Invited Talks
Day 1

Semantic Memory and Multi-Trial learning

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Adapting to environmental changes is critical for our survival. The brain's ability to build up knowledge about the world that enables us to benefit from our previous experience has been a long-standing, central topic in psychology and neuroscience. However, research into the neurobiology underlying knowledge build-up and updating is now just beginning. In my lab we develop new rodent tasks (e.g. Object Space Task and the HexMaze) to tap into how animals' build-up knowledge from experiences. We also use one session learning tasks (e.g. watermaze) for translation applications in humans and rodents. We combine these tasks with electrophysiology, pharmacology, functional MRI and immediate early gene expression analysis to investigate how memories become long lasting and which role location specific plasticity and sleep has in the process. This approach has revealed surprising results. The hippocampus optimizes but is not necessary for multi-trial memory and the cortex is an independent, fast but adaptive learner. In our semi-naturalistic memory task setting, the 9x5m HexMaze, spatial memory and navigation persist without the hippocampus – only necessary for one-session learning and computations like sophisticated path optimization. These optimizations occur during sharp-wave ripple oscillations, when hippocampal and cortical circuits engage in a bidirectional exchange.

Rapid neocortical learning – systems memory consolidation or parallel encoding?

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Rapid neocortical learning – systems memory consolidation or parallel encoding?
Recent evidence suggests that there are conditions under which the neocortex can establish declarative memory traces much more rapidly than traditionally assumed by systems consolidation theories. My lab's aims to better understand these conditions in the human brain by identifying learning-induced changes in activation and microstructure with the help of functional, diffusion-weighted and quantitative MRI. In this talk, I will show how memory reactivation benefits neocortical memory formation across the cortical hierarchy, from early sensory to highest-order association cortex, and for different aspects of memory, from perceptual detail to concept formation. Finally, I will discuss the contribution of hippocampal activity to these rapidly emerging neocortical memories

Ultrafast fMRI for revealing information flow in the brain

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Functional MRI (fMRI) has transformed neuroscience, but it is still most often acquired with relatively low temporal resolution (TR ≈ 1–2 s). This provides ample information on *where* activity occurs, yet the coarse sampling makes it difficult to infer on dynamics and timing of activity across regions – which can be essential for understanding information flow through neural circuits. Here, we present ultrafast fMRI experiments in rodents at high magnetic field, that sample BOLD signals at tens of milliseconds resolution, thereby enabling direct estimation of BOLD timing parameters. These timings reveal ordered sequences of regional engagement following sensory stimulation, providing an in vivo readout of the circuit's neural information flow. We further show that BOLD timing offers unique sensitivity to aberrant circuitry in a model of visual plasticity. Furthermore, we demonstrate how ultrafast fMRI can provide insight into spontaneous activity: intrinsic oscillatory modes can be uncovered from resting-state data, providing a complementary view of spontaneous brain activity beyond static correlation maps. In addition, we show that canonical visual representations (e.g., retinotopy) are captured in ultrafast resting-state signals, and that layer-resolved ultrafast fMRI can separate feedforward from feedback components of processing, and reveal subcortical plasticity eg following ischemia. Finally, we discuss how advanced fMRI paradigms, validated with electrophysiology and behavioral measurements, can be leveraged to dissect the mechanisms underlying the continuity illusion. Our work suggests promising vistas for future applications of ultrafast fMRI in health and disease.

Invited Talks
Day 2

Evolutionary preserved connectional patterns in the cortico-entorhino-hippocampal network

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An often-used model for episodic memory is strongly anchored in splitting the entorhinal cortex into medial and lateral subdivisions and their respective connectivity patterns along the transverse and radial axes of the hippocampus. Functional studies, partially complemented by patterns of cortical connectivity, provided arguments to present this 'Dual-Stream model' as handling spatial versus non-spatial streams or alternatively allocentric versus egocentric streams of information. This model has found support in a variety of species, though it is mainly based on rodent and to a lesser extent non-human primate data.

