iNAV 2024 Poster Abstracts

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1. OPTOGENETICALLY DE-ENERGIZED MITOCHONDRIA OF PARVALBUMIN-POSITIVE INTERNEURONS IMPAIR SPATIAL PROPERTIES WITHIN THE CA1 REGION OF THE HIPPOCAMPUS

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Parvalbumin-positive (PV+) interneurons within the hippocampal system are crucial for maintaining spatial memory functions that are otherwise impaired in neurodegenerative diseases. To maintain such an extensive control, PV+ interneurons require a high energy demand, which requires highly functional mitochondria. Previous studies have shown dysregulations of mitochondria within the hippocampus are apparent early on in cases of Alzheimer's Disease (AD), even preceding the major pathological hallmarks: tau aggregation, amyloid-beta plaques, and impairments in memory. Optogenetic tools have been instrumental in discovering and understanding the function of neurons within various different brain networks. Recently developed methods have expanded their use to allow for light-control of intracellular organelles, such as mitochondria. To understand how the mitochondria of PV+ interneurons contribute to learning and memory functions regulated by the hippocampal circuit, we utilized a previously developed optogenetic construct, mitoChR2, which targets the inner mitochondrial membrane. In the presence of light, the channel opens and causes a disruption of the proton motive force that drives ATP production, thus decreasing the amount of ATP produced, in essence "de-energizing" mitochondria. Through the use of this technique in conjunction with performing electrophysiological recordings in freely moving PV-cre mice, we discovered "de-energized" mitochondria impaired the firing activity of interneurons and consequentially altered spatial properties of place cells within the hippocampus during exploration of a familiar environment. Our findings emphasize the importance of mitochondria in learning and memory mechanisms and suggest mitochondria be considered for potential therapeutic targets for the treatment of AD.

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2. THE ENTORHINAL CORTEX'S PHASE CODE FOR NAVIGATION

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Grid cells in medial entorhinal cortex not only show spatially organized firing but also systematic phase advances and delays with respect to the population's multi-unit activity (MUA), which exhibits regular peaks every 120 milliseconds (theta-rhythm). Based on an analysis of 483 grid cells from Gardner et al. (2023), cells' phase- and firing-patterns fall into different classes. Conjunctive grid cells that are tuned both to head direction and spatial location tend to be phase-locked to the MUA. Other grid cells fire 180 degrees out of phase with the MUA.
Most grid cells, though, harbor a hidden head-direction signal in the temporal phase relative to the MUA. These cells often fire rapid bursts of spikes whose timing is a function of both head direction and spatial position, thereby multiplexing body-centered and world-centered information. The ensemble activity, measured in terms of the temporal phases, spans a 3-torus composed of two loops for the spatial coordinates and one loop for the head direction.
By exploiting dihedral symmetries, I show how an ideal observer can decode these temporal phases.

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3. MODERATING EFFECTS OF SPATIAL NAVIGATION TASK VARIATIONS: META-ANALYSIS ON MILD COGNITIVE IMPAIRMENT.

1. Dorota Kossowska-Kuhn, Florida State University 2. Gillian Gouveia, Florida State University
3. Dr. Neil Charness, Florida State University

Background: Dementia exerts a significant global impact on societies and individuals. Spatial disorientation emerges as one of the initial symptoms of Alzheimer's Disease (AD) (Coughlan et al., 2018). In our Meta-analysis on spatial navigation in Mild Cognitive Impairment (MCI) we obtained the standardized mean difference (Hedge's g) between this population and cognitively healthy older adults at the level of g = .88, which corresponds to the large effect size.
Methods: The potential moderators such as year of study publication, country of study, age of participants in each population, gender, education, forms of test administration (i.e., real-world, virtual reality), type of measure (time, accuracy), type of task (i.e., A Maze, Environment Navigation, Money Road Map Test) were coded for moderator analysis.
Results: Moderator analysis for 125 effect sizes across 47 studies, involving 2916 participants (1415 with MCI, 1501 cognitively healthy older adults) revealed that both age and the type of task were statistically significant ($p < .05$).
Conclusion: Further discussion on the definition of spatial navigation skills is essential to reach a consensus regarding the tasks used for assessments. Given the potential role of spatial navigation as an early marker of dementia, the significance of understanding this complex skill is paramount.

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4. CONJUNCTIVE ENCODING IN HUMAN PLACE AND TIME CELLS AND THEIR RELATION TO SPATIAL MEMORY

Thomas Donoghue, Sandra Maesta Pereira, Salman E Qasim, Ansh Patel, Habiba Azab, Elliot H Smith, Raissa Mathura, John Myers, Adrish Anand, Joshua Adkinson, Tyler S Davis, Hernan G Rey, John D Rolston, Timothy EJ Behrens, Matt Botvinick, Sameer A Sheth, Joshua Jacobs

To navigate a dynamic world, the brain must be able to keep track of the 'when' and 'where' of actions in the world, as well as be able to integrate these information streams together to plan future actions. Work in animal models has demonstrated that single-neurons, especially in the medial temporal lobe (MTL), can encode place and time, as well as conjunctive encoding of such information – providing a potential mechanism for encoding this information as required for navigating complex environments. In this work, we extend this work into the human brain, examining single-unit responses collected from the MTL and surrounding regions of neurosurgical patients with implanted microwires. Patients (n=23) completed a computer-based virtual navigation task, including navigation decisions (alternating directions across subsequent trials at a choice point), as well as a spatial memory component in which subjects learn and then recall specified locations. In this data, we first replicate that we find single neurons in the human brain that encode place or time, with firing rates relating to subjects' virtual spatial position or elapsed time during stationary periods. We then looked for conjunctive encodings (or 'splitter cells'), finding novel results whereby single neurons in the human brain encode a conjunctive representation of multiple features, including for current location + future turn direction and current time + future turn direction. Finally, we analyzed the relationship between conjunctive encodings, neural responses to the chest-encounter events, and behavioral performance on the memory component of the task (computed as the distance error between response and true locations), finding that single-neuron activity related to behavioral performance on the task. Overall, our results serve to further establish conjunctive encoding in the human brain altogether contributing to the scientific understanding of how we navigate through space and time.

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5. HIPPOCAMPAL RIPPLES FACILITATE REPRESENTATION LEARNING AND INFERENCE

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While hippocampal ripples and replays have been implicated in the construction of cognitive maps of physical space in rodent literature, their role in humans in non-spatial spaces is less clear. Human replay research relies on decoding processes, which complicates linking findings to the dynamics of region-specific brain computations, such as the burst-like occurrences of hippocampal ripples. Here, stereo electroencephalography (sEEG) recordings were obtained from 38 epileptic patients. Subjects first learned the ranks of two feature dimensions by adjacent pairs, followed by a 5-minute rest, after which they were asked to perform inference on compounds composed of these feature objects. Across all subjects, there were 181 contacts in the hippocampus, 92 contacts in the EC, and 3136 contacts in the neocortical area, with 877 contacts in the DMN. During learning, we observed that hippocampal ripples integrate discrete experiences into structured sequences at the inter-trial interval, increasing with learning experiences and predicting feature inference performance. In subsequent rest periods, hippocampal ripple activity also increased, facilitating the formation of map representations. Notably, a significant grid-like code was detected in the theta band (3-7 Hz) of both the EC and the mPFC, representing the 2D discrete space. The strength of grid code was also positively correlated with hippocampal ripple activity during rest. Intriguingly, the hippocampus spontaneously dialogue with high gamma activity in the DMN, especially the mPFC, during rest periods. This dialogue, associated with task-related experiences, predicts subsequent relational inference performance on the compounds. In summary, our study elucidates the role of human hippocampal ripples in organizing discrete experiences into coherent structures, essential for the representation of cognitive maps in discrete spaces. This process is characterized by complex interactions with the DMN, especially the mPFC.

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6. HIPPOCAMPAL RIPPLE-ALIGNED MEDIAL PREFRONTAL ACTIVITY UNDERLIES COMPOSITIONAL INFERENCE

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The infinite use of finite means is at the core of biological intelligence. Our recent work designed a series of Lego-like problems that required the use of limited basic building blocks to construct different silhouettes, revealing that the hippocampal-prefrontal circuit supports compositional computation. This means the neural representation of a silhouette can be derived by adding and subtracting representations of related building blocks (Schwartenbeck et al., 2023). In other words, it is compositional if it can be represented by linear combinations of basic building blocks with specific relational configurations (e.g., placing one building block above another).
Utilizing stereo electroencephalography (sEEG) recordings in humans, this study further explores how hippocampal ripple and its associated neocortical activity (high gamma, 80~140 Hz) perform compositional inference. A total of 28 epileptic patients participated in this study, with 149 contacts in the hippocampus and 1,905 contacts in the neocortex.
Results showed that hippocampal ripple and ripple-aligned dmPFC activity, rather than vmPFC, represent relational configurations in silhouettes, suggesting that ripples build a bridge in the hippocampal-prefrontal circuit during compositional computation. We also observed that replay assembles building blocks according to the actual relational configurations of silhouettes. Importantly, the replay sequence varies as a function of ripple onset during inference, gradually converging on the correct relational configuration. The relationship between ripple onset and replay sequence is mediated by ripple-aligned mPFC activity, implying that hippocampal ripple coordinates with mPFC to facilitate replay in compositional computation. Together, our results highlight that coordinated interactions between hippocampal ripple and ripple-aligned mPFC activity constitute the computational cornerstone of compositional inference.

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7. REPLAY FLEXIBLY CONSTRUCTS TASK SPACE BASED ON CHANGING RULES

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The ability to adapt internal representations for changing rules is foundational to human flexible behavior. Previous studies have shown that through neural replay, past experiences can be

reorganized based on a learnt rule. However, it remains unclear how the internal representation of task space can be constructed entirely based on the rule and how it changes when the rule changes.
We designed a novel deductive inference task in a two-dimensional(2D) non-spatial space: 16 compounds arranged in a 4x4 grid. Importantly, subjects could only deduce the compounds rank from feature objects(one-rank difference) and the mappings from the features(two separate dimensions) to compounds. After acquiring this foundational knowledge, subjects were instructed to rest for 10 minutes. Subsequently, they performed deductive inferences solely on the compounds. Afterward, the ranking of feature objects was randomly altered, prompting a second rest period for the subjects to adapt to this rule change. Entire procedure was monitored using Magnetoencephalography(MEG).
There were 28 subjects completed the task. They were adept at zero-shot inference in both task spaces, with no behavioral differences observed between them. At the neural level, we observed replays of compound could represent a 2D map, but also multiple linear hierarchies, with no particular prioritization over the map. This directly contrasts with the replay results when gradually learning the 2D map(Ou et al. 2024). Notably, when feature rankings changed, the replay of changes in compound positions, rather than features, facilitated map updating. Furthermore, the greater the dissimilarity between the two maps—that is, the greater the necessity for updating—the more pronounced was the replay of compound position changes. These findings suggest that task spaces can be constructed and updated through replay, which are not tied to a single representation but are flexibly deployed in service of adaptive behavior.

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8. THE RELATIONSHIP BETWEEN GPS USE AND NAVIGATION ABILITIES: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Chiara Meneghetti, Department of General Psychology, University of Padova, Italy Francesca Pazzaglia, Department of General Psychology, University of Padova, Italy

In modern society, the widespread adoption of Global Positioning System (GPS) devices has become pervasive. Nevertheless, the influence of GPS use on individuals' navigation abilities remains poorly understood. We reviewed and meta-analyzed the available evidence on the associations between GPS use and navigation ability such as environmental knowledge, wayfinding, and sense of direction. The systematic review followed the PRISMA guidelines and was preregistered in the PROSPERO database (CRD42022378106). We searched the Web of Science, PsycInfo, and Scopus databases for experimental studies on GPS use and navigation abilities. We assessed the risk of bias using Joanna Briggs tools. Out of 907 articles, 23 studies met the inclusion criteria and were eligible for the review. The narrative synthesis showed negative associations between GPS use and performance in environmental knowledge and sense of direction measures. Moreover, a positive association emerged with wayfinding. When considering quantitative data, the results revealed a negative effect of GPS use on environmental knowledge ($r = -0.18$, 95% CI [−0.28, −0.08]) and sense of direction ($r = -0.25$, 95% CI [−0.39, −0.12]) and a positive but not significant effect on wayfinding ($r = 0.07$, 95% CI [−0.28, 0.41]). The current literature has methodological weaknesses that limit the quality of evidence, with 68% of the studies classified with a moderate to high risk of bias. Although evidence suggests that using GPS tools can have a negative impact on environmental knowledge and sense of direction but a limited effect on wayfinding, future studies should adopt standardized measurements and procedures to further confirm these results and delve more deeply into understanding how GPS could be used as an external aid to support navigation.

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9. DEVELOPING A COGNITIVE MAP FOR STRUCTURING AND ASSIMILATING KNOWLEDGE

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Structured knowledge, known as schema or cognitive map, is key to how we internally organize experiences. This study investigates its evolution from childhood to adulthood, a crucial process for the development of human intelligence. We examined 203 participants, aged 8 to 25 years, using magnetic resonance imaging (MRI). Our focus was on the maturing ability to infer unseen relationships using a cognitive map. Unbeknownst to the participants, objects were organized into a 2D map. Initially, participants were given piecemeal experiences of objects within each dimension. During the fMRI tasks, increasing cellular representation of cognitive map, grid-like pattern, was observed in the entorhinal cortex (EC), signaling schema development of the 2D map. Based on the schema, the medial prefrontal cortex (mPFC) started to represent distances within this map. These evolving neural representations are crucial for inferring unseen relationships. When new information was introduced, participants assimilated it by aligning with the existing grid pattern. As participants aged, the mPFC ability to encode distances between new and existing objects grows, aiding in making new inferences. The development of inference abilities was linked to the anatomical maturation of mPFC and EC, and their structural connections, particularly via the cingulum. These cognitive map measures also generalize to predict intelligence quotient. Together, our findings elucidate the neural underpinnings of cognitive map development and its significance in structuring and assimilating knowledge, a process vital for flexible behaviour.

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10. 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, our results associate different subregions of the entorhinal cortex with different parts of the hippocampal longitudinal axis and suggest that entorhinal cortex is a major convergence area of distributed cortical processing in humans. Finally, our results provided the opportunity to perform new analyses of the differences in cortical connectivity with the hippocampal memory system across species. 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 unimodal cortical input, transmodal cortical input to the hippocampal region was selectively preserved. Importantly, these changes in connectivity cannot be attributed to the increase in brain size across species. To conclude, 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.

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11. SPONTANEOUS EYE MOVEMENTS REFLECT THE REPRESENTATIONAL GEOMETRIES OF CONCEPTUAL SPACES

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Functional neuroimaging indicates that the human brain can represent the relational structure of concepts in memory using coding schemes typical of spatial navigation. Can we read out the internal representational geometries of conceptual spaces solely from human behavior? Here we report that their relational structure might be reflected in spontaneous eye movements.
We first asked participants to randomly generate numbers from 1 to 12, while we monitored their spontaneous gaze behavior with an eye-tracker. Left and right eye movements correlated with numerical differences between mentioned numbers, consistent with the left-right 1D geometry of the number space (mental number line): the smaller (or larger) the number, the more participants looked to the left (or right) of their visual field before mentioning it.
Then, participants randomly mentioned 12 colors, for which they had previously provided pairwise similarity judgments. We used these judgments to reconstruct subject-specific "color wheels" using multidimensional scaling and we observed that Euclidean distances between colors in these reconstructed spaces correlated with distances covered by bidimensional eye movements during the verbal fluency task: the closer two colors were in the color wheel, the smaller the distance between

their corresponding gaze fixation in visual space before they were mentioned, consistent with the 2D ring-like geometry of the color space.
Lastly, participants randomly generated animal names, for which the underlying representational geometry is complex and multidimensional. We observed that 1D horizontal eye movements correlated with low-dimensional similarity in a linguistic “frequency space”: the more similar (or different) the frequency values of two mentioned animals in language, the more participants looked to the left (or right).
These results suggest that the representational geometries used to internally organize conceptual spaces might be read out from gaze behavior.

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12. TEMPORAL REPRESENTATIONS ACROSS ALLOCENTRIC AND EGOCENTRIC REFERENCE FRAMES IN THE HIPPOCAMPUS AND PARIETAL CORTEX

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The brain is a time machine that allows us to mentally travel back and forth in time. Both the hippocampus and the parietal cortex are considered involved in this process, but their contributions are unclear. This fMRI study investigated whether the hippocampus and the parietal cortex play different roles in allocentric versus egocentric temporal representation, similar to their roles in the spatial domain. Before scanning, participants learned a fictional religious ritual comprising 15 events. These events followed a specific sequence, lasted for a given duration, and happened in different parts of the day (i.e., morning, afternoon, and evening). During scanning, each trial presented a pair of events. Participants judged either whether the two events happened in the same or different parts of the day or whether the second event occurred before or after the first one after self-projecting into the first event. In the former task, participants were outside the timeline and took a "survey" perspective. In the later task, participants were within the timeline and took a "route" viewpoint. We found that the activity in the hippocampus positively correlated with the temporal distance between the two events in both tasks, regardless of participants' perspectives, which suggests the hippocampus implements an allocentric temporal representation. On the contrary, the activity in the partial cortex correlated positively with temporal distance in the "survey" perspective but negatively in the "route" one, which suggests that the parietal cortex's activity varies according to participants' viewpoints and implements an egocentric temporal representation. Moreover, we found a region in the hippocampus positively correlated with event duration only in the "route" perspective, suggesting that the hippocampus represents retrospective temporal durations in sequential contexts.

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13. THETA PHASE PRECESSION AT ENCODING PREDICTS THE MEMORABILITY OF SENSORY-DRIVEN VECTOR FIELDS, & IS PRESENT IN MEMORY-DEPENDENT FIELDS AT RETRIEVAL

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Theta phase precession is thought to confer key computational advantages (e.g. temporal compression suiting spike- timing related plasticity, cognitive relations as phase distances, and population-level coding for directions and sequences). However, direct evidence speaking to: 1) its widely-theorised role in enhancing memorability; 2) its dependence upon sensory input, is lacking. We leveraged the Vector trace cell (VTC) phenomenon to examine these issues. VTCs in subiculum show a simple, unambiguous memory correlate: VTCs remember the distance and direction to a cue after the cue is removed, with a new 'trace field' which was not present before the cue was inserted. Regarding memorability, here we show that subsequently-remembered cue fields (those which become trace fields) exhibit higher levels of phase precession than subsequently-forgotten cue fields (those which produce no trace). Thus, phase precession does appear to enhance memorability, consistent with long-established theory. The second issue concerns the extent of phase precession in sensory-elicited vs memory-dependent firing. Phase precession in CA1 is strongly disrupted following deprivation of its Entorhinal, but not CA3, inputs; this could indicate that theta phase precession is largely sensory-driven and absent in memory-dependent fields. Here, however, we show that phase precession is robust in subicular VTC trace fields, i.e. when the cue that originally elicited the new vector field is no longer present. Thus, the much-theorised benefits of phase precession likely apply to memory-dependent fields. These findings have wide implications for oscillatory-based models of memory.

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14. HIPPOCAMPAL CODING IN A SOCIAL GROUP OF WILD BATS: REPRESENTATION OF IDENTITY, SEX, HIERARCHY, AFFILIATION, AND INTERACTIONS

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Social animals live in groups and interact volitionally in complex ways. However, little is known about neural responses under such natural conditions. Here we investigated hippocampal CA1 neurons in a mixed-sex group of 5–10 freely behaving wild bats, which lived 24/7 in a laboratory-based cave and formed a stable social network. In-flight, most hippocampal place-cells were socially modulated, and represented the identity and sex of conspecifics. Upon social interactions, neurons represented specific interaction-types. During active-observation, neurons encoded the bat's own position and head-direction, together with the position, direction, and identity of multiple conspecifics. Identity-coding neurons encoded the same bat across contexts. The strength of identity-coding was modulated by sex, hierarchy, and social-affiliation. Thus, hippocampal neurons form a multidimensional socio-spatial representation of the natural world.

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15. BEYOND AVERAGE: EXPLORING INDIVIDUAL ERROR COMPONENTS OF HUMAN PATH INTEGRATION

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Individuality is an important factor to investigate when trying to understand the neural mechanisms underlying complex cognitive tasks such as navigation. When navigating, people use various cues that are individually weighed and integrated. An important mechanism in navigation is path integration, i.e. the continuous tracking of walked angles and distances for self-localisation.
In previous studies, two main error components in path integration were identified. Firstly, at the population level, a systematic misjudgement of travelled angles was found, with people overshooting small angles and undershooting large angles. Secondly, at the individual level, there are indications of idiosyncratic biases, i.e. persistent differences between left and right turns. However, while these individual-level effects have been reported by several authors, they have not been analysed in further detail in the existing literature, because previous studies typically check for differences between left and right-hand trials at population level, where individual effects cancel out, and eventually mirror and pool the data.
In this study, we investigate angle misjudgements in a virtual reality visual path integration task, strictly at individual level, without pooling left and right trials. We can validate the existence of time persistent idiosyncratic tendencies to either left or right. Remarkably, also angle over- and undershooting, which in the past has been considered a systematic, population-wide error, shows large variance between individuals. Additionally, a re-analysis of data from several of the most influential, recent human navigation experiments reveals tremendous variance in path integration error components between individuals also across study paradigms. Thus, we emphasise the importance of considering individuality when interpreting results of former and future human navigation studies.

