Autobiographical Memory: Is the Role of the Hippocampus Time-Limited?

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ABSTRACT

The increasing prevalence of Alzheimer's and Parkinson's disease with age has accelerated research characterizing the pathology underlying these diseases. Memory deficits, particularly for episodic memory, contribute to the decline in the quality of life experienced by affected individuals as they fail to remember past experiences that bring them joy. Episodic memory includes recollections of events in one's past. When these recollections pertain to one's personal history, they are described as autobiographical memories (AMs). Understanding the pathology behind declining AM recollection can prove vital in designing pharmaceutical therapies and surgical guidelines to preserve an individual's ability to remember their personal history. Given the significance of maintaining retrieval abilities for autobiographical memories, it is important to explore the nature of hippocampal contribution to this process. Therefore, this review will assess the results from two studies assessing human AM retrieval abilities with respect to hippocampal volumes to determine whether the hippocampus is involved in the retrieval of remote autobiographical memories.

(Keywords: neurological disorders, memory deficits, episodic memory, autobiographical memory, hippocampal function)

INTRODUCTION

Global concern regarding population aging has emphasized the need to maintain and improve the quality of life as individuals age. Notably, the increasing prevalence of Alzheimer's and Parkinson's disease with age has accelerated research characterizing the pathology underlying these diseases (GBD, 2015; Neurological Disorders Collaborator Group, 2017; Lobo, *et al*., 2000).

Most neurodegenerative diseases are associated with cognitive impairments (Alzheimer's Association, 2013; Goldstein and Abrahams, 2013; Svenningsson, *et al*., 2012; Walker, 2007). Memory deficits, particularly for episodic memory, contribute to the decline in the quality of life experienced by affected individuals as they fail to remember past experiences that bring them joy. Episodic memory includes recollections of events in one's past. When these recollections pertain to one's personal history, they are described as autobiographical memories (AMs). Understanding the pathology behind declining AM recollection can prove vital in designing pharmaceutical therapies and surgical guidelines to preserve an individual's ability to remember their personal history. Interestingly, the nature of hippocampal contribution in remote AM recall has been heavily debated over the last several decades.

From one standpoint, clinicians have noticed a pattern of hippocampal contribution in remote memory recall that is time-dependent. Precisely, following hippocampal damage, recently acquired memories are lost, while more distant remote memories are spared. This finding has been reported in human neuropsychology studies and lesion experiments in animal models (Broadbent, *et al*., 2010; Scoville and Milner, 1957; Zola-Mrgan and Squire, 1990). The standard model of consolidation (SMC) accounts for these findings and asserts that consolidation results in the migration of retrieval routes from the hippocampus to the neocortex such that, over time, the hippocampus is not required for successful retrieval of a given event (Squire and Alvarex, 1995).

Contrasting the SMC, other studies have suggested the hippocampus does not contribute to memory retrieval as a function of time but instead encodes all information that is attended and binds the neocortical neurons that represent that experience into a trace (Nadel and Moscovitch, 1997). This perspective has been classified as the Multiple Trace Theory (MTT). Accordingly, a memory trace of an episode consists of a bound ensemble of neocortical and medial temporal lobe neurons which represents a memory of the consciously experienced event.

Given the significance of maintaining retrieval abilities for autobiographical memories, it is important to explore the nature of hippocampal contribution to this process. Therefore, this review will assess the results from two studies assessing human AM retrieval abilities with respect to hippocampal volumes to determine whether the hippocampus is involved in the retrieval of remote autobiographical memories.

The Relationship Between Hippocampal Subfield Volumes and Autobiographical Memory Persistence

Barry, *et al.* (2021) conducted a longitudinal study to investigate the relationship between the volume of specific hippocampal subregions and the degree of remote AM persistence. Per previous literature, they hypothesized the dentate gyrus and/or CA3 hippocampal volume is related to the preservation of event details over an extended period. Moreover, they believed the amount of AM internal details produced after a considerable delay relates to the volume of the pre/para-subiculum, and previous positive associations found between the subiculum volume and AM may be driven by the pre/para-subiculum.

