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Enhancement of Brain Functions During Aging Through Various Exercises: a Review Study

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Abstract

Introduction: Decline of brain and mental functions with aging is a natural biological phenomenon. Scientists have engaged themselves to find out the different ways to protect degeneration and enhance brain functions. Regular exercise is one of the potential area. However, there are controversial and inconclusive results which create further interest of research. Aim: To review scientific literature related to exercise effect on brain and mental function during aging. Methods: Searches were conducted through electronic databases- PubMed, Medline, Springer link, Elsevier, and Google Scholar. The searching terms were: brain function (brain function or cognition or memory or processing speed or learning or executive function) and physical exercise (physical exercise or exercise or stretching exercise or strength exercise). Initial search were 11 review studies and 57 randomized control trials. The current study selected 03 review and 08 randomized control trials studies after fulfillment of its requirement. Findings: Long term (>24 weeks) combination exercise (aerobic, strength and stretching) training can improve memory functions and processing speed in elderly people. Aerobic exercise training and strength training together can contribute to the improvement of episodic memory, executive functions and processing speed in healthy elderly people. Memory can be enhanced through aerobic exercise training and also by doing strength exercise training in healthy older adults. Interpretations: Changes in different brain and mental functions may be occurred due to structural and functional variations. The structural changes may include change in the volume of hippocampus, neurogenesis, angiogenesis, and so on. The physiological variations can include brain plasticity, increase in brain-derived neurotrophic factor (BDNF), enhancement of Default Mode Network (DMN), increase the activity of proteasome and neprilysin. Conclusions: Aging brain and mental functions may be enhanced through regular aerobic exercise training but different exercise has different impact on brain structure and functions.

Keywords: Aging, Exercise, Brain structure, Brain function.

1. Introduction

Regular physical activity and exercise have a positive impact on health and well-being. Despite of this knowledge, human society has become an increasingly sedentary (Voss et al., 2011).

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Research shows an estimation that less than 50 % of children (6–11 yrs.) and 8 % of adolescents (12–19 yrs.) are actively engaged with the recommended 60 min. of exercise most days of the week, whereas only less than 5 % of adults (20–59 yrs.) and elderly (60+ yrs.) are active with the recommended 30 min./day for this age group (Troiano et al., 2008). This inactivity may cause different kind of risk factors such as type II diabetes (Laaksonen et al., 2005) cardiovascular-related disease (Shiroma and Lee, 2010), osteoporosis (Kelley, 1998), colon and breast cancer (Lee, 2003), and mental disorder (DHHS. Physical Activity Guidelines Advisory Committee Report 2008).

Mammalian brains process complex information including sensations, movements and complicated cognitive functions using sequences of action potentials in a large population of neurons. To process multiple signals simultaneously, brains take advantage of neural networks consisting of more than ten billion neurons connecting to one another. The individual neurons are known to have synaptic connections to hundreds or thousands of other neurons (Windhorst and Johansson, 1999). These intricate connections make it difficult to study functions of individual neurons or connections. Furthermore, some of the functional regions are located in the deep brain regions such as thalamus, hypothalamus, and hippocampus and so on (Holdefer et al., 2010; Belmonte et al., 2004).

Cognitive functions are in broad range which can be divisible into seven categories: executive functions, episodic memory, working memory, reading ability, attention and processing speed (Nouchi et al., 2014). Cognitive functions decline with age. Elderly people might experience a decline in several cognitive functions such as memory (Salthouse, 2003), attention (Yakhno et al., 2007), executive functions (Royall et al., 2004; Coppin et al., 2006), and processing speed (Salthouse, 1996). Maintaining or improving cognitive functions in older adults is drawing increasing attention (Colcombe and Kramer, 2003; Valenzuela and Sachdev, 2009; Fernandez-Prado et al., 2012; Tardif and Simard, 2011; Lovden et al., 2010; Kawashima et al., 2005; Uchida and Kawashima, 2008; Nouchi et al., 2012). Researcher observed that physical exercise training can improve cognitive functions in healthy older people (Colcombe and Kramer, 2003; Valenzuela and Sachdev, 2009; Hogan, 2005; Angevaren et al., 2008; vanUffelen et al., 2008; Chan et al., 2012; Snowden et al., 2011).

