THE INFLUENCE OF DRAWING ON MEMORY FORMATION:

A LESION-BASED APPROACH

ADINA LEVI

A Thesis submitted to the Faculty of Graduate Studies in Partial Fulfillment of the Requirements

for the Degree of Master of Arts

GRADUATE PROGRAM IN PSYCHOLOGY,

YORK UNIVERSITY,

TORONTO, ONTARIO

July 2021

Abstract

The hippocampus plays a critical role in the formation of contextually rich memories, with research indicating that distinct neuronal representations within the hippocampus produce the foundation of these memories. Therefore, the more distinct the memory representation at encoding, the stronger the memory trace. However, patients with focal damage to the hippocampus show impairment in this memory storage system and their memories are thus more vulnerable to interference. Drawing has recently been utilized as an encoding strategy that creates particularly distinct representations as it incorporates a range of modalities, such as motor, visual and verbal domains. Thus, the goal of this study was to determine whether patients with hippocampal amnesia could benefit from the mnemonic strategy of drawing. Two patients, BR and BL, who have hippocampal damage and their matched control samples ($N = 10$ for each patient) completed a testing session via videoconferencing where they were instructed to either draw or write down a list of 30 words. After a delay of 10 minutes, they completed unexpected free recall and recognition tasks. Both patients displayed enhanced performance for the words that they had drawn, as opposed to written, on measures of recall and recognition. As individuals with hippocampal amnesia live with severe memory deficits which impacts their day-to-day life, research on developing strategies to reduce their memory impairment is of upmost importance.

Keywords: hippocampus, amnesia, drawing, memory

Dedication

I would like to dedicate my MA thesis to my parents, Joshua and Bronya Levi, for their unwavering love and constant support.

Acknowledgements

First, I would like to thank my incredible supervisors, Dr. Gary Turner and Dr. Asaf Gilboa, for their continued support, encouragement, patience and understanding during my Master's degree and in preparation for the thesis defense. My amazing defense committee, Dr. Shayna Rosenbaum and Dr. Suzanne MacDonald, provided wonderful insight throughout the defense. I would not have been able to complete this research project without the help from my incredible Research Assistant, Patricia Aguiar, who was instrumental throughout every step of the project. I am so grateful to the Psychology Graduate Office, and in particular, Lori Santos, Barbara Thurston, and Freda Ann Soltau, for the constant guidance and kind encouragement. Finally, I would like to thank my wonderful family and friends, and my fiancé, Yehuda, for the unconditional love and constant support throughout my studies.

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Introduction

Hippocampal Amnesia

The cognitive ability of memory has been studied for centuries, as memory is a critical component of the human experience. Loss of memory can lead to devastating consequences for individuals with age-related changes to memory, or for those with acquired brain dysfunction. The term amnesia is often used to describe those with critically impaired memory abilities with comparatively preserved cognitive functioning (Spiers et al., 2001). These deficits can be displayed through profound impairments in the encoding, maintenance, and/or retrieval of newly learned information, as well as the inability to retrieve pre-existing memories (Rosenbaum et al., 2012). Selective damage to a particular subset of brain regions, and in particular the hippocampus, has been associated with amnesia (Aggleton & Brown 1999).

From a neuroanatomical perspective, seminal findings connecting memory to the human hippocampus were conducted by Scoville and Milner (1957), with their case work on the now famous patient HM. Patient HM was an individual suffering from epilepsy, and, in an effort to reduce the severity of his seizures, had bilateral portions of the medial temporal lobe (MTL; specifically, the CA fields, dentate gyrus and subiculum) removed. As a result of the experimental neurosurgery, patient HM suffered from anterograde amnesia, a deficit which impaired his ability to form new memories (Scoville & Milner, 1957). He also experienced deficits in declarative memory, which impacts depictions of facts and experiences that can be consciously and explicitly reflected upon (Eichenbaum, 1997; Scoville & Milner, 1957). However, HM did retain most of his cognitive, language, perceptual and non-declarative memory abilities. This apparent brain-behavior relationship inspired a host of studies analyzing

the associations between the hippocampus and memory, particularly underscoring the role that the hippocampus plays in declarative memory.

Lesions to the MTL have been strongly associated with anterograde amnesia (memory deficits for information post-lesion damage) for explicit material (Tulving & Markowitsch, 1998). Spiers et al. (2001) noted bilateral hippocampal damage has consistently been associated with anterograde amnesia with particular impacts on episodic memory (personally experienced events that can be linked to a time and place; Tulving, 1972). While procedural and working memory may be largely spared, retrograde amnesia (memory loss for information acquired pre-lesion damage) and semantic memory impairments for post-lesion material may be observed (Cavaco et al., 2004; Squire & Zola, 1998). However, as first seen with patient HM, when focal brain damage affects the hippocampus bilaterally, preserved cognitive functioning can be observed in conjunction with severe declarative memory deficits (Clark & Maguire, 2016; Eichenbaum, 2004).

Animal studies have demonstrated that hippocampal lesions can lead to spatial and contextual memory deficits (Kim & Fanselow, 1992; Morris et al., 1986). In 1971, Marr and colleagues proposed an influential model implicating the hippocampus in memory retrieval, suggesting a role in reinstating patterns of cortical activity that occurred during the encoding of a memory. Later rodent models of hippocampal functioning supported this notion, and displayed the replaying of learned categorizations in the hippocampus and cortex post environmental training (Ji & Wilson, 2007). Further evidence in rodent studies has shown how the hippocampus creates distinct representations through neuronal networks of hierarchical organization (McKenzie et al., 2014). Distinct contexts are represented by hippocampal neurons, which in turn generate the retrieval of a contextual memory.

However, individuals with damage to the hippocampus demonstrate impairments in retrieving contextual memories (Chun & Phelps, 1999; Leutgeb et al., 2007; Winocur et al., 2012). Hassabis and colleagues (2007) understood this impairment to mean that the hippocampus may play a role in the development of new experiences by allowing distinct elements of previously encoded memories to be connected to a specific context (Yassa & Reagh, 2013). Furthermore, hippocampal dysfunction may lead to deficits in recombining details of contextual memory elements (Addis & Shachter, 2012). As many scenarios in day-to-day life share overlapping features, functional MRI (fMRI) data shows that the hippocampus protects memories from interference as representations of context-dependent memories undergo pattern separation depending on their overlapping components. In other words, the hippocampus helps protect against memory interference by separating overlapping memory representations (Koolschijn et al., 2019). In order to ensure that interference of overlapping or related information is lessened, a stable memory storage system is crucial; however, patients with hippocampal dysfunction possess an impaired system, and are particularly susceptible to interference. Thus, the more distinct the memory representation at encoding, the less overlap between elements of prior information, leading to decreased reliance on the hippocampus.

Hippocampally-Mediated Memory Processes

When an individual initially experiences an event or learns new information, cognitive encoding processes ensue (Tulving, 1983, Tulving et al., 1994). Information coming from sensory input is transformed into a stored representation which can subsequently be retrieved (Craik, 1983). Encoding procedures initiate the creation of a memory trace that can support the conscious recollection of information at a later time. According to Paller and Wagner (2002), this encoding procedure depends on two main aspects: first, the initial encoding transforms incoming sensory input into internal representations. This process may necessitate the retrieval of related

knowledge associated with the current information. Then, the memory trace is further developed by binding the internal representation in a manner that would ultimately enable the trace information to be retrieved. The representation may consist of contextual details, perceptual features, and autogenous thoughts that critically bind aspects of the representation to form a cohesive engram (Paller & Wagner, 2002).

The interaction between these two aspects of encoding is clearly illustrated in individuals with hippocampal amnesia, particularly regarding patterns of intact versus impaired functioning. These patients will likely be able to have a coherent conversation and perform typically on tasks that require immediate retrieval of newly learned information (Cave & Squire, 1992). Although they can produce internal representations, these individuals may display difficulty when attempting to recall information once the representation has been dropped from "online" conscious retention (Paller, 1997). Difficulty during the latter stage of encoding, where the enduring traces require consolidation, underlies the deficit patients experience (O'Reily & Rudy, 2001).

Initial studies of memory encoding by Burnham (1904) emphasized two components that contribute to the learning of new information: the physiological, neurochemical changes of memory encoding at the cellular and molecular level, as well as the psychological changes that involve the interaction of novel experiences with cognitive configurations to generate long-lasting memories. Thus, after the original encoding of new information, a cascade of neural activities stabilize and augment the target memory, thereby transforming it into an enduring and cohesive memory while contributing to its long-term storage (Nadel & Moscovitch, 1997; Stickgold, 2005).

Areas in the MTL, including the hippocampus, are critically implicated across memory stages, including initial memory encoding (Davachi & Wagner, 2002), the storage or consolidation of memory (Nadel & Moscovitch, 1997) and finally, memory retrieval (Diana et al., 2007; Wixted & Squire, 2011). In early memory processing stages, during the initial encoding process, the hippocampus displays activation in the minutes to hours following the encoding of episodic memories (Dudai et al., 2015). However, recent research has shown that transient signals from the hippocampus occurs in the earliest stages of encoding, with activation in the MTL 200-300 ms post-stimulus onset (Raynal et al., 2020). fMRI studies have also indicated activity in the MTL during encoding, in addition to further neocortical and frontal areas (e.g., dorsolateral and ventrolateral prefrontal cortex and parietal structures) displaying activation during the encoding of later retrieved items (Diana et al., 2007; Paller & Wagner, 2002, Schott et al., 2013). Neuroimaging evidence further displays that the regions involved in the encoding process are reactivated during the successful retrieval of the encoded information (Fenker et al., 2005; Johnson & Rugg, 2007).

