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## Chronic Exercise and Memory Interference

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CHRONIC EXERCISE AND MEMORY INTERFERENCE

by  
Lisa Marie Vogelgesang

A thesis submitted to the faculty of The University of Mississippi in partial fulfillment of  
the requirements of the Sally McDonnell Barksdale Honors College.

Oxford  
April 2021

Approved by

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## ABSTRACT

LISA MARIE VOGELGESANG: Chronic Exercise and Memory Interference

(Under the direction of Paul Loprinzi)

This online study examined whether chronic exercise is associated with attenuated memory interference. Sixty-three healthy, young adults completed an interference task (AB/AC-paradigm) and self-reported the number of days and minutes a day they engaged in moderate-to-vigorous physical activity. We found that proactive interference (PI), but not retroactive interference (RI), occurred but none of the exercise modalities significantly impacted PI. Future studies should evaluate whether different interference tasks display diverse sensitivities to exercise-induced changes in memory interference. Moreover, other potential modulating factors, such as the duration and intensity of the exercise should be controlled for.

*Keywords:* Declarative Memory; Exercise Modalities; Forgetting; Habitual Exercise; Learning

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## LIST OF ABBREVIATIONS

Arc mRNA	Messenger RNA (Ribonucleic acid) of Activity-regulated cytoskeleton-associated protein
BDNF-TrkB receptor pathway	Signal pathways that involve Brain-Derived Neurotrophic Factor (BDNF) and tropomyosin receptor kinase B (TrkB) receptors
BMI	Body Mass Index
CAMKII	Ca <sup>2+</sup> /calmodulin-dependent protein kinase II
CREB	cAMP (Cyclic adenosine monophosphate) response element-binding protein
GLUA1 AMPA receptors	Glutamate ionotropic receptor AMPA ( $\alpha$ -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor) type subunit 1
GLUA2 AMPA receptors	Glutamate ionotropic receptor AMPA ( $\alpha$ -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor) type subunit 2
LTM	Long-Term Memory
LTP	Long-Term Potentiation
mTOR-TOP pathway	Signal pathway that involves mechanistic target of rapamycin (mTOR)
MVPA	Moderate-to-vigorous physical activity
NMDA	N-methyl-D-aspartate receptor
PKM $\zeta$	“Truncated, persistently active isoform of atypical protein kinase C-zeta (aPKCzeta), which lacks the N-terminal pseudosubstrate regulatory domain” (Drier et al., 2002)
PI	Proactive Interference
PSD	Post Synaptic Density
Rac-PAK cascade	Signal pathway that involves p21 activated kinase (PAK)



RAVLT	Ray Auditory Verbal Learning Test
Repeated measured ANOVA	Repeated measured analysis of variance
Rho-Rock cascade	Signal pathway that involves Rho-associated protein Rho kinase (ROCK)
RI	Retroactive Interference
SD	Standard Deviation
STM	Short-Term Memory
UPS	Ubiquitin/proteasome system
VWFA	Visual Word Form Area

## **Background**

Proper memory function is important for our daily functioning. We rely on our ability to retrieve memories to evaluate and plan present and future behavior (Hassabis et al., 2007). Consequentially, it is important to look at factors that might impact factors that interfere with our memory.

### **Model Overview of Memory Interference**

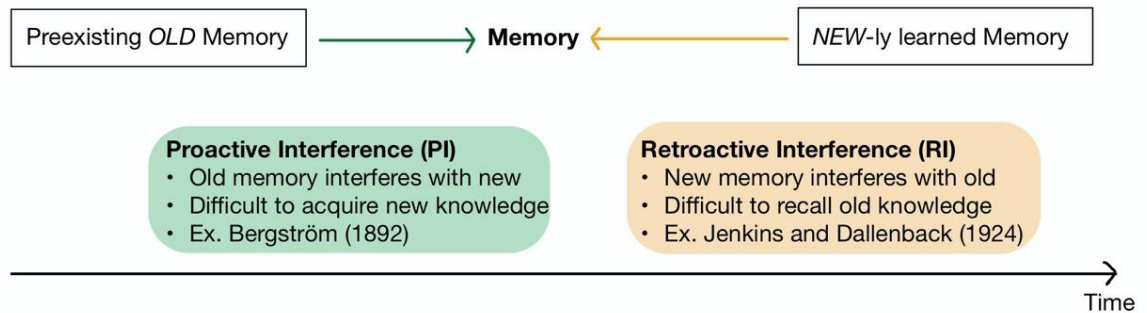
The concept of memory interference was first observed by Bergström in 1893. He let participants sort two decks of cards into two piles and measured the time they needed. When the location of the second pile changed, their sorting speed decreased (Bergström, 1893). This showed that information about the original location interfered with learning the latter location. Similarly, Jenkins and Dallenbach in 1924 showed that participants who slept after encoding retained more words compared to participants who did not sleep shortly after encoding. This showed that subsequent exposure to stimuli can interfere with previously encoded information.

The concept underlying these findings became to be known as interference. There are two kinds of interference, proactive and retroactive interference (Figure 1). Proactive interference (PI) occurs when preexisting memories interfere with the acquisition of new memory traces. Thus, it is difficult to acquire new knowledge. The study conducted by Bergström is an example of PI (Bergström, 1893). The preexisting memory of the original location of the second pile interferes with learning the new location. Therefore, participant's sorting speed got slower. Moreover, an inability to inhibit PI had also been associated with the induction of false memories and a reduction in leaning efficiency (Li

et al., 2020). The other kind of interference is retroactive interference (RI) and refers to newly learned material that is interfering with preexisting knowledge. As a result, it may be difficult to recall old memories. This effect was illustrated by Jenkins and Dallenback (1924): participants who were active and acquired new knowledge did not remember as many words that were previously learned compared to participants who slept and had no new input.

**Figure 1**

*Proactive and Retroactive Memory Interference*



### **From the Word on the Paper to the Image in our Mind**

In order to understand why memory interference takes place and we forget certain words from a list, it is helpful to first consider how we perceive visual stimuli such as words, how we process and comprehend the words, and how we form memories. This information will be discussed in the narrative that follows.

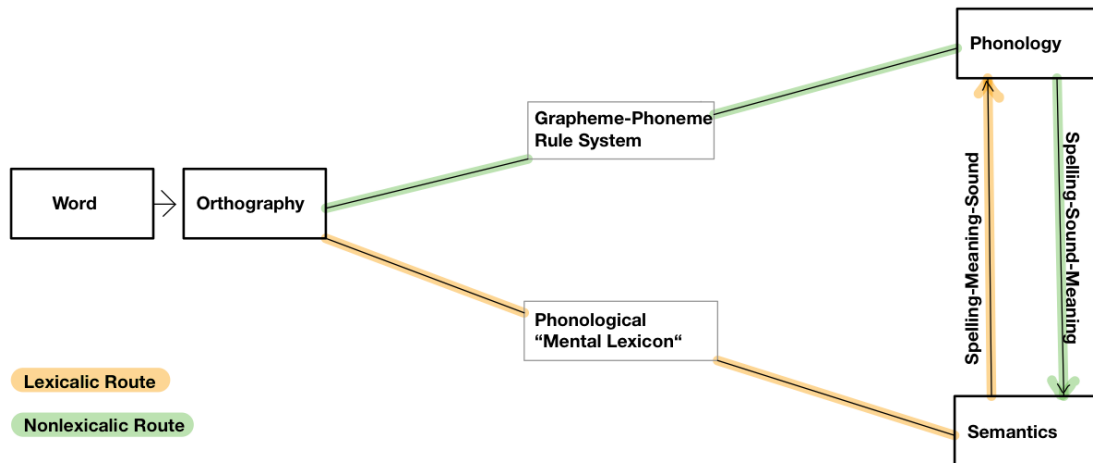
**Perception of Visual Stimuli.** Through perception by sensory organs, external stimuli are translated into electrical signals (Efron, 1969). In this section, I will be focusing on the perception and processing of visual stimuli since this study involves reading comprehension. Visual information is analyzed by two separate systems that serve different functions. Both underlying pathways originate in the primary visual cortex

(Figure 4) (Mishkin et al., 1983; Mishkin & Ungerleider, 1982). The ventral pathway serves the identification of objects and is also called the *what* stream. It connects the primary visual cortex through the dorsal visual areas with the parietal cortex (Walsh & Butler, 1996). The dorsal pathway focuses on the location of objects and is known as the *where* stream (Ungerleider and Pasternak, 2004, pp. 541–562). It runs from the primary visual cortex through the ventral visual area to the inferior temporal cortex (Walsh & Butler, 1996).

