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■ RESEARCH ARTICLE

Exercise, Episodic Memory, and Age: A Systematic Review

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ABSTRACT: Consistent long-term exercise has been understood to have broad positive effects on overall cognition, and there is also evidence supporting the benefits of exercise on episodic memory in particular. However, different forms of exercise, such as aerobic and resistance, can induce different physiological implications, changing the ways in which episodic memory is affected. This review paper aimed to investigate the ways and degrees to which different forms of long-term aerobic and resistance exercise affect episodic memory, as well as investigate the role that age plays in the magnitude of this effect. While both resistance and aerobic training were likely to illustrate an improvement in episodic memory performance, the results of long-term aerobic training were expected to have a greater positive impact on episodic memory. It was also expected that age would have a direct correlation on the magnitude of this effect. These hypotheses were supported by the findings of the review. Episodic memory likely experiences greatest improvement through exercise-induced neurogenesis and signalling pathways activated by increased levels of Brain-Derived Neurotrophic Factor (BDNF) and Insulin-like Growth Factor-1 (IGF-1), primarily as a result of aerobic and resistance exercise, respectively. Furthermore, it was found that the magnitude of this effect peaked within the age range of 55-68 years, potentially supporting the existence of a more exact optimal age for which exercise would have the most pronounced effect on episodic memory. Understanding the effect of both long-term aerobic and resistance training on episodic memory can have a widespread impact. It can unlock avenues to potentially enhancing memory and may help discover new methods to treat or prevent cognitive decline and neurodegenerative diseases.

KEYWORDS: Behavioral and Social Sciences; Cognitive Psychology; Cognition; Episodic Memory; Neurogenesis.

■ Introduction

Neurodegenerative diseases are a significant problem in the world today; they have an immense adverse effect on individuals' quality of life, social interactions, and mental health. It is estimated that they affect 15% of the global population and that percentage is significantly higher for the elderly, with aging being the primary risk factor for these diseases.[1-4] While there are a vast range of pharmaceutical methods to help prevent or even reduce the adverse effect of these diseases, recent evidence shows that exercise can actually have a significant effect on improving cognition,[5,6] and episodic memory in particular.[1,2]

These studies in relation to the effects of exercise on cognition and episodic memory typically focus on two distinct types: aerobic exercise and resistance exercise, both of which have distinct physical implications. Aerobic exercise stresses the body's cardiovascular and respiratory systems; it is rhythmic in nature and primarily utilizes large muscle groups that rely on energy in the form of adenosine triphosphate (ATP) extracted from aerobic metabolism.[7] Some examples include, running, dancing, and swimming. Resistance exercise, on the other hand, stresses the musculoskeletal system and involves the progressive use of resistance to exert force,[8] examples include weightlifting, push-ups, squats, and sit-ups.

Aerobic and resistance exercise have both been shown to improve episodic memory. Long-term exercise, both aerobic and resistance, have been shown to lower Whole Blood Viscosity (WBV) levels,[9,10] a measure of resistance to blood flow; WBV levels have been shown to be negatively correlated with cognitive performance.[11] Both forms of exercise also increase cerebral blood flow (CBF), improving cognition and episodic memory performance.[12,13]

Long-term aerobic exercise has been shown to increase Brain-Derived Neurotrophic Factor (BDNF) levels,[2,14,15] which can enhance plasticity and induce hippocampal neurogenesis,[15,16] improving episodic memory performance. The impact of long-term resistance training on BDNF levels has been shown to be much lower. Resistance training may also affect episodic memory through unique mechanisms. Resistance training was shown to be effective for inducing Insulin-like Growth Factor-1 (IGF-1) increase, which is correlated with improved cognition.[17,18]

Given the significant role BDNF production plays in improving episodic memory and inducing Long-term Potentiation (LTP),[2,19,20] which strengthens synapses and improves signal transmission between neurons, combined with the significant role aerobic exercise can play in increasing BDNF production, it is hypothesised that long-term aerobic exercise will have a greater impact on episodic memory than resistance exercise.

Both long-term aerobic and resistance training have positive effects on episodic memory performance.[1,21,22] However, there is a gap in the literature for comparative review and differences between the effects aerobic and resistance training have on episodic memory, which we intend to explore. Given that they have different physical implications, it is likely that the way

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they affect episodic memory and the degree to which they do so differs too.

