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Reviewers' comments:

Reviewer #1 (Remarks to the Author):

The manuscript reports results from a series of behavioural studies with control participants and an amnesic patient, and of an fMRI study. The authors used a VR task where they presented scenes while manipulating bodily self-consciousness (BSC: first-person synchronous avatar, first-person asynchronous avatar, and third-person asynchronous avatar). They observed the highest level of hippocampal reinstatement for scenes encoded under visuomotor and perspectival congruency. This was interpreted as demonstrating that hippocampal reinstatement depends on the bodily sensory context of the observer during encoding. The authors further argue that these results provide evidence for embodied hippocampal reinstatement by showing that the sensorimotor context of the observer's body at encoding impacts encoding- and retrieval-related hippocampal activity. The manuscript was well-written and clear, and the results are interesting and novel. I suggest below a few points of clarification, as well as further discussion of some of the results and their interpretation.

Abstract

"cortical-hippocampal reinstatement involved during encoding" would need to be rephrased (perhaps the authors meant reinstatement of encoding activity?)

Introduction

"Episodic memory (EM) refers to a form of long-term declarative memory associated with the recall of the sensory details of an event"

This is a quite an unusual definition of episodic memory (a classic recognition task with words may not produce rich recollection of sensory details)

Results

Results, page 9 : why do the authors think they observed no self-reference effect (advantage of 1st person perspective) in the recognition test in experiments 1 and 2? One could have thought that it could be due to the fact that the scenes were presented in the background and thus not associated with the avatar and their body. However, the authors report a significant effect on experiment 3, with intentional encoding. Could it be then that associating the avatar and the scenes was more likely to happen under intentional enclosing? Though the effect of agency was not significant in experiment 3, which was surprising. It would be good that the authors discuss these findings and how they can be integrated. The fMRI experiment was experiment 2, where there was no difference in recognition accuracy between the conditions. How do the authors interpret the discrepancy between the brain and behavioural results? Why do they think the hippocampus reinstatement activity correlated with recognition irrespective of condition? (figure 4A) How do they interpret the trial-by-trial results (figure 4B) in relation to the behavioural findings? It would be good to address these points in the discussion of the manuscript.

Did any of the control participant show the same pattern as the patient of better performance for asynchronous than synchronous 1st person perspective?

Reviewer #2 (Remarks to the Author):

Caveat. Though I'm well-versed in the empirical literature on episodic memory, I'm a philosopher, not an experimentalist. There are thus large parts of the paper about which I'll not allow myself to assess, and I will restrict myself to comments I feel legitimate to make.

1. Brief summary of the manuscript

MAJOR CLAIM

The paper explores the link between episodic memory (EM) and the sense of self, specifically bodily self-consciousness (BSC), i.e., an embodied multisensori-premotor form of self-consciousness that includes sense of agency, body ownership, 1PP, and selflocation. To do so, the authors design VR experiments with different in/congruent conditions between subjects' BSC and avatars designed to modulate BSC at encoding. These experiments provide evidence of a correlation between preserved sense of self at encoding (BSC/avatar congruency) and, on the one hand, better recognition performance, and on the other hand, stronger hippocampal reinstatement at retrieval. Overall, the core claim is that BSC at encoding contributes to episodic memory performance by boosting hippocampal reinstatement at retrieval due to a tight connection between premotor-sensory and hippocampal structures.

2. Overall impression of the work

MAJOR CLAIMS ARE NOVEL? OF INTEREST FOR OTHERS IN THE COMMUNITY

As far as I can see, the paper definitely contributes to better understand the neural circuitry underpinning memory (with the limitation pointed out below that I'm not sure they're talking about episodic memory). More specifically, it provides novel significant evidence for an embodied view of EM.

Maybe it's a minor point, but some relevant parts of the existing literature are missing and might qualify a bit the claimed novelty of the evidence provided.

1/ Regarding the embodied character of memory, for instance, Glenberg & Hayes, "Contribution of Embodiment to Solving the Riddle of Infantile Amnesia", 2016, is an important reference about the dependence of the hippocampus on motor development for it to play its role in EM. Iani, "Embodied memory", 2019, provides a whole body of experimental relevant evidence that suggests to downplay the claim that "sensory context of the observer's body at encoding and and its potential reinstatement during the retrieval process has only received scant attention."

2/ Regarding the experimental study of the role of the self in EM, some references might also lead the authors to qualify their claim as they say: "Although it has been claimed that EM is fundamental to establish a sense of self across time, this has never been shown experimentally." I think this is inaccurate. For instance, in a classic paper, Wheeler, Stuss, and Tulving, "Towards a Theory of Episodic Memory", 1997 claim: "Adult humans are capable of remembering prior events by mentally traveling back in time to reexperience those events. In this review, the authors discuss this and other related capabilities, considering evidence from such diverse sources as brain imaging, neuropsychological experiments, clinical observations, and developmental psychology. The evidence supports a preliminary theory of episodic remembering, which holds that the prefrontal cortex plays a critical, supervisory role in empowering healthy adults with autonoetic consciousness the capacity to mentally represent and become aware of subjective experiences in the past, present, and future."

The paper is interesting for the philosopher of memory I am. I'm interested in the embodied approach to episodic memory (Perrin, 2021), while very few philosophers have been so far. More work is needed, therefore, and the paper definitely provides empirical evidence and support for such an approach.

IS THE WORK CONVINCING?

Definitely.

WILL THE PAPER INFLUENCE THINKING IN THE FIELD?

Yes.

3. Specific comments, with recommendations for addressing each comment

Minor point. The abstract should be rephrased in order to make it clearer that it is a certain form of self-consciousness (BSC), considered from both a neural and a phenomenological point of view, that is studied in the paper. For instance, the authors say: "Although it has been claimed that EM is fundamental to establish a sense of self across time, this has never been shown experimentally." This is too general and inaccurate a claim, that does not reflect the specific point which the authors want to make, namely, certain multisensory and motor signals coming from the observer's body play a major role in the sense of oneself in EM.

Remarks about the core claim.

1/ The authors seek to study episodic memory, that is "long-term declarative memory", which "allows us to remember and relive past events and experiences". What they actually study, however, is very-short term—though autonoetic consciousness was tested one week later, recognition tests occurred one hour after encoding—recognition memory, which is different obviously. I know that there is some lexical variation in the empirical literature regarding the category of episodic memory between people who develop more neural approaches and those who develop more cognitive approaches. But since the authors explicitly refer to long-term episodic remembering and cite Tulving, there is a potential issue here.

2/ There are some potential blind spots in the core claims. The authors talk about the relation between BSC modulations at encoding and, at retrieval, recognition performance as well as hippocampal reinstatement. A natural question is: what happens in the hippocampus at encoding, in particular with respect to BSC? What about the storage in the hippocampus and the BSC network between encoding and retrieval? For instance, do the authors endorse the Hippocampal Index Theory about the relationships between the hippocampus and visuomotor structures, or do they have an alternative proposal about the functional role of the hippocampus? (some remarks p. 23 allude to HIT, but hearing more would be welcome) This question also comes to mind as one reads section "Hippocampal reinstatement ..." (p. 21 ff.).

Denis Perrin

Reviewer #3 (Remarks to the Author):

The paper reports on a series of studies aimed at investigating the role of the observer's body in episodic memory and its neural reinstatement during the retrieval processes. The research question is very timely and interesting as it fits into the research line addressing the role of the body representations in cognitive processing, and potentially the results could add very important information providing both behavioural and neuroimaging evidences that complement the current knowledge.

The manuscript is well written in the introduction and discussion whereas the methods section is hard to follow, and a lot of information is missing to replicate the study and understand in detail the protocol used. In addition, I have some concerns about some methodological choices that could have hindered the possibility to answer properly to the initial research question. Here below I will list my major comments.

- In general, as said above, the methods are poorly reported, and it is difficult for the reader to create a general picture of what happened in the different studies. I think that the authors should try to fill the gaps of missing information and put them in the correct paragraph (i.e. the description of the participant of the clinical study is included in the results and not in the participant section). As concerns the missing information, I would suggest including at least the following:

o A section dedicated to the VR environment (in the present version there are information here and there, and there is a video illustrating the scenes, but for clarity and reproducibility sake, a brief text with the different environments should be added, as supplementary material if not in the main manuscript)

o Which were the precise instructions for the incidental encoding? And for the intentional one?

o How did the participants answer to the object recognition task?

o What did the participants do during the delay between encoding and retrieval?
- BSC testing: why was this construct assessed in different environments (although reproducing the experimental conditions in terms of body involvement) and not right after each singular experimental task (therefore using the same scenes as the encoding)? I can't spot a real advantage of this choice. On the contrary, presenting different scenes with different objects in my opinion cannot rule out the possibility to have induced interference with those experienced during the experimental tasks (and this is especially true in the incidental memory task, when participants didn't know that they had to remember the object in the experimental scenes and not in the BSC scenes).

- VR environment: as I saw in the videos, the objects were very small and far away from the observer, to me sometimes difficult to recognize. Did the authors check for the object correct visual recognition beside the memory task? I guess the performance could be strongly affected if the objects are not properly identified.

- Considering the comment above, the experiment with incidental memory is affected by the set up itself: the participants were instructed only to move their hands and were surrounded by hardly recognizable objects that they did not know they had to remember. I would expect that the focus of their attention was allocated only to their virtual hands, so the memory recognition task basically assessed something that hadn't be properly encoded at all. Unfortunately, the fMRI study was conducted with this setup and not with the intentional encoding, whereby although the objects were the same, at least the participants had the opportunity to inspect them to try to remember. I agree that the incidental task is more similar to our everyday experience, but if my concern about the object correct identification is.

- well-founded, then the results of the imaging study are more difficult to interpret.

- The sample size calculation is not reported: did the authors run an a priori sample size calculation?