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16. A CONSISTENT MAP IN THE MEDIAL ENTORHINAL CORTEX SUPPORTS SPATIAL MEMORY

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The medial entorhinal cortex (MEC) is hypothesized to function as a “cognitive map” for memory-guided navigation. However, how this map develops during learning and influences memory remains unclear. To answer this question, we imaged MEC calcium dynamics while mice learned a novel virtual linear track over ten days. The mice exhibited different levels of spatial learning. In the “good performer” mice with successful learning, MEC calcium dynamics gradually became spatially consistent and then stabilized. Grid cells not only exhibited improved spatial tuning consistency, but also maintained stable phase relationships, suggesting a network mechanism involving both synaptic plasticity and rigid recurrent connectivity to shape grid cell activity during learning. Increased c-Fos expression in the MEC in novel environments further supports the induction of synaptic plasticity. These activity features were not observed in the “poor performer” mice with unsuccessful learning, indicating that a consistent map is specific for effective spatial memory. Furthermore, the difference in MEC spatial activity consistency between the good and poor performers was larger around cues and immediately before the reward, suggesting that consistent activity in these areas supports successful spatial memory. Indeed, optogenetic stimulation of the MEC in the good performers in a spatially random pattern in cue areas

disrupted their memory-guided navigation in a learned environment, supporting the necessity of consistent activity at cues for spatial memory. Moreover, optogenetic stimulation of the MEC in the poor performers in a spatially consistent pattern immediately before the reward improved their navigation in the environment, indicating the sufficiency of consistent activity before the reward for spatial memory. Thus, we demonstrated that the establishment of a spatially consistent MEC map during learning both correlates to, and is causally associated with, successful spatial memory.

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17. A CONTINUOUS ATTRACTOR MODEL WITH REALISTIC NEURAL AND SYNAPTIC PROPERTIES QUANTITATIVELY REPRODUCES GRID CELL PHYSIOLOGY

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Computational simulations with data-driven physiological detail can foster a deeper understanding of the neural mechanisms underlying cognition. We present a spiking continuous attractor network simulation of the medial entorhinal circuit that utilizes the wealth of experimental measurements from Hippocampome.org to study neural mechanisms of spatial navigation. Modeling the rodent hippocampal formation keeps the simulations computationally reasonable while also anchoring the parameters to empirical evidence. Biological characteristics included here are excitability, connectivity, and synaptic signaling of neuron types defined primarily by their axonal and dendritic morphologies. The key finding is that adding such realistic constraints to this popular theoretical model yields recordings that are remarkably similar to those of real grid cells in terms of spacing, size, orientation, and firing rates. Our simulations also recreate different scales of those properties, e.g., small and large fields, as found along the dorsoventral axis of the medial entorhinal cortex. Computational exploration of the spiking dynamics in specific neuron types and the synaptic activities between groups of neurons reveals that a broad range of neural properties can produce grid activity. The software is released open source to enable broad community reuse and encourage novel applications.

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18. EXPLORING THE ROLE OF PLASTICITY IN MODULATING HIPPOCAMPAL REPLAY

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Current understanding of hippocampal replay involves sequential activation of place-cell ensembles linked through plasticity. However, the plasticity rules that give rise to hippocampal (HpC) replay are poorly understood, particularly for bi-directional replays. Further, our understanding of HpC plasticity and its variation across online/offline (wake/sleep) states is limited, largely based on in-vitro studies. A novel model by Ecker et al. (2022) successfully produced spontaneous bi-directional replays in CA3 during offline states by incorporating a symmetric spike-timing-dependent plasticity (STDP) rule during exploration. We used this model to test the effects of different plasticity rules in the offline state on the structure and speed of replay. Our model shows that when long-term potentiation (LTP) or long-term depression (LTD) are applied to synapses with retrograde directionality counter to the direction of replay, replays respectively slow down or accelerate. Further, our model demonstrates that maintaining symmetric STDP leads to hyperactivity resembling epilepsy. Interestingly, asymmetric Hebbian STDP (H-STDP) biases the direction of replays, accelerating them, and ultimately eliminating them due to decoupling through synchrony (Lubenov and Siapas (2008)). In contrast, asymmetric anti-Hebbian STDP (AH-STDP) preserves replays in both directions, decreases their speed to a stable bound and decreases

mean network connectivity (aka “Synaptic Compression”). Our research thus clarifies the surprising correlation between extended exploration and slower replays identified by Berners-Lee (2022) and indicates a role for H-STDP in the degradation of sequences generated by the CA3 HpC region.

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19. THE EFFECTS OF UNRELIABLE VISUAL INFORMATION ON NAVIGATION

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Humans typically utilize vision in a dominant role for navigation and set it as the scaffolding for our perception of our environment. However, what happens when vision becomes actively unreliable? Will it impair user performance, be suppressed, or be used advantageously?
While such scenarios are rare in the real world, they are common in extended reality applications - e.g. virtual walls that a user sees but can walk through.
We created virtual mazes which could be solved via audio or visual cues. We then manipulated the sensory reliability by including invisible walls which are not perceived but still blocked passage, and ghost walls which could be perceived but did not block participants. Participants navigated identical layouts in each condition, and could solve these levels by ignoring the unreliable sensory modality and using only the other.
Participants easily completed these mazes using vision-only, and with some difficulty via audition-only. Partially unreliable vision degraded performance, though still above audio-only demonstrating utilization of the unreliable visual cues. Mazes whose entire visual input was false degraded performance to the level of audio only, though participants subjectively reported it as easier then audio-only and did not close their eyes indicating that they still relied on vision. When visual information was both false and constantly moved, preventing its use as landmarks or optic flow, participants did close their eyes, disregarding the false vision, but reported confounding nausea. In parallel, auditory incongruencies were easily suppressed across all unreliable auditory conditions.
This demonstrates human attachment to visual information for navigation, even when mostly or completely false, and the ability to glean practical advantages from it unless it is stripped from usability. More broadly it offers a tool for testing multisensory integration of sustained false sensory channels from a spatial perspective.

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20. COMPARATIVELY TESTING THE EFFECT OF REALITY MODALITY ON SPATIAL MEMORY

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Virtual and augmented reality hold great potential for understanding spatial navigation and memory. However, it is unclear what effect reality modality has on our perception and interaction with our spatial surroundings. Here, participants performed a spatial memory task using passthrough augmented reality in the real world and in a virtual environment reconstructed by scanning the real environment. The participants performed the task in the same room, using an identical interface, enabling us to isolate environmental and control factors and focus the difference between conditions

only on reality modality. We found no significant differences by reality modality for subjective measures such as reported immersion, difficulty, enjoyment and cyber-sickness, nor did we find objective differences in performance. These results suggest limited effects on spatial memory, and are promising for transfer between virtual and augmented scenarios.

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21. SCENE-SELECTIVE REGIONS ENCODE THE VERTICAL POSITION OF NAVIGATIONALLY RELEVANT INFORMATION IN YOUNG AND OLDER ADULTHOOD

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Position within the environment influences the navigational relevance of objects. However, the possibility that vertical position represents a central object property has yet to be explored. Considering that the upper and lower visual fields afford distinct types of visual cues and that scene-selective regions exhibit retinotopic biases, it is of interest to elucidate whether the vertical location of visual information modulates neural activity in these high-level visual areas. The occipital place area (OPA) and parahippocampal place area (PPA) demonstrate biases for the contralateral lower visual field, and contralateral upper visual field, respectively. Interesting insights could also be gained from studying older adulthood as recent work points towards an age-related preference for the lower visual field. In this study, 24 young adults (28.1 ± 4.0 yo) and 21 older adults (74.2 ± 5.2 yo) took part in a virtual navigation task while undergoing fMRI. Participants had to memorize the position of a goal with respect to objects situated in the upper (i.e., on balconies) and/or lower (i.e., on sidewalks) part of the environment. The objects’ vertical position as well as their relevance for navigation were modulated in four conditions. An independent functional localizer was performed to delineate the OPA and PPA from each subject. Functional MRI data during navigation were analyzed using representational similarity analysis and a least square separate approach. Results revealed that all three scene selective regions parsed the vertical position of useful objects independently of their subtending retinotopic biases. It therefore appears that representations in the higher-level visual system combined information about vertical position and navigational value for wayfinding purposes. This property was maintained in healthy aging emphasizing the enduring significance of visual processing along the vertical dimension for spatial navigation abilities across the lifespan.

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22. DECODING STABLE HIPPOCAMPAL TASKS IN CONTEXTUAL LEARNING

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This work uses advanced dimensionality reduction techniques to determine if, during navigation, representations of task- relevant stimuli found in the hippocampus (HPC) can be maintained against the background of remapped place cells. We trained rats in trace eyeblink conditioning (tEBC), an HPC-dependent conditioning task, in two different environments while recording HPC cellular activity using calcium imaging. This setup allowed us to investigate how representations of task-relevant stimuli, found in the HPC, can be maintained against the background of remapped place cells. We then used CEBRA, a dimensionality reduction technique, to analyze the neural data and assess the consistency of task representations across contexts. We found a remarkable consistency in HPC task representation despite environmental place cell remapping. We determined that the HPC effectively preserves task-related information even as place cells remap: We found similar embedding geometries of cellular representations in both environments, and established the ability of models trained in environment A to decode tEBC task parameters in environment B. This consistency highlights the HPC's adaptability and robustness in learning and memory processes. This novel finding research addresses a critical aspect of neuroscience: how the HPC adapts its encoding strategies to facilitate learning and memory that generalize across contexts. This research not only addresses a critical aspect of neuroscience, the adaptability of HPC encoding strategies navigatiom , but also demonstrates the invaluable role of advanced analytical techniques, like CEBRA, in uncovering the brain's mechanisms for learning and memory across varying contexts.

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23. GRID CELLS PERFORM PATH INTEGRATION IN MULTIPLE REFERENCE FRAMES DURING SELF-MOTION-BASED NAVIGATION

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With their periodic firing pattern, grid cells are considered a fundamental unit of a neural network contributing to path integration. Although their stable periodic firing pattern is well-suited to support path-integration-dependent behaviors, it has been observed primarily during behaviors involving minimal navigational demands. Thus, it needs to be clarified how grid cells fire in freely moving animals engaged in navigational tasks that depend on path integration. Here, we record the activity of grid cells in mice performing the AutoPI task, a task assessing homing based on path integration. Using single-cell analysis and grid-module-level decoding methods, we found that grid cells do not maintain constant anchoring during the task. Grid cell modules performed path integration over short trajectories but re-anchor to a task-relevant but randomly placed object. This re-anchoring involved translation of the grid map with minimal change in grid orientation. Our findings demonstrate that during navigation guided by self-motion cues, the phase of the grid network can change its anchor point when the animal encounters salient objects.

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24. DIFFERENTIAL NAVIGATION BEHAVIOUR IN OLDER ADULTS WITH AND WITHOUT VISUAL IMPAIRMENT

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Human vision is one key source of information for daily navigation. Impaired vision might affect one's navigation performance, limiting visually impaired patients' confidence for independent travel. Prior studies have shown behavioural and eye movement differences in navigation between the visually impaired and normal groups but many in laboratory- based virtual settings that involves passive video viewing. Few has investigated real life goal-oriented navigation that requires active exploration.
In this study, we explored how visually impaired individuals with age-related macular degeneration (AMD) processed visually salient information differently from their healthy counterparts in real life goal-directed navigation. Eye and gait movements were recorded with Tobii Pro Glasses 3 and three motion sensors. Participants recruited have a mean age of 66.99 (n = 21). All were asked to perform a guided-walk and backtracking from two designated points for three routes (a combination of indoor and outdoor). Each route took 15 minutes to complete. Spatially salient scenarios (e.g. crossing a street) were selected for areas of interest (AOIs) and interval of interest (IOIs) analysis. Gaze parameters (e.g. fixation count, fixation duration and amplitude of saccades) were compared between groups.
Data for the indoor route was reported. Results revealed that gaze behaviour were different between groups during backtracking, but not in the guided-walk. Specifically, those with visual impairment had significantly longer and more spread fixation ($p<0.05$), with a higher amplitude of saccades ($p<0.05$), only at the street crossing event. They also tended to fixate more on moving vehicles. These suggests higher demand on visual functions in cognitively challenging events. People with visual impairment may adopt different strategies in real life goal-directed navigation. Future studies could investigate the differences in navigation strategies and spatial representation formed.

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25. THE HUMAN GRID-LIKE SIGNAL FROM A RODENT GRID CELL PERSPECTIVE

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One of the most intriguing and researched neural firing patterns in neuroscience is the hexagonal tessellation of two dimensional space created by grid cell firing. Several years following the discovery of this phenomenon in rats, human fMRI recordings revealed higher BOLD activity during free navigation in virtual reality environments along a hexagonal set of directions. This effect became known as the 'grid-cell-like representations' in humans, or the Hexadirectional Signal. Because both grid cell firing and the hexadirectional signal are observed in homologue regions of the cortex and are both 6-fold symmetric in nature, it is easy to assume that they are causally related. While several hypotheses connecting the two have been posited, the way in which a single-neuron, 2D spatial firing pattern results in population-level angular tuning has never been thoroughly examined. In this work we build a probabilistic model of a population of grid cells firing modulated by the hemodynamic response to see if the hexadirectional signal emerges. We parameterize this model to simulate several grid cell configurations that have been previously hypothesized to cause this phenomenon. The model shows

that averaged grid cell firing alone, regardless of population configuration, does not produce the hexadirectional signal. However, the variance of firing rates does show detectable hexadirectional modulation in certain scenarios. In addition to modeling, we use datasets of single-cell recordings of rodent grid cells to extrapolate population activity of the same form we model and perform a parallel analysis. The results of this study have sizable implications for how future studies interpret the hexadirectional signal and for the methodology of how spatially modulated brain activity is detected in fMRI recordings.

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26. OBJECT LOCATION MEMORY AS A FUNCTION OF BOUNDARY PROXIMITY

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Spatial navigation is supported by an ensemble of spatially tuned cells that create an internal cognitive map of the environment, facilitating object location memory. Among these cells, are boundary cells which are suggested to support place- and grid cells, such that encounters with environmental boundaries (e.g., walls) correct their firing fields. However, the exact mechanistic description of how the boundary code emerges and guides behaviour is not yet known. A promising prediction comes from the Scale Invariant Path Integration (SIPI) framework, according to which boundary cells fire with decreasing accuracy the further away from the boundary the navigator is. Thus, if boundary encounters stabilise grid cells, this would result in an exponential decay of spatial memory performance and grid cell stability as a function of boundary proximity. To test this, the present study employs immersive Virtual Reality where participants remember 5 object locations that systematically vary as a function of boundary distance. To test the prediction of an exponential decay, the distance between true and estimated location will be analysed with General Linear Models. Shedding light on the impact of environmental boundaries on spatial memory could help understand navigation deficits in Alzheimer's Disease, people in genetic risk of which have been observed to navigate closer to environmental boundaries, possibly to stabilise grid cell firing fields.

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27. REFERENCE FRAME UTILIZATION AS A POTENTIAL MARKER OF AGING-RELATED DEFICITS IN SPATIAL NAVIGATION

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With advancing age, older adults (OAs) report impaired spatial navigation ability, an early indicator of aging-related cognitive decline. Specifically, OAs may demonstrate deficits in utilizing allocentric information and rely on egocentric cues during navigation, resulting in reference frame (RF) bias. While traditional navigation assessments have characterized aging-effects on RF bias, the application to complex, naturalistic, real-world-like navigation remains unclear. This study aimed to identify

interactions between RF bias, classified using a computerized Y-Maze task, with novel navigation measures in a naturalistic, virtual reality environment ("NavCity"). We also introduce a NavCity Allocentric Representation Assessment ("NARA") to quantify allocentric representation ("cognitive map") formation post-NavCity. Our hypothesis is that OAs with egocentric bias will exhibit the largest deficits in naturalistic navigation and "cognitive map" formation, compared to OAs without bias or younger adults (YAs). To test this hypothesis, YAs (N = 12; 18-35 years) and OAs (N = 12; 60+ years) completed NavCity (3 repetitions), NARA, and the Y-Maze. Independent t-tests and chi-squared tests evaluated group differences. Compared to YAs, OAs demonstrated increased NavCity mean completion time and distance traveled (both $p < .01$). However, rates of improvement across NavCity repetitions were similar between groups ($p > .05$). OAs exhibited lower NARA scores than YAs, reflecting decreased allocentric RF recall ($p < .001$). NavCity outcomes and NARA scores were correlated across groups ($p < .001$). OAs also exhibited greater prevalence of egocentric RF utilization on the Y-Maze, compared to YAs ($\chi2$ = 14.96, $p < .001$). Findings suggest that RF bias characterization may serve as a marker of aging-related navigational deficits. Next steps will identify neural mechanisms of aging-related navigation impairments to support preclinical markers for cognitive decline.
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28. DECONFOUNDING PATH FAMILIARITY, EFFICIENCY, AND SHORTCUT BEHAVIOR IN HUMAN SPATIAL NAVIGATION UNDER STRESS

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Navigating when stressed is a common situation that many encounter, such as running late to work or driving in bad weather. Some rodent studies suggest that stress may alter navigation from using efficient shortcuts to inefficient familiar paths. These findings, however, have been mixed in humans, with some studies linking stress and familiar path usage and others suggesting no effect. Some issues with past studies are that paths were either completely novel and more efficient or familiar but less efficient and that the stressors differed. In the current study, we used a within-subject design to deconfound path familiarity, efficiency, and stress on navigation in three conditions: a nonstressful control, a physical stressor (participants put one hand in ice water for 3 minutes), and a mental stressor (navigation occurred while the environment was on fire). In all conditions, participants first learned two predetermined paths (a more efficient inner path and a less efficient outer path) and four target stores in a large virtual environment on a desktop computer. The paths received different levels of familiarity: participants learned one path 8 times and the other path 4 times. Path familiarity and efficiency were counterbalanced across participants and conditions. After the stressors, participants completed 3 blocks of a navigation test prompting them to travel from one store to another. To assay the effectiveness of the stressors, salivary cortisol samples were collected before, immediately after, 15 mins after, and 30 mins after the stressor occurred. Preliminary results with a sample of 12 participants showed a numerical increase in cortisol for the physical stressor but not the control condition or the mental stressor. During the navigation test, excess path decreased over blocks indicating better performance as the navigation test progressed. Our preliminary results position us to look in more detail how stress affected path efficiency compared to familiarity.

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29. COGNITIVE MAP FORMATION AND VIRTUAL NAVIGATION IN BLIND SUBJECTS: AN FMRI STUDY

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Blindness significantly impacts the ability to acquire spatial information, build a cognitive map, and stay oriented in the environment. Possible consequences include reduced autonomy, increased anxiety, social isolation, and overall decreased quality of life. It is therefore important to investigate non-visual cognitive map formation and its underlying neural mechanisms, which are still poorly understood in this population. Therefore, we used fMRI to study the neural correlates of cognitive map formation through touch and audition in individuals with congenital and acquired blindness, and sighted individuals as controls. We used a three-phased game-like paradigm, designed to differentiate between 1) the formation of a cognitive map, 2) its retrieval, and 3) use during navigation. In phase 1 (maze exploration), participants used their fingers to learn the layout of a tactile maze containing multiple destinations. In phase 2 (drop-off), participants were randomly placed inside a virtual rendering of the same maze and were given a goal destination. In phase 3 (navigation), participants navigated in this virtual space with auditory feedback to reach the destination. Preliminary results reveal distinct neural patterns during navigation in each group: sighted controls showed a reliance on frontal, insular, and parietal cortices, and blind subjects significantly activated visual occipital areas and cerebellum, combined with a general deactivation in the rest of the brain. However, depending on if participants were forming, retrieving, or using their cognitive map, different activation patterns emerged across the navigation network (hippocampus, parahippocampal place area, retrosplenial complex, occipital place area), informing on their different spatial functions in blindness.

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30. SPATIAL INFORMATION IN NON-PLACE CELLS

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In this present study we investigated spatial memory encoding in the hippocampus of human refractory epilepsy patients using a virtual navigation task. Participants were asked to remember the locations of six items in a rectangular arena while receiving brain stimulation at either low (3 Hz) or high (8 Hz) theta. Concurrently, we recorded single neuron activity in the hippocampus.
Using a Gaussian Process Regression we successfully decoded the spatial position of the patient during the encoding phase of the experiment. Even after excluding previously identified place cells, our decoding analysis remarkably maintained its predictive power. This discovery challenges the notion that spatial information is exclusively sparsely coded in the hippocampus by highly selective place coding cells. Instead, this suggests a gradual decrease of spatial information within other neurons in the hippocampus, not classified as place cells. Although each neuron codes spatial information to a lesser degree, collectively this broad ensemble of neurons contained significant spatial information.

