Regional Deficits With Impacts on Functioning Cognition

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Abstract

Our team reviewed several clinical documents ranging from 1990 to 2025 that dealt with cognitive delay due to cell death within the medial temporal lobe (MTL). The team specifically filtered out patients presenting with injuries in different cortices. Injuries focused within our review include stroke, traumatic brain injury (TBI), and immunological disorders– with priority on cellular disruption due to cell death. After review, it is prevalent that when cell death occurs within the MTL, patients struggle with the formation of new memories and recall. When injuries occur within neurological tissues specialized for memory consolidation, like the hippocampus, negative symptoms were found to be severe, with partial or total loss of new memory formation.

Keywords: MTL, STM, LTM, hippocampus, cognition, memory, delay, RAM, HDD, SSD

Regional Deficits with Impacts on Functioning Cognition

As humans, we are bombarded with hundreds of different stimuli throughout our day. Thankfully, after information is collected by sensory organs, several cognitive functions help us filter, store, and respond to information in our environment. This, the processing of information, is paramount for organisms to perform higher cognitive functions. One of the mechanisms used to execute cognitive tasks is termed ‘working memory.’ Working memory is a cognitive function that stores small amounts of information, which can then be used to perform necessary and relevant tasks (Cowan, 2014). Think of working memory as a computer's random-access memory (RAM). It serves as an accelerated, but limited in capacity, workspace. Comparatively, our hippocampus resembles the shared responsibilities, such as those of a computer's hard drive. The hippocampus is a much larger workspace responsible for three phases of memory: registration, storage, and retrieval of relevant information (Fogwe et al., 2025). Both systems work in tandem to help individuals learn and react to their environments, affecting an individual's reaction time and recall accuracy (Draheim et al., 2016).

The purpose of this paper is to explore the relationship between our working memory and the hippocampus in relation to an individual's ability to perceive and respond to data; continued by comparing findings of normal cognitive functions to those who have suffered from regional deficits. By exploring the impact of regional cell death, we hope to show the important relationship the hippocampus and working memory share in assisting us with higher cognitive processing.

Neurological Anatomy

The brain consists of two temporal lobes, situated prominently on both sides of the brain- mirrored across the sagittal plane. These lobes sit in the middle of our cranial fossa, which are interior skeletal depressions to support the temporal lobes. Our ears are situated parallel to our cranial fossa. Continuing with the temporal lobe, it is accepted that these lobes assist with eight different cognitive functions, such as speech perception and production, hearing, episodic memory, phonological understandings, social and visual encoding, and finally semantic memory (Patel et al., 2025). The medial temporal lobe (MTL) sits deeper within the temporal lobes, closer to the brain's midline (the sagittal plane) (Baars & Gage, 2018). The structures found within the MTL are understood to be our hippocampus, amygdala, perirhinal cortex, parahippocampal cortex, and finally the entorhinal cortex (Raslau et al., 2015). These structures are integral for the formation, storage, and retrieval of our memories. The complex circuitry of our MTL helps with the formation of episodic memories, and with the help of the hippocampus, allows us to encode, organize, and formulate a structure to our memories (Dickerson & Eichenbaum, 2010). Due to the intricacies and density of neural tissues found within the MTL, our MTL not only assists with long-term memory storage but also assists with other memory functions such as working memory. This could be due to the temporal lobe's neural highway connections with other cortical lobes.

In terms of working memory, our prefrontal cortex (PFC) is believed to be responsible for this higher cognitive function (Funahashi, 2017). The prefrontal cortex is situated in the front of the brain, right behind the forehead and above the eyes. This cortex can be divided into two regions: the dorsolateral prefrontal cortex and ventrolateral prefrontal cortex (Hathaway & Newton, 2025). Recent studies have found that lesions within the dorsolateral PFC inhibit the efficiency of working

memory. The dorsolateral PFC is located on the outer (dorsal) surface of the brain and on the top (dorsal) of the brain (located around your hairline).