- Study design: it is unexpected to me the use of 3 experimental conditions instead of 4. As I understood, the authors crossed two variables, motor syncronicity and visual perspective, but then one of the four combinations is missing (i.e. SYCRONY3PP). Can the authors justify this choice? The issue arise also from the analyses, where the lack of the fourth condition prevents from fitting a full 2x2 model which would have allowed to detect the main effects of perspective and syncronicity plus their interaction.

- In study 4, the authors tested the patient 1 week after the VR experience, in analogy with the protocol with healthy participants. If this is correct to guarantee a comparable paradigm, I am wondering how reliable the answers of a patient suffering from a severe amnesia could be, if tested after such a long delay. The authors stated that she was able to remember the scenes under consideration, but still this is a qualitative report not supported by objective data.

Some minor-changes suggestions will follow:

- The abstract could be improved as currently doesn't mirror the complexity and richness of the studies (again, some methodological information should be added here to give the reader a first glance of the research)

- Line 94: what is the number (61) referred to?

- Lines 833-836: there are parentheses apparently not closed
- Line 842: what do the authors mean for "for each condition"?

- For the patient study, a table summarizing the neuropsychological tests and related scores could be helpful to support authors' statements about the patient's cognitive profile

Dear Reviewers,

We are happy to resubmit a revised version of our manuscript entitled "**Embodiment in** episodic memory through premotor-hippocampal coupling" (COMMSBIO-24-0615-T), by Nathalie Heidi Meyer*, Baptiste Gauthier*, Sara Stampacchia, Juliette Boscheron, Mariana Babo Rebelo, Jevita Potheegadoo, Bruno Herbelin, Florian Lance, Vincent Alvarez, Elizabeth Franc, Fabienne Esposito, Marilia Morais Lacerda and Olaf Blanke.

We thank you for the evaluation of our manuscript. We have thoroughly examined each of the comments and have updated the manuscript accordingly.

Below, we provide a comprehensive point-by-point response (in green) addressing each comment raised. All changes in the revised manuscript are indicated in **bold and are underlined**.

Nathalie Heidi Meyer, Baptiste Gauthier & Olaf Blanke

Reviewer #1 (Remarks to the Author):

The manuscript reports results from a series of behavioural studies with control participants and an amnesic patient, and of an fMRI study. The authors used a VR task where they presented scenes while manipulating bodily self-consciousness (BSC: first-person synchronous avatar, first-person asynchronous avatar, and third-person asynchronous avatar). They observed the highest level of hippocampal reinstatement for scenes encoded under visuomotor and perspectival congruency. This was interpreted as demonstrating that hippocampal reinstatement depends on the bodily sensory context of the observer during encoding. The authors further argue that these results provide evidence for embodied hippocampal reinstatement by showing that the sensorimotor context of the observer's body at encoding impacts encoding- and retrieval-related hippocampal activity. The manuscript was well-written and clear, and the results are interesting and novel. I suggest below a few points of clarification, as well as further discussion of some of the results and their interpretation.

We thank Reviewer 1 for these encouraging comments. We answer in detail to each comment below:

1.Abstract

"cortical-hippocampal reinstatement involved during encoding" would need to be rephrased (perhaps the authors meant reinstatement of encoding activity?)

We agree and have updated the abstract of the revised manuscript (page 2, line 30) as follows:

Revised manuscript: "Episodic memory (EM) allows us to remember and relive past events and experiences **and has been linked to** cortical-hippocampal reinstatement **of encoding activity**."

2. Introduction

"Episodic memory (EM) refers to a form of long-term declarative memory associated with the recall of the sensory details of an event"

This is a quite an unusual definition of episodic memory (a classic recognition task with words may not produce rich recollection of sensory details)

We have improved the definition in the revised manuscript, which now reads as follows: (page 4, line 50)

Revised manuscript: "Episodic memory (EM) refers to a form of long-term declarative memory associated with the explicit recall of the sensory, **perceptual and emotional** details of a past event."

Results

3. Results, page 9: why do the authors think they observed no self-reference effect (advantage of 1st person perspective) in the recognition test in experiments 1 and 2? One could have thought that it could be due to the fact that the scenes were presented in the background and thus not associated with the avatar and their body. However, the authors report a significant effect on experiment 3, with intentional encoding.

a) Could it be then that associating the avatar and the scenes was more likely to happen under intentional enclosing?

Reviewer 1 asks why we did not observe an advantage of the 1PP condition vs 3PP condition in experiments 1 and 2 and why we did observe such an effect of intentional (Experiment 3) vs. incidental encoding (Experiments 1 and 2). Indeed, under intentional encoding in Experiment 3, we observed better recognition performance for scenes encoded under visuomotor and perspectival congruency: performance in SYNCH1PP was better when compared to scenes encoded with visuomotor-perspectival mismatch (ASYNCH1PP; ASYNCH3PP). This effect was not present in Experiments 1 and 2, when participants encoded the scene under incidental encoding (i.e., they were not told that the experiment was about memory).

These data are compatible with the reviewer's proposal that potential effects between the avatar and the other visual objects, as manipulated by visuomotor and perspectival congruency, are more likely present under intentional vs. incidental encoding. Our data also support this proposal. Under incidental encoding (Experiments 1 and 2), participants may have paid less attention to the scene and its objects and may have more likely focused on the avatar and its movements and less on the visual objects. This 'attention-on-the-avatar' interpretation is compatible with our finding of an effect of object laterality (better performance for right-sided objects vs left-sided objects), as reported in the original manuscript. This object laterality effect was only found for the experiments performed with incidental encoding (i.e., Experiments 1 and 2; note that participants in all three experiments only performed right hand movements). However, as stated in the original manuscript (page 11, lines 265-281), this laterality effect (in Experiments 1 and 2) was found irrespective of the three conditions and therefore, does not depend on our SoA manipulation. Thus, participants were better at recognizing scenes in which the changed object was on the right side, that is on the same side as the moving upper limb. This laterality effect was absent in Experiment 3. To summarize and as Reviewer 1 suggests, the association between avatar and scene (objects) seems more prominent under intentional encoding and could explain why the behavioral effect is observed under intentional encoding and not incidental encoding. Future work will have to investigate these interesting questions further. This point has now been added in a new section of the discussion in the revised manuscript (pages 25-26, lines 701-723).

Revised manuscript: "We note that we did not find a difference between conditions in recognition performance under incidental encoding instructions (Experiments 1 and 2). Although we did expect such a difference (as found in Experiment 3), we speculate that this may have resulted from different processes associated with the different instructions given at the beginning of Experiments 1-2 versus Experiment 3. Under incidental encoding, the participants were not instructed to pay particular attention to the scene and thus may have been more likely to focus on the avatar and its movements. This interpretation is supported by the fact that we found an effect of object laterality under incidental encoding (Experiments 1 and 2), but not under intentional encoding (Experiment 3). Thus, participants were better at recognizing scenes in which the change occurred on the right side (i.e., the same side where their avatar's limb was moving). However, as our participants were above chance level in all three experiments, the fact that the attention towards the avatar was most likely emphasized during incidental encoding did not prevent them from performing the task. Moreover, we observed a reduced SoA under visuomotor and perspectival incongruency across the three experiments. Hence, even if there may have been a different focus of attention between experiments performed under incidental versus intentional encoding, the SoA was manipulated in the same way in all three experiments. Furthermore, as we observe differences of hippocampal reinstatement (Fig. 3D) between the conditions in our imaging results in Experiment 2 we assume that these differences are due to our experimental SoA manipulation at encoding, but that the incidental instruction gave rise to smaller difference of performance which may explain the absence of behavioral effect in the present study. Future studies should further test differences in episodic memory, depending on SoA and incidental versus intentional encoding."

b) Though the effect of agency was not significant in experiment 3, which was surprising. It would be good that the authors discuss these findings and how they can be integrated.

We thank Reviewer 1 for pointing this out. Although there was no statistically significant difference for the sense of agency (SoA) ratings when comparing the conditions SYNCH1PP and ASYNCH1PP in Experiment 3, we note that the results in this experiment are going in the same direction as those from Experiments 1 and 2 (i.e., higher SoA in SYNCH1PP than in ASYNCH1PP and ASYNCH3PP). Thus, numerically, the SoA ratings (continuous ratings between 0 and 1) in the SYNCH1PP condition was of 0.63 (sd \pm 0.23) for Experiments 1 and 2, and 0.69 (sd \pm 0.23) in Experiment 3, whereas the SoA in ASYNCH1PP condition was 0.56 (sd ± 0.28) in Experiments 1 and 2 and 0.65 (sd \pm 0.26) in Experiment 3). In Experiments 1 and 2, the difference between SYNCH1PP and ASYNCH1PP using a linear mixed model is comprised within a confidence interval between -0.43 and -0.08, while the standard coefficient is of -0.26 (these results were obtained applying the function 'effectsize' from the package 'effectsize' in R to the model described in the manuscript). In Experiment 3, the confidence interval is comprised between -0.45 and 0.11, and the standard coefficient is -0.17, therefore the difference is not significant. However, when we performed additional analysis pulling the three experiments

together, SoA was consistently higher in the SYNCH1PP compared to the two other conditions, independent of Experiment (SYNCH1PP compared to ASYNCH1PP: estimate = -0.059, t = -3, p = 0.003; SYNCH1PP compared to ASYNCH3PP: estimate = -0.08, t = -4.28, p <0.001), with a confidence interval between -0.38 to -0.08, and a standard coefficient of -0.23, which is similar to what is obtained when applying the model on Experiments 1 and 2 only. Thus we consider that although the effect is not significant in Experiment 3, it is still present overall and that the SoA is reduced under visuomotor and perspectival mismatch.