While long-term aerobic and resistance training have been shown to improve episodic memory amongst older adults, some evidence suggests that the effect may be more significant for specific older age ranges.[23] Additionally, when analysing the effect of exercise on variables positively correlated with cognition, this picture becomes clearer. Age has been shown to reduce CBF,[24] reduce hippocampal BDNF levels,[14] and reduce IGF-1 levels.[25] Furthermore, age has been shown to increase WBV,[26] which is negatively correlated with cognitive performance.

Reviewing past literature and analysing the results of their studies, we will explore whether aerobic and resistance exercise have differing effects on episodic memory, precisely what those effects are, and whether the impacts of exercise on episodic memory differ based on age. As justified earlier in the introduction, it is hypothesised that long-term aerobic exercise will have a greater impact on episodic memory than resistance exercise. Moreover, it is hypothesised that the impact of both forms of exercise on episodic memory will be more pronounced with higher ages; the impact on older adults will be stronger than the impact on younger adults.

Discussion

Aerobic Exercise on Episodic Memory:

Evidence shows that long-term aerobic exercise has been shown to improve episodic memory performance,[1,2] particularly through increases in CBF and increases in BDNF,2 which can induce hippocampal neurogenesis,[15] potentially improving episodic memory.[27,28] Neurogenesis is a process by which new neurons are formed in the brain (See Figure 1),[29] where neural stem cells become mature neurons. Neurogenesis creates new neurons and increases plasticity;[27] evidence shows that this mechanism can potentially improve episodic memory.[27,28]

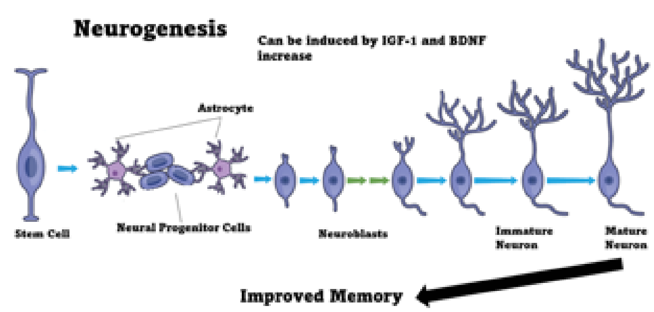

Figure 1: Process by which IGF-1 and BDNF induce neurogenesis and improve episodic memory. Through neurogenesis, neural stem cells grow into mature neurons, increasing plasticity and potentially improving memory. *Figure adapted from Stuttershock*.

Kattenstroth *et al.*, conducting a 24-week study amongst elderly individuals (n=35; range: 60-94 years) measuring the effect of dance,[1] a form of aerobic exercise, on cognition and other variables. The intervention group took part in a 1-hour dance session every week for the duration of the study. Cognitive performance and episodic memory were tested using the Repeatable Battery of Neuropsychological Status (RBANS). Scores were calculated at the start and conclusion of the study and displayed a statistically significant improvement in RBANS score ($p \leq 0.001$), which includes episodic memory.

Aerobic exercise can affect episodic memory through a number of mechanisms, including increased CBF and decreased WBV. However, the most significant factor for improvement is increased BDNF levels. BDNF can induce neurogenesis, which can enhance plasticity and improve episodic memory.[30-32] In addition, BDNF can improve episodic memory through activation of molecular pathways (See Figure 2).

Seifert *et al.*, conducted a 3-month randomized controlled study amongst healthy sedentary men (n=12) where participants engaged in aerobic exercise for approximately 1 hour each day.[33] The aerobic exercise mainly consisted of cycling; however, some participants opted to participate in other exercises such as rowing, swimming, and running. Participants performed the exercise at 70% of maximal heart rate and this was adjusted after 6 weeks to account for any changes in heart rates. At the conclusion of the trial, there were statistically significant improvements in VO_2 max (maximum oxygen that can be utilized during exercise) ($p<0.05$), a metric for cardiovascular fitness. Additionally, statistically significant improvements were found for BDNF levels, specifically BDNF levels in blood from the internal jugular vein ($p<0.05$), which carries deoxygenated blood back to the heart.[34]

While this study did not explore the effects of aerobic exercise on episodic memory, the improvements in BDNF levels suggest potential mechanisms through which episodic memory could be improved (See Figure 1 and Figure 2).

Resistance Exercise on Episodic Memory:

Long-term resistance training has been shown to improve cognition and episodic memory performance.[17,35] However, the exact mechanisms through which this occurs, those specifically related to resistance training, are somewhat unclear. We will explore how some correlated variables, including WBV, CBF, and IGF-1 levels, can cause an improvement in episodic memory.

