Oct 25th, 2023

Dear Editor,

Please consider our manuscript titled "Hippocampal neural fluctuation between memory encoding and retrieval states during a working memory task in humans" for publication as a Research Article in *iScience*.

In this study, we present novel insights into the neural dynamics of the medial temporal lobe, particularly the hippocampus, during a working memory task in humans. Our research is grounded in the calculation of low-dimensional neural trajectories based on multiunit activity recordings. The key findings of our investigation can be summarized as follows:

First, we discovered that the neural trajectory of the hippocampus displays a memory load-dependent pattern in the distance between its encoding and retrieval states. This observation sheds light on the cognitive processes underpinning working memory, highlighting the hippocampus as a crucial player in this dynamic.

Second, our study reveals a transient increase in hippocampal neural activity during hippocampal sharp-wave ripple (SWR) events, which are established biomarkers for various cognitive functions. This finding underscores the significance of SWRs in the context of working memory, suggesting their involvement in memory-related processes.

Lastly, our research uncovers intriguing fluctuations in the direction of hippocampal neural trajectories during the retrieval phase. These fluctuations reflect a dynamic balance between encoding and retrieval states, with a pronounced shift toward the retrieval state during SWR events. This phenomenon aligns with the specific requirements of different trial types and is supported by previous studies, offering a fresh perspective on hippocampal information processing during working memory tasks.

We hereby certify that this study constitutes original research that has not been previously published and is not under consideration for publication elsewhere, in whole or in part, in any language.

We suggest the following potential reviewers for this paper:

1. Prof. Ph.D. Lluís Fuentemilla Garriga

Cognition & Brain Plasticity Unit, [University of Barcelona](https://scholar.google.com/citations?view_op=view_org&hl=en&org=15918451262755526508), Spain

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Reason: He is the corresponding and last author of a related study (Saint Amour di Chanaz et al., *Current Biology*, 2023). Moreover, as the first author, he published a related paper titled “Theta-Coupled Periodic Replay in Working Memory” in Current Biology in 2010.

2. Prof. Ph.D. Johannes Sarnthein

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Reason: He is the last author of the dataset we used in the manuscript.

3. Prof. Ph.D. Colin Lever

Psychology Department, the University of Durham, United Kingdom

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Reason: He has experience working with hippocampal neural processing during working memory tasks.

4. Prof. Ph.D. Bernhard P Staresina

Department of Experimental Psychology, University of Oxford, United Kingdom

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Reason: He found a correlation between hippocampal activities during the encoding and retrieval phases of a working memory task in humans.

5. Associate Prof. Ph.D. MD. Anli A. Liu

Department of Neurology at NYU Grossman School of Medicine, USA

[anli.liu@nyumc.org](mailto:anli.liu@nyumc.org)

Reason: She published a paper for a consensus statement on detection of hippocampal sharp wave ripples.

6. Postdoctoral fellow. Ph.D. Yitzhak Norman

Department of Neurobiology, Weizmann Institute of Science, Rehovot 76100, Israel

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Reason: He found a correlation between sharp-wave ripples and spontaneous recall in humans.

We appreciate your consideration of our manuscript and look forward to your response.

Sincerely yours,

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