

Sixth International Conference on the
FUNCTIONAL ARCHITECTURE OF MEMORY
19th -21st June 2024

SPEAKERS

David Berron (DZNE, Magdeburg, DE)
Svenja Brodt (MPI Tübingen, DE)
Jozsef Csicsvari (Institute of Science and Technology, AT)
Christian Doeller (MPI for Human Cognitive and Brain Sciences, DE)
Stefan Köhler (Western University, CA)
Thomas McHugh (Riken Center for Brain Science, JP)
Sanja Mikulovich (LIN, DE)
Morris Moscovitch (University of Toronto, CA)
Ora Ohana (Center for Molecular Neurobiology Hamburg, DE)
Charan Ranganath (University of California, Davis, USA)
Stefan Remy (LIN/OvGU Magdeburg, DE)
Magdalena Sauvage (LIN/OvGU Magdeburg, DE)
Monika Schönauer (Freiburg University, DE)
Oliver Stork (OvGU Magdeburg, DE)
Motoharu Yoshida (LIN/DZNE Magdeburg, DE)

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General information

1. Registration/ Badge pick-up

The check-in for the conference and the respective badge pick-up on 19th June starts at 9:00am.

2. 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 / Willy-Brandt-Platz* and take the tram line 9 (direction: *Reform*). 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](#).

3. Wifi

Eduroam

LIN-Conference (Access Code: meet@LIN)

4. 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).



5. 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.

6. Conference Dinner (Thursday June 20th)

www.restaurant-die-kirche.de



For participants who registered for the conference dinner transport:

Departure from the LIN: 5:30 p.m. sharp.

Return: pick-up at the drop off point at 9 p.m. sharp. Going either to Motel One (city centre) **or** to the LIN.

Alternatives: 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 (direction *Leipziger Straße*) or tram line 9 (direction *Reform*) and get off at *Brennecke Straße* (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 June 19th	Time	Thursday June 20th	Time	Friday June 21st
09:30 - 09:40	"Welcome" Prof. Dr. Sauvage	09:30 - 10:10	Stefan Köhler (Western University, CA) Dissociations and associations between pattern separation and statistical learning	09:30 - 10:10	Jozsef Csicsvari (Institute of Science and Technology, AT) REM and non-REM sleep antagonistically influence reactivation drift in the hippocampus
09:40 - 10:50	Data Blitz Session Part I	10:10 - 10:50	Oliver Stork (OVGU, DE) Local circuit mechanisms in the dentate gyrus controlling fear memory strength and specificity	10:10 - 10:50	Monika Schönauer (Univ. Freiburg, DE) Reactivation drives memory consolidation during wakefulness and sleep
10:50 - 11:00	Coffee	10:50 - 11:20	Coffee	10:50 - 11:20	Coffee
11:20 - 12:00	Data Blitz Session Part II	11:20 - 12:00	Charan Ranganath (Univ. of CA, USA) Crashing the Gates of Memory	11:20 - 12:00	David Berron (DZNE Magdeburg, DE/ Lund Univ., SE) Novel unsupervised and remote visual memory assessments for disease-stage specific detection, prognosis and monitoring of cognitive impairment in Alzheimer's disease
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	Morris Moscovitch (Univ. of Toronto, CA) Memory consolidation and re-organization: Details, gist and schemas	14:00 - 14:40	Thomas McHugh (Riken Center for Brain Science, JP) Subcortical modulation of hippocampal memory	14:00 - 14:40	Christian Doeller (MPI for Human Cognitive and Brain Sciences Leipzig, DE) Structuring experience in cognitive spaces
14:40 - 15:20	Magdalena Sauvage (LIN/ OVGU) Medial temporal lobe memory subnetworks across time and dimensions	14:40 - 15:20	Stefan Remy (LIN/ OVGU, DE) The medial septum - cell-type diversity, circuit connectivity and relevance for behaviour	14:40 - 15:20	Motoharu Yoshida (DZNE) Persistent firing in single cells support working memory and spatial representation
15:20 - 15:40	Coffee	15:20 - 15:25	Group picture (in front of the LIN)	15:20 - 15:40	Coffee
15:40 - 16:20	Svenja Brodt (MPI for Biological Cybernetics, DE) The hippocampal contribution to rapid neocortical learning	15:25 - 15:40	Coffee	15:20 - 15:40	Coffee
15:40 - 16:20		15:40 - 16:20	Sanja Mikulovic (LIN, DE) "Learning to be good" engages the dorsal hippocampus: focus on emotional contagion and helping behavior	15:40 - 16:20	Ora Ohana (Center for Molecular Neurobiology Hamburg, DE) The activity-regulated gene Arc/Arg3.1 orchestrates a critical period in the development of learning, memory, and hippocampal networks
16:20 - 17:00	Open Discussion	16:20 - 17:00	Open Discussion	16:20 - 17:00	Open Discussion

Data Blitz Sessions Overview

09:40 - 10:50	Data Blitz Session Part I (talk: 5mins; questions: 1min)
	<p>Lioudmila Sosulina (LIN Magdeburg/ DZNE Bonn, Germany) Locus coeruleus modulates medial septum network</p>
	<p>Sara Enrile Lacalle (OvGU Magdeburg/ CBBS, Germany) Amygdalar modulation of memory engrams in the hippocampus: Spotlight on sex differences</p>
	<p>Oliver Barnstedt (OvGU Magdeburg, Germany) A hippocampus-accumbens code guides goal-directed appetitive behavior</p>
	<p>Andreas Schulz (LIN Magdeburg, Germany) Dopamine dependent potentiation of acoustic evoked potentials in the striatum</p>
	<p>Anwasha Das (LIN/ OvGU, Magdeburg, Germany) "Can we learn while doing nothing?" – Role of medial temporal lobe in offline performance improvements during human motor sequence learning</p>
	<p>Björn Hendrik Schott (LIN Magdeburg/ Univ. Medic. Center Göttingen, Germany) Preserved inhibitory temporo-parietal effective connectivity predicts explicit memory performance in older adults</p>
	<p>Erika Atucha (LIN Magdeburg, Germany) Identification and mobilization of neural resources for recognition memory in young and old populations</p>
	<p>Panagiotis Iliopoulos (OvGU/ DZNE, Magdeburg, Germany) Prefrontal-hippocampal task-based connectivity is inversely linked to mnemonic discrimination performance</p>

