

The Effects of Aerobic Exercise on The Neural Basis of Memory Functions in Elderly Individuals: A Systematic Review

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Abstract

This systematic review aims to investigate the effects of aerobic exercise on the neuroal basis of memory functions in healthy elderly individuals. The search was conducted in accordance with PRISMA and covered three electronic databases, namely PubMed, Scopus, and Web of Science, for peer-reviewed published, and original research. Six studies met the inclusion criteria and were included in the review. The studies utilized various behavioral or cognitive tasks related to memory, including the Sternberg Working Memory Task, Spatial Memory tests, and neuroimaging techniques such as magnetic resonance imaging (MRI). This systematic review suggests that aerobic exercise can improve memory in healthy elderly individuals, including spatial, working, and short- and long-term memory. As revealed by neuroimaging techniques, memory function improvement was accompanied by changes in brain structure and function in memory-processing regions. These findings provide evidence that aerobic exercise can improve the neurological basis of memory function in healthy elderly individuals. The beneficial effects of aerobic exercise on memory have significant implications for the aged population. Memory loss is a common and often debilitating issue in older adults, and the ability to recall and learn new information is crucial for maintaining independence and quality of life. Therefore, aerobic exercise is a promising intervention to improve memory function in healthy elderly individuals.

Keywords: Aerobic exercise, memory function, healthy older adults, neuroimaging, cognitive aging

The Effects of Aerobic Exercise on The Neural Basis of Memory Functions in Elderly Individuals: A Systematic Review

Memory is undoubtedly one of the most remarkable aspects of human nature, as it shapes who we are and how we perceive and understand the world around us. It is responsible for learned skills, language, personal experiences, and more (Thompson & Madigan, 2013). However, as individuals age, our cognitive functions particularly memory, tend to decline gradually impacting our independence and quality of life (Harada et al., 2013; Jia et al., 2023).

Researchers have suggested various interventions to improve cognitive performance in elderly individuals. Among these interventions, aerobic exercise has emerged as a potential non-pharmacological intervention that may prevent or delay age-related memory decline and even improve cognitive function in individuals with mild cognitive impairment or dementia (Hillman et al., 2008; Northey et al., 2018).

Prior research has indicated that aerobic exercise can enhance various memory functions, including long-term memory, working memory, and episodic memory, by increasing neuroplasticity, neurogenesis, or cerebral blood flow in the brain, with the help of behavioral/cognitive memory tasks (Erickson et al., 2009; Erickson et al., 2011)

The potential benefits of aerobic exercise on memory and cognitive function become even more significant, given that memory is integral to who we are and how we experience the world around us. Therefore, exploring the effects of aerobic exercise on memory function in the elderly population is of utmost importance in maintaining healthy brain cognitive ability.

Memory

Human memory is a multi-component system that relies on many behavioral and cognitive processes, attention, rehearsal, and retrieval. Memory is specialized for different types of information, including verbal, visual, and spatial (Alexandrov & Fedoseev, 2012). Memory is a fundamental cognitive skill that enables individuals to acquire, store, and recall knowledge. It is a complicated system involving numerous processes and systems in the brain (Squire, 2004). The process of memory involves three key components: encoding, storage, and retrieval (Thompson, 2005; Tulving & Craik, 2000).

Short-term memory and long-term memory are two distinct types of memory systems that differ in terms of their capacity, duration, and retrieval processes, with short-term memory referring to the temporary storage with limited capacity, exhibiting temporal decline, and lasting a few seconds to a minute (Baddeley, 2012; Thayer, 2016). In contrast,

long-term memory is a relatively permanent store that can hold unlimited information for days, weeks, or even a lifetime (Cowan, 2014).

The process by which newly acquired information is stabilized and transformed into a more permanent form of memory (from short-term to long-term) is known as memory consolidation (Squire et al., 2015).

According to Baddeley (2010), working and short-term memory are two separate categories but frequently confounded. Baddeley (2010) discusses how working and short-term memory are often used interchangeably, even though they refer to different aspects of memory. Baddeley (2010) further explains that confusion between these two types of memory arises from working memory relying on activating the information held in short-term memory (Baddeley, 2010).

The term *working memory* involves actively manipulating and processing information. It refers to the type of memory responsible for carrying out activities, and it is considered an essential component of various cognitive processes, including problem-solving, reasoning, decision-making, language, comprehension, and learning (Cowan, 2014; Cowan, 2017).

Camina and Güell (2017) reported that long-term memory classifies as either non-declarative or declarative memory. Non-declarative memory, also referred to as implicit memory, is a type of memory that is typically unconscious and automatic, supporting the acquisition and use of skills and habits such as riding a bike or typing on a laptop keyboard (Camina & Güell, 2017)

On the other hand, declarative or explicit memory refers to the conscious recollection and knowledge of facts or events and includes both episodic and semantic memories (Riedel & Blokland, 2015; Squire, 2004). Semantic memories are general knowledge and information about the world, whereas episodic memories contain recollections of personal experiences and events (Riedel & Blokland, 2015).

Research has revealed that memory processing is a complicated and dynamic process involving connections across various brain areas (Squire, 2004; Tulving & Craik, 2000). Individual variations in brain anatomy and function can also influence different stages of memory processing (Tulving & Craik, 2000). Brod et al. (2013) and Corkin (2002) reported that the medial temporal lobe, specifically the hippocampus and prefrontal cortex regions, play a critical role in coordinating the formation and application of knowledge. The entorhinal cortex, perirhinal cortex, and parahippocampal cortex surround the hippocampus and have a role in memory function (Brod et al., 2013; Garcia & Buffalo, 2020; Schacter & Addis, 2007). The medial temporal lobe supports long-term declarative memory (Doxey & Kirwan, 2015; Milner, 2005).

The prefrontal cortex is responsible for working memory and attention (Baddeley, 2003), whereas the amygdala is responsible for emotional memory (Phelps, 2004). The brain's capacity to learn and use spatial memory representations is crucial for successful navigation in familiar and unfamiliar settings; this ability enables individuals to navigate and orient themselves within their environment (He et al., 2021; Maguire et al., 2000; Thayer, 2016).

The function of the hippocampus is to process information from all sensory modalities (Doxey & Kirwan, 2015). According to research, the hippocampus is involved in various memory processes, including spatial memory, associative memory (Maguire et al., 2000; Ranganath & Ritchey, 2012), and episodic memory (Davachi, 2006). The hippocampus is a crucial component in absorbing correlations between environmental inputs, creating brain representations of those associations, and using this knowledge to move fluidly through various environments (Maguire et al., 2000; Thayer, 2016).

How Aging Affects Memory

The aging population raises concerns about cognitive decline, associated with declines in various aspects of cognitive performance, impacting daily functioning, quality of life, and independence (Salthouse, 2010). One of the most prominent challenges scientists face today is slowing down the detrimental effects of aging (Kirkland & Tchkonja, 2017). A growing body of research has explored various interventions that may help to promote healthy aging and delay cognitive decline (Ngandu et al., 2015). These include lifestyle factors such as exercise, diet, and social engagement, as well as pharmacological and cognitive interventions. For instance, Hillman et al. (2008) discussed the effects of exercise on the brain and cognition.

Studies on the healthy human brain have consistently shown a decline in cognitive function with age, with declines in processing speed, attention, memory, and executive function (Salthouse, 2010). This decline has been observed in individuals over 40 and is even more pronounced in those over 70 (Alexandrov & Fedoseev, 2012; Fjell et al., 2014). Episodic memory is the long-term memory that suffers the most from age-related loss, while working-memory performance deteriorates with aging (Nyberg et al., 2012).

One of the effects of aging on the brain is that the gray matter and brain volume of older individuals tend to decrease (Sullivan & Pfefferbaum, 2006). The prefrontal cortex, which is involved in executive tasks, including working memory and decision-making, can be significantly impacted by this volume decrease (Raz et al., 2007). With a considerable decrease in gray matter volume seen in older adults, the brain's frontal lobe is particularly susceptible to alterations brought on by aging (Salat et al., 2004). Specific brain areas, such as the frontoparietal cortex and striatum, have more significant gray matter destruction than the temporal cortex and hippocampus (Alexandrov & Fedoseev, 2012).

The hippocampus, a crucial component of memory formation and consolidation, is another brain region significantly impacted by aging (Raz et al., 2007). According to Small et al. (2011), the hippocampus experiences significant structural changes as it ages, including a decrease in volume and the loss of dendritic spines. According to longitudinal research, older individuals experience a hippocampus volume reduction of up to 2-3% annually (Raz et al., 2007).

Normal aging mainly affects explicit spatial memory, not implicit memory (Alexandrov & Fedoseev, 2012). During aging, there is a reduction in brain volume and gray matter in certain areas, including the frontal lobe and hippocampus (Sullivan & Pfefferbaum, 2006). However, a form of compensation in normal aging makes the left and right hippocampus active throughout the encoding phase, whereas the left prefrontal cortex is less activated (Park & Reuter-Lorenz, 2009). The left and right prefrontal regions are equally involved in the retrieval, but there is a shift towards greater right frontal activation in older adults (Cabeza, 2002).

Aerobic Exercise

Aerobic exercise (also referred to as endurance activities) is a type of physical activity that is oxygen-dependent and requires the body's metabolic system to utilize oxygen to obtain energy from fat and carbohydrate, to fulfill the energy demands of the muscles during exercise (Millstein, 2013; Muscella et al., 2020).

Aerobic exercise is defined as any activity that uses major muscle groups such as arms and legs rhythmically; it also stimulates and focuses on breathing (lung capacity) and increases and improves cardiovascular fitness to regulate and distribute oxygen more rapidly and effectively throughout the body. Peak oxygen consumption (VO_2), or a person's maximal oxygen uptake during an exercise, is the criterion measure for aerobic capacity (Patel et al., 2017).

Patel et al. (2017) have shown that aerobic exercises such as walking, jogging, running, hiking, cycling, aerobic dance, or swimming can improve cardiovascular health by strengthening the heart muscles and increasing oxygen utilization.