**Dual Route Theory – Processing and Comprehension of Words.** Early research demonstrated that some functions/features including language are lateralized, meaning that one hemisphere dominates over the other (Breedlove & Watson, 2020, p. 632). In about 90-95 % of humans, the left-hemisphere is specialized for language (Breedlove & Watson, 2020, p. 637). While there are different theories on how reading out loud takes place, it is agreed upon that dual routes lead to reading comprehension (Coltheart, 2005). Reading comprehension aims to transform the printed word into meaning (Coltheart, 2006). During reading, two routes, the **nonlexical** and **lexical route**, are utilized to analyze the information conveyed through the language and finally access the meaning of the written word (Figure 2). The former aims to analyze the sounds of words and letters (*phonology*) while the latter focuses on their meaning (*semantics*) (MacCarthy & Warrington, 1999).

**Figure 2**

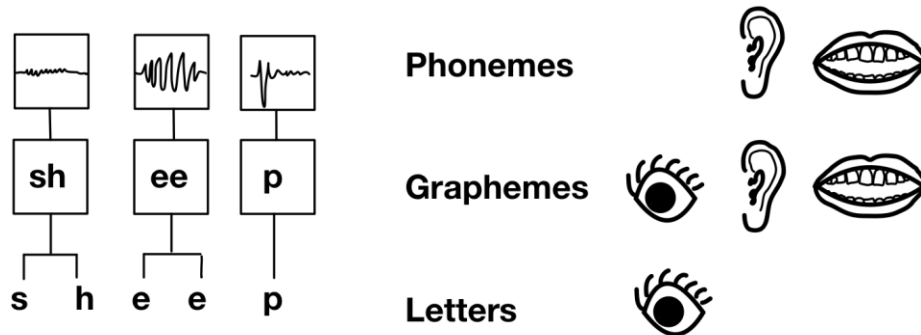
*Dual Route Theory*



**Nonlexical Route.** Words are comprised of letters which form graphemes. Graphemes are written versions of phonemes. For instance, the word ‘sheep’ has five letters but only three graphemes (Figure 3). The nonlexical route uses a grapheme-phoneme rule system to associate letters (orthography) such as s-h-e-e-p through graphemes sh-ee-p with phonemes (Coltheart, 2005). The phonemes help to create a full phonemic representation which is used to assess the meaning of the word (Coltheart, 2005)

**Figure 3**

*Nonlexical Route: A Grapheme-Phoneme Rule System*



**Lexical Route.** The lexical route relies on a ‘mental lexicon’. In this ‘mental lexicon’, memories about the spelling and pronunciation of words and letter strings are stored (Coltheart, 2005; Seidenberg, 1995). This information is directly associated with the meaning (Jobard et al., 2003). The association gets stronger as individuals come across words more frequently and the ‘mental lexicon’ gets larger as individuals gain reading experience (Jobard et al., 2003).

**Associated Brain Regions.** A meta-analysis conducted by Jobard et al., (2003) compared 35 neuroimaging studies to investigate which brain areas are involved in reading. They found that, at first, the left occipitotemporal region, which is also known as Visual Word Form Area (VWFA), is activated. The occipitotemporal region is in the ventral route and located between the inferior temporal and fusiform gyri (Jobard et al., 2003).

Interestingly, the lexical and nonlexical routes show different activation patterns supporting the dual route theory. When the nonlexical route is activated, left lateralized brain structures, such as superior temporal areas, supramarginal gyrus, and the opercular part of the inferior frontal gyrus, are especially active. In contrast to that, the lexical route is associated with activity in the VWFA and semantic areas, which include the basal

inferior temporal area, the triangular part of inferior frontal gyrus, as well as the posterior part of the middle temporal gyrus (Jobard et al., 2003).

### **How the Image in Our Mind Gets Stored**

After addressing at how written words are perceived and processed in the brain, we will now explain how they are stored in our memory so that they can be recalled later on. First, we will give an overview about how memory formation takes place on a synaptic level. Secondly, we will discuss the widely accepted division of memory into long-term memory (LTM) and short-term memory (STM).

**On A Synaptic Level – The Memory Trace.** While the processes on a synaptic level are generally known, it is not yet completely understood how behavioral experiences are made/translated into memories. Most researchers believe that interaction with the environment leads to behavioral experiences, which generate memory traces and ultimately strengthen synapses in specific regions of the brain (Rudy, 2014, p. 153; Squire, 1992). Assuming this persistent strengthening of the synapses, also known as long-term-potential (LTP), is the underlying mechanism of memory formation, there are four overlapping states that a synapse undergoes (Figure 5).

**Stages of Memory Formation.** The four stages that ultimately lead to strengthening of the synapse include generation, stabilization, consolidation, and maintenance. During generation, calcium enters the spine through NMDA receptors. Calcium in combination with calmodulin activates CAMKII, a kinase whose autophosphorylation facilitates that additional GLUA1 AMPA receptors, become trapped in the post synaptic density (PSD) (Rudy, 2014, pp. 63–68). Moreover, actin filaments are disassembled, which helps to trap even more GLUA1 AMPA receptors in the PSD. While the generation of a memory trace

is achieved in about one minute, the stabilization of the trace takes about 10-15 minutes. More calcium continues to enter the spine, which activates several cascades, such as the Rho-Rock cascade and the Rac-PAK cascade. Both cascades ultimately facilitate actin polymerization. Moreover, the Rac-PAK cascade also contributes to the crosslinking and reorganization of actin filaments. Both processes as well as several other cell adhesion molecules are necessary for the spine to get enlarged and stabilized (Rudy, 2014, pp. 68–79). However, the stability of the synapse is still temporary. During consolidation, translation and transcription processes take place to make the memory trace more resistant to disruption. This process takes about 2 to 4 hours. Multiple calcium recourses are recruited based on the strength of the stimulus. This allows genomic signaling cascades, such as the mTOR-TOP pathway and the BDNF-TrkB receptor pathway to activate transcription factors like CREB (and enhance translation the capacity of Arc mRNA), which further induce transcription and translation of new proteins. Besides, the Ubiquitin/proteasome system (UPS) degrades proteins that inhibit translation or transcription processes, which further supports consolidation (Rudy, 2014, pp. 83–123). The last stage, the maintenance stage, aims to maintain the memory trace despite having to replace synaptic molecules. The exact underlying processes are not fully understood yet. The atypical kinase PKM $\zeta$  is a promising maintenance molecule that might facilitate the replacement of GLUA1 AMPA receptors though GLUA2 AMPA receptors. Through inhibition of GLUA2 AMPA receptors endocytosis, the synapse stays strengthened and the consolidated trace can be maintained (Rudy, 2014, pp. 129–141).

**Division of Memory – STM and LTM.** Typically, memory is divided into long-term memory (LTM) and short-term memory (STM) (Cowan, 2008). In contrast to the LTM,



the STM has a limited capacity and can hold about  $7 \pm 2$  chunks of information. Moreover, it decays over time (Cowan, 2008).

Long-term memory is typically divided into declarative and nondeclarative memory. Declarative memory is often referred to as explicit memory and is further subdivided into semantic memory (memory for facts) and episodic memory (memory for episodes and events) (Loprinzi et al., 2017). Nondeclarative memory, also called implicit memory, involves, for instance, memory about skills and habits, and memories acquired through procedural learning, classical conditioning, and non-associative learning (Squire, 1992).