Future analyses will include the effect of stimulation on the stability and emergence of place cells, their reinstatement during verbal and spatial retrieval, and the relationship between place cell firing and hippocampal theta events.

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31. MULTIMODAL NEUROIMAGING REVEALS DIFFERING BRAIN STRUCTURES UNDERLYING PATH INTEGRATION IN YOUNG AND MIDLIFE ADULTS

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Path integration is a component of human spatial navigation that involves the continuous updating of position and orientation during movement. Our previous findings suggest that there are negligible effects of early aging on the LOOP task, a measure of path integration ability. Briefly, participants were guided in a circle, providing them proprioception and visual optic flow but no landmarks, and had to indicate when returned to the start of the circle. Men and women made similar errors during path integration but rely on different strategies: women overshoot the target and men undershoot. However, the extent to which brain structure contributes to path integration performance across the lifespan remains unclear. To address this question, we analyzed white matter integrity, hippocampal and hippocampal subfield volume, and whole brain cortical thickness to examine the relationship between brain structure and path integration performance on the loop task in young (ages 18-35, n = 23 and midlife (ages 45-55, n = 43) adults. We found that total hippocampus and subfield volumes are associated with strategy preference in midlife adults, but not overall accuracy during path integration. In contrast, young adults hippocampal volume was associated with accuracy but not strategy. In midlife, white matter integrity in the fornix – a major output tract of the hippocampus – corresponds to both path integration accuracy and strategy use, but this relationship differs between men and women. In the young adults, white matter integrity in the fornix corresponds to better accuracy overall but is not related to strategy. This suggests that brain structure corresponds to path integration abilities but that this relationship changes during midlife and may be influenced by sex. These results provide us with a greater understanding of human spatial navigation across the lifespan and may have implications for our understanding of age-related disorders.

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32. BRAIN NETWORK DYNAMICS OF HUMAN NAVIGATIONAL LEARNING

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Navigation is a fundamental, yet complex, human behavior with large individual differences. While many studies have identified multiple brain regions involved in spatial navigation in known environments, considerably less is known about the brain circuits involved in learning a new environment, and whether individual differences are present during learning. In the present study, healthy young adults (n=93) completed a challenging maze learning task during fMRI scanning. Participants were given 16 minutes to explore a virtual hedge maze and learn the locations of 9 objects. Next, their memory was tested in a series of 48 (>= 45 sec) test trials, each of which started at one object with instructions to find another object using the paths of the maze (e.g. clock -> lamp), without feedback. Accuracy ranged from near 0% to 100% correct, enabling us to quantify the neural and behavioral differences that distinguish between poor, average, and exceptional performers. We conducted dynamic community detection to analyze the flexibility of brain network nodes (how often a brain area changes communities) followed by a seed-to-seed connectivity analyses to understand how brain regions communicate with each other. To explore dynamic changes in brain connectivity, we segmented these analyses into the first exploration, second exploration, and test phases. Then we identified psychophysiological interactions (PPIs) to investigate the task-related modulation of connectivity patterns and the relationship between the PPIs, behavioral and performance metrics, and results of additional tasks, to identify sources of individual differences in navigational learning. Preliminary imaging results from the dynamic community analysis suggest that an overall increased flexibility across the whole brain predicts better navigational performance. The results of this study will illuminate how brain regions dynamically interact during navigational learning.

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33. ADAPTIVE FIRING EXPLAINS ANTICIPATORY CODING, THETA SWEEPS AND REPLAY IN SPATIAL TUNING CELLS

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Spatial cognition in the brain emerges from the coordination of distinct neuronal types, each encoding navigational elements such as position, head direction, and velocity. Although various spatial firing patterns—anticipatory coding, phase precession, and non-local replay—have been identified, their underlying mechanisms and interrelations remain unclear.
Our study proposes a unified framework suggesting that these phenomena are interconnected expressions of adaptive neuronal firing within spatially tuned circuits. We introduce an attractor network model that captures the dynamic attributes of head direction cells, place cells, and grid cells. Incorporating adaptive firing mechanisms into our model, we reproduce known phenomena such as anticipatory firing, theta sweeps, and non-local replay across different neuronal types and provide explanations for these observations. The model elucidates mechanisms behind anticipatory coding in head direction and place cells [1,2], explains asymmetric tuning curves as a function of running or scanning direction [2,3], establishes a link between head scanning speed and the degree of anticipatory firing [3] and predicts a positive correlation between the amount of anticipatory firing and phase precession. Furthermore, we extend these insights to grid cell firing, validating with data [4] that these dynamics are also present in grid cell activity.
Our theoretical analysis reveals how varying adaptation strengths in neuronal firing can modulate these sequential firing patterns, offering a comprehensive explanation for the observed behaviors in spatial tuning cells. This adaptive firing framework not only reconciles various seemingly disparate phenomena but also deepens our understanding of the neural mechanisms underpinning spatial cognition, including navigational planning, decision-making, and memory consolidation.

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34. AGE DIFFERENCES IN EVERYDAY SPATIAL NAVIGATION BEHAVIORS

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A large body of literature demonstrates age-related deficits in navigation performance, with older adults having greater difficulty forming and using flexible representations of environments. However, we have limited understanding of the degree to which these objective deficits impact daily life. There is a dearth of research investigating age differences in real-world, daily navigation behaviors. The goals of the current study were to examine everyday spatial navigation behaviors of younger and older adults, and to investigate their predictors and associations with objective performance. Younger (n=53, age range 18-35) and older (n=86, age range 60-83) adults reported any trips outside the home for up to 14 days. Participants answered questions about the trip, including the destination and length of the trip, whether the destination was new or familiar to them, and whether they made any navigation errors or got lost on the way. Participants also completed the Wayfinding Anxiety Scale and a virtual cognitive mapping task. Younger and older adults reported a similar number of trips outside the home (p=.10), and a similar proportion of trips to new destinations (p=.06). Of trips to new destinations, younger and older adults had similar proportions of trips during which they got lost (p=.10) or made an error (p=.49). There were no age differences in wayfinding anxiety (p=.76). Older adults had worse cognitive mapping performance (p=.001). For older adults, higher wayfinding anxiety was related to fewer trips taken (p=.01). Cognitive mapping performance was associated with more errors traveling to familiar destinations (p=.01) for older adults, but not with getting lost to familiar destinations (p=.52), getting lost to new destinations (p=.06), or errors to new destinations (p=.42). Results highlight potential age similarities in some daily navigation behaviors, and the role of wayfinding anxiety and objective performance for older adults' daily navigation behaviors.

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35. IDENTIFYING MECHANISMS INVOLVED IN ACUTE ALCOHOL-INDUCED AMNESIA

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Alcohol intoxication can impair episodic (autobiographical) and spatial (navigational) memory. These memories are formed and maintained in different subareas of the hippocampal formation, including the hippocampus proper (HC) and the medial entorhinal cortex (MEC). The rhythmic activity within these regions is in turn orchestrated by GABAergic projection neurons of the medial septum (MS). The effects of alcohol on these systems are largely unexplored. In this project, we examine the effects of acute alcohol intoxication on functional cell types and network-level activity in and between these regions by performing in vivo electrophysiological recordings in behaving mice. Alcohol administration at a dosage of 1.7 g/kg intraperitoneally impairs the performance of a reference memory task on the 8-arm radial maze. In an open-field environment, the same dose of alcohol causes a reduction in the firing rate of fast-spiking cells in the MS, MEC, and HC, with the strongest effect in the MEC. The firing

rate of grid cells in the MEC, but not of place cells in the HC, is reduced by alcohol. At the network level, alcohol causes a reduction of the LFP theta frequency in both the MEC and HC. Phase precession, a temporal coding property of spatially selective cells, is affected by alcohol in grid cells in the MEC, but not in place cells in the HC. Hence, we infer that the MEC is more susceptible to alcohol than the HC.

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36. REMAPPING AND THETA SEQUENCES IN MOUSE HIPPOCAMPAL FORMATION FOLLOWING ALTERED SPATIAL TRANSITIONS

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Flexible behaviours in spatial navigation require a model of the environment. Spatial representations found in the hippocampus (HPC) and medial entorhinal cortex (MEC) are candidates for implementing a cognitive map and facilitating flexibility though how updates to such a model are made in a dynamic environment remains unclear.
HPC and MEC neurons have been suggested to encode state relationships reflecting a predictive map of future occupancy. We test this with a task that manipulates the transition statistics of a familiar environment and ask how changes are reflected in HPC and MEC coding and examine the role of replay in this dynamic environment.
Our task changes a line state space into a loop. Mice forage in a familiar circular linear track with a barrier preventing full transition, creating a line state space. The barrier is removed, changing the transition statistics and allowing mice to fully navigate a loop state space. Thus, mice experience that locations previously on either side of the barrier are connected. After exposure to the loop, the barrier is reinserted and animals run again in the original line environment. Rest sessions are recorded to study offline replay.
We recorded spatial cells in HPC or MEC of 6 mice in this task. Both HPC (362 units) and MEC (384 units) show remapping, however the greatest remapping occurs in HPC between the two line environments, perceptually identical except for the intervening experience of transitions around the loop. MEC in contrast showed less remapping. These results suggest a role for the hippocampus in integrating current and previous transition statistics into a cognitive map. The MEC representations in contrast, may reflect a more stable and generalisable map.
Both prospective theta sweeps and replay provide a read out of the current map. Whether or not they cross the barrier enables us to see when changes to the map occur. We are currently analysing recent data to answer this question.

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37. IDENTIFYING SOURCES OF PATH INTEGRATION ERROR USING BAYESIAN HIERARCHICAL MODELING

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Path integration is a neural computation by which self-motion cues are continuously integrated to keep track of one's position and orientation in space. Path integration performance has the potential to be a sensitive cognitive marker in clinical research and for the detection of early Alzheimer's disease. To characterize errors in path integration performance, we propose a two-level Bayesian hierarchical approach that provides a distributional estimate of individual factors that might contribute to the error. By applying this approach to path integration data from participants with self- reported cognitive decline and control participants, we found that the noise accumulated with traveled distance was the dominant source of error that differed between the two groups. We believe this approach could be broadly useful in identifying sources of path integration error and advancing the understanding of neural mechanisms underlying cognitive decline.

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38. MULTISENSORY REPRESENTATIONS OF SELF-MOTION DIRECTION AND SPEED IN THE DROSOPHILA NAVIGATION CENTER

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In order to navigate through the world, the brain must compute movement of the self and the environment from ambiguous sensory experience. For example, vision (as optic flow) and mechanosensation (from the vestibular system) provide information about the direction and speed of self-motion, with different temporal dynamics. Integrating these signals could allow the brain to distinguish whether the motion was self-generated or produced by an external force.
In this work, we use the exquisitely detailed circuitry of the navigation center in the fruit fly brain to examine how multisensory integration of mechanosensory airflow and visual optic flow sensation produces neuronal representations of self-motion direction and speed. We find that one population of input neurons to the navigation center integrates visual and mechanosensory information about the direction of travel. Mechanosensory responses are fast and transient while visual responses are slow and sustained, reflecting the different dynamics of these two sensory systems. A second input population represents both speed and direction based on mechanosensory cues. Comparing the responses of these neurons to those of their upstream partners suggests that speed information is accentuated, while direction information is suppressed, along this pathway.
Based on these data, we constructed computational models of each neuron population's responses. Using these models, we are exploring the navigational computations that are possible from different combinations of their activity, such as the direction of a wind acting on the fly.
This work deepens our understanding of how multisensory integration can be used to disambiguate sensory experience during movement.

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39. UNRAVELLING PATH INTEGRATION DEFICITS IN HEALTHY AGING AND EARLY ALZHEIMER'S DISEASE

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Path integration deficits are apparent in healthy older adults and Alzheimer's disease (AD) patients. Yet, it remains unclear which specific aspects of the path integration process are most affected and whether these processes are differentially affected in older adults and those with AD. It is possible that AD-related deficits are primarily driven by grid cell dysfunction as a result of AD related pathology, whereas, in healthy aging the deficits arise primarily due to degradation of sensory inputs resulting in nosier representations. Subjective Cognitive Decline (SCD) is currently considered the earliest symptomatic stage of preclinical AD, hence detecting cognitive deficits within this group to provide a window into the emergence of AD. Our study utilized immersive virtual reality to examine path integration deficits in healthy older adults and those with SCD. Participants were exposed to multisensory self-motion cues while navigating short, curved paths in a virtual environment. Our findings revealed impaired path integration performance in the SCD group, independent of general cognitive status, visuospatial working memory, subjective spatial abilities, and balance. To further dissect the sources of these errors, we employed a computational model, identifying memory leak and randomly accumulating noise as prominent factors, particularly pronounced in the SCD group. Furthermore, we observed a link between blood-derived neurofilament light chain levels and accumulating noise, suggesting neural degeneration as a significant factor driving noisier location estimates. Additionally, we will present findings from blood-based NPTX2, a biomarker of synaptic activity, elucidating its association with sources of path integration error. These insights promise a more mechanistic understanding of path integration deficits in early AD.

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40. INTEGRATION OF MOTOR AND VISUAL INFORMATION IN THE ZEBRAFISH HEAD DIRECTION SYSTEM

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Animals can use different strategies to navigate. They may guide their movements by relying on external cues in their environment or by using an internal cognitive map of the space around them. In many species, the heading direction of the animal is represented by heading direction neurons and can be affected by both motor and visual information. We recently discovered, for the first time in a vertebrate, a topographically organized heading direction system in the larval zebrafish hindbrain. This network functions in the absence visual inputs and shows similar dynamics and efficiency in the presence of visual feedback and in darkness. Here, we investigate how visual inputs are integrated downstream of this network. We used light sheet and two-photon calcium imaging to detect visually responsive neurons in the anterior hindbrain and interpeduncular nucleus, in which head direction is integrated. Furthermore, we identified neurons with receptive fields responses and show that these neurons send excitatory projections to the interpeduncular nucleus. Finally, we show that the representation of visual information is anatomically organized in a way that matches the organization of the heading signal in the interpeduncular nucleus. Our findings point to a potential mechanism that allows zebrafish to generate a more accurate representation of their heading direction by integrating efference copies with visual information.

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41. TESTING THE USE OF ABSTRACT INFORMATION DURING NAVIGATION

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Every day, we navigate through space using our brain's spatial navigation network, including the so-called neuronal compass, i.e., the head-direction cells (HDCs). Several studies have investigated how HDCs integrate visual and self-motion cues to track head direction during navigation. However, humans routinely use abstract cues like signs, maps, or verbal directions to orient. This implies that higher cognitive regions may feed abstract information into the HDC system. Here we test whether rodents can use abstract information for navigation and whether such information can anchor HDC. We define "abstract information" as a stimulus whose physical location in allo or egocentric coordinates is uninformative, but who conveys information about one's location. To test this, we train rats in a food-foraging task in which they need to learn the position of an unmarked zone that triggers a reward and auditory cue upon entry. Both the clicker and pellet dispensers are located above the center of the arena, such that the location of the auditory cue is devoid of spatial information. Thus, the feedback acts as an abstract cue according to our definition, conveying information about the animal's location in the zone. We control for visual and odor cues by lightproofing the setup, illuminating it with invisible LEDs, and rotating the floor to make odor cues unreliable. After training, rats can learn the task. In the next steps, we will place the animals in complete darkness and record the response of HDC. We hypothesize that rats will get disoriented in darkness but that, upon re-entering the zone, the auditory cue will inform them of their current position, reorienting both the rats and the HDCs. This project will allow us to understand how cognitive information updates the HDCs. A positive outcome would indicate the influence of higher-order brain areas on the HDCs circuit and would be the first demonstration of the ability of HDCs to integrate abstract information.

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42. SPATIAL NAVIGATION TRAINING ENHANCES HIPPOCAMPAL EPISODIC MEMORY RETRIEVAL

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The hippocampus (HPC) exhibits high plasticity and varies across individuals based on experience (e.g. London taxi drivers). Given its vulnerability in aging and various memory disorders, there is both necessity and possibility for hippocampal cognitive training. Episodic memory (EM), a complex HPC function integrating what, where, and when information, is challenging to train directly. Spatial memory training has been more widely studied, but its generalizability to general HPC functions like EM and the exact nature of its modification of hippocampal activity remains unexplored.
In this study, we investigated the transfer of navigational training to a non-navigational what-where-when binding EM task and its corresponding changes in hippocampal activity. 33 participants underwent a 2-week navigation training on sequences of 8 locations on each trial; half of the subjects (feedback group) re-enacted the sequence after a delay and received feedback. To test the transfer effect, a novel EM task - requiring participants to remember events that objects (what) moved into boxes (where) in a specific order (when) - was administered in the fMRI scanner before and after the navigational training.
Through training, both navigation and EM were enhanced in the feedback group. We found that where-when binding was essential for successful EM and significantly improved by training. Training also

enhanced activation of the cortico- hippocampal memory network during EM retrieval. Notably, subiculum activity was tightly correlated to the enhancement of spatiotemporal binding; the enhancement in encoding-retrieval pattern reinstatement was also strongest in the subiculum and parahippocampal gyrus.
In summary, training fundamental spatiotemporal processes of navigation enhanced EM accuracy and hippocampal engagement during retrieval, extending existing knowledge on hippocampal plasticity and providing neurocognitive evidence for the development of navigation-based memory training tools.

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43. SPONTANEOUS SPATIAL CHUNKING IN HUMAN NAVIGATIONAL MEMORY

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Grouping information into larger chunks has been reported in multiple domains as a way to increase memory capacity. While spatial memory may benefit from such efficient organization of information, chunking in navigation has not been extensively studied. In this study, we explored the extent to which human adults chunk space in a multi-goal navigation task and examined its impact on memory. To understand the mechanisms underlying such behavior, we conducted further experiments to identify various factors that contributed to spatial chunking.
In the first experiment, 17 participants (mean age 24.4) collected eight sequentially-presented coins in each trial, and then, after a short interference task, were asked to mark each coin's location in the correct order. Each subject completed a total of 65 trials across seven sessions. We observed a prototypical response pattern of nine nodes (3x3), across various square-shaped rooms. Participants responded at a node even when their responses were far from the target. Although the pattern remained invariant across different contexts and sessions, it became more evident across the coin sequence, demonstrating its potential role in increasing cognitive capacity for encoding multiple targets.
In subsequent experiments, we investigated factors shaping spatial chunking by altering the properties of the room, such as removing two walls (n=14), and varying room size (n=14) and shape (n=18). While the presence and layout of proximal boundaries were important for node formation, room size did not significantly affect the chunking patterns.
Overall, this study found that in addition to the well-known effects of boundary-based spatial place coding, geometry- driven spatial chunking guides human navigation, particularly under high cognitive load induced by multiple targets.

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44. EVALUATING THE RELATIONSHIP BETWEEN PATH INTEGRATION TASKS: TRIANGLE COMPLETION AND LOOP CLOSURE

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Path integration, an animal's ability to update its position and orientation over time, supports successful navigation. Homing tasks like Triangle Completion and Loop Closure are commonly used to assess this ability. While Triangle Completion requires participants to judge the direction and distance back to the start location after walking two legs of a triangle, Loop Closure involves indicating when one has returned to the starting point while walking in a circle. Both tasks involve path integration but likely utilize different frames of reference (i.e., allocentric vs. egocentric). This investigation is the first to study the relationship between these two tasks by measuring performance from the same subjects in walking, immersive virtual reality. Over 200 healthy, young adults completed both tasks, and neuroimaging data were additionally collected from a subset of ~100 individuals to understand the underlying neural mechanisms associated with performance differences between the tasks. We predicted a significant correlation between performance on these tasks and expected self-reported strategies to reveal more allocentric representations for Triangle Completion and egocentric representations for Loop Closure. Behaviorally, we observed surprisingly moderate correlations between Triangle and Loop measures. Contrary to our hypothesis, we discovered that participants who primarily reported using allocentric strategies for Triangle Completion exhibited poorer performance compared to those who did not, and conversely, those who primarily employed egocentric strategies for Loop Closure showed poorer performance compared to their counterparts who did not. Neuroimaging data will be analyzed to uncover the neural substrates underlying these performance differences. By examining the shared and unique contributions of these tasks to path integration ability more generally, this study deepens our understanding of the cognitive and neural processes that support navigation.