Aerobic exercise can be performed at different levels of intensity, such as moderate-intensity level or high (also referred to as "vigorous") -intensity level. However, using moderate-intensity aerobic exercise for extended periods is a commonly recommended approach to improving overall fitness (World Health Organization: WHO, 2022). The talk test is a simple, valid, and reliable indicator of relative exercise intensity, high-intensity (in which respiration and heart rate will increase and one is unable to talk for more than a few words without pausing for a breath) is more challenging to perform than moderate-intensity

activity (breathing and heart rate will be increased, one will be able to talk but not sing) (Foster et al., 2008).

Effects of Aerobic Exercise and Aging

Regular aerobic exercise has numerous benefits for mental health, physical functioning, and cognitive performance. Maintaining a regular exercise routine allows the body to continue experiencing the inherent advantages of physical exercise, which include an expansion and strengthening of the cardiac muscle, enhancement of the strength of respiratory muscles, improvement of circulation efficiency, and reduction of blood pressure as documented by Bouaziz et al. (2017) and Fletcher et al. (1992). This, in turn, can help individuals retain a high degree of personal independence in later life and improve the overall quality of life (QoL) (Bouaziz et al., 2017; Lazzar, 2018). Regular aerobic exercise can also improve mental health and psychological well-being, including reducing stress and depression, increasing cognitive performance, and improving mood substantially (Bouaziz et al., 2017; Diloranzo et al., 1999; Mead et al., 2008).

Furthermore, aerobic exercise can reduce depression symptoms and improve mood in patients with moderate to severe major depression (Heissel et al., 2023; Morres et al., 2019; Xie et al., 2021). Additionally, regular exercise reduces the risk of diabetes and improves insulin sensitivity (Colberg et al., 2010; Colberg et al., 2016; Snowling & Hopkins, 2006).

Regular aerobic exercise provides significant health benefits for older adults, including preventing and modifying severe health conditions such as cardiovascular diseases (CVD), mortality, and metabolic syndrome. Also, older adults demonstrate enhanced mobility and improved quality of life through aerobic exercise (Bouaziz et al., 2017; Perez-Terzic, 2012; Stewart et al., 2005; Tian & Meng, 2019).

Other health benefits included in longitudinal research have indicated that regular aerobic exercise slows down the progress of cognitive decline in older adults, improves cognitive functions, contributes to an increase in brain volume, and maintains the brain's cognitive ability, particularly memory (Colcombe et al., 2006; Erickson et al., 2011).

Although aerobic exercise appears to have beneficial effects, the maximum health benefits achieved with aerobic exercise depend on the intensity level and duration of the activity. Moderate to high-intensity activity may be required to attain the previously mentioned benefits. The World Health Organization (WHO) recommends that individuals aged 18–64 and older should engage in training at least 2–3 times per week for at least 150 minutes at a moderate-intensity level; or at least 75 minutes at a high-intensity level (World Health Organization: WHO, 2022).

Neurological Effects of Aerobic Exercise

According to Denham et al. (2014), Erickson et al. (2015), and Gligoroska and Manchevska (2012), aerobic exercise has a wide variety of neurological effects, including

several enhancements to the brain structure, brain function, and cognition. A regular aerobic exercise regimen of two to three times per week has both short- and long-term effects, including promoting neuroplasticity (which increases the production of neurotrophic factors such as brain-derived neurotrophic factor (BDNF) and insulin-like growth factor 1 (IGF-1)), exercise-induced neurogenesis (i.e., the increases in gray matter volume), effects on neurochemistry (releases neurotransmitters like serotonin, dopamine, and norepinephrine that improve mood and emotional states by promoting positive effects). It reduces the biological response to psychological stress.

BDNF plays an essential role in the differentiation and maturation of neurons and their survival and maintenance. BDNF enhances and participates in synaptic plasticity, which is crucial for memory and learning (Lu et al., 2014). Furthermore, high protein BDNF in the hippocampus and cerebral cortex has been linked to elevated hippocampal volume and improved memory functions. Moreover, due to the role that BDNF plays in plasticity, the protein may be able to protect against age-related structural and functional degradation (Erickson et al., 2011; Mackay et al., 2017). These findings show evidence that aerobic exercise significantly impacts BDNF levels in healthy individuals.

Like BDNF, IGF-1 is a neurotrophic factor important for cognition, neurogenesis, and neuronal survival. IGF-1 decreases with age and is thought to make old adults more susceptible to sarcopenia (Ashpole et al., 2015). Exercise increases circulating growth hormone (GH), the main stimulator of IGF-1 production. Physical activity is associated with increased levels of IGF-1. Hence, the duration and intensity of physical activity determine the amount of IGF-1 released (Sundari & Arsani, 2022).

The Present Thesis and Aim

There is growing interest in understanding the underlying neural mechanisms of the effects of aerobic exercise on memory functions in elderly individuals. Understanding the neural mechanisms underlying these effects may help identify the most robust findings and potential gaps in knowledge that could guide future research and develop more effective interventions to promote healthy cognitive aging (Erickson et al., 2009).

Therefore, this systematic review aims to provide a comprehensive overview of the current evidence regarding the effects of aerobic exercise on the neural basis of memory functions in elderly individuals. The effects of aerobic exercise focusing only on either the cognitive or the executive functioning of older adults have been the subject of several previous reviews and meta-analyses or any physical exercise that, aside from aerobic exercise, related to specific components of memory functioning (e.g., Hall et al., 2001; Kelly et al., 2014; Levin et al., 2017; Ludyga et al., 2016; Xiong et al., 2021; Young et al., 2015).

Furthermore, the purpose of this systematic review is to investigate whether aerobic exercise can improve the neural basis of memory functions in healthy elderly individuals.

Specifically, this review will examine the effect of aerobic exercise on different types of memory, including episodic memory, spatial memory, working memory, and short- and long-term memory. To achieve this, we will consider studies that have used various behavioral or cognitive tasks related to memory, including the Sternberg Working Memory Task and spatial memory tests. Additionally, we will consider studies that have utilized neuroimaging techniques such as magnetic resonance imaging (MRI). Moreover, we have chosen to focus on these types of memory because previous research has primarily investigated their relationship with aerobic exercise (Erickson et al., 2009; Erickson et al., 2011). Thus, we include them in our systematic review.

Additionally, we choose to focus on aerobic exercise, rather than other types of training, because aerobic exercise is readily accessible, requires no specialized expertise or any specific equipment, is more directly linked to cardiovascular fitness, and slows down the progress of cognitive decline, which researchers have also linked to memory function—not just in elderly individuals whose memory functions are impaired or declining.

The thesis will investigate the research question: Does aerobic exercise affect any neural basis structure/function or brain areas associated with memory functions in healthy adults (aged 50 +) with no known cognitive impairments, motor disabilities, or disease?

Methods

Search Strategy

The search procedure in this systematic review was carried out in accordance with the PRISMA guidelines (Moher et al., 2009). The literature search was conducted on March 14, 2023, using the well-known electronic databases PubMed, Web of Science, and Scopus to find relevant studies. The following search string was used: ((((((memory OR ("memory performance" OR "memory function" OR "recall" OR "spatial memory" OR "working memory" OR "hippocampus" OR "hippocampal volume" OR "hippocampus function" OR "gray matter"))) AND (aerobic exercise OR ("aerobic training" OR "cardiovascular exercise" OR "endurance activities")))) AND (elderly OR ("older")))) AND (MRI OR ("magnetic resonance imaging" OR "EEG" OR "electroencephalography" OR "functional magnetic resonance imaging" OR "fMRI")) NOT (animal* OR ("rat*" OR "rodent*" OR "mice")) NOT (Parkinson* OR ("dementia" OR "schizophrenia" OR "Alzheimer" OR "autism")) NOT (patient*)) NOT (cognitive impairment* OR ("cognitive dysfunction" OR "cognitively impaired"))).

The search terms were all adjusted according to the database used, and the search was not limited to any time period. The search yielded 280 articles (PubMed n = 177; Scopus n = 53; Web of Science n = 50). All articles were exported into the Rayyan software, a helpful web tool for systematic reviews to save time and extract relevant data very quickly (Ouzzani et al., 2016). After the removal of duplicates, a total of 106 articles remained. Among these, 61 articles were excluded, and 45 articles proceeded to full-text review. 39 of the 45 remaining articles were deemed irrelevant and eliminated, and six articles were included in the qualitative review. Reasons for exclusion: wrong participant group (n = 16), did not analyze changes in the brain related to aerobic exercise (n = 6), studies on rats and animals (n = 7), reviews or meta-analysis (n = 4), wrong outcome (n = 6). The remaining articles were assessed based on full-text reading (see Figure 1 for a PRISMA flow diagram).