***LTM – The Declarative Memory System.*** Three brain regions belong to the declarative memory system including the cerebral cortex, the parahippocampal region, and the hippocampus (Loprinzi et al., 2017). As shown in Figure 7, the parahippocampal cortex is in close proximity to the hippocampus and it facilitates the communication between the hippocampus and the cortical association areas that are located across the cerebral cortex (Eichenbaum, 2012). The parahippocampal cortex receives input from several cortical association areas. As mentioned, visual information is first processed in the primary visual cortex. After passing through secondary and tertiary stages of sensory processing, the processed information is sent to the visual association cortexes. Information about the location (where) is sent to the parietal lobe through the dorsal stream. Information about the object itself (what) is sent to the temporal lobe through the ventral stream (Ungerleider and Pasternak, 2004, pp. 541–562; Walsh and Butler, 1996).

Information from the ventral and dorsal streams are passed to the parahippocampal cortex (Burwell et al., 1995). After that, information enters the entorhinal cortex and then, information from these two streams are combined in the hippocampus (Figure 6). During encoding, internal representations are formed. In the perirhinal and entorhinal cortex, internal representations of new items are formed. In the entorhinal and parahippocampal cortex, internal representations regarding the context are formed. Not only do the information from the dorsal and ventral stream combine in the hippocampus, they also get associated with context (Figure 6) (Loprinzi et al., 2017). Moreover, the hippocampus projects back to the parahippocampal region, which then also projects back to neocortical regions (Loprinzi et al., 2017).

**How/Why do we Forget?** On a synaptic level, many memory traces are generated without having initial functional significance (Rudy, 2014, p. 236). Therefore, there is often no need to remember every consolidated trace, such as what we had for breakfast three weeks ago. According to Hardt et al. (2013), the likelihood that a memory trace is maintained is increased through either recall or repetition of the behavioral experience. In both instances, the memory trace is reactivated and/or new information are added to the trace (Hardt et al., 2013). Nonetheless, many day-to-day behavioral experiences are forgotten. Currently, there are two theories of forgetting established in the literature. The *Active Decay Theory* claims that unused memory traces are actively degraded by molecular processes (Hardt et al., 2013). Considering the important role of AMPA receptors and PKM $\zeta$  play in the generation and maintenance of memory traces, it seems plausible that memory traces may decay if AMPA receptors are removed from the post

synaptic density or the PKM $\zeta$  cascade is disrupted (Hardt et al., 2013; Rudy, 2014, p. 237).

The *Interference Theory*, which we are focusing on in this paper, claims that forgetting is due to additional experiences that either overwrite already existing memory traces or generate new traces, which consequentially interfere with the retrieval of the preexisting memory traces (Rudy, 2014, p. 237).

### **Theoretical Attributes Behind Memory Interference**

There are several theories that potentially attribute to proactive and/or retroactive memory interference. These include, for instance, *Irwin's Two-factor Model for Unlearning*. According to Irwin (1940), when learning alternative associations (e.g. the word pair hero – project from List 2), the original associations (e.g. hero – jacket from List 1) might be weakened. The old and new responses are competing with each other when asked to recall. Hence, this theory aims to describe retroactive memory interference (Melton & Irwin, 1987). Another theory that might underly retroactive memory interference is the *Changed-trace Theory*. This theory states that after a memory trace is created (e.g., the memory trace “hero – jacket” when learning List 1), new information can change and overwrite the original trace (e.g., the new word “project” that is paired with “hero” in List 2 would overwrite the original trace so the new memory trace would be “hero - project”) (Lanz et al., 2012). The *Multiple-trace* and the *Search of Associative Memory (SAM) Theory* do not focus on active weakening or overwriting of the original trace that may take place during the encoding of new/changed information. Rather, those two theories emphasize that each item/stimulus creates a distinct memory trace. The *Multiple Trace Theory* then states that when two memory traces are similar to each other,

the stronger trace will likely be retrieved over the weaker trace (McGeoch & Underwood, 1943; Melcher, 2011; Shimamura et al., 1995). The *Search of Associative Memory (SAM) Theory* does not focus on the similarity of distinct memory traces but on their individual strengths. According to this theory, each stimulus creates a memory trace. However, the traces vary in strengths. For instance, the association “hero - jacket” (List 1) might be stronger for a participant that just got a new jacket. Hence, it is easy for her to form an association between those two words. It may be harder for the participant to associate “hero” with “project” (List 2), thus the memory trace of “hero - project” is not as strong. Consequentially, when presented with the cue word “hero - \_\_\_” during the recall, the participant will be more likely to recall “jacket” than “project” (Irlbacher et al., 2014).

Besides the just mentioned theories, there are several other explanations that are discussed in detail elsewhere (Loprinzi et al., 2018).

### **Measurement of Memory Interference**

There are different ways to measure memory interference depending on the memory type that researchers are evaluating. For measuring memory interference in episodic memory, the type of memory we are looking at, the Ray Auditory Verbal Learning Test (RAVLT) as well as AB/AC word tasks are commonly used. In this study we are utilizing an AB/AC paradigm which is a paired associate learning task. Paired associate learning tasks typically consist of several wordlists that contain word- or symbol-pairs (e.g., dog-table). Participants are asked to memorize them and later recall them (e.g., dog-\_\_\_). There are several different models which include, for instance, the AB-AC model. The AB-AC model consists of two wordlists (Wordlist 1 and Wordlist 2). List 1 consists of eight AB and DE word-pairs and List 2 contains eight AC and FG

word-pairs. Only “A” words were presented in List 1 as well as List 2, potentially causing memory interference (for instance, List 1 AB = hero – apple, List 2 AC = hero – project). These words pairs were used to measure memory interference, while the other word pairs (DE and FG), the control word pairs, do not contain repeating words.

In the cued recall, participants engage in a “modified modified free recall” (Barnes & Underwood, 1959), which tests both lists simultaneously. Individuals are presented with one left-hand word at a time and are instructed to type in the corresponding word(s) (for instance “hero - \_\_\_\_\_, \_\_\_\_\_”). From the 12 cue words (A, D, F words), four are paired with two responses (four AB/AC word-pairs), and eight are only paired with one response (four DE and four FG word-pairs). All word-pairs appeared for 18 seconds on the screen until it automatically advanced to the next slide. Proactive interference takes place when participants recall less AC word-pairs compared to FG word-pairs. Retroactive interference occurs when participants recall less AB word-pairs compared to DE word-pairs. Now that we have an understanding of how to measure memory interference, the following narrative will briefly discuss the literature on exercise and memory, as well as memory interference

### **Effect of Exercise on Memory**

Research suggests that exercise activates memory-related pathways (Loprinzi et al., 2017). For instance, exercise has been shown to increase hippocampal volume in animal models as well as improved learning (Erickson et al., 2011).

As mentioned earlier, the parahippocampal cortex projects via two pathways, a short and a long one, to the hippocampus (Figure 4). There is evidence that exercise may increase dendritic spine density in the entorhinal cortex as well as in the C1 (Stranahan et

al., 2007), which are beneficial changes in/for the hippocampus (Loprinzi et al., 2017). Furthermore, acute physical exercise is thought to increase neural activity in several brain regions, such as the medial prefrontal cortex, amygdala, and the hippocampus (Loprinzi et al., 2018). These brain regions play an important role in memory mechanisms. When there is increased neural activity in these brain regions, pattern separation may be enhanced, which in turn, may lead to decreased memory interference (Lanier et al., 1986, 1989, 1990). There are studies indicating that exercise may have advantageous effects on all levels of memory formation, including generalization, stabilization, consolidation, and maintenance (Loprinzi et al., 2018; Loprinzi et al., 2017 Loprinzi et al., 2021). Even prior to encoding, exercise may help to facilitate priming of neuronal cells to encode memories (Loprinzi et al., 2017).

**Acute Exercise.** Acute exercise may impact memory function through altering mood, long-term-potential, and executive functioning (Loprinzi, 2019). Research indicates that acute exercise may help to facilitate stabilization of memory traces. Besides, it may induce synthesis of plasticity-related proteins, which are crucial for tagging nearby synapses (Loprinzi et al., 2018). However, the effects vary based on several factors, such as the timing, intensity, duration, and modality of utilized exercise (Loprinzi, 2019).

**Chronic Exercise.** In 2017, a meta-analysis evaluated 17 studies, which utilized chronic training protocols in 18-50-year-old adults. Seventy-one percent of the studies found a favorable effect of chronic exercise on memory function (Loprinzi et al., 2018).