Combination exercise (aerobic, strength and stretching) training can improve executive functions, episodic memory and processing speed (Nouchi et al., 2014). Aerobic exercise training and strength training can contribute to the improvement of executive functions, episodic memory and processing speed in healthy elderly people (Colcombe and Kramer, 2003; Snowden et al., 2011). There is a direct correlation between increased levels of physical activity, increased hippocampal volume and enhanced spatial memory (Phillips et al., 2014). Exercise enhances Brain derived neurotrophic factor (BDNF), which plays a critical role in the learning process (Berchtold et al., 2005).

The objective of this study was to review scientific research related to exercise effect on brain function during aging.

2. Methods

Search Strategy

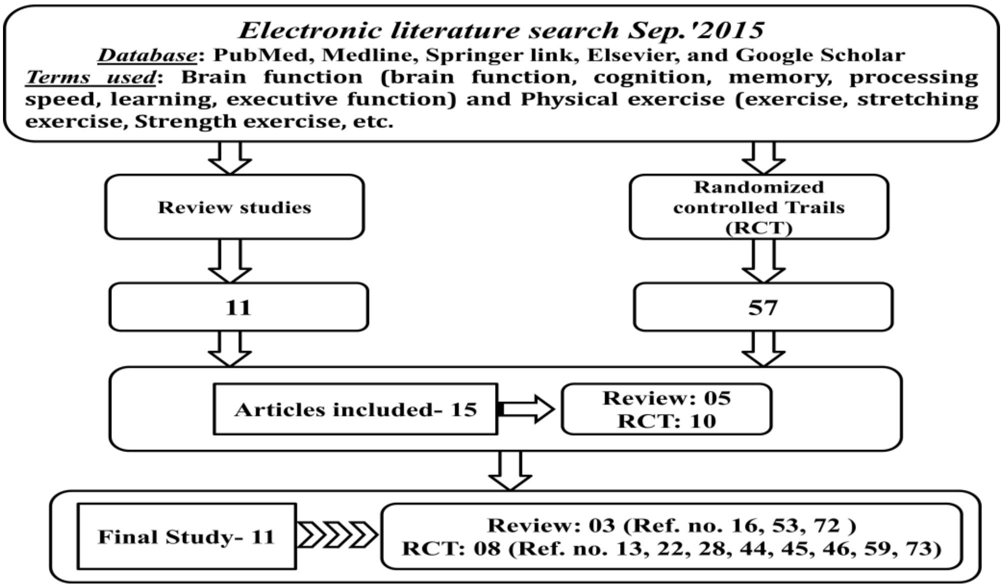
PubMed, Medline, Springer link, Elsevier and Google Scholar databases were systematically searched for Randomized Controlled Trials (RCTs) and Review work using terms related to brain function (brain function OR cognition OR memory OR processing speed OR learning OR executive function) and physical exercise (physical exercise OR exercise OR stretching exercise OR strength exercise). The search was performed in September' 2015 and repeated in April' 2016.

Inclusion and Exclusion criteria

The trials selected in this review had to meet the following inclusion criteria: RCTs; participants were involved in physical exercise with acute or chronic intervention period and reported the effect on brain functions. The review articles also involve the effect of different exercises on brain functions. The effect on brain functions included structural and functional changes.

Our initial search identified 11 review studies and 57 RCTs. Out of the total 68 studies, 23were excluded after reading the abstracts, and 30 studies were somehow unmatched the requirement of present study. The remaining 15 studies, 4 studies failed as insufficient information. The current study reported 03 review and 08 RCTs studies to complete its requirement.

