What is the role of the hippocampus in remote autobiographical memory recall?

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Contents

1. Abbreviations

AM	Autobiographical memory
fMRI	Functional magnetic resonance imaging
FT	Future thinking
MTL	Medial temporal-lobe
MTT	Multiple trace theory
SCT	Standard consolidation theory

2. Introduction

In 1957, Scoville and Milner carried out memory tests on patients with bilateral medial temporal-lobe (MTL) resections. They discovered that whenever bilateral hippocampal damage occurred, memory deficits followed. If the resection spared the hippocampus, the patient was free from memory deficits. From this they concluded that the hippocampus is important for normal memory function. Remote autobiographical memories (AMs) are explicit distant memories of information and experiences relating to oneself. This essay will investigate the role of the hippocampus in remote AM recall, outlining theories that paved the way to our current understanding.

3. Methods

A broad search was carried out on PubMed in March 2020 using a combination of the terms: autobiographical, episodic, memory, recall, retriev*, hippocamp*, medial temporal lobe, amnesia, loss, impair* (Fig 1.).

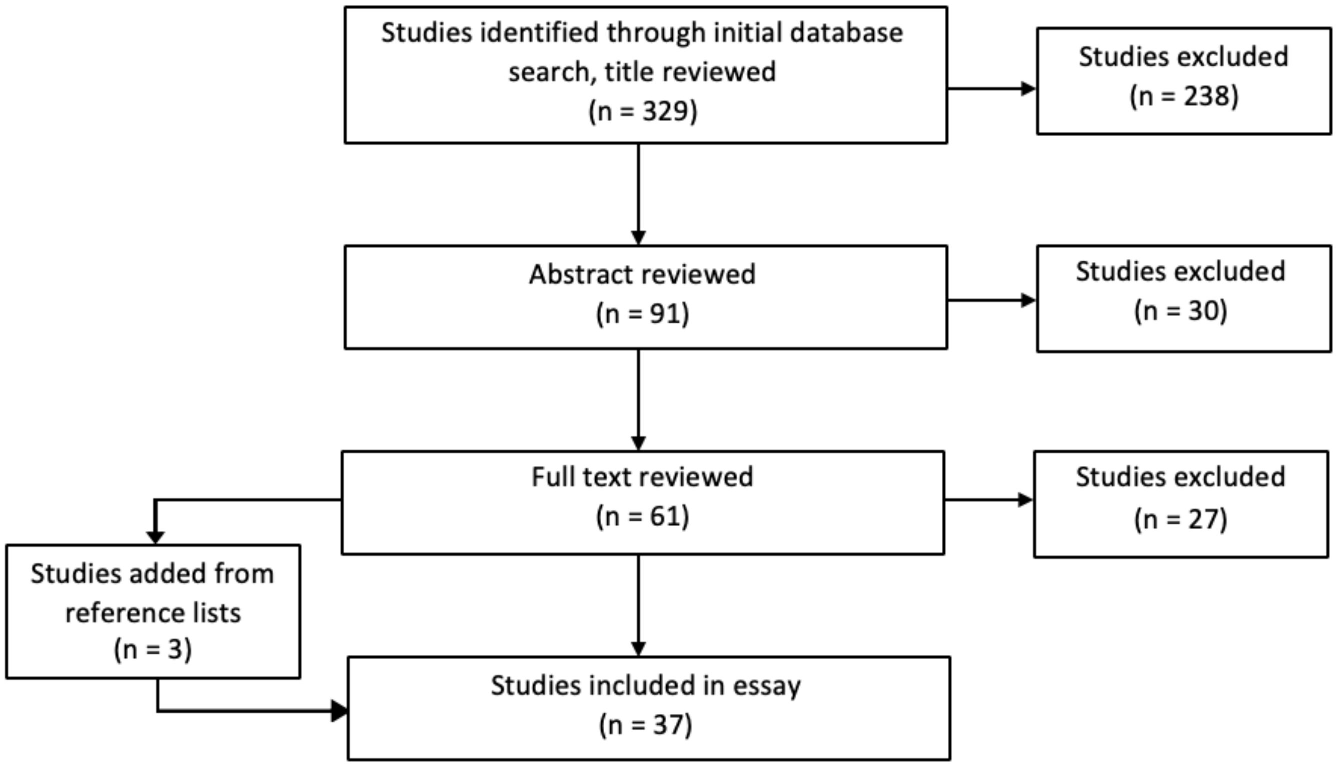

Figure 1. Flow diagram of literature selection process
Studies were included if they contained information on the role of the hippocampus in memory recall of healthy individuals, or the consequences of medial temporal lobe damage. Studies were excluded if their methods were poor, or if they were not available in English. References of selected papers were analysed to identify key studies not obtained from the initial searches.