Formative research has displayed hippocampal involvement during encoding at the cellular level, noting hippocampal cells rapidly encode perceptual and behavioural features of an experience (Shapiro & Eichenbaum, 1999). Based on animal studies, Moser and Moser (1998) proposed that the formation of a memory trace does not occur in the hippocampus as a solitary, integrated unit, but rather they emphasize the roles of isolated subfields within the hippocampus contributing to different functions of encoding. Moser and Moser (1998) note that the posterior hippocampus in primates, and the dorsal hippocampus in rodents, are the key areas of activation during encoding. Early animal research on encoding mechanisms has demonstrated that lesions of the primate hippocampus impair recently, as opposed to remotely, acquired memory (Zola-

Morgan & Squire, 1990). This finding has led to the idea that the hippocampus is associated with memory acquisition, but is less involved in the retrieval of stored memory traces. However, other studies with human subjects have emphasized activation of the anterior hippocampus during memory encoding, while the posterior hippocampus was engaged during memory retrieval (Lepage et al., 1998). Studies using positron emission tomography (PET) scans in human participants found left hippocampal engagement during item encoding (Nyberg et al., 1996), and further studies have shown activation in the medial and posterior, as opposed to anterior, hippocampus during both encoding and retrieval (Greicius et al., 2003).

From a behavioural as opposed to neuroanatomical perspective, there are certain conditions that can optimize or enhance the encoding process. Although initial research by Atkinson & Shiffrin (1968) described a memory model that did not differentiate between separate rehearsal methods, later studies emphasized that the rehearsal technique at encoding strongly impacts the subsequent memory performance (Craik & Lockhart, 1972; Craik & Tulving, 1975). Usually, superficial forms of encoding (i.e., rote rehearsal) of information is associated with reduced retention, while a deeper level of encoding (i.e., semantic aspects or contextual details) of the information is associated with better retention (Craik, 1983). Memories that can be retrieved successfully are the result of processes completed during the experience itself, which typically involve perceptual and conceptual elements. In particular, certain methods of encoding (ones that are contextually rich, elaborate and meaningful) are associated with increased levels of retention (Craik, 1983).

The levels-of-processing theory proposed by Craik and Lockhart (1972) emphasize the association between deep, semantic connections with material at encoding with subsequent enhanced retention. To-be-remembered material can either undergo a surface-level version of

rehearsal, with the result of this kind of rote activity being the maintenance of information in working memory, or, a more elaborative form of rehearsal, which involves a cascade of cognitive functioning incorporating deeper (e.g., semantic) associations with the material (Craik & Lockhart, 1972; Woodward et al., 1973). This method of encoding involves creating a detailed and rich association with the to-be-remembered information that leads to increased memory consolidation based on the deep encoding mechanism (Craik & Watkins, 1973).

However, the levels-of-processing approach does not differentiate between the retention of memories from separate events that were similarly encoded in a semantically elaborative manner. Therefore, a further understanding of the encoding process was proposed by Jacoby et al., (1979) which emphasizes the relationship between the distinctiveness of encoding elements and subsequent retention of the material. If the initial encoding is more extensive and requires effort, the result from this elaborative practice is reflected in a distinct memory trace. Subsequently, the distinctive trace is highly discriminable from other memory records and can be retrieved with ease, as opposed to traces with overlapping features which are not highly discriminable from other memory records and thus are more difficult to retrieve. Therefore, differentiation of the encoded trace is a result of deeper processing which leads to a distinctive trace that can be more precisely specified and thus successfully retrieved (Carr et al., 2015; Craik, 2012). Thus, the distinctive memory trace leads to decreased reliance on the hippocampus for succeeding memory retrieval.

There is abundant evidence that the hippocampus is associated with the capacity to encode distinct neural representations of discrete events or stimuli (Yassa & Reagh, 2013). Furthermore, damage to the hippocampus can disrupt encoding-related processing of new information (Scoville & Milner, 1957). As such, enhancing the separability of representations at

encoding, consistent with levels of processing theory, should improve subsequent memory performance in individuals with hippocampal damage. In the next section we review evidence for a novel encoding strategy, drawing, that may support encoding and subsequent retrieval, by recruiting extra-hippocampal structures, in patients with hippocampal damage.

Drawing and Memory Consolidation

A variety of consolidation encoding approaches have been introduced in populations of healthy individuals, which appear to improve declarative memory performance (Ullman & Lovelett, 2018). Specifically, using drawing as a mechanism to boost memory performance has been emphasized as a useful mnemonic strategy, as it incorporates elements of elaborative, pictorial and motor encoding methods which enable the development of a contextually rich representation at encoding (Fernandes et al., 2018). However, other elaborative methods have also been proposed. For example, spaced repetition (also known as distributed practice or the spacing effect) is a method that involves establishing a temporal space between repeated items, which has been shown to increase memory retention for learned stimuli (Cepeda et al., 2006). Another mnemonic mechanism, known as the generation effect, involves increased memory performance for words that participants generated themselves, compared to words they were asked to passively read (Slamecka & Graf, 1978). Retrieval practice, or the testing effect, displays how the mnemonic strategy of retrieving learned information from memory enhances recollection when compared to re-studying the information (Roediger & Butler, 2011). Retrieval practice enhances the knowledge gained as the consolidated memory can further be adaptably retrieved and integrated to new environments (Roediger & Butler, 2011). As well, gesture-based learning, or the enactment effect, is a strategy that involves word learning with accompanying contextually suitable gestures. This method has also been shown to improve learning or retention

at the item level (Engelkamp & Zimmer, 1989; Macedonia, 2014). Further mnemonic strategies include the method of loci, or the memory palace, which involves cognitively mapping to-be-remembered information into imaginable settings, and has been shown to increase item-level retention of information (Lea, 1975). Finally, tasks that require deep encoding, which engages a semantically powerful level of processing (as opposed to surface-level processing), was proposed to improve memory performance compared to tasks that do not engage this deep semantic elaboration (Craik & Lockhart, 1972).

Although the previous elaborative strategies emphasized process-based methods, modality-based methods have also been proven useful. When compared to words, images are better remembered, and this is known as the picture-superiority effect (Paivio et al., 1968; Paivio 1971). The notion behind this effect is a theoretical dual coding described by Paivio et al. (1968) as pictures can be dually characterized by their verbal descriptions and their visual qualities. Based on this reasoning, a recent strategy that has displayed beneficial effects after enhanced encoding processes is drawing (Fernandes et al., 2018). Drawing not only employs this dual coding technique, but its effect may enhance encoding through the motor movement and elaborative processes required to create a personalized visual representation of to-be-remembered information. In a series of studies, Fernandes et al. (2018) and Wammes et al. (2016) have shown that drawing, as opposed to writing, target material improves both free recall and recognition memory performance. This phenomenon has been dubbed the “drawing effect” and integrates semantic, visual, and motor components of studied material. Furthermore, when compared to other encoding strategies (e.g., passively viewing an image, visualizing an image, semantic elaboration), drawing, and specifically the active motor aspect, enhances long-term memory retention (Wammes et al., 2019).

Fenandes et al. (2018) hypothesized that the drawing effect has particularly robust mnemonic qualities due to the amalgamation of other active encoding strategies. When prompted with a verbal cue and instructed to draw it, participants must first generate a mental image of the word, gathering semantic information about that word from memory. They must then design the image, and apply that design through a motor movement onto a page. Once the image is created, it is again viewed. Each of these steps taps into enhanced encoding strategies; first, image generation and semantic elaboration (Craik & Lockhart, 1972; Slamecka & Graf, 1978), then, enactment strategies (Engelkamp & Zimmer, 1989), and finally, the picture-superiority effect (Paivio et al., 1968). These prolific encoding strategies produce a strong and distinct memory representation which results in enhanced recall and recognition performance of the to-be-remembered information (Fernandes et al., 2018).

Studies on patients with MCI and dementia suggest that studying pictures, compared to words, can increase memory performance (Ally et al., 2009). As drawing not only involves studying a picture, but creating one, the mechanism supporting the benefits of images rather than words underscore the advantages seen by increased memory performance when compared to writing. Certain mechanistic features account for the increased memory performance in patients with memory disorders, specifically in terms of the neural structure and function. Areas in the brain that are often associated with memory disorders include the frontal and medial temporal lobes, and specifically the hippocampus and entorhinal cortex in the medial temporal lobes are affected (Clark & Maguire, 2016; Eichenbaum, 2004; Gomez-Isla et al., 1996), while primary visual cortices and ventral visual pathway are typically unaffected (Arndt et al., 1996). Therefore, one interpretation for why patients with memory disorders display benefits of studying pictures compared to words is that they employ intact areas of the brain that are

necessary for visual perceptual processing (Ally, 2012). Indeed, the mnemonic benefits of the drawing effect have recently been displayed in both healthy adult populations, as well as in individuals with probable dementia (Meade et al., 2020).

Given the beneficial effects of drawing as an encoding method, it is critical to both MTL-damaged patients and researchers to identify practical mnemonic strategies by which individuals with hippocampal amnesia can advance their declarative memory functioning. The notion that patients with hippocampal amnesia may benefit from mnemonic strategy of drawing has been rarely studied, although gesturing, a separate active encoding strategy, has displayed enhanced effects of word learning in these patients. This mnemonic benefit has been attributed to the engagement of brain regions outside of the hippocampus (e.g., striatum) involved in non-declarative memory processes such as procedural memory that supports motor and cognitive skill knowledge (Hilverman et al., 2018). As drawing also involves non-hippocampally-mediated processes, such as motor and visual modalities, hippocampal amnesic patients may benefit from drawing-based memory encoding strategies.