Study Design: Sixteen right-handed individuals (14 female) selected three photographs corresponding to eight distinct time points (2 weeks, 4 months, 8 months, 12 months, 16 months, 20 months, 24 months, and 5 years) in their past relative to the time of taking part in this study (Barry, *et al.*, 2021). On two separate visits 8 months apart, the participants described, in as much detail as possible, the specific AM elicited by their chosen photograph.

The experimenters scored the memories according to the Autobiographical Interview procedure. Details provided for each memory were scored as either “internal” (episodic) or “external” (semantic). Internal details were composed of five subcategories: event details referred to happenings, specific individuals present, weather conditions, actions that were physical or emotional, or reactions elicited in others.

External details consisted of any references to details from events other than the one being recalled, general knowledge or facts, events that were ongoing rather than specific to a particular time, or an extended state of being. Using a manual segmentation protocol, Barry, *et al.* (2021) performed partial correlations between the subregion volumes and the ratio of internal details produced from Visit 1 to Visit 2, with age, gender, and total hippocampal volume. They specifically analyzed the following regions: the dentate gyrus/CA4, CA3/2, CA1, subiculum, pre/para-subiculum, and uncus.

Study Results: By the second visit, Barry, *et al*. (2021) reported the participants produced significantly fewer details about subjective thoughts and emotional states compared to their first visit. A significant positive correlation was found between the volume of the left pre/para-subiculum and the amount of internal detail produced, as illustrated by Figure 1. Further analysis of the subcategories of internal memory details reveals a significant positive correlation with specific event details over time, perceptual observations, and thoughts and emotions.

Study Assessment: Overall, Barry, *et al.* (2021) identified a positive relationship for facets of the autobiographical memories benefitting from a greater volume of the left pre/para-subiculum. They concluded their findings to expand existing functional evidence highlighting a link between the left pre/para-subiculum and AM recall. It is important to note the results Barry, *et al*. (2021) obtained are based on correlation analysis, hence causality cannot be concluded.

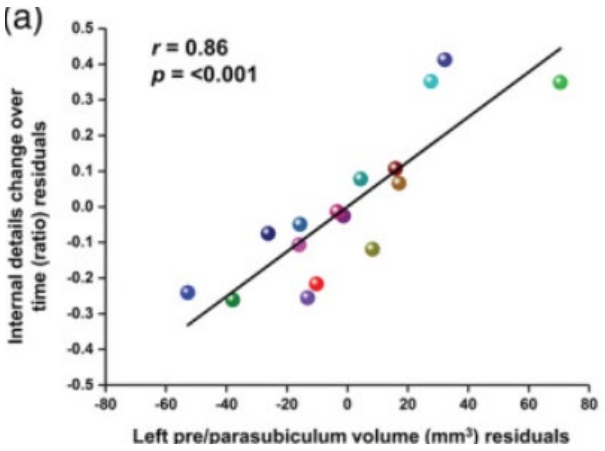

Figure 1: The Correlation between the Residuals of the Change in Memory details over time and the Residuals of the Pre/Para-subiculum Volume after Controlling for Age, Gender, and Total Hippocampal Volume, and are centered around zero (Barry, *et al.,* 2021).

Specifically, Barry, *et al*. (2021) do not prove the decrease in detail recall for autobiographical memories is caused by decreased volume in the left pre/para-subiculum. The positive correlation they identified could be caused by a third variable including reductions in neocortical areas that were not controlled for in their analysis (Chiang, *et al*., 2015).

This correlation Barry, *et al.* (2021) identified can be further investigated through lesion studies in animal models. Neurotoxin-induced ablation or optogenetic inhibition of the left pre/para-subiculum can be done to assess whether recall of episodic memories is affected in contextual "episodic-like" memory tasks (Celerier, *et al*., 2004; Dere, *et al*., 2003; Dere, *et al*., 2007). However, the assessment of episodic memory in animal models, particularly mice, poses limitations when generalizing to humans. Notably, the neural network between mice and humans differ greatly (Hodge, *et al*., 2019).

Moreover, human episodic memory assessments typically use memories formed from childhood or many years before the experiment. Mice model tasks do not account for this extended period of consolidation and do not accurately reflect human episodic memory processing (Celerier, *et al*., 2004; Dere, *et al*., 2003; Dere, *et al*., 2007).

