

Local Organizer

Prof. M. Sauvage, Leibniz-Institute for Neurobiology/ OvGU,
Functional Architecture of Memory Dept., Germany

Sponsors

The DFG logo is the text 'DFG' in a large, bold, blue, sans-serif font.

LIN

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Functional Architecture of Memory Conference

May 25th – 27th 2016

General Information

Key Information

1. Way to the conference centre (see map page 9)



Address:

Leibniz Institute for Neurobiology (LIN)
Center for Learning and Memory
Research
Ebbinghaussaal
Brenneckestr. 6
39118 Magdeburg

By car:

Coming from Berlin or Hannover via A2 depart at 'Magdeburg-Zentrum' and follow the city highway (Magdeburger Ring) to exit 'Wiener Straße' (approx. 12 km). Turn right 3 times and follow signage "Uniklinik Magdeburg". Enter the campus of the University hospital and turn left at the ZENIT building.

Coming from Halle/Leipzig via A14 depart at 'Sudenburg', follow signage Magdeburg-Zentrum on the city highway (Magdeburger Ring) to exit Fermersleber Weg (approx. 7 km). Turn right twice, follow signage "Uniklinik Magdeburg". Enter the campus of the University hospital and turn left at the ZENIT building.

By public transport:

From Magdeburg station "Hauptbahnhof" (main entrance) take the tram Line 6 (direction: "Leipziger Chaussee") to the stop "Universitätsklinikum" (approx. 10 min) or "Brenneckestraße" (approx. 15 min).

From the city center take the tram Line 9 (direction: "Reform") to the stop "Universitätsklinikum" (approx. 10 min) or "Brenneckestraße" (approx. 15 min).

From the tram stop "Brenneckestraße" turn right into Brenneckestraße and after approx. 400m the yellow-brown institute's building appears on the right (see map on page 9).

If you miss the transfer to the restaurant, you can go by tram (Line 6) from the stop “Brenneckestraße” or “Universitätsklinikum” to the 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 “Die Kirche”.

Alternatively, you can call a cab (0049 391 73737).

In case that you miss your transfer from the restaurant, walk along the main road from “Die Kirche” to the town entrance of Magdeburg and use the tram (Line 6). This goes directly to the town center if you need to get off for Motel One (use the stop “Allee Center” and walk up Breiter Weg and take a left after the Grüne Zitadelle Building, then go straight towards Motel One). If you wish to go back to the LIN, keep going on tram line 6 until “Universitätsklinikum” or “Brenneckestraße” (see map next page).

No specific events are organized for Wednesday 25th or Friday 27th but speakers and participants are encouraged to reconvene for drinks at Hasselbachplatz at “The Lion” on the evening at 21:00. The meeting point is in front of the pub at Keplerstraße 7. Wearing your badges would help finding each other.

For participants, our tips for dinner on those two days:

Please refer to the map in the “Recreational Info” chapter of this booklet (page 46) to find a choice of restaurants you might like to visit.



Functional Architecture of Memory Conference

May 25th – 27th 2016

Program



Time	Wednesday May 25th	Time	Thursday May 26th	Time	Friday May 27th
09:30 - 10:10	"Welcome" M. Sauvage E. Gundelfinger (Head of the LIN) Data Blitz Session	09:30 - 10:10	Axel Mecklinger (Univ. Saarland, Germany) ERP evidence for multiple familiarity signals in the word frequency mirror effect	09:30 - 10:10	Norbert Fortin (UC Irvine, USA) Hippocampal neural mechanisms underlying the memory for sequences of events
10:10 - 10:50	Data Blitz Session	10:10 - 10:50	Serge Leach (CNRS & Univ. Paris-Sud, France) Neural substrate of recollection of past occasional events in a number-inspired episodic memory task in rats	10:10 - 10:50	John Distcheroff (Northwestern University, USA) Differential responsivity of neurons in perirhinal cortex, basal entorhinal cortex and dentate gyrus during time-bridging learning
10:50 - 11:20	Coffee	10:50 - 11:20	Coffee	10:50 - 11:20	Coffee
11:20 - 12:00	Data Blitz Session	11:20 - 12:00	Michael Yassa (UC Irvine, USA) Establishing hippocampal-neocortical traces for discrimination and recognition memory	11:20 - 12:00	Motokazu Yoshida (DZNE/JIN, Germany) Cellular mechanism for acute memory reactivation in the hippocampus
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	Erinac Düzel (DZNE, Germany) Encoding and retrieval of hippocampal memory traces: Studies in the aged human brain and in individuals with subjective memory complaints	14:00 - 14:40	Liset Menendez de la Prida (IC - CSIC, Spain) On the role of temporal coordination of hippocampal-entorhinal microcircuits in episodic-like memory deficits	14:00 - 14:40	Inah Lee (Seoul Univ., South Korea) Delineating functional circuits for remembering visual scenes and objects
14:40 - 15:20	Magdalenä Sauvage (LIN/ OVGU, Germany) Emergence and fate of the memory trace	14:40 - 15:20	James Knierim (Johns Hopkins Univ., USA) Functional dissociations along the CA3-CA2-CA1 transverse axis	14:40 - 15:20	Rebecca Burwell (Brown Univ., USA) Perirhinal and posthinal interactions in the representation of context
15:20 - 15:40	Coffee	15:20 - 15:40	Coffee	15:20 - 15:40	Coffee
15:40 - 16:20	Michael D. Rugg (UT Dallas, USA) Hippocampal-neocortical interactions supporting episodic retrieval	15:40 - 16:20	Raymond Kesner (Utah Univ., USA) Role of the dorsal dentate gyrus in processing spatial and spatial context information as well as conjunctive encoding and the role of the ventral dentate gyrus in processing anxiety, olfactory and reward value pattern separation	15:40 - 16:20	Elizabeth Buffalo (Univ. of Washington, USA) Toward an understanding of the hippocampal cognitive map
16:20 - 17:00	Open Discussion - Moderator M. Rugg	16:20 - 17:00	Open Discussion - Moderator M. Yassa	16:20 - 17:00	Open Discussion - Moderator N. Fortin