Data Blitz Sessions Overview

11:20 - 12:00	Data Blitz Session Part II (talk: 5mins; questions: 1min)
	Larissa Fischer (DZNE Magdeburg, Germany) Longitudinal changes in medial temporal lobe functional connectivity and episodic memory performance with age and Alzheimer’s pathology
	Daniel Reznik (MPI Leipzig, Germany) Evolution and topography of cortical connectivity with the medial temporal lobe in humans
	Iryna Schommartz (Goethe Univ. Frankfurt, Germany) Out of Sight, Out of Mind: Differential Predictions of Subsequent Memory by Eye Gaze Patterns in Children and Adults
	Markus Fendt (OvGU Magdeburg, Germany) Orexinergic modulation of chronic jet lag-induced deficits in mouse cognitive flexibility



Data Blitz Session Abstracts

Locus coeruleus modulates medial septum network

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The locus coeruleus (LC) is known as the main source of norepinephrine in the brain, to project throughout the brain and to be vulnerable in the early stages of memory impairment pathologies, including Alzheimer's disease. One of the target areas is the medial septum (MS) and diagonal band of Broca (DBB), which are involved in sleep and arousal regulation, oscillatory and locomotor behaviour, as well as exploration, learning and memory. We hypothesised that arousal mediated by LC activity may act on MS/DBB neurons to drive locomotion. Using Cre-targeted calcium imaging in awake head-fixed mice, we demonstrate that catecholaminergic LC projections into the MS are activated during locomotion initiation and positively correlate with the animal's pupil diameter but not its velocity. Optogenetic stimulation of these projections *in vivo* also induces locomotion initiation. Microelectrode array optogenetic data *in vitro* confirms the alteration of the firing properties of the network: we observe units with increased and reduced firing frequency upon stimulation of TH+LC fibres. Single-cell RNA-seq and spatial transcriptomic expression analysis reveals the differential expression for RNA of noradrenergic receptors in different cell types in the MS of neuronal and non-neuronal origin. These findings suggest that the LC acts as an important modulator for the MS, orchestrating medial septal network activity in multiple ways.

Amygdalar modulation of memory engrams in the hippocampus: Spotlight on sex differences

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The interaction of amygdala and hippocampus, critical for the formation of persistent emotional memories, may play a central role in the pathophysiology of posttraumatic stress disorder (PTSD). However, with amygdala hyperactivity as hallmark of PTSD, it is still not clear whether amygdala hyperresponsiveness prior to a traumatic event is a predisposing factor for the development of PTSD or is an acquired condition upon trauma.

To address this question, in the current study we investigated the effect of heightened amygdala activity on fear memory, anxiety and the formation of hippocampal fear engrams in male and female mice using chronic chemogenetic activation of basolateral amygdala (BLA) for a period of one week prior to fear conditioning. We observed an enhanced anxiety-like behavior and hyperactivity in the elevated plus maze in female but not in male mice. Moreover, chronic BLA activation elicits higher foot-shocked induced cFos expression in both sexes in comparison to control mice.

By contrast, amygdala hyperactivity led to the loss of specificity of background context fear memory in both sexes, together with increase in cFos expression in the hippocampus. However, aberrant reactivation engram patterns in the presence of ambiguous contextual threats were present only in male mice. Collectively, these data support the notion that amygdala hyperactivity might underlie the fear-induced metaplasticity in the hippocampal circuits relevant to pattern separation and completion functions.

A hippocampus-accumbens code guides goal-directed appetitive behavior

Oliver Barnstedt

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The dorsal hippocampus (dHPC) is a key brain region for the expression of spatial memories, such as navigating towards a learned reward location. The nucleus accumbens (NAc) is a prominent projection target of dHPC and implicated in value-based action selection. Yet, the contents of the dHPC→NAc information stream and their acute role in behavior remain largely unknown. Here, we found that optogenetic stimulation of the dHPC→NAc pathway while mice navigated towards a learned reward location was both necessary and sufficient for spatial memory-related appetitive behaviors. To understand the task-relevant coding properties of individual NAc-projecting hippocampal neurons (dHPC→NAc), we used in vivo dual-color two-photon imaging. In contrast to other dHPC neurons, the dHPC→NAc subpopulation contained more place cells, with enriched spatial tuning properties. This subpopulation also showed enhanced coding of non-spatial task-relevant behaviors such as deceleration and appetitive licking. A generalized linear model revealed enhanced conjunctive coding in dHPC→NAc neurons which improved the identification of the reward zone. We propose that dHPC routes specific reward-related spatial and behavioral state information to guide NAc action selection.

Dopamine dependent potentiation of acoustic evoked potentials in the striatum

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Auditory memory, at least of complex auditory stimuli, depends on auditory cortex as well cortico-hippocampal and cortico-striatal circuits. While for the cortico-striatal pathway it is known that training in auditory discrimination tasks potentiates cortico-striatal synapses, it remains unknown so far, whether dopamine is necessary for plastic changes of these synapses. To assess the role of dopamine on these synapses we employed Mongolian gerbils in a passive listening task with frequency modulated tones. The presentations of a subset of tones was paired with optogenetic stimulation of the ventral tegmental area (VTA). We recorded local field potentials in two different sites in the striatum, in the posterior and the dorsal lateral striatum. The magnitudes of the auditory evoked potentials (AEP) in the striatum were increased after VTA stimulation in the dorsal striatum but not in the posterior striatum. Systemic application of a dopamine antagonist prevented the increase of the AEP and tended to decrease AEP amplitudes after VTA stimulation. Magnitudes of AEP without VTA stimulation did not change. In summary, dopamine seems to be required for the increase of striatal AEP and consequently for potentiation of auditory striatal synapses, however in the current study we did not distinguish between possible pathways, like cortico-striatal or thalamo-striatal connections.