As such, the goal of this study is to determine whether patients with hippocampal amnesia may benefit from the mnemonic effects of drawing, and display enhanced recall and recognition performance for drawn as compared to written word stimuli. Based on the evidence that non-hippocampally-mediated, multi-process and multi-modal encoding approaches enhance memory performance, we predict that patients with hippocampal amnesia will benefit from the mnemonic effects of drawing and display enhanced recall and recognition performance on drawn compared to written words. Theoretically, this process would generate a memory trace from a multi-modal experience that requires less hippocampal support and would therefore show relative preservation in these memory impaired patients.

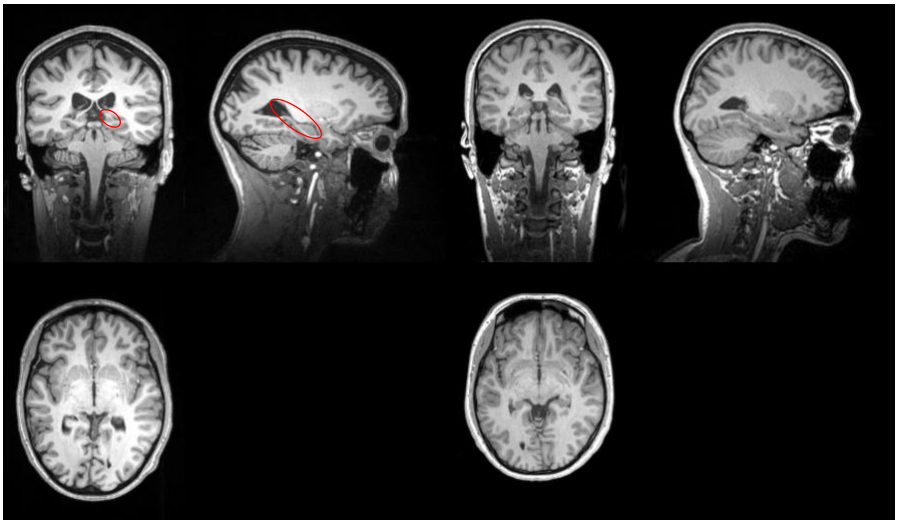
Methods

Participants and Procedure

Two patients with MTL damage, in addition to age, sex, and education matched controls completed this study via Zoom (distance-delivered given the COVID-19 pandemic). The first patient, BR, is 39-year-old, female, and has 16 years of education. At the age of 18, BR suffered from anoxia which resulted in bilateral hippocampal damage. Specifically, reduced hippocampal volume was seen, in addition to small globus pallidus lesions and possible cerebellum degeneration (see Figures 1-3). The overall hippocampal MTL cortices displayed degeneration, and based on the subfield analysis, there was a pattern of greater reduction in the CA1 subfield compared to other subregions when analyzing the percent-volume compared to controls (see Table 1).

Figure 1

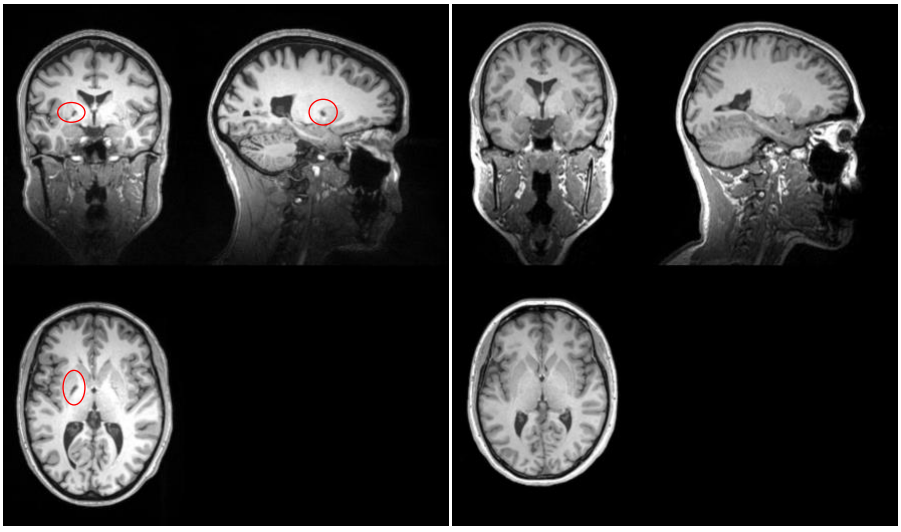
3T MR Images for BR and Matched Control



Note. Comparison between BR (left) and a matched control (right) noting hippocampal damage. From left to right: coronal, sagittal and axial views.

Figure 2

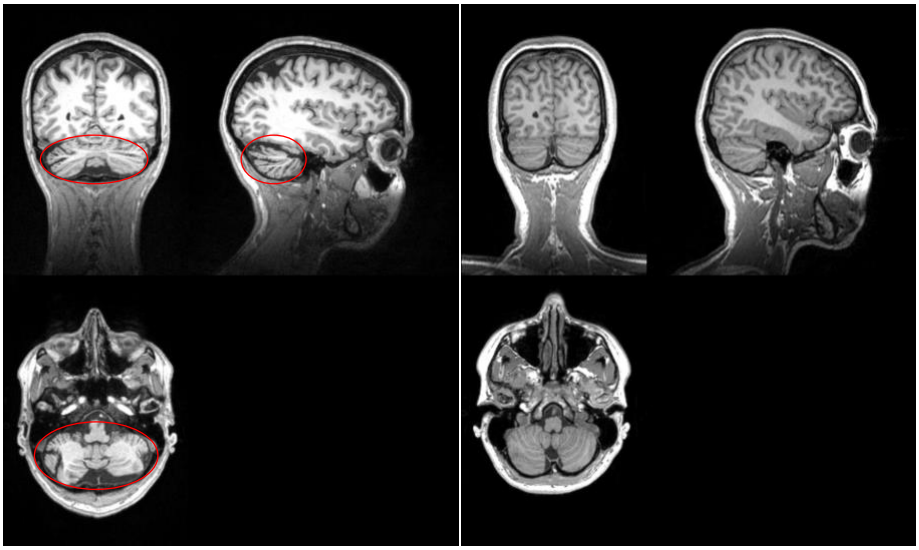
3T MR Images for BR and Matched Control



Note. Comparison between BR (left) and a matched control (right) noting small lesions to the globus pallidus. From left to right: coronal, sagittal and axial views.

Figure 3

3T MR Images for BR and Matched Control



Note. Comparison between BR (left) and a matched control (right) noting possible cerebellum degeneration. From left to right: coronal, sagittal and axial views.

BR's amnesic profile can be seen in the results of her neuropsychological battery, where she scored in the impaired range on measures of delayed memory, with typical intellectual and executive functioning (see Figure 4). Specifically, on the California Verbal Learning Test II (CVLT-II; Woods et al., 2006), which measures episodic verbal learning and memory, BR displays moderately impaired scores for both the immediate free recall portion of the test, as well as the total number of words recalled. She also exhibits profound impairment on both the long delay free recall section, and the long delay cued recall portions of the task. BR's long delay recognition scores are in the severely impaired range. Furthermore, on the Logical Memory I and II (LM) test from the Wechsler Memory Scale (Wechsler, 1997), which is designed to measure verbal episodic memory, BR's scores are in the low average range on the LM-I (immediate recall) section. On the LM-II (delayed recall) section, she similarly has scores in the

low average range, and on the final section, the LM Recognition (delayed recognition) segment, her score is average. On the Rey-Osterrieth Complex Figure task (ROCF; Rey, 1941; Osterrieth, 1944), which assesses visuospatial/constructional ability and visual memory, BR displays borderline scores on the immediate and delayed conditions, while she had high average performance on the copy condition. In sum, BR's neuropsychological profile in a variety of delayed memory tests indicate impaired performance.

Table 1

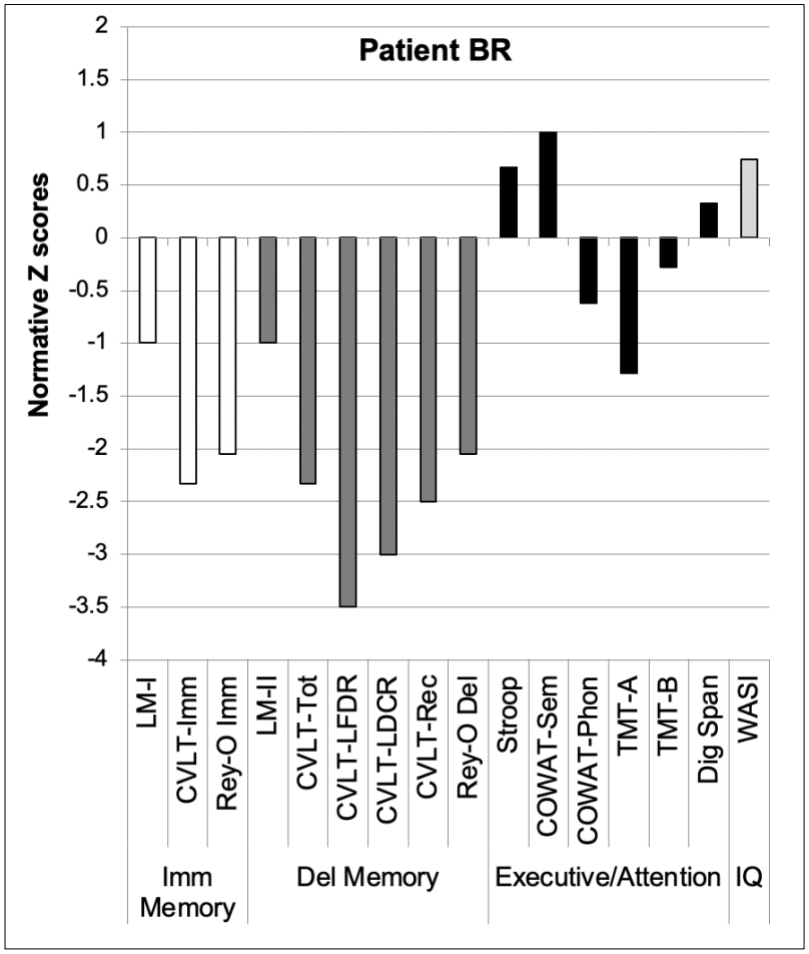
Volumetric Data: BR's Percentage Volume Relative to the Means of Six Healthy Controls

	CA1	CA23DG	Sub	AntHipp	PostHipp	PHC	PRC	ERC	HPC
Left Hemisphere	60%	88%	46%	56%	27%	84%	103%	84%	58%
Right Hemisphere	58%	85%	45%	49%	41%	94%	121%	108%	58%

Note. Manual segmentation of the hippocampus was completed using the Olsen-Amaral-Palombo (OAP) protocol which is used for volumetric investigations of the MTL (e.g., Olsen et al., 2017). Abbreviations: Sub, Subiculum; AntHipp; Anterior Hippocampus; PostHipp, Posterior Hippocampus; PHC, Parahippocampal Cortex; PRC, Precuneus; ERC, Entorhinal Cortex; HPC, hippocampus.

