg.

Hegelstraße

The Hegelstraße street begins at the Cathedral and runs in a southerly direction. The popular boulevard was built between 1880 and 1920, during the Gründerzeit era, and is lined with magnificent representative buildings.

Hasselbachplatz

At Hasselbachplatz, which is named after a former major of Magdeburg (1809-1882), you can marvel at the city's most magnificent Gründerzeit-style facades. This district is home to many pubs, bars and restaurants and is well worth a visit, especially in the evening.

Gruson Greenhouses

The Gruson Greenhouses are a traditional botanical garden featuring the exotic collection of plants. The facility preserves and continues the botanical legacy of Magdeburg's industrialist and plant collector Hermann Gruson (1821-1895).

The Elbauenpark including Millennium Tower

With its unique Millennium Tower, the world's tallest wooden construction of its kind, the Elbauenpark is well worth a visit 365 days a year. The Millenium tower is hosting interactive exhibitions of 6000 years of evolution of science and technology while the park itself offers themed gardens, a butterfly house, a deer enclosure and a climbing park

Waterway Junction

The water-saving lock Rothensee and the longest canal bridge in Europe (918 m) which spans the river Elbe, the double ship lift Hohenwarthe and the connecting canals are all part of a gigantic building project to connect the waterways of Hanover, Magdeburg and Berlin.

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