The flow chart showing below for describing the method at a glance-



Findings from the final studies

i. Exercise enhances memory function

Brain-derived neurotrophic factor (BDNF) plays a critical role in memory functions (Berchtold et al. 2005). Exercise is associated with favourable changes in BDNF (Coelho et al., 2013; Erickson et al., 2013). Hippocampus is a brain region important in memory (Cotman and Engesser-Cesar 2002). One Randomized Controlled Trail (RCT) study using MRI (Magnetic resonance imaging) showed the increase of the brain volume in the hippocampus (Erickson et al., 2011). Enhanced Default Mode Network (DMN) was associated with better memory performance (Hampson et al., 2006). Aerobic exercise training led to increase the DMN (Voss et al., 2010).

Combination exercise training for 42 weeks improved memory (Williams and Lord 1997). Long term (>24 weeks) combination exercise training can improve memory functions in elderly people (Colcombe and Kramer 2003; Snowden et al., 2011; Williams and Lord, 1997; Smith et al., 2010; Tseng et al., 2011). Combination exercise training improved certain cognitive functions such as memory functions (Williams and Lord, 1997; Lautenschlager et al., 2008). RCT studies have revealed that aerobic exercise training alone and strength exercise training alone improved memory in healthy older people (Cassilhas et al., 2007; Perrig-Chiello et al., 1998; Hassmen and Koivula, 1997). Aerobic exercise training and strength training can contribute to the improvement of episodic memory in healthy elderly people (Colcombe and Kramer, 2003; Snowden et al., 2011). Functional MRI study reported that aerobic exercise training led to increase the DMN (Voss et al., 2010) which includes the posterior cingulate, ventral and superior frontal medial cortices, and bilateral lateral occipital, middle frontal, hippocampal and parahippocampal, and middle temporal cortices (Fox et al., 2005). There is a direct correlation between increased levels of physical activity, increased hippocampal volume and enhanced spatial memory (Phillips et al., 2014).

ii. Exercise enhances learning

Exercise enhances BDNF, which plays a critical role in the learning process (Berchtold et al., 2005). BDNF involves in increasing the volume of Hippocampus and it is a brain region important in learning (Cotman and Engesser-Cesar, 2002).

iii. Exercise enhances processing speed

Aerobic exercise training and strength training can contribute to the improvement of processing speed in healthy elderly people (Colcombe and Kramer, 2003; Snowden et al., 2011). Combination exercise training for 42 weeks improved processing speed (Williams and Lord, 1997).

One fMRI study demonstrated greater activity in the middle frontal gyrus after aerobic exercise training for 6 months. Middle frontal gyrus is associated with performance of processing speed (Colcombe et al., 2004).

iv. Exercise enhances executive functions

Enhanced DMN was associated with better performance of executive functions (Andrews-Hanna et al., 2007). A recent study using resting state fMRI has shown that aerobic exercise training led to increase the DMN (Default Mode Network) (Voss et al., 2010). Aerobic exercise training and strength training can contribute to the improvement of executive functions in healthy elderly people (Colcombe and Kramer, 2003; Snowden et al., 2011). One FMRI study demonstrated greater activity in the middle frontal gyrus, which is associated with performance of executive functions after aerobic exercise training for 6 months (Colcombe et al., 2004).

3. Discussion on the findings

1. Structural changes

Exercise is associated with maintenance or improvement in brain volume (Colcombe et al., 2006; Erickson et al., 2014). MRI of older adults has shown that a certain type of exercise training selectively changes the brain structure. One RCT study using MRI showed the increase of the brain volume in the hippocampus, which has an important role in memory functions, after walking exercise training for 1 year (Erickson et al., 2011). There is a direct correlation between increased levels of physical activity, increased hippocampal volume (Phillips et al., 2014).

2. Brain plasticity

Brain plasticity or neuroplasticity is the ability of the brain to functional change throughout the life. Human neuroimaging studies have revealed brain plasticity after exercise training (Erickson et al., 2011). Animal studies reported that some molecules such as BDNF, insulin-like growth factor (IGF-1), and vascular endothelial growth factor (VEGF) have a central role in brain plasticity, including neurogenesis, angiogenesis, and synaptic plasticity (Monteggia et al., 2004; Neeper et al., 1995; Ding et al., 2006; Chen et al., 2005). Exercise has the ability to enhance brain plasticity and encoding in a manner that may translate directly into structural change of neurons or synapses (Widenfalk et al., 1999).