What has become 'neglected' is a previously described organizational principle of the mammalian entorhinal cortex into rostro-caudal band-like zones, based on intrinsic connectivity patterns associated with connections along the hippocampal long axis.

In my talk I will present data from a variety of different species, including humans, supporting this band-like organization into at least three parallel zones, leading to a revised anatomical blueprint, which has been remarkably preserved in mammalian phylogeny. This provides support for a more complex functional framework of the entorhinal-hippocampal circuitry**,** allowing for a more flexible view on hippocampal-dependent functions, particularly addressing the complexity of conscious memory as representing integrated factual, emotional and social aspects.

Entorhinal Cortex Subnetworks and Memory Recall Across the Lifespan

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The entorhinal cortex (EC) is among the first brain regions affected in Alzheimer's disease, and its functional connectivity with the hippocampus is altered during aging. The medial and lateral EC differentially process spatial and non-spatial information; however, their specific contributions to memory recall remain poorly understood. Moreover, it is still unclear how EC subregions contribute to memory recall across the lifespan, whether these dynamics differ from those of prefrontal cortical areas, and how they evolve over timescales relevant to human memory.

Our studies demonstrate that selective spatial and non-spatial dentate gyrus-dependent memory deficits can be traced to the innervation of distinct EC subregions, extending beyond the classical medial-versus-lateral EC distinction. Furthermore, longitudinal analyses of memory recall over one year in mice reveal a circuit-specific and time-dependent reconfiguration of cortico-entorhino-hippocampal networks. These findings identify the EC, alongside the prefrontal cortex, as a dynamic hub for remote memory recall.

Shared early impairments of medial entorhinal cortex function across distinct Alzheimer's disease etiologies

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The medial entorhinal cortex (MEC) harbors diverse spatially and object-tuned cell types essential for spatial coding and episodic memory, and is among the earliest regions affected in neurodegenerative diseases. Here, we examined how early neurodegeneration alters MEC cellular coding, network dynamics, and behavior in two Alzheimer mouse models of distinct etiology. Specifically, we performed in vivo electrophysiology, immunohistochemistry and behavioral assays in models that reflect the manifestation of a tauopathy and amyloidopathy, respectively, to identify common impairments. In both models, the earliest deficits manifested as instability of spatial context representations at the cellular and behavioral level. These impairments preceded model-specific disruptions in grid cell coding and altered theta oscillations. We further identified reduced parvalbumin-positive (PV+) septal projections as a likely contributor to MEC dysfunction. In contrast, object-vector coding remained intact, highlighting spatial context instability as an early marker of MEC impairment.

Representational Dynamics in the Hippocampus and Medial Prefrontal Cortex during Spatial Learning

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We recorded neural activity from hippocampal area CA1 and the medial prefrontal cortex (mPFC) in rats performing two spatial tasks on a radial eight-arm maze: a combined spatial reference and working memory task and a cue-guided association task. Using a combination of tetrodes and Neuropixel probes, we tracked individual cell activity and population-level manifolds across multiple days of learning and task execution. The results described below apply to both paradigms.

At the single-cell level, we identified a form of flickering in which neurons transitioned between discrete alternative firing fields across trials. In CA1, this flickering was primarily learning-induced; as animals reached task proficiency, these cells transitioned systematically toward stable, single-field representations. In contrast, mPFC cells exhibited persistent, random flickering that remained uncoordinated across the population and did not diminish with increased task familiarity.

Population-level manifold analysis using UMAP further differentiated these regional dynamics. In CA1, manifolds primarily encoded spatial variables, such as arm identity and position. In the mPFC, however, manifolds better differentiated task-relevant variables, including relative arm location and trial progression. However, as animals gained experience, mPFC representations of trial progression weakened, while spatial decoding improved, suggesting a shift in representational priority.