We added these results to the supplementary text (page 33, lines 267-286 of the supplementary documents) and to the revised results and discussion section of the main text (see below):

Revised supplementary manuscript: "Intentional encoding. Higher SoA and better recognition performance for intentional encoding when immersed with visuomotor and perspectival congruency (behavior, Experiment 3)

Although there was no significant difference for SoA ratings when comparing the conditions SYNCH1PP and ASYNCH1PP in Experiment 3, we note that the results in this experiment are going in the same direction as those from Experiments 1 and 2 (i.e., higher SoA in SYNCH1PP than in ASYNCH1PP and ASYNCH3PP). We compared the effect size from Experiments 1 and 2 with the effect size of Experiment 3 regarding the difference between SYNCH1PP and ASYNCH1PP. In Experiments 1 and 2, the difference between SYNCH1PP and ASYNCH1PP was comprised within a confidence interval between -0.43 and -0.08, while the standard coefficient is of -0.26. In Experiment 3, the confidence interval is comprised between -0.45 and 0.11, and the standard coefficient is of -0.17. Accordingly, the difference is not significant. However, when we performed additional analysis pulling the three experiments together, the SoA was consistently higher in the SYNCH1PP compared to the two other conditions, independent of Experiment (SYNCH1PP compared to ASYNCH1PP: estimate = -0.059, t = -3, p = 0.003; SYNCH1PP compared to ASYNCH3PP: estimate = -0.08, t = -4.28, p < 0.001, with a confidence interval between -0.38 to -0.08, and a standard coefficient of -0.23, which is similar to what is obtained when applying the model on Experiments 1 and 2 only."

We also added a short text in the revised results section (page 9-10, lines 235-250):

Revised manuscript: "Intentional encoding. Higher SoA and better recognition performance for intentional encoding when immersed with visuomotor and perspectival congruency (behavior, Experiment 3)

Experiment 3 was similar in all aspects, except that participants were told before the encoding session that their memory for the scenes would be tested subsequently (intentional encoding). As in Experiments 1 and 2, participants' SoA was higher in SYNCH1PP compared to ASYNCH3PP (**Fig. 2C**; estimate = -0.11, t = -3.16, p = 0.002; the comparison between the SYNCH1PP and the ASYNCH1PP condition was not significant, but similar in direction compared to Experiments 1 and 2 (estimate = -0.04, t = -1.2, p = 0.23). **To investigate whether the SoA effect was comparable to what was observed under incidental encoding, we compared the effect size of Experiments 1 and 2 with the one of Experiment 3 and ran additional analysis, confirming a similar SoA effect across all three experiments (for detail see Supplementary text).** The average ratings for the control items were significantly different between conditions (SYNCH1PP compared to ASYNCH1PP: estimate = -0.01, t = -0.56, p = 0.58; SYNCH1PP compared to ASYNCH3PP: estimate = -0.028, t = -1.5, p = 0.13)."

A short statement about this has been added to the discussion of the revised version of the manuscript (discussion: page 25, lines 691-700):

Revised manuscript: "<u>Successful manipulation of SoA leads to significant</u> <u>decrease of recognition performance under intentional encoding</u>

As expected, the disruption of visuomotor and perspectival congruency applied in the ASYNCH1PP and ASYNCH3PP conditions significantly reduced the SoA under incidental encoding (Experiments 1 and 2), similar to what is observed and reported in the literature (Haggard, 2017; Kannape and Blanke, 2013; Padilla-Castañeda et al., 2014). Although the SoA difference between SYNCH1PP and ASYNCH1PP did not differ significantly between conditions under intentional encoding (Experiment 3), the SoA was also higher in SYNCH1PP compared to ASYNCH1PP, showing that participants felt a higher SoA with preserved visuomotor and perspectival congruency across all experiments (see Supplementary material). "

4. The fMRI experiment was experiment 2, where there was no difference in recognition accuracy between the conditions.

a) How do the authors interpret the discrepancy between the brain and behavioural results?

Reviewer 1 asks us to discuss the behavioral and fMRI data of Experiment 2, pointing to fMRI differences across conditions that are not present in the behavioral results. First, we note that we obtained a reduction of sense of agency for both incidental encoding (Experiments 1 and 2) and intentional encoding (Experiment 3). Therefore, we induced a successful manipulation of bodily self-consciousness in both experiments. We did expect to find better recognition performance when the scenes were encoded under preserved visuomotor and perspectival congruency (SYNCH1PP); however, this result was only found under intentional encoding (Experiment 3) and not under incidental encoding (Experiments 1, and 2), which include the experiment performed with the MRI acquisition.

We agree with Reviewer 1 that divergence of behavioral and fMRI should be considered carefully. However, we also note that we do link behavioral and fMRI data. Thus, we show stronger hippocampal reinstatement for scenes encoded under preserved visuomotor and perspectival congruency (associated with a higher SoA) and link this result with recognition performance as we were able to show that hippocampal reinstatement was associated with a better recognition performance, as reported in previous studies (Danker et al., 2017; Ritchey et al., 2013; Tompary et al., 2016; Xiao et al., 2017). Further associating behavior and hippocampal activity, our trial-by-trial analysis (see Fig. 4B) also linked the hippocampal reinstatement (fMRI) with memory performance and showed that this association was held only when the scenes were encoded under preserved visuomotor and perspectival congruency. Thus, although averaged reinstated hippocampal activity across conditions and average recognition performance across conditions were not associated, more fine-grained analysis (correlation analysis, single trial analysis) linked recognition performance with hippocampal reinstatement.

This has been added in the discussion section of the revised manuscript (page 22-23, lines 574-611; see revised text below comment 4c)

b) Why do they think the hippocampus reinstatement activity correlated with recognition irrespective of condition? (figure 4A)

In addition to our previous response we note that in Fig. 4A of the original manuscript, we report a positive correlation between hippocampal reinstatement and recognition performance, showing that the greater the similarity between hippocampal encoding

activity and the averaged hippocampal recall activity across all trials, the better was our participants' recognition performance. This analysis did not reveal an interaction between recognition performance depending on the experimental conditions, implying that regardless of the different encoding conditions, hippocampal reinstatement is associated with recognition performance (i.e., independent of the three experimental conditions). These findings link hippocampal reinstatement to recognition performance and are compatible with the behavioral data that did not reveal differences across conditions. Accordingly, the data reported in Fig. 4A reveal a more general relationship between episodic memory and hippocampal reinstatement that does not depend on the present experimental conditions, compatible with previous reports (Danker et al., 2017; Ritchey et al., 2013; Tompary et al., 2016; Xiao et al., 2017), showing that hippocampal reinstatement is a neural proxy for memory processes. However, while previous research, such as Tompary et al. (2016), demonstrated this relationship for much simpler stimuli (like word lists or object pictures), the present data extend hippocampal reinstatement to more naturalistic and immersive visual scenes, as tested in VR. This has been clarified in the discussion section of the revised manuscript (page 22-23, lines 574-611; see revised text below comment 4c)

In addition, we show that hippocampal reinstatement derived from successful trials was reduced under visuomotor and perspectival mismatch. Thus, a strong similarity of the encoding and the recall activity pattern in the hippocampus (i.e., a strong hippocampal reinstatement), improves memory performance, but independent of the condition. Hence, we rather found that participants tend to have stronger hippocampal reinstatement for successful trials when scenes were encoded under preserved visuomotor and perspectival congruency (Fig. 3D). This could be interpreted as a facilitated way for the hippocampus to have a similar encoding activity at retrieval when the scenes were encoded under preserved visuomotor and perspectival congruency.

c) How do they interpret the trial-by-trial results (figure 4B) in relation to the behavioural findings? It would be good to address these points in the discussion of the manuscript.

Reviewer 1 asked us to address the trial-by-trial results depicted in Fig. 4B, in which we found a significant interaction between conditions and hippocampal reinstatement to explain part of the memory performance in Experiment 2. In the trial-by-trial findings, when the original scene (i.e., same scene than the one presented at encoding, but without the avatar) was presented during the recognition task, the strength of the hippocampal reinstatement explained our participants' recognition performance, but only for the SYNCH1PP condition, which corresponds to the condition with preserved visuomotor and perspectival congruency. This suggests that the hippocampal activity during recall is more similar to the hippocampal activity at encoding for scenes encoded with preserved SoA, compared to scenes encoded under disrupted visuomotor and perspectival congruency (as in ASYNCH1PP and ASYNCH3PP). We suggest two potential interpretations: (1) one possibility is that during encoding, when SoA is preserved (under visuomotor and perspectival congruency, SYNCH1PP condition) the memory trace formation at encoding is better integrated into the hierarchy of the medial temporal lobe, including the hippocampus (Shimamura, 2010). Accordingly, the reinstatement of the hippocampal encoding activity is facilitated at retrieval in these conditions compared to the conditions with visuomotor and perspectival mismatch. (2) Another possibility is that different brain regions might be involved depending on

visuomotor and perspectival congruency. Under preserved visuomotor and perspectival congruency, the hippocampus seems to be involved, but it might be possible that when encoding a scene under disrupted visuomotor and perspectival congruency, the hippocampus is less reinstated and some other regions - not identified in this study- are more reinstated. Overall, this result indicates that hippocampal reinstatement is stronger for scenes encoded under preserved visuomotor and perspectival perspectival congruency.