“Can we learn while doing nothing?” – Role of medial temporal lobe in offline performance improvements during human motor sequence learning

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Accumulating evidence points to the hippocampus as a generic sequence generator. This role may extend to sequences of movements. Motor sequence learning results in plastic changes in medio-temporal lobe, evident in human fMRI studies, and may induce offline replay of trained movement sequences, evident in MEG⁵. Buch et al. have proposed that hippocampal replay supports the rapid offline performance improvements typically observed across rest periods of a few seconds that are interspersed between training of a movement sequence. These so-called ‘micro-offline gains’ (MOG) are thus considered a form of rapid motor memory consolidation.

We report six experiments that challenge this view. Our data indicate that MOG reflect neither offline learning, nor (sequence-specific) replay, but are (at least partly) mediated by sequence planning, enabled by breaks from continuous practice. Sequence planning, too, involves medial temporal lobe. Thus, by classifying MEG data during breaks, we are currently examining the role of medial temporal lobe, in particular parahippocampal regions, for break-induced sequence planning. Furthermore, we aim to explore theta sequences or ‘look ahead’ activity during rest periods, to deepen our understanding of hippocampal involvement in the context of micro-offline performance improvements.

Preserved inhibitory temporo-parietal effective connectivity predicts explicit memory performance in older adults

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Background: Successful encoding of novel information into episodic memory traces is associated with increased activation of the hippocampus and temporo-occipital cortical structures like the parahippocampal place area (PPA). On the other hand, midline brain structures like the precuneus, which is prominently involved in memory retrieval, typically show encoding-related deactivations. Older adults exhibit lower episodic memory performance and reduced precuneus deactivations. However, it is still unclear how the hippocampus interacts with temporo-occipital and medial parietal structures to facilitate successful memory formation and whether these interactions are affected by aging.

Methods: Here, we used dynamic causal modeling (DCM) of functional magnetic resonance imaging (fMRI) data from three independent cohorts to elucidate the information flow between the hippocampus, the PPA, and the precuneus during episodic memory formation for visual scene stimuli. We then tested the relationship between effective connectivity of the memory network using Bayesian robust correlations.

Results: In 117 young, healthy adults, we observed pronounced excitatory connectivity from the PPA to the hippocampus and inhibitory connections from the PPA to the precuneus. Both were further up-regulated during successful encoding. This pattern could be replicated in two cohorts of young and older adults (N = 58 young, 83 older; 64 young, 84 older). Older adults exhibited attenuated negative PPA-precuneus connectivity, which correlated negatively with memory performance.

Discussion/Conclusion: Our results provide insight into the network dynamics underlying encoding-related activations and deactivations and suggest that age-related differences in memory-related network activity manifest in altered temporo-parietal neocortical rather than hippocampal connectivity.

Identification and mobilization of neural resources for recognition memory in young and old populations

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Previous studies indicate that successful performance on high demand recognition memory tasks requires medial temporal lobe (MTL) and prefrontal cortex (PFC) functional integrity. The MTL and the PFC are composed of vastly distinct functional subregions, including the hippocampal (CA1 and CA3) and parahippocampal subareas (PER, POR, LEC, MEC), and the Anterior cingulate (ACC), Prelimbic (PrL) and Infralimbic (IL) cortices. The extent to which each of these subareas might serve as a neural resource for recognition memory in young impaired or aging organisms is however not well-understood. To address this question, we first compared brain activity between high and low performers in young and older mice (2 and 18 months-old, respectively) performing an object-in-place task, sensitive to hippocampal and PFC lesions (Barker and Warburton, 2015). Second, we investigated if cognitive training (repeated training in the object-in-place task) improved performance on the task and studied changes in MTL and PFC areas' activity in young and older mice. To do so, we detected the expression of the RNA of the immediate early genes Arc and Homer1A, commonly used to map cognitive functions (Guzowski et al., 2001; Sauvage et al., 2013; 2019; Nakamura and Sauvage, 2016), and compared between groups the proportion of cells that had been activated during both memory formation and retrieval (i.e. Arc/Homer1A+ reactivated cells). Preliminary results show that a limited number of brain areas might serve as neural resource for recognition memory in older compared to younger adults. In addition, cognitive training improved memory performance in both young and older mice but at a different rate. Finally, brain activity patterns following the final training session, reveal that cognitive training might lead to changes at the neural level that favor a reversion of the effect of aging on brain integrity. These findings might be instrumental in developing targeted interventions to slow down or restore age-related cognitive decline.

Prefrontal-hippocampal task-based connectivity is inversely linked to mnemonic discrimination performance

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Successful memory relies on the process of mnemonic discrimination (MD) to establish distinct representations. Despite extensive research on the role of medial temporal lobe (MTL) areas in MD, little is known about MTL interactions with prefrontal (PFC) and visual (VIS) areas. Here, we investigated task-based functional connectivity patterns during MD, focusing on major MTL-PFC-VIS areas. Fifty-four young adults (M = 23.76 years) underwent a cognitive task differentiating similar objects and scenes ('lures'; correct response: 'new') from repeated items ('repeats', correct response: 'old'). Stimuli were presented in 12-item sequences with the first six being new images, while each of the subsequent six could be either a lure or a repeat trial. Task-based 3T functional magnetic resonance imaging (fMRI) data were acquired (2 mm isotropic, TR= 2.2 secs) and modeled with generalized psychophysiological interaction analysis. All connectivity analyses focused on the LD contrast (correct lures versus repeats).