Blitz Sessions – Wednesday morning, May 25th
 see page 14 for invited talks in the afternoon

Time	Wednesday May 25 th	Time	Wednesday May 25 th
09:30 - 09:45	"Welcome" M. Sawag, E. Gundelfinger (lead of the LIN)	10:50 - 11:20	Coffee
09:45 - 10:50	Data Blitz Session (5 minute talk and 2 minute discussion afterwards)	11:20 - 12:00	Data Blitz Session (5 minute talk and 2 minute discussion afterwards)
	Marion Inostroza (Univ. of Tübingen) Onology of object-place recognition memory consolidation in rats		Caroline Chwiesko (Ruhr University Bochum) Exposure to familiar and novel stimuli yields hippocampal BOLD responses for opposite contrasts depending on the duration of the habituation to the stimuli; a fMRI study in awake rats
	Monika Schönauer (University of Tübingen) Hippocampal dependence in declarative memory		Lea Himmer (University of Tübingen) Sleep accelerates memory systems consolidation
	Erika Attwucher (LIN Magdeburg) Effects of the selective inactivation of CA3 and CA2 on familiarity and the selective involvement of the deep layers of the perirhinal and lateral entorhinal cortices		Guilherme M. Gomes (LIN Magdeburg) Hippocampus-dependent cognitive function is impaired in Jacob mouse mutants
	David Berron (OVG Univ. & DZNE Magdeburg) Strong evidence for pattern separation in human dentate gyrus		Klaus G. Reymann (LIN Magdeburg) Dopamine agonists rescue amyloid β -induced LTP impairment by Src-family tyrosine kinases
	Svenja Brodt (University of Tübingen) Rapid and hippocampus-independent memory formation in the perirhinal cortex		
	Catherine M. Sweeney-Reed (OVG University Magdeburg) Pre-stimulus thalamic theta power predicts human memory formation		

Time	Wednesday May 25th
09:30 - 10:10	<p><i>"Welcome" M. Sauvage (09:30 - 09:45)</i></p> <p><i>E. Gundelfinger (Head of the LIN)</i></p> <p><i>Data Blitz Session (09:45 - 10:10)</i></p>
10:10 - 10:50	<i>Data Blitz Session</i>
10:50 - 11:20	<i>Coffee</i>
11:20 - 12:00	<i>Data Blitz Session</i>
12:00 - 13:00	<i>Lunch Break</i>
13:00 - 13:50	<i>Students/Speakers round table</i>
14:00 - 14:40	<p><i>Emrah Düzel (DZNE, Germany)</i></p> <p>Functional anatomy and plasticity of hippocampal memory circuits: Studies in the aging human brain and in individuals with subjective memory complaints</p>
14:40 - 15:20	<p><i>Magdalena Sauvage (LIN/ OvGU, Germany)</i></p> <p>Emergence and fate of the memory trace</p>
15:20 - 15:40	<i>Coffee</i>
15:40 - 16:20	<p><i>Michael D. Rugg (UT Dallas, USA)</i></p> <p>Hippocampal-cortical interactions supporting episodic retrieval</p>
16:20 - 17:00	<i>Open Discussion - Moderator M. Rugg</i>

Time	Thursday May 26th
09:30 - 10:10	Axel Mecklinger (Univ. Saarland, Germany) ERP evidence for multiple familiarity signals in the word frequency mirror effect
10:10 - 10:50	Serge Laroche (CNRS & Univ. Paris-Sud, France) Neural substrate of recollection of past occasional events in a human-inspired episodic memory task in rats
10:50 - 11:20	<i>Coffee</i>
11:20 - 12:00	Michael Yassa (UC Irvine, USA) Establishing hippocampal-neocortical traces for discrimination and recognition memory
12:00 - 13:00	<i>Lunch Break</i>
13:00 - 13:50	<i>Students/Speakers round table</i>
14:00 - 14:40	Liset Menendez de la Prida (IC - CSIC, Spain) On the role of temporal coordination of hippocampal-entorhinal microcircuits in episodic-like memory deficits
14:40 - 15:20	James Knierim (Johns Hopkins Univ., USA) Functional dissociations along the CA3-CA2-CA1 transverse axis
15:20 - 15:40	<i>Coffee</i>
15:40 - 16:20	Raymond Kesner (Utah Univ., USA) Role of the dorsal dentate gyrus in processing spatial and spatial context information as well as conjunctive encoding and the role of the ventral dentate gyrus in processing anxiety, olfactory and reward value pattern separation
16:20 - 17:00	<i>Open Discussion- Moderator M. Yassa</i>

Time	Friday May 27th
09:30 - 10:10	<p>Norbert Fortin (UC Irvine, USA) Hippocampal neural mechanisms underlying the memory for sequences of events</p>
10:10 - 10:50	<p>John Disterhoft (Northwestern University, USA) Differential responsivity of neurons in perirhinal cortex, lateral entorhinal cortex and dentate gyrus during time-bridging learning</p>
10:50 - 11:20	<p><i>Coffee</i></p>
11:20 - 12:00	<p>Motoharu Yoshida (DZNE/LIN, Germany) Cellular mechanism for active memory retention in the hippocampus</p>
12:00 - 13:00	<p><i>Lunch Break</i></p>
13:00 - 13:50	<p><i>Students/Speakers round table</i></p>
14:00 - 14:40	<p>Inah Lee (Seoul Univ., South Korea) Delineating functional circuits for remembering visual scenes and objects</p>
14:40 - 15:20	<p>Rebecca Burwell (Brown Univ., USA) Perirhinal and postrhinal interactions in the representation of context</p>
15:20 - 15:40	<p><i>Coffee</i></p>
15:40 - 16:20	<p>Elizabeth Buffalo (Univ. of Washington, USA) Towards an Understanding of the Hippocampal Cognitive Map</p>
16:20 - 17:00	<p><i>Open Discussion- Moderator N. Fortin</i></p>