Figure 4

Neuropsychological, Cross-Domain Profile for BR



Note. Measures completed by BR, which are noted in normative Z scores: Logical Memory I & II (LM) from the Wechsler Memory Scale, California Verbal Learning Test (CVLT), Rey-Osterrieth Complex Figure task (Rey-O), Stroop Task, Controlled Oral Word Association Test (COWAT), Trail Making Test (TMT), Digit Span, and the Wechsler Abbreviated Scale of Intelligence (WASI).

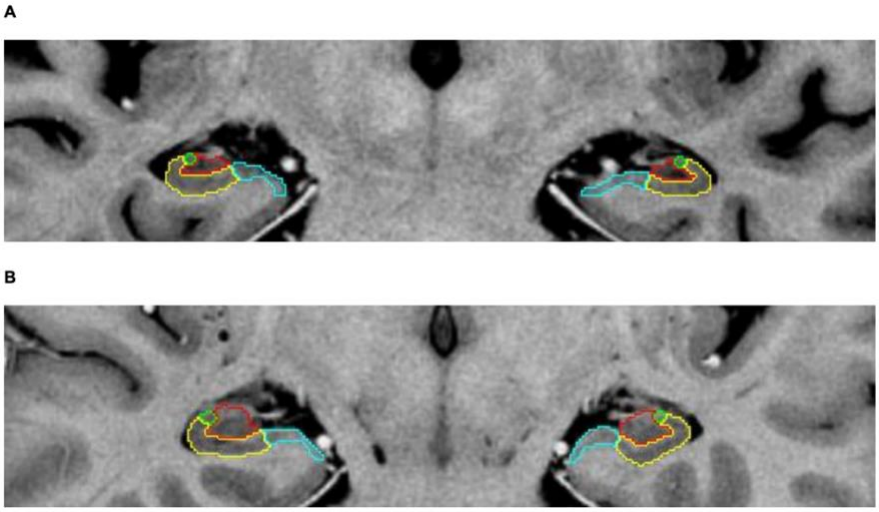
However, on measures of other cognitive abilities, BR's performance is in the typical range. On the Wechsler Abbreviated Scale of Intelligence II (WASI-II; Wechsler, 2011), BR's performance is in the average range on tests such as the Block Design (which measures visuospatial and motor skills), Vocabulary (which assesses word knowledge and verbal

formation), and Matrix Reasoning (which measures visual processing, and abstract, spatial perception), Similarities (which measure non-verbal problem solving). Her scores on indices of Verbal Comprehension and Perceptual Reasoning are in the average and high average ranges, respectively. Her performance on tests that measure executive and attentional abilities, such as the Digit Span, Stroop Task, and Controlled Oral Word Association Test (COWAT; Benton et al., 1994), and Trail Making Test (TMT) A & B (Reynolds, 2002) are within the low average to average range. BR's Full Scale Intelligence Quotient (FSIQ) is in the high average range (see Table 3 for a comprehensive list of tests). Therefore, although her performance on the measures of delayed memory fell into the impaired range, she displayed normal executive and intellectual functioning.

The second patient, BL, is a 61-year-old, male, with 13 years of education. BL was diagnosed with anoxic brain injury following cardiac arrest. This incident resulted in bilateral ischemic lesions in the hippocampus, particularly affecting the dentate gyrus, and a portion of the CA3, while the CA1 subfield and surrounding entorhinal and perirhinal cortices were relatively spared (see Figure 5). Atrophy to the cerebral cortex and slight increase in ventricle size were seen in MRI examinations (see Table 2; Kwan et al., 2015; Baker et al., 2016). Furthermore, volumetric analysis of BL's hippocampus and surrounding MTL cortices have displayed decreased size of the dentate gyrus (approximately 50% smaller) than 119 age-matched controls, while the CA1 subfield was 8% larger (Baker et al., 2016; Mueller & Weiner, 2009).

Figure 5

Segmentation of BL's Hippocampus Compared to an Age-Matched Control[1]



Note. This 3T MRI scan displays the manual segmentation of BL's discrete lesions to the hippocampus (volumetric quantification compared to 119 age-matched controls; Mueller & Weiner, 2009). Border description: red (CA3 subfield and DG); green (CA1-2 transition); yellow (CA1 subfield); blue (subiculum). (A) BL's hippocampus (B) Control hippocampus.

[1] Information from Baker et al., 2016, *Current Biology*

Table 2

Volumetric Data: BL's Percentage Volume Relative to the Means of Healthy Controls[2]

	IOG	LOTG	LG	AG	SMG	SPL	Pre	ITG
Left Hemisphere	85%	91%	111%	111%	74%	73%	82%	112%
Right Hemisphere	94%	99%	97%	111%	96%	85%	74%	99%

DG	CA1
50% smaller	8% larger

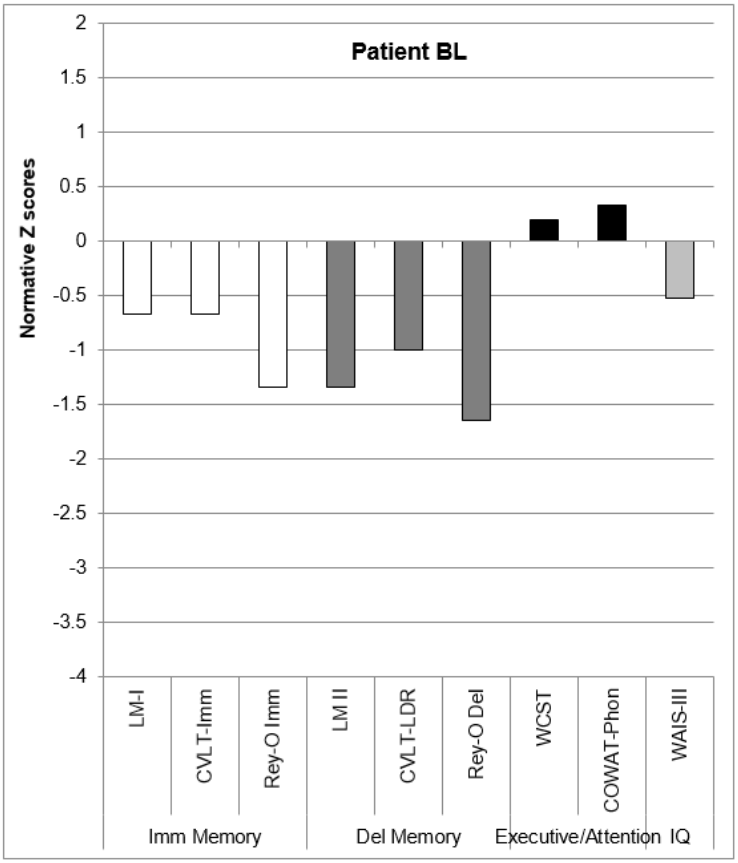
Note. Whole brain analysis volumetric percentages relative to eight healthy controls were derived using automated segmentation methods (i.e., FreeSurfer) and included IOG, LOTG, LG, AG, SMG, SPL, Pre and ITG (Baker et al., 2016). Manual hippocampal segmentation comparisons relative to 119 healthy controls (Mueller & Weiner, 2009) which excluded hemispheric differences included decreased DG volume relative to controls, with increased CA1 volume. Abbreviations: IOG, Inferior Occipital Gyrus; LOTG, Lateral Occipito-Temporal Gyrus; LG, lingual gyrus; AG, angular gyrus; SMG, supramarginal gyrus; SPL, superior parietal lobule; Pre, precuneus; ITG, inferior temporal gyrus; DG, dentate gyrus, CA1, cornu ammonis 1.

In terms of BL's neuropsychological test performance, he displayed below average memory performance on tests of immediate and delayed recall (see Figure 6). While his results on the LM-I were in the average range, his scores on the LM-II were borderline. BL's score on the immediate free recall portion of the CVLT-II was average, and the long delay free recall score was low average. His recognition score for the CVLT-II was average. BL's performance on recall for both the immediate and delayed sections of the ROCF were in the borderline range. BL's neuropsychological profile indicates a deficit in delayed memory abilities. Furthermore, although not a clinical test, BL completed the Mnemonic Similarity Task (MST) which is a behavioural discrimination test that assesses recognition memory (Baker et al., 2016). BL's performance on this task indicated an inability to successfully discern between previously seen images and similar (lure) ones, indicating a selective insensitivity to lure information.

[2] Information from Baker et al., 2016, *Current Biology*.

Figure 6

Neuropsychological, Cross-Domain Profile for BL



Note. Measures completed by BL, which are noted in normative Z scores: Logical Memory I & II (LM) from the Wechsler Memory Scale, California Verbal Learning Test (CVLT), Rey-Osterrieth Complex Figure task (ROCF), Wisconsin Card Sorting Task (WCST), Controlled Oral Word Association Test (COWAT), and the Wechsler Abbreviated Scale of Intelligence III (WASI-III).