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45. DECODING SPATIAL POSITION FROM HUMAN HIPPOCAMPAL LOCAL FIELD POTENTIAL DATA DURING VIRTUAL NAVIGATION AND MENTAL SIMULATION

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Decades of work in rodents suggest that goal-directed movement is a powerful driver of hippocampal low-frequency "theta" oscillations. While also present in humans, hippocampal movement-related "theta" oscillations typically manifest at a lower frequency and in shorter bursts. Additionally, robust theta oscillations are observed during verbal memory tasks, suggesting that human hippocampal theta rhythms may be more intimately tied to memory processes than to movement and raises questions about its functional relevance. To explore the role of movement and memory-related processing in eliciting hippocampal theta oscillations, we conducted a study with neurosurgical patients, who navigated paths in a virtual environment and subsequently engaged in mental simulation of the paths while undergoing intracranial EEG monitoring. We observed that mental simulation of a recently navigated route resulted in theta activity that was greater power, higher frequency, and longer duration than those during navigation. This raised the possibility that these oscillations relate primarily to

mnemonic content, suggesting that we might be able to decode memory for spatial position from mental simulation using the navigation data. We first tested whether we could decode position from local field potential data (LFP) while patients navigated (as has been shown in rodents). A random forest algorithm was trained to decode spatial position during navigation using average power across log-spaced frequency bands from 2 to 100 Hz. We were able to decode the segments that patients occupied at levels above chance using the navigation LFP data. Second, we wished to apply the classifier trained during navigation to the LFP data recorded during the mental simulation task. Our findings help to resolve differences in low-frequency hippocampal oscillations for navigation compared to episodic memory and provide hints into why human low-frequency oscillations may differ from those of the rodent.

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46. MOUSE NAVIGATION WITHOUT HIPPOCAMPUS OR NEOCORTEX

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In humans, the neocortex (CTX) plays essential roles in sensory processing and motor control. Furthermore, the interplay between the neocortex and hippocampus (HPC) is necessary for the formation, retention, and recall of memories. It is commonly assumed that this applies to rodents as well. Here we tested these ideas using a mouse mutant that lacks the dorsal forebrain, including the hippocampus and most of the neocortex.
We studied the acortical (ACT) mutant in four naturalistic tasks: escape from predator, hunting of prey, navigation in a complex labyrinth, and long-term spatial memory ranging from hours to weeks. Some of the experiments were repeated on mice with acute lesions to the cortex and hippocampus.
We found that ACT mice are proficient in all these behaviors. On tasks that require learning, they take ~3x longer to mastery than normal mice. For example, the ACT animals - like normal mice - exhibit one-shot learning of a reward location in a complex maze. However, it takes them longer to discover that location. As a rule, the ACT mouse's behavior includes more repetition and less exploration. In addition, we found a few subtle deficits consistent with known cortico- spinal pathways.
We conclude that the neocortex and hippocampus are not necessary for escape, pursuit, navigation, or learning. The absence of CTX/HPC introduces behavioral changes that slow the learning process but do not eliminate learning, or memory, or spatial navigation based on that memory. Our findings call attention to the power of subcortical pathways in all these functions. We conclude that rodents use CTX/HPC in ways that are categorically different from primates.

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47. NAVIGATING MUSIC AS A COGNITIVE MAP

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Neurodegeneration in Alzheimer’s disease (AD) severely damages the brain regions implicated in cognitive maps supporting spatial navigation and memory. Studies applying virtual reality and GPS measurements demonstrated the resulting deterioration of spatial navigation ability, while other findings suggested that acoustic and spatial processing share neural substrates within the brain regions critically damaged by AD pathology. Importantly, the late-developing pathology in the regions encoding long-known music implies intriguing prospects for capitalizing on the potential of music as a mnemonic device to support the declining spatial navigation function. Notable findings on the demonstrated correspondence of acoustic frequency to spatial elevation and analog neuronal

responses to changes in frequency and location indicate that music can reflect the spatial properties of navigation. Therefore, this poster puts forward a novel framework for mapping music to spatial coordinates to improve spatial navigation in neurocognitive disorders such as AD.
Running along the line of evidence on cognitive maps in domains other than spatial navigation, such as the acoustic domain, the proposed experimental paradigm draws on behavioral and neurophysiological methods to explore the potential application of music as a mnemonic device for spatial cognitive maps. The first stage of research encompasses the pitch-based design of a virtual reality navigation experience quantified by functional magnetic resonance imaging, with a focus on the hypothetical role of the brain regions preserved the longest in AD in supporting associative spatial-acoustic learning.
Learning whether translating spatial coordinates onto long-known music may effectively “transfer” the declining memory of familiar routes onto the acoustic cognitive maps can be the first step of tapping into the potential of preserved long- term musical memory in AD to conserve the fading spatial memory.

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48. MAPPING A SCENE FROM AFAR: ALLOCENTRIC REPRESENTATION OF VIEWED LOCATIONS IN THE HUMAN BRAIN

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Spatial neuroscience has revealed a great deal about how humans and animals encode allocentric cognitive maps learned through bodily exploration. In theory, these maps could also be learned from afar, through visual perception alone. Consistent with this idea, recent work has revealed boundary, object, and landmark vector cells in the rodent hippocampal formation that represent the world “out there”. However, we have little evidence for similar representations in the human brain, nor do we understand how such representations might be constructed from visual inputs processed by “scene” areas such as the parahippocampal place area (PPA), occipital place area (OPA), and retrosplenial complex (RSC). To address these issues, we scanned participants with fMRI while they attended to locations within a virtual courtyard, viewed from outside the courtyard. Stimuli were images taken from 4 possible viewpoints outside and slightly above the courtyard, spaced 90 degrees apart. Within each image was an indicator object (a car), in one of six possible allocentric locations; on each trial, participants reported whether the indicator object was facing the same or different allocentric direction as in the previous trial (one-back task). The task was designed to direct attention to the location of the indicator object within the allocentric framework of the courtyard without requiring explicit reporting of that location. Two behavioral studies (N=30 each) using similar task designs showed that reaction times were faster and accuracy greater when the same courtyard location was repeated in sequence, thus providing evidence for an allocentric representation of viewed locations. Preliminary fMRI analyses suggest that multivoxel patterns in RSC distinguish between these allocentric locations, whereas multivoxel patterns in PPA and OPA distinguish between views of the courtyard. These findings provide new information about how the world “out there” is represented across the human brain.

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49. PREDICTIVE REPRESENTATIONS WITH EPISODIC REPLAY IN THE HUMAN BRAIN MEDIATE MULTI-GOAL SPATIAL NAVIGATION

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What are the neural and computational mechanisms underlying human spatial navigation? Previous studies have suggested that reward prediction and replay might underlie key navigational components such as credit assignment, memory consolidation, and planning. However, these mechanisms are usually tested with relatively simple paradigms, and it is unclear what role they might play in ecologically realistic navigational tasks involving rapidly changing goal locations. To investigate this issue, we scanned participants (N=15) with fMRI while they performed a "taxi-cab" task in a virtual city with multiple possible goals. We found that a successor representation model incorporating episodic replay (DYNA-SR) fit the observed human behavior better than alternative mechanistic models such as Q-learner (model-free) and value iteration (model-based). To identify the possible neural systems underlying DYNA-SR, we analyzed BOLD activity in terms of several components of the model. We observed parametric tracking of successor state values in bilateral hippocampus ($p < 0.05$, nonparametric ROI analysis) and parametric tracking of successor prediction error in retrosplenial complex, parahippocampal place area, occipital place area, and superior parietal cortex. The latter set of regions bears striking overlap with the cortical network that has recently been proposed to mediate visuospatial memory (Steel et al., 2023). Lastly, we found evidence for remote prospective episodic replay in the right posterior hippocampus (p

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50. RELIANCE ON SPATIAL CUES ACROSS MULTIPLE VIRTUAL NAVIGATION TASKS

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Different strategies can be used to navigate towards a goal. Previous research has demonstrated that individuals with an increased genetic risk for Alzheimer's disease exhibit altered navigational patterns in a variety of virtual navigation tasks. Specifically, risk carriers tend to show a reduced preference to walk towards the center in a virtual arena, walk closer to a landmark in an open field, and tend to walk to the boundary in a maze-like field. However, the relationship between these patterns remains unclear. In the present study, we aimed to investigate the relationship between these patterns by conducting four spatial navigation tasks with the same sample of participants. Additionally, we included

four event segmentation tasks to explore a potential link between event boundaries and spatial boundaries. Our results revealed that across tasks, participants showed similar effects of spatial cues, with better performance when walking towards the center or landmark and when the goal was closer to the center or landmark. Interestingly, reliance on spatial cues in a task was more common among participants with lower overall performance. While some tasks showed significant correlations in performance, we did not find any correlation between movement preferences. In the event segmentation tasks, we found that participants had an enhanced recall of contextual information at boundaries and needed more time to mentally replay segments of a movie that contained a boundary. However, we did not find any relationship between these event segmentation effects and navigational patterns. Overall, our findings provide valuable insight into how individuals differ in their use of spatial cues for navigation.

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51. CAN DECREASED HIPPOCAMPAL THETA IN OLDER ADULTS BE RESTORED BY SPATIAL TRAINING?

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Despite the existence of a few studies showing the potential benefit of repeated navigational training on the hippocampus, the underlying effects of such cognitive improvement have not yet been described in detail. Given the well- described function and importance of hippocampal theta oscillations in spatial memory, measuring changes in hippocampal intracranial EEG (iEEG) over the course of spatial training may reveal specific hippocampal functional correlates associated with an increase is navigation performance and memory. In this study, we specifically investigated the possibility that hippocampal theta power may change over the course of repeated trials of spatial navigation with feedback on every trial.
We used iEEG recordings across the whole brain in 69 presurgical epilepsy patients (ages 19 to 61), while they performed a computer-based task in which participants were passively driven to a target location and then asked to freely return to that location after being teleported to a random place in the virtual arena. First, we found that hippocampal theta (3-6Hz) power during the encoding phase was significantly lower in the older participants. In addition, the decrease in hippocampal theta was more pronounced in low-performing older participants. Next, we tested how hippocampal theta power was modulated over multiple trials (48 trials), with feedback on the target and response on every trial. Theta power gradually increased during the course of the task both in the younger and older participants; moreover, this increase in theta was associated with improved spatial navigation and memory, both in terms of the heading direction and distance estimation from the wall boundary.
Although it is not clear how much training is required to gain a long-term benefit in hippocampal navigation and memory function, these results are hopeful in providing a potential neural mechanism that can be recovered, at least in part, by targeted cognitive training.

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52. SPATIAL MODULATION OF SENSORY ACTIVITY IN MULTIPLE BRAIN REGIONS

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Spatial navigation is a complex form of goal-directed behavior that depends on cognitive processes such as perception. A key center is the hippocampal formation, where well-known ‘place cells’ and ‘grid-

cells' encode the animal's position. Spatial coding has been found in other brain regions, including the anterior thalamic nucleus and cortical regions that were considered purely sensory such as the visual cortex. Here we ask whether spatial coding is restricted to specific regions or widely distributed across the brain. Additionally, we ask whether spatial and sensory coding occur in separate populations, or integrate within single neurons.
We used Neuropixels probes to record from 2121 well-isolated neurons across 22 regions in 24 mice navigating a virtual linear corridor. The corridor consisted of two sensory identical halves. The visual contrast of landmarks in the corridor varied across trials. In a subset of trials the landmarks were also the source of an auditory stimulus. The gain of the running wheel varied to decouple physical and virtual position. We quantified the response of each neuron in the corridor as a function of virtual position, sensory intensity, reward, and running speed, using linear ridge regression.
Regions included visual, somatosensory, retrosplenial, and motor cortex, the hippocampal formation, the dorsal thalamus, striatum, and midbrain. Activity of 5-45% (across regions) of neurons was modulated by position in the corridor. 2-55% of neurons were modulated by sensory intensity or reward, and 34-95% by running speed. There was a positive correlation between the number of neurons modulated by virtual position or sensory intensity and the number of neurons that were modulated by both.
These results indicate that spatial coding is widely distributed across the brain, and that the proportion of neurons integrating sensory and spatial information increases with a higher percentage of neurons modulated by either.

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53. BEHAVIOR-DEPENDENT THETA RHYTHM GENERATION IN THE MEDIAL SEPTUM AND THE SUPRAMAMMILLARY NUCLEUS

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Cortical synchrony has been considered to play a crucial role in integrating distributed information across the brain. While previous studies suggested that theta oscillations can modulate functional interactions between the prefrontal cortex and the hippocampus depending on behavioral demands, how such interregional synchrony is desirably controlled at the neural circuit level remains unclear. The primary sources of theta oscillations have been identified in two subcortical regions - the supramammillary nucleus (SuM) and the medial septum (MS) - and we hypothesize that the modulations of these two oscillators may underlie dynamic interregional coupling. To test this idea, we performed simultaneous recordings from the SuM, MS, medial prefrontal cortex (mPFC), and hippocampal CA1 region in rats performing an open- field foraging or a T-maze alternation task. Our recordings revealed high theta coherence between the CA1 and either the SuM or the MS, whereas rather low coherence between the SuM and the MS. Moreover, theta rhythms generated by SuM and MS neuronal spiking displayed distinct frequencies, indicating independent generation of theta oscillations in these two regions. When the animals approached a T-junction on the maze, the theta frequency in the SuM became slower, whereas such changes were not observed in the MS, leading to enhanced spike-time coordination of SuM neurons relative to the CA1 theta. Similarly, we observed enhanced coordination between SuM neuronal spiking and the mPFC theta rhythm, which indicates an increased influence of SuM-generated theta oscillations on both the CA1 and the mPFC during trajectory decisions, likely facilitating information transfer in prefrontal-hippocampal circuits. Our findings illuminate a novel mechanism of oscillatory coupling via theta frequency modulations, allowing for dynamic coordination across multiple brain regions in accordance with behavioral demands.

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54. THE SPATIAL PERFORMANCE ASSESSMENT FOR COGNITIVE EVALUATION (SPACE): USING DEFICITS IN NAVIGATION TO DETECT COGNITIVE IMPAIRMENT

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The Spatial Performance Assessment for Cognitive Evaluation (SPACE) is a novel serious game for the early detection of cognitive impairment. In this study, we investigated whether the various spatial tasks in SPACE can predict cognitive impairment as measured by the Montreal Cognitive Assessment (MoCA). A total of 348 participants (f = 197; age = 21-76) completed SPACE and a socio-demographic questionnaire. Results revealed that the Age ($\beta = -0.20$; $p < 0.001$), Gender ($\beta = -0.26$; $p = 0.013$), and the Visuospatial ($\beta = -0.12$; $p = 0.016$) and Perspective taking ($\beta = -0.20$; $p = 0.001$) tasks in SPACE significantly predicted 20% of the variance in MoCA scores. Surprisingly, none of the demographic variables representing risk factors of dementia were found to be significant. To further investigate the relationship between the tasks in SPACE and MoCA, we conducted a Principal Component Analysis (PCA). Results from the PCA revealed that the Visuospatial and Perspective taking tasks in SPACE loaded in the same component as the MoCA (PC1 = 27% of the variance), while the navigation tasks in SPACE (i.e., Path integration, Pointing, and Mapping) loaded in another component (PC2 = 23% of the variance). More importantly, we were able to identify two clusters of participants. The first cluster performed well on the MoCA and badly on the navigation tasks in SPACE. The second performed well on the navigation tasks in SPACE and badly on the MoCA. We argue that including additional navigation tasks as part of cognitive assessments may increase their sensitivity. We further provide age norms for each of the tasks in SPACE.

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55. REPLAY LEARNS EFFICIENT MAP REPRESENTATION TO AVOID ONLINE PLANNING

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To quickly adapt to novel environments, we form a 'cognitive map' from past experiences. Such a map in a two- dimensional (2D) world is represented by grid cells, characterized by hexagonal firing patterns. Forming this map requires the integration of fragmented experiences. Spontaneous 'replay' of experiences is thought to be crucial in this process. However, little is known about what should be replayed in learning a cognitive map, its resulting neural representation of the 2D world, and its role in future flexible behavior. Using Magnetoencephalography, we have successfully scanned more than 10 hrs per human subject (35 in total) throughout the learning and inference process. Unbeknownst to the

subjects, this was a 5 * 5 non-spatial grid with two independent dimensions. In learning each dimension, subjects were given piecemeal experiences with only a one-rank difference within a dimension. We found that replay of the 2D map—not just direct memories—started to emerge during rest when learning the 2nd dimension. This offline replay complemented learning, prioritized weakly learned information. It was stronger in the central than the boundary area of the map. Its strength was positively related to the grid cell-like representation of the 2D world and predictive of future novel inference performance. On the task of novel inferences, there were two types of replays, differing in speed (slow vs. fast), representation, and functions. While the fast ON-task replay is similar to offline replay, the slow ON-task replay is the opposite. It only represented trial-specific information, appeared earlier in the inference trials, and was negatively related to the grid-like representation and trial-by-trial inference performance. This study offered unique insight into the distinct role of replay in representation learning and inference. It suggested replay facilitates representation learning, and a sufficiently learned representation alleviates the reliance on online planning.

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56. AGE-RELATED IMPAIRMENTS IN REACTIVATION OF LANDMARK AND TURN SEQUENCES DURING NAVIGATIONAL MEMORY

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Past studies have reported that aging individuals show a decline in spatial memory due to diminished use of landmarks and map-based strategies during navigation. To examine the EEG correlates underlying age-related impairments in landmark memory, we conducted a passive navigation task in which subjects were passively navigated through an environment and subsequently asked to identify an overhead map indicating the route and the destination of the navigational path. We recorded scalp EEG and eye-gaze during navigation (encoding) and map-viewing (retrieval) in younger (age: 20-47, n=32) and older subjects (age: 48-65, n=30).
First, we hypothesized that similar cortical neural activities related to landmark processing during encoding (navigation) and retrieval should be indicative of successful memory reactivation. We calculated EEG pattern similarity between navigation and retrieval period and compared across timepoints in which subjects viewed landmarks or turns – the two important navigational cues in our task. We found higher spectral similarity during landmark viewing and turning compared to other timepoints in younger subjects, but not in older subjects, particularly during landmark viewing, suggesting a failure to reactivate landmark-specific information.
Second, we found a replay-like pattern related to turn representations, characterized by a transition from stronger reactivation for earlier turns to stronger reactivation for later turns over the retrieval period. Furthermore, we found that higher landmark reactivation at the early stage of retrieval predicted significant replay-like patterns of turn sequence reactivation, particularly in younger subjects. These results suggest that: 1) the reactivation of neural patterns during landmark processing and turn sequences in navigation provide an EEG marker for navigational memory and that 2) the spatial memory decline in older adults is associated with their failure to reactivate landmark information.

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57. OBJECT VECTOR CODING IN THE HUMAN BRAIN

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A key property of mammalian navigation is that locations of interest are often stored with respect to local or global landmarks. In rodents, this coding scheme has been related to vectorial information derived from object vector cells(e.g., Deshmukh and Knierim, 2013; Hinman et al., 2019), which encodes both the distance and direction towards local objects. In humans, so-called egocentric bearing cells have been observed in the medial temporal lobe (Kunz et al., 2021), but cognitive maps are generally thought to be stored in an allocentric reference frame.
In this study, we examined object vector coding in healthy young adults with fMRI. Participants first learned four target locations in relation to a fixed landmark in a virtual environment, with the landmark providing both directional and distance information. Even though we ensured that visual input was identical across the four test locations, we were able to decode the target positions from multivariate BOLD response patterns in the caudate nucleus, lateral occipital cortex and precuneus. Furthermore, model-based representational similarity analysis revealed that the lateral occipital cortex and the precuneus were sensitive to the allocentric direction towards the landmark, while the caudate nucleus might encode the distance component. Together, these results point towards a distributed code of allocentric object vectors in the human brain, which complements the boundary related processing typically observed in the entorhinal cortex and the subiculum.

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58. UNRAVELING THE TEMPORAL DYNAMICS OF HIPPOCAMPAL REPLAY POST-REMAPPING

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The hippocampus is critical for memory encoding, with neuronal "replay" posited to aid this function across contexts in various species. When a rat runs on a linear track, "place cells" in the hippocampus fire at different locations along the track. Employing this concept, we developed a Bayesian decoder that interprets an animal's track trajectory from its ongoing neuronal spiking activity. This tool also assesses hippocampal replays during sharp-wave ripples when the rat is at rest. Even minor environmental changes can trigger a total or partial remapping of these place cells, but how this impacts hippocampal replay is not well understood. In a previous experiment, rats ran ~20 laps for a water reward on a track, which was then shortened, followed by another ~20 laps. We hypothesized that replays reflect the most recent experience—long track replays on the long track, short track replays on the shortened track. In contrast, we found distinct replays of both track lengths after, but not before, the track was shortened, indicating the hippocampus balances recent and remote experiences. Analysis of place cells active in both track configurations showed firing rate changes during replays proportional to those during laps. We next built a decoder that produces the relative likelihood that a given period of neural activity corresponds to the long or short track. This showed that replay of the shortened track begins immediately after the length change and is interleaved with continued replays of the long track. Even minor differences in the firing rates of cells between tracks contributed significantly to discrimination by the decoder. Some cells became active only on the short track, even though it is a spatially restricted segment of the long track. Studying this topic can provide insight into fundamental principles of memory encoding and retrieval across overlapping contexts, leading to a broader understanding of memory in health and disease.