Kilic-Toprak *et al.*, conducted a 12-week study measuring the hemorheological response to progressive resistance training amongst young men.[9] Seven exercises, training both upper and lower body, were selected and participants measured their 1RM (1 Rep Max), which is their maximum weight for 1 repetition, to calculate weight to be lifted during the study. Participants began in the first week by performing 1 set of 8-12 repetitions with a weight 40-60% of 1RM for each exercise three times a week. Participants progressively increased both the weight and the number of sets, concluding the study with 3 sets of 8-12 repetitions for 75-80% of 1RM. 1RMs for all exercises were calculated and statistically significant improvements were found for all exercises ($p<0.005$). At the end of the experiment, pre-exercise measurements of WBV at standard (40%) haematocrit and plasma viscosity decreased significantly, ($p=0.05$) and ($p=0.041$) respectively, which has been linked to increases in CBF and thus may improve episodic memory.[13,36,37] While this study did not explore the direct effects of exercise on episodic memory, it highlighted important potential mechanisms.

(n=62).[17] After complementary exclusion criteria, participants were assigned to one of three groups: Control (n=23), experimental moderate (n=19), and experimental high (n=20). The experimental groups had three 1-hour sessions per week; the experimental moderate group performed at a weight 50% of their 1RM while the experimental high group performed at weight 80% of their 1RM. After the 24-week trial, both the experimental moderate and experimental high group recorded statistically significant improvements in their 1RM weight lifted for each exercise ($p<0.001$); assessing episodic memory, statistically significant improvements were observed for both the experimental moderate ($p=0.02$) and experimental high ($p=0.02$) groups. There was no statistically significant difference for neuropsychological test scores or for 1RM weight when comparing the experimental moderate to experimental high group, suggesting the effect on episodic memory is not significantly affected by the intensity of resistance training. When testing for IGF-1 levels, there were significant increases for both the experimental moderate ($p=0.02$) and experimental high ($p<0.001$) groups, illustrating a clear correlation between IGF-1 levels and episodic memory performance. IGF-1 is one of the primary mechanisms through which resistance exercise can improve cognition and episodic memory.[38-40] Similar to BDNF, IGF-1 can induce neurogenesis (See Figure 1) which can improve episodic memory.41 In addition, IGF-1 can enhance memory through signalling pathways (See Figure 2).

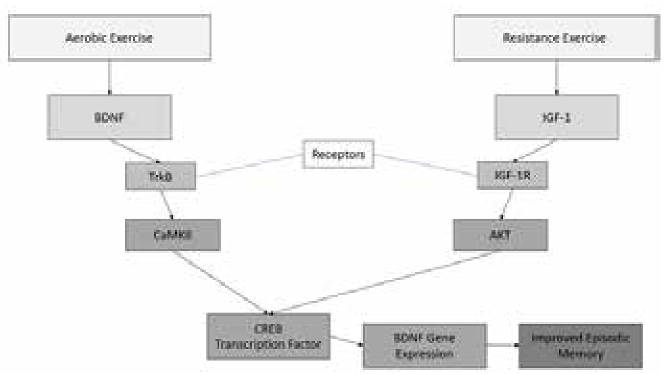

Figure 2: Potential model through which aerobic and resistance exercise can improve episodic memory through signalling pathways. Aerobic and resistance exercise increase levels of BDNF and IGF-1, respectively. Both BDNF and IGF-1 bind to their respective receptors, tropomyosin receptor kinase B (TrkB) and insulin-like growth factor 1 receptor (IGF-1R), which activates the receptors and induces autophosphorylation. This subsequently leads to the phosphorylation and activation of the kinases protein kinase b (AKT) and calmodulin-dependent protein kinase II (CaMKII). Activated AKT and CaMKII phosphorylate cAMP-response element binding protein (CREB). Phosphorylated CREB can regulate gene expression, inducing LTP and potentially improving episodic memory.

Note: While both aerobic and resistance exercise can affect IGF-1 and BDNF levels, the figure shows potential pathways through which each form of exercise would have the most significant impact.

Comparing Aerobic and Resistance Exercise on Episodic Memory:

Having established the different ways in which long-term aerobic and resistance exercise can affect episodic memory, it is important to identify the differences in the ways they affect episodic memory as well as the magnitude of the impact they have.