3. Standard consolidation theory

Clues to the function of the hippocampus in memory recall should come from observing the consequences of hippocampal dysfunction. MTL damage can produce a graded retrograde-amnesia (Rempel-Clower *et al.,* 1996; Reed and Squire, 1998; Bayley *et al.,* 2003), whereby recent memories are more vulnerable to loss than distant memories. For example, Bayley *et al.* asked patients with hippocampal amnesia and healthy controls to recall events from the first third of their life. The recollected memories were scored by how well they described the event. There was no difference between the patients and controls. However, this alone is not sufficient to say remote memory is unaffected. Perhaps hippocampal damage causes details to be lost from memories. To address this, Bayley *et al.* compared the number of details per autobiographical narrative and found this too was the same between patients and controls. Additionally, participants were made to reproduce elements of their narratives after a median 14-month delay. Eighty-eight percent of patient recollections were confirmed, demonstrating high validity of recollections. The observation that patients with MTL damage can recall distant AMs with the same level of detail as those with intact MTLs implies that the hippocampus is not important for remote AM recall. Such evidence supports the standard consolidation theory (SCT; McClelland *et al.,* 1995; Squire and Alvarez, 1995). This model proposes that upon learning, information is initially stored across hippocampal and neocortical modules. Over time, the hippocampus mediates a reorganisation of the memory trace such that neocortical modules are strongly bound together, and this neocortical representation becomes independent of the hippocampus. Such a theory explains the preservation of remote memories: as memories are consolidated, they become resistant to loss by hippocampal damage as the hippocampus becomes progressively less involved in representing them. However, not all patients have preserved remote memories.

4. Multiple trace theory

A number of patients with hippocampal damage suffer from loss of remote memories (Sanders and Warrington, 1971; Viskontas *et al.,* 2000; Cipolotti *et al.,* 2001). For example, Viskontas *et al.* compared AM recall of 25 MTL damage patients with 22 age- and education-matched controls. They observed impaired recall of childhood episodic memories in patients compared to controls. This is in direct contrast to what the SCT would predict. However, all patients had temporal lobe epilepsy, and the mean age of seizure onset was 10.9 years. A proponent of the SCT could argue that childhood seizures may have disrupted the hippocampal childhood memory traces before they were consolidated in the cortex, or interfered with the consolidation process, as opposed to disrupting a hippocampal remote memory trace. Indeed, there is evidence for epilepsy disrupting memory consolidation (Martin *et al.,* 1991; Kapur *et al.,* 1997; Blake *et al.,* 2000). However, Viskontas *et al.* show that remote semantic memories of patients are intact, suggesting that seizures did not interfere with the general process of memory consolidation. These studies implicate the hippocampus as being crucial for remote AM recall, supporting the multiple trace theory (MTT; Nadel and Moscovitch, 1997). The MTT states that memory traces are initially stored across hippocampal and neocortical modules and that re-activations of the memory trace lead to the accumulative formation of new hippocampal traces. In this model, the hippocampus is always required for AM storage and retrieval.

5. Evidence from functional imaging studies

The conflicting evidence in patients with MTL damage highlights the need to study healthy individuals. Functional imaging in healthy patients can identify whether the hippocampus is active during remote AM recall. Such studies have identified that the hippocampus is active during both remote and recent AM recall (Conway *et al.,* 1999; Ryan *et al.,* 2001; Gilboa *et al.,* 2004). It's important to note that in some cases the MTL was more active during recent than remote memory recall (Niki and Luo, 2002), which at first implies the hippocampus is less important for recalling remote memories. However, remote and recent memories have different phenomenological characteristics. For example, recent memories tend to be more vivid, detailed and emotional than remote memories (Johnson *et al.,* 1988). It is possible that these phenomenological differences could account for the differences in hippocampal activity. Furthermore, the above studies were all cross-sectional. Therefore, differences in hippocampal activation could be due to different phenomenological features of the different memories, as opposed to differences in memory age. To resolve this, longitudinal studies comparing hippocampal activity during recall of the same memory across time can be used. A further limitation of these studies is that, apart from Gilboa *et al.*, they treat the hippocampus as one unit. In reality, the hippocampus can be divided into a number of subdomains and different subdomains may be involved differently in memory recall (van Strien *et al.,* 2009). Bonnici *et al.* (2012; 2018) overcame both these limitations. They measured hippocampal functional magnetic resonance imaging (fMRI) activity during recall of a recent (2 week) and a remote (10 year) memory, and then again for the same memories two years later. Additionally, activity along the hippocampal longitudinal axis was segmented into an anterior and posterior portion. They found that the hippocampus as a whole was equally involved in the recall of recent and remote memories. However, the posterior hippocampus better represented remote compared to recent memories (10 year vs 2 week), with no difference when both memories were remote (2 year vs 12 year). These findings show that the hippocampus, particularly the posterior domain, is important for remote autobiographical memory recall. However, this anterior-posterior separation is still an oversimplification. In reality, the hippocampus likely contains multiple graded domains (Strange *et al.,* 2014).