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59. TOWARD A MORE NUANCED UNDERSTANDING OF THE SENSE OF DIRECTION AND PERSONALITY TRAIT RELATIONSHIP

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Although there are notable associations between higher-order personality factors and sense of direction (SOD) (Condon et al., 2015), little is known about how finer descriptions of personality disposition relate to SOD. Using data from the Synthetic Aperture Personality Assessment (https://sapa-project.org; SAPA), we tested (N = 24,298) and cross-validated (N = 24,298) the utility of the SAPA Personality Inventory (SPI) 5 factors, SPI 27 facets, and SPI 135 personality nuances/items for predicting SOD, measured with the Santa Barbara Sense of Direction Scale (Hegarty et al., 2002).
Personality facets of high intellect (cross-validated r = .32), wellbeing (.27), industry (.25), charisma (.25), and adaptability (.20), as well as low anxiety (-.27) had the strongest associations with SOD ($p < .001$). Personality items relating to high confidence, flexibility, as well as quick learning and thinking had the strongest item-level associations with SOD. The SPI- 135 nuances/items had the greatest predictive utility for SOD (cross-validated multiple R = .51), followed by personality facets (.44), and personality factors (.39). Additionally, an empirically identified selection of the 30 most predictive personality items from the full set of 135 items predicted SOD almost as well as the full set (cross-validated multiple R = .49). Overall, an in-depth understanding of the complexity in personality trait and SOD associations is important for understanding why there are stark individual differences in SOD.

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60. TWO-PHOTON IMAGING OF MOUSE HIPPOCAMPUS DURING VIRTUAL NAVIGATION OF OPEN ARENAS

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Two-photon (2P) microscopy is a pivotal tool to visualize neuronal activity in the brain, providing essential insights into the neural substrates of cognition and behavior. However, traditional tabletop 2P imaging setups require head-fixed animals exploring mostly linear virtual reality (VR) environments, limiting the observation of neural dynamics associated with naturalistic behaviors, while miniature head-mounted 2P devices are more difficult to adapt to additional functionality than tabletop rigs. This project overcomes these limitations by incorporating 2P imaging with two-dimensional virtual reality (2D VR). In our setup, mice explore in a 2D virtual environment with free rotation in the horizontal plane. The angular displacement is recorded synchronously with imaging, facilitating the subsequent un-rotation of each frame to a fixed orientation. Imaging registration and Z-drift correction are implemented every 5 minutes as imaging is carried out. The semi-online imaging process ensures the precise tracking of neuronal populations within a substantial field of view. Our preliminary data show place cell dynamics as mice navigate in 2D VR, showcasing the ability to monitor neuronal assemblies over successive days and across both superficial and deep layers in the hippocampus. This novel 2P 2D VR methodology augments our capacity to investigate complex navigational behaviors, potentially broadening the range of cognitive processes for which we can study neural activity in the hippocampus and other areas.

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61. CROSS-SPECIES COMPARISON OF THE ABILITY TO CREATE AND USE AN ALLOCENTRIC SPATIAL REPRESENTATION NAVIGATING IN A VIRTUAL ENVIRONMENT

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The ability to create and use an allocentric representation of the environment is considered a hallmark of efficient and flexible navigation. However, the nature of the representation in different species -whether Euclidean, graph-like, or a collection of viewpoint memories- has been debated, particularly in the context of virtual navigation.
We hypothesize that an allocentric representation is acquired by integrating external and self-motion information when navigating a novel environment, and enables optimized responses to environmental perturbations, such as finding shortcuts. To characterize the ability of humans and rhesus monkeys to form spatial representations from virtual navigation, we developed a novel experimental protocol based on the virtual environment of the Starmaze task. To best mimic conditions in humans and monkeys, no instructions were given to humans. Both species used a joystick to navigate while their virtual coordinates and eye movements were recorded.
The task involved a training phase where humans and monkeys had to alternately navigate toward a visible cue, which changed location each time, and a non-visible reward that remained fixed relative to the unchanged environment. To test participants' representations, we introduced environmental perturbations, including a change in maze geometry from the Starmaze structure to an open arena, teleportation, and suppression of all distal cues.
Ongoing analyses will allow us to assess the ability of humans and monkeys to memorize the location of an invisible reward and to anticipate the location of their heading target based on environmental information, indicating whether they formed a representation of the environment through navigation. In addition, we will determine whether they used self-motion information to find their target or could generalize spatial information acquired in one geometry to another, which will help to characterize the underlying cognitive representations.

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62. REPRESENTATIONAL DRIFT AS A RESULT OF IMPLICIT REGULARIZATION

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Recent studies show that, even in constant environments, the tuning of single neurons changes over time in a variety of brain regions. This representational drift has been suggested to be a consequence of continuous learning under noise, but its properties are still not fully understood. To investigate the underlying mechanism, we trained an artificial network on a simplified navigational task. The network quickly reached a state of high performance, and many units exhibited spatial tuning. We then continued training the network and noticed that the activity became sparser with time. Initial learning was orders of magnitude faster than ensuing sparsification. This sparsification is consistent with recent results in machine learning, in which networks slowly move within their solution space until they reach a flat area of the loss function. We analyzed four datasets from different labs, all demonstrating that CA1 neurons become sparser and more spatially informative with exposure to the same environment. We conclude that learning is divided into three overlapping phases: (i) Fast familiarity with the environment; (ii) slow implicit regularization; (iii) a steady state of null drift. The variability in drift dynamics opens the possibility of inferring learning algorithms from observations of drift statistics.

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63. THE EFFECT OF AGE AND ENVIRONMENTAL SYMMETRY ON HUMAN NAVIGATION IN COMPLEX ARCHITECTURAL SPACES.

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Recent navigation studies show that older people rely on geometric cues (i.e. the surface layout of space) to a larger extent than young, potentially due to an age-related deficit in processing landmarks. General validity of these data is questioned by the fact that these studies were conducted in small-scale (vista) spaces, since it is known that the use of geometric cues is affected by environmental size. Here we tested young and aged adults in a navigation task performed in large-scale (~500m2) architectural spaces composed of multiple (~20) rooms. Subjects equipped with head-mounted displays searched for objects hidden in the virtual space by moving through the open physical space of the same size. In 3 experimental conditions we assessed the effect of environmental symmetry on performance in the presence or absence of landmarks. We show that older navigators learned object locations as fast as younger ones in an asymmetric environment, whereas their performance was significantly worse in a rotationally symmetric one, despite the presence of landmarks. Moreover, subjective reports indicate reliance of older navigators on landmarks, despite the objective evidence that landmarks had no effect on their performance, confirming the difficulty in landmark use in the older population. These data confirm landmark-processing deficits and reliance on geometry as a general effect of age on spatial navigation.

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64. LONG TERM POTENTIATION DIFFERENTIALLY AFFECTS CODING OF SPATIAL LOCATION AND HEAD DIRECTION AFTER SPATIAL LEARNING IN THE MORRIS WATER MAZE

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Hippocampal place and head direction (HD) cells activity has long been proposed to mediate the representation of one's location and the heading direction in space. Yet, how place and HD neuronal population dynamics change with spatial learning and how this activity drives navigation to a learned goal is poorly understood. To address these questions, using calcium imaging with wire-free

miniaturized microscopy we imaged the activity of hippocampal CA1 neurons during spatial learning of a target oriented two-dimensional navigational task, the Morris Water Maze. Using generalized linear models we were able to disentangle activity of the place and HD cells in CA1 as animals navigate in the maze. We found that spatial and HD firing selectivity significantly increased as mice learned to navigate to the goal (n=10 animals). Concomitantly, the prediction of spatial location and HD from the population activity using deep learning-based decoders showed a significant improvement after learning. Further, we investigated the synaptic mechanisms driving these improvements in hippocampal spatial and HD neural selectivity, and assessed whether they are necessary for learned goal navigation. We performed identical experiments in glutamate receptor subunit 1 (GluA1) mutated mice that have impaired long-term potentiation (LTP) in CA1 without any deficiency in the normal synaptic transmission (Zhou et al., 2018). Preliminary findings show LTP-deficient animals have a significant improvement in spatial selectivity during learning similarly to littermate controls, however HD selectivity did not improve in the LTP deficient mice (n=5). Consistent with these findings, decoding of the spatial location from the CA1 population during spatial learning improved in the LTP- deficient mice, but the HD decoding prediction did not improve. Therefore, LTP reduction differentially impacts HD and place coding during spatial learning.

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65. EFFECTS OF STRESS AND CORTISOL INCREASES ON EXPLORATION AND SPATIAL LEARNING

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The effects of stress and stress-dependent cortisol increases on spatial cognition are a significant research interest in the field. This study investigates the effects of stress and elevated cortisol levels on spatial cognition utilizing two distinct modalities: a first-person virtual navigation task, known as Virtual SILCton, and a two-dimensional grid-based foraging task. Stress was induced in participants through a socially evaluated cold-pressor task, an established method for eliciting stress responses in a controlled laboratory setting. Salivary cortisol levels were measured before and after stress induction to quantify physiological stress responses. Next, participants were tasked with freely exploring the Virtual SILCton environment, with the goal of learning the locations of landmark buildings. Participants then completed a series of on-site pointing accuracy tests between each of the buildings as a measure of spatial learning. After the end of this task, a third saliva sample was collected for cortisol measurement, before participants proceeded to the second spatial learning task. The second modality, the grid-search task, tested spatial cognition in a more abstract, less immersive environment. Participants were required to locate and remember the positions of resources across a series of grids. This task assessed spatial memory and strategy in a context distinct from first-person navigation tasks, offering insights into what shared fundamental processes underlie spatial memory and navigation. Data collection for this experiment has concluded. We discuss the relationship between stress induction, cortisol levels, and spatial exploration and learning in alignment with our pre-registered hypotheses and analytical plans. In our pre-registration, we predict a positive relationship between cortisol increases from baseline and exploration in both environments, as well as a positive relationship between cortisol concentrations and spatial learning performance.

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66. HEXADIRECTIONALLY SYMMETRIC MODULATION OF EEG POWER DURING VIRTUAL NAVIGATION

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The entorhinal grid cells are part of the brain network for processing spatial information, with firing fields tessellating a plane with triangular grids. The current study investigated whether non-invasive EEG can record hexadirectionally symmetric modulation of neural activity, hypothesised to originate from populations of putative grid cells. While studies employing fMRI, intracranial EEG, and MEG have established the methodology to read out the medial temporal signal on the macroscopic level, the application of scalp EEG to capture such dynamics in humans is not yet established.
Participants (N = 41) performed a first-person perspective navigation task following predefined trajectories to move along lines with varying orientations, evenly sampling the 360 degrees angular space. Using the DICS beamformer, we estimated the voxel-wise power of virtual channels. Log-transformed powers from four regions of interest (bilateral hippocampi and parahippocampal cortices) and five frequency bands (theta, alpha, beta, and low and high gamma) extracted from the translating segments with constant headings were included in the analysis.
We found a significant modulation of high gamma power (60-120 Hz) in bilateral source-localized hippocampal voxels ($p < .05$, Bonferroni corrected). Additional effects were found in the left hippocampus in the low gamma (60-30 Hz) band and in the left parahippocampal cortex in the high gamma band. Such cyclic modulation was absent in control symmetries (4, 5, 7, and 8-fold) or the other frequency bands analysed. The phase of the hexadirectional signal (putative orientations of grid-cell-like activity) in participants for whom the hexadirectional modulation was significant were not clustered across different individuals (Rayleigh test, $p = .67$). These findings serve as a foundation for investigating medial temporal circuits including the hippocampus and the entorhinal cortex in humans, leveraging the high temporal resolution and mobility of EEG.

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67. INTEGRATION OF BEHAVIORALLY-RELEVANT VISUAL INFORMATION INTO A HEADING DIRECTION REPRESENTATION OF LARVAL ZEBRAFISH

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Spatial cognition involves the study of how we acquire, organize, use and correct knowledge of our spatial environment. Within it, navigation can be defined as the process of reaching a specific destination or goal, located in space. Many different cell types, like place cells, grid cells and head-direction cells, have been identified as representing self position and orientation. These neurons are involved in generating an internal cognitive map of the animal's environment, supported by persistent, continuously updated neuronal activity. Although place and grid cells have been mainly studied in mammals so far, head-direction cells have also been found in flies. This suggests these representations

may be widespread in the animal kingdom. In our laboratory, we have identified a heading direction circuit also in larval zebrafish, involving neurons that share features with those of the mammalian dorsal tegmental nucleus. Original studies identified this circuit based on experiments carried out either in complete darkness or in open-loop (without visual reafference). However, for the heading direction network to be useful, it must be possible to calibrate its representation in order to remove the integration of errors. This can happen, for example, by anchoring the heading representation to a visual stimulus or landmark. Here, we investigate how an external, behaviorally-relevant stimulus can influence the network's activity. We develop a behavioral paradigm involving a visual stimulus that the fish can track and control in closed-loop. Our findings reveal a consistent phototactic response to the presented stimulus. Due to its demonstrated behavioral relevance, this stimulus could potentially affect the head-direction activity, which makes it interesting in the context of spatial navigation. However, more experiments are ongoing in order to achieve a clear understanding of the underlying neural correlates of this behavior.

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68. REPLAY WITHOUT SHARP WAVE RIPPLES IN A SPATIAL MEMORY TASK

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Understanding how memory replay works is important for understanding how the brain accomplishes memory consolidation and planning. In the hippocampus, memory replay in the form of sequenced reactivations of place cells is thought to be broadcast to the rest of the brain via sharp wave ripples. This relationship is so ingrained historically that replay is usually found by detecting ripples first. Here, we report that in rats performing an open field spatial memory task, replays can readily occur in the absence of ripples or population bursts, indicating that, contrary to prevailing theories, ripples are not a prerequisite for the expression of replay. In addition, we report the existence of "ripple fields", locations encoded by replays that, independent of their direction of approach, predict the occurrence of ripples. By manipulating the spatial and reward contingencies of the task, we demonstrate that ripple fields track changes to the underlying hippocampal map, consistent with ripples conveying information about the incorporation of novel experiences. Ripple fields were also matched across rats experiencing similar contexts, highlighting the robustness of ripple generation as a function of context. These findings challenge as well as extend existing theories about the relationship between hippocampal replay and ripples, shedding new light on the neural mechanisms underlying memory processing and spatial cognition.

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69. WHY DO YOU GET LOST? A ROLE FOR SPATIAL PROXIMITY-BASED LANDMARK COMPETITION

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When multiple landmarks can be used to locate a goal, attention resources can favor the most salient ones at the expense of others. This can lead to a competition effect, overshadowing (OS), which impacts memory. As a result, we can get lost. However, little is known about the factors determining when we observe OS. We designed a paradigm to parametrically assess the dependence of OS on

spatial distance. In two between-subjects studies, participants were trained to find a hidden goal located in the center of an open virtual environment relative to four distinct landmarks arranged in the shape of a cross. Critically, in Exp1 the landmarks were at different distances from the goal in different groups (Close, Medium and Far). Two of them ("target landmarks") were placed at 50 and 70 Virtual Units (VU) across all groups. Following training, goal location memory relying on each of the four landmarks was separately tested, and goal localization error was assessed. Of interest was how well they performed with the target landmarks. Results revealed that landmarks near the goal more effectively overshadowed landmarks far from it, such that when a target landmark was the closer of the options in the array, test performance was good, but when it was relatively farther, performance was worse. In Exp2, a fourth Control Group was trained only with the 50+70 VU landmarks, validating Exp1 results were due to OS. Critically, results also showed a gradient of OS depending on the overall goal-landmark proximities in the array: OS effects were strong in the Close Group, but attenuated in the Far Group where the target landmarks were relatively more proximal, revealing relative distance as a critical determinant of OS. In a third within-subjects study, we examine fMRI correlates in the frontoparietal and medial temporal circuitry. We will characterize the neural bases of OS in navigation, unpacking mechanisms behind goal-landmark proximity effects and associated navigation strategies.

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70. REPRESENTING OBJECT VECTORS IN THE HUMAN BRAIN

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The entorhinal cortex (EC) in the medial temporal lobes (MTL) constitutes a core area for spatial navigation, yet its precise function in humans is not fully understood. This fMRI project investigation in human participants is inspired by recent observations of object-vector cells in rodent entorhinal cortex, which supposedly represent allocentric geometric relationships between the self and objects in the external world. The objective is to identify neural representations associated with object-vector processing in humans, using high-field fMRI at a field strength of 7T (Siemens MAGNETOM Terra).
We developed a new spatial updating task which required participants to point in the direction of a local object from different perspectives in allocentric vs egocentric conditions, while we systematically manipulated distance (close-far) and direction (ahead-behind) to the object. Spatial memory performance, eye movements and brain activity (TR=2, volumes=288, voxels=1.25mm iso) were recorded in 48 young healthy participants (18-35 yo).
Preliminary analyses indicate equally good performance in the two conditions, with the environmental background being more critical to successful allocentric trials, as indicated by gaze distribution during the task. The task yielded activity in main navigation (eg. RSC, PRC, PHC) and scene-selective (eg. OPA, PPA) areas. Condition comparison showed higher activity in dorso-medial and ventro-lateral processing streams during the allocentric and egocentric conditions, respectively, also extending to the MTL. Furthermore, EC activity varies with distance to the intramaze object.
Studying how the human brain processes object vectors may be key in understanding EC spatial function in humans and could help us identify and characterize EC functional changes that occur in early Alzheimer's disease.

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71. CAN A GLOBAL COMPASS CUE RESOLVE LOCAL LANDMARK AMBIGUITY IN SPARSE AND CLUTTERED VIRTUAL ENVIRONMENTS?

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In our daily life, we rely on various strategies to navigate, with two key methods being path integration and the use of landmarks. In path integration, the spatial self-location is continually updated by integrating travel time, speed, and acceleration. However, systematic errors tend to occur within this integration, often resulting in an underestimation of travelled distances and angles. Therefore, it can be helpful to additionally use landmarks. Landmarks can complement path integration by providing external directional cues. However, relying on just one or two ambiguous landmarks or trying to distinguish between clusters of landmarks in a cluttered environment can lead to imprecise and inaccurate navigation.
Consequently, the inclusion of a global directional compass cue could be of vital importance to improve navigation success. Unlike local landmarks, a global directional cue is world-centered and unaffected by minor movements of the viewer. This stability could resolve existing ambiguity in internal representations of environmental features and help with the integration of other spatial cues. Therefore, we ask: Can a global compass cue resolve local landmark ambiguity in sparse and cluttered virtual environments?
In our experiment, the participants were asked to perform a triangle completion task within a virtual environment, in which they are displaced via two legs of a triangle and have to return to their starting position afterwards. We varied the degree of clutter by the number of trees in the surround (0, 1, 10, or 99) and altered the sun azimuth to provide a global compass cue by its position and the direction of cast shadows. By investigating whether the sun can resolve the existing ambiguity from the local landmarks and path integration in cluttered environments, we demonstrate the efficacy of compass cues and highlight their limitations.

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72. CAVE CRYSTAL QUEST: A NOVEL PATH INTEGRATION TASK FOR ISOLATING ANGULAR ENCODING AND PRODUCTION ERRORS

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Path integration tasks, such as triangle completion, involve the updating of self-location by integrated linear and angular movements and the production of a return trajectory. This navigation skill is inherently prone to inaccuracies due to encoding and production errors. Despite ongoing debate regarding which type of error—encoding or production— predominantly contributes to inaccuracies in path integration among healthy populations, recent research focusing on early Alzheimer's Dementia (AD) highlighted angular encoding gain as a significant source of errors in a triangle completion task (Castegnaro, Ji et al., 2023).
Here, we propose a novel path integration task, conceived as an immersive virtual reality game named 'Cave Crystal Quest,' whereby participants are required to provide linear and angular responses separately. In a counterbalanced design, we aim to disentangle the contributions of angular encoding and production errors by requiring identical responses to different initial turns and different responses to identical initial turns (see Chrastil and Warren, 2017). We also ensure that the test can be run in a small narrow space for ease of use.

The task is validated by showing sensitivity to dissociable encoding and production errors in young healthy participants, and will be assessed for its potential to provide a cognitive read-out of early progression towards AD.

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73. INVESTIGATING AND MODELLING THE EFFECT OF AGEING ON THE HEAD DIRECTION SYSTEM IN HUMANS

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The head direction (HD) system, which acts as an internal compass, is central to our sense of direction. This study focuses on creating a behavioural read-out of the HD system while participants can freely move their bodies and heads. This method allows us to investigate changes in the HD system that can emerge during aging. While many studies have described a general, age-related decline of spatial navigation skills, it is unknown if and how the HD system is affected. Moreover, existing HD models cannot adequately assess aging and the consequences of physiological changes (e.g. neuronal death). Therefore, this project aimed to explore the effect of aging on the HD system by using immersive virtual reality (iVR) and a neurobiologically informed modelling approach.
To achieve this, we created an iVR task with an environment composed of a unique landmark and a multicoloured cylinder surrounding the participant. The goal was to retrieve the landmark location by turning towards it after a self- rotation while the cylinder was not visible. As participants were physically rotating, it gave a proper heading measure, and we quantified angular error as the difference between their answers and the correct position of the landmark. In addition, to test for the accumulation of noise over time, a delay period was introduced in half of the trials before answering. Overall, we found that older participants showed larger angular errors than young participants. Moreover, older participants were more impacted by the delay period than the young participants, suggesting a faster accumulation of noise while being static.
To better characterise the differences between the two age groups, we also created a model based on ring attractor networks, a neural network architecture well established for modelling the HD system. We assessed aging by implementing three distinct sources of noise. We found that each source impacted and modified the behaviour of the HD attractor dynamics differently.