However, on measures of executive and attentional functions, BL performs in the normal range. Specifically, his scores on the Letter Fluency task are average, as are his scores on the Wisconsin Card Sort Task (Grant & Berg, 1993), and the COWAT (Benton et al., 1994). Furthermore, his FSIQ from the WAIS-II also falls within the average range for general

intellectual functioning. Therefore, BL's neuropsychological profile indicates impairment in the domain of memory, while other cognitive functioning appears to remain intact.

A sample of healthy control participants were recruited through the Rotman Research Institute database and through word of mouth. These participants were matched to the patients on age, gender, and years of education. To match BR, 10 healthy control participants were recruited and were thus all female, with ages ranging from 35 – 45 years (M = 40.4, SD = 3.8) and years of education ranging from 14 – 17, (M = 16.3, SD = 1.15). 10 matched controls were similarly recruited to match BL and were thus all male. Ages ranged from 56 – 66 (M = 60.1, SD = 3.784), and years of education ranging from 13 – 17 (M = 16.1, SD = 1.370). All participants provided their informed consent prior to participating in the experiment, and were compensated with a $15 Amazon e-Gift card for their participation in the approximately 1-hour long task.

Table 3

Neuropsychological Tests and Normative Z-scores for BR and BL

Test	BR's Z-Score	Description	BL's Z-Score	Description
CVLT (Immediate FR)	-2.33	Moderate impairment	-0.67	Average
CVLT (LDFR)	-3.50	Profound impairment	-1.00	Low average
CVLT (LDCR)	-3.00	Profound impairment	n/a	n/a
CVLT (Rec)	-2.50	Severe impairment	0.00	Average
CVLT (Total)	-2.33	Moderate impairment	n/a	n/a
LM-I (Immediate)	-1.00	Low average	-0.67	Average
LM-II (Delayed recall)	-1.00	Low average	-1.34	Borderline
LM Recognition (Delayed)	-0.67	Average	n/a	n/a
ROCF (Copy)	1.01	High Average	n/a	n/a
ROCF (Immediate)	-2.05	Borderline	-1.34	Borderline
ROCF (Delayed)	-2.05	Borderline	-1.64	Borderline
Block Design	0.33	Average	n/a	n/a
Vocabulary	0.25	Average	n/a	n/a
Matrix Reasoning	0.00	Average	n/a	n/a
Similarities	0.25	Average	n/a	n/a
Verbal Comprehension	0.61	Average	n/a	n/a
Perceptual Reasoning	0.75	High Average	n/a	n/a
Digit Span	0.67	High average	n/a	n/a
Stroop Task	0.67	High Average	n/a	n/a
Letter Fluency	n/a	n/a	0.33	Average
COWAT - Semantic Fluency	1.00	High Average	n/a	n/a
COWAT - Phonemic Fluency	-0.62	Average	0.33	Average
Trail Making Test A	-1.28	Low average	n/a	n/a
Trail Making Test B	-0.28	Average	n/a	n/a
WCST	n/a	n/a	0.20	Average
WASI-II FSIQ	0.67	High average	-0.54	Average

Note. List of neuropsychological tests administered to BR and BL, as well as normative Z-scores and descriptions for each score. Abbreviations: CVLT, California Verbal Learning Test; FR, Free recall; LDFR, Long-delay free recall; LDCR, Long-delay cued recall; Rec, Recognition; LM, Logical Memory; ROCF, Rey-Osterrieth Complex Figure; COWAT, Controlled Oral Word Association Test; WCST, Wisconsin Card Sort Test; WASI, Wechsler Abbreviated Scale of Intelligence; FSIQ, Full-scale intelligence quotient.

Materials

Target Items. An 80-item word list that consisted of a selection of verbal labels was created by Wammes et al. (2016) to guarantee that each of the words could be drawn easily (e.g., complex words to draw such as 'ballerina' were avoided in place for simple words such as 'pants'). This was done to reduce the amount of time required for participants to generate each drawing without necessitating excessive visual details to distinguish drawings. This word list consisted of words ranging in length of between 3 and 11 letters (M = 5.56, SD = 1.79), and in number of syllables from 1 to 4 (M = 1.63, SD = 0.72).

Notebook. Prior to the experiment, participants were sent a standardized notebook to use during the task to ensure controlled encoding settings. The notebook had 8.5 x 11inch pieces of unlined, blank white paper.

Filler Task. This distractor task lasted 1-minute, and consisted of simple arithmetic questions created from a list of 50 three-number questions. Each question consisted of numbers that ranged from 1-20. Half of the equations were true (e.g., 4 + 5 = 9), while half were false (e.g., 2 + 11 = 15), and participants were asked to determine whether the calculation was true or false.

Procedure

Prior to the experiment, participants were sent a Zoom link by the experimenter, and the entire study participation was completed via video-conferencing. Participants were reminded to have the notebook they were sent handy, to leave their phone in another room, and to use headphones during the experiment (to avoid any interfering noise). The experimenter shared one screen when launching the experiment using PsychoPy3.0.6 (Peirce et al., 2019), and had a second screen to view the participant during the task. Participants were informed that they

would be presented with a list of words on the screen, with a prompt to either write down or draw the word that they see. Importantly, there was no mention to participants that their memory for these words would later be assessed, i.e., this was a period of incidental encoding. If the prompt was to draw, they were instructed to draw a picture of the word for 40 seconds, using any extra time to elaborate on the details of the picture. If the prompt was to write, they were instructed to repeatedly write the word for 40 seconds on the page. After 40 second period had elapsed, the experimenter asked the participant to turn over to a new piece of paper with each new word or picture they were asked to write down. Once they were finished with each trial, they were instructed to turn the page over so that it was facing down and so that they did not see it again (ensuring no review of the drawings or words). The experimenter pressed the spacebar on their computer between each new trial, with the next prompt and word appearing. Prior to starting the task, participants completed two demonstration trials (one with a draw prompt, and one with a write prompt) to ensure that they understood the task instructions and procedure before beginning the task.

Encoding

From the 80-item word list created by Wammes et al. (2016), 30 words were randomly selected to be used for the encoding process (see Appendix A). Of those words, 15 were randomly assigned to the drawing condition, and 15 were assigned to the writing condition. Participants viewed their screen and saw either the draw or write prompt for 1 second, followed by a 500ms fixation point before the target word was displayed on the screen for 40 seconds. During this period, participants either drew or repeatedly wrote the word that was presented on the screen. Once the 40 seconds had elapsed, the experimenter reminded the participant to turn to

a new page in the notebook and clicked on the spacebar so that the next prompt and word would be displayed.

Once the encoding portion was finished and the 30 words had been either drawn or written down, participants were told that the experimenter would now be going to prepare the next part of the experiment, which would take approximately ten minutes. They were asked to turn off the light in their room, relax, close their eyes, and feel free to think about anything that came to their mind while the experimenter organized the next part of the study (Dewar et al., 2012). They were also told that the experimenter would be turning off their camera and audio so as not to disturb them during this time, and were reminded to remain in their seat during this time and just relax. The experimenter was able to ensure that participants were adhering to the instructions and not completing another activity (e.g., opening a book) through the Zoom call. The screen had a grey background with no stimuli presented and was timed to last for 9 minutes. Once the 9 minutes had elapsed, the experimenter turned their camera and audio back on and informed the participant that they were ready to continue the experiment.

Retention

Following the period of rest, a short interference task was used to ensure that any deliberate rehearsal during the post-encoding period was disrupted. Prior to the free recall and recognition portions of the task, this filler task acts as an interruption of any potential rehearsal strategies used to keep information within short term memory (McGhee et al., 2020). Participants were told they would next be shown some simple equations in the center of the screen, which had the words ‘TRUE’ and ‘FALSE’ beneath the equations on the left and right side of the screen, respectively. As the experimenter was sharing their screen and inputting the response from the participant on their end of the Zoom call, participants were instructed to say

"true" aloud if the equation was true, and "false" aloud if the equation was false. The experimenter would then click the left arrow key if they said true, and the right arrow key if they said false. Each equation was displayed on the screen until the participant's response was recorded. A 500ms inter-stimulus blank screen followed each equation, and the task lasted for 1-minute.

Free Recall

Following the filler task, participants were told that earlier in the experiment, they saw a variety of words on their screen and either drew them or wrote them down. In this portion of the task, they were instructed to try and recall aloud to the experimenter as many of the words as possible, regardless of whether they had drawn them or wrote them down. The experimenter recorded each of the words provided. Once the participant indicated that they could no longer recall any more words from the list, or was silent for 30 seconds, the experimenter probed them to determine whether they had any other words to report before moving onto the next portion of the task.

Recognition

Following the free recall segment, participants were given a recognition memory task, which consisted of 80 words in total, comprised of the 30 target words they had encoded, and 50 new, lure words. Participants were told that they would be presented with a list of words one at a time, and that some of these words were words they had either drawn or written down (targets) and that some of the words were new (lures). If they had seen the word during the encoding period, regardless of whether they had drawn it or written it down, they were instructed to say "yes" aloud. If the word was new, they were instructed to say aloud "no". Similar to the presentation of the filler task, on the left and right side of the screen beneath the presented words

were prompts for 'YES' and 'NO'. The experimenter would click the left arrow key if the participant said yes, and the right arrow key if the participant said no. The words were presented in a random order, consistent across participants. There was no time limit to the recognition memory task, and the experiment automatically ended once the responses to all 80 words had been recorded.