Functional Architecture of Memory Conference

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Data Blitz Session

Ontogeny of object-place recognition memory consolidation in rats**Marion Inostroza^{1,2} and Jan Born¹**

¹ *Institute of Medical Psychology and Behavioral Neurobiology and Center for Integrative Neuroscience, University of Tübingen, Tübingen, Germany.*

² *Departamento de Psicología, Universidad de Chile, Santiago, Chile.*

Sleep has been identified as a state that optimizes the consolidation of newly acquired memory. Our previous studies in adult rats showed that a short period of sleep after encoding is critical for maintaining episodic-like memory and spatial memory (Inostroza et al., 2013); however, little is known about the role of sleep in episodic memory ontogeny and its components. It has been suggested that object-place recognition (OPR, “where”) emerges between PD21 and PD26 (Westbrook et al., 2014). We investigated: 1) the time point when the consolidation of the “where” component of the episodic memory emerges and, 2) the contribution of the learning experience to this emergence. We tested two groups of rats on postnatal day (PD) 18 and PD25 in the OPR task. We used a 3-hour retention interval between encoding and retrieval to test for memory consolidation. During this interval, the rats were undisturbed to ensure regular morning sleep. Later we performed three OPR re-tests at successive time-points for each of the two groups (PD20, PD22, PD24 and PD27, PD29, PD31 respectively). Neither PD18 nor PD25 groups expressed memory for the spatial location after the 3-hour sleep retention interval. However, during the 3rd re-test at PD31 we found a significant preference for the displaced object, suggesting the delayed emergence of OPR memory that had been previously consolidated. Ongoing experiments aim to test the role of sleep in OPR memory consolidation.

Hippocampal dependence in declarative memory

Monika Schönauer

Institute of Medical Psychology and Behavioral Neurobiology, University of Tübingen

The dual-storage model of declarative memory describes the hippocampus as a fast-learning system and the neocortex as one that incorporates new information only gradually. The slow process during which memories become independent of the hippocampus and are integrated into neocortical memory networks is called systems memory consolidation. New evidence suggests that this process does not necessarily require months or years to complete as previously assumed, but can occur within days if the new memory can be integrated with existing schemas. It is still unclear whether systems consolidation occurs for every type of declarative memory, and under which circumstances rapid neocortical integration takes place. Using an associative memory paradigm, we compared brain activity during recall of word lists that had been associated beforehand either with autobiographical events, with spatial positions, or with other list words. After a brief interval, word lists were recalled and brain activity recorded with fMRI. Astonishingly, the hippocampus was only active when words had been associated with detailed, scenic autobiographical memories. For words that had been associated to existing semantic schemas like other words or locations on a well-known path, recall did not activate the hippocampus but only neocortical areas. Together, our data support the idea that a main role of the hippocampus is to process detailed, scenic long-term memories. We show that under specific conditions, e.g. when words are associated to pre-existing semantic schemas, the neocortex acts as a fast-learning system and rapid integration into existing neocortical memory networks occurs.

Cellular evidence for the lack of contribution of CA1 and CA3 to familiarity and the selective involvement of the deep layers of the perirhinal and lateral entorhinal cortices

Erika Atucha^{1,2,3}, Artem Karew¹, Takashi Kitsukawa⁴, Magdalena Sauvage^{1,2,3}

¹*Mercator Research Group1, Functional Architecture of Memory unit, Ruhr-University Bochum, Germany*

²*Otto von Guericke University, Medical Faculty, Functional Neuroplasticity, Magdeburg, Germany*

³*Leibniz-Institute for Neurobiology, Functional Architecture of Memory Dpt, Magdeburg, Germany*

⁴*KOKORO-biology group, Osaka University, Osaka, Japan.*

Recognition memory relies on two memory retrieval processes, recollection and familiarity. Recollection reflects the retrieval of specific information about events whereas familiarity is described as a vague feeling of déjà vu. While it is well-accepted that the hippocampus supports recollection, it is still unclear whether it also supports familiarity or whether the parahippocampal region, especially the perirhinal (PER) and lateral entorhinal cortices (LEC), does. One of the reasons why this remains elusive is the low accessibility, in humans, to imaging techniques with spatial resolution high enough to dissociate the source of activity among adjacent brain regions. Importantly, studies in rodents have brought evidence for a functional segregation of the hippocampal subfields CA1 and CA3 along their proximodistal and longitudinal axes as well as between the PER and the LEC and their deep and superficial cell layers, but their contribution to familiarity has not been studied yet. Here, we combined an odor memory task yielding judgements based on familiarity with high resolution molecular imaging involving the detection of the immediate early gene *Arc* and mapped cellular activity in these areas. We report that even the ventral part of CA1 and CA3, thought to process the most odor stimuli, failed to be recruited while the deep layers of the PER and the LEC, believed to contribute to more cognitive processes than their superficial layers, were. These data provide robust cellular evidence for the lack of contribution of the hippocampus to familiarity and for the engagement of the parahippocampal region during this process.