6. Beyond memory

The dentate gyrus (DG) contains over a third of human hippocampal neurons. These DG neurons constantly renew, and an 80-year-old human has DG neurons with an average age of ~40 years (Spalding *et al.,* 2013). Memories are encoded within the connections between neurons, and a loss of these connections should lead to a loss of memories. However, 80-year-old humans can have memories far preceding the age of 40, suggesting the hippocampus is not storing memories. The hippocampus participates in many cognitive functions beside memory recall and commonalities between these functions could highlight the role of the hippocampus. AM recall, future thinking (FT; Addis *et al.,* 2007) and atemporal scene imagination (Hassabis *et al.,* 2007a) activate an extensively overlapping set of brain regions, including the hippocampus. Furthermore, damage to the hippocampus impairs the ability to imagine future scenarios (Rosenbaum *et al.,* 2005; Andelman *et al.,* 2010) and atemporal scenes (Hassabis *et al.,* 2007b). It is important to note that patient K.C., the focus of the Rosenbaum *et al.* study, had extensive multifocal damage beyond the MTL. His deficits can therefore not be attributed solely to hippocampal disruption. The hippocampus is also involved in spatial navigation (Moser *et al.,* 2008; Miller *et al.,* 2018), and hippocampal damage can impair complex navigation. For example, Maguire *et al.* (2006) found that a taxi driver, T.T., with bilateral hippocampal damage could not navigate large-scale complex spaces. T.T. had very focal bilateral hippocampal damage, giving confidence that the observed deficits were solely due to hippocampal loss-of-function. However, this is just a single case study, hence the generalisability is limited. Therefore, AM, FT, imagination, and spatial navigation all utilise the hippocampus.

7. Scene construction theory

Scene construction is common to AM, FT, imagination, and spatial navigation, which led to the scene construction theory of hippocampal function (Hassabis and Maguire, 2007; Maguire and Mullally, 2013). This theory proposes that the primary role of the hippocampus is in constructing spatially coherent scenes. Indeed, Clark *et al.* (2019) show that performance on scene construction, AM, FT, and spatial navigation tasks is related, and that this relationship is mediated by scene construction. In this paradigm, the role of the hippocampus in AM recall is the reconstruction of neocortical memory traces into a coherent visual scene. The neocortical modules are then consolidated and persist in the neocortex, while the reconstructed scene exists only transiently in the hippocampus. Each time the memory is recalled, the hippocampus again reconstructs a coherent visual scene from the neocortical trace. Therefore, memory impairments due to hippocampal damage are the result of an inability to reconstruct neocortical traces into a scene, as opposed to disruption of the memories themselves. This theory is strengthened by the observations it explains. For example, the accuracy of recalled memories decreases overtime (Anderson *et al.,* 2000), while the level of detail is unchanged (Campbell *et al.*, 2011). In the scene reconstruction paradigm, neocortical elements absent from the original memory trace could be erroneously incorporated into the reconstructed visual scene, and then consolidated with the original memory trace in the neocortex (Barry and Maguire, 2019). Remote memories are likely to have undergone more reconstructions than recent memories, and hence would be more prone to accumulating errors.

8. Conclusion

In summary, the most convincing role for the hippocampus in remote AM recall is that of scene reconstruction: the hippocampus uses neocortical memory traces to reconstruct a visual scene. This theory is congruent with the many cognitive processes of the hippocampus, explains why the hippocampus is always required for memory recall, and why remote memories are vulnerable to error accumulation.

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