Özkaya *et al*., conducted a 9-week study amongst older people (60-85), aiming to measure the effects of both aerobic and resistance exercise on cognition, utilizing Event-related potentials (ERPs), which are "electrophysiological neural responses time-locked to a stimulus".[13,42] The aerobic intervention group performed aerobic exercise on a running track 3 times a week at an intensity 70% of heart rate reserve. The resistance exercise group also performed exercise 3 times a week, performing 7 different exercises each session. Intensity started at 60% of 1RM on the first session and increased each session to end at 80% of 1RM. When analysing results, both the aerobic and resistance exercise groups showed improvement in ERP measurements. However, when comparing the resistance group and the aerobic group, the resistance training group showed statistically significant differences in terms of timing ($p<0.05$).[13] These findings suggest that resistance training may affect cognition slightly different to aerobic exercise, leading to improved sensory processing and encoding of memories.[2,13]

Interestingly, a 6-month study conducted by Jonasson *et al*., that compared the effects of aerobic exercise and resistance/toning exercise on cognition contrasts this.[43] Cognition was measured through a "cognitive score" which included several aspects such as episodic memory, executive function, and processing speed. It was found that the aerobic group, compared to the resistance group, had a significant improvement in "cognitive score" ($p=0.01$), likely indicating that aerobic exercise has a greater effect on episodic memory when compared with resistance training.

Cassilhas *et al*., 2012 conducted an 8-week study and investigated the molecular mechanisms through which aerobic and resistance exercise affected spatial memory in adult male Wistar rats.[44] The results of the experiment allowed for a clear comparison between aerobic and resistance training on several important variables. It was found that resistance training, compared to aerobic exercise, had a greater increase in serum IGF-1 levels ($p<0.05$). While hippocampal IGF-1 levels were similar between the aerobic and resistance groups, only the resistance group had a significant increase in hippocampal IGF-1R expression ($p<0.001$) and the downstream phosphorylated AKT expression when compared with the control ($p<0.05$). On the other hand, hippocampal BDNF levels were found to be significantly higher in the aerobic exercise group when compared to all other groups ($p<0.001$); levels of TrkB expression, a receptor for BDNF, was found to be significantly higher for the aerobic group when compared with the resistance group ($p<0.05$). Also, only the aerobic exercise group had a significant increase in hippocampal CaMKII expression compared with the control group($p<0.05$). While this experiment was completed with rats acting as the subject, results from previous studies involving humans appear to be at least partially in agreement with results of this study.[44]

The results of the study, as well as other studies,[2,44] show that resistance exercise likely affects episodic memory through IGF-1/IGF-1R and AKT pathway while aerobic exercise does

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so through BDNF/TrkB and CaMKII pathway (See Figure 2). Given evidence that suggests long-term aerobic exercise is more effective than resistance training (that does not influence VO_2 max) in improving cognition and episodic memory,[43] it may be true that the BDNF/TrkB and CaMKII pathway is more effective in improving episodic memory performance.

Interestingly, while Jonasson *et al*., found that aerobic exercise was more effective for improving episodic memory and cognition as a whole, Cassilhas *et al*., found that both the resistance and aerobic group were equally as effective in improving spatial memory.[43,44] While this may indicate that the mechanisms that affect spatial memory and episodic memory are different, further research with larger sample sizes is required to comprehensively evaluate this effect.

Age On the Relationship Between Exercise and Episodic Memory:

We have established that both aerobic and resistance training may enhance episodic memory, but what are the implications of this. Being able to enhance memory through exercise can have broad applications including implementing exercise programs into school to improve academic performance and enhance teaching/learning. However, perhaps the most important application could be to counteract the cognitive effects of aging and potentially prevent consequential neurodegenerative conditions.[45] Interestingly, there is evidence to show that the effect of exercise on episodic memory is more significant in older adults.

A study conducted by Hayes *et al*., measured the effect of aerobic exercise on a number of cognitive factors (including episodic memory) amongst both younger and older adults.[23] The participants were thus split into two groups: the young adult group (n=29; range: 18-31 years; mean=21.2) and older adult group (n=31: range: 55-82 years; mean=64.5)). The study presented interesting results; physical activity was only shown to significantly affect the results of the older adult group, and only for visual episodic memory and the face-name memory task while exercise did not significantly influence any results for the young adult group. The findings from this study may suggest that there is a correlation between age and the magnitude of the effect of exercise on episodic memory, potentially as a result of cognitive decline. This may be due to the fact that younger adults are closer to their peak in cognitive performance and hence have less capacity to improve; the opposite may be true for older adults. However, the paucity of studies surrounding the effect of exercise on cognition in younger individuals, likely due to relevance of potential applications, means that the effect cannot be appropriately identified and compared to that on other age groups.