Strong evidence for pattern separation in human dentate gyrus

David Berron^{1,2}, Hartmut Schütze¹, Anne Maass^{1,2}, Arturo Cardenas-Blanco², Hugo J. Kuijff³, Dharshan Kumaran⁴, Emrah Düzel^{1,2,4}

¹ *Institute of Cognitive Neurology and Dementia Research, Otto-von-Guericke-University Magdeburg, 39120 Magdeburg, Germany*

² *German Center for Neurodegenerative Diseases (DZNE), Site Magdeburg, 39120 Magdeburg, Germany*

³ *Image Sciences Institute, University Medical Center Utrecht, 3584 CX Utrecht, the Netherlands*

⁴ *University College London, Institute of Cognitive Neuroscience, London, WC1N 3AR, United Kingdom*

The hippocampus is proposed to be critical to distinguishing between similar experiences by performing pattern separation computations that create orthogonalized representations for related episodes. Previous neuroimaging studies have provided indirect evidence that the dentate gyrus and CA3 hippocampal subregions support pattern separation, by inferring the nature of underlying representations from the observation of novelty signals. Here, we use ultra high-resolution functional magnetic resonance imaging (fMRI) at 7 Tesla and multivariate pattern analysis (MVPA) to provide compelling evidence that the dentate gyrus (DG) subregion specifically sustains representations of similar scenes that are less overlapping than in other hippocampal (e.g. CA3) and MTL regions (e.g. entorhinal cortex). Thereby our study provides a mechanistic link between novelty signals and the underlying representations and demonstrates strong evidence that the human DG performs pattern separation.

Rapid and hippocampus-independent memory formation in the parietal cortex

Svenja Brodt

*Institute of Medical Psychology and Behavioral Neurobiology, Eberhard Karls
Universität Tübingen, Silcherstr. 5, 72076 Tübingen, Germany*

Previous evidence indicates that the brain stores memory in two complementary systems, allowing both rapid plasticity and stable representations at different sites. For memory to be established in a long-lasting neocortical store, many learning repetitions are considered necessary after initial encoding into hippocampal circuits. To elucidate the dynamics of hippocampal and neocortical contributions to the early phases of memory formation, we closely followed changes in human functional brain activity while volunteers navigated through two different initially unknown virtual environments. In one condition, they were able to continuously encode new information about the spatial layout of the maze. In the control condition no information could be learned, because the layout changed constantly. Our results show that the posterior parietal cortex (PPC) encodes memories for spatial locations rapidly, beginning already with the first visit to a location and steadily increasing activity with each additional encounter. Hippocampal activity and connectivity between PPC and hippocampus, on the other hand, are strongest during initial encoding, and both decline with additional encounters. Importantly, stronger PPC activity related to higher memory-based performance. Compared to the non-learnable control condition, PPC activity in the learned environment remained elevated after a 24-hour interval, indicating a stable change. Our findings reflect the rapid creation of a memory representation in the PPC, which belongs to a recently proposed parietal memory network. The emerging parietal representation is specific for individual episodes of experience, predicts behavior and remains stable over offline periods, and must therefore hold a mnemonic function.

Pre-stimulus thalamic theta power predicts human memory formation

Catherine M. Sweeney-Reed^{1*}, Tino Zaehle¹, Jürgen Voges^{1,2}, Friedhelm C. Schmitt¹, Lars Buentjen¹, Klaus Kopitzki^{1,2}, Alan Richardson-Klavehn¹, Hermann Hinrichs^{1,2,3}, Hans-Jochen Heinze^{1,2,3}, Robert T. Knight⁴, Michael D. Rugg⁵

¹ *Departments of Neurology and Stereotactic Neurosurgery, Otto von Guericke University, Leipziger Strasse 44, 39120 Magdeburg, Germany*

² *Department of Behavioral Neurology, Leibniz Institute for Neurobiology, Otto von Guericke University, Leipziger Strasse 44, 39120 Magdeburg, Germany*

³ *German Centre for Neurodegenerative Diseases (DZNE), Otto von Guericke University, Leipziger Strasse 44, 39120 Magdeburg, Germany.*

⁴ *Helen Wills Neuroscience Institute and Department of Psychology, University of California, Tolman Hall, MC 3192 Berkeley, California 94720, USA*

⁵ *Center for Vital Longevity and School of Behavioral and Brain Sciences, University of Texas, Dallas, TX 75235, USA*

Pre-stimulus theta oscillatory power in the medial temporal lobe and the neocortex is associated with whether memories are successfully formed. Lesion, imaging, and animal studies, and more recently human electrophysiological studies have demonstrated a role for the dorsomedial (DMTN) and anterior thalamic nuclei (ATN) in memory processing. We analyzed human intrathalamic recordings from 7 patients who received electrodes implanted for deep brain stimulation treatment for intractable focal epilepsy. The patients were shown a series of 200 photographic scenes, which they judged as indoors or outdoors, during data recording. In a subsequent memory test, the images were shown again in random order, intermixed with 100 new scenes, and the patients judged whether the scenes were old or new. The electrophysiological encoding data were re-referenced to a bipolar montage and epoched 1 s before to 2 s after stimulus presentation and labeled according to whether memory formation was successful. A time-frequency decomposition was performed using the wavelet transform, and power was calculated. Mean pre-stimulus theta power in the right DMTN was greater preceding successful than unsuccessful memory encoding. Pre-stimulus theta power was correlated with behavioral performance and with previously determined post-stimulus correlates of successful memory formation, namely frontal-right ATN theta-gamma cross-frequency coupling,



early frontal theta phase alignment, and late right ATN gamma phase alignment. Our findings extend our knowledge of brain structures whose pre-stimulus activity is associated with memory formation from cortical to include subcortical.