We identified three significant connectivity clusters during MD displaying: 1) reduced VIS-to-VIS and VIS-MTL connectivity, and increased connectivity between 2) VIS-PFC and 3) hippocampal-PFC regions. Higher LD task connectivity between the hippocampus and PFC areas (inferior and superior frontal gyrus) was linked to poorer MD performance. Additionally, higher connectivity in the HIPP-PFC network was associated with poorer MD in an independent out-of-scanner mnemonic discrimination task. Our results suggest a key role of VIS-to-VIS, VIS-MTL, VIS-PFC, and PFC-hippocampal connectivity during successful MD. They also highlight an inverse relationship between HIPP-PFC connectivity and MD performance, which might reflect compensatory mechanisms or reduced processing efficiency.

Longitudinal changes in medial temporal lobe functional connectivity and episodic memory performance with age and Alzheimer's pathology

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The medial temporal lobe (MTL) and posteromedial cortex (PMC) are crucial for episodic memory. However, they are vulnerable to aging and early Alzheimer's disease (AD). Both processes might elicit distinct functional connectivity (FC) changes, which is however not well understood. We hypothesized that resting-state FC strength involving those regions would decrease with age with no or low AD pathology but increase with early AD pathology.

We analysed longitudinal 3-Tesla resting-state fMRI data from cognitively unimpaired older adults (OA; PREVENT-AD cohort). We assessed FC at baseline and after 24 months (FU24) in A β and p-tau CSF-characterized OA with available longitudinal p-tau₁₈₁/A β ₁₋₄₂ ratio (N=70). First, we investigated effects of p-tau₁₈₁/A β ₁₋₄₂ ratio on FC controlling for age, *APOE*, sex and education. Second, we tested the association between FC and change in delayed memory recall via multiple regression. In another sample of A-T⁺ OA (N=100), we investigated the effects of ageing independent of AD pathology.

P-tau₁₈₁/A β ₁₋₄₂ ratio at baseline and FU24 was related to increasing FC between anterior hippocampus and superior precuneus as well as parahippocampal cortex and superior precuneus over time ($p = 0.032$). Higher baseline FC was associated with longitudinally increasing memory in *APOE4* non-carriers and decreasing memory in *APOE4* carriers ($p = 0.026$). In A-T⁺ OA, FC between MTL and PMC decreased over time with posterior hippocampus, parahippocampal cortex, inferior and medial precuneus involved. Our results provide novel longitudinal evidence incorporating age, *APOE*, A β and tau indicating specific memory-related FC changes in cognitively unimpaired OA.

Evolution and topography of cortical connectivity with the medial temporal lobe in humans

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Tract-tracing studies in non-human primates indicate that different subregions of the medial temporal lobe (MTL) are connected with multiple brain regions. However, no clear framework defining the distributed anatomy associated with the human MTL exists. This gap in knowledge originates in notoriously low MRI data quality in the anterior human MTL and in group-level blurring of idiosyncratic anatomy between adjacent brain regions comprising the MTL. To overcome these challenges, we intensively scanned four human individuals and collected whole-brain data with unprecedented MTL signal quality that allowed us to explore in detail the cortical networks associated with MTL subregions within each individual. We discovered biologically meaningful networks associated with the hippocampus, entorhinal cortex, perirhinal cortex and parahippocampal area TH. Furthermore, consistent with animal tract-tracing data, we associate subregions of the entorhinal cortex with different parts of the hippocampal longitudinal axis. Finally, our results provided the opportunity to perform new analyses of cross-species differences in cortical connectivity with the hippocampal memory system. In a further comparison between the rat, marmoset, macaque and human, we demonstrate that mammalian evolution has been associated with an increasingly dominating role of transmodal input compared with unimodal input to the hippocampal region and that unlike the unimodal cortical input, transmodal cortical input was selectively preserved. Importantly, these changes in connectivity cannot be attributed to the increase in brain size across species. Our findings define the anatomical constraints within which human mnemonic functions must operate and provide a comparative anatomical framework describing the evolutionary trajectory of human memory.



Out of Sight, Out of Mind: Differential Predictions of Subsequent Memory by Eye Gaze Patterns in Children and Adults

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Eye movements are implicated in the formation, retrieval, and reconstruction of memory. In adults, prolonged dwelling times are associated with enhanced memory recall. Additionally, gaze fixations during the encoding phase correlate with functional activity in the hippocampus. However, the extent to which eye gaze patterns predict subsequent memory across different time delays, and how these patterns differ between children and adults, remains uncertain. To address this, we examined whether eye-gaze patterns during the encoding of naturalistic scenes could predict memory performance in children aged 6 to 11 and in young adults after extended time delays. Furthermore, we explored how representational similarity in eye gaze patterns between the encoding and retrieval phases relates to subsequent memory performance in these two groups.

Orexineric modulation of chronic jet lag-induced deficits in mouse cognitive flexibility

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Cognitive flexibility and working memory are important executive functions mediated by the prefrontal cortex and can be impaired by circadian rhythm disturbances such as chronic jet lag (CJL) or shift work. In the present study, we used mice to investigate whether (1) simulated CJL impairs cognitive flexibility, (2) the orexin system is involved in such impairment, and (3) nasal administration of orexin A is able to reverse CJL-induced deficits in cognitive flexibility and working memory. Mice were exposed to either standard light-dark conditions or simulated CJL, consisting of series of advance time shifts. Experiment (1) investigated the effects of a mild CJL protocol on cognitive flexibility using the attentional set shifting task. Experiment (2) used a stronger CJL protocol and examined CJL effects on the orexin system utilizing cFOS and orexin immunohistochemistry. Experiment (3) tested whether nasal orexin application can rescue CJL-induced deficits in cognitive flexibility and working memory, the latter by measuring spontaneous alternation in the Y-maze. The present data show that CJL (1) impairs cognitive flexibility, and (2) reduces activity of orexin neurons in the lateral hypothalamus. (3) Nasal administration of orexin A rescued CJL-induced deficits in working memory and cognitive flexibility. These findings suggests that executive functions impairments by circadian rhythm disturbances such as CJL are caused by dysregulation of orexinergic input to the prefrontal cortex. Compensation of decreased orexinergic input by nasal administration of orexin A could be a potential therapy for CJL- or shift work-induced human deficits in executive functions.