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74. HEAD-FIXATION ALTERS NEURAL CIRCUIT DYNAMICS OF HEAD-DIRECTION SYSTEM DURING IMMOBILITY

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Head-fixation in rodent models has become a prominent method for studying neural circuits, yet its impact on neural dynamics remains unclear. Here, we specifically explored the influence of head-fixation on the dynamics of the mouse thalamic head direction (HD) system, revealing impaired population coordination during stationary periods. Using a 2D virtual reality (VR) setup, which enables mice to rotate their heads in the horizontal plane, and chronic Neuropixel recordings of HD cells in anterior thalamus, we discovered that stationary periods in head-fixed animals represent a distinct brain state. This was evident through an altered pairwise correlation structure and off-ring manifold activity. To isolate contribution of head-fixation from VR, we developed a custom head-fixation apparatus that allows mice to freely explore an open-field arena while maintaining an immobile head relative to their body. Interestingly, despite the mice being exposed to all sensory cues, the HDC exhibited similar alterations during stationary periods as observed in VR. Crucially, we show that in both conditions, the fundamental property of HDC, firing exclusively at their preferred direction, is compromised when the head is restrained. During periods of immobility, HDC with preferred directions close to the current orientation reduce their activity, whereas other non-preferred HDC increase their firing, leading to off-ring manifold activity. Simulations of ring-attractor models indicate that disruption of recurrent connectivity of the HD attractor, resulting in non-preferred head direction firing, leads to off-ring manifold dynamics, as observed in experimental data. Collectively, these findings suggest that stationary periods in head-fixed mice signify a distinct brain state of HD system, potentially due to the lack of gravity cues. Future studies should consider potential impact of head- fixation on the specific system under investigation.

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75. REPRESENTATIONS OF IMPOSSIBLE NON-EUCLIDEAN SPACE

Andrew McAvan - Vanderbilt University Tim McNamara - Vanderbilt University

Typically, research into human spatial navigation is conducted with environments that attempt to simulate the real world as closely as possible. However, it is equally important to test humans in spaces that contradict their real-world knowledge of the physical structure of the world; it is just as important to study what we cannot do as it is to study what we can do. Our aim in this project was to explore and exploit a fundamental aspect of Euclidean geometry –namely a space's internal size corresponding to its external dimensions. Here we compare human responses on various measures between two room conditions: A normal space consistent with Euclidean geometry and a non-Euclidean space in which the internal size was larger than its external measurements would allow. The non-Euclidean space was created by making the internal dimensions of two adjoining rooms larger than the external dimensions of the two rooms; in effect, the two rooms overlapped internally. By utilizing fully immersive virtual reality, we tested participants' knowledge of the space that they explored and found that those within the non-Euclidean condition were not able to reconcile the impossible space when tested on it. Specifically, participants in the non-Euclidean condition walked more and spent more time in the environment during learning, created maps that more closely resembled the Euclidean condition (with no map demonstrating the impossible overlap), had increased pointing errors and in some instances, even pointed to where objects would have been in the Euclidean space (180 degrees off from the correct location). These findings provide evidence that people are unable to form a memory of a physically impossible, spatial layout, and rely instead upon their Euclidean prior knowledge of how an environment can be structured.

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76. NEURAL CORRELATION OF GAZE IN LANDMARK OR GEOMETRY -BASED NAVIGATION

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Navigation is a crucial skill for both humans and animals as they exploit resources in their environment. Humans heavily depend on vision, utilizing visual landmarks to generate trajectories to goals in simple or complex environments. In the present research, we aimed to investigate the neural correlation of gaze and trajectory patterns during landmark-based or geometry-based navigation. Rhesus macaques are employed as an effective model for examining processes underlying navigation and were trained to locate a hidden reward in a rectangular virtual arena featuring three salient landmarks. In 25 percent of the trials, these landmarks were intentionally occluded. We have mapped the spatial gaze patterns in both landmark-based and non-landmark environments to analyze the animals' navigational strategy. In addition, the activity of neurons in hippocampus, the retrosplenial and the posterior cingulate cortices were recorded during the tasks. Our preliminary data show that gaze patterns are differentially distributed between landmarks and the floor of the arena, depending on landmark availability. This suggests that animals learned to rely on either the geometry of the environment or the landmarks.

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77. STABLE SPATIAL REPRESENTATION UNDER CEREBELLAR MONITORING

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Spatial navigation relies on internal calculations of direction and distance (self-motion) from sensory information, continuously updating to stay in register with the external environment. However, the brain mechanisms underlying the integration of self-motion information into the brain's navigation system remain unclear. In this poster, we first present our recent findings demonstrating that cerebellar mechanisms are necessary for the continuous updating of position and direction information in hippocampal place cells (Zhang et al 2023). Additionally, we show that cerebellar mechanisms contribute to the generation of a single and stable head-direction signal in the cortico-subcortical head-direction system (Fallahnezhad et al 2023). Our convergent findings on place and head-direction cells suggest that the cerebellum likely acts as a hub for processing internal sensory cues that are crucial for hippocampal function. Subsequently, using a dual viral tracing approach, we identified a disynaptic pathway connecting the cerebellum and hippocampus via a brainstem nucleus. We are currently employing optogenetic axonal inhibition of the cerebellar projections to the brainstem nucleus while simultaneously monitoring neuronal activity in the hippocampus of freely behaving mice to investigate the function of this pathway.

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78. THE EMERGENCE OF NEURAL MECHANISMS FOR MEMORY SPECIFICITY DURING POST-NATAL DEVELOPMENT

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Episodic memory, or memory for events, emerges late in humans. Prior to this, individuals experience infantile generalization (IG): impaired memory recall and positioning of specific events within their spatial-temporal framework (Nelson and Gruendel, 1981). An explanation is the immaturity of the mechanisms by which the brain reduces the overlap between neural representations with contextual similarities, to produce separate memories (pattern separation; PS) and retrieves memories from incomplete sensory information (pattern completion; PC). In development, an inability to separate similar memories and an over association of sensory information could lead to a bias of generalization over specificity (Keresztes et al., 2018; Ramsaran et al., 2019). Prevailing theories suggest that PS and PC occur in the dentate gyrus (DG) and CA3 regions sub-regions of the hippocampus respectively (Marr, 1971). In addition, the hippocampal subfield CA3 has also been implicated in PS (Goodsmith et al., 2019). Therefore the developmental immaturity of this brain circuit, in particular the unusually late maturation of granule cells in the DG, could be causally linked to IG. This data represents the first awake behaving electrophysiological recordings of different cell types of the DG-CA3 circuit in developing rats. In addition, we evaluated the PS ability of these cells in rats exposed to varied spatial contexts, assessing their encoding capability for memories with similar or distinct contextual elements across the onset of hippocampal memory (P16-P32). We found no evidence of PS in granule cells, suggesting that their protracted maturation may not be the primary factor behind IG. In contrast, mossy cells developed PS after weaning implying PS functions through distinct mechanisms in the two cell types and underscoring the significance of mossy cells in the emergence of memory specificity during the postnatal period in rats.

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79. STUDYING 3D NAVIGATION IN THE SPONTANEOUSLY BEHAVING COMMON MARMOSET

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During their daily activities, non-human primates need to orient in their environment in order to locate themselves, remember relevant sites, and plan routes. Common marmosets (Callithrix jacchus) are New World monkeys, equipped with accurate foveal vision similar to humans, and renowned for their exceptional climbing ability. Therefore, they are an ideal and human-relevant model for investigating navigation in intricate settings.
We designed and built multiple setups (up to 4m3) to study navigation in freely behaving marmosets. We use a marker- based motion capture system (Optitrack; 24 cameras) to robustly track multiple animals' head movements simultaneously in 3D, and we plan to use data-loggers (White Matter) to record up to 64 channels of neuronal data.
We are interested in the head direction cells coding of the 3D space which until now has been studied in freely moving rodents or in animals passively being rotated. Thanks to their climbing proficiency, marmosets are an interesting model to study 3D orientation. Accordingly, we easily trained them to locomote for several minutes on the floor and ceiling of a cage, and demonstrate that the resulting head motion efficiently covers 3D rotation space. The further use of this setup will lay the groundwork for future research in the field of 3D orientation.

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80. INVESTIGATING THE NEURAL BASES OF EPISODIC MEMORY AND NAVIGATION IN CHILDREN AND YOUNG ADULTS

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Cognitive maps and episodic memory are often linked, but there is no agreement regarding the nature of the overlap, if any, and whether relations wax or wane over development. We used a real-world encoding task and structural MRI to investigate how these cognitive functions are related.

Participants (n = 130) were led along a staged tour where they interacted with and learned facts about 16 objects. Episodic memory was evaluated with an autobiographical free recall and a cued recognition test. Spatial memory was evaluated by testing route efficiency, judgement of relative direction (JRD), and map building. T1- and T2-weighted images were acquired from 116 participants in a 3.0T Siemens scanner. Bilateral CA1-2, DG-CA3, and Sub volumes were automatically segmented using the Bender et al. (2018) atlas, manually corrected, and adjusted for intercranial volume.
Behavioral results indicate the measures of spatial and episodic memory contribute to two components, accounting for 85.6% of the total variance. Navigation measures of route efficiency and map building and memory measures of spatiotemporal details and free recall contribute strongly to the first factor. The second factor includes perceptual and event details and JRD. Although the two factors are strongly correlated ($r = .81$, $p < .001$), factor congruence analysis shows that across age, the two factors are distinct. These behavioral findings suggest that navigation and episodic memory are neither cleanly delineated nor the same construct but overlap due to shared task demands and neural substrates.
Ongoing analysis explores correlations with HPC and subfields volumes.

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81. THE COMMON MARMOSET AS A NOVEL MODEL FOR MULTIMODAL SELF-MOTION SENSING

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Spatial orientation and Navigation require precise and accurate integration of visual, vestibular and motor efference copies. Comprehending the interplay between these sensory modalities is primordial for understanding their contributions to navigation, in the context of virtual reality setups or experiments with sensory deficits models, where only a subset of these cues are present.
To date, empirical and theoretical evidences into self-motion processing in non-human primates (NHP) stems from macaques. However, in the recent years, common marmosets (Callithrix jacchus) are emerging as a new NHP model in neuroscience. Their small size, active and agile nature makes them ideal to investigate navigation and self-motion in laboratory settings. The first step towards this goal is to characterize their vestibular function.
We have built a marmoset rotator in which the animal and/or the visual surround can be rotated independently, and performed a series of experiments to evaluate the vestibular functions and the visual-vestibular interaction in common marmosets. Our experimental observations are in agreement with previous finding in humans and macaques. Furthermore, we successfully adapted the mathematical models of the vestibular system in humans and macaques to marmosets.
Together, our experiments demonstrate that the principles of rotation perception in common marmosets is analogous to other primate models. These findings will be the basis of further investigations of the vestibular system in marmosets, and of model-based studies of how the vestibular sense contributes to spatial orientation.

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82. WALKING IN CIRCLE: THE ROLE OF THE VESTIBULAR SYSTEM?

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In many stories, lost individuals in deserts, jungles or snowstorms often end up walking in circles, feeling hopeless as they realise they've crossed their own tracks. This phenomenon is universal and surprisingly enough we still know very little about it.
Previous empirical studies have demonstrated the occurrence of circling behaviour in real settings such as forests, deserts, and open fields and have dispelled the misconceptions that it may be attributed to

biomechanical factors such as leg length or strength. Building upon these researches, we sought to replicate and further investigate this behaviour in controlled laboratory settings. Specifically, we aimed to examine the involvement of the vestibular system.
Through extensive experimentation involving over 100 young participants, we encountered challenges in pinpointing a consistent variable associated with the circling behaviour. The variability and randomness observed made identifying a discernible pattern difficult, making it even more difficult to pinpoint the role of the vestibular system.
Parallely, we addressed the question of how visual impairment affects this behaviour, hypothesising that individuals accustomed to relying less on visual cues to navigate may exhibit superior ability to maintain a straight-ahead position. Preliminary results do not confirm it. This result speaks indirectly in favour of the implication of the vestibular system.
These findings contribute to our understanding of circling behaviour and underscore the complexity of human navigation processes.

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83. REGIONAL SPECIALIZATION OF RETROSPLENIAL CORTEX IN VISUAL AND SPATIAL CODING

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The retrosplenial cortex (RSC) is a multimodal association hub, integral for sensory visual and spatial contextual signals for navigation. In rodents, RSC receives inputs from a variety of cortical and parahippocampal areas and shows landmark and place-correlated responses. However, RSC inputs and response properties are anatomically and functionally diverse and have rarely been characterized, particularly along the anterior-to-posterior spectrum, this axis covers a substantial area of the rodent cerebral cortex and has recently been implicated in exhibiting distinct functionalities in contextual memory.
We investigated functional and anatomical regional specialization in mouse RSC using in vivo cellular imaging and genetic brain-wide input mapping. We measured the calcium activity in head-fixed running mice in response to spatial location and visual stimuli, and mapped the long-range inputs to these regions. Our results suggested while both anterior RSC (aRSC) and posterior RSC (pRSC) show position-related and visually evoked activity, each region specializes in processing distinct signal modalities. Position tuning is more pronounced and reliable in aRSC than in pRSC. This enhanced position activity correlates with denser inputs from cortical areas carrying position-tuned signals (motor, somatosensory, entorhinal areas and dorsal subiculum). In contrast, visual responses are more pronounced and more reliable in pRSC than in aRSC. Enhanced pRSC visual responsiveness correlates with denser inputs from primary and higher visual areas.
Altogether, the results indicate regional specialization suggesting complementary functional roles of aRSC and pRSC in the integration of visuospatial information. aRSC could be implicated in the rapid processing of visual cues and landmarks, enabling efficient route planning and execution. pRSC may be more involved in the integration of contextual information and the formation of cognitive maps.

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84. PLACE CELL FIRING PROPERTIES AND REACTIVATION IN A MOUSE MODEL OF ALZHEIMER'S DISEASE

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Alzheimer's disease (AD) research has primarily focused on pathological brain changes, with less emphasis on functional alterations. Those studies investigating neural function have often used transgenic models, which are affected by APP gene overexpression, potentially confounding results. To better understand the functional consequences of AD pathology, we focused on the hippocampus, a region crucial for memory and one of the first affected in AD. We employed the APP NL-G-F knock-in mouse model, which avoids APP overexpression, to explore memory functions, place cell activity, and their reactivation in AD.
We conducted chronic single-cell ephys recordings from region CA1 of the hippocampus in AD mice and wild-type controls. As the APPNL-G-F model exhibits saturated amyloid plaques by 7 months (Saito et al. 2014), we recorded from mice of 7-18 months. Memory performance was assessed using a radial arm maze task with reward configuration changing across days, providing two distinct measures of memory performance: recall of reward locations across trials and recall of previously visited locations within trials. AD mice showed impaired recall for previously visited locations, while recall for reward locations remained intact.
Ephys findings showed that place cells in this AD model have lower firing rates and smaller firing fields than controls. The stability of firing fields across sessions was reduced, and the correlation between ratemaps for inbound and outbound running was diminished, suggesting increased directional specificity in AD mice. Reactivation patterns during stationary rest and subsequent sleep recordings were also assessed. While reactivation rates did not differ between AD mice and controls, the content of reactivations varied, indicating qualitative differences in the replay of prior experiences. These results provide insights into the impact of amyloid pathology on hippocampal function and memory performance in a conservative mouse model of AD.

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85. A METHOD FOR IDENTIFYING EGOCENTRIC BEARING CELLS IN THE BRAIN

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Humans and other animals use different reference frames for spatial navigation and spatial memory. By means of allocentric reference frames, they represent spatial information relative to the external environment. By means of egocentric reference frames, in contrast, they represent spatial information relative to themselves. Recent empirical findings in rodents, bats, and humans indicate that the hippocampal formation does not only contain neural cell types underlying allocentric reference frames but that there are also cell types specialized in representing egocentric spatial information. The analytical detection of egocentrically tuned cells is non-trivial, however, and allocentrically tuned cells may be mistaken as egocentric cells in some cases. Here, we present an analysis method for identifying egocentric bearing cells, following up on our previous work (Kunz et al., Neuron, 2021). These cells increase their spiking activity at particular egocentric directions relative to local reference points in the environment. We show that our method reliably detects egocentric bearing cells (with and without distance tuning); that it detects their reference points with good accuracy; and that it does not incorrectly identify allocentric place or direction cells as egocentric bearing cells. In contrast, our results show that egocentric bearing cells can be mistaken as allocentric direction cells and that egocentric bearing cells with distance tuning can be mistaken as allocentric place cells. Our method may thus help

investigate egocentrically tuned cells in humans and other animals, and it may help advance our understanding of how the brain accomplishes spatial navigation and spatial memory.

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86. THE HEAD DIRECTION SYSTEM IS HORIZONTALLY TUNED IN A THREE-DIMENSIONAL ENVIRONMENT

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Spatial orientation and wayfinding are fundamental characteristics that address basic life needs. Animals and humans use various types of neurons in several brain regions that encode different aspects of spatial orientation. Directional heading is one of these aspects, encoded by the head direction (HD) network. Each cell in this system fires as a function of a specific preferred direction. In other words, each HD cell fires when the animal's head is pointing in a specific direction within the horizontal (azimuthal) plane. Nevertheless, terrestrial animals often encounter three-dimensional structures while navigating in any given natural environment. Thus, it is important to understand how neurons represent a three- dimensional environment in the brain. In this study, we focused on the three-dimensional properties of HD cells, and specifically, we posed the question of whether HD cells of a freely moving rat are modulated by tilt plane. To address this question, we monitored HD cells from the antero-dorsal thalamus nuclei (ADN) of freely moving rats in a three- dimensional environment constructed as a hilly terrain. Traveling in this hilly terrain, led to sampling of different degrees of tilt orientation by the rats. Our hypothesis was that HD cell activity will be aligned with the horizontal plane of the environment, regardless of the tilt orientation of the rat's head, since rats are terrestrial animals, and their head is generally aligned with the horizontal plane of their locomotion. Results revealed that HD cells in the ADN were not modulated by the tilt orientation of the head, even when the rats locomoted in a three-dimensional environment. This finding is consistent with the notion that HD cells encode the direction of the head with respect to the current plane of locomotion.

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87. COGNITIVE MAPS IN REASONING AND MENTAL MODELS: A NOVEL MEASURE OF ABSTRACT SPATIAL REPRESENTATIONS

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Recent evidence has shown that the brain's system for navigating the environment, the cognitive map, is also recruited when spatially representing and reasoning about information that is not inherently spatial. These findings imply that the cognitive map underlies navigation through abstract, metaphorical space as well as physical space. Despite the neural evidence, there have been few behavioral studies investigating the relationship between abstract spatial representations and individual differences in spatial cognition. Here we present four behavioral studies that support this link. A novel task measured two cognitive processes: the integration of multiple relations into a unified spatial representation and the inferences of novel relations from this representation. Participants were tasked with representing premises relating objects on two dimensions in space and answered inference problems based on their representation. The structure of the created representations varied widely, with some participants spontaneously creating a uniform grid pattern and others creating less structured representations. The type of information, i.e., concrete spatial information compared to abstract non-spatial information, did not affect task performance. Individual differences in

representations and reasoning performance correlated with performance on a measure of spatial scanning (the Hidden Figures Test, previously shown to predict verbal reasoning ability) and with path integration ability, known to rely on grid cells, a key neural component of the cognitive map. This evidence is consistent with the view that a common cognitive map system underlies the representation of both physical and abstract spaces.