Exposure to familiar and novel stimuli yields hippocampal BOLD responses for opposite contrasts depending on the duration of the habituation to the stimuli: a fMRI study in awake rats

Caroline Chwiesko^{1,2}, Benoit Boulat², Dirk Wiedermann⁵, Mathias Hoehn⁵ and Magdalena Sauvage^{1,2,3,4}

¹*International Graduate School of Neuroscience, Ruhr University Bochum, Germany*

²*Mercator Research Group, Ruhr-University Bochum, Germany*

³*Leibniz Institute for Neurobiology, Functional Architecture of Memory Dpt, Magdeburg, Germany*

⁴*Otto von Guericke University; Medical Faculty, Magdeburg, Germany*

⁵*Max-Planck- Institute for neurological research, Cologne, Germany*

The specific nature of information processing in the hippocampus (HIP) and its precise mechanisms is still poorly understood. We have been the first to report HIP BOLD signal in awake rats in relation to a fMRI cognitive paradigm testing for the memory for odors: we showed a greater BOLD effect for 'old' than for 'novel' odors in rats (old-new contrast). This pattern is consistent with some reports in humans using a similar paradigm. However, other studies also reported HIP BOLD responses for the opposite contrast (new-old). We speculated that these opposite results might stem from the use of different cognitive strategies for discriminating 'new' from 'old' stimuli: either the retrieval of 'old' items or a novelty-based strategy. Extensive habituation to the odor stimuli might favorize this latter strategy in animals. Hence, to test this hypothesis, we investigated HIP BOLD responses in awake rats with the same block design paradigm but habituated rats to the odors for 13 weeks instead of 5. In this case, exposure to familiar and novel odors yielded HIP BOLD signal for the opposite contrast (new-old) than that observed when habituation lasted 5 weeks (old-new). Our results suggest that the duration of the familiarization to the stimuli might indeed affect the cognitive processes at stake during the task. These findings might help explaining the discrepancy existing in the literature in humans and showed this translational approach to be a valuable tool for contributing in solving major debates in human memory research.

Sleep accelerates memory systems consolidation

Lea Himmer

Institute of Medical Psychology and Behavioral Neurobiology, University of Tübingen

Consolidation during sleep is assumed to modify the traces of memories in the brain, supporting the emergence of neocortical representations. We examined the effects of repeated learning and sleep on the declarative memory trace as seen in brain activity. Participants learned a list of nouns in seven repetitions in an fMRI scanner. A second session employing the same task followed 12 hours later. Half of the to be learnt words were identical to the previous session, whereas the other half consisted of new nouns. Subjects were randomly assigned to attend the first session in the morning or in the evening, thus spending the time in-between awake or sleepings. We find that hippocampal and medial prefrontal cortex (mPFC) activity decrease over encoding repetitions, while activity in the precuneus and inferior parietal lobule increases, indicating the build-up of a parietal memory representation. After a 12-hour offline period, we find discrepant activity patterns over repetitions for the sleep and wake groups. The sleep group shows further decrease of hippocampal activity only for new words, but not for old words, whereas this was seen for all words in the wake group. Moreover, the sleep group shows enhanced neocortical activity for words learned the previous day. Our findings demonstrate the distinctive paths memories take during consolidation in sleep and wakefulness. Retention during wakefulness leaves the memory trace unchanged and we still witness ongoing consolidation during additional learning. Offline reprocessing during sleep, however, strengthens the neocortical representation, thus enabling memory formation to complete ahead of time.

Hippocampus-dependent cognitive function is impaired in Jacob mouse mutants

Guilherme M. Gomes¹; Jorge Bergado-Acosta²; Pingan Yuanxiang¹, Oliver Stork³; Michael R. Kreutz¹

¹*RG Neuroplasticity, Leibniz Institute for Neurobiology, Magdeburg, Germany*

²*Pharmacology Department, Otto von Guericke University, Magdeburg, Germany*

³*Institute of Biology, Otto von Guericke University, Magdeburg, Germany*

NMDA receptors (NMDAR) have a well-established role in the control of plasticity-related gene expression and long-term information storage. Recently, we identified Jacob, a protein messenger that encodes and transduces the synaptic or extrasynaptic origin of GluN2B NMDA receptor (NMDAR) signals to the nucleus. Deletion of the Jacob gene in principal neurons of the forebrain results in severely impaired Hebbian plasticity and a blunted expression of immediate early genes that encode synaptic scaling factors. However, an unresolved issue is how for instance the absence of NMDAR-dependent LTP and LTD at hippocampal CA1 synapses affects memory formation.

Jacob deficient mice show increased anxiety and deficits in hippocampus-dependent behavioral paradigms, like contextual fear conditioning, 3-chamber social task and Y-maze reference memory. Deletion of the Jacob gene in principal neurons of the forebrain also results in severely impaired behavioral flexibility. The most prominent learning deficit was found in reversal learning. Collectively, the data show defective hippocampus-dependent information processing, which might be explained by deficient synaptic scaling processes.

Dopamine agonists rescue amyloid β induced LTP impairment by Src-family tyrosine kinases

Klaus G. Reymann

Neuropharmacology, Leibniz Institute for Neurobiology, Brennekestrasse 6, 39118, Magdeburg, and German Center for Neurodegenerative Diseases, Magdeburg, Germany

Soluble forms of oligomeric amyloid beta (A β O) are involved in the loss of synaptic plasticity and memory, especially in early phases of Alzheimer's Disease (AD). Stimulation of dopamine D1/D5 receptors (D1R/D5R) is known to increase surface expression of synaptic AMPA and NMDA receptors and facilitates the induction of the late phase of long-term potentiation (LTP), probably via a related mechanism. In this study we show, that the D1/D5R agonist SKF38393 protects LTP of hippocampal CA1 synapses from the deleterious action of A β O. Unexpectedly the D1R/D5R mediated recovery of LTP is independent of protein kinase A (PKA) or phospholipase C (PLC) pathways. Instead we found that inhibition of Src-family tyrosine kinases (SFK) completely abolished the protective effects of D1R/D5R stimulation in a cellular model of learning and memory. Since SFK inhibitors are in clinical testing because they prevent A β O induced synapse loss this finding raises some concerns with their use in attempting to restore synaptic plasticity, which is impaired already at an early stage of AD.