We discuss these points (4a, 4b, 4c) in the discussion section of the revised manuscript (page 22-23, lines 574-611):

Revised manuscript: "Hippocampal reinstatement reflects recognition performance and the visuomotor and perspectival congruency of the encoded scenes

Although averaged reinstated hippocampal activity across conditions and average recognition performance across conditions were not associated, more fine-grained analysis (correlation analysis, single trial analysis) linked recognition performance with hippocampal reinstatement. We found that the hippocampal reinstatement of encoding activity across the experimental conditions was correlated with participants' recognition performance, consistent with previous work using visual or auditory stimuli (Liang and Preston, 2017; Tompary et al., 2016). Thus, hippocampal reinstatement - reflected by the average hippocampal activity across all trials - correlated with average recognition performance (Fig. 4A). This is consistent with the idea that successful EM retrieval depends on the degree of remobilization of activity observed during encoding (Danker et al., 2017; Tompary et al., 2016), i.e. reactivation of the hippocampal engram (Josselyn et al., 2015). Neural reactivation of the hippocampus during EM retrieval and its link with memory performance has been demonstrated previously (Danker et al., 2017; Ritchey et al., 2013; Tompary et al., 2016; Xiao et al., 2017). Yet this earlier work presented single or paired stimuli at encoding (i.e., pictures, word cues, whereas the present results report hippocampal reinstatement in a richer sensory context with action-embedded 3D scenes using immersive VR in fMRI with incidental encoding, closer to encoding conditions in our everyday life. We did not expect necessarily a difference between conditions in this latter analysis, as it has been shown previously that hippocampal reinstatement is linked with recognition performance, more generally. Our finding is compatible with previous data on hippocampal reinstatement and recognition performance in a range of tasks (Danker et al., 2017; Ritchey et al., 2013; Tompary et al., 2016; Xiao et al., 2017). Although there was no condition-dependent effect for the relationship between hippocampal reinstatement and memory performance on average, these findings were extended by our additional trial-by-trial analyses showing that hippocampal reinstatement reflects the successful recognition of the original scene presented during encoding, but only when analyzed for single trials. Moreover, this was found only when encoding was done with visuomotor and perspectival congruency in the SYNCH1PP

condition (Fig. 4B). This suggests that the hippocampal activity during recall is more similar to the hippocampal activity at encoding for scenes encoded with preserved SoA, compared to scenes encoded under disrupted visuomotor and perspectival congruency (as in ASYNCH1PP and ASYNCH3PP). This could be due to better reinstatement of the hippocampal encoding activity at retrieval in the preserved visuomotor and perspectival congruency condition compared to the conditions with visuomotor and perspectival mismatch (i.e., Shimamura 2010), or participation of other brain regions to reinstatement when the scenes were encoded in conditions with disrupted visuomotor and perspectival congruency (ASYNCH1PP; ASYNCH3PP). Hence, the successful recognition of the scene observed at encoding is critically linked to the reactivation of the hippocampal encoding activity during retrieval, extending previous evidence about the hippocampal encoding activity during retrieval, extending previous evidence about the hippocampal encoding activity during retrieval, extending previous evidence about the hippocampal encoding activity during retrieval, extending previous evidence about the hippocampus' role in pattern separation to discriminate between previously encoded events and new events (Amer and Davachi, 2023; Lohnas et al., 2023, 2018; Staresina et al., 2013)."

5.Did any of the control participant show the same pattern as the patient of better performance for asynchronous than synchronous 1st person perspective? The reviewer asks for more detail comparing the patient's behavioral results with those obtained in healthy participants. None of our participants showed the same or a larger difference than the patient. More specifically, from our 24 participants, only 7 participants showed slightly better performance in the ASYNCH1PP condition compared to SYNCH1PP. Importantly, 5 of these participants had only a very minor ASYNCH1PP > SYNCH1PP difference of 0.075; 2 participants showed a slightly bigger difference of 0.1, which however was still inferior to the patient's difference between conditions (0.16). Moreover, when comparing the patient's score with participants from Experiment 3 (intentional encoding), using a Crawford test, we found that the patient's score was significantly lower compared to the healthy participants as reported in the original text (page 19, line 492; MParticipants = 0.06, SD = 0.11, p = 0.036). Additional analysis also showed that the patient has a significantly lower score specifically in SYNCH1PP (patient's score = 0.58) compared to the healthy participants (M = 0.77, SD = 0.11, p = 0.048). Whereas her score in the ASYNCH1PP (0.73) is not significantly different from the healthy participants (M = 0.70, SD = 0.13, p = 0.4) (see figure below).

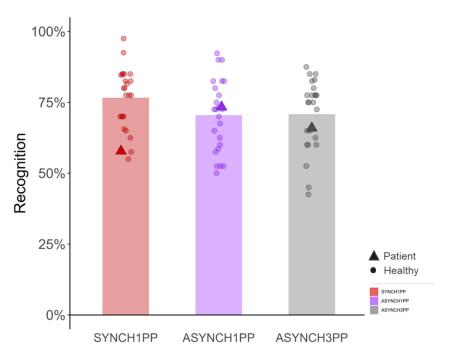


Figure 1 : Recognition performance of healthy participants from Experiment 3 (intentional encoding) depicted by dots, and for the patient (depicted by triangle) in the three conditions (SYNCH1PP, red, ASYNCH1PP, purple and ASYNCH3PP grey).

Overall, these results show that the patient exhibited a unique pattern of performance relatively to the performance of healthy participants in comparable experimental conditions. We have added this more detailed description to the results section of revised manuscript.

Revised manuscript: (page 19, lines 490 - 500): "The accuracy difference the patient showed between SYNCH1PP and ASYNCH1PP was significantly different from that observed in healthy participants (Experiment 3) (mean = 0.06, sd \pm = 0.11, p = 0.036; the comparison SYNCH1PP-ASYNCH3PP was not significantly different compared to healthy participants (mean = 0.06, sd \pm = 0.13, p = 0.148). From our 24 participants, only 7 participants showed slightly better performance in the ASYNCH1PP condition compared to SYNCH1PP. Five of these participants had only a very minor ASYNCH1PP > SYNCH1PP difference of 0.075. Two participants did show a slightly bigger difference of 0.1, which was still smaller than the patient's difference between conditions (0.16). Thus, no participant showed a performance difference that was larger or comparable with the patient's, supporting the results of the Crawford test."

Reviewer #2 (Remarks to the Author):

Caveat. Though I'm well-versed in the empirical literature on episodic memory, I'm a philosopher, not an experimentalist. There are thus large parts of the paper about which I'll not allow myself to assess, and I will restrict myself to comments I feel legitimate to make.

1. Brief summary of the manuscript

MAJOR CLAIM

The paper explores the link between episodic memory (EM) and the sense of self, specifically bodily self-consciousness (BSC), i.e., an embodied multisensori-premotor form of self-consciousness that includes sense of agency, body ownership, 1PP, and self-location. To do so, the authors design VR experiments with different in/congruent conditions between subjects' BSC and avatars designed to modulate BSC at encoding. These experiments provide evidence of a correlation between preserved sense of self at encoding (BSC/avatar congruency) and, on the one hand, better recognition performance, and on the other hand, stronger hippocampal reinstatement at retrieval.

Overall, the core claim is that BSC at encoding contributes to episodic memory performance by boosting hippocampal reinstatement at retrieval due to a tight connection between premotor-sensory and hippocampal structures.

2. Overall impression of the work

MAJOR CLAIMS ARE NOVEL? OF INTEREST FOR OTHERS IN THE COMMUNITY

As far as I can see, the paper definitely contributes to better understand the neural circuitry underpinning memory (with the limitation pointed out below that I'm not sure they're talking about episodic memory). More specifically, it provides novel significant evidence for an embodied view of EM.

We thank Reviewer 2 for this positive feedback about our study and the valuable comments and suggestions. We respond below to each of the comments raised by Reviewer 2.

Maybe it's a minor point, but some relevant parts of the existing literature are missing and might qualify a bit the claimed novelty of the evidence provided.

1. Regarding the embodied character of memory, for instance, Glenberg & Hayes, "Contribution of Embodiment to Solving the Riddle of Infantile Amnesia", 2016, is an important reference about the dependence of the hippocampus on motor development for it to play its role in EM. Iani, "Embodied memory", 2019, provides a whole body of experimental relevant evidence that suggests to downplay the claim that "sensory context of the observer's body at encoding and and its potential reinstatement during the retrieval process has only received scant attention."

We thank Reviewer 2 for indicating these relevant references. We have added them to the revised introduction (page 4, line 69). Iani et al. (2019) is a good review of the role

of the body in memory, which discusses the different sensorimotor contributions of the body in memory. Thanks. Glenberg & Hayes (2016) focused mainly on the link between hippocampal development and the motor system, which is a bit further away from the current research questions. However, it will add other theoretical and biological evidence in favor of the role of the body in memory and we have also added it.

Revised manuscript (page 4, lines 68-78):

"However, the sensory context of the *observer's body* at encoding and its potential reinstatement during the retrieval process has only received scant attention. Thus, **although previous authors have speculated about the importance of the observer's body in episodic memory (Iani at al., 2019, Glenberg & Hayes, 2016), there are only very few laboratory-based empirical studies that have tested whether sensory bodily inputs - such as tactile, proprioceptive, or vestibular stimuli and their integration with motor signals of the observer's body at encoding and retrieval - impact EM. This neglect is surprising because the body provides a rich set of sensory-motor inputs during encoding and may provide cues that aid memory formation for visual and auditory stimuli. The few studies that have been carried out revealed that congruent body posture between encoding and retrieval facilitates retrieval of words (Rand and Wapner, 1967) and personal events (Dijkstra et al., 2007, <u>lani et al., 2019</u>). However, none of these studies investigated whether neural reinstatement, as described for the visual and auditory context (Bosch et al., 2014; Wheeler et al., 2000), applies to the bodily sensory context."**

2. Regarding the experimental study of the role of the self in EM, some references might also lead the authors to qualify their claim as they say: "Although it has been claimed that EM is fundamental to establish a sense of self across time, this has never been shown experimentally." I think this is inaccurate. For instance, in a classic paper, Wheeler, Stuss, and Tulving, "Towards a Theory of Episodic Memory", 1997 claim: "Adult humans are capable of remembering prior events by mentally traveling back in time to reexperience those events. In this review, the authors discuss this and other related capabilities, considering evidence from such diverse sources as brain imaging, neuropsychological experiments, clinical observations, and developmental psychology. The evidence supports a preliminary theory of episodic remembering, which holds that the prefrontal cortex plays a critical, supervisory role in empowering healthy adults with autonoetic consciousness—the capacity to mentally represent and become aware of subjective experiences in the past, present, and future."

The paper is interesting for the philosopher of memory I am. I'm interested in the embodied approach to episodic memory (Perrin, 2021), while very few philosophers have been so far. More work is needed, therefore, and the paper definitely provides empirical evidence and support for such an approach.