Invited Talks Day 1



Memory consolidation and re-organization: Details, gist and schemas

Morris Moscovitch

Dept. of Psychology, University of Toronto, Canada

The presentation is organized around the natural history of a memory, and its representation in humans, from the initial experience to its retention and retrieval over different durations, from short to very long. Among the factors we'll examine are the effects of prior knowledge, attention and pre-encoding neural activity on different parts of the long axis of the hippocampus and neocortex, especially medial pre-frontal cortex, in memory encoding, retention and retrieval.

Medial temporal lobe memory subnetworks across time and dimensions

Magdalena Sauvage

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

³Center for Behavioral Brain Sciences (CBBS), Magdeburg, Germany

Why some of us remember events more clearly than others and why memory loses precision over time is a major focus in memory research. Using optogenetic manipulations and neuronal activity mapping, we show here that the recruitment of specific neuroanatomical pathways within the medial temporal lobe (MTL) of the brain might define the precision of the memory recalled over the lifespan (Lux et al, eLife, 2016; Atucha et al, Cell Rep. 2024). These pathways include the hippocampal subfields CA1, CA3 and the parahippocampal areas MEC, LEC, POR and PER. In addition, we report evidence for the existence of MTL subnetworks preferentially processing spatial or non-spatial information for which the synchronization of CA3 neuronal activity with CA1 theta oscillations during memory recall plays an important role. (Nakamura et al, J. Neurosc. 2013; Beer and Vavra, Plos Biol. 2018; Ku et al., Cell Rep., 2024).



The hippocampal contribution to rapid neocortical learning

Svenja Brodt

Max Planck Institute for Biological Cybernetics, Tübingen, Germany

Recent evidence suggests that there are conditions under which the neocortex can establish declarative memory trace much more rapidly than traditionally assumed by systems consolidation theories. Our research aims to better understand these conditions by combining functional and diffusion-weighted MRI. In a recent study, we investigated human memory formation of unfamiliar abstract visual stimuli and found evidence for rapid neocortical memory traces for semantic as well as episodic information, most strikingly a concept representation in early visual cortex. In this talk, I will discuss the contribution of the hippocampus to these rapidly emerging neocortical memories.



Invited Talks Day 2



Dissociations and associations between pattern separation and statistical learning

Stefan Köhler

Department of Psychology & Western Centre for Brain and Mind, University of Western Ontario, London, Ontario, Canada

To function effectively in daily life, we must be able to discriminate between similar events as well generalize across these events. For example, we must discriminate when trying to remember where we parked our car this morning rather than yesterday. And we must generalize across experiences from multiple days in order to realize that one part of the parking lot tends to have more empty spots than another. Pattern separation (the creation of distinct representations of similar inputs) and statistical learning (the rapid extraction of regularities across multiple inputs) are two processes that may support these distinct functional roles in human learning and memory. Computational modeling suggests that both processes rely on hippocampal functioning. At present, however, there is limited research that has directly compared behavioural expression of pattern separation versus statistical learning and corresponding neural mechanisms. Moreover, neural data for a role of the hippocampus in extracting statistical regularities in the auditory modality is scarce. To shed light on these issues, I will describe evidence from a single-case study in an individual with a highly selective hippocampal lesion and from a comparative study in younger and older adults. We employed behavioural tasks that were optimized for comparison of pattern separation and statistical learning with speech-based material. We found that behavioural markers of pattern separation are impaired following dentate-gyrus damage as well as in healthy aging; by contrast the implicit expression of statistical learning remained intact. Associations between the two processes emerged when behavioural expression of knowledge required the explicit retrieval of high-fidelity representations. Overall, these findings point to higher vulnerability of pattern separation as compared to statistical learning in behaviour. Finally, I will present data from an ongoing study with intracranial sEEG recordings that directly addresses whether the hippocampus plays a role in statistical learning in our behavioural paradigm.

Local circuit mechanisms in the dentate gyrus controlling fear memory strength and specificity

Oliver Stork

Department of Genetics and Molecular Neurobiology, Institute of Biology, and Center of Behavioral Brain Sciences, Otto-von-Guericke University Magdeburg, Germany

The dentate gyrus (DG), frequently regarded to as gate to the hippocampus, is critical for the formation of episodic memories integrating multimodal sensory input and computing pattern separation. The DG is also known as a key site for the emotional modulation of memory formation, with a peculiar involvement of its dorsal portion in integrating cognitive and emotional aspects of behavior.

We have investigated, in mice, the local circuit mechanisms in the DG that are involved in these processes, using contextual fear conditioning as a model of memory formation and stress-induced pathology. In our studies, Neuropeptide Y (NPY) has emerged as a key transmitter that modulates the storage of fear memories and engram formation in the DG. Most NPY in the DG hilus is expressed in so-called hilar perforant path associated neurons, which we found to be involved both in salience encoding and in the generalization of remote fear memories. We observed that NPY is profoundly decaying in the ageing DG in a sex-dependent manner, along with the decay of perforant path-induced long-term potentiation. Reduced NPY function not only mediates ageing-induced functional decline, but moreover enhances vulnerability to behavioral pathology in a rodent model of post-traumatic stress disorder. While the DG is dispensable for a mere retrieval of contextual fear memories, it showed a remarkable lateralization concerning the induction of synaptic plasticity and engram formation following fear conditioning, facilitating induction of network oscillations in CA3 and its computation of context similarity. We therefore propose that the local hilar circuitry via NPY shapes memory ensemble formation in the DG to encode context specificity and context salience, and thus may lend itself to counteract stress- and aging-induced functional loss in hippocampal function. In fact, replenishing NPY recovered plasticity in ageing mice and the specificity of generalized remote fear memories in our hands could be recovered by exposure to a reminder training along with an increased memory representation as cellular engram.