In 2010, a study was conducted using fMRI to show the cooperative involvement between our PFC and MTL while encoding memories. The results found evidence that these two brain regions hold significant correlations when processing certain memories (Jenkins & Ranganath, 2010). This shows evidence of a strong neural network connecting our PFC and our MTL during sensory exposure, data processing, and encoding for memory. A more defined review of the cooperative nature between our PFC and MTL will be expanded within the hippocampus section of the paper.

Comparing Neural Regions with Digestible Terminology

The brain and its memory systems have been compared to modern computers and their memory systems. A computer has two types of memory. The first is called random access memory, or RAM. The second is the hard disk drive, often called a hard drive or HDD. RAM is a quick, temporary storage for information. The RAM storage capacity is also relatively small compared to the hard drive. This is where information is manipulated, for example, in calculations. If the information in RAM is to be used later, it must be saved to the hard drive. There it is, ideally permanently stored, barring component failure.

The brain has three memory systems, but they act similarly to a computer's. The first is called working memory. This is where perceptions, or information, are first stored and can be manipulated, not unlike RAM. Further, short-term memory is where information that needs to be remembered temporarily goes after working memory. There are also limits on the amount of information that can be stored in both working and short-term memory. Working memory and short-term memory can then be directly compared to RAM because they are both temporary

storage; only small amounts of information can be stored there, and they serve as “holding spots” for information that will be stored for a longer period of time (Buschman & Miller, 2022).

In terms of the brain, that larger, more permanent storage is called long-term memory. While there are multiple types of long-term memory, such as semantic, episodic, and procedural, they will not be the focus of this analogy (Neher et al., 2015). This is primarily located in the hippocampus and stores significantly more information than can be held in working memory and short-term memory. This is also the location from which memories that are no longer in short-term memory are retrieved. This is very similar to the function of a computer’s hard drive. However, the analogy is not perfect as there is some interplay between the hippocampus and short-term memory (Husain, 2024). Because there is some interconnectedness between the hippocampus, long-term storage, and short-term memory, one could argue that a solid-state drive (SSD) might be a more apt comparison to the hippocampus. An SSD works the same as an HDD in a computer, except it has no moving parts and performs significantly faster than a traditional HDD. Because of the increased speed, to a user, there is seemingly very little difference between RAM and SSDs, just as a person doesn’t experience much difference between their short-term and long-term memory.

Working Memory

The term working memory emerged during the 1970s from Baddeley and Hitch (Goldstein, 2019). Baddeley proposed the theory of working memory to better represent dynamic processes that occurred over time, but could not be explained by short-term memory. Prior to then, there had not been a distinction between short-term memory and working memory. However, they refer to different types of memory. Short-term memory ranges from thirty seconds to two minutes and its ability is to retain information for a short time. Our current understanding of working memory

refers to the ability to manipulate the information presented while being held in limited-capacity storage (Goldstein 2019).

Baddeley explained working memory with a model that includes three components: the phonological loop, visuospatial sketchpad, and the central executive. The phonological loop allows rehearsal through the articulatory rehearsal process, and the ability to hold a limited amount of information for a few seconds through the phonological store. The visuospatial sketchpad is what is in use when visualizing a picture in the mind. The central executive takes on most of the work by managing these two aspects together, deciding how attention is divided between the two, and retrieving necessary information from long-term memory as needed.

While this model was an advancement in understanding working memory, it was still lacking. Baddeley saw that it failed to explain the phenomena of expansion through the use of methods, like chunking. He saw that it was fit to add another component called the episodic buffer. The episodic buffer is a component theorized to store information, connect to long-term memory, and connect the visuospatial sketchpad and phonological loop to long-term memory.
Working memory gives a better indication of learning as opposed to intelligence quotient (IQ). This is because working memory measures the potential for learning while IQ only measures what has been learned (Alloway & Copello, 2013). Working memory is necessary for mental arithmetic, reading comprehension, and language. Phonological awareness is a foundational reading skill that allows people to break down words into parts, like recognizing rhyming words, or the ability to name pictures quickly (Alloway & Copello, 2013). The measurement of each student's phonological awareness accurately predicted their reading proficiency. The theory behind why working memory is so critical for reading skills is that it is like a Post-it Note: it keeps relevant speech sounds in mind, matches them up with letters, and then combines them to allow minds to