These results indicate that representational change in the hippocampus and mPFC follows distinct trajectories. While the hippocampus undergoes a structured stabilization of spatial maps during learning, the mPFC maintains a persistent flexibility. This divergence suggests that the mPFC may prioritize the encoding of dynamic task rules over the stable environmental representation maintained by the hippocampus.

Active single-cell memory

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The prevailing view holds that neurons operate primarily as input-output units, becoming active only when they receive sufficiently strong synaptic inputs from other neurons. On the other hand, *in vitro* experiments have long indicated that neurons can maintain their activity through intrinsic cellular mechanisms under certain neuromodulatory conditions, thereby acting as memory elements. However, whether individual neurons act as memory elements and support cognition *in vivo* remains unclear. In my talk, I will first present the cellular and molecular mechanisms of active single-cell memory—*intrinsic persistent firing*—in hippocampal and entorhinal neurons, as evidenced by *in vitro* electrophysiological recordings. I will then discuss the role of intrinsic persistent firing in the maintenance of hippocampal and entorhinal spatial representations, and its contribution to spatial working memory performance in behaving mice. These findings redefine neurons as active contributors to information retention, beyond their traditional role as passive input-output units and potentially reshaping our understanding of neural computation.

Medial septal circuits in exploratory locomotion: cellular correlates of brain state changes

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Transitions between rest, locomotion, sleep, and other behaviors are accompanied by distinct neuronal activity patterns, or brain states, that can be observed in network dynamics. The medial septum and diagonal band of Broca (MSDB) are key regulators of hippocampal and cortical activity and are thought to play an important role in shaping such state transitions. However, the functional contribution of specific MSDB cell types and the integration of locomotion-related input by individual hippocampal and MSDB neurons remains incompletely understood.

Using single-cell RNA sequencing, we characterized the cellular heterogeneity of the MSDB and identified novel genetic subclusters and transcriptional gradients that provide new molecular access points for circuit dissection. We further identified a glutamatergic projection from the MSDB to the ventral tegmental area (VTA) that is critically involved in exploratory locomotion.

Combining circuit-specific manipulation with machine-learning-based behavioral analysis, we show that activation of this pathway selectively promotes exploratory behaviors such as sniffing, whisking, and rearing. In addition, the circuit directly targets distinct VTA neuron populations, including dopaminergic neurons.

These findings link molecularly defined MSDB cell types to behavioral state transitions and brain-state dynamics, providing new insight into how basal forebrain circuits organize behavior.

Invited Talks
Day 3

Development and lesion-induced plasticity in the primate medial temporal lobe

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The hippocampal formation, often considered as one functional unit, is the central component of a large brain network essential for the processing of spatial and episodic memories. Yet, it is now well established that different hippocampal structures and circuits contribute to different types of information processing. In the first part of my talk, I will discuss the differential postnatal maturation of distinct hippocampal regions and layers and putative functional circuits from a global perspective that takes into consideration the work of many other researchers who have contributed to our current understanding of various hippocampal functions. Both neuroanatomical and molecular data suggest that the differential maturation of distinct hippocampal circuits underlie the emergence and maturation of different hippocampus-dependent memory processes, ultimately leading to the emergence of episodic memory concomitant with the maturation of all hippocampal circuits.

In the second part of my talk, I will discuss experimental studies on the plasticity of medial temporal lobe structures following restricted hippocampal lesions. I will show that populations of immature neurons found in the entorhinal and perirhinal cortices are differentially affected by hippocampal lesion occurring shortly after birth or in adulthood. In neonate-lesioned monkeys, the number of immature neurons in the entorhinal and perirhinal cortices was generally higher than in controls. The number of mature neurons was also higher in layer III of area Er of neonate-lesioned monkeys, but no differences were found in layer II of area 36. In adult-lesioned monkeys, the number of immature neurons in the entorhinal cortex was lower than in controls but did not differ from controls in the perirhinal cortex. The number of mature neurons in layer III of area Er did not differ from controls, but the number of small, mature neurons in layer II of area 36 was lower than in controls. In sum, hippocampal lesions impacted populations of mature and immature neurons in discrete regions and layers of the entorhinal and perirhinal cortices, which are interconnected with the amygdala and provide major cortical inputs to the hippocampus. These structural changes may contribute to some functional recovery following hippocampal injury in an age-dependent manner.