However, just as with acute exercise, the impact of chronic exercise may depend on different parameters, such as the duration and intensity of chronic exercise. Loprinzi et al. (2020) suggested that aerobic and resistance exercise may positively impact aspects of

memory function, such as increased cerebral blood flow, protein synthesis, neurochemical alterations and neurogenesis (Loprinzi et al., 2020). This effect tends to be especially present when combining aerobic and resistance exercise. Interestingly, aerobic and resistance may enhance memory function via different mechanisms. The effects within those modalities seem to vary as well. For instance, low external load, high external load, and body weight resistance training seem to induce different neurotrophic changes, and thus, may lead to different effects on memory function (Loprinzi et al., 2020). However, the precise underlying effects are still unclear. Research in animal models suggests that chronic exercise induces increased synthesis of noradrenaline and dopamine, as well as increased tyrosine hydroxylase mRNA expression in the brain. These processes, as well as activation of the noradrenalin and dopamine pathways through chronic exercise, may contribute to enhanced memory function (McMorris, 2016).

**Exercise and Memory Interference.** The review paper by Li et al. (2020) evaluated ten studies that investigated the effect of chronic and acute exercise on PI in either humans, beagles, or mice. All seven of the studies involving chronic exercise found a positive effect on the cognitive tasks tested. For instance, Suwabe et al. (2017) conducted a study in which they divided up 75 participants into two groups based on a median split of aerobic fitness. Aerobic fitness levels were taken as an indicator for habitual physical exercise. Suwabe et al. (2017) examined performance on a discrimination task, which served as an indicator for PI. They found that the higher fitness group performed better on the discrimination task. Hence, they suggested that chronic exercise benefits memory discrimination (Suwabe et al., 2017). Regarding acute bouts of exercise, Suwabe et al.

(2017) found that, in one of three studies, a positive effect of exercise occurred, while the other two studies did not find a significant effect of acute exercise on the cognitive task. In a study conducted by Wingate et al. (2018), the researchers utilized an AB/AC paradigm to measure PI or RI. However, they did not find significant differences in PI nor in RI between participants that engaged in a 15 minute brisk walk on a treadmill compared participants that did not exercise before the cognitive task (Wingate et al., 2018). However, as mentioned, there are a variety of pathways and mechanisms through which exercise may facilitate memory. Both, Wingate et al. (2018) as well as Li et al. (2020) emphasize that more experimental work is needed to understand the effects and underlying mechanisms between acute and chronic exercise and PI and RI.



## **Justification For The Experiment**

Proper memory function is essential for our daily functioning. We need to remember past experiences and facts in order to plan future and present behavior (Hassabis et al., 2007). Therefore, it is crucial to investigate factors that might impact memory functioning.

One way of testing an aspect of memory functioning is to test memory interference. The concept of memory interference was first evaluated by Bergström (Bergström, 1893) in 1892. The concept of memory interference refers to the observation that daily information can interfere with memory. There are two kinds of interference, proactive and retroactive interference. Proactive interference (PI) occurs when preexisting memories interfere with the acquisition of new memories. Thus, it is difficult to acquire new knowledge. For instance, when rearranging the drawers in the kitchen, it is hard to remember the new location of, for example, the spoons. The memory of the old location of the spoons is interfering with the new information. The other kind of interference is retroactive interference (RI), which refers to newly learned material that is interfering with preexisting knowledge. As a result, it is difficult to recall old memories. This effect was illustrated by Jenkins and Dallenbach in 1924. They showed that participants who slept after encoding, retain more words they previously learned compared to participants who did not sleep shortly after encoding. This showed that subsequent exposure to stimuli can interfere with previously encoded information (Jenkins and Dallenbach, 1924).

In order to measure memory interference, paired associate learning tasks are often used. These typically consist of several wordlists that contain word- or symbol-pairs (e.g., “dog - table”). Participants are asked to memorize them and later recall them (e.g., “dog - \_\_\_\_”). An example of a paired associative learning task is the AB-AC model, which consists of two wordlists (Wordlist 1 and Wordlist 2). List 1 consists of eight AB and DE word-pairs and List 2 contains eight AC and FG word-pairs. Only “A” words are presented in List 1 as well as List 2, potentially causing memory interference (for instance, List 1 AB = “hero – apple”, List 2 AC = “hero – project”). These words pairs were used to measure memory interference while the other word pairs (DE and FG), the control word pairs, do not contain repeating words. During cued recall, participants engaged in a “modified modified free recall” task (Barnes & Underwood, 1959), which tests both lists simultaneously. Individuals are presented with one left-hand word at a time and are instructed to type in the corresponding word(s) (for instance, ”hero - \_\_\_\_\_, \_\_\_\_\_”). From the 12 cue words (A, D, F words), four are paired with two responses (four AB/AC word-pairs), and eight are only paired with one response (four DE and four FG word-pairs). Proactive interference takes place when participants recall less AC word-pairs compared to FG word-pairs. Retroactive interference occurs when participants recall less AB word-pairs compared to DE word-pairs.

Several studies have looked at the impact that acute exercise has on aspects of memory functioning (Crawford & Loprinzi, 2019, 2019; Scudder et al., 2012; Stranahan et al., 2007; van Dongen et al., 2016). Research suggests that acute exercise may positively impact long-term-potentiation and help facilitate the stabilization of memory traces (Loprinzi et al., 2018, Loprinzi, 2019). However, the majority of studies, which

have evaluated the relationship of exercise and memory interference, concentrated on acute exercise. Hence, the relation between chronic exercise and memory interference, as well as its potential underlying mechanisms, are still yet unknown. The goal of the present study is to see if chronic exercise is associated with attenuated memory interference. In order to do this, we utilized an online study to deliver the memory test as well as questions regarding participant's exercise behavior. Based on the beneficial effect acute exercise has on memory interference, we hypothesized that chronic/habitual exercise will attenuate memory interference. Moreover, as mentioned, Loprinzi et al. (2020) suggested that aerobic and resistance exercise may have unique effects on select mechanisms of memory, cerebral blood flow, protein synthesis, neurochemical alterations and neurogenesis (Loprinzi et al., 2020). This effect tends to be especially present when combining aerobic and resistance exercise (Loprinzi et al., 2020). Thus, given this prior review, which demonstrates that different exercise modalities may have unique effects on the mechanisms of memory function, we evaluated whether there are unique associations between different exercise modalities on memory interference.

## **Methods**

### **Study Design and Participants**

German participants who were residing in Germany during the time they took part in the study were recruited via email, social media (link in Instagram Story), and word of mouth. Through an anonymous link, participants were sent the Qualtrics survey. Two-hundred and thirty-one participants started the experiment, and among these 231, 207 completed the experiment. The study was approved by the Institutional Review Board at the University of Mississippi and all participants provided consent online to participate before starting the survey. In order to complete the study, participants had to (a) be aged 18 to 35, (b) be concussion free for the past 30 days, (c) be free of a learning disorder, and (d) use a laptop/desktop computer (no cell phone) to complete the experiment. If any of those eligibility requirements were not met, the online survey automatically ended, and the data was excluded. Among the 207 participants, we excluded 144 participants, leaving a final sample of 63.

### **Memory Task**

The online survey was set up as a within-subjects design that could be completed on a Laptop/desktop computer only. All instructions and words/stimuli were presented in German. The individual creating the survey was also a fluent in German. After consenting to participate, all participants received the same instructions to the memory task that followed. For the memory task, all individuals saw two lists, which each contained eight word-pairs (for instant the word-pair “dog-table”). All words were chosen from the Toronto Word Pool (Friendly et al., 1982) and had an imagery score greater than 6 and were semantically unrelated.

Each word-pair was presented on the screen for five seconds and then the screen automatically advanced to the next word-pair. After List 1, participants had 20 seconds to solve simple arithmetic problems (20-second distractor test between the two lists). After short instructions, participants saw the second list, which also contained eight word-pairs. Within both lists, the order of the word-pairs was randomized.