read words (Alloway & Copello, 2013). Children who suffer reading challenges also tend to present with a limited capacity for processing and storing information. Low working memory scores also align with poor computational skills and poor performance with arithmetic word problems. Overall, academic performance is better predicted by working memory performance as opposed to standardized testing, and IQ (Alloway & Copello, 2013).

Hippocampus

In 1953, Henry Gustav Molaison lost his abilities to form new declarative memories after undergoing a surgical procedure to remove the hippocampus, and nearby temporal lobe structures (Knierim, 2015). Since then the hippocampus has become one of the most investigated brain structures. This paved the way to investigate long-term potentiation, and the pre-eminent model of the cellular basis of memory (Knierim, 2015). Knierim states “the hippocampus plays a critical role in memory formation by providing the brain with a spatiotemporal framework within which the various sensory, emotional, and cognitive components of an experience are bound together.” The hippocampus is often described as an elongated structure that lies deep in the medial temporal lobe (Knierim, 2015). There are several ways to image the hippocampus such as magnetic resonance imaging (MRI), computed tomography (CT), diffusion tensor imaging (DTI), positron emission tomography (PET), and single photon emission computed tomography (SPECT; Lang et al., 2024). In the past, the hippocampus was thought to be used primarily for long-term memory. However, current research shows that the hippocampus is also used during working memory. As expressed within the Neurological Anatomy portion of the paper, our prefrontal cortex (PFC) and medial temporal lobe (MTL), share a cooperative role in a cognitive function known as working memory. New research has shown that the hippocampus may be more involved with working memory than previously expressed. In the past, researchers believed that the hippocampus only assisted in long-

term memory. If, however, we refer to working memory as a cognitive system that stores data in a readily available state, if only for a short time, it is reasonable to see that the hippocampus may play a role in how that collected data is utilized (Li et al., 2023). Working memory is a system that handles different levels of cognitive-memory loads. Most working memory tasks held by researchers typically explore how well a participant can recall different memory loads. In a recent study that explored the relationship between the hippocampus and working memory, it was hypothesized that a damaged hippocampus might negatively affect working memory. The trial found that under low memory loads, there was no statistical significance between a healthy participant and one with a damaged hippocampus. However, it was found that as the memory load increased participants started scoring poorly, when they had damage to their hippocampus (Marcelle et al., 2025). This was also seen in individuals with hippocampal atrophy. Another study used an intracranial electroencephalography (iEEG) to record hippocampal activity while stimulating an individual's working memory (Li et al., 2023). It was found that when presented with a new stimulus, not only did the prefrontal cortex engage, assisting with working memory, but the hippocampus also engaged simultaneously. This provides evidence that the hippocampus may be assisting with the process of working memory. The hippocampus is now being explored as a potential supportive cognitive cortex for the process of working memory by supporting the maintenance of newly gathered information. This maintenance then ensures that relevant data is accurately transferred and stored within the hippocampus and other cortices.

Clinical Significance

We can see the importance of the medial temporal lobe, specifically the hippocampus, in dealing with working memory through patients who have suffered from various maladies that have affected the hippocampus.

Anti-N-Methyl-D-Aspartate receptor (NMDAR) encephalitis is an autoimmune disorder in which antibodies target NMDARs in limbic structures such as the hippocampus (Finke, 2013). Patients diagnosed with anti-NMDAR encephalitis often show reduced working memory capacity, which may be related to hippocampal damage. In these patients there is a reduction in gray matter volume in the medial temporal lobe structures, particularly the hippocampus (Finke, 2013), and these hippocampal volume reductions have been shown to correlate with memory performance.