Sleep-dependent memory formation in the developing brain

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Early life is characterized by remarkable learning capacities, yet memories formed during infancy often appear inaccessible later in life, a phenomenon commonly referred to as infantile amnesia. Increasing evidence from rodent research suggests that these early experiences are not simply forgotten but can persist in latent forms and influence learning and behavior in adulthood. Understanding how such memories are formed and stabilized during early development remains a central challenge in memory research.
I will present findings from studies in rats investigating how sleep supports memory formation during infancy. The developing brain differs substantially from the adult brain in both neural organization and sleep architecture. In particular, early life is characterized by a high proportion of REM sleep and immature coordination between hippocampal and cortical networks. These developmental features raise the possibility that the mechanisms supporting sleep-dependent memory consolidation during infancy differ from those described in adults.
Using behavioral paradigms assessing spatial and schema-like memory together with electrophysiological recordings, our work examines how hippocampal and medial prefrontal networks interact with sleep dynamics across development. The findings suggest that infancy represents a distinct state of the memory system, in which sleep plays a critical role in shaping how early experiences are processed and stored over the long term.

Neurobiological mechanisms underlying the developmental emergence of episodic memory

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Memories for events (i.e., episodic memories) formed in early development differ from those in adulthood in at least two regards. First, these memories tend to be less precise (i.e., infantile generalization). Second, they tend to be rapidly forgotten (i.e., infantile amnesia). My talk will focus on the neurobiological mechanisms that account for these different operating characteristics of episodic memory in the developing brain. With respect to infantile generalization, our studies have shown that maturation of inhibitory hippocampal microcircuits is necessary for the formation of adult-like, precise memories for events. With respect to infantile amnesia, our studies have revealed that developmentally-regulated myelination of prefrontal cortical circuits is necessary for the formation of adult-like, enduring event memories. Similar to developing sensory systems—where cortical circuit refinement occurs during defined windows of heightened brain plasticity known as critical periods—our work suggests that similar refinement of hippocampal and prefrontal cortical circuits underlies the emergence of adult-like episodic memory function.

Are medial temporal lobe subregions "specialized" for particular classes of visual stimuli?

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A long-standing question in cognitive neuroscience concerns whether medial temporal lobe (MTL) subregions are specialized for processing particular classes of visual stimuli. Influential accounts have proposed category-selective roles for MTL structures—for example, that perirhinal cortex supports object representations whereas parahippocampal cortex preferentially processes scenes and spatial contexts. However, alternative frameworks suggest that functional organization within the MTL may instead reflect differences in representational or integrative demands rather than strict stimulus categories.

In this talk, I will review evidence bearing on this debate. First, I will present findings from an fMRI study examining associative inference, a form of memory that requires integrating information across overlapping episodes. Although several MTL subregions exhibited scene sensitivity in an independent functional localizer, these same regions were recruited during encoding to support associative inference even when episodes were linked by faces. These findings suggest that regions often characterized as scene-selective may contribute more generally to integrating disparate elements of experience.

I will then present recent work from my laboratory examining visual discrimination performance in individuals with mild cognitive impairment. Behavioral, structural, and functional measures indicate that perceptual discrimination deficits emerge early along the continuum from healthy aging to cognitive impairment and relate to interactions between perirhinal cortex integrity and anterior temporal network functional connectivity.

Together, these findings challenge strictly category-based interpretations of MTL function and instead support a view in which MTL subregions contribute to distinct representational computations that are recruited flexibly depending on task demands.