Analysis

In order to compare the patients' performance to that of the control group, we implemented methods developed by Crawford et al. (1998, 2002, 2010) which allow for the analysis of single-patient neuropsychological case studies. This statistical methodology uses a modified t-test to compare the difference between patients and matched control samples performance on either single or multiple measures. We used the Singlims.exe software made publicly available (accessible from: https://homepages.abdn.ac.uk/j.crawford/pages/dept/psychom.htm) in order to compare the differences in free recall for drawn versus written words between patients and the controls. We used a separate software developed by Crawford et al., (2005, 2010) to assess for the difference in the size of the drawing effect (i.e., analyzing the difference in proportion of drawn compared to written recalled words). Specifically, the Revised Standard Difference Test (RSDT) was utilized. This software implements methods that determine whether a difference lies between a single-case (patient) performance on two tasks, by analyzing the difference in comparison with a matched control sample. The RSDT.exe software similarly performs the Singlims.exe analysis, which allows for the calculation of both single and multi-test comparisons. This software is also accessible by the above link. Finally, when comparing memory performance results for the control groups, paired sample t-tests were calculated.

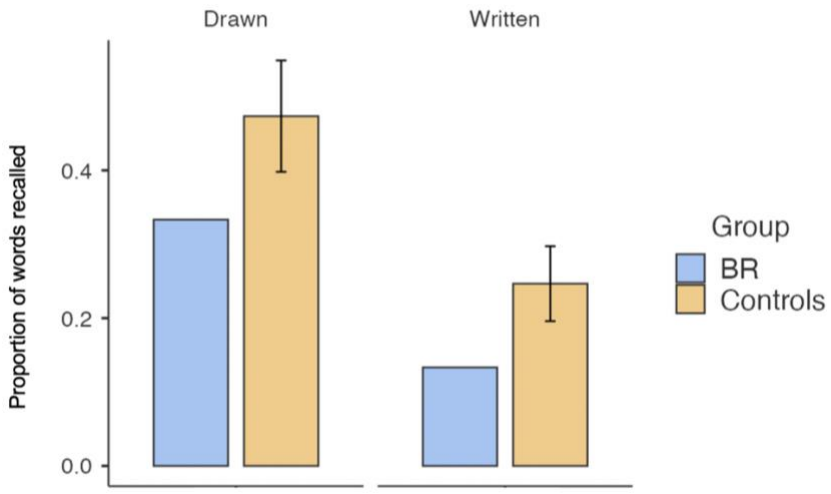
Results

Free Recall: BR

BR recalled a larger proportion of drawn words (0.333) compared to written words (0.133), resulting in a proportional difference of words recalled between conditions of 0.2. Interestingly, BR indicated awareness into her increased recall for drawn words, with a statement saying that she “could remember the drawings better than the words”. BR’s matched control group similarly recalled a significantly larger proportion of drawn words ($M = 0.473$, $SD = 0.238$) compared to written words ($M = 0.247$, $SD = 0.160$), $t(9) = 2.459$, $p = 0.022$, $d = 1.116$ (see Figure 7).

Figure 7

Free Recall Performance of BR Compared to Controls



Note. BR recalled a higher proportion of drawn words (0.333) than written words (0.133). The control group recalled a significantly larger proportion of drawn words (M = 0.473, SD = 0.238) compared to written words (M = 0.247, SD = 0.160).

Next, we compared BR's free recall performance to that of the control group. The results indicated that no evidence for a significant difference between the drawn words recalled by BR (0.333) and controls (M = 0.473, SD = 0.238), t = -0.560, p = 0.294, d = 0.831. When comparing BR to controls on written word performance, we similarly found no evidence for a significant difference in recall of BR (0.133) and controls (M = 0.247, SD = 0.160), t = -0.673, p = 0.259, d = 0.997.

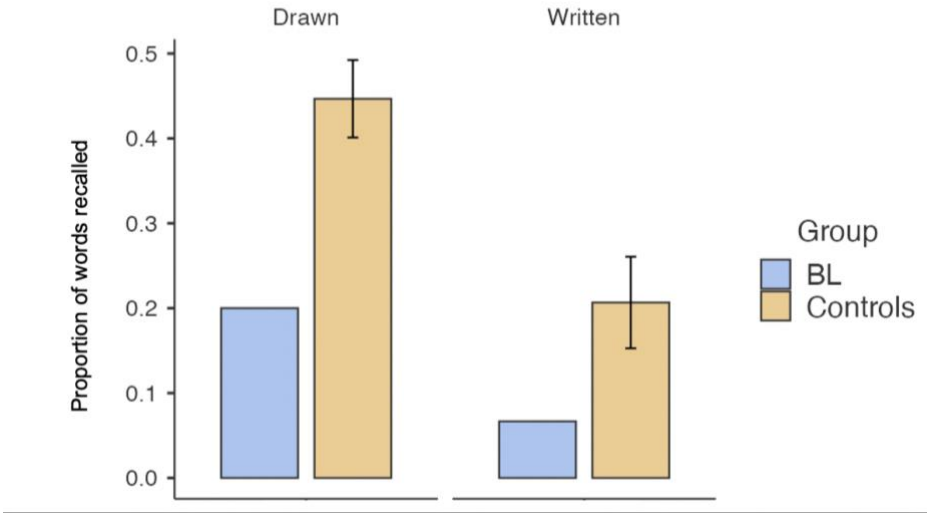
Next, we assessed for the difference in the size of the drawing effect (i.e., analyzing the difference in proportion of drawn compared to written recalled words). The results from this analysis indicated no evidence for a significant difference in the drawing effect between BR (0.2) and controls (M = 0.226, SD = 0.078), $t(9)$ = 0.083, p = 0.935, d = 0.094.

Free Recall: BL

In terms of BL's free recall, he recalled a larger proportion of drawn words (0.2) than written words (0.067), with an overall difference between drawn and written words of 0.133. Similarly, the control sample displayed a significant difference between the drawn ($M = 0.447$, $SD = 0.144$) and written words ($M = 0.207$, $SD = 0.171$), $t(9) = 3.398$, $p = 0.032$, $d = 1.520$; see Figure 8).

Figure 8

Free Recall Performance of BL Compared to Controls



Note. BL recalled a higher proportion of drawn words (0.2) than written words (0.067). The control group recalled a higher proportion of words that were drawn (M = 0.447, SD = 0.144) compared to words that were written (M = 0.207, SD = 0.171).

Next, using the modified t-tests developed by Crawford et al., (1998, 2002, 2010), we used the Singlims.exe software to analyze the differences between BL and the controls for their recall for the drawn and written words. The findings display no evidence for a significant difference for the drawn words by BL (0.2) and controls (M = 0.446, SD = 0.144), t = -1.632, p = 0.137, d = 2.414. We next analyzed BL's recall performance for the written words (0.0667) compared to the controls (M = 0.207, SD = 0.171), and again found no evidence for significant differences between the two groups, t = -0.782, p = 0.454, d = 1.158.

In order to analyze the difference in the size of the drawing effect, we used the RSDT.exe developed by Crawford et al., (2005, 2010). The findings did not display evidence for a

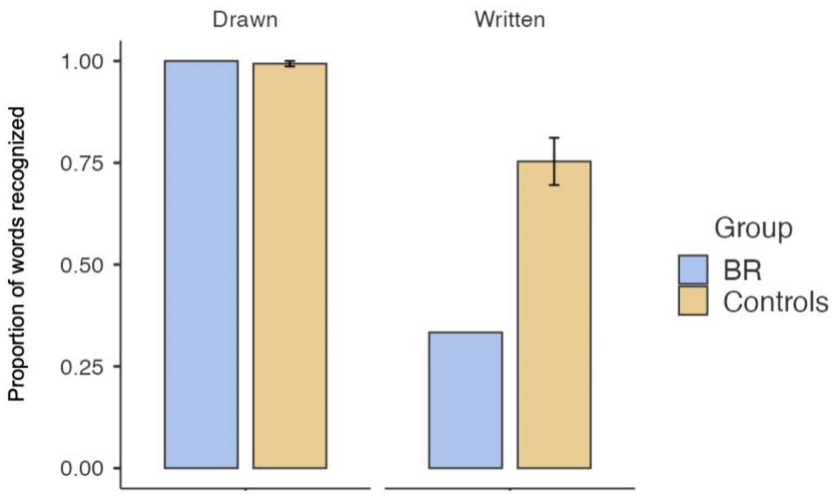
significant difference in the magnitude of the drawing effect between BL (0.133) and the control participants (M = 0.24, SD = 0.209), $t(9)$ = 0.060, p = 0.563, d = 0.722.

Recognition: BR

BR correctly recognized all of the drawn words, and the control group had a similarly high proportion of recognition for the drawn words (M = 0.993, SD = 0.021). She performed at ceiling and correctly recognized all the drawn words (15 in total) compared to recognizing only 5 of the written words. She therefore recognized a decreased proportion of written words (0.333) while the controls recognized a higher proportion (M = 0.753, SD = 0.183). She also incorrectly recognized 2 out of the 50 lure items. Similarly, the control group recognized significantly more drawn words (M = 14.9, SD = 0.316) compared to written words (M = 11.3, SD = 2.751), $t(9)$ = 4.111, p = 0.0006, d = 1.839, with a mean value of M = 0.7 for incorrectly recognizing false alarms (SD = 1.567; see Figure 9).

Figure 9

Recognition Performance of BR Compared to Controls



Note. BR recognized all of the drawn words, and the control group also recognized a high proportion of the drawn words (M = 0.993, SD = 0.021). For the written items, BR recognized a proportion of words 0.333, while the controls recognized a higher proportion (M = 0.753, SD = 0.183).

We next analyzed whether BR and the controls differed in their recognition responses for drawn and written words using the Singlims.exe software (Crawford et al., 2002, 2005). There was no evidence for significant differences between the recognized drawn words by BR (15) and controls (M = 14.9, SD = 0.316), t = 0.32, p = 0.385, d = 0.447. However, for written words, BR correctly recognized a total of 5, while controls recognized a higher amount, (M = 11.3, SD = 2.751), leading to a significant difference, t = -2.184. p = 0.028, d = 3.239.