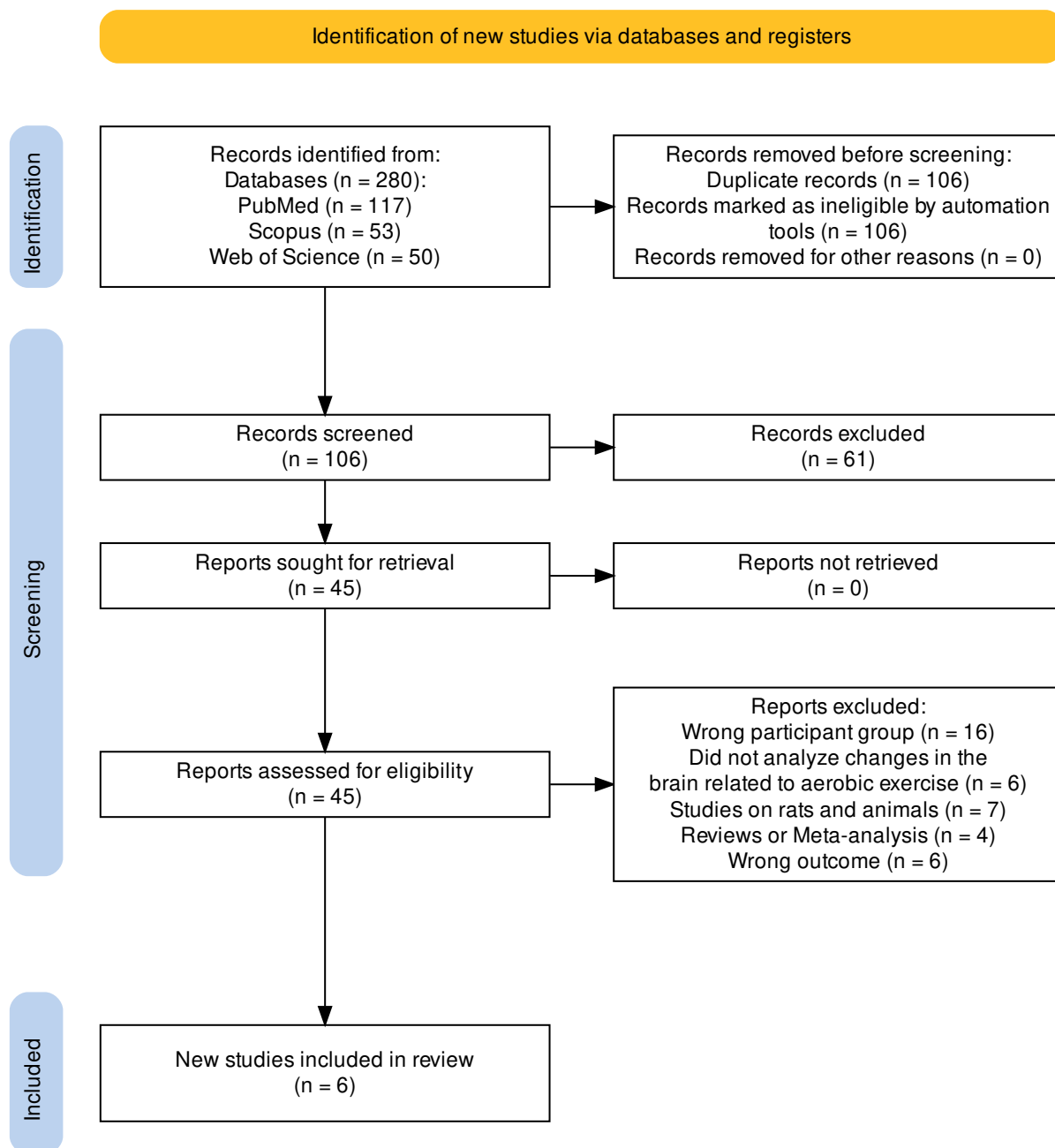
Inclusion and Exclusion Criteria

The studies we will review must involve at least one brain-scanning method, such as Magnetic resonance imaging (MRI), Functional magnetic resonance imaging (fMRI), and Electroencephalography (EEG), or neurobiological mechanism, such as BDNF, or cognitive/behavioral function measures (spatial memory task, Wechsler Memory Scale). We will also incorporate research on randomized controlled trials (RCTs), community-based studies, scholarly publications, and peer-reviewed periodicals. In addition, we will include journals with an Impact Factor (IF) greater than 1.5 to eliminate low-quality journals and studies. Articles written in English and publications that are not outdated between 1999 and 2023 will only be included to focus on important and current facts.

We will exclude studies involving children, animals, or adults suffering from cognitive deficits or neuropsychiatric illnesses such as Dementia, Schizophrenia, or Alzheimer's. Additionally, we will exclude meta-analyses and systematic reviews. We will include studies on different age groups (children, young, middle-aged) if data for elderly individuals are reported separately. To minimize the number of hits, we will filter out studies that do not pertain to neuroscience.

Data Extraction

This systematic review includes six (n=6) articles that met the inclusion criteria (see above). Based on all included studies, the following data were extracted: authors with publications date, study design and country, number of participants and gender, intervention, type of measure, and outcome measure (see Table 1).

Figure 1*PRISMA flow chart*

Note: A PRISMA Flow Diagram illustrates the literature search process (Moher et al., 2009).

Results

Table 1 presents descriptive information about the six studies that met the inclusion criteria. Although this review aimed to find and include studies using one or more of the following methods: MRI, fMRI, or EEG, there were studies using the methods ERP, VO₂peak, and BDNF that fulfilled the inclusion criteria.

Study Characteristics

Across the six studies, there were 496 participants in total, allocated to the intervention or control group. Participants' ages ranged from 55 to 88 years, with a mean age of 71.5 years. All of the studies included in this review consisted of both genders, and the participants were predominantly female (female n=296, male n=200). In addition, three studies (Chang et al., 2013; Colcombe et al., 2006; Erickson et al., 2011) reported that the participants were right-handed. Among the six studies, three were conducted in the United States (Colcombe et al., 2006; Erickson et al., 2011; Erickson et al., 2009), one in Canada (Kovacevic et al., 2020), one in China (Chang et al., 2013), and one in Japan (Nishiguchi et al., 2015).

Regarding the study design, four out of six studies used Randomized controlled trials (Colcombe et al., 2006; Erickson et al., 2011; Erickson et al., 2009; Nishiguchi et al., 2015). While Kovacevic et al. (2020) and Chang et al. (2013) used Community-Based studies. Five studies, namely Chang et al. (2013), Colcombe et al. (2006), Erickson et al. (2011), and Kovacevic et al. (2020), incorporated an active control group, which involved toning and stretching activities, whereas one study used a non-active control group (Nishiguchi et al., 2015). Conversely, Erickson et al. (2009) conducted a comparative analysis between individuals with higher and lower aerobic fitness levels.

Four studies (Colcombe et al., 2006; Erickson et al., 2009; Erickson et al., 2011; Nishiguchi et al., 2015) that were included in this review involved MRI or fMRI as neuroimaging methods (see Table 1). Only one study (Chang et al., 2013) included ERP, whereas Kovacevic et al., (2020) involved BDNF.

Memory Measurements

This review identified different outcome measurements related to memory: neuroimaging and neuroelectric techniques (EEG, fMRI, MRI, and ERP), as well as BDNF and VO₂ max. The behavioral measures were: Sternberg Working Memory Task, Spatial memory task, Mnemonic Similarity task, and Wechsler Memory Scale-Revised (WMS-R). The study conducted by Colcombe et al. (2006) did not incorporate behavioral tasks; however, the utilization of functional magnetic resonance imaging (fMRI) in conjunction with VO₂ max measurements yielded indirect evidence supporting improved brain health and cognitive function, including memory.

Neuroimaging/Neuroelectric Measures

In the study by Chang et al. (2013), the participants' brain activity was recorded using EEG while they completed the working memory exercise. The researchers examined the individuals' ERPs to assess their cerebral activity during the working memory task.

The ERP data showed that higher physical activity was associated with significantly larger P3 amplitude ($11.16 \pm .72 \mu\text{V}$) compared to lower physical activity ($8.17 \pm .72 \mu\text{V}$) ($p < .005$). The P3 component had a significantly larger amplitude at Fz and Pz ($10.12 \pm .60 \mu\text{V}$, $10.51 \pm .51 \mu\text{V}$) compared to Cz ($8.36 \pm .67 \mu\text{V}$) ($p < .005$). The higher physical activity group had a shorter P3 latency ($446.73 \pm 78.01 \text{ ms}$) than the lower physical activity group ($569.56 \pm 116.87 \text{ ms}$) at Cz ($p < .01$); the higher physical activity group also had a significantly larger N1 amplitude compared to the lower physical activity group ($p < .001$). The N1 component had the largest amplitude at Fz ($-4.0 \pm 0.24 \mu\text{V}$) compared to Cz ($-3.38 \pm 0.21 \mu\text{V}$) and Pz ($-1.59 \pm 0.19 \mu\text{V}$) (both $ps < .01$). The N1 component had a significantly longer latency during in-set probe trials compared to out-of-set probe trials ($p < .05$) (Chang et al., 2013).

The study by Colcombe et al. (2006) included additional twenty young adults to serve as controls for the (MRI) but did not participate in the exercise intervention. The MRI analyses revealed that the aerobic exercisers compared to the control groups (the older toning and stretching control group, or the younger control group), showed a greater increase in volume in both gray and white matter primarily located in the prefrontal and temporal cortices—these regions are often reported to show substantial age-related deterioration and are thought to subserve higher-order cognition, such as working memory. Specifically, the regions showing the greatest increase in volume were the anterior cingulate cortex (ACC), supplementary motor area (SMA), right inferior frontal gyrus (rIFG), and the left superior temporal lobe (lSTL) (Colcombe et al., 2006).