A review conducted by Aghjayan *et al*., explored the effect of aerobic exercise on episodic memory during late adulthood.[46] The review analysed 36 articles and explored the effect of various factors including age, intervention duration, and gender on how much episodic memory was impacted. To investigate the effect of age, all samples were split into two groups using a median split: young-old group (55-68 years) and old-old group (69-85 years). Interestingly, they found a significant effect for the young-old group ($p<0.001$) but not for the old-old group ($p=0.418$). While the previous study from Hayes *et al*., showed significant results for the older group (range: 55-82 years; mean=64.5), given that the mean age was 64.5,[23] it is possible that the results do not contradict those found by Aghjayan *et al.*, This results from these studies, while somewhat difficult to interpret together, both support that age indeed has an impact on the effect of exercise on episodic memory. Furthermore, these results may also suggest that there is an optimal age for this effect, as further explained below.

The results from Aghjayan *et al*., and Hayes *et al*., both support that there is likely an optimal age-range within late adulthood in which aerobic exercise, or exercise as a whole, will have the greatest effect on episodic memory.[23,46] Due to the lack of studies with younger or middle-aged participants, it is difficult to provide conclusive justification for these reasons. For the study conducted by Hayes *et al*., the younger group may be peaking in terms of "neural integrity and cognitive performance" and thus the impact and potential improvement is significantly reduced.[23] For the review and analysis by Aghjayan *et al*., it is possible that the young-old group (55-68 years) performed better than the old-old group (69-85 years) due to increased prevalence of neuropathological issues and cognitive decline. It is possible that beyond a certain stage, the levels of potential improvement are significantly reduced. While further studies that compare this effect across several age groups are necessary, this evidence may indicate that exercise is better served as a preventative measure to improve episodic memory in late adulthood as opposed to a form of treatment once substantial cognitive decline has occurred.

■ Conclusion

In this review, we analysed several studies to determine the mechanisms through which aerobic and resistance exercise can affect episodic memory as well as how variables like age can impact the magnitude of this effect. Both aerobic and resistance exercise can affect various factors such as CBF and WBV,[9,10] which have been shown to have positive and negative correlations with episodic memory, respectively.[11-13] Based on results identified in the studies presented, it is likely that the increased levels of BDNF from aerobic exercise and IGF-1 from resistance exercise contribute most significantly to improvements in episodic memory and cognition as a whole. As discussed, the increased levels of BDNF and IGF-1 can induce neurogenesis (See Figure 1), which creates new neurons, enhances plasticity, and can enhance memory. In addition, both BDNF and IGF-1 can activate signalling pathways, which can regulate gene expression, inducing LTP and improving episodic memory.

Our analysis in this review has identified gaps in the current literature and direction for further studies. While evidence was found to support a number of mechanisms through which resistance exercise can affect episodic memory including CBF and most notably, through IGF-1, there are a lack of studies that measure these variables simultaneously, meaning that certain conclusions are drawn across studies, where methods are likely inconsistent. Future studies should measure a large range of variables including hemodynamic effects, effects on IGF-1, and others not yet explored.

There is a paucity of studies that compare the effects of aerobic and resistance exercise on episodic memory in humans. As a result, we resorted to using some experiments with rat subjects and others where other aspects of cognition were the focus to attempt to draw conclusions. While the hypothesis that aerobic exercise would be more effective in improving episodic memory was partially supported by the results of the studies, the lack of comparative studies with human subjects means the hypothesis cannot be conclusively confirmed. Further studies should focus on comparing the effects of aerobic and resistance exercise on episodic memory in human subjects and do so with large sample sizes to improve accuracy. When analysing the effect of exercise on episodic memory with age as a variable, it was found that the magnitude of the effect may be more pronounced within a specific age range: approximately ages 55-68. The results of the studies analysed also indicated that exercise has no statistically significant effect on episodic memory for young adults (18-31 years) and much older adults (69+ years). Possible justification could be that young adults are peaking in terms of cognitive ability and hence may not have much room to improve while much older adults may be unable to significantly improve due to increased levels of cognitive decline. However, the lack of studies comparing age ranges makes these conclusions difficult to draw and substantiate. Further research should focus on incorporating age as a measured variable to be able to determine this.

To close, it was found that both aerobic and resistance exercise can affect episodic memory through various mechanisms, some similar and some contrasting. Additionally, it was also found that age may play a significant role in the magnitude of this effect. Further research should focus on aforementioned areas to enhance knowledge in these areas, potentially allowing exercise to eventually serve as a useful method of improving episodic memory and a preventative measure for cognitive decline and neurodegenerative disorders.

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