LUKAS ALEXANDER LEUBE

Imaginary systems? Perspectives on hippocampal function beyond memory

Opinion

Viewing the hippocampus as a structure specifically dedicated to memory is no longer viable. However, functional characterization of this structure and its involvement in learning and memory is still necessary. This perspective article argues that the hippocampus principally processes spatial contexts or scenes. It highlights findings on hippocampal involvement in episodic prospection, navigational planning and online perception. Finally, it discusses how the hippocampus may analogically process non-spatial information via representation in a conceptual cognitive space. The relevance of spatial mnemonic techniques for further research is emphasized.

Keywords: Hippocampus, memory, spatial cognition, episodic prospection

"[Simonides] inferred that persons desiring to train this faculty [of memory] must select places and form mental images of the things they wish to remember and store those images in the places, so that the order of the places will preserve the order of the things, and the images of the things will denote the things themselves, and we shall employ the places and images respectively as a wax writing-tablet and the letters written on it." - Cicero (undated)

INTRODUCTION

Historically, the hippocampus and, by extension, the whole medial temporal lobe (MTL) has been conceptualized as containing or representing a system dedicated to long term memory (LTM). This MTL - LTM hypothesis was originally formulated in response to observations of (anterograde) amnesia in patients that suffered bilateral hippocampal lesions (Scoville & Millner, 1957). More recent investigations using functional neuroimaging have shown that metabolic activity in the

hippocampus is associated with the acquisition of novel information as well as its subsequent retrieval (Lepage, Habib & Tulving, 1998; Zeineh, Engel, Thompson & Bookheimer, 2003). Models of long term potentiation (LTP) have demonstrated that the hippocampus is capable of inducing long lasting changes to the strength of synaptic connections. This process is a prerequisite for hebbian learning, which likely enables the formation of new memories (Bliss & Collingridge, 1993). Considering these findings, it stands without question that the hippocampus participates in the encoding and retrieval of mnemonic representations.

However, the conceptualisation of the hippocampus and MTL as a system that is specifically dedicated to memory should be called into question. Gaffan (2002), for instance, maintained that the MTL - LTM system hypothesis is harmful because it may impede scientific progress. He argued that it is emblematic of an approach that localizes cognitive functions "intuitively and in a haphazard and piecemeal fashion" (Gaffan, 2002). He contrasted it to viewing the brain as a hierarchical processing system, which he considered more appropriate. Following this

line of reasoning, the hippocampus may participate as a crucial component in a multilevel process that results in the phenomenological experience of remembering, but it ultimately cannot be the sole locus of memory.

Gaffan (2002) raised several convincing arguments in favor of this hierarchical view. He presented evidence that (1) memories are not stored in the MTL, that (2) the prefrontal cortex and its connections with the MTL are likewise essential for normal memory functioning and that (3) the hippocampus is involved in perceptual processes (Gaffan, 2002). Since then, more evidence in favor of these arguments has emerged. Memory engrams have been found in the posterior parietal cortex, rather than the hippocampus (Brodt, Gais, Beck, Erb, Scheffler & Schönauer, 2018). The medial prefrontal cortex seems to play an important role in memory consolidation and retrieval for recent as well as distant memories (Leon, Bruno, Allard, Nader & Cuello, 2010). Furthermore, the hippocampal involvement in online perception (meaning the instantaneous automatic processing of one's current sensory input) has been repeatedly demonstrated (Aly, Ranganath & Yonelinas, 2013;

Chadwick, Mullally & Maguire, 2013). Collectively, these findings demonstrate that the hippocampus and (long-term) memory cannot be linked to each other in a one-to-one fashion. This raises the following question: What then precisely is the function of the hippocampus and how does it play into learning and memory?

Past, Future and Presence: Modelling of spatial contexts

Similar to the deliberations presented by Gaffan (2002), Nadel and Hardt (2011) likewise argue against the MTL - LTM system hypothesis. In their comprehensive review on "memory systems" they conceptualize episodic (and thus hippocampus-dependent) memory as entailing a specific spatial context (Nadel & Hardt, 2011). This is in line with how Tulving originally defined episodic memory as entailing "temporo-spatial relations" (Tulving, 1972). However, Nadel and Hardt (2011) note that the hippocampus is also involved in the initial acquisition of non-episodic

information. Such knowledge may then be "semantisized" in a brain wide consolidation process and become independent from the hippocampus (Nadel & Hardt, 2011). Importantly, the gain of hippocampal independence entails a loss of contextual specificity. One might infer from this that the hippocampus principally processes spatial contexts or scenes. The presence of a spatial context can be considered the defining feature of episodic memory that distinguishes it from semantic information.