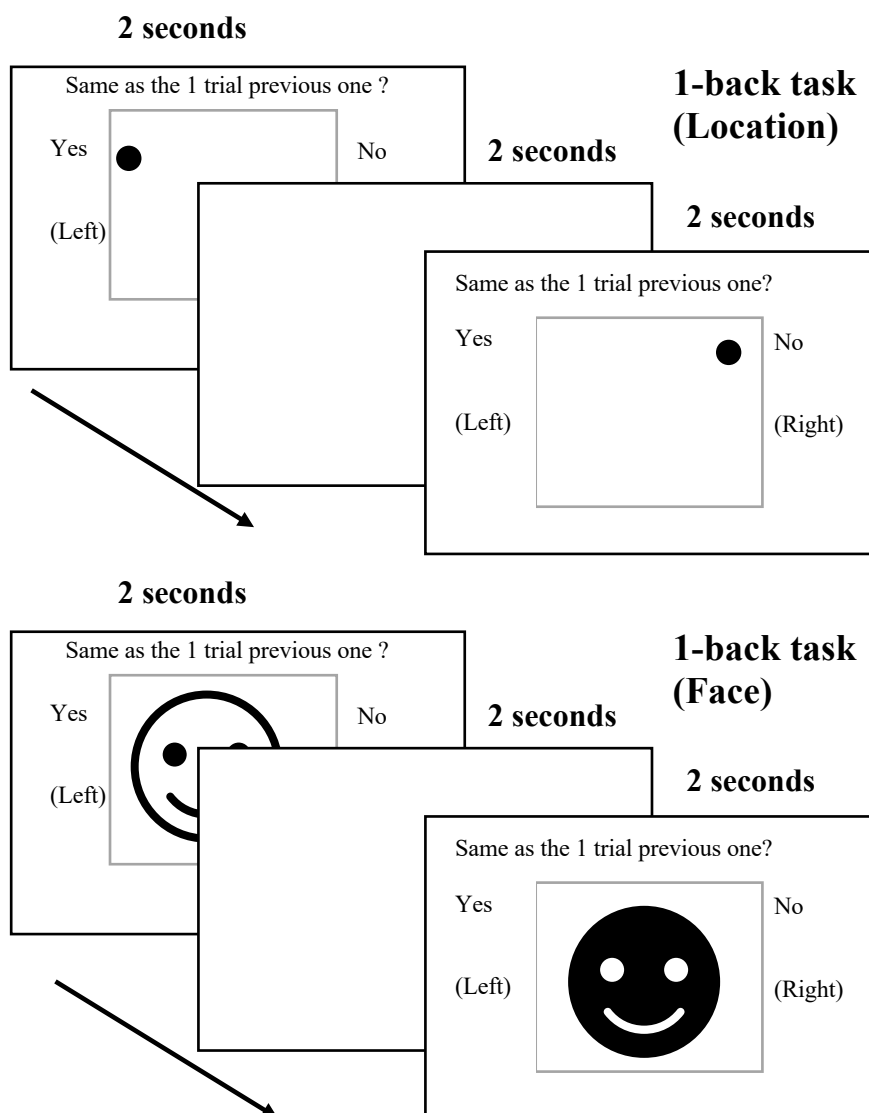
In the study by Erickson et al. (2009), the authors used MRI to measure the left and right hippocampus volume. The result showed greater volumes in the left and right hippocampus were strongly correlated with higher aerobic fitness levels. Even after accounting for age, sex, and overall brain capacity, this association was still significant. Specifically, they found that after accounting for age, sex, and years of education, fitness measurements explained 7.8% and 12.2% of the variance in right and left hippocampal volume, respectively.

In a study by Erickson et al. (2011), MRI was used to collect images before, after six months, and after the completion of the intervention. The findings indicated increased

hippocampus size in the group that underwent aerobic exercise. Specifically, there was a 2.12% and 1.97% increase in volume for the left and right anterior hippocampus, respectively, while the volume of the posterior hippocampus remained unchanged. Conversely, the stretching control group exhibited a decline in volume for the anterior hippocampus (1.40% and 1.43%, respectively) but no significant change in the volume of the posterior hippocampus. Additionally, to further investigate the regional specificity of the intervention, two regions were used as controls: the thalamus and caudate nucleus. Results revealed that the volumes of these regions were unaffected by the intervention (Erickson et al., 2011).

Nishiguchi et al. (2015) assessed the effect of a 12-week multimodal exercise program, encompassing both physical and dual-task exercises, on brain activation associated with visual short-term memory. The researchers used fMRI to evaluate the effects of the intervention on cognitive function, particularly memory, and the efficiency of brain activation. The fMRI data collected during a visual short-term memory task, known as the n-back task ($n = 1, 0$), was designed to assess attention and visual short-term memory (see Figure 2). The fMRI data were analyzed using a region of interest (ROI) approach to examine changes in activation within specific brain regions. The fMRI findings revealed that the intervention group exhibited reduced brain activation associated with face and location tasks in several brain regions, including the bilateral prefrontal cortex. Furthermore, none other regions displayed significantly increased brain activation associated with the face and location tasks. These results suggest that participants could perform the task with less neural effort, as the intervention enhanced the efficiency of their brain activation (Nishiguchi et al., 2015).

Figure 2
n-back task ($n = 1, 0$)



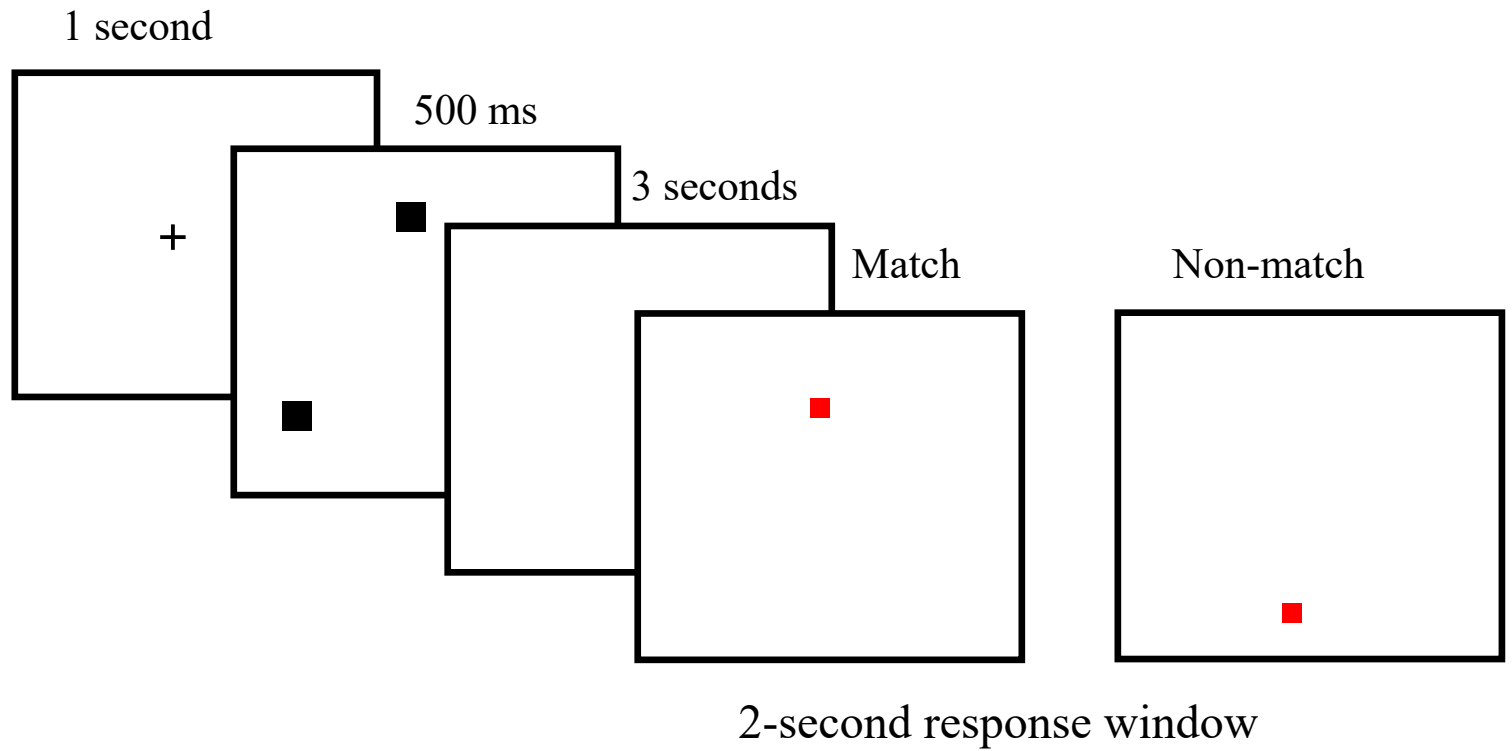
Note. This is a modified version from Nishiguchi et al. (2015). The task comprised different variations for location, face stimuli, and rest periods. During the 0-back task, participants monitored stimuli and indicated whether it was the same as the previous trial. In the location 1-back task, participants monitored the position of a black dot and indicated if it was in the center of the screen. In the face 1-back task, participants identified the sex of neutral faces of young Japanese people (it is essential to mention that the figure depicted emoji representations of faces). During the rest phase, participants fixated on a cross in the center of the screen.

Direct Measures of Memory

Chang et al. (2013) assessed Working Memory (WM) performance using a modified version of the Sternberg WM task (SWM). The SWM task is a popular cognitive task in which participants must memorize a series of items known as the memory set and then determine whether or not a probe item is part of the memory set. The participants were shown a series of letters (memory set), followed by a probe letter, and asked to indicate whether the probe letter was part of the memory set or not. Working memory performance was tested using the reaction time and response accuracy of participants.

The results demonstrated that better performance on the SWM task was correlated with higher levels of physical exercise. In particular, the high physical activity group considerably outperformed the low physical activity group in terms of hit rate (percentage of right answers) ($p < .05$). In addition, the high physical activity group outperformed the low physical activity group in terms of reaction time on successful trials ($p < .05$). According to these results, older individuals who engage in more physical activity may do better while using their working memory (Chang et al., 2013).

In the study by Erickson et al. (2009), spatial memory was evaluated using Spatial Memory task (see Figure 3). The results showed that higher aerobic fitness levels were associated with better performance on the spatial memory task in older adults. Specifically, participants with higher aerobic fitness levels demonstrated higher hit rates and lower false alarm rates than those with lower fitness levels.

Figure 3*Spatial Memory Task*

Note. This is a modified version from Erickson et al. (2009; 2011). Display the spatial memory task used in Erickson et al. (2009) and Erickson et al. (2011). Participants were shown one, two, or three black dots on the screen and asked to remember where they were after a three-second delay (two-item condition shown here). Later, a red dot appeared in either the same or a different location than the target dots (match condition). If the red dot was in a match trial, participants had to press the “m” key; otherwise, they had to press the “x” key. The task assessed spatial memory and response time.