Crashing the Gates of Memory

Charan Ranganath

University of California, Dept. of Psychology, Davis, USA

Traditional theories of memory implicitly assume that memories are formed and retrieved constantly, and recordings of place cells are likewise often interpreted to suggest a continuous encoding of spatial contexts in the hippocampus. Evidence for this view, however, has largely come from humans who are asked to encode lists of unpredictable, arbitrarily organized lists, or in animals that have little to no prior knowledge about the contexts in which they are studied. However, most of the details of real world events are forgotten, and we know that neuromodulators prioritize encoding and retention of information that is motivationally significant, novel, or surprising. Thus, it is likely that motivation and prior knowledge have a powerful influence that shapes, or even gates the episodic memory encoding and retrieval.

In this talk, I will present results from computational simulations and recordings suggesting that entorhinal layer IIa cells (including grid cells) play a role in pattern separation, rather than systematic maps. I will then present work from fMRI and intracranial EEG studies showing that the hippocampus seems to interact with neocortical networks in the service of episodic and spatial memory primarily at significant moments such as event boundaries, start points, and goal locations. Moreover, cortico-hippocampal processing during the predictable elements of experience appear to be counterproductive for memory. These findings potentially suggest a radical reinterpretation of findings from studies of place cells in rats and fMRI and intracranial recordings of list memory in humans, and point to the importance of functional interactions (rather than informational handoffs) between the neocortex and hippocampus.



Subcortical modulation of hippocampal memory

Thomas McHugh

Riken Center for Brain Science, Japan

The hippocampus plays a crucial role in episodic memory; the who, what, where memories that define our lives. In the rodent, its well-defined anatomy and physiology make the structure an ideal model system; amenable to circuit manipulations and observations designed to test hypotheses concerning how memories are formed, consolidated and used. Here I will present our recent work in mice which combines anatomical characterization, genetic intervention and in vivo recording to address how non-cononical hippocampal output can influence neuromodulation, circuit dynamics and memory. Specifically, I will focus on the CA2 region and how its activity can impact both local and distal circuits, including our identification and characterization of a novel descending glutamatergic projection from CA2 pyramidal cells to PV+ neurons in the medial septum that can regulate cholinergic tone and bidirectionally modify both the encoding and consolidation of hippocampal dependent memory.



The medial septum - cell-type diversity, circuit connectivity and relevance for behavior

Stefan Remy

Department of Cellular Neuroscience, Leibniz Institute for Neurobiology, Magdeburg, Germany.
German Center for Neurodegenerative Diseases (DZNE), Magdeburg, Germany,
Center for Behavioral Brain Sciences (CBBS), Magdeburg, Germany,
German Center for Mental Health (DZGP), partner site Halle-Jena-Magdeburg, Magdeburg, Germany,

The medial septum and the diagonal band of Broca (MSDB) is a strongly connected subcortical brain region. Among others, it receives inputs from the hippocampus, the amygdala, the supra-mammillary nuclei, the thalamus and the ventral tegmental area and projects to the entire hippocampal formation, the amygdala, the ventral tegmental area and the hypothalamus. It can be regarded as a pivotal node within an ascending pathway from the brainstem and the hypothalamus that conveys sensory and motor information to the limbic system. Moreover, we and others have shown that it is directly involved in behavioural execution. In my talk, I will present new data on the cell type diversity within the MSDB and on how distinct subpopulation of MSDB neurons drive exploration and motor behavior, while controlling activity patterns in the hippocampal formation, such as theta oscillations, that are aligned with the specific behaviors.

'Learning to be good' engages the dorsal hippocampus: focus on emotional contagion and helping behavior

Sanja Mikulovic

Leibniz Institute for Neurobiology (LIN), Magdeburg, Germany

Emotional contagion, the capacity to internally simulate another's emotional state, plays a crucial role in modulating prosocial behaviors. This includes rescue behaviors, wherein individuals in a safe context intervene to release a trapped conspecific from an aversive context. However, little is known about the neural mechanisms underlying the learning of these behaviors or more generally about the mechanisms involved in learning prosocial behaviors. This study explores the involvement of the dorsal hippocampus (dHPC), associated with contextual learning, in emotionally charged helping behavior in mice. Male and female mice were trained to rescue a distressed familiar conspecific of the same sex by opening a door under two conditions: the trapped mouse in a dry or flooded chamber. Cold water in the flooded chamber induced higher emotional arousal in the victim, resulting in reduced latency for rescuing by the helper. Silencing the dHPC prior to sessions significantly impaired rescue behavior, increasing latency and reducing the total number of helpers. C-fos expression after dHPC silencing suggested that emotional processing related areas were less engaged during the task. A decoder model, trained with 1-p calcium imaging and manually annotated behavioral data, revealed that ~10% of dHPC cells exhibited correlated activity with helping behavior, showing increased activity after the release of the victim. The number of task-related cells decreased over days. These findings suggest that the dHPC is engaged during learning of rescue behavior, hinting at a contextual or episode-like memory component in the acquisition of this behavior.