Functional Architecture of Memory Conference

May 25th – 27th 2016

Invited Talks



**Functional anatomy and plasticity of hippocampal memory circuits:
Studies in the aging human brain and in individuals with
subjective memory complaints**

Emrah Düzel

DZNE, Germany

I will present data on the functional organization of domain-specific hippocampal memory circuits in humans as revealed by fMRI studies at 3 and 7 Tesla. I will show how these circuits are affected in aging and in individuals with subjective memory complaints. Furthermore, I will present data on how physical exercise affects these memory circuits.

Emergence and fate of the memory trace

Magdalena Sauvage

Leibniz Institute for Neurobiology (LIN) / Otto-von-Guericke University Magdeburg,
Germany

Many debates about the function of the hippocampus are still sparking memory research: if the same part/cells of the hippocampus contribute to the formation and the retrieval of memory, if the hippocampus is exclusively involved in retrieving recent memories and not older ones, and if the hippocampus is necessary for the reconsolidation of memory. One of the reasons why these issues are still highly debated is the scarce availability of techniques with high spatial and temporal resolution in humans. Here, we address these questions using translational behavioral paradigms in rodents combined to a high resolution molecular imaging technique based on the detection of the immediate-early genes *Arc* and *Homer1A* and/or optogenetics. We found that, only in the dorsal part of the hippocampal subfield CA1, activation during encoding is predictive of memory performance. Also, in this area, only half of the cells recruited during memory formation are reactivated during memory retrieval (Nakamura et al, hippocampus, 2015). In addition, by studying the retrieval of memories up to one-year old in mice (the equivalent of 40 years-old memories in humans), we showed that both CA1 and the hippocampal subfield CA3 contribute to the retrieval of recent and early remote memories but that only CA1 is engaged for the retrieval of very remote ones, indicating a shift from a greater contribution of the trisynaptic loop to that of the temporoammonic pathway (Lux et al, eLife, 2016). Finally, we demonstrated that CA1 is necessary for memory reconsolidation (Lux et al, Cerebral Cortex, 2015).



Hippocampal-cortical interactions supporting episodic retrieval

Michael Rugg

UT Dallas, USA

It is generally accepted that the hippocampus plays a central role in the encoding and subsequent reactivation of patterns cortical activity representing experienced events. I will discuss fMRI findings suggesting that successful episodic retrieval is associated with enhanced hippocampal activity, the cortical reinstatement of patterns of encoding-related activity, and enhanced cortico-cortico functional connectivity. Each of these neural signatures of successful recollection is robustly correlated across subjects with memory performance. The implications of these findings for a systems-level understanding of successful episodic retrieval will be discussed.

ERP evidence for multiple familiarity signals in the word frequency mirror effect

Axel Mecklinger

University Saarland, Germany

The word frequency mirror effect describes the observation that low frequency words produce lower false alarms and higher hit rates than high frequency words in recognition memory tasks. Recent dual process models consider absolute familiarity, an item's baseline familiarity at a given point in time responsible for the false alarm differences and recollection for the hit rate differences. An early dual processes model (Mandler, 1980; *Psych. Rev.*) assumes an additional relative familiarity mechanism, i.e. an incremental change in absolute familiarity as a function of study event. In this talk I will show that it is possible to map these processes on event-related potential (ERP) effects in an old/new recognition memory task. A contrast between high and low frequency new words is taken as index of absolute familiarity. This effect was observed between 300 and 600 ms and was topographically distinct from a mid-frontal old/new effect in the same time interval, which was larger for low frequency than for high frequency words, as one would expect for an ERP correlate of relative familiarity. A later occurring parietal old/new effect associated with recollection was only obtained for low frequency items (Bridger, Bader & Mecklinger, 2014, *Neuropsychologia*). The data support the view that word frequency affects three qualitatively distinct memory processes and indicate that recognition judgments for high and low frequency words can be based on functionally distinct but interwoven familiarity mechanisms.

Neural substrate of recollection of past occasional events in a human-inspired episodic memory task in rats

Serge Laroche

CNRS & University Paris-Sud, France

In search for the mechanisms underlying complex forms of human memory such as episodic recollection, a primary challenge is to dispose of adequate animal models amenable to neurobiological investigation. Here, we developed a task that provides means to quantitatively evaluate the ability of rats to form and recollect a combined knowledge of What happened, Where and in Which context/occasion (referred to as episodic-like memory) after limited encounter of specific episodes, based on odour-drink associations (What) in distinct locations (Where) within different multisensory enriched environments (in Which context/occasion). Analyses of individual recollection profiles show that rats are able to form and recollect, in a hippocampal-dependent manner, an accurate, long-term integrated episodic-like memory that can last at least 24 days. Placing rats in a contextually challenging recollection situation at recall reveals the ability for flexible use of episodic memory. Cellular imaging of c-Fos and Zif268 brain activation reveals that episodic memory recollection recruits a distributed network of hippocampal-prefrontal cortex structures that correlates with the accuracy of recollection performance. Finally, we provide evidence that adult hippocampal neurogenesis contributes significantly to faithful recall of episodic memory.



Establishing hippocampal-neocortical traces for discrimination and recognition memory

Michael Yassa

UC Irvine, USA

Recent work on the role of the medial temporal lobes in episodic memory has highlighted pattern separation as a key computation in which the hippocampus is involved. Several studies have also noted that there is a dorsoventral axis in the hippocampus that may be related to the precision or granularity of representation in memory. I will discuss recent data from our lab that uses a pattern separation task, with repeated exposure to study stimuli to assess the instantiation of hippocampal-neocortical traces and the involvement of dorsal and ventral hippocampus differentially in discrimination and recognition judgment. I will also share behavioral data suggesting that repetition enhances target recognition but degrades high-precision discrimination, consistent with a semanticization process, in which memories become more generalized. The data are discussed within the context of Competitive Trace Theory, a new candidate theory that harmonizes across the Standard Model of Systems Consolidation and Multiple Trace Theory.