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88. NAIVE NAVIGATION STRATEGIES UTILIZE LOCAL PERCEPTUAL INFORMATION AND ARE MODULATED BY DESTINATION PROXIMITY

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Little is known about route selection in unexplored environments. Given naiveté, humans likely depend on local information that can approximate globally optimal solutions. Past research has found that humans minimize the angular deviation between path direction and goal direction (Fajen & Warren, 2003; Hochmair & Karlsson, 2005), select shorter initial segments (Bailenson et al., 1998) and reduce turning angle (Dalton, 2001; Van Tilburg & Igou, 2014), titled the “least angle strategy” (LAS), “initial segment strategy” (ISS) and “action continuation strategy” (ACT), respectively. While there is independent evidence for each strategy, few studies have compared their influence when they are in conflict (Baxter & Warren, 2020), nor measured how their influence may change at different stages of navigation.
To explore these questions, we created a maze of 3 walls or ‘layers’ which each contained 2 doors, the positions of which were randomized between trials. Participants (N=34) were asked to navigate to a goal beacon visible above the walls. In Experiment 1, this beacon was always visible. In Experiment 2, it was only visible for 2s at trial start, and then disappeared. The results from both experiments show that LAS, ACT and ISS had a significant influence on route decisions. However, the dominant strategy changed across layers. Participants were much more likely to minimize angular deviation from the goal (LAS) in the middle layer but tended to choose the nearest door (ISS) in the final layer. Participants were less influenced by LAS when the beacon was invisible. We calculated the expected metabolic cost (Brown et al., 2021) of all paths and found that agents who used only LAS performed best, but not significantly better than humans. Agents that used only ISS or ACT were less efficient. These results suggest that humans use different kinds of information to guide naive navigation at different stages of their journey, and their strategy tends to be energy efficient.

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89. INFERRING A RING-ATTRACTOR STRUCTURE FROM SINGLE-CELL ACTIVITY IN THE ZEBRAFISH HEAD-DIRECTION SYSTEM

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A head direction (HD) cell fires when an animal faces a particular azimuthal direction (Taube and Bassett 2003). Recurrent connections between cells tuned to distinct head directions are thought to create a ring-attractor network that continuously encodes the heading of the animal; this ring-attractor serves as an internal compass (Ajabi et al. 2023).
In the Drosophila HD system, there is strong evidence for a ring-attractor network with three functional rings that integrates angular head velocity (AHV) through velocity-dependent inputs to two lateral rings

(Turner-Evans et al. 2017), but the exact structure of the ring-attractor is still unknown in many other species' HD systems. For example, an alternative mechanism to integrate AHV relies on an AHV-dependent modulation of synaptic couplings (Zhang 1996; Zittrell et al. 2023).
Here, we put forward a theoretical framework to show how AHV differentially affects the firing of HD cells across different network architectures. This framework allows us to infer the ring-attractor structure from single-cell activity without reference to the anatomical location of cells within putative ring-like structures. Different AHV tuning profiles among sub-ensembles of HD cells correspond to separate functional rings.
We first illustrate that the theory correctly predicts the three functional rings present in Drosophila, each of which exists on a separate anatomical structure. The same approach applied to zebrafish data (Petrucco et al. 2023) indicates that the zebrafish HD system is composed of three functional rings, too. Moreover, while the left and right functional rings do not lie on separate anatomical structures in the zebrafish, they do exhibit a significant degree of anatomical lateralization.
This approach is general and can be easily extended to other ring-attractor systems and species.

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90. INTEGRATION OF SYNTHETIC CUES DURING SPATIAL NAVIGATION

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Mobile organisms use spatial cues to navigate effectively in the world. Recent research indicates that humans can optimally combine visual and body-based cues during homing. However, technological advances (e.g., virtual and augmented reality) have introduced novel synthetic cues for navigation, such as digital overhead maps, relevant to the evolution of GPS and assisted GPS technologies.
We examined whether human navigators integrate visual landmarks, self-motion, and synthetic (dynamic overhead map) cues during navigation in immersive VR. Conflict among three cues was introduced by independently rotating landmarks (Exp 1) or the landmarks represented in the synthetic map (Exp 2), or by rotating both simultaneously in the same (Exp 3) or opposite directions (Exp 4) by 15o around the participant. The overhead map maintained a north-up orientation in Exps 1-4. All cues were available along the outbound path and manipulated prior to the homing response. In Exp 5, the orientation of the synthetic map was either north-up or forward-up for two groups. Response variability in the combined condition was consistent with cue integration models for landmarks+self-motion and landmarks + map cues, suggesting that navigators only integrated two cues when all three were available. Notably, compared with the north-up map, the forward-up map enhanced homing precision with self-motion cues, even after the map was removed prior to the homing response.
Exp 6 manipulated the availability of a forward-up map on the outbound and homing paths. We found that with the access to the forward-up map along the outbound path, response variability was smaller than when using self-motion cues only but was larger than when both cues were available during both the outbound and homing paths. The egocentric nature of the forward-up map enhanced the precision of self-motion cues along the outbound path, and this integrated representation was partially intact during the homing response.

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91. LOST IN TRANSLATION: EGO-ALLO REFERENCE FRAME TRANSFORMATION IS DISTINCT FROM ALLO-EGO TRANSLATION

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The ability to build and maintain an accurate spatial representation of our environment is essential for spatial orientation and for navigation, both fundamental everyday tasks. Yet as with all cognitive abilities, there are large individual differences in people's abilities. Characterizing the different factors which underlie this incredibly complex process is critical for understanding the source of the variance. A common distinction made in the navigation literature, is between egocentric (self-centered) and allocentric (world-centered) reference frames, which are postulated to involve different brain circuits. To examine the relationship between these two reference frames and their unique contributions, we test the translation process between them, while also accounting for memory load, an oft-neglected variable in spatial orientation abilities. We designed a virtual reality (VR) experiment with two components: in the first, participants explore virtual arenas in complete darkness, and receive auditory cues to indicate that they have reached an object location. At the end, they must draw a map of the arena, translating the egocentric information to an allocentric representation. Conversely, participants receive a map with object locations, and must indicate where those objects would be with respect to their own position, translating allocentric to egocentric information, with or without having to first memorize the map. Our results indicate that these two transformations are indeed behaviorally distinct, and that memory load interacts with them in a non-trivial manner which varies across participants. These findings will facilitate a deeper understanding of the mechanisms underlying individual differences in spatial abilities, and can serve as a basis for studying what goes wrong in diseases such as Alzheimer's.

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92. HEXADIRECTIONAL MODULATION OF GRID CELL FIRING IN RODENTS

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A method for non-invasive detection of grid cell activity has been successfully applied to functional neuroimaging in humans. This method looks for "hexadirectional" modulation of macroscopic activity by running direction with 6-fold rotational symmetry, i.e. 6 peaks and troughs within the 360o range of directions (Doeller et al. 2010). Despite its successful use in several studies in humans, it is still not clear what aspects of physiology produce the hexadirectional modulation (Khalid et al. 2024). Two suggestions concern: i) non-linear processes, such as firing rate adaptation, that would affect activity differently when running along 3 axes of the grid pattern (when some cells fire a lot and other a little) compared to running between grid axes (when all cells fire at more similar rates); ii) the contribution of directionally modulated "conjunctive" grid cells whose directional tuning might be aligned to grid axes. Here we examined the firing of grid cells in freely foraging rats for evidence of hexadirectional modulation (HM), bearing in mind the confounding effects on firing rates of inhomogeneous sampling of locations, directions and speeds by behaving animals (Burgess et al. 2005). We found weak but consistent HM effects such that firing is reduced when running aligned to the grid axes, suggestive of

the presence of firing-rate adaptation. We did not find stronger HM in populations of conjunctive grid cells compared to pure grid cells, suggesting that these are not the main driver of any HM effects. Further analyses investigate the HM modulation in grid cell firing in terms of variables such as trajectory which might influence firing rate adaptation, and methodological details that would optimize the ability to detect HM in data from rodents and humans. Overall, our findings begin to provide a way to understand the macroscopic HM signal in terms of microscopic neuronal physiology.

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93. REPRESENTING ACTION PLANS AND THEIR OUTCOMES VIA HIPPOCAMPAL-ENTORHINAL COGNITIVE MAPS AND NEOCORTICAL MOTOR MODELS

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Goal-directed action selection requires weighing alternative actions against each other based on their expected outcomes in the external world. However, the neural mechanisms underlying these computations are still unknown. Here, we hypothesize that cognitive maps generated in the hippocampal-entorhinal system could organize available action plans in a relational manner according to their expected outcomes, supporting flexible goal-directed behavior. We used a novel immersive virtual reality paradigm to train participants to associate arbitrary actions with two independent outcome dimensions. To test participants' knowledge of action-outcome relations, we asked participants to compare the action combinations while recording brain activity with fMRI. Our results indicate that the distance between relative positions of action combinations in a two-dimensional action-outcome space was represented in the hippocampus, while the general structure of the space elicited a grid-like signal in the entorhinal cortex. We also identified action-related processes in the supplementary motor area, which showed a stronger response to comparisons between similar vs. dissimilar motor plans. Crucially, the connectivity between hippocampus and supplementary motor area was modulated by the distance between action combinations in the action-outcome space, suggesting this circuit may play a key role in action selection. In sum, we find evidence that cognitive maps, in coordination with more cortical motor representations, could enable efficient action selection by encoding multiple relationships between different action plans.

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94. INVESTIGATION OF SPATIAL REPRESENTATIONS IN THE POSTRHINAL CORTEX OF DEVELOPING ANIMALS

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To navigate in space, animals rely on knowledge of their spatial location and properties of the environment, such as boundaries and objects. In parahippocampal areas, these external landmarks are represented in relation to each other (allocentric) as well as in relation to the animal (egocentric). Postrhinal cortex (POR) maps the surrounding space in both egocentric and allocentric reference

frames, representing a potential locus for switching between them. Previous work has shown that POR neurons are tuned to egocentric bearing of boundaries during open field exploration. In a trained visual discrimination task, POR neurons code associations between objects and place, as well as the animal's own motor response.
Learning association between objects and a specific place relies on hippocampal functions but emerges late in development (p30; Ainge & Langston 2012). We hypothesised that solving this task requires switching between egocentric viewpoints and allocentric reference frames. This function depends on structures, including POR, displaying both spatial correlates, which might develop later than the hippocampus.
To test this hypothesis, we recorded from POR of adult (p70) and developing (p21-32) rats during exploration and found two distinct populations of neurons. One encodes the presence of objects, without discriminating object location or identity. The other encodes egocentric bearing and/or distance of boundaries, but not objects. In younger animals, object coding is more prominent, while egocentric boundary selectivity is broader and lacks distance preference. In both age groups, about half of the cells display conjunctive allocentric directionality.
This work is relevant to interpret behavioural findings on the emergence of object-place associative recognition. Results advance our understanding of how POR contributes to contextual processing by mapping the geometry of the environment, as well as the spatial distribution of objects in this environment.

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95. NEUROBIOLOGY OF NAVIGATION IN THE REAL WORLD: HEAD-DIRECTION CELLS SERVE AS A NEURAL COMPASS IN BATS NAVIGATING OUTDOORS ON A REMOTE OCEANIC ISLAND

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Navigation is crucial for animals and humans. Historically, studies of navigation followed two very different approaches: On one hand, ethologists and ecologists tracked animals in the wild, focusing on sensory cues and navigational strategies in real-world environments. On the other hand, neuroscientists recorded neural activity from animals navigating indoors in small laboratory enclosures, and discovered place cells, grid cells, and head-direction cells. However, these neurons were never recorded during real-world navigation, outdoors. To bridge the gap between these two approaches, we conducted the first study of neurons in the brain's "navigation circuit" during outdoors navigation. We focused on head- direction cells, which represent the animal's orientation, and are commonly called "neural compasses". Natural conditions pose several challenges for these neurons to maintain their direction: First, animals move over large geographical spaces. Second, celestial cues such as the moon and sun – the most prominent distal visual cues outdoors – move substantially and disappear completely. However, to this day, no study tested if head-direction cells exist outdoors – and if they do: are they stable over geographical space, and stable to movement of celestial cues – two key properties crucial for any compass. To this end, we developed wireless electrophysiology and high-accuracy positional tracking, and recorded hundreds of single neurons in the presubiculum – a key hub of head-direction cells – while bats were flying and navigating outdoors on a remote oceanic island. We found head-direction cells, which exhibited both key properties of a compass: They showed stable directional tuning over the island's space, and were stable over time – maintaining the same preferred direction regardless of appearance, disappearance, or rotation of the moon. Together, our results suggest that head-direction cells serve as a neural compass during real-world navigation outdoors.

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96. LINKING PLACE AND VIEW: ORGANIZING SPACE THROUGH SACCADES AND FIXATIONS BETWEEN PRIMATE POSTERIOR PARIETAL CORTEX AND HIPPOCAMPUS

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Humans primarily rely on vision to explore and guide actions in space. The posterior parietal cortex (PPC) is thought to withhold a unified representation of the visual space allowing to direct saccades to salient cues, while the hippocampus (HPC) provides a memory-based cognitive map of the environment. How do these two representations interact during navigation? To probe the link between view and place, we compared neural activity in the PPC and HPC of macaques navigating in a virtual maze. When analyzed as a function of the animal's virtual position, more neurons in the PPC displayed spatial selectivity compared to the HPC. We hypothesized that such modulation by self-position in the PPC might stem from processing visual cues of the environment through exploratory saccades and fixations. However, we established that position-selectivity was not solely correlated with simple oculomotor dynamics. Rather, spatial selectivities in the PPC and the HPC originated from cells driven by direct fixations of maze paths or landmarks. However, while a substantial proportion of PPC and HPC cells displayed selectivity towards landmarks' spatial and/or visual features, we also revealed different task-related maze segmentation between regions. Indeed, when animal gazed at paths, activity in PPC revealed anticipation of reward while that of the HPC suggested reward outcome processing. On the other hand, when animals gazed at a landmark already present in the field of view, PPC activity tended to occur close to intersections, while that of HPC was more spatially distributed. Finally, at the population level, neurons in both regions anticipated landmarks before they appeared in the field of view, suggesting a shared knowledge of the spatial layout and a collective active role in memory-guided visual exploration across regions. Taken together, these findings shed light on the neural processes linking place and view, through action- and memory-driven exploration of objects in space.

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97. DYNAMIC SEQUENTIAL INTERACTIONS OF SPATIAL UNCERTAINTIES SHAPE HUMAN NAVIGATIONAL STRATEGIES, THEIR ERRORS, AND VARIABILITY

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Goal-directed navigation requires sequentially integrating uncertain, noisy, and ambiguous information from various internal and external spatial cues, representing them internally, planning, and executing motor actions. Yet, a comprehensive computational account explaining how these elements interact in complex open-field environments and how they give rise to different navigational biases and variability is lacking. Importantly, models based on perceptual cue integration (Nardini, 2008) do not explicitly account for internal representations, motor planning, and the sequentiality of perception and action. Here, we introduce an optimal control under uncertainty model (Kaelbling et al., 1998), which provides a computational-level explanation of how noisy sequential egocentric landmark observations form an uncertain allocentric cognitive map and how this internal map is used both in route planning and during execution of movements, giving rise to different navigational strategies. We find that the dynamic interaction of state-dependent sensory uncertainty, time-dependent internal representation

uncertainty, and signal-dependent motor variability across space and time provides a unifying account of a wide range of behavioral phenomena in three previously published studies that employ a variant of the triangle completion task with landmarks (Nardini et al., 2008; Chen et al., 2017; Zhao et al., 2015). Our model not only explains behavior previously deemed contradictory under cue integration models concerning the integration of landmark and self-motion cues but quantitatively predicts human navigational biases and variability in a single unifying and theoretically principled optimal control under uncertainty framework. These findings offer new insights into human navigation, suggesting novel directions for future research in neuroscience and behavioral science by connecting brain activity with internal states and allowing for making behavioral predictions.

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98. AN ARTIFICIAL NEURAL NETWORK MODEL OF COGNITIVE MAP DEVELOPMENT

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Navigation is supported by a network of neurons whose activity is tuned to self-location and orientation in space, such as place cells, head direction (HD) cells, grid cells, and boundary responsive cells. The post-natal development of these neurons in rats follows a specific timeline which has been well characterized in recent studies.
Our work seeks to shed light on the mechanisms driving the maturation of spatial neurons because it remains unclear. Specifically, we created a new Recurrent Neural Network (RNN) model to explore whether the emergence of navigation primarily drives place cell development. We trained the network made of 500 units to form predictions of the upcoming stimuli, exploiting past and current sensory and vestibular information, while the agent explored a squared environment. We then analysed the activity of the RNN's units employing established metrics for characterizing place cells and HD cells. When we trained with a simulated adult rat's trajectory, we found that 22% of the units were classified as place cells, 10% as HD cells, and 26% as both place and HD cells. When we trained with a simulated baby rat's trajectory - which corresponds to the navigational statistics of P8-14 rats - 1% of the units were classified as place cells, 14% as HD cells, and 1% as both. Hence, we found that not only the network was less prone to encode information into spatially tuned units, but also that almost all the spatially tuned units were classified as HD cells, consistent with the stage of development of hippocampal neurons at around P12.
Our early results show that the development of cells likely mirrors behaviour, which in turn is dictated by the environment and other factors. We are currently investigating if this extends to other stages of navigational statistics and other types of spatial neurons. In general, our predictive framework suggests interesting developmental manipulation of rats' movements which can then be tested in real-world experiments.

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99. WHEN SECONDS COUNT: UNDERSTANDING NAVIGATION STRATEGIES OF FIREFIGHTERS IN NORTH AMERICA

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How do first responders successfully arrive to all the unique addresses they are called to for emergencies? This work investigates how firefighters are trained to navigate their response areas, seeks to understand what navigation tools are available to ensure successful navigation, and how

firefighters use these tools. Using an online survey, we collected training, navigational aid details, and demographic data from over 200 firefighters across North America. Our analysis identified that firefighter navigation training is predominantly carried out informally and that firefighters use a variety of methods to create robust cognitive maps of their response areas. They also use an assortment of navigation tools to supplement their cognitive maps including generic aids such as Google Maps, as well as fire service specific aids such as mapbooks or software applications. Redundancy within navigation aids was important, with most participants having access to technology and non-technology navigational tools. These results expand our understanding of professional navigators, provide additional insight on navigation under time stress, and create an opportunity to refine navigation training curricula for first responders.

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100. AN AUTOMATED TACTILE DISCRIMINATION LEARNING TASK FOR FREELY-MOVING MICE.

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Sensory discrimination tasks are valuable tools to study neuronal mechanisms of perception and learning. In recent years, novel discrimination tasks have been developed for electrophysiological or imaging studies in head-fixed mice. However, discrimination tasks in which neurophysiological recordings are implemented into a more ecologically realistic setting with freely moving animals are still relatively scarce, especially for somatosensory studies. This study introduces a tactile discrimination task for freely moving mice, integrating electrophysiology and calcium imaging with cellular resolution. In this go/no-go paradigm, mice learn to discriminate between different aperture widths in order to forage for food rewards on a linear platform. We demonstrate that the task is whisker-dependent and that mice reliably discriminate aperture differences as small as 6 mm. The automation of the setup minimizes confounding factors; for example, the experimenter can leave the room during the recordings. The setup's high flexibility facilitates investigations into diverse behavioral features, including tactile discrimination thresholds, valence-dependent behavior, and cognitive flexibility following a reversal of the task rule. The learning is highly stereotypical and reproducible across individual mice, with approximately 500 trials to reach expert level and approximately 1000 trials to relearn the rule after rule switching. We further demonstrate that electrophysiological recordings and calcium imaging can be conducted in the same paradigm such that multiple behavioral read-outs (learning progression, whisker motion, whisker touch, reward licking) can be synchronized with respective electrophysiological and imaging data, providing valuable data to help elucidate neural mechanisms of cognition and sensory processing.

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101. THE IMPACT OF STRESS-INDUCED TRAINING ON RESILIENCE TO STRESS AND NAVIGATION EFFICIENCY

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Stress reduces the use of efficient shortcut strategies and increases reliance on less efficient familiar routes in a learned environment (Brunye et al., 2017; Brown et al., 2020; Varshney et al., 2024). This raises questions of whether exposing people to stress during learning can enhance people's resilience to stress and mitigate its impact on navigation efficiency, which are addressed in this study.
Participants (N = 50) were randomly assigned to control or stressful conditions and familiarized with a desktop virtual environment featuring 12 landmarks via six laps of a guided route. For the initial three laps, both groups learned in the same environment. In the subsequent three laps, the stressful condition was exposed to stressful stimuli, including threatening music, a timer, black fog, and randomly placed walls obstructing the learned path. The control group navigated without these stressors but encountered white fog in order to control visibility for both groups. Participants' acquisition of configural knowledge of the environment was assessed using a Judgment of Relative Direction (JRD) task. They were then tasked with navigating to goal locations for 24 trials in an ambulatory immersive virtual environment, with half of these trials including the stressors from the learning phase of the stressful condition. After each wayfinding trial, participants rated their perceived stress level on a 1-7 scale.
The two groups did not differ in JRD performance, suggesting they acquired similar environmental knowledge. The stressful condition reported significantly lower perceived stress during stressful wayfinding trials than those in the control condition. However, there was no difference in navigation efficiency between the two conditions. These findings suggest that while learning under stress may reduce perceived stress during later navigation in the same environment, prior exposure to stress does not enhance navigational efficiency under stress.