Invited Talks Day 3

REM and non-REM sleep antagonistically influence reactivation drift in the hippocampus

Jozsef Csicsvari

Institute of Science and Technology Austria, Klosterneuburg, Austria

Hippocampal reactivation of waking neuronal activity patterns in sleep is an important initial step for memory consolidation. For intermediate sleep duration (<5h), published work suggests relatively stable reactivation, albeit some studies indicated that reactivation is the strongest only within the first 30 min to 1 h of sleep. It is, however, unclear whether reactivated assemblies are static or whether they reorganize gradually over prolonged sleep. Here, we monitored the reactivation of CA1 assembly patterns over ~20 hours of sleep/rest periods using radiotelemetry recordings from at least 16 independently movable tetrodes. Before sleep, animals performed a goal-learning paradigm on a cheeseboard maze and recalled the goal locations after the prolonged sleep periods. We tested to what degree reactivated assembly patterns are similar to those seen before or after sleep. We found that they were initially (<5h) similar to those seen before sleep, but later, they gradually transformed and started to resemble those seen in the subsequent recall session. Periods of rapid eye movement (REM) sleep and non-REM (NREM) sleep had antagonistically influenced this reactivation drift: NREM periods accelerated the assembly drift, while REM had an opposing influence, moving similarity backward towards pre-sleep patterns. Only rate-changing pyramidal cells contributed to the drift, while stable firing rate cells maintained unaltered reactivation patterns. Our data suggest that during prolonged sleep periods, reactivated spatial assemblies reorganize. Such a reactivation drift might contribute to daily cognitive map changes or to encoding new learning situations.

Reactivation drives memory consolidation during wakefulness and sleep

Monika Schönauer

University of Freiburg, Department of Psychology, Neuropsychology, Freiburg, Germany

New memories are initially labile and have to be consolidated into stable long-term representations. Current theories assume that this is supported by a shift in the neural substrate that supports the memory, away from rapidly plastic hippocampal networks towards more stable representations in the neocortex. Rehearsal, i.e. repeated activation of the neural circuits that store a memory, is thought to crucially contribute to the formation of neocortical long-term memory representations. This may either be achieved by repeated study during wakefulness or by a covert reactivation of memory traces during offline periods, such as quiet rest or sleep.

We investigate memory consolidation in the human brain by non-invasive in-vivo imaging of functional brain activity (fMRI, EEG) and microstructural plasticity (DW-MRI). We demonstrate that active rehearsal of learning material during wakefulness can facilitate rapid systems consolidation, leading to an immediate formation of lasting memory engrams in the neocortex, even when participants study complex episodic narratives. These representations, observed in both brain activity and brain microstructure, satisfy general mnemonic criteria: They are long-term stable, drive behavior, and code the specific content of what has been learnt. Importantly, also offline periods, such as sleep, hold a crucial role in stabilizing memories. Using multivariate pattern analysis on brain imaging data, we show that humans spontaneously reprocess previously studied episodic narratives during sleep. This reactivation not only benefits memory retention, but is also reflected in the content of dreams. Online and offline reactivation may thus jointly contribute to forming lasting memories and shape the content of our conscious experiences not only during wakefulness, but also during sleep.

Novel unsupervised and remote visual memory assessments for disease-stage specific detection, prognosis and monitoring of cognitive impairment in Alzheimer's disease

David Berron

German Center for Neurodegenerative Diseases (DZNE), Leipziger Straße 44, Magdeburg, Germany
Clinical Memory Research Unit, Department of Clinical Sciences Malmö, Lund University, Sweden

Traditional pen-and-paper neuropsychological assessments have originally not been developed for Alzheimer's disease and are thus neither sensitive to subtle cognitive changes in the earliest stages of Alzheimer's disease (AD) nor to cognitive change over time, limiting their use for early detection, prognosis and monitoring of cognitive performance in clinical trials. Digital visual memory assessments via mobile devices that incorporate recent knowledge on the spatio-temporal distribution of Alzheimer's disease pathology have the potential to complement and facilitate cognitive assessment in clinical and research settings.

Here we used three remote and unsupervised digital visual memory tasks – the Mnemonic Discrimination task for Objects and Scenes (MDT-OS), the Object-in-Room recall task (ORR) and the Complex Scene Recognition task (CSR) that all have been shown to differentially engage memory networks in the MTL and the neocortex. We investigated whether these remote and unsupervised digital memory assessments can predict and detect cognitive decline across several independent samples including cognitively unimpaired older adults, individuals with subjective cognitive decline and patients with mild cognitive impairment. Our results demonstrate the potential of novel visual memory assessments delivered via unsupervised digital memory assessments using smartphones for early detection and prognosis in AD and show that high frequency remote longitudinal monitoring is sensitive to changes in episodic memory in MCI patients. Together these results suggest that memory tests that rely on different parts of the episodic memory network can serve as disease-stage specific cognitive markers for AD.



Structuring experience in cognitive spaces

Christian Doeller

Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany

The fundamental question in cognitive neuroscience—what are the key coding principles of the brain enabling human thinking—still remains largely unanswered. Evidence from neurophysiology suggests that place and grid cells in the hippocampal-entorhinal system provide an internal spatial map, the brain’s SatNav—the most intriguing neuronal coding scheme outside the sensory system. Our framework is concerned with the key idea that this navigation system in the brain—potentially as a result of evolution—provides the blueprint for a neural metric underlying human cognition. Specifically, we propose that the brain maps experience in so-called ‘cognitive spaces’. In this talk, I will give an overview of our theoretical framework and experimental approach and will present show-case examples from our fMRI, MEG and virtual reality experiments identifying cognitive coding mechanisms in the hippocampal-entorhinal system and beyond.