List 1 consisted of eight AB and DE word-pairs and List 2 contained eight AC and FG word-pairs. Only “A” words were presented in List 1 as well as List 2 (for instance, List 1 AB = “hero – apple”, List 2 AC = “hero – project”). Those words pairs were used to measure memory interference, while the other word pairs (DE and FG), the control word pairs, did not contain repeating words. In cued recall, participants engaged in a “modified modified free recall” task (Barnes & Underwood, 1959), which tests both lists simultaneously. Individuals were presented with one left-hand word at a time and were instructed to type in the corresponding word(s) (for instance “hero - \_\_\_\_\_, \_\_\_\_\_”). From the 12 cue words (A, D, F words), four were paired with two responses (four AB/AC word-pairs), and eight were only paired with one response (four DE and four FG word-pairs) (Table 5). In recall, participants were presented with one cue word at a time and asked to fill in the word(s) the cue word was previously paired with. After 18 seconds, the screen advanced to the next slide.

The proportions of correctly recalled AB, DE, AC, and FG-word pairs are calculated. For example, if participants correctly recalled 3 out of 4 AC words pairs, a numeric value of 0.75 is reported in the results (participants correctly recalled 75% of AC word pairs). To calculate proactive memory interference, the numeric value of correctly recalled FG word pairs is subtracted from the numeric value of correctly recalled AC

word pairs ( $PI = AC - FG$ ). For instance, if a participant correctly recalled 75% of AC words and 50% of FG words, his/her proactive interference score would be .25 ( $PI = 0.75 - 0.5 = 0.25$ ). Retroactive interference is calculated by subtracting the proportion of correctly recalled DE word pairs from the proportion of correctly recalled AB word pairs ( $RI = AB - DE$ ) (Crawford et al., 2021).

### **Physical Exercise Assessment**

After completing the memory task, participants were asked to self-report their habitual physical activities. Physical activity was defined as “*Moderate or strenuous activities that increase your heart rate and breathing with physical effort being required. These activities should be lasting at least 10 minutes in duration.*” Participants were given a list containing 14 activity categories (for instance biking, running/jogging/treadmill, weightlifting/resistance exercise). Exercise categories were selected based on two studies that looked into the types of exercise German adults engaged in from 2017 to 2019 and also from the National Health and Nutrition Examination Survey conducted by the CDC (Centers for Disease Control and Prevention, 2005; Repenning et al., 2019; Spenidid Research, 2018). The specific questioning was based on the Global Physical Activity Questionnaire, which has demonstrated evidence of reliability and validity (Cleland et al., 2014; Irlbacher et al., 2014). For each category, individuals indicated (1) if they participated in the activity, (2) on average, how many days a week they engage in moderate to strenuous exercise for this specific activity, and (3) on average, how many minutes per day they engage in moderate to strenuous exercise at that level.

## **Quality control measures**

Participants were asked whether they currently smoke (for instance cigarettes or vaping), consumed alcohol within the last 12 hours, consumed caffeine within the last 3 hours, and engaged in physical exercise within the last 3 hours. Participants also self-reported their height and weight, in which body mass index ( $\text{kg}/\text{m}^2$ ) was subsequently calculated. Further, participants were asked if they cheated in any way during the experiment (e.g., wrote down the words); these participants ( $n = 0$ ) were excluded for the analyses. Moreover, participants used a Likert scale (response options included “strongly disagree”, “disagree”, “neutral”, “agree” to “strongly agree”) to indicate (1) how hard it was to concentrate during the memory task, (2) the extent to which they had trouble focusing their attention during the memory task, and (3) the extent of difficulty they experienced blocking out distracting thoughts during the memory task.

## **Analyses**

A Spearman correlation analysis was used to evaluate the association of levels of moderate-to-vigorous physical activity with proactive/retroactive memory interference. Separate correlation analyses were computed for proactive and retroactive memory interference and separate analyses were computed for each of the modalities of exercise. The exercise modalities that were statistically significantly ( $p < .05$ ) associated with memory interference were then considered for inclusion in a repeated measured ANOVAs that involved three factors: (1) List (two levels: List 1 vs List2), (2) Interference/Non-Interference (two levels: Interference vs. Non-Interference), and (3) Meeting Exercise Guidelines (two levels: Meeting vs. Not Meeting Guidelines).

## Results

Characteristics of the sample are shown in Table 1. Participants, on average, were 23.2 years of age, with the sample being predominately male (57.7%). The mean body mass index of the sample was 22.4 kg/m<sup>2</sup>.

**Table 1**

*Descriptive Statistics*

Variable	Point Estimate	SD
Age, mean years	23.2	3.6
BMI, mean kg/m <sup>2</sup>	22.4	2.7
% Female	42.3	
% Daily smoker	0.0	
% Daily alcohol drinker	11.1	

Note: BMI, body mass index

### Physical Exercise Assessment

Physical activity estimates, across each of the 13 exercise modalities, is shown in Table 2. Across these 13 exercise modalities, the lowest to highest weekly MVPA in minutes per week (SD), respectively, occurred for Football (0), Cheerleading/Gymnastics (2.4 (SD = 15.5)), Basketball (4.3 (SD = 25.2)), Tennis (5.2 (SD = 18.3)), Dance (6.2 (SD = 33.7)), Soccer (8.8 (SD = 41.8)), Swimming (15.8 (SD = 52.4)), Handball (19.5 (SD = 76.2)), Fitness Classes (28.8 (SD = 63.5)), Biking (46.9 (SD = 66.6)), Weightlifting (74.6 (SD = 107.4)), Running (94.8 (SD = 122.3)), and Walking/Hiking (102.3 (SD = 127.6)).

**Table 2**

*Physical Activity Estimates*

Physical Activity	MVPA per week
Football	0
Cheerleading/Gaymnastics	2.4 (SD = 15.5)
Basketball	4.3 (SD = 25.2)



Tennis	5.2 (SD = 18.3)
Dance	6.2 (SD = 33.7)
Soccer	8.8 (SD = 41.8)
Swimming	15.8 (SD = 52.4)
Handball	19.5 (SD = 76.2)
Fitness Classes	28.8 (SD = 63.5)
Biking	46.9 (SD = 66.6)
Weightlifting	74.6 (SD = 107.4)
Running	94.8 (SD = 122.3)
Walking/Hiking	102.3 (SD = 127.6)

*Note.* MVPA, moderate-to-vigorous physical activity

### Memory Task

Table 3 displays the memory results. The mean (SD) values AB, DE, AC, and FG, respectively, were 0.51 (0.31), 0.50 (0.33), 0.29 (0.30), and 0.50 (0.32). In a 2 (List: List 1 vs. List 2) x 2 (Interference vs. Non-Interference) rANOVA, we observed a significant main effect for List,  $F(1, 62) = 20.34, p < .001, \eta^2 = .08$ , and main effect for Interference/Non-Interference,  $F(1, 62) = 19.60, p < .001, \eta^2 = .06$ , which was qualified by a List x Interference/Non-Interference interaction,  $F(1, 62) = 13.45, p < .001, \eta^2 = .08$ . The interaction was investigated with separate Tukey corrected comparisons of List for each Interference/Non-Interference level. List 1 Interference (AB accuracy) was not different than List 1 Non-Interference (DE accuracy),  $p = .99$ , suggesting no evidence of retroactive interference. However, List 2 Interference (AC accuracy) was worse than List 2 Non-Interference (FG accuracy),  $p < .001$ , demonstrating evidence of proactive interference. We also computed sensitivity analyses (rANCOVA) that controlled for each of our quality control measures (smoking, alcohol, caffeine, exercise prior to the memory task, and their concentration and distraction during the memory task), but these rANCOVA analyses produced a similar pattern of results from our rANOVA.

### Table 3

### *Memory Results*

	AB Value	DE Value	AC Value	FG Value
Mean	.51	.50	.29	.50
Std. Deviation	.31	.33	.30	.32

Table 4 displays the correlations depicting the relationship between weekly engagement in MVPA for each of the 13 (football was excluded because no participants engaged in this modality) exercise modalities with PI and RI. As shown in Table 4, the correlation coefficient (Spearman rho) ranged from -.26 to .23. Tennis was inversely associated with RI ( $r = -.26, p = .03$ ), but this should be interpreted with caution; as demonstrated above in the rANOVA analyses, we did not observe a statistically significant RI effect. None of the physical activities were associated with PI, all  $ps > .07$ .