We thank Reviewer 2 for his comments and added this important reference to the paper (Wheeler, Stuss and Tulving, 1997) in the Introduction (pages 4-5, lines 87-90):

Revised manuscript: "However, despite prominent proposals that self-consciousness is an essential part of EM, as argued by Endel Tulving (Tulving, 1985;2002, <u>Wheeler,</u> <u>Studdy and Tulving, 1997</u>), the impact of experimental alterations of BSC during encoding on later retrieval processes has only recently been investigated."

Concerning the abstract, we rephrased the all abstract as detailed in the next comment of Reviewer 2.

IS THE WORK CONVINCING? Definitely. WILL THE PAPER INFLUENCE THINKING IN THE FIELD? Yes.

3. Specific comments, with recommendations for addressing each comment

Minor point. The abstract should be rephrased in order to make it clearer that it is a certain form of self-consciousness (BSC), considered from both a neural and a phenomenological point of view, that is studied in the paper. For instance, the authors say: "Although it has been claimed that EM is fundamental to establish a sense of self across time, this has never been shown experimentally." This is too general and inaccurate a claim, that does not reflect the specific point which the authors want to make, namely, certain multisensory and motor signals coming from the observer's body play a major role in the sense of oneself in EM.

The abstract has been rephrased as follows (page 2, lines 29-40):

Revised manuscript: "Episodic memory (EM) allows us to remember and relive past events and experiences <u>and has been linked</u> to cortical-hippocampal reinstatement <u>of encoding activity</u>. <u>While EM is</u> fundamental to establish a sense of self across time, <u>this claim and its link to the sense of agency (SoA)</u>, <u>based on</u> <u>bodily signals, has not been tested experimentally</u>. <u>Using real-time sensorimotor</u> <u>stimulation, immersive virtual reality, and fMRI we manipulated the SoA</u> and report stronger hippocampal reinstatement for scenes encoded under preserved <u>SoA</u>, reflecting recall performance <u>in a recognition task</u>. We link <u>SoA</u> to EM showing that hippocampal reinstatement is coupled with reinstatement in premotor cortex, a key <u>SoA</u> region. We extend these findings ina severe amnesic patient whose memory lacked the normal dependency on <u>the SoA</u>. Premotor-hippocampal coupling in EM describes how <u>a key aspect of the bodily</u> self at encoding is neurally reinstated during the retrieval of past episodes, enabling a sense of self across time."

Remarks about the core claim.

4. The authors seek to study episodic memory, that is "long-term declarative memory", which "allows us to remember and relive past events and experiences". What they actually study, however, is very-short term—though autonoetic consciousness was tested one week later, recognition tests occurred one hour after encoding—recognition memory, which is different obviously. I know that there is some lexical variation in the empirical literature regarding the category of episodic memory between people who develop more neural

approaches and those who develop more cognitive approaches. But since the authors explicitly refer to long-term episodic remembering and cite Tulving, there is a potential issue here.

We agree with this general concern and note that it is present in many studies on episodic memory. First, there is indeed some lexical variation in the details concerning distinctions between long-and short-term memory. According to the APA dictionary short-term memory extends to at best delays of a few minutes, with no opportunity to consolidate memory either by offline (sleep) or online consolidation (awake rest). Long-term memory, on the contrary, is defined as starting from a delay of at least one hour, aligning with the typical onset of hippocampal consolidation processes (Dudai, 2011; McGaugh, 2015; Moscovitch et al., 2016; Squire et al., 2015)

Second, one of our main interests and longer-term goals is to understand how aspects of bodily self-consciousness, such as SoA, interact with long-term memory processes that occur weeks or months after the encoding of an event. When citing the work of Endel Tulving, we do refer to these long-term and self-related aspects of autobiographical memory. However, investigating the behavioral and neural mechanism that link bodily self-consciousness with these very long-term memories is very challenging, simply because of the length and cost of performing such long studies, as well as the amount of confounds (emotions, valence, rehearsal of the events, delay between encoding and retrieval) with longer-term autobiographical memories, and the lack of control on the encoding situation.

Third, our approach is a tradeoff between having virtual scenes and body movements that were richer and closer to real life-like scenario compared to simpler stimuli such as words and 2D objects that have been classically used as stimuli in most previous imaging studies (Squire et al., 2000, Moscovitch et al., 2010, Rugg et al., 2012, Davachi et al., 2017). In addition, we wanted to keep a controlled encoding scenario without the usual confounds attached to autobiographical memory recall (emotions, valence, rehearsal of the events). This is one of the difficulties when studying longterm episodic memory, often reported and discussed in the literature (Smith, 2019). Some approaches use life-like events (thus uncontrolled events with unknown content) and focus on the retrieval part, while some other approaches opt for rather simple, but well controlled stimuli to investigate encoding and retrieval processes. We here tried to find a balance between both approaches. Using virtual reality brings the experimental scenario closer to life-like events while keeping a controlled environment (the view is 3D, we can control the view of the body to make it as close to real life, track movement to keep the visual feedback of motor movement as in real life). It also enables to quantify memory performance objectively as we know what was presented during encoding and therefore whether what was recall is correct or not. However, this approach is based on the encoding of events that are most likely not important enough in the life of the participants to be remembered in the longer term, and hence, a delay of one week or one month to test the recognition of these participants seemed too long when designing the study. We think that both approaches are needed (test longer-term memory based on real events, and test memory with a shorter delay between encoding and recall to ensure a good control of the events and potential confounds), and hope that future studies will continue our work and develop related memory paradigms and investigate the neural mechanism linking bodily self-consciousness and episodic memory under different long-term delay of retrieval.

Finally, concerning the recognition task, this approach was used extensively in the memory field (Davachi et al., 2017, Tompary et al., 2016) and also previously used to investigate the link between bodily self-consciousness and episodic memory by our group (Bréchet et al., 2019, 2020, Gauthier et al., 2020), showing behavioral effects characterized by a reduction of memory performance when bodily self-consciousness was manipulated, as well as difference of functional connectivity between the hippocampus and parahippocampus (Gauthier et a., 2020). Hence, we thought this approach was well suited for the present study (studying the neural mechanisms linking bodily self-consciousness and episodic memory), as it allowed us to have several trials and thus better quantification of memory performance. This was also important for the fMRI analysis as it allowed us to do trial-by-trial analysis and uncover patterns of activity across trials that differ between conditions.

We added this limitation in the revised version of the manuscript, in the discussion section (page 27, lines 768-782):

Revised manuscript: "Study limitations

This study did not aim to separate the specific mechanisms associated with the firstperson perspective or with visuo-motor synchrony, but to provide first evidence into the neural mechanisms linking BSC and EM. Therefore, we tested the effects of graded conditions, from preserved BSC (SYNCH1PP), to moderate (ASYNCH1PP), to strong BSC alterations (ASYNCH3PP). Future studies may investigate the specific effects of perspective and congruency on the behavioral, neural, and clinical mechanisms leading to the present coupling of BSC and EM.

Additionally, this study tested memory using a recognition task at a one-hour delay, whereas long-term episodic memories expand over much larger time periods. We used a one-hour delay as it corresponds to the onset of the hippocampal consolidation process associated with long-term memory (Dudai et al., 2004, Squire et al., 2015, McGaugh et al., 2015, Moscovitch et al., 2016). A recognition task was chosen as it allowed us to obtain many repeated trials that were critical to obtain sufficient data for the fMRI analysis (Experiment 2). We encourage future studies to measure memory with longer delays (days, weeks, etc) and with autobiography relevant stimulus material and presented in immersive VR scenarios."

5. There are some potential blind spots in the core claims. The authors talk about the relation between BSC modulations at encoding and, at retrieval, recognition performance as well as hippocampal reinstatement. A natural question is:

a) what happens in the hippocampus at encoding, in particular with respect to BSC?

Thanks for this interesting question. At encoding, the BSC contrast (SYNCH1PP > ASYNCH1PP + ASYNCH3PP) did not reveal any difference in hippocampal activity. However, our results show that hippocampal reinstatement was higher in SYNCH1PP as compared to ASYNCH1PP and ASYNCH3PP. This suggests that the hippocampus has a similar level of activity in the different conditions during the encoding, but that

the reinstatement of its activity at retrieval is facilitated for scenes encoded under preserved visuomotor and perspectival congruency. Based on these results, it seems that the BSC level at encoding activates a BSC network and does not modulate hippocampus differently. However, the BSC manipulation differently influences the reinstatement of the hippocampal activity during retrieval.

This has been added to the revised discussion (page 24, lines 660-668).

"Several studies have demonstrated that hippocampal activity during encoding is coupled with the reactivation of other cortical regions, during the retrieval process^{14,82}. In particular, activation of visual cortex has been linked with hippocampal activity, at encoding and retrieval, and it has been suggested that hippocampal reinstatement mediates the reinstatement of cortical areas during retrieval (Gordon et al., 2014; Staresina et al., 2013). <u>We did not find any difference of hippocampal activity</u> between conditions during the encoding session alone, suggesting that neural processes between encoding and retrieval and not during the encoding process itself, mediated this effect. In our study, we found that the reinstatement of the left hippocampus was linked to left dPMC reinstatement, at the single trial level (Fig. 5B)."

b) What about the storage in the hippocampus and the BSC network between encoding and retrieval?

Reviewer 2 is asking about the consolidation process between encoding and the retrieval session. Although this is also a very interesting question, our experiments were not setup to investigate this directly. Because our participants had a break during the encoding and retrieval session, we also did not record any additional measurements (neither behavioral nor neural) during that period. Therefore, we can only speculate about the consolidation process. In the standard model of memory consolidation, a one-hour delay corresponds to a storage of the compressed encoding information in the hippocampus, which would enable the reinstatement of the corresponding neocortical activity during the first explicit recall (Dudai and Eisenberg, 2004) Thus, it is possible that the neural differences observed in Experiment 2 (stronger hippocampal reinstatement, positive reinstatement coupling between hippocampus and dPMC for scenes encoded under SYNCH1PP) could be due to differences in consolidation that happened between encoding and retrieval. However, as mentioned above this was not investigated in the present study.

c) For instance, do the authors endorse the Hippocampal Index Theory about the relationships between the hippocampus and visuomotor structures, or do they have an alternative proposal about the functional role of the hippocampus? (some remarks p. 23 allude to HIT, but hearing more would be welcome) This question also comes to mind as one reads section "Hippocampal reinstatement ..." (p. 21 ff.).