Secondly, of the 16 participants recruited in this study, 14 were females. Various studies have identified sex differences in episodic memory tasks, however, whether these differences arise specifically in the retrieval process for AM remains inconclusive (Pauls, *et al*., 2013; Young, *et al*., 2017). Moreover, previous literature has reported extensive sex differences in hippocampus anatomy and synaptic plasticity which are both facets of AM processing (Gall, *et al*., 2021; van Eijk, *et al*., 2020).

Despite these limitations, Barry, *et al.* (2021) provide meaningful functional data contradicting the SMC. The positive correlation between the left pre/para-subiculum volume and the amount of detail recalled in autobiographical memories illustrates the continuous involvement of the hippocampus in remote episodic memory.

The Neuroanatomy of Remote Memory

Bayley, *et al.* (2005) conducted a volumetric analysis of patients with medial temporal lobe (MTL) damage, extensive MTL damage, and MTL plus neocortical damage (MTL+ group) to assess the recall abilities of remote autobiographical memories concerning these damaged areas.

Lesion Assessment: Using magnetic resonance imaging (MRI), Bayley, *et al*. (2005) distinguished their participants into 4 groups. The MTL damage group consisted of 3 patients (R.S., G.W., and J.R.W.) with substantial hippocampal volume reductions. Other regions of the brain were preserved, except for patient R.S. who exhibited abnormally small parietal lobes. The extensive MTL damage group included 2 patients (E.P. and G.P) with reduced volumes in the hippocampus, para-hippocampal gyrus, fusiform gyrus, and the insular cortex. Three patients (H.C., P. H., and G. T.) were assigned to the MTL+ group as they had reduced volumes in medial temporal lobe structures and additional reductions in one or more of the major lobes.

Autobiographical Memory Assessment: With the patients described and 26 healthy controls who were matched according to age and education, Bayley, *et al.* (2005) collected autobiographical memories using a modified version of the Crovitz test of autobiographical memory. Participants were asked to recollect an AM that involves a given stimulus word (e.g.,

bottle or river) from the first third of their life before the onset of their amnesia. Narratives were recorded and scored.

For an episodic memory referring to a specific time and place, three points were awarded. Two points were given for memories with some specificity but were not specific to one time and place (i.e., they did not recall a specific event). For a vague reference to memories without any reference to time or place, one point was awarded. Zero points were given for a generic response or no response. Furthermore, the participants underwent the AM Interview (AMI).

This standardized test quantifies the recall of autobiographical incidents and personal facts from childhood (until age 18) and two later periods. Following published procedures, participants were asked to recall three unique events from childhood (autobiographical memory) along with 12 facts about their childhood (personal semantic memory). Results were compared to findings for 13 controls.

Interestingly, the MTL group and their controls scored a maximum of three points (provided unique autobiographical memories) in response to most of the 24 cue words (MTL patients, 21.6 memories; controls, 22.9 memories). The MTL+ group, however, was significantly impaired at recalling autobiographical memories and received one point for most of their memories in response to the cue words. In other words, they were able to recall some general information without reference to a specific time or place. Secondly, Bayley, *et al.* (2005) reported the MTL+ group performed significantly worse in recalling autobiographical memories and personal semantic memory in the AMI.

Study Assessment: Bayley, *et al.* (2005) went on to conclude that the ability to retrieve remote memories depends on neocortical regions. However, they neglected the variation seen across the scores assessing memory for autobiographical events in the MTL+ group. In Figure 2, H.C. performed significantly better in recalling autobiographical incidents from childhood compared to G.T. and P.H. This finding becomes interesting when cross-referenced with the specific volume reduction seen in these patients.

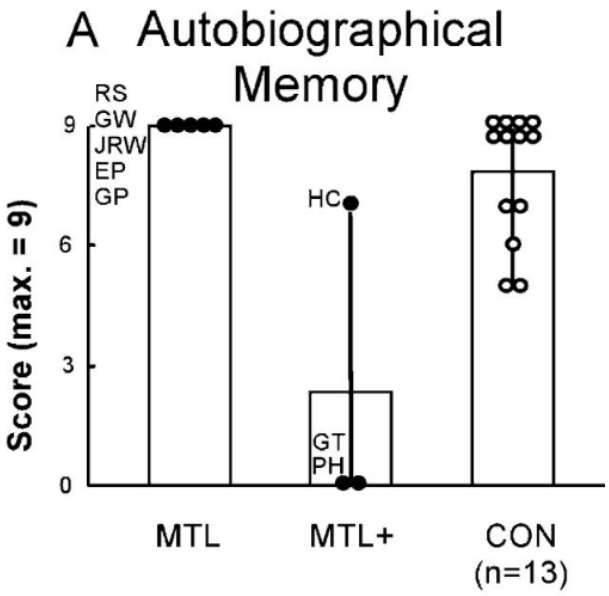

Figure 2: Scores on Items that Assessed Memory for Autobiographical Events (Bayley, *et al.,* 2005)