**Table 4**

*Spearman rho correlations (p-value) between each exercise modality (expressed as a continuous variable) and retroactive (RI) and proactive (PI) interference.*

<b>Exercise Modality</b>	<b>RI</b>	<b>PI</b>
Football	-	-
Cheerleading/Gaymnastics	-.10 (.41)	-.08 (.54)
Basketball	.16 (.19)	-.12 (.35)
Tennis	-.26 (.04)	.06 (.63)
Dance	-.13 (.31)	-.11 (.39)
Soccer	.09 (.49)	.04 (.75)
Swimming	-.15 (.22)	.05 (.69)
Handball	.07 (.58)	-.08 (.52)
Fitness Classes	-.002 (.98)	.18 (.15)
Biking	-.03 (.80)	.12 (.34)
Weightlifting	.19 (.14)	-.15 (.23)
Running	-.16 (.20)	.03 (.81)
Walking/Hiking	.12 (.36)	-.02 (.89)
Total MVPA	-.01 (.95)	.02 (.87)

*Notes:* Values in parentheses represent the  $p$ -value associated with the Spearman rho correlation. A dash (-) indicates no correlation was computed given that no participants engaged in this modality of exercise. RI, retroactive interference; PI, proactive interference.

## Discussion

The goal of the present study was to evaluate if chronic exercise is associated with attenuated memory interference. We utilized an online study to deliver a memory test as well as questions regarding participant's exercise behavior. Findings by Loprinzi et al. (2020) suggest that aerobic and resistance exercise may have unique effects on select mechanisms of memory, cerebral blood flow, protein synthesis, neurochemical alterations and neurogenesis (Loprinzi et al., 2020), which seem to be especially present when aerobic and resistance exercise are combined (Loprinzi et al., 2020). Hence, we further aimed to evaluate whether there are unique associations between different exercise modalities on memory interference. The main findings of this study are as follows. We observed evidence of PI, but notably, none of the physical activity modalities were reliably associated with attenuating memory interference.

In this study we found that PI, but not RI, occurred but none of the exercise modalities significantly impacted PI. It might be speculated that the AB/AC paradigm is not successful in eliciting PI and RI. However, several other studies that utilized the same paradigm combined with acute exercise showed otherwise (Crawford et al., 2021; Crawford & Loprinzi, 2019). It might be further speculated that only acute, but not chronic exercise, significantly impacts memory interference. However, Li et al. (2020), who reviewed several studies, found that chronic exercise seems to consistently reduce PI. All seven studies reviewed by Li et al. (2020) reported significant effects of chronic exercise on memory interference and suggest that it significantly reduces PI. For instance, Suwabe et al. (2017) utilized a mnemonic discrimination task and found that chronic exercise at high aerobic intensity reduces PI. Seventy-five college students between 18

and 24 years of age completed the study. To assess the level of habitual exercise, participants completed a graded exercise task at least 48 hours prior to the mnemonic discrimination task. Based on the  $\text{VO}_{2\text{peak}}$  results from the graded exercise tests, participants were divided into a higher or lower fitness group. Their results showed that aerobic fitness was a mediator variable of the effect of chronic exercise on memory interference (Suwabe et al., 2017). A study conducted by Heisz et al. (2017) found significant effects of chronic exercise on memory interference. They used a mnemonic similarity task, which includes high interference to assess memory interference. Participants, who completed a 20-minute high-intensity training, three times per week for a total of 6 weeks, showed significantly reduced memory interference compared to participants who did not engage in an exercise protocol.

While the sample characteristics, the AB/AC memory paradigm, and the physical exercise assessment demonstrate evidence of validity, there are several other factors that may modulate the effect of chronic exercise on memory. As discussed earlier, different exercise modalities may impact memory function differently (Loprinzi et al., 2020). For instance, aerobic and resistance exercises may enhance memory function via different mechanisms, and even the effects within those modalities seem to vary. For instance, low external load, high external load, and body weight resistance training seem to induce different neurotrophic changes, and thus, may lead to different effects on memory function (Loprinzi et al., 2020). In this study, most participants did not engage in only one exercise modality, but often in a combination of aerobic and resistant exercises. Hence, the results for RI and PI for the different categories may not be seen completely

separate from each other. This might be a reason why we did not find significant differences between exercise modalities.

Despite different modalities, which may moderate the effect of chronic exercise on memory (Loprinzi et al., 2020), Loprinzi (2019) suggested that the intensity, duration, and temporality may also modulate the effect of acute exercise on memory function. Hence, these factors may also play a modulating role in the effect of chronic exercise on memory interference. The main difference between the present study the study conducted by Heisz et al. (2017) is in the intensity and duration of exercise. In the present study, we asked participants to report the number of days and minutes a day they exercise. However, we focused on whether PI and RI differ among exercise modalities and did not take the different time spans participants exercise at a time into consideration for the analysis. We asked participants to report their moderate-to-vigorous physical activities. Hence, there is a range of intensities participants might have exercised at.

In contrast to that, participants in Heisz et al. (2017) strictly controlled for a high intensity. Participants exercised at a high intensity level for 20 minutes, three times per week, for a total of six weeks and showed decreased memory interference afterwards. As discussed by Crawford et al. (2021), Loprinzi (2019), and Loprinzi et al (2021), the duration and intensity of exercise may influence memory function differently. So far, there is limited research on the effects of different durations and intensities of chronic exercise on memory interference. However, since duration and intensity seem to impact memory function differently, they may also impact PI and RI differently.

It becomes clear that future research is needed to understand the effect of chronic exercise on PI and RI. The relationship is complex and seems to be modulated by various

factors, such as, modality, intensity, duration, and temporality of exercise. Future work should continue to explore the impact of chronic exercise on PI and RI in a controlled environment, while trying to hold these modulators at a constant level. Moreover, we did not find significant results using the AB/AC paradigm but Heisz et al. (2017) were successful in finding significant results using the mnemonic discrimination task. Therefore, future research should examine whether different interference tasks show diverse sensitivities to exercise-induced changes in memory interference.

It is important to consider the limitations of this study when interpreting the results. First, the sample of this study was relatively small ( $N = 63$ ) and consisted of young adults aged between 18 and 35. Hence, our findings cannot be generalized to other populations. Moreover, since we sent out a link to the study via email and through Instagram, the sample was relatively homogenous, as most of my friends and followers are very active people who are closely affiliated with sports. Thus, even a generalization of the results within the age group of 18 to 35-year-olds would not be applicable. Second, we did not observe participants completing the study. Despite applying a time frame (300-1500sec) to complete the study and quality control measures (“Did you cheat in any way during the experiment (e.g., wrote down the words)?”), participants could have cheated. Thirdly, we could not control for external factors, such as the room participants took the study in or the level of noise surrounding them, during the study. Another limitation of the study is that the habitual physical exercise was self-reported, which is prone to bias. We did not take into account the duration they have been engaged in the different exercise modalities and if/how much their pensum of MVPA varies. Lastly, this

was a cross-sectional design, thus, preventing the ability to determine the directional relationship between MVPA and memory.

There are several strengths of this study. We controlled for several quality control measures (such as smoking, alcohol, caffeine, exercise prior to the memory task, and their concentration and distraction during the memory task) and applied strict exclusionary criteria (time limitation to complete the study, age limit, no concussion, no learning disorder, completion from a laptop/desktop computer (no cell phone)) to control for potential confounding variables.

In conclusion, the present study does not provide evidence that chronic exercise is associated with attenuated memory interference. Moreover, engagement in different exercise modalities do not seem to modulate participants' PI and RI. While several studies have found a positive effect of chronic exercise on memory interference, especially on PI, the results of this study did not support this association. Future research is needed to better understand the relationship between chronic exercise and memory interference.