The hippocampus is a central component of the memory system and also a key node of the default mode network (DMN). The study conducted MRIs of resting state functional connectivity within the DMN and revealed decreased connectivity in patients with anti-NMDAR encephalitis (Finke, 2013). Disrupted hippocampal connectivity within this network may contribute to memory deficits. One of the major components of the DMN, the medial prefrontal cortex (mPFC), is involved in working memory processes and its interaction with the hippocampus is essential for memory maintenance. Furthermore, diffusion tensor imaging (DTI) revealed reduced white matter integrity, particularly within the cingulum bundle (Finke, 2013). Damage to the cingulum has been associated with impairments in working memory because it serves as a major structural pathway connecting the hippocampus with anterior DMN regions such as the mPFC. Disruption of this pathway may therefore reduce hippocampal-prefrontal connectivity and contribute to working memory impairment observed in patients with anti-NMDAR encephalitis.

Medial temporal lobe (MTL) damage has been shown to directly impair working memory precision rather than simply reducing memory capacity. In a study examining epilepsy patients before and after neurosurgical resection, individuals with hippocampal lesions demonstrated “a significant increase in recall variability, indicating reduced visual working memory (VWM) precision after surgery” (Choo et al., 2025). This impairment reflected a degraded quality of

representations rather than a failure to store information because there was no significant change in the ability to recall information (Choo et al., 2025). Voxel-based lesion mapping further revealed an association between hippocampal damage and increased recall variability overlapping with the entorhinal-hippocampal circuit (Choo et al., 2025). The authors conclude that “hippocampal lesions selectively impaired VWM precision, without affecting recall success rates” and that “the hippocampal circuitry preferentially supports the quality rather than quantity of retained VWM content” (Choo et al., 2025). These findings challenge the view that says hippocampal function is only confined to long-term memory and instead demonstrate that the hippocampus plays a critical role in maintaining the constancy of working memory representations. Clinically, this supports the argument that hippocampal disruption, whether due to surgical resection, autoimmune inflammation, or other medial temporal pathology, can lead to measurable working memory impairment.

Findings from Feigenbaum et al. (1996) provide additional support for the idea that the hippocampus plays a role in working memory. Spatial working memory involves the encoding of specific and contextual information within the spatial domain (Feigenbaum et al., 1996). In this study, individuals with bilateral hippocampal damage showed impairments on tasks that required them to briefly hold and organize information, especially when they had to understand relationships between different pieces of information, such as spatial or contextual details. This suggests that the hippocampus is involved in working memory when tasks require binding or organizing information, rather than just storing long-term memories. Furthermore, one of the core features of working memory is the maintenance of that information across time. Feigenbaum et al. (1996), found that damage to the right temporal lobes were impaired in their ability to recall the locations of objects, more importantly this impairment was only seen when there was a delay in the

presentation of material and recall. The authors propose that damage to the hippocampus affects a person's ability to maintain flexible mental representations needed for ongoing cognitive tasks, showing that working memory deficits can result from medial temporal lobe dysfunction (Feigenbaum et al., 1996).

Results

In the following section, results will be presented from studies showcasing the relationship between working memory and the hippocampus. Findings from each of these studies will be provided and whether or not these support the hypothesis outlined in the introduction of this paper: damage to the hippocampus affects an individual's ability to perceive and respond to data.

Medial temporal lobe lesions reduce visual working memory precision

The paper "Medial temporal lobe lesions reduce visual working memory precision" included 40 participants (22 male, 18 female), 19 with "hippocampal lesions," 17 with "extra hippocampal lesions, and 4 without a "surgical resection after intracranial EEG recordings" (Choo et al., 2025).

From this study, it found "participants with hippocampal lesions exhibited a selective increase in VWM recall variability, with no evident change in the rate of uniform (i.e., random) recall responses." Furthermore, research found a "significant increase in SD [standard deviation] after surgery… indicating a reduced memory precision." Finally, "the probability of recall success showed no significant change" (Choo et al., 2025).