3. Neurogenesis

Growth and development of neurons and formation of new neurons can be stated as neurogenesis. MRI has shown that a certain type of exercise training selectively changes the brain function, and brain connectivity in the older adults (Erickson et al., 2011). VEGF is also heavily involved in neurogenesis (Ding et al., 2006; Fabel et al., 2003). Exercise effects on VEGF content and messenger RNA (mRNA) expression seem to be dependent on the dose of exercise (Ding et al., 2006). IGF-1 is essential for nerve growth, as well as neurotransmitter synthesis and release (Anlar et al., 1999). Exercise increased the IGF-1 levels (Fabel et al., 2003; Cotman and Berchtold, 2002). IGF-1may protect from hyperglycemia-induced oxidative stress and neuronal injuries, by regulating mitochondrial inner membrane potential, possibly by the involvement of uncoupling protein 3 (Gustafsson et al., 2004). Various findings suggest that improved cognitive function during an exercise may be ascribed to the cerebral neural activation associated with the exercise (Ogoh et al., 2014). The effects of exercise appear to be very complex and could include neurogenesis via neurotrophic factors (Cotman and Engesser-Cesar, 2002; Neeper et al., 1995; Cotman and Berchtold, 2002; Adlard and Cotman, 2004; Adlard et al., 2005; Johnson and Mitchell, 2003; Molteni et al., 2004; Oliff et al., 1998; Lazarov et al., 2005). Exercise increases neurogenesis, and this one of the processes by which exercise benefits brain function (Van Praag et al., 1999). Resistance training may enhance brain function through several pathways which includes improvement in the structural integrity of the brain (growth of new neurons) and increased production of neurochemical promoting growth, differentiation, survival, and repair of brain cells (Voss et al., 2011). Exercise is associated with improved cerebral blood flow and neuronal connectivity (Ogonovszky et al., 2006) and neurogenesis (Coelho et al., 2013; Molteni et al., 2004)

4. Angiogenesis

Angiogenesis is the growth of capillary blood vessels from the existing vasculature. The effects of exercise appear to be very complex and could include increased capillarization (Cotman and Engesser-Cesar, 2002; Neeper et al., 1995; Cotman and Berchtold, 2002; Adlard and Cotman, 2004; Adlard et al., 2005; Johnson and Mitchell, 2003; Molteni et al., 2004; Oliff et al., 1998; Lazarov et al., 2005). Resistance training may enhance brain function through several pathways which includes improvement in the structural integrity of the brain (growth of new blood vessels) (Voss et al., 2011).

5. Brain-derived neurotrophic factor (BDNF)

BDNF is a neurotrophic factor which is important for nourishment of neurons and overall brain health. One study showed 20 % increase in the hippocampus abundance of BDNF mRNA from control levels after 2–7 nights of running (Salthouse, 2003; Neeper et al., 1996). Three weeks of exercise demonstrated that the effect of exercise on BDNF mRNA levels was not merely a short-term, transient effect. It is found that BDNF mRNA and its receptor; Tyrosine receptor kinase β (trkB) increased in the hippocampus after 6 weeks of voluntary wheel running (Widenfalk et al., 1999). Maintenance of cerebral BDNF level is important for effective neural function and longevity (Schinder and Poo, 2000). BDNF acts to increase levels of important synaptic proteins like - synaptobrevin, synaptophysin, and synaptotagmin. It has direct relationship with neuronal communication. Hippocampal BDNF mRNA level was increased with either exercise or the antidepressant tranylcypromine. BDNF plays a critical role in the learning process, memory, locomotion, behaviours, and a wide range of stress responses (Berchtold et al., 2005). The expression and protein content of BDNF have been shown to be upregulated by exercise and oxidative stress (Mattson et al., 2004). If exercise is terminated abruptly BDNF levels initially fall below normal before returning to control levels by 30 days and this is due to depression (Widenfalk et al., 1999). Exercise is associated with favourable changes in brain derived neurotrophic factor (Coelho et al., 2013; Erickson et al., 2013).