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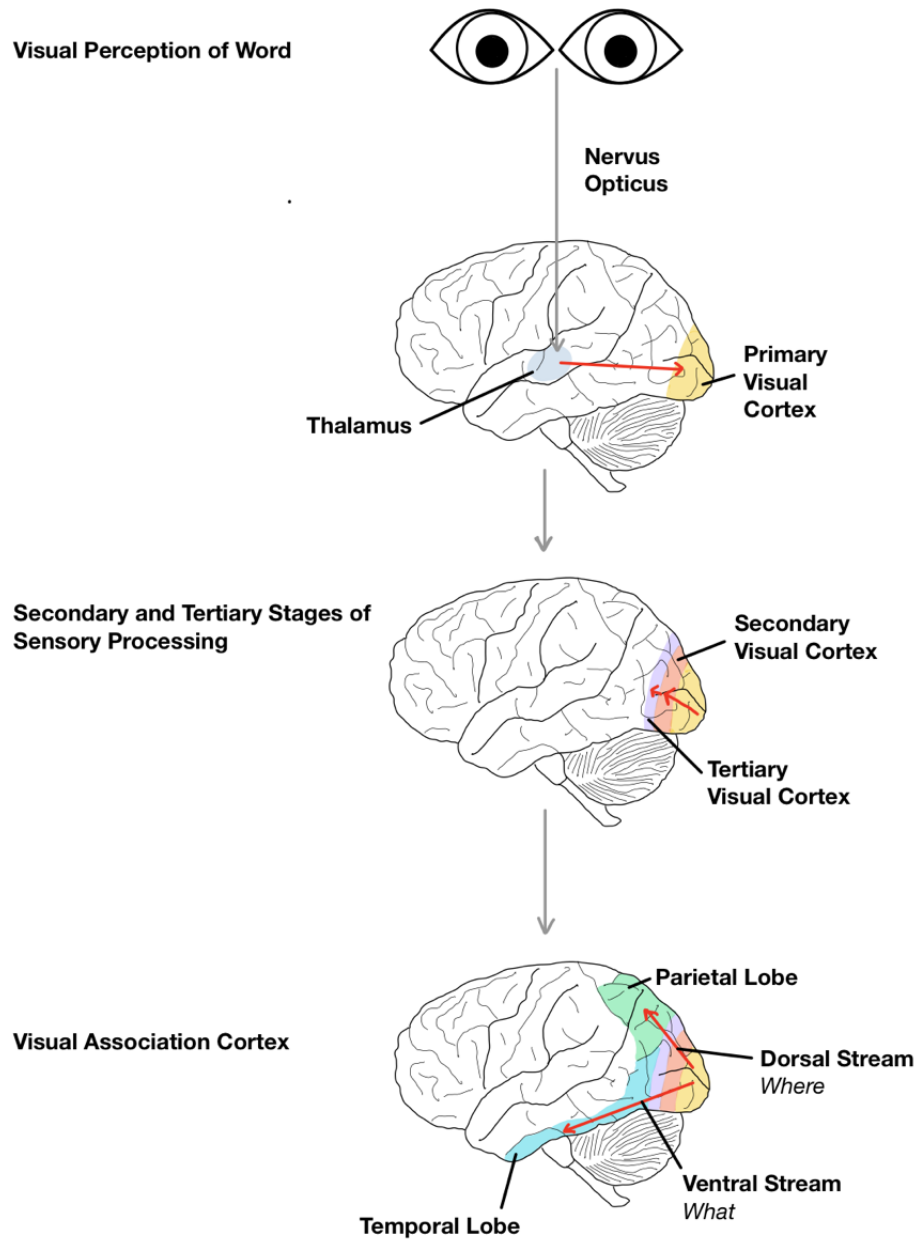
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APPENDIX