H.C. has bilateral volume reductions of the frontal, parietal, and occipital lobes, but only a 7% and 12% volume reduction of the left and right hippocampus, respectively. G.T. has reduced volume of the lateral temporal lobes, along with 89% and 67% volume reduction of the left and right hippocampus, respectively.

Patient P.H. exhibited volume reductions of 54% in the left and 34% of the right hippocampus, along with the reduced volume of the left frontal lobe.

Although H.C. reported the greatest extent of neocortical volume reductions, H.C. is still able to recall internal details to a substantially higher degree than P.H. and G.T. This discrepancy may hint toward a more dynamic role of the hippocampus and neocortex in AM recall that has been reported by previous studies as well (Goshen, *et al.*, 2011; Hogeveen, *et al*., 2020).

Precisely, the hippocampus and neocortex both maintain a memory trace and play a role in AM recall; however, upon damage to either region, the undamaged region may be able to compensate for the damaged region by using its respective memory trace. This phenomenon can explain why the MTL group was able to retrieve autobiographical memories amidst hippocampal

volume reductions. For patients P.H and G.T in the MTL+ group, their extensive damage to both the hippocampus and neocortex could have affected memory traces in both regions thereby explaining their poor recall of autobiographical memories.

Lastly, H.C. may have been able to recall autobiographical memories to a high degree as the hippocampus, with limited reduced volume, maintained its memory traces and compensated for the damages across the neocortex.

DISCUSSION AND CONCLUSION

Taken together, the results of Barry, *et al.* (2021) and Bayley, *et al.* (2005) provide evidence supporting the MTT and constant contribution of the hippocampus to AM recall. In the first study, Barry, *et al.* (2021) identified a significant positive correlation between the volume of the left pre/para-subiculum and the amount of internal detail produced in AM recall. Although this relationship was not proved to be causal, it supports previous findings in the literature that have also illustrated a similar relationship.

Secondly, Bayley, *et al.* (2005) reported participants with hippocampal and neocortical volume reductions demonstrated a poor ability to recall autobiographical memories. The case of H.C., who performed well in AM recall, hints at the hippocampus and neocortex engaging in a dynamic role to recall autobiographical memory. Specifically, the hippocampus and neocortex both maintain a memory trace for AMs; however, damage to either region leads to a compensatory mechanism whereby the undamaged region supports the recall of the targeted AM. Assessing this compensatory mechanism is crucial for understanding pathologies. For instance, global activity measures through fMRI where elevated correlates of activity in a specific brain region may not represent a pathology but rather compensatory recruitment supporting the underperforming process of a defected brain region.

In conclusion, this review provides support for further research to continue investigating the mechanism behind the hippocampal contribution to AM recall regardless of how old the memory is. To further establish whether hippocampal contribution to AM recall is time-dependent, future studies should focus on collecting data regarding the ability of individuals with neocortical brain abnormalities to recall remote memories. If individuals with neocortical deficiencies but healthy hippocampal regions can recall autobiographical memories with a high degree of detail, this would provide further evidence supporting the contribution of the hippocampus to episodic memory regardless of how remote the memory is.

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APPENDIX

The Relationship Between Hippocampal Subfield Volumes and Autobiographical Memory Persistence (Barry, *et al*., 2021): This study was obtained through PubMed using the search term “hippocampus and autobiographical memory recall”.

The Neuroanatomy of Remote Memory (Bayley, *et al*., 2005): This study was obtained through the

introduction of a study titled “Human hippocampal CA3 damage disrupts both recent and remote episodic memories” by Thomas D. Miller and colleagues. The Miller, *et al.* (2020) study was obtained through a PubMed search using the search term “Human hippocampal damage and episodic memory”.

SUGGESTED CITATION

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