In Erickson et al. (2011) study, spatial memory was evaluated using the same task as in the previous study Erickson et al. (2009) (see Figure 3). The participants completed the task at baseline, after six months, and following the intervention. The findings revealed that both groups exhibited memory improvements, as indicated by a significant increase in accuracy from the initial to the final testing sessions for the aerobic exercise [$t(2,51) = 2.08$; $P < 0.05$] and the stretching control [$t(2,54) = 4.41$; $P < 0.001$] groups. Furthermore, the results were consistent with those of Erickson et al. (2009), that higher baseline and post-intervention aerobic fitness levels were linked to better performance on the spatial memory task.

An altered Mnemonic Similarity Task was used in the recent study by Kovacevic et al. (2020) to assess high-interference memory in older individuals. Participants rated each of the 60 photos of familiar objects indoors or outside during the encoding phase. Then they had to categorize objects as "Old" (repetition), "Similar" (lures), or "New" (foils) in a forced-choice recognition task. Through the use of the lure discrimination index, performance was evaluated. In the mnemonic similarity task, the participant's ability to distinguish between similar but distinct items was found to be enhanced by high-intensity aerobic exercise. In particular, compared to the stretching and toning control group, the lure discrimination index rose 8.8% (95% CI [3.5%, 14.1%], $p = 0.002$) in the high-intensity exercise group. It implies that aerobic exercise at a high intensity may enhance high-interference memory in elderly individuals (Kovacevic et al., 2020).

Indirect Measures of Memory

VO₂ Max. One study used Peak oxygen uptake (VO_{2peak}) to assess cardiorespiratory fitness (Colcombe et al., 2006). The results showed that during the 6-month intervention, the VO_{2peak} of the aerobic fitness training group increased significantly (16.1%), whereas the older control participants did not change significantly (5.3%).

The relationship between VO₂ peak and age, sex, and years of education was significantly correlated in the study by Erickson et al. (2009) ($r = -0.41$, $p < 0.001$), as well as with years of education ($r = 0.23$, $p = 0.003$). With age, sex, and years of schooling included as factors in a hierarchical linear regression analysis, VO₂ peak strongly predicted adjusted right hippocampus volume ($p < 0.001$) and left hippocampal volume ($p < 0.001$), with the greater hippocampal volume being related to higher levels of aerobic fitness. Fitness metrics explained 7.8% and 12.2%, respectively, of the variance in the right and left hippocampus volumes after adjusting for age, sex, and years of schooling.

BDNF. Kovacevic et al. (2020) assessed Serum BDNF levels in participants before and after a 12-week exercise program. There was no significant difference in BDNF levels before or after the exercise program ($F [2,54] = 0.21, p = 0.81$). Changes in BDNF levels did not correlate with changes in cardiorespiratory fitness or memory performance, nor did baseline BDNF levels predict changes in these outcomes (r s ranging from -0.01 to 0.14 , all p s > 0.05). These data show that, at least in the short term, BDNF may not play a significant role in the cognitive advantages of exercise in older individuals.

Table 1
Characteristics of Included Studies

AUTHORS & DATE	STUDY DESIGN & COUNTRY	PARTICIPANTS & GENDER	INTERVENTION	TYPE OF MEASURE	OUTCOME MEASURE
Chang et al., (2013)	Community-Based China	N= 40 (21 female; 19 male)	Light to moderate aerobic exercise (e.g., walking, jogging) Low levels of exercise (e.g., stretching)	Event-Related Potential (ERP) Sternberg Working Memory Task	ERP showed enhanced P3 and N1 amplitudes and shorter P3. Higher physical activity group exhibited better performance on the memory task (p= .05)
Colcombe et al., (2006)	Randomized Controlled Trial (RCT) USA	N= 59 (32 female; 27 male)	Aerobic exercise Stretching control group & young adults (control group)	Magnetic resonance imaging (MRI) Maximal Oxygen Uptake (VO ₂)	Increased volume in both grey and white matter in the prefrontal and temporal cortical. 16.1% increase in VO ₂ peak
Erickson et al. (2009)	Randomized Controlled Trial (RCT) USA	N= 165 (109 female; 56 male)	Higher levels of aerobic fitness exercise Lower fitness levels (control group)	Magnetic resonance imaging (MRI) Spatial Memory Task	Increased hippocampal volume in the left and right hippocampi Higher levels of aerobic fitness were associated with better performance on the spatial memory task

Erickson et al. (2011)	Randomized Controlled Trial (RCT) USA	N= 120 (73 female; 47 male)	Aerobic walking group Stretching control group	Magnetic resonance imaging (MRI) Spatial Memory Task	2.12% and 1.97% increase in volume for the left and right anterior hippocampi Memory improvements and increase in accuracy for the aerobic exercise (P < 0.05) and the stretching control (P < 0.001) groups
Kovacevic et al. (2020)	Community-Based Canada	N= 64 (39 female; 25 male)	High-intensity interval training (HIIT); Moderate continuous training (MCT); and stretching control (CON)	Levels of Brain- derived neurotrophic factor (BDNF) Mnemonic Similarity task (test memory)	No significant differences in BDNF were found between groups HIIT and MCT induced better memory performance than CON
Nishiguchi et al. (2015)	Randomized Controlled Trial (RCT) Japan	N= 48 (22 female; male 26)	Dual task–based multimodal exercise class in combination with walking exercise Non-active control group	Functional magnetic resonance imaging (fMRI) Wechsler Memory Scale-Revised (WMS-R)	Reduced brain activation associated with face and location in bilateral prefrontal cortex. Higher scores on the immediate recall (WMS-LM I: F = 7.44, P = .009) and the delayed recall (WMS-LM II: F = 7.80, P = .008)

Discussion

This systematic review aimed to investigate the effects of aerobic exercise on the neurological foundation of memory skills in healthy individuals aged 50 and older. The review employed various methodologies, including behavioral or cognitive tests, neurobiological mechanisms, and neuroimaging/neuroelectric measures, to explore the impact of aerobic exercise on different forms of memory, such as spatial, working, short-term, and long-term memory.

The findings of the six studies reviewed consistently demonstrated a positive association between aerobic exercise and enhanced memory function in older individuals. Neuroimaging studies revealed that aerobic exercise, in particular, was linked to increased gray and white matter volume in brain regions crucial for higher-order cognition, including working memory. EEG and ERP studies indicated that higher levels of physical activity were associated with larger P3 and N1 amplitudes and shorter P3 latencies, which are markers of improved cognitive processing speed and working memory. Additionally, most studies examined the effects of aerobic exercise on cognitive task performance in older adults, consistently showing that those who engaged in regular aerobic exercise outperformed inactive older adults in tasks related to memory and attention.

These findings align with previous research that has demonstrated faster response speeds on spatial working memory tasks in older individuals with higher physical exercise levels, as observed in the study by Pontifex et al. (2009). Furthermore, the results of Chang et al. (2013) are in line with previous ERP research by Hillman et al. (2006), who found that older adults with higher physical activity levels exhibited larger P3 amplitudes during trials requiring greater executive control.

Similarly, Kovacevic et al. (2020) reported that higher-intensity aerobic exercise had more significant cognitive benefits in older adults compared to lower-intensity exercise, highlighting the potential advantages of higher intensity workouts in this population. On the other hand, Heisz et al. (2017) demonstrated that high-intensity exercise improved memory in sedentary older individuals over a 12-week intervention, emphasizing the importance of exercise intensity in memory enhancement. These studies addressed contradictions in the literature regarding exercise and memory, suggesting that typical moderate continuous exercise may not significantly impact memory in older individuals. Previous exercise programs involving low-to-moderate intensity exercise failed to show memory benefits in older adults over short periods (12 weeks). However, Kovacevic et al. (2020) revealed that

high-intensity exercise can improve cognition in older adults during a short intervention period.

Nishiguchi et al. (2015) reported improved cognitive performance and brain efficiency in elderly individuals, highlighting the potential benefits of combining physical and cognitive exercise regimens in older adults. These findings support and expand on previous research suggesting that physical activity alone or combined with cognitive training can enhance cognitive function in elderly individuals. Only one previous study, conducted by Fabre et al. (2002), which employed physical and cognitive workouts for 12 weeks or less, found improvements in working memory and memory performance in individuals with normal cognition.

The studies by Colcombe et al. (2006), Erickson et al. (2009), and Erickson et al. (2011) collectively demonstrated the positive effects of aerobic exercise on brain structure and memory function in aging individuals. Earlier research has also reported the beneficial effects of exercise on brain structure and cognition, including neuron proliferation and survival, growth of capillary beds, and increased dendritic spines. Additionally, both human and animal studies have shown that aerobic activity promotes the growth and survival of cells in the hippocampus, enhances synaptic plasticity, and provides protection against damage (Black et al., 1990; Cotman & Berchtold, 2002; Van Praag et al., 1999). These findings further support the notion that regular aerobic exercise benefits the cognitive health of aging individuals.

Although the study conducted by Colcombe et al. (2006) primarily focused on investigating the correlation between aerobic exercise and increased brain volume among older individuals, it did not directly examine the specific impact on memory function. However, we have included this study in our review due to evidence suggesting that enhanced brain volume is associated with improved memory function (Erickson et al., 2011). Additionally, Colcombe et al. (2006) used VO₂peak to measure cardiorespiratory fitness, which indirectly supports the correlation between VO₂peak and cognitive performance. It has been observed that individuals with lower VO₂ max experience a faster rate of cognitive deterioration over time, particularly in verbal and visual memory tasks (Wendell et al., 2014).

These findings hold significant implications for society and individuals in mitigating the cognitive decline of healthy older adults. At the individual level, this review contributes to the growing body of evidence suggesting that aerobic exercise is a simple and evidence-based intervention that improves the quality of life for older adults by preserving their

independence, facilitating engagement in social activities, and enhancing daily task performance. At the societal level, physicians and policymakers need to acknowledge the importance of this knowledge, guiding prevention and treatment strategies for cognitive decline, as well as planning safe outdoor spaces and affordable fitness programs. Addressing these barriers through community initiatives and policy changes has the potential to increase exercise rates among older adults.