Deficits in spatial working memory after unilateral temporal lobectomy in man

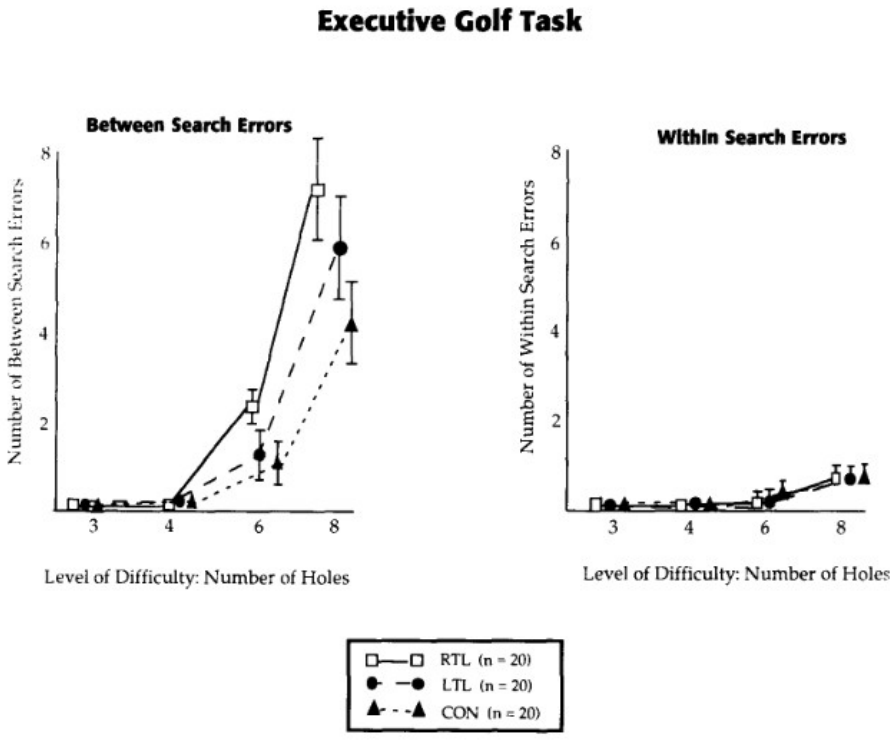
Forty neurosurgical patients and 20 controls were tested in this study, which utilized a computerized representation of a golf course. The study divided possible errors into two categories: 'Within search errors' are defined as "during a single search sequence, the subject 'guesses' the

same hole more than once while searching for the correct hole into which the golfer will putt the ball." 'Between search errors' are defined as " subject 'guesses' a hole which already contains a ball."

Accordingly, it found "On 'between search errors' there was a significant group effect with the right temporal lobe group making significantly more errors than controls. This effect was more significant as the problem difficulty increased. However, while there was no significant difference between the right and left temporal groups, the left temporal groups were also impaired when compared to controls." Furthermore, "On multiple analyses of variance comparing all three groups [right temporal lobe, left temporal lobe, and control] together and each individual group with each other group, there were no significant differences for 'within search errors for any of the three groups at any level of difficulty" (Feigenbaum et al., 1996).

Figure 1

Search Errors Divided Between RTL, LTL, and Control



Note. From “Deficits in spatial working memory after unilateral temporal lobectomy in man” by Feigenbaum et al. (1996).

Finally, “...when compared on ‘within search errors,’ very few errors were made by subjects in any of the three groups on the rotate task. When comparing the three groups for ‘between search errors’ there was a significant difference between the RTL and LTL groups and only a very small (not quite significant) difference between the LTL and control groups” (Feigenbaum et al., 1996).

Functional and structural brain changes in anti–N-methyl-D-aspartate receptor encephalitis

“Twenty-four patients with anti-NMDAR [anti–N-methyl-D-aspartate receptor] encephalitis after the acute stage of the disease were studied.” “Patients showed substantial deficits of executive functions, working memory, and verbal long-term memory, whereas attention, visuospatial abilities, and language were intact.” Patients also “showed significantly reduced functional connectivity between the aDMN [anterior default mode network] and the anterior hippocampus bilaterally” (Finke et al., 2013).