Does Reviewer 2 refer to the theory in which the hippocampus acts as a reactivator of brain regions (mainly in the neocortex), involved at encoding (Tanaka and McHugh, 2018; Teyler and DiScenna, 1986)? In that case, our results are compatible with this theory as we observe premotor-hippocampal coupling, characterized by stronger hippocampal reinstatement that was associated with stronger dorsal PMC reinstatement. Moreover, this was only found for the scene encoded with preserved bodily self-consciousness (SYNCH1PP). These findings are in line with the theory

proposed by Timothy Teyler (Teyler and DiScenna, 1986) and further elaborated by others under the concept of hippocampal-neocortical axis or transformation trace theory (Moscovitch et al., 2016; Nadel et al., 2000; Sekeres et al., 2018, 2017) Importantly, our results add the component of the bodily self and its related sense of agency to this theory, and link sensorimotor processes and the bodily self via premotor and hippocampal coupling of their reinstatement, which was so far not considered in the current proposition of the Hippocampal Index Theory, as far as we know.

This was already discussed in the manuscript (page 24, lines 660-671); we now added two additional references:

Revised manuscript: "Several studies have demonstrated that hippocampal activity during encoding is coupled with the reactivation of other cortical regions, during the retrieval process^{14,82}. In particular, activation of visual cortex has been linked with hippocampal activity, at encoding and retrieval, and it has been suggested that hippocampal reinstatement mediates the reinstatement of cortical areas during retrieval ^{14,21}. In our study, we found that the reinstatement of the left hippocampus was linked to left dPMC reinstatement, at the single trial level (Fig. 5B). Together with past experimental work, this observation extends the widely accepted theory that the hippocampus indexes sensory information of EM stored in visual and auditory regions (Nadel et al., 2000, Sekeres et al., 2017; 2018, **Teyler and DiScenna, 1986, Tanaka and McHugh 2018**) to indexing sensorimotor information stored in dPMC."

Reviewer #3 (Remarks to the Author):

The paper reports on a series of studies aimed at investigating the role of the observer's body in episodic memory and its neural reinstatement during the retrieval processes. The research question is very timely and interesting as it fits into the research line addressing the role of the body representations in cognitive processing, and potentially the results could add very important information providing both behavioural and neuroimaging evidences that complement the current knowledge.

The manuscript is well written in the introduction and discussion whereas the methods section is hard to follow, and a lot of information is missing to replicate the study and understand in detail the protocol used. In addition, I have some concerns about some methodological choices that could have hindered the possibility to answer properly to the initial research question. Here below I will list my major comments.

We thank Reviewer 3 for the positive evaluation of our manuscript and apologize if any information was missing. Below is an answer to each comment raised by Reviewer 3.

We note here at the beginning that we have thoroughly revised and extended the method section. We feel that these changes improved the method section and will help the reader to follow the experimental procedures and analyses that we performed. However, this has increased the word count of the revised manuscript and we hope this is acceptable.

- In general, as said above, the methods are poorly reported, and it is difficult for the reader to create a general picture of what happened in the different studies. I think that the authors should try to fill the gaps of missing information and put them in the correct paragraph (i.e. the description of the participant of the clinical study is included in the results and not in the participant section). As concerns the missing information, I would suggest including at least the following:

1. A section dedicated to the VR environment (in the present version there are information here and there, and there is a video illustrating the scenes, but for clarity and reproducibility sake, a brief text with the different environments should be added, as supplementary material if not in the main manuscript)

Although this was mentioned in the original manuscript, we agree that the description was too short and additionally spread among different sections (page 29, lines 829-841, page 31-32, lines 943-952). We added a new single section to the main text of the revised version of the manuscript (page 32, lines 959-974) called "VR scenes" placed immediately after the section "VR display" in the methods section and now give more details about the generation of the VR scenes.

Revised manuscript: <u>"VR scenes</u>

We designed four virtual scenes for this study. For the encoding session, three virtual indoor scenes were used (Living room, Changing room, Cabin). Each scene contained 18 objects placed in front of the participants in their visual field (See Supplementary text for the detailed list of objects). Critically, for each participant, a scene was associated with a different condition. For example, whereas the living room was associated with the SYNCH1PP condition for participant 1, it was associated with ASYNCH3PP for participant 2, etc. This was pseudorandomized across participants prior to the beginning of the experiment, ensuring that each scene was associated with an equal number of times with the different conditions. When the scene was associated with the condition of ASYNCH3PP, the point of view was similar compared to the other conditions (i.e., the distance between the observer and the objects remained the same) and only the avatar was shifted by 2 virtual meters to a position in front of the observers.

The fourth scene, used only for the BSC session, was a different scene, an outdoor scene in a forest. To ensure similar visual complexity compared to the other three conditions (used during the encoding session), we also placed 18 objects in this scene."

Revised manuscript, supplementary text page 33, lines 252-264:

"<u>Methods</u>

VR scenes

Each scene contained the following objects: Living room: mug, tennis ball, gloves, soccer ball, slippers, coat, forks, umbrella, toy-train, radio, phone, carpet, pillow, bottle, fan, bucket, soap, golf swing; Changing room: dice, knife, shoes, bike, teapot, basketball, apron, alarm clock, plant, glasses, sledge, camera, vase, chair, Ping-Pong racket, guitar, diving mask, beanbag; Cabin: pen, ice skate shoes, broom, tie, book, skis, tennis racket, belt, water can, pants, remote controller, skate, treadmill, microwave, cane, computer, calculator, helmet; BSC scene (forest): hammer, pocket clock, sponge, box gloves, snowboard, flipflop, scooter, socks, bowling ball, bowtie, baseball bat, vacuum cleaner, paddle, cane, coffee maker, dumbbell, smoking pipe, phonograph."

o Which were the precise instructions for the incidental encoding? And for the intentional one?

This was indicated in some detail in the original manuscript (page 28, lines 823-824, and page 29, lines 852-859), but probably not in sufficient detail. We added details of

the instructions that we used in the revised text and added this in the "encoding session" section, as follows (page 29, lines 852-859):

Revised manuscript: "Encoding was incidental in Experiments 1,2 and 4. Thus, participants were not told that they participated in a memory experiment and that their object recognition was going to be tested (participants were told that they were participating to a technical feasibility study testing a new VR environment). This was different in Experiment 3, where encoding was intentional. We instructed the participants to pay close attention to the scene during encoding and told them they would be tested on the scene one hour later. We did not specify which type of memory test would be performed and what kind of questions would be asked. The rest of the experimental design was the same between Experiments 1, 2, 3 and 4."

3. How did the participants answer to the object recognition task?

This was also indicated in the original manuscript in some detail (page 30, lines 878-881), but was given in the BSC assessment section. This placement was done because this part of the experiment also involves button press responses and precedes the recognition section. We have now added more detail to the revised manuscript in the recognition task session as follows (page 30, lines 890-898):

Revised manuscript: "One hour after the encoding session, participants were presented with the encoded scenes again. Participants were exposed to each tested scene for 10 seconds <u>after which a white square appeared on a grey background.</u> They were then asked to respond yes <u>(right button press)</u> or no <u>(left button press)</u> with their index finger to the question: "Is there any change in the room compared to the first time you saw it?". <u>Once they had answered, the white square disappeared</u> and another scene was shown for 10 seconds. They were instructed just before the start of the recognition session that they would have to answer concerning the original scenes seen during the encoding session. Some of these scenes were identical to the encoded scenes (original scene), and others were modified (changed scene)."

4. What did the participants do during the delay between encoding and retrieval?

During the break, the participants were not monitored in detail by us and free to walk in our research institute and the cafeteria. They were told not to consume any alcohol or drugs. This has now been added to the revised method section (page 30, lines 883-888):

Revised manuscript: "Break

At the end of the encoding and BSC session, participants left the MR/mock scanner environment and had a one hour break during which they were free, but asked to stay in the buildings of our research campus (we asked them not to consume any alcohol or drugs). One hour after the break they returned to the

<u>MR scanner (Experiment 2) or mock replicate of the scanner (Experiments 1 and 3) to start the recognition session.</u>"

5. BSC testing: why was this construct assessed in different environments (although reproducing the experimental conditions in terms of body involvement) and not right after each singular experimental task (therefore using the same scenes as the encoding)? I can't spot a real advantage of this choice.

Reviewer 3 asks us to clarify the choice we made in the experimental design, specifically the reason why BSC was not assessed with the same scenes that we used for the encoding session. This is a key aspect of our experimental setup and we reiterate that it is important that a different fourth scenes was used for the BSC assessment. We had briefly indicated the reasons for this choice in the original manuscript (page 8, lines 187-188).

The four different scenes were necessary, because of the use of a different environment for each of the three experimental conditions. Additionally, a fourth scene for the BSC session was done to avoid any confound of the experimental scene itself with the memory encoding session. In fact, during the design of the study, we thought about three different possible ways to test BSC (including the solution Reviewer 3 is suggesting):

First, as Reviewer 3 suggests, we could have tested BSC immediately after each encoded scene and thus in the exact same scene as the scene used for encoding. However, this has two main disadvantages in our opinion: (1) Because we would have to ask questions about SoA and related aspects of bodily self-consciousness, this may have directed the participants' attention more generally to the body and its movements and would have confounded the encoding of subsequent scenes. (2) It may have also made participants more aware of the differences between the different conditions (i.e., more aware of the delay of the movement). We wanted to avoid both confounds.