Furthermore, we assessed recognition memory by using the d-prime (d') statistic as a measure of sensitivity for recognition accuracy scores. Specifically, d' takes into account the total number of hits, regardless of condition, and false alarm rates and is used to ensure that both groups of participants recognized the encoded words above the chance level. The results

indicated that BR, with a d' = 2.181, and controls (M = 3.744, SD = 1.279) performed above the level of chance, and were not significantly different from each other $t(9) = -1.164$, $p = 0.274$, $d = 1.728$.

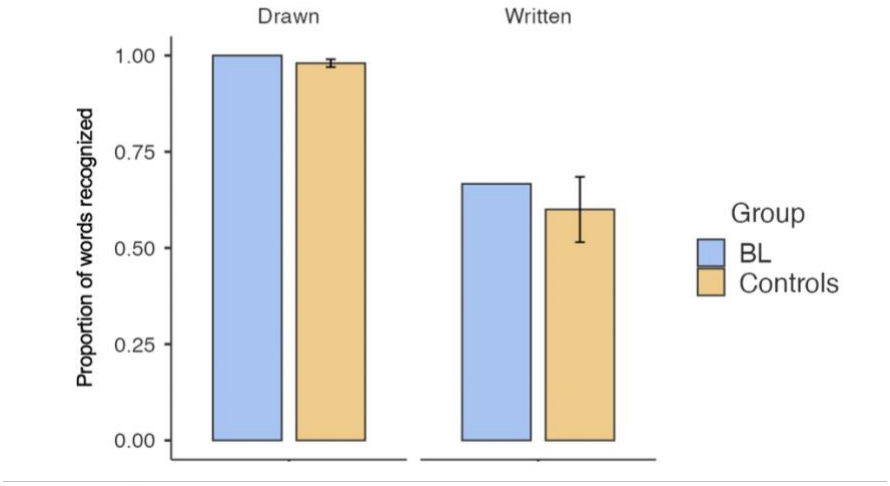
We used the RSDT to analyze the drawing effect for the recognition results. There was no evidence for a significant difference in the size of the drawing effect for BR (10) and the controls (M = 3.6, SD = 2.434), $t(9) = 1.785$, $p = 0.108$, $d = 3.688$. However, the result of a one-tailed calculation displays a value of $p = 0.054$, indicating borderline significance. Therefore, in terms of her performance on the recognition task, it appears that BR displays marginally differing results ($p = 0.054$) compared to control sample.

Recognition: BL

BL correctly recognized each of the drawn words, and the control group also recognized a high proportion of the drawn words (M = 0.98, SD = 0.032). He correctly recognized all 15 of the drawn words, and 10 of the written words, i.e., a proportion of 0.666, with the control group recognizing a similar proportion of words (M = 0.6, SD = 0.269). He also incorrectly identified 3 out of the 50 lure items. The control group recognized significantly more drawn words (M = 14.7, SD = 0.483) than written words (M = 9.00, SD = 4.028), $t(9) = 4.443$, $p = 0.0003$, $d = 1.987$, with a false alarm mean of $M = 0.5$ for incorrectly recognizing lures (SD = 0.707; see Figure 10).

Figure 10

Recognition Performance of BL Compared to Controls



Note. BL recognized each of the drawn words, with the control condition also recognizing a high proportion of the drawn words ($M = 0.98$, $SD = 0.032$). BL recognized a proportion of 0.666 of the written words, with the control group recognizing a similar proportion of written words ($M = 0.6$, $SD = 0.269$).

Next, we analyzed whether a difference in recognition results existed between BL and controls. For the drawn words, there was no evidence for a significant difference in recognition between BL (15) and the control group ($M = 14.7$, $SD = 0.483$), $t = 0.592$, $p = 0.568$, $d = 0.878$. The analysis for the written words also displayed no evidence for a significant difference in recognition performance between BL, who correctly recognized 10 of the written words, compared to the controls ($M = 9.00$, $SD = 4.027$), $t = 0.237$, $p = 0.818$, $d = 0.351$. BL's and the controls sensitivity index indicated performance above chance, with a d' = 2.522, and $M = 3.269$, $SD = 0.997$, and were not significantly different, $t(9) = -0.712$, $p = 0.247$, $d = 1.059$.

Finally, the RSDT was used to study the drawing effect in terms for the scores on recognition. This analysis indicated no evidence for a difference in the drawing effect for BL (5) compared to the control group ($M = 5.7$, $SD = 4.057$), $t(9) = 0.237$, $p = 0.818$, $d = 0.244$.

Table 4

Free Recall and Recognition Data: BR and Controls

Participant ID	Free Recall Drawn Proportion	Free Recall Written Proportion	Recognition Drawn # of Hits	Recognition Written # of Hits	# of False Alarms	d'
BR	0.3333	0.1333	15	5	2	2.1814
DR_001	0.5333	0.4	15	15	0	6.0454
DR_002	0.4	0.2	15	7	1	2.6767
DR_005	0.2	0.2	15	12	1	3.3353
DR_007	0.6	0	14	10	0	3.1680
DR_009	0	0.2667	15	7	0	2.9493
DR_011	0.4667	0.2	15	12	0	3.6079
DR_013	0.4	0.2667	15	12	0	3.6079
DR_014	0.6667	0.2	15	11	5	2.3923
DR_018	0.8	0.6	15	15	0	6.0454
DR_019	0.6667	0.1333	15	12	0	3.6079

Table 5

Free Recall and Recognition Data: BL and Controls

Participant ID	Free Recall Drawn Proportion	Free Recall Written Proportion	Recognition Drawn # of Hits	Recognition Written # of Hits	# of False Alarms	d'
BL	0.2	0.0667	15	10	3	2.5222
DR_003	0.2667	0.2667	14	9	0	3.0543
DR_004	0.4667	0.5333	15	13	0	3.8274
DR_006	0.4667	0.2667	15	12	1	3.3353
DR_008	0.2667	0.0667	14	6	0	2.7571
DR_010	0.2667	0.2	15	8	2	2.4786
DR_012	0.5333	0.2	14	12	0	3.4371
DR_015	0.6	0.4	15	15	1	5.7728
DR_016	0.4	0	15	2	1	2.2216
DR_017	0.5333	0	15	5	0	2.7571
DR_020	0.6667	0.1333	15	8	0	3.0543

Discussion

The goal of this study was to determine whether the beneficial mnemonic effect of drawing would increase memory performance in patients with focal hippocampal damage. The findings demonstrate that this strategy enhances performance on both recall and recognition measures in hippocampal amnesia patients, and the size of this effect is similar to that observed in healthy matched control participants.

BR demonstrated increased free recall for the drawn compared to written words, and the number of drawn words recalled was comparable to the control group. Similarly, the number of written words she recalled was not display evidence for a significant difference compared to the matched control sample. BL also recalled a higher proportion of drawn compared to written words, with his free recall results on both the drawn and written words not displaying evidence for differing significantly from the control group. These findings indicate that although the two patients suffer from hippocampal amnesia, which characteristically impairs memory for delayed recall, the paradigm of implementing drawing as an encoding strategy can boost memory performance to the level of healthy controls.

The finding that BR's free recall performance was comparable to controls is particularly interesting given aspects of her neuropsychological profile. On measures of episodic verbal learning and memory, assessed by the CVLT-II, BR's free recall scores were in the impaired range on the total number of words recalled. She also exhibited borderline performance in the long delay free recall section, and profound impairment on the long delay cued recall portion of the task. Furthermore, on the ROCF, a measure of visual memory which involves drawing a series of arbitrary shapes, BR displayed impaired scores on the immediate and delayed conditions. However, this study displays that with a 10-minute delay, that included an interference task, BR was able to successfully recall more drawn words than written words, a

result that is in line with the healthy participants. In a similar vein, BL's neuropsychological profile indicated low average performance on the long delay free recall portion of the CVLT-II. As well, his performance on recall for both the immediate and delayed sections of the ROCF were in the borderline range. However, he too demonstrated free recall results with evidence that they were not significantly different from healthy controls. Compared to other methods of encoding, this finding of enhanced free recall in both patients who previously displayed difficulty in this domain is indicative of the strong mnemonic benefits of utilizing drawing as an encoding strategy.

Both patients performed at ceiling and correctly recognized all of the drawn words from encoding, in line with the performance of both control groups. However, BR recognized a significantly smaller proportion of written words than the controls, while BL's recognition for the written words displayed evidence that were not significantly different from the controls. It is possible that the differences in neural substrates between the two patients may contribute to this difference in recognition task performance. Specifically, although both patients have bilateral hippocampal damage, there are some differing areas that are impaired; while BR has damage to the CA1 sub region of the hippocampus, the CA1 and subfield surrounding the hippocampus in BL was relatively spared. Rodent research has shown that the CA1 region of the dorsal hippocampus is critically involved in the consolidation pathway for recognition memory tasks and displays activation during the recognition of familiar material (Wan et al., 1999). Importantly, the CA1 region of the medial temporal lobe is the final destination of the pathway for the consolidation of recognition memory tasks (Mello-Carpes & Izuierdo, 2013). Perhaps the damage to BR's CA1 subfield thus impacted her recognition for the written words, while the drawn words did not undergo decline due to the stronger encoding mechanism that had been

employed. Conversely, the CA1 subfield in BL was undamaged, and he did not display impaired performance on the recognition task. Nonetheless, the encoding strategy used for the drawn words boosted recognition memory compared to the written words.