The results of three articles were presented in this section. Each of these results showcased a different study, engaging patients in varying tasks. The article by Choo et al. (2025), which focused upon medial temporal lobe lesions, supported the supposition that the working memory is supported by the hippocampus. Furthermore, it found that damage to this area of the brain resulted in “reduced memory precision” (Choo et al., 2025). Feigenbaum et al. focused upon patients’ working memory after lobectomies in both the left and right temporal lobes. An example of the effects this study described were the increased amount of “between search errors” compared with controls (Feigenbaum et al., 1996). Finally, in a study upon patients with anti-NMDAR encephalitis, extensive damage was found to “executive functions, working memory, and verbal long-term memory” (Finke et al., 2013).

Each of these studies focused upon the hippocampus and the effects of the damage to this part of the brain, confirming the hypothesis proposed earlier. These studies confirmed that damage to the hippocampus affects an individual's ability to perceive and respond to data. Further evaluation of the results of each of these studies will be described in the discussion section.

Discussion

The findings within our study demonstrate an advancing theory that the hippocampus has a close relationship with the cognitive function working memory. Our study synthesizes and analyzes dozens of previously published research articles to explore if there is a connection between the two variables, by reviewing cellular deficits within targeted cortices, such as the medial temporal lobe. After reviewing these articles, we have agreed to accept our alternative hypothesis, that damage to the hippocampus affects an individual's ability to perceive and respond to data.

Research done by Marcelle et al., Li et al., and Jenkins & Ranganath developed a profound connection between an individual's working memory and hippocampus. Their work explored the theoretical nature that a high memory load within the working memory arouses neurons within the hippocampus. Hippocampal arousal was found utilizing an iEEG while clients performed working memory tasks (Li et al., 2023). Research has also found a communication link between the prefrontal cortex and medial temporal lobe (Jenkins & Ranganath, 2010). These findings help create a strong argument that the two cognitive regions share a complex interrelationship. Continued literature reviews have found that damage to the medial temporal lobe has negative effects on an individual's visual working memory (Finke et al., 2013). An additional study held by Choo et al., concluded that lesions with the medial temporal lobe negatively affected patient's ability to formulate memories and utilize visual working memory effectively.

It is based on the reviews of current scientific literature that we accept our hypothesis and have found a strong relationship between the hippocampus and working memory, through studying cellular death.

Limitations

Our research is limited simply by the natural limitations that follow literature reviews. We were unable to verify, replicate, or test the potential findings within our references. However, the quality of our references has been explored and found to be competent, though small sample sizes, regarding specific references, could skew potential statistical results. There are also the risks of selection bias during the process of reference review and implementation within our study. Selection bias was avoided by finding multiple references conducting similar research which concluded in the acceptance of their hypothesis. These references were then compared to research with potentially disputing claims.

Recommendations

We recommend that further research is needed to find the exact relationship between working memory and the hippocampus. Current literature agrees that there is a connection; however, the exact importance of this connection is difficult to define due to limited studies. FMRI and iEEG tests seem to be the most effective tests in exploring this correlation and should be used in future studies as deemed relevantly warranted. The test iEEG can pose health complications and these should be discussed with the patients before the study starts.

Conclusion

This paper set out to explore the relationship between our working memory and the hippocampus in relation to an individual's ability to perceive and respond to data by exploring the impact of regional deficits and cell death. We first defined the neural regions, working memory, and the function of the hippocampus in an effort to understand the possible impacts to patients after damage had occurred. After this, research was presented which was found to support the authors' suppositions that damage to the hippocampus may affect the ability to perceive and respond to data. With this foundation of understanding provided, it may be beneficial to conduct further literature reviews to understand other forms of cell damage to the hippocampus and to compare and contrast the differences in findings.

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