**Figure 4**

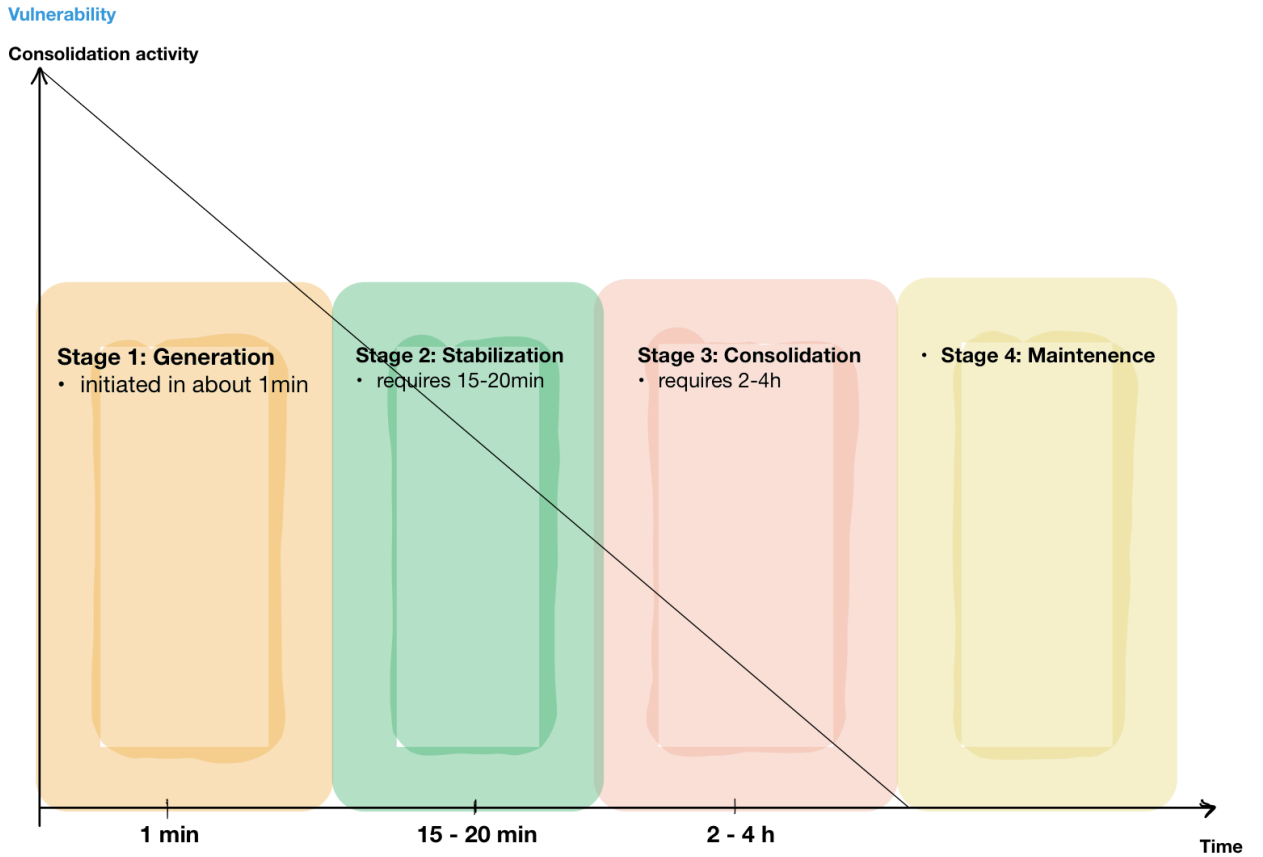
*Visual Perception of Words*





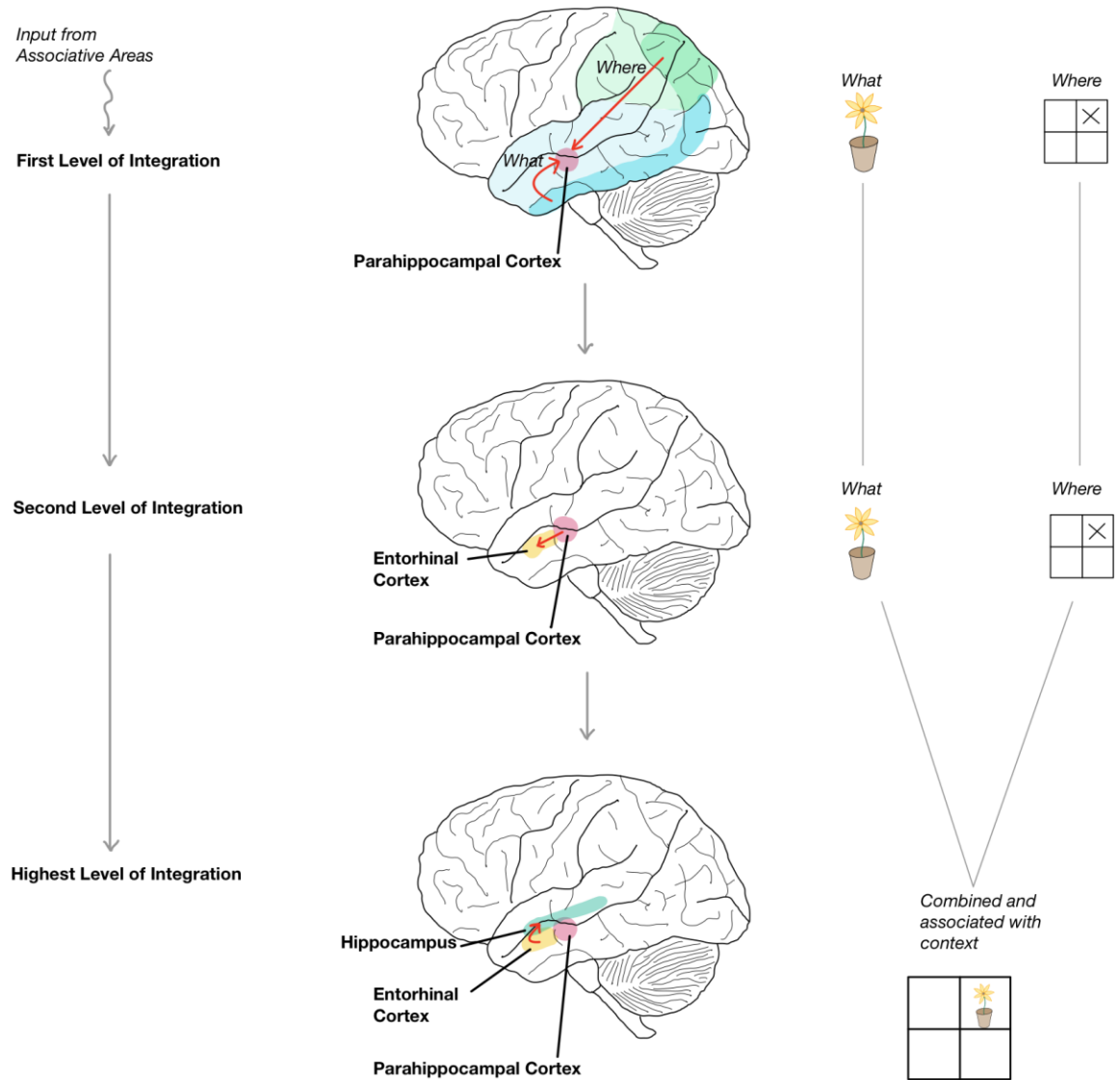
**Figure 5**

*Stages of Memory Formation on a Synaptic Level*



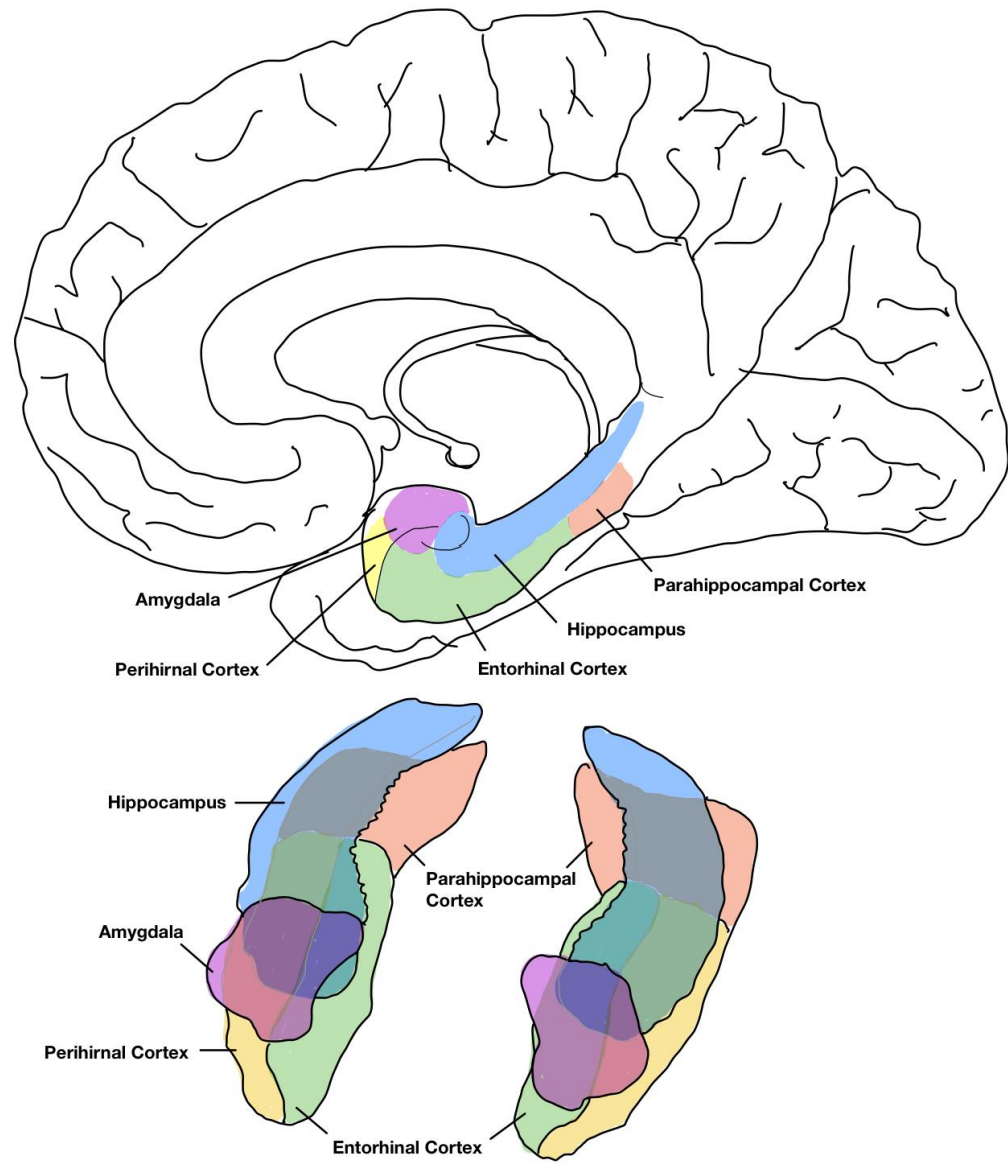
**Figure 6**

*Processing of Visual Information*



**Figure 7**

*Anatomy of the Medial temporal Lobe*



**Table 5**

*Wordlists utilized in this study*

Cued Recall List 1 AB, DE	Cued Recall List 2 AC, FG	MMFR AB, DE, AC, FG	Cued Recall List 1 AB, DE	Cued Recall List 2 AC, FG	MMFR AB, DE, AC, FG
Canoe – Garden	Ocean – Echo	Coffee – Anchor, jacket	Kanu – Garten	Ozean – Echo	Kaffee – Anker, Jacke
Hero – Apple	Hero – Project	Detail – Silver	Held – Apfel	Held – Projekt	Detail – Silver
Coffee – Anchor	Patent – Orange	Ocean – Echo	Kaffee – Anker	Patent – Orange	Ocean – Echo
Detail – Silver	Uncle – Climate	Uncle – Triumph, climate	Detail – Silber	Onkel – Klima	Onkel – Triumph, Klima
Author – Finger	Number – Fever	Patent – Orange	Author – Finger	Nummer – Fieber	Patent – Orange
Uncle – Triumph	Model – Hotel	Insect – Singer	Onkel – Triumph	Model – Hotel	Insekt – Sänger
Theater – Baby	Coffee – Jacket	Author – Finger, Object	Theater – Baby	Kaffee – Jacke	Author – Finger, Objekt
Insect – Singer	Author – Object	Number – Fever	Insekt – Sänger	Author – Objekt	Nummer – Fieber
		Canoe – Garden			Kanu – Garten
		Hero – Apple, Project			Held – Apfel, Projekt
		Theater – Baby			Theater – Baby
		Model – Hotel			Model – Hotel

*Note.* Bolded items represent AB/AC pairs, in which the “A” words repeat. The Table on the left represents the words in English, where their German equivalent shown on the Table on the right