Persistent firing in single cells support working memory and spatial representation

Motoharu Yoshida

Leibniz Institute for Neurobiology (LIN), Magdeburg, Germany
Deutsches Zentrum für Neurodegenerative Erkrankungen (DZNE), Magdeburg, Germany

Action potentials are fundamental units of neural computation underlying cognitive functions. It is generally believed that neurons respond with action potentials only during sufficiently large synaptic input. On the other hand, *in vitro* studies have been pointing out for many years that cholinergic neuromodulation enables individual neurons to persistently fire for tens of seconds triggered by a transient input, potentially serving as an element of memory. However, whether this ability of individual neurons to support persistent firing underlies *in vivo* neural activity and contributes to cognitive functions remains unclear. Here, we developed an *in vivo* model in which this ability of individual cells to support persistent firing was disrupted using knockdown of TRPC4 channels selectively in the hippocampus or the medial entorhinal cortex. I demonstrate that this manipulation significantly impaired spatial working memory performance and reduced persistent activity of neurons at certain phases of the task *in vivo*. I further demonstrate the link between this lack of sustained activity and spatial representation in these areas. These results challenge the generally accepted view of action potential generation and suggest that intrinsic cellular mechanism of persistent firing is essential for working memory and spatial representation.

The activity-regulated gene *Arc/Arg3.1* orchestrates a critical period in the development of learning, memory, and hippocampal networks

Ora Ohana

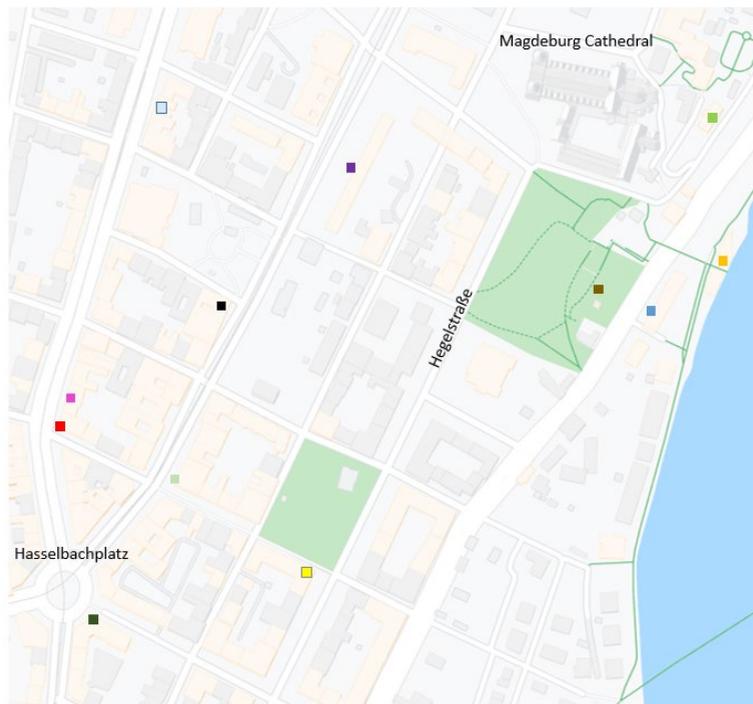
Center for Molecular Neurobiology Hamburg and Institute of Molecular and Cellular Cognition, Germany

The hippocampus is essential for learning and memory and spatial navigation in adult mammals. These higher brain functions emerge during early postnatal development and mature until early adulthood. The genetic and molecular factors underlying the maturation process remain largely unknown. In my talk, I will present our recent studies on the role of the activity-regulated and memory-linked gene *Arc/Arg3.1* in the maturation of hippocampal network activity, synaptic plasticity, and cognitive function. For this study, we generated conditional KO (cKO) mice in which *Arc/Arg3.1* was deleted during or after postnatal development. We used behavioral tests, biochemical analyses, *in vivo* and *in vitro* electrophysiology, and fMRI to assess spatial cognition, memory, and hippocampal network activity in adult *Arc/Arg3.1* cKO mice. We show that early postnatal expression of *Arc/Arg3.1* exerts a life-long influence on the microarchitecture of hippocampal circuitry, network oscillations, inter-areal connectivity, and ultimately, learning and memory. Our findings are congruent with the hypothesis that learning and memory undergo a critical period in development, akin to sensory critical periods.



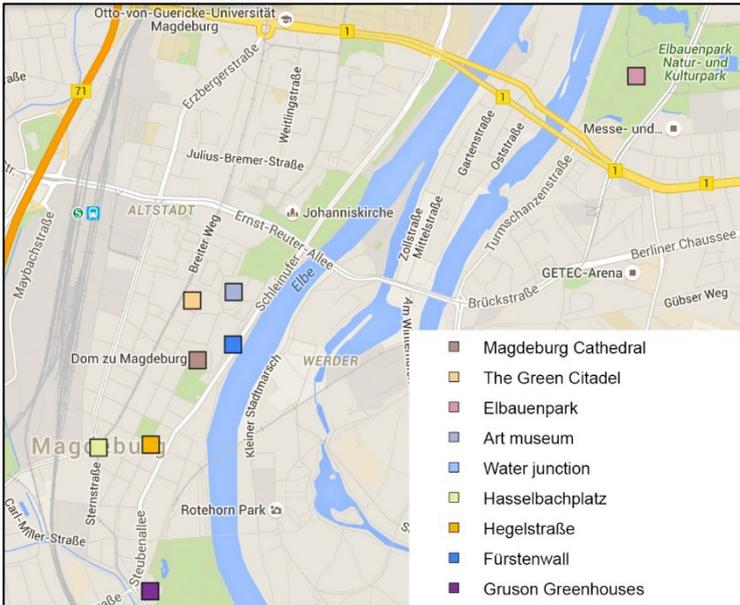
Recreational Information

Restaurants



■ Berner & Brown Tapas Bar	€€	■ Restaurant Balkan	€€
■ Toro Grosso	€€€	■ Indian Palace	€€
■ Culinaría	€€€	■ Thai Sawadee Restaurant	€€
■ Sakura	€€	■ Milchkuranstalt (Biergarten)	€
■ Kazoku Izakaya	€€	■ BOTANICA (vegan)	€€
■ Sen Viet BBQ & Soup	€€	■ HOF LIEFERANT	€€

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 Hundertwasser. 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 Millennium 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.