Evidence for the hippocampus' role in processing spatial information is not restricted to memory research. The following will perhaps highlight some key findings regarding hippocampal involvement in episodic prospection, navigational planning and online perception in order to elaborate on its function beyond memory.

Episodic prospection or "future simulation" is the mental construction of possible future scenarios. It engages a similar network of brain regions as episodic remembering, which includes the hippocampus (Schacter, Addis & Szpunar, 2017). A popular method for researching episodic prospection using fMRI

is the experimental recombination paradigm. Here, participants have to generate lists of familiar *objects*, *persons* and *places* prior to testing. During imaging, they are then asked to imagine novel future scenes in which these three aspects are combined. Crucially, this experimental approach allows for both manipulation of the novelty of these scenarios as well as controlling for the amount of specific detail that is generated. As it turns out, the hippocampus is more engaged during imagination of novel combinations and its activity correlates with the amount of specific detail contained within them (Schacter, Addis & Szpunar, 2017). Furthermore, populations that usually perform worse on measures of delayed recall, such as depressive patients or older adults, also show peculiarities in episodic prospection: Their scenes seem to lack detail and appear to be less specific and more stereotypical (Schacter, Addis & Szpunar, 2017). Importantly, cognitive deficits have been associated with hippocampal volume loss in both depression (Sheline, Sanghavi, Mintun & Gado, 1999) as well as aging (Reichel, Bedenk, Czisch & Wotjak, 2017). The hippocampus might thus model the spatially coherent scene

that underlies the respective imagination. Naturally, the creation of a novel and detailed scene would place more demands on the hippocampus than generating a stereotypical and thus quasi-semantic context.

The ubiquitous involvement of the hippocampus in spatial navigation is well documented, primarily in rodents. Evidence shows that the hippocampus contains "place cells" that are tuned to specific locations within a given environment. Furthermore, distinct neural populations seem to "preplay" movement trajectories during route planning (Bendor & Spiers, 2016). An investigation by Brown and colleagues (2016) demonstrated that this mechanism is also present in humans. They were able to relate hippocampal activation to prospective navigational goals, as well as intervening locations along the planned route.

Critically inclined people might object that these future oriented mental activities (episodic prospection and route planning) still essentially constitute memory processes, as they require retrieval of previous knowledge. However, there is also experimental evidence showing that the hippocampus is

involved in online perception. In particular, it seems to contribute to the perception of an environment as a continuous whole. Simply stated, the hippocampus is involved in extrapolating visual information beyond the actual stimulus. In an experimental setting, this phenomenon can be demonstrated with the boundary extension effect (Intraub & Richardson, 1989). This effect describes the phenomenon of people judging a visual stimulus (such as a picture) to be smaller during repeated viewings compared to the initial presentation. As it can be detected less than 50 ms after viewing a stimulus, boundary extension is undoubtedly part of online perception (Intraub & Dickinson, 2008). Chadwick and colleagues showed that the boundary extension effect correlates with functional connectivity between the hippocampus and the visual cortices (Chadwick, Mullally & Maguire, 2013). Boundary extension is a form of elaborative processing, which would be a necessary step in modelling spatial contexts as part of online perception

Accounting for the described findings, Zeidman and Maguire (2016) recently proposed an anatomical model, which differentiates functional roles within the hippocampus in

relation to the processing of spatial scenes. Principally, they make a distinction between the anterior and the posterior hippocampus. In this model, the anterior part is explicitly involved in the construction of spatial scenes during episodic simulation, while the posterior part has a more perceptual function. Taken together, there is substantial evidence that the hippocampus principally processes spatial contexts or scenes, both during perception of current spatial environments as well as during episodic imagery.

Pseudo-spatial properties of abstract information

Thus far, the present article has argued that the hippocampus principally models spatial contexts or scenes. However not all types of information, whose acquisition depends on the hippocampus, seem to have spatial properties. Eichenbaum and Cohen (2014) reasoned that the hippocampus also processes non-spatial bits of information in terms of their trajectories in conceptual "memory space". This implies that the same principles governing the processing of spatial relations apply to

other types of information, e.g. conceptual similarity or temporal distance.