Role of adult-born dentate neurons in successful cognitive aging

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Aging is accompanied by a decline in memory but these alterations are extremely variable between subjects: some individuals preserve cognitive abilities (Resilient, Res), whereas others show a clear substantial cognitive decline incapacitating in everyday life (Vulnerable, Vul). These inter-individual differences have also been described in rodents especially in tasks measuring spatial memory abilities. We believe that understanding the processes underlying such individual differences is a key step to predict, prevent or slow age-related cognitive disorders.
Spatial memory processes depend upon the hippocampus and more particularly upon the creation of new neurons in the dentate gyrus. Aging is associated with an exhaustion of the pool of new neurons and their delayed maturation. However, it remains unknown if aging influences the integration and role of adult-born hippocampal neurons (ABNs) generated early in adult life and whether this is influenced by the cognitive status of the individuals. We will show that long-lived ABNs support successful cognitive aging by preserving their synaptic inputs onto the proximal segments of their dendrites, and that these proximal synaptic sites also demonstrate a maintenance of their mitochondrial homeostasis. Furthermore, by-passing the reduced inputs of ABNs in vulnerable rats through direct optogenetic stimulation successfully improved their memory abilities. Overall, our data indicate not only the rate of neurogenesis but also the that the maintenance of long-lived ABNs integration within the neuronal network is essential for successful cognitive aging, highlighting their potential as a therapeutic target for restoring cognitive functions in old age.

Medial temporal lobe network changes in aging and early Alzheimer's disease

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The medial temporal lobe (MTL) is among the earliest brain regions affected by aging and Alzheimer's disease, including the early accumulation of neurofibrillary tau tangles in the superficial layers of the entorhinal cortex. Facilitated by amyloid-related hyperactivity, tau is thought to propagate along functional pathways to the neocortex, with the posteromedial cortex (retrosplenial cortex, precuneus) among the earliest affected regions. Functional MRI studies in older adults at risk for Alzheimer's disease often report increased hippocampal activity or connectivity, and it remains debated whether this reflects pathological hyperexcitability or compensatory network responses. To investigate how aging and early Alzheimer's pathology affect connectivity within the MTL and between the MTL and posteromedial regions, longitudinal multimodal imaging studies including Alzheimer's biomarkers are essential.
In this talk, I will first present longitudinal 3T functional MRI findings from the Prevent-AD cohort examining how MTL connectivity changes over time in cognitively normal older adults at increased risk for Alzheimer's disease. These analyses reveal differential trajectories along the hippocampal long axis, with aging and Alzheimer's-related processes associated with distinct changes in connectivity of the anterior versus posterior hippocampus with the posteromedial cortex. In healthy aging, functional connectivity strength between the posterior hippocampus and the precuneus, as well as within the posteromedial cortex, decreased and was associated with poorer longitudinal episodic memory performance. In contrast, increased connectivity between the anterior hippocampus and the superior precuneus was related to higher baseline Alzheimer's disease pathology. Associations between hippocampal connectivity and episodic memory were further moderated by APOE4 genotype, suggesting that genetic risk shapes the relationship between network organization and memory performance. To probe local circuit alterations within the MTL in relation to tau pathology, I will then present ultra–high-field 7T fMRI data in cognitively normal older adults that map layer-specific intrinsic functional connectivity within the MTL circuit. Specifically, we examine how layer- and subfield-specific connectivity relates to MTL tau burden and whether these associations are moderated by APOE4 genotype or astroglial reactivity.

Together, our studies suggest that aging and Alzheimer's pathology are associated with specific alterations in functional connectivity within MTL subregions and between the MTL and posteromedial cortical regions supporting episodic memory. Early alterations may reflect a complex interplay between hyperactivity, tau propagation along memory networks, and potentially compensatory connectivity changes that transiently support memory function in the face of emerging pathology.