On the role of temporal coordination of hippocampal-entorhinal microcircuits in episodic-like memory deficits**Liset Memendez de la Prida**

IC – CSIC, Spain

Deficits of episodic memory are present during normal aging and in many neurological conditions including Alzheimer's disease and certain forms of epilepsy but the mechanisms both in health and disease remain elusive. More importantly, we still lack integrative theories to understand a range of cognitive co-morbidities affecting these different neurological conditions. Here, we show our data obtained in animal models of temporal lobe epilepsy (TLE), a disease affecting the temporal lobe circuitry in particular, using a combination of multi-site local field potential (LFP) and single-cell recordings in behaving rats. Similar to human, TLE rats exhibit a disruption of episodic-like memory as tested with the 'What-Where-When' paradigm, which can be related to deficits of LFP theta oscillations (4-12 Hz) recorded during the task. Strikingly, changes of theta coherence and theta-gamma coordination are distinctly related with the temporal and spatial components of the task. Such impaired coordination of hippocampal-entorhinal activity is hardwired in the TLE-reorganized microcircuits along the proximal (close to CA3) to distal (close to subiculum) axis of the dorsal hippocampus. We discuss the implication of these findings as candidate mechanisms of cognitive co-morbidities in diseases affecting structures of the temporal lobe.

**Functional dissociations along the CA3-CA2-CA1 transverse axis****James Knierim**

Johns Hopkins University, USA

Most computational models of the hippocampus regard the different components of the hippocampus (e.g., the dentate gyrus, CA3, and CA1 regions) as composed of functionally homogeneous units. Anatomical and functional differences along the longitudinal axis have been reported, but less attention has been paid to gradients along the transverse axis (i.e., along the CA3-CA2-CA1 pyramidal cell layer). We recorded place cells along this axis as rats ran laps on a circular track with salient local and global cues. In mismatch probe sessions, the local and global cues sets were rotated relative to each other. Proximal CA1 cells behaved much like the dentate gyrus, in that they remapped the mismatch environment (which we interpret as evidence of pattern separation), whereas distal CA3 (and CA2) cells responded in a more coherent fashion under the control of the local cue set (which we interpret as a form of pattern completion). Proximal CA1 formed a split local-global representation, which we interpret as the result of a conflict between CA3 and medial entorhinal cortex inputs. In contrast, distal CA1 was controlled by the global cues, which we suggest may reflect the dominant influence of head direction cell inputs in this region in the absence of a competing, coherent spatial signal from its major afferents (proximal CA3 and lateral entorhinal cortex). These differences in the CA1 output may reflect the specific requirements of pattern separation/completion in the CA3 circuit to support the different functions of the parallel processing loops along the transverse axis.



Role of the dorsal dentate gyrus in processing spatial and spatial context information as well as conjunctive encoding and the role of the ventral dentate gyrus in processing anxiety, olfactory and reward value pattern separation

Raymond Kesner

Utah University, USA

Based on research with rats data will be presented to support an episodic memory role for the dorsal dentate gyrus subregion of the hippocampus in mediating conjunctive encoding of visual with spatial information, as well as episodic memory for spatial distance, height of objects, slope, and spatial context. Data will also be presented for the ventral dentate gyrus subregion of the hippocampus in mediating episodic memory for odors, social recognition and reward value. Also, data will be presented to support a role for the CA3 subregion of the hippocampus in mediating cue-based pattern completion for object information as well as cue-based pattern completion for relapse following cocaine conditioning. Finally, based on neurogenesis within dentate gyrus, it appears that there is a role for the dentate gyrus in mediating long-term memory.



Hippocampal neural mechanisms underlying the memory for sequences of events

Norbert Fortin

UC Irvine, USA

The ability to remember temporal relationships among events or stimuli is fundamental to perception, cognition and adaptive behavior. This type of temporal organization is also an essential feature of episodic memory, as the memory for individual events includes information about the order in which they occurred, and yet the neural mechanisms underlying this important capacity remain poorly understood. While considerable research indicates hippocampal activity can represent sequences of locations and can provide timing signals at different timescales, direct evidence of coding for the memory of sequential relationships among nonspatial events is lacking. In this seminar, I will primarily focus on a recent experiment in which we addressed this issue by recording neural activity in CA1 as rats performed a nonspatial sequence memory task we recently developed, a task that shows strong behavioral parallels in rats and humans and depends on the hippocampus in both species. We found that hippocampal activity differed depending on the temporal context of items—in this case, whether they were presented in or out of sequence. This nonspatial sequence coding was present at the level of individual neurons, neuronal ensembles, and local field potentials, and paralleled sequence memory performance across sessions. These findings provide compelling evidence that sequence coding extends beyond the domain of spatial trajectories and is thus a fundamental function of the hippocampus. I will conclude by summarizing our ongoing work in rats and humans aimed at elucidating the contributions of other structures, specifically the prefrontal cortex, perirhinal cortex and nucleus reuniens.