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102. BEHAVIORAL INVESTIGATION OF ALLOCENTRIC AND EGOCENTRIC SPATIAL MEMORY IN HUMANS

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Spatial navigation and spatial memory rely on world-centered (allocentric) and self-centered (egocentric) representations of the environment. To identify determinants of allocentric and egocentric spatial memory recall, we developed a new task (the "Garden Game") and conducted a behavioral study with this task. During the encoding period of each trial, participants navigated a virtual garden environment with a square boundary and encountered two animals at different locations within the environment. Participants were asked to memorize the positions of these animals both relative to their starting position (egocentrically) and relative to the environment (allocentrically). Three trees and four fences served as environmental landmarks. After encoding, participants were asked to recall the animals' locations in abstract allocentric and egocentric reference frames. For both types of recall, we estimated memory performance as the distance between the participant's response location and the animal's correct position. Our results show that performance improved for both egocentric and allocentric memory recall throughout the task, with allocentric performance showing stronger improvements for animals that had the same encoding location across trials. Regarding landmarks, allocentric memory performance was better for objects close to the boundary and the corners. For egocentric recall, animals positioned in front of and close to the player's starting position were easier to remember. Feedback during allocentric retrieval improved subsequent allocentric retrieval, whereas egocentric feedback did not improve subsequent egocentric performance. Time elapsed between encoding and retrieval was associated with impaired performance. Overall, our study sheds light on the behavioral determinants of allocentric and egocentric spatial memory in humans. In the future, the Garden Game may constitute a useful tool for studying the neural basis of allocentric and egocentric cognitive maps.

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103. DISRUPTED ORIENTATION AFTER PATH INTEGRATION BY ABSENCE OF ANTICIPATED PREVALENT SPATIAL VIEWS

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Previous research indicated that removing expected landmarks disrupts homing abilities after walking. This study investigated when this disruption occurs, which spatial representations are impacted, and whether lessening landmark prevalence mitigates this disruption. In immersive virtual environments, against three landmarks, participants learned the location of a home object alone (Experiments 2 and 3), plus two additional objects (Experiment 1), or plus four additional objects (Experiments 4 and 5). They then navigated an outbound path originated from the home object. After participants' views were blocked briefly, landmarks were revealed for nine standard paths/trials but removed in a subsequent catch trial, except in Experiment 3 where a curtain kept landmarks concealed. In Experiment 5, landmarks were rotated instead of being removed in the second catch trial. Participants replaced the home object in standard trials but all objects in catch trials. Baseline trials, which were identical to the catch trials except for no landmarks throughout the trials, followed catch trials. The results showed larger homing errors in first catch trails than baseline trials only when landmarks were removed (Experiment 2) but not when the curtain concealed the landmarks (Experiment 3). For experiments with multiple objects, participants' represented position and heading were calculated with a bi-dimensional regression between the replaced and correct locations. Experiment 1 showed disrupted homing and heading estimates but intact position estimates, while Experiments 4 and 5 showed no disruption. In addition, participants followed rotated landmarks in Experiment 5. These findings extend the updating spatial view theory: participants update spatial views of environments using path integration, and the absence of anticipated primary spatial views disrupts orientation. Although reducing the prevalence of landmarks mitigates disruption, landmarks still indicate orientations.

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104. GRID-LIKE ENCODING OF LONG LISTS WITHIN A MEMORY PALACE

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Memory palace techniques enhance memory for ordered lists by visualisation along a familiar route. We asked whether its success reflects the embedding of 1D lists into 2D spaces supported by the high-capacity grid-codes found in entorhinal cortex. Participants learned a memory palace inspired by Harry Potter, containing 36 objects arranged in a 6x6 square array, by navigating through it in virtual reality (VR). They then learned lists of 36 words in order by associating them with the objects along a route connecting them in an East-West or North-South raster pattern. We predicted that involvement of grid coding would modulate fMRI activity while encoding lists along either route according to its orientation

relative to that participant's grid orientation. Consistent with our hypothesis, modulatory effects were found in entorhinal, orbitofrontal, ventromedial prefrontal cortices and amygdala, and the strength of the entorhinal grid-like signal during navigation correlated with faster encoding of the words into the memory palace.

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105. EFFECTS OF OLDER AGE ON WAYFINDING DECISIONS

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Literature proposes that the mechanism of wayfinding decisions is based on multiple cognitive strategies. Correlational analyses yielded that in young adults, decisions were mainly based on strategy-specific mechanisms ($r_{within-maze} = 0.52 > r_{within-frame} = 0.19$), not on mechanisms specific for an egocentric or allocentric reference fame ($r_{within-frame} = 0.19 \approx r_{between-frames} = 0.20$), but moderately on generalized mechanisms ($r_{between-frames} = 0.20 > 0$) (Bock et al., 2024). Given that wayfinding performance is known to be impacted in older adults, we now investigate how age affects wayfinding accuracy and whether different strategies are affected differently. In addition, we explore whether the intrinsic mechanisms of wayfinding decisions are also influenced by older age. Old adults were asked to take six trips along a given route through five virtual mazes, each designed for decision-making at intersections by a particular strategy. The first trip through each maze was externally guided, and the subsequent five trips were self-guided. Across all mazes, older adults had significantly lower decision accuracy compared to young adults, and this discrepancy was more pronounced in mazes which require substantial cognitive processing. Correlational analyses yielded that like in young adults, decisions in older ones were also mainly based on strategy-specific mechanisms ($r_{within-maze} = 0.42 > r_{within-frame} = 0.06$). However, unlike in young adults, decisions in older ones were modestly based on mechanisms specific for an egocentric or allocentric reference frame ($r_{within-frame} = 0.06 > r_{between-frames} = 0.01$), but not on generalized mechanisms ($r_{between-frames} = 0.01 \approx 0$). We conclude that older age had a negative effect on wayfinding decisions, that this effect varied depending on the cognitive load of the strategy used, and that older adults rely almost exclusively on strategy- specific mechanisms for decision-making at intersections.

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106. NAVIGATING IN DIFFERENT ENVIRONMENTS: DOES CONTEXT MATTER?

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People navigate in various types of environments, including indoor and outdoor environments. These differ in availability of navigation cues such as distal landmarks, clear boundaries, and regular grid structures. Navigating different environments has profound effects on our spatial abilities, raising questions of whether learning different environments draws on the same or diverse perceptual and cognitive processes. Individual differences studies can shed light on this issue, but most studies have focused on navigation of a single environment, and different measures of spatial knowledge acquisition have been used across studies. People (n=88) learned the layout of two environments: a grid-like maze and a campus-like open environment. After learning each, their knowledge was measured by three

tasks: pointing, map- reconstruction, and wayfinding. We also examined how Sea Hero Quest performance related to performance in the two environments. Confirmatory factor analysis assessed whether the measures reflect a common ability to learn spatial layout, separate abilities associated with different environments, or separate abilities associated with different measures of spatial learning. All tasks across the two environments were significantly correlated. Confirmatory factor analyses suggested the environment matters; the best fitting model indicated separate factors for the grid-like maze and the outdoor environment. However, these two factors were highly related, indicating they reflect common underlying abilities. There was no evidence that different measures of learning (pointing, map reconstruction, and wayfinding) define separate abilities, adding to their validity as configural knowledge measures. Sea Hero Quest performance was generally unrelated to performance in the two environments, suggesting that this task depends on different abilities.

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107. A NEURAL CIRCUIT FOR SPATIAL ORIENTATION DERIVED FROM BRAIN LESIONS

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There is disagreement regarding the major components of the brain network supporting spatial cognition. To address this issue, we applied a lesion mapping approach to the clinical phenomenon of topographical disorientation. Topographical disorientation is the inability to maintain accurate knowledge about the physical environment and use it for navigation. A review of published topographical disorientation cases identified 65 different lesion sites. Our lesion mapping analysis yielded a topographical disorientation brain map encompassing the classic regions of the navigation network: medial parietal, medial temporal, and temporo-parietal cortices. We also identified a ventromedial region of the prefrontal cortex, which has been absent from prior descriptions of this network. Moreover, we revealed that the regions mapped are correlated with the Default Mode Network sub-network C. Taken together, this study provides causal evidence for the distribution of the spatial cognitive system, demarking the major components and identifying novel regions.

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108. SIMULTANEOUS BODY- AND ENVIRONMENT-STABILIZED PROCESSES OF OBJECT LOCATIONS IN MIXED REALITY ENVIRONMENTS

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People, during locomotion, can simultaneously maintain their relations to some objects (e.g., their glasses) in a body- stabilized manner and change their relations to other objects (e.g., a desk) in an environment-stabilized manner. Previous studies have shown that although people cannot engage in body-stabilized processes for real objects on the floor, they could for virtual objects on the floor by a verbal instruction such as "everything will move with you while you rotate." The goal of the current study was to investigate the extent to which people can use both processes when both virtual and real objects are present on the floor. Participants learned an object array and then either maintained their original perspective or turned 180° to face the opposite perspective. Participants judged relative directions from imagined perspectives based on the memories of the object array. The actual and imagined perspectives were aligned or misaligned. Better performance for aligned than misaligned perspectives (sensorimotor alignment effects) indicates environment-stabilized processing, while no sensorimotor alignment effect indicates body-stabilized processing. In Experiments 1 and 2, participants learned only virtual objects with and without body-stabilized verbal instructions. In Experiment 3, via a Mixed Reality HMD, participants learned both virtual and real objects with body-stabilized verbal instructions. The results showed sensorimotor alignment effects in Experiments 1 and 3 but not in Experiment 2. These results suggest that both virtual and real objects, if presented together, are processed as an environment-stabilized integrated system even with body-stabilized instructions.

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109. EFFICIENCY OF HUMAN WAYFINDING BY HORIZONTAL, VERTICAL AND THREE-DIMENSIONAL COGNITIVE MAPS.

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Human wayfinding often relies on cognitive representations of the environment, commonly referred to as “cognitive maps”. Depending on task demand, these maps can capture the spatial relationships in the horizontal plane only (like road maps), in the vertical plane only, or in all three dimensions of space. This study investigates whether horizontal, vertical and 3D maps are equally refined, thus enabling comparable wayfinding performance. Participants were guided through a virtual 3D maze where a distinct object was shown at each intersection. Subsequently, they had to revisit these objects in a different order, while their accuracy and decision time at each intersection were recorded. In three experimental conditions, the objects were placed at twelve neighboring intersections in a horizontal plane, in a vertical plane, or in 3D. The recorded data revealed a higher accuracy in the horizontal plane compared to both the vertical plane and 3D, with no significant difference between the latter two. In contrast, decision time did not differ between conditions. We conclude that with the same amount of learning and the same number of objects, cognitive representations of horizontal space were more refined than those of vertical and 3D space, as quantified by accuracy. However all three representations were retrieved at a similar speed, as quantified by decision time. This outcome has implications in several areas such as neurorehabilitation, VR gaming, and urban design.

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111. QUANTITATIVE MODELING OF THE EMERGENCE OF MACROSCOPIC GRID-LIKE REPRESENTATIONS

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Grid cells are neurons in the entorhinal cortex that are thought to perform computations in support of spatial navigation. As direct recordings of grid cells from the human brain are only rarely possible, functional magnetic resonance imaging (fMRI) studies proposed and described an indirect measure of entorhinal grid-cell activity, which is quantified as a hexadirectional modulation of fMRI activity as a function of the subject's movement direction through a virtual environment. However, the contributing role of the aggregated activity of grid cells to this modulation remains unclear. Our research addresses the unresolved question concerning the origin of hexadirectional modulation of activity in the entorhinal cortex, as observed in fMRI, iEEG, and MEG studies (e.g. Doeller et al., Nature, 2010; Staudigl et al., Curr Biol, 2018; Convertino et al., Brain, 2023). Here, we explored three hypotheses through both numerical simulations and analytical calculations: head-direction tuning (conjunctive grid by head-direction cell hypothesis); firing-rate adaptation (repetition suppression hypothesis); or a bias towards a certain grid phase offset (structure-function mapping hypothesis). Our findings indicate that, in principle, all three hypotheses can account for hexadirectional modulation of sum grid-cell activity in ideal conditions. However, when including grid-cell properties found in the literature, our simulations most strongly support the conjunctive grid by head-direction cell hypothesis. In contrast, our simulations do not support the structure-function mapping hypothesis. With respect to the repetition-suppression hypothesis, our simulations are insufficient to substantiate or refute it, and further experiments on the adaptation properties of single grid cells are required.

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112. THE MEMORY ADVANTAGE: EXPLORING SUPERIOR EPISODIC MEMORY IN SUPERAGERS THROUGH GRID CELL COMPUTATIONS

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Grid cells in the entorhinal cortex (EC) are central to spatial coding: via the grid cell system encoding primarily positional information alongside organising general knowledge and nonspatial experience. Moreover, grid cell activity is shown to be interrupted by aging (Stangl et al., 2018). On the other hand, SuperAgers, older adults with superior episodic memory, are shown to have preserved EC (reduced NFTs and larger ERC layer II neurons) in post-mortem studies even in advanced age (Gefen et al., 2021). Episodic memory is also suggested to critically rely on computations in this grid cell computation in the entorhinal cortex (EC): spatial position ('Where'), sequence of events ('When'), and the content of the experience ('What') (Sugar and Moser, 2019). In this study, we asked whether grid cell computations can help us understand the mechanisms explaining why episodic memory is preserved in Superagers.

Two groups of old adults, Normal Control and SuperAgers, are recruited for a series of tasks to measure their grid cell activity and episodic memory performance. SuperAgers are classified by using the protocol established by Harrison et al., 2012 with the Ray Auditory Verbal Learning test as the main cut-off. Grid cell activities are calculated via GridCat (Stangl et al., 2017) using the parametric modulation technique. Individual entorhinal cortex masks are created via a semi- automated pipeline utilising ASHS (Yushkevich et al., 2014) followed by manual correction. Blood biomarkers such as Abeta 42 were acquired as well. Our preliminary analysis shows that both preserved episodic memory and grid cell integrity in superior aging can be preserved even in the presence of AD pathology such as ß-amyloid loads.

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113. NEW DEVELOPMENTS IN UNDERSTANDING THE SPATIAL INPUTS TO THE HUMAN HIPPOCAMPUS FOR NAVIGATION AND MEMORY

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Hippocampal and parahippocampal gyrus spatial view neurons in primates respond to the spatial location being looked at. The representation is allocentric, in that the responses are to locations “out there” in the world, and are relatively invariant with respect to retinal position, eye position, head direction, and the place where the individual is located. The pathway for this spatial view information was analysed in humans. Whole-brain effective connectivity was measured with magnetoencephalography between 30 visual cortical regions and 150 other cortical regions using the Human Connectome Project Multimodal Parcellation atlas in 21 participants performing a 0-back scene memory task. In a ventromedial visual stream, V1-V4 connect to the ProStriate region where the retrosplenial scene area is located. The ProStriate region has connectivity to ventromedial regions VMV1-3 and VVC. VMV1-3 and VVC connect to the medial parahippocampal gyrus PHA1-3, which, with the VMV regions, include the parahippocampal scene area. The medial parahippocampal PHA1-3 regions have effective connectivity to the hippocampus, entorhinal cortex, and perirhinal cortex. Diffusion topography in 171 HCP participants at 7T supported this hierarchical organisation. An implication is that spatial view information is computed by feature combinations for parts of viewed scenes, very different to the local place representations in rodents. It is proposed that hippocampal spatial view cells provide a basis for navigation to a series of viewed landmarks, with the orbitofrontal cortex reward inputs to the human hippocampus providing the goals for navigation.

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114. BARCODING OF EPISODIC MEMORIES IN THE HIPPOCAMPUS OF A FOOD-CACHING BIRD

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The hippocampus is critical for episodic memory. Although hippocampal activity represents place and other behaviorally relevant variables, it is unclear how it encodes numerous memories of specific events in life. To study episodic coding, we leveraged the specialized behavior of chickadees – food-caching birds that form hippocampal-dependent memories at well-defined moments in time whenever they cache food for subsequent retrieval. We developed novel methods for high- density silicon probe recordings in freely moving birds along with mm-precision 3D postural tracking, enabling the first characterization of hippocampal activity during caching behavior. Our recordings during caching revealed very sparse, transient barcode-like patterns of firing across hippocampal neurons. Each "barcode" uniquely represented a caching event and transiently reactivated during the retrieval of that specific cache. Barcodes co-occurred with the conventional activity of place cells, but were uncorrelated even for nearby cache locations that had similar place codes. Relative to the place code, barcodes were high-dimensional and transient. We also observed neurons with location-independent tuning for the contents of cache sites. We propose that animals recall episodic memories by reactivating hippocampal barcodes, which could be associated with memory content like place and cached items. Similarly to computer hash codes, these patterns assign unique identifiers to different events and could be a mechanism for rapid formation and storage of many non-interfering memories. We also develop a computational model which forms memories by storing barcodes as attractor states in a RNN and associating these states with spatial inputs. The model reproduces experimental findings and makes novel predictions of hippocampal dynamics when deciding between alternative routes to retrieve nearby caches, which are being tested in ongoing experiments.

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115. INDEPENDENT CONTRIBUTIONS OF GLOBAL PRIOR AND LOCAL PRIOR IN HUMAN SPATIAL NAVIGATION

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The usage of prior experiences often manifests in the central tendency phenomenon, meaning that single estimations are attracted to the mean of the stimulus distribution. However, investigations of how prior experiences influence current response in human spatial navigation is very limited, which is the goal of the current study. We examined i) whether people use spatial prior experiences by exhibiting the central tendency effect, and ii) whether there is a unitary prior or multiple priors driving the central tendency phenomenon by disentangling local prior (preceding response) from global prior (accumulative response distribution). We used a spatial location reproduction task implemented in desktop VR. In three experiments, participants first learned the location of a target and then moved back to the remembered location. The procedure included landmark-only, self-motion-only, combination, and conflict conditions. First, we consistently observed the central tendency phenomenon, confirming the usage of prior experiences in current judgments. Second, while the influence of local prior was eliminated
by the cue-switching manipulation, the central tendency effect was unaffected, indicating minimal contributions of local prior to the central tendency effect during cue-switching. Third, we contrasted different reference frames within the landmark condition. We found that both local prior and global prior were defined in the egocentric instead of allocentric reference frame, and they exerted independent influences on the current localization response, except that the effect of the egocentric

local prior was abolished with additional working memory load. Taken together, our findings showed that spatial priors were used by human navigators and their localization judgments were influenced by an unstable local prior and a stable global prior.

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116. EVIDENCE FOR HIPPOCAMPAL INVOLVEMENT IN CUE INTEGRATION IN HUMAN SPATIAL NAVIGATION

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Landmarks and path integration cues are two fundamental types of information utilized in spatial navigation. In daily life, people often combine these two information sources to enhance their navigation performance. While past studies have investigated the neural mechanism behind each navigation mode separately, it remains unexamined how these two information sources are combined in the human brain. In the current study, we employed a combination of fMRI at 3T, desktop virtual reality, and fMRI adaptation analysis. Using a novel linear track navigation task, we contrasted the utilization of singular cues to their combined use. The results showed that participants performed significantly better under the combination condition compared to the single-cue conditions. Consistent with the behavioral findings, we observed adaptation effect in the hippocampus, in that the hippocampal activation decreased as the distance between the current location and the previous location decreased, but only when in the combination condition. Further scrutiny of the hippocampal subregions showed a relatively strong adaptation effect in the subiculum. Additionally, we explored the functional network structure of the medial temporal lobe and the retrosplenial cortex during navigation and found that the hippocampus served as a hub, regardless of the cue condition. Taken together, our findings provide the first evidence that the human hippocampus plays an important role in effective cue integration during spatial navigation.

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117. EVENT CODING OF SUBICULUM NEURONS IN VIRTUAL ENVIRONMENTS

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The subiculum is the critical interface between the hippocampus and cortical regions. We reported previously that a class of subicular neurons organized their firing fields according to task events in a hippocampal-dependent memory task (Lee et al., J Neurosci 2018). In this study, we verified the previous findings in more controlled experimental conditions. We hypothesize that the subiculum reorganizes the fine-grained positional information fed from the hippocampus into behaviorally meaningful representations according to task demands. To test this hypothesis, we developed a VR-based memory task for rats to record such task structure-based representation in the subiculum. In the VR task, the rat ran on a circular track to obtain drops of honey water while experiencing two virtual environments filled with different visual landmarks. The reward was always given at a fixed position (0°), but the start location was pseudo-randomly selected from one of three positions (90°, 180°, 270°) for each trial. Once reaching the reward position, the rat was required to choose one of the two lick

ports associated with the environment to receive a reward. Each trial ended as the rat came back to the start position again after obtaining the reward. While the rat learned the task, spiking activities of single units and local field potentials were recorded from the CA1 and subiculum simultaneously by a multi-electrode drive equipped with 24 tetrodes. Our preliminary data suggest that some subicular neurons not only encode task events by representing event boundaries (e.g., the start of the trial) but also flexibly change their firing fields as the event boundaries shift. We plan to further examine the detailed properties of task event-based coding in the subiculum, including the influence of learning on the event-bound representations as the rats learn the association between the environments and the behavioral responses.

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