Limitations

Several limitations can be identified in this review. Firstly, the small sample sizes in the included studies limit the generalizability of the results, as smaller sample sizes may not accurately represent the wider population. Three studies had fewer than 60 participants, with the study by Chang et al. (2013) having the smallest sample size of only 40 participants.

Secondly, selection biases may have influenced some of the findings, as seen in the study by Chang et al. (2013). The comparison between groups with higher and lower physical activity levels may have been influenced by selection bias.

Thirdly, most studies relied on self-reported physical activity measurements, which may not always provide an accurate representation of actual physical activity levels. Self-reporting can be subject to recall bias or social desirability bias, potentially impacting the reliability of the data.

Fourthly, the duration and intensity of exercise interventions varied across studies, making it challenging to compare results and determine the optimal exercise regimen for cognitive benefits. For example, Kovacevic et al. (2020) and Nishiguchi et al. (2015) implemented 12 weeks of intervention, but the specific exercise protocols and intensity levels differed.

Fifthly, a follow-up assessment after the intervention was not conducted in the study by Nishiguchi et al. (2015), thus limiting our knowledge of any potential long-term effects of the intervention.

Lastly, it is important to acknowledge that this review was subject to language bias, as it only included articles published in English. This exclusion of non-English articles may have limited the scope of the review and potentially introduced bias in the findings.

These limitations should be taken into consideration when interpreting the results of this review and highlight areas that require further research to address these limitations and provide more robust evidence.

Future Research

Future research could explore the impact of exercise intensity on memory performance in older adults, building upon the findings of Kovacevic et al. (2020), who demonstrated that higher-intensity aerobic exercise had a greater effect on memory compared to lower-intensity exercise in healthy older individuals. It would be valuable to

investigate the underlying mechanisms that mediate the relationship between exercise intensity and cognitive outcomes in this population.

Additionally, future studies should examine the potential cognitive benefits of varying exercise durations through physical and cognitive training regimens for older individuals. For example, Nishiguchi et al. (2015) reported positive outcomes with a 12-week program combining cardiovascular exercise and cognitive training among older adults in the community. Further investigations could explore whether extending the duration of such programs or increasing their intensity would yield even more significant effects on cognitive function.

By addressing these research gaps, we can gain a deeper understanding of how exercise intensity and duration influence memory performance in older adults, which can inform the development of optimized exercise interventions for cognitive enhancement in this population.

Ethical and Societal Aspects

All six studies obtained ethics committee approval. All participants provided informed consent by signing a written form except the study by Nishiguchi et al. (2015). There were no reports of ethical dilemmas, conflicts of interest, or participants' exposure to any risks related to the aerobic exercises or different methodologies used. Moreover, none of the studies involved participants with psychiatric or physiological disorders; all studies exclusively enrolled healthy older adults.

From a societal perspective, research investigating the effects of aerobic exercise on the health of older adults holds significant importance, particularly given the challenges posed by the growing aging population. The potential benefits of aerobic exercises, such as improvements in physical and mental health, cognitive function, mobility, and social engagement, are crucial for enhancing the quality of life for this population. This research area is valuable to society as it offers a non-pharmacological and cost-effective intervention that may be easily accessible depending on the type of activity. However, it is essential to consider individual circumstances and limitations when implementing such interventions to ensure safety and effectiveness.

Conclusions

The research examined in this systematic review provides evidence supporting the beneficial impact of aerobic exercise on memory function in healthy older individuals. The findings from the research on cognitive task performance and neuroimaging consistently demonstrate that aerobic exercise improves memory function, increases brain volume, and enhances cognitive task performance in older individuals. Interestingly, moderate- to high-intensity exercise appears to be more advantageous for memory function compared to low-intensity exercise. Based on these results, regular physical activity emerges as a crucial

component of a healthy lifestyle to preserve cognitive function as individuals age. These research findings imply that regular aerobic exercise benefits older individuals' cognitive task performance, brain structure, and overall cognitive function.

References

- Alexandrov, A. K., & Fedoseev, L. M. (2012). Long-Term Memory. Nova Science Publishers, Inc.
- Ashpole, N. M., Sanders, J. N., Hodges, E. L., Yan, H., & Sonntag, W. E. (2015). Growth hormone, insulin-like growth factor-1 and the aging brain. *Experimental Gerontology*, 68, 76–81. <https://doi.org/10.1016/j.exger.2014.10.002>
- Baddeley, A. D. (2003). Working memory: looking back and looking forward. *Nature Reviews Neuroscience*, 4(10), 829–839. <https://doi.org/10.1038/nrn1201>
- Baddeley, A. D. (2010). Working memory. *Current Biology*, 20(4), R136–R140. <https://doi.org/10.1016/j.cub.2009.12.014>
- Baddeley, A. D. (2012). Working Memory: Theories, Models, and Controversies. *Annual Review of Psychology*, 63(1), 1–29. <https://doi.org/10.1146/annurev-psych-120710-100422>
- Black, J. H., Isaacs, K. R., Anderson, B. J., Alcantara, A. A., & Greenough, W. T. (1990). Learning causes synaptogenesis, whereas motor activity causes angiogenesis, in cerebellar cortex of adult rats. *Proceedings of the National Academy of Sciences of the United States of America*, 87(14), 5568–5572. <https://doi.org/10.1073/pnas.87.14.5568>
- Bouaziz, W., Vogel, T., Schmitt, E., Kaltenbach, G., Geny, B., & Lang, P. O. (2017). Health benefits of aerobic training programs in adults aged 70 and over: a systematic review. *Archives of Gerontology and Geriatrics*, 69, 110–127. <https://doi.org/10.1016/j.archger.2016.10.012>
- Brod, G., Werkle-Bergner, M., & Shing, Y. L. (2013). The Influence of Prior Knowledge on Memory: A Developmental Cognitive Neuroscience Perspective. *Frontiers in Behavioral Neuroscience*, 7. <https://doi.org/10.3389/fnbeh.2013.00139>
- Cabeza, R. (2002). Hemispheric asymmetry reduction in older adults: The HAROLD model. *Psychology and Aging*, 17(1), 85–100. <https://doi.org/10.1037/0882-7974.17.1.85>
- Camina, E., & Güell, F. (2017). The Neuroanatomical, Neurophysiological and Psychological Basis of Memory: Current Models and Their Origins. *Frontiers in Pharmacology*, 8. <https://doi.org/10.3389/fphar.2017.00438>
- Chang, Y. K., Huang, C. L., Chen, K. C., & Hung, T. M. (2013). Physical activity and working memory in healthy older adults: An ERP study. *Psychophysiology*, 50(11), 1174–1182. <https://doi.org/10.1111/psyp.12089>
- Colberg, S. R., Sigal, R. J., Fernhall, B., Regensteiner, J. G., Blissmer, B., Rubin, R. R., Chasan-Taber, L., Albright, A. L., & Braun, B. (2010). *Exercise and Type 2 Diabetes*. *Diabetes Care*, 33(12), e147–e167. <https://doi.org/10.2337/dc10-9990>

- Colberg, S. R., Sigal, R. J., Yardley, J. E., Riddell, M. C., Dunstan, D. W., Dempsey, P. C., Horton, E. S., Castorino, K., & Tate, D. F. (2016). Physical Activity/Exercise and Diabetes: A Position Statement of the American Diabetes Association. *Diabetes Care*, *39*(11), 2065–2079. <https://doi.org/10.2337/dc16-1728>
- Colcombe, S. J., Erickson, K. I., Scalf, P. E., Kim, J. S., Prakash, R., McAuley, E., Elavsky, S., Marquez, D. X., Hu, L., & Kramer, A. F. (2006). Aerobic Exercise Training Increases Brain Volume in Aging Humans. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences*, *61*(11), 1166–1170. <https://doi.org/10.1093/gerona/61.11.1166>
- Corkin, S. (2002). What's new with the amnesic patient H.M.? *Nature Reviews Neuroscience*, *3*(2), 153–160. <https://doi.org/10.1038/nrn726>
- Cotman, C. W., & Berchtold, N. C. (2002). Exercise: a behavioral intervention to enhance brain health and plasticity. *Trends in Neurosciences*, *25*(6), 295–301. [https://doi.org/10.1016/S0166-2236\(02\)02143-4](https://doi.org/10.1016/S0166-2236(02)02143-4)
- Cowan, N. (2014). Working Memory Underpins Cognitive Development, Learning, and Education. *Educational Psychology Review*, *26*(2), 197–223. <https://doi.org/10.1007/s10648-013-9246-y>
- Cowan, N. (2017). The many faces of working memory and short-term storage. *Psychonomic Bulletin & Review*, *24*(4), 1158–1170. <https://doi.org/10.3758/s13423-016-1191-6>
- Davachi, L. (2006). Item, context and relational episodic encoding in humans. *Current Opinion in Neurobiology*, *16*(6), 693–700. <https://doi.org/10.1016/j.conb.2006.10.012>
- Denham, J., Marques, F. Z., O'Brien, B. J., & Charchar, F. J. (2014). Exercise: Putting Action into Our Epigenome. *Sports Medicine*, *44*(2), 189–209. <https://doi.org/10.1007/s40279-013-0114-1>
- Dilorenzo, T. J., Bargman, E. P., Stucky-Ropp, R. C., Brassington, G. S., Frensch, P. A., & LaFontaine, T. (1999). Long-Term Effects of Aerobic Exercise on Psychological Outcomes. *Preventive Medicine*, *28*(1), 75–85. <https://doi.org/10.1006/pmed.1998.0385>
- Doxey, C. R., & Kirwan, C. C. (2015). Structural and functional correlates of behavioral pattern separation in the hippocampus and medial temporal lobe. *Hippocampus*, *25*(4), 524–533. <https://doi.org/10.1002/hipo.22389>
- Erickson, K. I., Prakash, R. S., Voss, M. W., Chaddock, L., Hu, L., Morris, K., White, S. M., Wójcicki, T. R., McAuley, E., & Kramer, A. F. (2009). Aerobic fitness is associated with hippocampal volume in elderly humans. *Hippocampus*, *19*(10), 1030–1039. <https://doi.org/10.1002/hipo.20547>