In addition to the differences in neural substrates that may impact the patients' recognition results, we can gain further insight from these differing recognition performance scores from their neuropsychological profile. On the CVLT-II, BR's long delay recognition scores were in the severely impaired range, while BL's recognition scores were average. It is possible that the role of the CA1 subfield is displayed in these differing results well. However, even with the damaged CA1 subfield in BR, her recognition for the drawn words was at ceiling, further underscoring the powerful effect of drawing as an encoding mechanism. Interestingly, on both measures of recall and recognition, there was no evidence to display a significant difference in the drawing effect between the patients and controls. Therefore, this finding indicates that although patients with hippocampal amnesia experience declarative memory deficits, the benefits of enhanced memory seen in the drawing effect is similar to the experience of a matched control sample.

Our research provides evidence for drawing being an enhanced encoding strategy, as it facilitates the integration of both the fundamental verbal memory trace, while also incorporating multisensory information from the encoding procedure (Wammes et al., 2018). The rich elaborative encoding process that is involved in drawing contributes to the distinct representation created (Fernandes et al., 2018). This strong memory trace consists of three separate, yet integrated factors: the semantic elaboration tactic employed when determining how to complete the drawing, proposed by Craik & Lockhart (1972), gesture-based learning, initially described by Engelkamp & Zimmer (1989) that involves motor information from the act of drawing out the

image, and the dual coding that is exhibited in the picture-superiority effect (Paivio et al., 1968). Wammes et al. (2018) outlined how each aspect of this integrated trace is displayed as participants can retrieve particular contextual features from the initial encoding procedure for drawn, compared to written, items. The successful retrieval of a memory trace is driven by recollection-based memory, which is comprised of contextually rich details from the initial encoding (Gardiner, 2001; Tulving, 1983). Each of these encoding steps protects the memory trace from interference as a distinct representation of the word has been created (Craik et al., 2012). The distinctiveness of the encoded memory is a result of elaborative mechanisms that result in a differentiated trace that can be more uniquely specified and subsequently, retrieved with ease (Carr et al., 2015). Importantly, the hippocampus is able to protect the memory trace from interference by separating overlapping representations (Koolschijn, 2019). However, patients with damage to the hippocampus are impaired in this ability and are left with memory traces that are particularly vulnerable to interference (Craik et al., 2012).

Therefore, although the encoding process is disrupted in MTL patients, there are certain mechanisms that can enhance encoding in these patient populations. Our results display the evident impact that the drawing effect has on patients, while also highlighting the underlying neurocognitive mechanisms involved. As discussed earlier, the act of drawing involves creating a strong memory trace by engaging in a rich, multi-modal elaborative encoding process that combines visual, motor, and semantic components. These elements are each associated with regions that are functionally distinct from the hippocampus, and therefore, we propose that drawing supports word-learning by specifically engaging in non-declarative memory processes.

For example, drawing employs the undamaged visual pathways to direct the perceptual elements of the task. When the primary visual cortices and ventral visual pathway are intact in

hippocampal amnesic patients, the benefits of studying pictures as opposed to words likely rely on the engagement of perceptual processing systems (Ally, 2012). Previous studies of patients with hippocampal amnesia have also displayed the benefit of the visual modality as they displayed increased recognition for pictures opposed to words. Specifically, Barbeau et al. (2005) found that when material was encoded in the verbal modality, amnesic patients performed poorly on recall and recognition tests. However, when encoding engaged the visual modality, typical performance was seen on tests of visual recognition. This result is particularly in line with our findings which showed patients BR and BL performing at ceiling on the recognition portion of the test in particular. Work by Aggleton & Shaw (1996), Vargha-Khadem et al. (1997), Mayes et al. (2002), and Yonelinas et al. (2002) have found that while patients with hippocampal lesions display severe impairment in recall memory, recognition memory is may be slightly more preserved. This, in addition to the picture-superiority effect seen in patients with memory disorders, can explain the increased benefit on memory for drawn words, and specifically on the recognition test as displayed in our study.

The incorporation of motor information may also add to the neurocognitive mechanistic account for the drawing effect. Previous research has shown that the act of gesturing can enhance a memory trace when learning words through recruitment of the motor system in healthy controls (Ianì & Bucciarelli, 2017) and hippocampal patient populations (Hilverman et al., 2018). Specifically, Hilverman et al. (2018) theorize that this memory boost is attributable to the activation of extra-hippocampal brain regions that are engaged in non-declarative memory processes. Presumably, our study displays that drawing similarly taps into non-hippocampal-mediated processes, including the motor modality that is associated with regions left intact. As drawing requires deliberate motor engagement relevant to the word-learning task, this act may

recruit procedural memory, i.e., components of the non-declarative memory system (Knowlton, Mangels, & Squire, 1996; Hilverman et al., 2018). Indeed, the benefits of employing the motor modality during memory encoding dissipate when the motor action is unrelated to the task (Ianì & Bucciarelli, 2017).

Finally, the semantic elaboration that is required when determining how to draw a picture of a word recruits prior knowledge, and is a feature of memory encoding that may have effects on subsequent memory strength (Lockhart et al., 1990; Craik, 2002). Semantic evaluations enhance the mental representation and enrich the encoding process which result in boosted subsequent memory performance (Amlein et al., 2019). Our findings are inconsistent with some previous literature, which described patients with hippocampal damage displaying impaired performance on tasks of semantic elaboration (Race et al., 2013). However, in that study, encoding took place in the verbal modality. As the semantic elaboration during encoding in our task recruited motor and visual components as well, it is possible that the amalgamation of the multi-sensory features contributed to the patients' enhanced memory for drawn words.

As we found evidence indicating that BR and BL performed comparably to controls on this declarative memory task for both drawn and written words, we should also take into account the brief period of rest they experienced post-encoding. Post-encoding sleeping is a well-known memory consolidation phenomenon which enhances memory performance for learned information (Stickgold, 2005) as during sleep, hippocampal-dependent memories undergo reactivation, leading to enhanced memory traces (Ellenbogen et al., 2006). However, even brief periods of wakefulness while an individual is not engaging in sensory stimulation or a cognitively demanding task can improve memory performance (Cowan et al., 2004; Craig et al.,

2015; Dewar et al., 2012). The enhanced performance on this declarative memory task should thus also consider the effects of enhanced consolidation that accompanies periods of rest.

Limitations and Future Directions

The nature of completing research on patient populations includes the caveat of a small number of participants, both in terms of the patients and matched controls. Thus, the results of this case-study should be replicated in larger groups of participants in order to confirm the effects seen with the drawing effect consolidation method that produces enhanced memory performance. Continuing to research these findings in populations with damage to the hippocampus would support the generalization of these results.

In future work we would like to propose the investigation of the drawing effect across a wide range of patients with varying severity of memory dysfunction; although BR and BL fall under the hippocampal amnesic range, perhaps patients with higher levels of memory impairment may also benefit from the mnemonic memory boost. Furthermore, as BR and BL performed comparably to controls in most aspects testing, and it would be interesting to increase the level of challenge to determine whether the drawing effect holds with increased interference. Here we included a longer resting period and relatively brief (1-minute) interference period. Thus, we are unable to evaluate the extent to which the drawing effect was impacted by post-encoding rest. Future work should specifically manipulate rest and interference epochs to distinguish these effects from the primary drawing versus writing manipulation.

Conclusion

Although drawing has been shown to be a superior encoding method compared to writing, with benefits such as improved declarative memory performance in a variety of populations (Ferdandes et al., 2018), it was not known whether patients with damage to the

hippocampus would similarly benefit from the mnemonic strategy. Furthermore, as the memory deficits experienced by individuals with hippocampal amnesia are extensive, developing tools or strategies that can ameliorate their impairment is of upmost importance. This study provides evidence that hippocampal amnesia patients do show enhanced memory performance after encoding drawn information. Our evidence displays how patients recalled a comparable amount of both drawn and written words as the control participants, yet overall recalled a larger proportion of drawn words compared to written ones (see Figures 7 and 8). Furthermore, the patients recognized more drawn words than written words, with false alarm rates similar to controls (see Figures 9 and 10).

Ultimately, these findings demonstrate that drawing pictures as an encoding strategy is beneficial for boosting memory performance in hippocampal amnesic patients. Our results provide further evidence for the efficacy of the drawing effect by displaying the beneficial impact drawing has on patients with hippocampal amnesia and adds to the robust findings that previously demonstrated these effects in populations with MCI and dementia (Ally, 2012). Drawing particularly allows for the advantage of enhancing day-to-day memories by creating a visual depiction of images or graphical information as a method to remember daily events. Incidentally, one of the patients commented on the study, noting enhanced recollection of the drawn, compared to written, words and said “they should publish that for people with brain injuries so they could use it as a tool. I’m going to tell my husband that”, indicating insight into the stark potential benefits that drawing can have on day-to-day life. Continuing to research strategies that can lead to enhanced memory performance is a critical step forward in enriching the life of individuals with memory deficits. Here, we show that drawing can be utilized as a tool to improve the memory, and subsequently, lives, of those with memory impairments.

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Appendix

80-Item Target Word List[1]

airplane	couch	kite	ruler
ant	cow	knife	sailboat
axe	desk	ladder	scissors
balloon	doll	lamp	screwdriver
banana	door	lemon	sheep
bee	drum	lion	shoe
beetle	duck	lips	skirt
blouse	ear	monkey	spider
boot	elephant	mushroom	spoon
broom	flute	owl	stool
butterfly	fork	pants	stove
camel	frog	peanut	strawberry
cannon	giraffe	pear	sweater
carrot	glove	penguin	toaster
cat	grapes	pepper	trumpet
caterpillar	guitar	pig	turtle
cherry	hammer	pineapple	violin
clock	harp	pumpkin	wagon
coat	jacket	rabbit	whistle
corn	kettle	rooster	wrench

[1] Information from Wammes et al., 2016, *The Quarterly Journals of Experimental Psychology*.