Differential responsivity of neurons in perirhinal cortex, lateral entorhinal cortex and dentate gyrus during time-bridging learning**John Disterhoft**

Northwestern University, USA

Acquisition of temporal associative tasks is hippocampus-dependent, while consolidated performance is not. However, it remains unknown how afferent information to the hippocampus from surrounding areas relates to associative learning. Here we recorded single-unit firing in three regions of the medial temporal lobe (MTL) while rabbits underwent trace eyeblink conditioning, and again after a month-long consolidation period. Perirhinal cortex (PR) responded to both conditioned (CS; whisker vibration) and unconditioned (US; corneal airpuff) stimuli in a similar manner before and after learning. In contrast, lateral entorhinal cortex (latEC) showed conditioning-specific associative neuronal activity and dentate gyrus (DG) showed trace-bridging associative, responses well before behavioral criterion was reached. This information was carried by high firing-rate neurons in each region. Spiking activity was similar on trials with or without conditioned responses, indicating that these three regions do not directly control behavioral output. Encoding of temporal association in latEC and DG decreased post-consolidation, when behavior was optimized. Together these findings demonstrate that the MTL forms early associations, rather than controls behavior, and suggest that retention of remotely-acquired memories involves regions outside of the MTL. The associative activity in entorhinal cortex is of special relevance because EC is the site of earliest pathologic changes in Alzheimer's Disease, when initial difficulties in learning and memory are noted.

Cellular mechanism for active memory retention in the hippocampus

Motoharu Yoshida

Leibniz Institute for Neurobiology (LIN) and German Center for Neurodegenerative Diseases (DZNE) Germany

The hippocampus is crucial for temporal association tasks that require short-term (< 30s) memory retention. These tasks also require an intact cholinergic projection from the medial septum to the hippocampus. However, it remains unclear what cellular mechanisms support short-term memory retention in the hippocampus. We investigated cholinergic cellular modulations and its role in the hippocampus using in vitro electrophysiological recordings and computational simulations. First, I will present that a cholinergic activation supports persistent firing in hippocampal CA1 and CA3 pyramidal cells. Persistent firing is a repetitive neural spiking, which lasts for more than 30 sec after being triggered by a brief stimulation. This persistent firing seems to be supported by the transient receptor potential cation (TRPC) channels. Although recurrent synaptic excitation is widely thought to support persistent firing, these results indicate that hippocampal neurons may support persistent firing through an intrinsic mechanism within individual cells. Second, I will present that this persistent firing may support more robust in vivo-like persistent firing compared to the mechanism based on recurrent synaptic excitation, using computational simulations. Third, I will present that persistent firing in individual cells is achieved through a fine balance between the TRPC and potassium channels. When the cholinergic activation is relatively strong, neurons responded with an ictal-like activity with depolarization block. Such ictal-like activity was also seen when potassium channels were blocked, agreeing with the role of cholinergic modulation and the potassium channels in mesial temporal lobe epilepsy. Finally, I will talk about the roles of other neuromodulators on persistent firing.



Delineating functional circuits for remembering visual scenes and objects

Inah Lee

Seoul University, South Korea

The hippocampal memory system is important for spatial navigation while remembering events experienced during the navigation. While an animal is engaged in such episodic mnemonic situations, memories of visual scenes in the animal's background serve as strong contextual information with which memories of individual objects and other cognitive factors can be associated together. Our laboratory has been investigating the neural mechanisms (in the medial temporal lobe) underlying contextual decision making using visual scenes. So far, we have confirmed that the dorsal hippocampus is indispensable to making spatial/nonspatial choices in a particular visual background scene because rats with dorsal hippocampal inactivation show chance-level performance in the task. It appears that this scene-specific mnemonic behavior is a unique function of the hippocampus because inactivations of other regions in the extrahippocampal cortical areas do not result in such devastating impairment in performance except for when the medial entorhinal cortex is inactivated. Since objects are often remembered with visual background in episodic memory, we also investigate how object memory is formed and retrieved in the perirhinal cortex. In my talk, I will briefly overview some of our behavioral and electrophysiological data that can provide insights into how object perception/memory is processed in the perirhinal cortex.

Perirhinal and postrhinal interactions in the representation of context

Rebecca Burwell

Brown University, USA

A widespread view of the medial temporal lobe memory system posits that object information reaches the hippocampus via the perirhinal cortex and spatial information arrives to the hippocampus via the postrhinal cortex. The perirhinal and postrhinal cortices each project to the hippocampus both directly and indirectly through the lateral and medial entorhinal areas. By one view, the spatial pathway conveys both spatial and contextual information to the hippocampus. By another view, the hippocampus, itself, configures spatial and object information into representations of context. Neither view takes into account 1) the evidence that both the perirhinal and postrhinal cortices are necessary for contextual memory, and 2) the robust, reciprocal connections between the perirhinal and postrhinal cortices. I will present the anatomical, experimental lesion, and electrophysiological evidence that the perirhinal and postrhinal cortices are part of a circuit that supports representation of context. Although both the perirhinal and postrhinal cortices are important for contextual fear conditioning, the question of whether direct perirhinal-postrhinal interactions are necessary for contextual learning has not been addressed. We have evidence from disconnection lesion studies that such perirhinal-postrhinal interactions are not necessary for contextual fear conditioning, but are necessary for a context-guided version of spontaneous object recognition. Our findings support the view that context is encoded upstream of the hippocampus and that such representations are made available to the hippocampus for episodic memory and associative learning and to other brain regions for other context-guided cognitive processes.

Towards an Understanding of the Hippocampal Cognitive Map

Elizabeth Buffalo

University of Washington, USA

While it has long been recognized that medial temporal lobe structures are important for memory formation, studies in rodents have also identified exquisite spatial representations in these regions in the form of place cells in the hippocampus and grid cells in the entorhinal cortex. Spatial representations entail neural activity that is observed when the rat is in a given physical location, and these representations are thought to form the basis of navigation via path integration. Recent studies in nonhuman primates have suggested that similar kinds of spatial representations can be identified, even in the absence of physical movement through an environment. I will discuss recent work from my lab that addresses similarities and differences between spatial responses as identified in rodents and primates. I will also discuss areas of opportunity for future research to further our understanding of the function of the hippocampal formation and the nature of the cognitive map.



Functional Architecture of Memory Conference

May 25th – 27th 2016

Recreational Info



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