6. Default Mode Network (DMN)

DMN is a network of interacting brain regions which is helpful in remembering the past and planning for the future. Enhanced DMN was associated with better memory performance (Hampson et al., 2006) and better performance of executive functions (Andrew-Hanna et al., 2007). One study using resting state fMRI (Voss et al., 2010) have shown that aerobic exercise training led to increase the DMN, which includes the posterior cingulate, ventral and superior frontal medial cortices, and bilateral lateral occipital, middle frontal, hippocampal and parahippocampal, and middle temporal cortices (Fox et al., 2005).

7. cAMP response element binding protein (CREB)

CREB is a cellular transcription factor which has important role in neuronal plasticity and long-term memory formation in the brain and has been shown to be integral in the formation of spatial memory. When BDNF was blocked, the exercise-induced increases in CREB mRNA levels, as well as the phosphorylation of CREB, were prevented (Vaynman et al., 2003; Vaynman et al., 2004). Exercise does not simply upregulate the content and expression of BDNF in different brain regions, but also impacts downstream effectors of BDNF; namely, the transcription factor CREB. CREB DNA binding sites contribute to the activation of BDNF mRNA transcription, and this process can regulate by Reactive Oxygen Species (ROS). BDNF acts through trkB receptors that activate CREB, thus creating a positive loop for the cascades (Zou and Crew, 2006).

8. Gene Expression

Gene expression is the process by which information from a gene is used in the synthesis of a functional gene product. It has been discovered that in addition to BDNF, exercise induces changes in other genes known to be associated neuronal activity, synaptic structure, and neuronal plasticity (Tong et al., 2001).

9. Proteasome and Neprilysin

Proteasomes are protein complexes inside all eukaryotes and archaea, and in some bacteria while neprilysinis an enzyme that in humans is encoded by the metallo-endopeptidase (MME) gene. The effects of exercise appear to be very complex and could include decreased oxidative damage, and increased proteolytic degradation by proteasome and neprilysin (Cotman and Engesser-Cesar 2002; Neeper et al., 1995; Cotman and Berchtold, 2002; Adlard and Cotman, 2004; Adlard et al. 2005; Johnson and Mitchell, 2003; Molteni et al., 2004; Oliff et al., 1998; Lazarov et al., 2005). Regular exercise training also attenuated the age-related accumulation of Reactive carbonyl derivative (RCD) in the brain, increased the activity of the proteasome complex, and improved brain function (Radak et al., 2001b). Voluntary exercise decreases the accumulation of beta-amyloid in the brain. Exercise increases the activity of neprilysin, which is responsible for the degeneration of beta-amyloid (Tseng et al., 2011). Ogonovszky et al. (2005a) has given moderate training, very hard training, and overtraining to rats and found, even with hard training and overtraining, beneficial effects on brain function and lowered accumulation of RCD.

4. Conclusions

The combination exercise training would increase the BDNF, IGF-1, and VEGF levels. The increase BDNF, IGF-1, and VEGF levels might contribute to exercise induced neurogenesis and angiogenesis. Neurogenesis and angiogenesis would engender changes in the brain structure, brain function and brain connectivity, which are related to cognitive functions.

ROS and the changes in redox homeostasis could play a role in the very complex mechanism by which exercise training benefits the brain. The relationship between ROS concentration and brain function can be characterized by a bell-shaped curve, both low and high levels of ROS could impair brain cell function. Low levels of ROS might cause insufficient gene expression for redox homeostasis while high levels of ROS exceed the adaptive tolerance of cells, resulting in significant oxidative damage, apoptosis, and necrosis. Oxidizing enzyme, cytokines, and mitochondria are potent generators of ROS in the brain during exercise.

Finally, the improvements of executive functions, processing speed, and episodic memory can be expected to be enhanced by increasing the brain volume of hippocampus, which is related to memory. Greater activity in the middle frontal gyrus which is important for executive functions and processing speed and enhancing the DMN is associated with executive functions and memory could be improved through the combination exercise training. The phenomenon of exercise related to brain functions might be interpreted in a different way that exercise attenuates the inactivity-caused deteriorative effects on the CNS.

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