Accordingly, we decided to test BSC in a separate block after the end of the three encoding sessions. There were again two different ways to test BSC:

We could have still used the same scenes than the one used during the encoding session, but in that case, we would not know whether the participants would remember the moment of the encoding session or the moment of the BSC assessment (which is slightly different from the encoding session as it contains questions, and a virtual threat going into the virtual body). This would have affected mainly the measure of autonoetic consciousness that we also acquired in all healthy participants one week after the encoding session (a second manuscript about the sense of agency in autonoetic consciousness is submitted elsewhere) because it would have been impossible to discriminate whether participants were reliving the moment of encoding or the moment of BSC assessment, or would mix both. This is the reason why we finally decided to go for a fourth virtual scene that was different from the other three scenes but included the same manipulation of visuomotor and perspectival congruency to test BSC. This was done in an effort to minimize the potential confounds that could be raised due to the use of a similar environment for different sessions.

This has been clarified in the revised results section (page 8, lines 187-192).

Revised manuscript: "we used a different complex outdoor scene, to avoid any interference with the encoding of the three scenes used during encoding and recognition sessions (Fig. 1B). More specifically, we used a fourth scene for the BSC assessment to avoid that participants may have focused differently on the body (and therefore avoiding potential interference with the encoding process), and to minimize their awareness of the different experimental conditions concerning the bodily manipulations."

6. On the contrary, presenting different scenes with different objects in my opinion cannot rule out the possibility to have induced interference with those experienced during the experimental tasks (and this is especially true in the incidental memory task, when participants didn't know that they had to remember the object in the experimental scenes and not in the BSC scenes).

Reviewer 3 states that adding a fourth scene for the BSC assessment might have interfered in the encoding process, especially for Experiments 1 and 2, for which the instructions were incidental. We think that this is not the case in our task and detail the reasons below. We do agree with Reviewer 3, that presenting a fourth scene for BSC is another additional information and signals during encoding. While we cannot ensure that there was no interference with the encoding process in general, we carefully designed the BSC assessment with an outdoor scene to ensure it was different from the other indoor scenes, to avoid any confusion between scenes during the autonoetic consciousness task (performed a week after encoding). Critically, we note that in case that the fourth scene would have added interference in the encoding process, this interference should be similar across scenes (and therefore across conditions) so it cannot explain differences across conditions. Also, we did not retest the fourth scene during the retrieval phase of the experiment. Finally, one could argue that in real life, one also constantly encodes meaningless information along with meaningful information and thus our experimental paradigm is not so different than a life-like situation (which is one of the aims of this novel paradigm). Moreover, we reached a performance above chance level in the incidental encoding Experiment (Experiments 1 and 2) confirming that the task was feasible for healthy participants. This shows that participants were able to perform the task despite the addition of the fourth environment.

7. VR environment: as I saw in the videos, the objects were very small and far away from the observer, to me sometimes difficult to recognize. Did the authors check for the object correct visual recognition beside the memory task? I guess the performance could be strongly affected if the objects are not properly identified.

Reviewer 3 is concerned about the visual aspects of our virtual scene and objects, indicating that they may have been too small and too difficult to recognize, as shown on the figures and the video (provided as supplementary material). Reviewer 3 also asked whether participants were able to correctly recognize the different objects and how this may have affected memory performance. Several arguments allow us to exclude this possibility.

First, we state that it is difficult to represent in an image or a video, what is seen in an immersive VR headset. The field of view is larger in VR and stereoscopic rendering providing depth perception (important to identify some objects) is not depicted in a 2D image. Therefore, the objects appear indeed smaller in the screen captures (used for the figure). The same is true for the videos, in comparison to how the stimuli were seen in VR. Thus, all visual objects in the VR scenes that we developed were clearly and effortlessly seen and recognized by our participants. However, this was not tested formally as it would have interfered strongly with the encoding process and affected both our recognition task and autonoetic consciousness data. However, for every experiment (1,2,3 and 4) we always ensured that the view was clear and that the participants' view was not blurred while we were setting up the VR headset. This was checked at the very beginning of the experiment for each participant while fitting the headset by presenting a white cross on a gray background and asking them to adjust the virtual headset (for Experiments 1 and 3) and the lenses of the virtual google (for Experiment 2). This was checked again during the familiarization phase (by presenting the empty forest scene and asking them to report if anything was blurry). We note that our lab has extensive expertise in VR in cognitive neuroscience, having used many different VR technologies since 2007.

Even if the concern of Reviewer 3 about the performance being strongly affected by stimulus visibility would be correct, our participants were above chance level even during incidental encoding (67%), indicating that they were able to perform the task. To investigate whether one scene could have led to a decreased performance due to differences in object visibility, we compared the performance level of each scene (irrespective of conditions) under incidental encoding instruction (in Experiments 1 and 2). We found that participants had comparable recognition performance that was above chance level for all scenes ("Changing room" recognition performance: 70%, "Living room" recognition performance: 65%, "Cabin" recognition performance: 65%). This shows that the present task was feasible, despite different objects and scenes.

8. Considering the comment above, the experiment with incidental memory is affected by the set up itself: the participants were instructed only to move their hands and were surrounded by hardly recognizable objects that they did not know they had to remember. I would expect that the focus of their attention was allocated only to their virtual hands, so the memory recognition task basically assessed something that hadn't be properly encoded at all. Unfortunately, the fMRI study was conducted with this setup and not with the intentional encoding, whereby although the objects were the same, at least the participants had the opportunity to inspect them to try to remember. I agree that the incidental task is more similar to our everyday experience, but if my concern about the object correct identification is well-founded, then the results of the imaging study are more difficult to interpret.

Reviewer 3 indicates three points here (1) The fact that the focus of attention may have been directed towards the moving virtual upper limb, thereby interfering with the encoding of the objects; (2) a previous concern is repeated (that the objects may have been hardly recognizable; see our response above that this is not true); (3) these two concerns challenge the interpretation of our fMRI results.

Regarding the first point, the fact that the participants encoded the scene under incidental instruction showed indeed a bias towards a better recognition for the objects that were on the right. Under incidental encoding (Experiments 1 and 2), participants may have paid less attention to the scene and its objects and may have more likely focused on the avatar and its movements and less on the visual objects. This 'attentionon-the-avatar' interpretation is compatible with our finding of an effect of object laterality (better performance for right-sided objects vs left-sided objects), as reported in the original manuscript. This object laterality effect was only found for the experiments performed with incidental encoding (i.e., Experiments 1 and 2; note that participants in all three experiments only performed right hand movements). However, as stated in the original manuscript (page 11, lines 265-281), this laterality effect (in Experiments 1 and 2) was found irrespective of the three conditions and therefore, does not depend on our SoA manipulation. Thus, participants were better at recognizing scenes in which the changed object was on the right side, that is on the same side as the moving upper limb. This laterality effect was absent in Experiment 3. To summarize and as Reviewer 1 suggests, the association between avatar and scene (objects) seems more prominent under intentional encoding and could explain why the behavioral effect is observed under intentional encoding and not incidental encoding. Future work will have to investigate these interesting questions further. This point has now been added in a new section of the discussion in the revised manuscript (pages 25-26, lines 701-723).

Revised manuscript: "We note that we did not find a difference between conditions in recognition performance under incidental encoding instructions (Experiments 1 and 2). Although we did expect such a difference (as found in Experiment 3), we speculate that this may have resulted from different processes associated with the different instructions given at the beginning of Experiments 1-2 versus Experiment 3. Under incidental encoding, the participants were not instructed to pay particular attention to the scene and thus may have been more likely to focus on the avatar and its movements. This interpretation is supported by the fact that we found an effect of object laterality under incidental encoding (Experiments 1 and 2), but not under intentional encoding (Experiment 3). Thus, participants were better at recognizing scenes in which the change occurred on the right side (i.e., the same side where their avatar's limb was moving). However, as our participants were above chance level in all three experiments, the fact that the attention towards the avatar was most likely emphasized during incidental encoding did not prevent them from performing the task. Moreover, we observed a reduced SoA under visuomotor and perspectival incongruency across the three experiments. Hence, even if there may have been a different focus of attention between experiments performed under incidental versus intentional encoding, the SoA was manipulated in the same way in all three

experiments. Furthermore, as we observe differences of hippocampal reinstatement (Fig. 3D) between the conditions in our imaging results in Experiment 2 we assume that these differences are due to our experimental SoA manipulation at encoding, but that the incidental instruction gave rise to smaller difference of performance which may explain the absence of behavioral effect in the present study. Future studies should further test differences in episodic memory, depending on SoA and incidental versus intentional encoding."

Concerning the interpretation of our fMRI results, we found that hippocampal reinstatement was stronger for successful trials (Fig. 3D), and linked hippocampal reinstatement with memory performance (Fig. 4A). Importantly, the association between hippocampal reinstatement and memory performance has been reported in several studies (Danker et al., 2017; Tompary et al., 2016), supporting the interpretation that hippocampal reinstatement is a marker of the memory process. Finally, the trial-by-trial analysis showed that the correct recognition of the original scene could be explained by hippocampal reinstatement when scenes were encoded under preserved visuomotor and perspectival congruency. This result is important, as it shows that the neural mechanism linking bodily self-consciousness with episodic memory is mainly emphasized when the original scene is correctly identified. To sum up, we believe that if the objects were hardly recognizable as stated by Reviewer 3, or if t too much attention would have been directed at the avatar, our participants would not have been able to perform the present task and would have not reached above chance memory performance, and would not be associated with the present fMRI results.

9. The sample size calculation is not reported: did the authors run an a priori sample size calculation?

We based our sample size on previous studies published with a similar experimental design and expected comparable effect sizes (Bréchet et al., 2020, 2019; Gauthier et al., 2020; Iriye and Ehrsson, 2022). These studies recruited between 16 and 33 participants. Moreover, for the condition-scene matching randomized across participants, we needed at least 24 to be sure to match the lower bound of the sample size if any participants had to be removed.