- Erickson, K. I., Voss, M. W., Prakash, R. S., Basak, C., Szabo, A., Chaddock, L., Kim, J. S., Heo, S., Alves, H., White, S. M., Wojcicki, T. R., Mailey, E., Vieira, V. J., Martin, S. A., Pence, B. D., Woods, J. A., McAuley, E., & Kramer, A. F. (2011). Exercise training increases size of hippocampus and improves memory. *Proceedings of the National Academy of Sciences*, *108*(7), 3017–3022. <https://doi.org/10.1073/pnas.1015950108>
- Erickson, K. I., Hillman, C. H., & Kramer, A. F. (2015). Physical activity, brain, and cognition. *Current Opinion in Behavioral Sciences*, *4*, 27–32. <https://doi.org/10.1016/j.cobeha.2015.01.005>
- Fabre, C., Chamari, K., Mucci, P., Massé-Biron, J., & Prefaut, C. (2002). Improvement of Cognitive Function by Mental and/or Individualized Aerobic Training in Healthy Elderly Subjects. *International Journal of Sports Medicine*, *23*(6), 415–421. <https://doi.org/10.1055/s-2002-33735>
- Fjell, A. M., McEvoy, L. K., Holland, D., Dale, A. M., & Walhovd, K. B. (2014). What is normal in normal aging? Effects of aging, amyloid and Alzheimer’s disease on the cerebral cortex and the hippocampus. *Progress in Neurobiology*, *117*, 20–40. <https://doi.org/10.1016/j.pneurobio.2014.02.004>
- Fletcher, G. F., Blair, S. N., Blumenthal, J. A., Caspersen, C. J., Chaitman, B. R., Epstein, S. E., Falls, H. F., Froelicher, E. S., Froelicher, V. F., & Piña, I. L. (1992). Statement on Exercise: Benefits and Recommendations for Physical Activity Programs for All Americans. *Circulation*, *94*(4), 857–862. <https://doi.org/10.1161/01.cir.94.4.857>
- Foster, C., Porcari, J. P., Anderson, J. J., Paulson, M., Smaczny, D. M., Webber, H., Doberstein, S. T., & Udermann, B. E. (2008). The Talk Test as a Marker of Exercise Training Intensity. *Journal of Cardiopulmonary Rehabilitation and Prevention*, *28*(1), 24–30. <https://doi.org/10.1097/01.hcr.0000311504.41775.78>
- Garcia, A. P., & Buffalo, E. A. (2020). Anatomy and Function of the Primate Entorhinal Cortex. *Annual Review of Vision Science*, *6*(1), 411–432. <https://doi.org/10.1146/annurev-vision-030320-041115>
- Gligoroska, J. P., & Manchevska, S. (2012). The Effect of Physical Activity on Cognition - Physiological Mechanisms. *Materia Socio-Medica*, *24*(3), 198. <https://doi.org/10.5455/msm.2012.24.198-202>
- Hall, C. D., Smith, A. D., & Keele, S. W. (2001). The impact of aerobic activity on cognitive function in older adults: A new synthesis based on the concept of executive control. *European Journal of Cognitive Psychology*, *13*(1–2), 279–300. <https://doi.org/10.1080/09541440126012>
- Harada, C. N., Love, M. N., & Triebel, K. L. (2013). Normal Cognitive Aging. *Clinics in Geriatric Medicine*, *29*(4), 737–752. <https://doi.org/10.1016/j.cger.2013.07.002>

- He, Q., Han, A. T., Churaman, T. A., & Brown, T. I. (2021). The role of working memory capacity in spatial learning depends on spatial information integration difficulty in the environment. *Journal of Experimental Psychology: General*, *150*(4), 666–685. <https://doi.org/10.1037/xge0000972>
- Heissel, A., Heinen, D., Brokmeier, L. L., Skarabis, N., Kangas, M., Vancampfort, D., Stubbs, B., Firth, J., Ward, P. B., Rosenbaum, S., Hallgren, M., & Schuch, F. B. (2023). Exercise as medicine for depressive symptoms? A systematic review and meta-analysis with meta-regression. *British Journal of Sports Medicine*. <https://doi.org/10.1136/bjsports-2022-106282>
- Heisz, J. J., Clark, I. B., Bonin, K., Paolucci, E., Michalski, B., Becker, S., & Fahnestock, M. (2017). The Effects of Physical Exercise and Cognitive Training on Memory and Neurotrophic Factors. *Journal of Cognitive Neuroscience*, *29*(11), 1895–1907. https://doi.org/10.1162/jocn_a_01164
- Hillman, C. H., Erickson, K. I., & Kramer, A. F. (2008). Be smart, exercise your heart: exercise effects on brain and cognition. *Nature Reviews Neuroscience*, *9*(1), 58–65. <https://doi.org/10.1038/nrn2298>
- Hillman, C. H., Kramer, A. F., Belopolsky, A. V., & Smith, D. (2006). A cross-sectional examination of age and physical activity on performance and event-related brain potentials in a task switching paradigm. *International Journal of Psychophysiology*, *59*(1), 30–39. <https://doi.org/10.1016/j.ijpsycho.2005.04.009>
- Jia, J., Zhao, T., Liu, Z., Liang, Y., Li, F., Li, Y., Liu, W., Li, F., Shi, S., Zhou, C., Yang, H., Liao, Z., Li, Y., Zhao, H., Zhang, J., Zhang, K., Kan, M., Yang, S., Li, H., . . . Cummings, J. (2023). Association between healthy lifestyle and memory decline in older adults: 10 year, population based, prospective cohort study. *BMJ*, e072691. <https://doi.org/10.1136/bmj-2022-072691>
- Kelly, M., Loughrey, D. G., Lawlor, B. A., Robertson, I. H., Walsh, C., & Brennan, S. (2014). The impact of exercise on the cognitive functioning of healthy older adults: A systematic review and meta-analysis. *Ageing Research Reviews*, *16*, 12–31. <https://doi.org/10.1016/j.arr.2014.05.002>
- Kirkland, J. L., & Tchkonina, T. (2017). Cellular Senescence: A Translational Perspective. *EBioMedicine*, *21*, 21–28. <https://doi.org/10.1016/j.ebiom.2017.04.013>
- Kovacevic, A., Fenesi, B., Paolucci, E. O., & Heisz, J. J. (2020). The effects of aerobic exercise intensity on memory in older adults. *Applied Physiology, Nutrition, and Metabolism*, *45*(6), 591–600. <https://doi.org/10.1139/apnm-2019-0495>
- Lazzer, S., Rejc, E., & Del Torto, A. (2018). Benefits of aerobic exercise training with recommendations for Healthy Aging. *Annales Kinesiologiae*, *8*(2), 111–124. <https://doi.org/10.35469/ak.2017.135>

- Levin, O., Netz, Y., & Ziv, G. (2017). The beneficial effects of different types of exercise interventions on motor and cognitive functions in older age: a systematic review. *European Review of Aging and Physical Activity*, 14(1).
<https://doi.org/10.1186/s11556-017-0189-z>
- Lu, B., Nagappan, G., & Lu, Y. (2014). BDNF and Synaptic Plasticity, Cognitive Function, and Dysfunction. In *Handbook of experimental pharmacology* (pp. 223–250). Springer Science+Business Media. https://doi.org/10.1007/978-3-642-45106-5_9
- Ludyga, S., Gerber, M., Brand, S., Holsboer-Trachslers, E., & Pühse, U. (2016). Acute effects of moderate aerobic exercise on specific aspects of executive function in different age and fitness groups: A meta-analysis. *Psychophysiology*, 53(11), 1611–1626.
<https://doi.org/10.1111/psyp.12736>
- Mackay, C., Kuys, S., & Brauer, S. G. (2017). The Effect of Aerobic Exercise on Brain-Derived Neurotrophic Factor in People with Neurological Disorders: A Systematic Review and Meta-Analysis. *Neural Plasticity*, 2017, 1–9. <https://doi.org/10.1155/2017/4716197>
- Maguire, E. A., Gadian, D. G., Johnsrude, I. S., Good, C. D., Ashburner, J., Frackowiak, R. S. J., & Frith, C. D. (2000). Navigation-related structural change in the hippocampi of taxi drivers. *Proceedings of the National Academy of Sciences of the United States of America*, 97(8), 4398–4403. <https://doi.org/10.1073/pnas.070039597>
- Mead, G., Morley, W., Campbell, P., Greig, C. A., McMurdo, M. E. T., & Lawlor, D. A. (2008). Exercise for depression. *Cochrane Database of Systematic Reviews*.
<https://doi.org/10.1002/14651858.cd004366.pub3>
- Milner, B. (2005). The Medial Temporal-Lobe Amnesic Syndrome. *Psychiatric Clinics of North America*, 28(3), 599–611. <https://doi.org/10.1016/j.psc.2005.06.002>
- Millstein, R. (2013). Aerobic Exercise. *Encyclopedia of Behavioral Medicine*. Springer, New York, NY. https://doi.org/10.1007/978-1-4419-1005-9_1087
- Moher, D., Liberati, A., Tetzlaff, J., & Altman, D. G. (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Medicine*, 6(7), e1000097. <https://doi.org/10.1371/journal.pmed.1000097>
- Morres, I., Hatzigeorgiadis, A., Stathi, A., Zourbanos, N., Arpin-Cribbie, C. A., Krommidas, C., & Theodorakis, Y. (2019). Aerobic exercise for adult patients with major depressive disorder in mental health services: A systematic review and meta-analysis. *Depression and Anxiety*, 36(1), 39–53. <https://doi.org/10.1002/da.22842>
- Muscella, A., Stefàno, E., Lunetti, P., Capobianco, L., & Marsigliante, S. (2020). The Regulation of Fat Metabolism during Aerobic Exercise. *Biomolecules*, 10(12), 1699.
<https://doi.org/10.3390/biom10121699>
- Ngandu, T., Lehtisalo, J., Solomon, A., Levälähti, E., Ahtiluoto, S., Antikainen, R., Bäckman, L., Hänninen, T., Jula, A., Laatikainen, T., Lindström, J., Mangialasche, F., Paajanen,