This idea is very appealing, because it makes sense from an evolutionary perspective. The hippocampus might have been a purely spatial structure originally, which is in line with the close neural link between olfactory identification and spatial navigation (Dahmani, Patel, Yang, Chakravarty, Fellows & Bohbot, 2018). However, over time its function might have become generalized and transferred upon other dimensions that can be described in spatial terms. One has to consider and appreciate the fact that we as humans resort to spatial schemata for representation of all types of information. On an intuitive level, one can realize that by considering how our language deals with abstract concepts. To give a few examples: We characterize personality traits, such as self-esteem, as being *high* or *low*. Time is moving *forward.* Political views are organized on a spectrum from *right* to *left.* This of course is very anecdotal. However, there is more far reaching evidence for mental representation of higher order knowledge in spatial terms. The spatial numerical associations of response codes (SNARC) effect for instance

shows that mental representations of number magnitudes have spatial properties (Wood, Willmes, Nuerk & Fischer, 2008).

These pseudo-spatial attributes of human knowledge become most apparent when one considers the effectiveness of spatial mnemonic strategies. A particularly popular one in educational settings is "mind-mapping". It means arranging information that is to be encoded on a two dimensional plane (i.e. a blackboard or a piece of paper). Here different conceptual dimensions can be displayed in spatial terms: Distance can express similarity, size can indicate importance, connections can imply belonging to a category, etc. Several investigations have shown that encoding information with mind-maps leads to superior recall when compared to simply studying said information in a text (Hallen & Sangeetha, 2015; Lalyanasundaram, Abraham, Ramachandran, Jayaseelan, Bazroy, Singh & Purty, 2017). One possible explanation of this effect is that spatially arranging information facilitates hippocampal processing.

A similar case can be made for the mnemonic techniques employed by participants in "memory championships". These

people compete on tasks like remembering extraordinary long digit spans. Maguire and colleagues have shown that their brains do not show any structural differences compared to controls (Maguire, Valentine, Wilding & Kapur, 2002). Rather, their superior memory performance stems from proficient use of spatial mnemonics, such as the "method of places" (Maguire et al., 2002). In the quote, which prefaces this article, Cicero describes this technique. It associates each bit of information with a location in an imaginary scene. Despite necessitating the encoding of *additional* information, this method is very effective (Maguire et al., 2002). It could very well serve as a metaphor for hippocampal function at large: The spatial scene in which the "images" are placed represents the pseudo-Euclidean cognitive space that is processed by the hippocampus, whereas the "images" themselves represent the bits of information that are encoded.

In recent years evidence for this view has been emerging: The hippocampal circuit has been shown to process auditory spectral (Constantinescu, O'Reilly & Behrens, 2016), and other types of stimulus feature information (Theves, Fernandez &

Doeller, 2019) in a manner that is analogous to spatial information.

CONCLUSION

The present article has argued that the hippocampus principally processes spatial contexts or scenes. This function is a critical component of visuospatial perception and any form of episodic imagery, meaning both episodic recall and prospection, as well as counterfactual imagery. Furthermore, it is crucial for any activity requiring spatial reasoning, such as navigational planning. Analogous to spatial scenes containing objects, the hippocampus may process constellations of abstract information via representation in a conceptual cognitive space. In order to reach a better understanding of how the hippocampus processes non-spatial information, future research could investigate the working mechanisms of spatial mnemonic aids. Techniques such as "mind-mapping" and the "method of places" might ultimately be effective because they organize information in a form, which

is more readily processed by the hippocampus, e.g. by adding spatial and/or associative components. This kind of hippocampal "spatialization" could ultimately be a domain-general aspect of human cognition.

REFERENCES

Aly, M., Ranganath, C., & Yonelinas, A. P. (2013). Detecting changes in scenes: The hippocampus is critical for strength-based perception. *Neuron*, *78*(6), 1127-1137.

Bendor, D., & Spiers, H. J. (2016). Does the hippocampus map out the future? *Trends in cognitive sciences*, *20*(3), 167-169.

Bliss, T. V., & Collingridge, G. L. (1993). A synaptic model of memory: long-term potentiation in the hippocampus. *Nature*, *361*(6407), 31.

Brodt, S., Gais, S., Beck, J., Erb, M., Scheffler, K., & Schönauer, M. (2018). Fast track to the neocortex: A memory engram in the posterior parietal cortex. *Science*, *362*(6418), 1045-1048.

Brown, T. I., Carr, V. A., LaRocque, K. F., Favila, S. E., Gordon, A. M., Bowles, B., ... & Wagner, A. D. (2016). Prospective representation of navigational goals in the human hippocampus. *Science*, *352*(6291), 1323-1326.