We have added the following sentence in the method section of the revised manuscript (page 31, lines 935-940):

Revised manuscript: "We based our sample size on previous studies published with a similar experimental design, or similar research question (Bréchet et al., 2020, 2019; Gauthier et al., 2020; Iriye and Ehrsson, 2022). These studies recruited between 16 and 33 participants. We aimed to recruit 24 participants in each study to ensure that we would have four participants encoding the scene with a similar scene-condition association. For the fMRI study, we recruited 5

more participants, in case we had to exclude participants based on motion or other imaging artefact."

10. Study design: it is unexpected to me the use of 3 experimental conditions instead of 4. As I understood, the authors crossed two variables, motor syncronicity and visual perspective, but then one of the four combinations is missing (i.e. SYCRONY3PP). Can the authors justify this choice? The issue arise also from the analyses, where the lack of the fourth condition prevents from fitting a full 2x2 model which would have allowed to detect the main effects of perspective and syncronicity plus their interaction.

We agree with Reviewer 3 that adding a fourth condition (SYNCH3PP) would have allowed to additionally disentangle between effects of synchrony and perspective in our study. However, our main limiting constraint was the experiment time, because the current experiment was already quite long with the present three experimental conditions (i.e., 2.5 hours without counting the break). Adding a fourth scene for the encoding session would have not only increased the tiredness of the participants but also the task difficulty (as each new scene added in the recognition task corresponds to 45 more trials and a heavier memory load), especially given the fMRI acquisition. To save time, and avoid increasing the task difficulty, we opted for the creation of a gradient, in which SYNCH1PP would be the condition where bodily self-consciousness was not manipulated, ASYNCH1PP was the condition with bodily self-consciousness manipulation while ASYNCH3PP was strongly manipulating bodily self-consciousness. This gradient induction was sufficient to answer our main research question (what are the neural mechanisms associating bodily self-consciousness, as manipulated by visuomotor and perspectival congruency with episodic memory?). We could thus compare SYNCH1PP (the preserved bodily self-consciousness condition) with ASYNCH1PP and ASYNCH3PP (the disrupted bodily self-consciousness conditions), using a linear mixed model. We believe that this was sufficient to answer our main research question, while minimizing the level of tiredness of participants and the task difficulty.

We agree that a 2x2 design would have allowed us to investigate further questions such as those concerning differential contributions of visuomotor synchrony versus perspective in the neural mechanisms associating bodily self-consciousness and episodic memory. While we acknowledge that this is a very interesting and valid question, we explained in the discussion in the limitations section (page 27, lines 768-774), that this was not our main aim.

11. In study 4, the authors tested the patient 1 week after the VR experience, in analogy with the protocol with healthy participants. If this is correct to guarantee a comparable paradigm, I am wondering how reliable the answers of a patient suffering from a severe amnesia could be, if tested after such a long delay. The authors stated that she was able to remember the scenes under consideration, but still this is a qualitative report not supported by objective data.

First, we like to state that we tested the patient one hour after the encoding session in the recognition task, similarly to the healthy participants. Additionally, we tested the patient's autonoetic consciousness one week after the encoding session (as indicated by Reviewer 3), again similar to the study in healthy participants (but not reported in the present manuscript). The recognition task allowed us to obtain objective behavioral

data from the patient. Importantly, her performance was above chance level in the three conditions (58% in SYNCH1PP, 73% in ASYNCH1PP and 66% in ASYNCH3PP). We agree with Reviewer 3 that the data collected for autonoetic consciousness are subjective (equally for both healthy participants and the patient). Of course, when we tested the patient, we did not know whether and what she would be able to remember. For the present paper, we found it important to also report the autonoetic consciousness results of the patient (subjective rating data), as it was part of our experimental protocol. Although the patient was able to remember the scene encoded under strong visuomotor and perspectival mismatch (ASYNCH3PP), the ratings of the patient are very low, as expected for an amnesic patient. However, she could at least remember weakly only the ASYNCH3PP scene, while she could not at all remember the scenes encoded with preserved visuomotor and perspectival congruency. Hence these results, although subjective, go in the same direction than her objective behavioral data in the recognition task (and are opposite to those observed in healthy participants. We felt it was important to add these patient data.

We are currently continuing testing the patient with different experimental paradigms on memory performance and also autonoetic consciousness. In these new experiments, using different VR paradigms we have been able to confirm the reported dissociation between conditions with preserved and altered visuomotor and perspectival congruency.

Some minor-changes suggestions will follow:

12. The abstract could be improved as currently doesn't mirror the complexity and richness of the studies (again, some methodological information should be added here to give the reader a first glance of the research)

We have revised the abstract as follows (page 2)

Revised manuscript: "Episodic memory (EM) allows us to remember and relive past events and experiences <u>and has been linked</u> to cortical-hippocampal reinstatement <u>of encoding activity</u>. <u>While EM is</u> fundamental to establish a sense of self across time, <u>this claim and its link to the sense of agency (SoA)</u>, <u>based on</u> <u>bodily signals, has not been tested experimentally</u>. <u>Using real-time sensorimotor</u> <u>stimulation, immersive virtual reality, and fMRI we manipulated the SoA</u> and report stronger hippocampal reinstatement for scenes encoded under preserved <u>SoA</u>, reflecting recall performance <u>in a recognition task</u>. We link <u>SoA</u> to EM showing that hippocampal reinstatement is coupled with reinstatement in premotor cortex, a key <u>SoA</u> region. We extend these findings ina severe amnesic patient whose memory lacked the normal dependency on <u>the SoA</u>. Premotor-hippocampal coupling in EM describes how <u>a key aspect of the bodily</u> self at encoding is neurally reinstated during the retrieval of past episodes, enabling a sense of self across time."

13. Line 94: what is the number (61) referred to? We corrected it, it was a referencing issue

14. Lines 833-836: there are parentheses apparently not closed We corrected it as follows (page 31, lines 915-920)

Revised manuscript: "including questions from the "Memory characteristic questionnaire" (19 questions, Johnson et al., 1988), part B of the "Episodic autobiographic memory interview" (EAMI; 8 questions, Irish et al., 2011), two questions from the "affected limb intentional feeling questionnaire" (ALFq, Crema et al., 2022) and one additional question related to our research question ("I remember the movement and gesture I was doing with my body during the event", ordinal scale, See Table <u>S21</u> for a list of all the questions)."

15. Line 842: what do the authors mean for "for each condition"?

As each scene was encoded under one specific condition, measuring autonoetic consciousness for each scene enabled us to measure autonoetic consciousness associated with the different conditions (i.e., the visuomotor and perspectival manipulation applied at encoding: SYNCH1PP, ASYNCH1PP and ASYNCH3PP).

We are updating the text as follows to make that explanation clearer in the text (page 31, line 913)

Revised manuscript: "We also tested the patient and the healthy participants' autonoetic consciousness for each condition <u>(and therefore each scene encoded)</u>, at one week after the encoding."

16. For the patient study, a table summarizing the neuropsychological tests and related scores could be helpful to support authors' statements about the patient's cognitive profile

A table summarizing the different neuropsychological score of the patient assessed by the neuropsychologist during her stay at the hospital is now added as Supplementary Table S19. We refer to the table in the text, page 17, lines 425-426.

Revised manuscript (page 17, lines 421-426): "Repeated neuropsychological examinations revealed a severe EM deficit affecting retrograde events (early childhood to adulthood without temporal gradient) and a moderate anterograde EM deficit. Learning for verbal memory was normal, but deficient for delayed recall (normal after indication). Visuo-spatial memory was at the inferior limit of the norm. There was a mild-to-moderate semantic memory deficit (i.e., public events and celebrities; <u>See</u> Table S19 for a summary of the performance on the neuropsychological tests)."

Test	Raw scores	VIN	IN	SIN	Ν	SSN	SN	VSN
Orientation								
Orientation	Oriented in 4				Х			
Questionnaire	modes : 18/29							
(Von Cramon	Temporal							
& Säring,	orientation : 5/5,							
1982)	spatiale : 5/5,							
	personal : 4/5,							
	situation : 4/5							
Mnesic								
function								

Short-term memory Empan verbal WAIS-IV (Welcher, 2011) Empan	4			Х				
visuospatial Corsi (CHUV, 1985)	5				Х			
Rivermead	Name: 4				Х			
Behavioural	Personal				Х			
Memory Test	objects : 8							
(Wilson et al.,	Delayed images:			Х				
2008)	13 Delayed history:				v			
	Delayed history: 5				Х			
	Orientation and							
	date : 9	Х						
TEMPau	0-17 y.o. global	Х						
(Piolino et al.,	score: 3,	Х						
2008)	episodic score 1	Х						
	18-30 y.o. global	Х						
	score: 6,	V						
	episodic score 2	Х						
	>30 y.o. global							
	score: 6,							
	episodic score 2							
	Last 5 years							
	global score: 5,							
	episodic score 2							
	Last 12 months							
	global score: 2,							
	episodic score 1	V						
EVE-10 Batteries	Public events : 38% correct	Х						
(Thomas-								
Antérion et	Famous people :		Х					
al., 2006)	54% correct							
Screening	No provoqued				Х			
confabulation	confabulation							
Modified	32/32				Х			
Camel and								
Cactus test								
Table S19.								
Neuropsychological tests performed in amnesia patient.								

Summary of the main tests performed three months prior to Experiment 4. VIN = very inferior to the norm, IN = inferior to the norm, N = norm, SIN = Slightly inferior to the norm, SSN = Slightly superior to the norm, SN = superior to the norm, VSN = very superior to the norm. y.o. = years old.

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REVIEWERS' COMMENTS:

Reviewer #1 (Remarks to the Author):

The authors have appropriately revised and clarified their manuscript, I have no further comments.

Reviewer #2 (Remarks to the Author):

The authors have done a thorough job on the revisions. I am now happy to recommend acceptance.

Reviewer #3 (Remarks to the Author):

The authors have satisfactorily answered to all my comments