- T., Pajala, S., Peltonen, M., Rauramaa, R., Stigsdotter-Neely, A., Strandberg, T. E., Tuomilehto, J., . . . Kivipelto, M. (2015). A 2 year multidomain intervention of diet, exercise, cognitive training, and vascular risk monitoring versus control to prevent cognitive decline in at-risk elderly people (FINGER): a randomised controlled trial. *The Lancet*, *385*(9984), 2255–2263. [https://doi.org/10.1016/s0140-6736\(15\)60461-5](https://doi.org/10.1016/s0140-6736(15)60461-5)
- Nishiguchi, S., Yamada, M., Tanigawa, T., Sekiyama, K., Kawagoe, T., Suzuki, M., Yoshikawa, S., Abe, N., Otsuka, Y., Nakai, R., Aoyama, T., & Tsuboyama, T. (2015). A 12-Week Physical and Cognitive Exercise Program Can Improve Cognitive Function and Neural Efficiency in Community-Dwelling Older Adults: A Randomized Controlled Trial. *Journal of the American Geriatrics Society*, *63*(7), 1355–1363. <https://doi.org/10.1111/jgs.13481>
- Northey, J. M., Cherbuin, N., Pumpa, K. L., Smee, D. J., & Rattray, B. (2018). Exercise interventions for cognitive function in adults older than 50: a systematic review with meta-analysis. *British Journal of Sports Medicine*, *52*(3), 154–160. <https://doi.org/10.1136/bjsports-2016-096587>
- Nyberg, L., Lövdén, M., Riklund, K., Lindenberger, U., & Bäckman, L. (2012). Memory aging and brain maintenance. *Trends in Cognitive Sciences*, *16*(5), 292–305. <https://doi.org/10.1016/j.tics.2012.04.005>
- Ouzzani, M., Hammady, H., Fedorowicz, Z., & Elmagarmid, A. (2016). Rayyan-a web and mobile app for systematic reviews. *Systematic Reviews*, *5*(1), 1–10. <https://doi.org/10.1186/s13643-016-0384-4>
- Patel, H., Alkhwam, H., Madanieh, R., Shah, N., Kosmas, C. E., & Vittorio, T. J. (2017). Aerobic vs anaerobic exercise training effects on the cardiovascular system. *World Journal of Cardiology*, *9*(2), 134. <https://doi.org/10.4330/wjc.v9.i2.134>
- Park, D. C., & Reuter-Lorenz, P. A. (2009). The Adaptive Brain: Aging and Neurocognitive Scaffolding. *Annual Review of Psychology*, *60*(1), 173–196. <https://doi.org/10.1146/annurev.psych.59.103006.093656>
- Perez-Terzic, C. (2012). Exercise in Cardiovascular Diseases. *PM&R*, *4*(11), 867–873. <https://doi.org/10.1016/j.pmrj.2012.10.003>
- Phelps, E. A. (2004). Human emotion and memory: interactions of the amygdala and hippocampal complex. *Current Opinion in Neurobiology*, *14*(2), 198–202. <https://doi.org/10.1016/j.conb.2004.03.015>
- Pontifex, M. B., Hillman, C. H., Fernhall, B., Thompson, K. R., & Valentini, T. A. (2009). The Effect of Acute Aerobic and Resistance Exercise on Working Memory. *Medicine and Science in Sports and Exercise*, *41*(4), 927–934. <https://doi.org/10.1249/mss.0b013e3181907d69>

- Ranganath, C., & Ritchey, M. (2012). Two cortical systems for memory-guided behaviour. *Nature Reviews Neuroscience*, *13*(10), 713–726. <https://doi.org/10.1038/nrn3338>
- Raz, N., Rodrigue, K. M., Kennedy, K. M., & Acker, J. R. (2007). Vascular health and longitudinal changes in brain and cognition in middle-aged and older adults. *Neuropsychology (Journal)*, *21*(2), 149–157. <https://doi.org/10.1037/0894-4105.21.2.149>
- Riedel, W. J., & Blokland, A. (2015). Declarative memory. *Cognitive Enhancement*, 215–236. https://doi.org/10.1007/978-3-319-16522-6_7
- Salat, D. H., Buckner, R. L., Snyder, A. Z., Greve, D. N., Desikan, R. S., Busa, E., Morris, J. C., Dale, A. M., & Fischl, B. (2004). Thinning of the Cerebral Cortex in Aging. *Cerebral Cortex*, *14*(7), 721–730. <https://doi.org/10.1093/cercor/bhh032>
- Salthouse, T. A. (2010). Selective review of cognitive aging. *Journal of the International Neuropsychological Society*, *16*(5), 754–760. <https://doi.org/10.1017/s1355617710000706>
- Schacter, D. L., & Addis, D. R. (2007). The cognitive neuroscience of constructive memory: remembering the past and imagining the future. *Philosophical Transactions of the Royal Society B*, *362*(1481), 773–786. <https://doi.org/10.1098/rstb.2007.2087>
- Small, S. A., Schobel, S., Buxton, R. B., Witter, M. P., & Barnes, C. A. (2011). A pathophysiological framework of hippocampal dysfunction in ageing and disease. *Nature Reviews Neuroscience*, *12*(10), 585–601. <https://doi.org/10.1038/nrn3085>
- Snowling, N. J., & Hopkins, W. G. (2006). Effects of Different Modes of Exercise Training on Glucose Control and Risk Factors for Complications in Type 2 Diabetic Patients. *Diabetes Care*, *29*(11), 2518–2527. <https://doi.org/10.2337/dc06-1317>
- Squire, L. R. (2004). Memory systems of the brain: A brief history and current perspective. *Neurobiology of Learning and Memory*, *82*(3), 171–177. <https://doi.org/10.1016/j.nlm.2004.06.005>
- Squire, L. R., Kasri, N. N., Wixted, J. T., & Morris, R. W. (2015). Memory Consolidation. *Cold Spring Harbor Perspectives in Biology*, *7*(8), a021766. <https://doi.org/10.1101/cshperspect.a021766>
- Stewart, K. J., Bacher, A. C., Turner, K. M. E., Lim, J., Hees, P. S., Shapiro, E. S., Tayback, M., & Ouyang, P. (2005). Exercise and risk factors associated with metabolic syndrome in older adults. *American Journal of Preventive Medicine*, *28*(1), 9–18. <https://doi.org/10.1016/j.amepre.2004.09.006>
- Sullivan, E. V., & Pfefferbaum, A. (2006). Diffusion tensor imaging and aging. *Neuroscience & Biobehavioral Reviews*, *30*(6), 749–761. <https://doi.org/10.1016/j.neubiorev.2006.06.002>

- Sundari, L. P. R., & Arsani, N. L. K. A. (2022). Regular physical exercise increase of growth hormone (GH) and insulin-like growth factor-1 (IGF-1) activity in elderly improve the aging process and quality of life: A mini review. *Biomedical and Pharmacology Journal* 15(2), 883–890. <https://doi.org/10.13005/bpj/2422>
- Thayer, E. A. (2016). *Spatial, Long-and Short-term Memory: Functions, Differences and Effects of Injury*.
- Thompson, R. F. (2005). In Search of Memory Traces. *Annual Review of Psychology*, 56(1), 1–23. <https://doi.org/10.1146/annurev.psych.56.091103.070239>
- Thompson, R. F., & Madigan, S. A. (2013). *Memory: The Key to Consciousness*. Princeton University Press.
- Tian, D., & Meng, J. (2019). Exercise for Prevention and Relief of Cardiovascular Disease: Prognoses, Mechanisms, and Approaches. *Oxidative Medicine and Cellular Longevity*, 2019, 1–11. <https://doi.org/10.1155/2019/3756750>
- Tulving, E., & Craik, F. I. M. (Eds). (2000). *The Oxford Handbook of Memory*. Oxford University Press.
- Van Praag, H. M., Christie, B., Sejnowski, T. J., & Gage, F. H. (1999). Running enhances neurogenesis, learning, and long-term potentiation in mice. *Proceedings of the National Academy of Sciences of the United States of America*, 96(23), 13427–13431. <https://doi.org/10.1073/pnas.96.23.13427>
- Wendell, C. R., Gunstad, J., Waldstein, S. R., Wright, J. G., Ferrucci, L., & Zonderman, A. B. (2014). Cardiorespiratory Fitness and Accelerated Cognitive Decline With Aging. *The Journals of Gerontology*, 69(4), 455–462. <https://doi.org/10.1093/gerona/glt144>
- World Health Organization: WHO. (2022, October 5). *Physical activity*. Retrieved Mars 8, 2023, from <https://www.who.int/news-room/fact-sheets/detail/physical-activity>
- Xie, Y., Wu, Z., Sun, L., Zhou, L., Wang, G., Xiao, L., & Wang, H. (2021). The Effects and Mechanisms of Exercise on the Treatment of Depression. *Frontiers in Psychiatry*, 12, 705559. <https://doi.org/10.3389/fpsy.2021.705559>
- Xiong, J., Ye, M., Wang, L., & Zheng, G. (2021). Effects of physical exercise on executive function in cognitively healthy older adults: A systematic review and meta-analysis of randomized controlled trials. *International Journal of Nursing Studies*, 114, 103810. <https://doi.org/10.1016/j.ijnurstu.2020.103810>
- Young, J. R., Angevaren, M., Rusted, J., & Tabet, N. (2015). Aerobic exercise to improve cognitive function in older people without known cognitive impairment. *The Cochrane Library*. <https://doi.org/10.1002/14651858.cd005381.pub4>