Chadwick, M. J., Mullally, S. L., & Maguire, E. A. (2013). The hippocampus extrapolates beyond the view in scenes: an fMRI study of boundary extension. *Cortex*, *49*(8), 2067-2079.

Cicero, M. T. (undated). *De oratore*, II, lxxxvi. Translation: Sutton, W. & Rackham, H. (1942). Harvard University Press.

Constantinescu, A. O., O'Reilly, J. X., & Behrens, T. E. (2016). Organizing conceptual knowledge in humans with a gridlike code. *Science*, *352*(6292), 1464-1468.

Dahmani, L., Patel, R. M., Yang, Y., Chakravarty, M. M., Fellows, L. K., & Bohbot, V. D. (2018). An intrinsic association between olfactory identification and

spatial memory in humans. *Nature communications*, *9*(1), 4162.

Eichenbaum, H., & Cohen, N. J. (2014). Can we reconcile the declarative memory and spatial navigation views on hippocampal function? *Neuron*, *83*(4), 764-770.

Gaffan, D. (2002). Against memory systems. *Philosophical Transactions of the Royal Society of London B: Biological Sciences*, *357*(1424), 1111-1121.

Hallen, D., & Sangeetha, N. (2015). Effectiveness of Mind Mapping in English Teaching among VIII Standard Students. *Journal on English Language Teaching*, *5*(1), 45-50.

Intraub, H., & Dickinson, C. A. (2008). False memory 1/20th of a second later: What the early onset of boundary extension reveals about perception. *Psychological Science*, *19*(10), 1007-1014.

Intraub, H., & Richardson, M. (1989). Wide-angle memories of close-up scenes. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *15*(2), 179.

Kalyanasundaram, M., Abraham, S. B., Ramachandran, D., Jayaseelan, V., Bazroy, J., Singh, Z., & Purty, A. J. (2017). Effectiveness of mind mapping technique in information retrieval among medical college students in Puducherry-A pilot study. *Indian journal of community medicine: official publication of Indian Association of Preventive & Social Medicine*, *42*(1), 19.

Lepage, M., Habib, R., & Tulving, E. (1998). Hippocampal PET activations of memory encoding and retrieval: the HIPER model. *Hippocampus*, *8*(4), 313-322.

Maguire, E. A., Valentine, E. R., Wilding, J. M., & Kapur, N. (2003). Routes to remembering: the brains behind superior memory. *Nature neuroscience*, *6*(1), 90.

Nadel, L., & Hardt, O. (2011). Update on memory systems and processes. *Neuropsychopharmacology*, *36*(1), 251.

Reichel, J. M., Bedenk, B. T., Czisch, M., & Wotjak, C. T. (2017). Age-related cognitive decline coincides with accelerated volume loss of the dorsal but not ventral hippocampus in mice. *Hippocampus*, *27*(1), 28-35.

Schacter, D. L., Addis, D. R., & Szpunar, K. K. (2017). Escaping the past: Contributions of the hippocampus to future thinking and imagination. *The hippocampus from cells to systems* (pp. 439-465). Springer, Cham.

Scoville, W. B., & Milner, B. (1957). Loss of recent memory after bilateral hippocampal lesions. *Journal of neurology, neurosurgery, and psychiatry*, *20*(1), 11.

Sheline, Y. I., Sanghavi, M., Mintun, M. A., & Gado, M. H. (1999). Depression duration but not age predicts hippocampal volume loss in medically healthy women with recurrent major depression. *Journal of Neuroscience*, *19*(12), 5034-5043.

Theves, S., Fernandez, G., & Doeller, C. F. (2019). The Hippocampus Encodes Distances in Multidimensional Feature Space. *Current Biology*.

Tulving, E. (1972). Episodic and semantic memory.

Wood, G., Willmes, K., Nuerk, H. C., & Fischer, M. H. (2008). On the cognitive link between space and number: a meta-analysis of the SNARC effect. *Psychology Science*.

Zeidman, P., & Maguire, E. A. (2016). Anterior hippocampus: the anatomy of perception, imagination and episodic memory. *Nature Reviews Neuroscience*, *17*(3), 173.

Zeineh, M. M., Engel, S. A., Thompson, P. M., & Bookheimer, S. Y. (2003). Dynamics of the hippocampus during encoding and retrieval of face-name pairs. *Science*, *299*(5606), 577-580.