

# Underlying mechanisms for physical activity-induced brain plasticity

## Abstract

Physical activity is an important component in daily life which become more important when comes to health-related complications. Physical activity regardless the type and intensity, can bring beneficial effect for general health and can improve skills in several aspects including learning tasks and response to stimuli along with other health benefits. By recruiting regular physical activity and exercise, which happened for athletes, some structural and functional changes may occur in some regions of brain including increase in network connection, increase the speed of message transformation, increase in gray matter, synaptic plasticity and brain plasticity. There are several suggested mechanisms for physical activity-induced brain plasticity including increase in gene expression, BDNF, IGF-1, VEGF and activation of cellular cascade. Although the beneficial effects of physical activity on brain flexibility is well known which is reviled in athletes, the most effective type of activity which can affect brain flexibility the most, is not clear yet.

**Keywords:** brain plasticity, physical activity, cellular mechanism, gene expression, health

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## Introduction

Physical activity is considered as a component of healthy life style which can play a preventative role in prevention of many diseases. The importance and beneficial effects of regular physical activity for public in all age groups with various of biological characteristics and differences, has made public health authorities to provide and publish guidelines for physical activity for different individuals in order to improve public health status, as a result of physical activity status modification as a part health lifestyle along with healthy dietary pattern. Although researchers have approved the beneficial effect of physical activity on general health and chronic disease prevention and/or management, physical activity seems to have more beneficial effect than what can be perceived. Physical activity may affect central nervous. System along with other systems in the body and can highlight the connection between different systems including central nervous system and cardiovascular system. The purpose of this study is to highlight some possible mechanisms that physical activity can help brain health and brain plasticity and discuss which type of physical activity can affect brain plasticity and synaptic plasticity more.

Physical activity can affect brain plasticity in several pathways. It has been suggested that physical activity cab affect methylation status and as a result, affect gene expression. Physical activity can demethylate the gene promotor which can activate the gene expression.<sup>1-5</sup>

Studies have suggested that physical activity can improve BDNF level which can increase neural and brain plasticity, as a result of increase in BDNF and N-methyl- aspartic acid receptor, activity of regulated cytoskeleton associated protein- Arc will increase which increase brain plasticity especially after recruiting aerobic exercise in childhood and adolescent.<sup>6-9</sup> Although the effect of aerobic studies on aerobic endurance and capacity and brain health has been indicated in previous research, the results are in consistent. This has made researcher to investigate more about the mechanisms and underlying pathways that physical activity can affect brain plasticity. Another method to assess , is PCR enzyme reaction time which can be considered as a suitable indicator for assessing brain activity. Results on the study which evaluate the effect of high intensity

interval training and moderate continuous activity, has suggested that even physical activities in higher intensities can affect PCR reaction time, increase in angiogenesis and myokines involved in brain and neural plasticity.<sup>10-12</sup> According to the results derived from previous studies, it can be concluded that the exact type of physical activity which seems to be the most effective, is not clear yet. Although, it has been approved that physical activity, regardless its characteristics, can increase NPY, IL-6, angiogenesis related factors including VEGF, histone acetylation, cellular cascade activation (AMPK, PI3K, GTPase) and mRNA involved in BDNF expression, which can lead to neurogenesis and increase in brain plasticity. Histone modification is one of the principal factors in gene expression regulation via histone-acetyl transferase (activates transcription) and histone deacetylase (inhibits gene expression). Physical activity can induce histone acetyl transferase in hippocampus and suppress deacetylase activity which can be related to neuron apoptosis and brain plasticity.<sup>13-15</sup> On the other hand, physical activity can affect DNA methylation which is related to gene expression. Studies have indicated that both short term and long-term physical activity can increase BDNF gene expression and decrease the activity of neurotrophic factor p75 receptor, which is responsible for neural cell necrosis and death.

Chromatin repair, is another mechanism which physical activity can affect brain plasticity via epigenetic pathways. It seems that chromatin recovery and reconstruction can increase BDNF gene expression and transcription and enhance phosphorylation of proteins involve in expression and activation of calcium-calmodulin complex dependent protein kinase, which can be result in brain plasticity.<sup>16,17</sup>

Other mechanisms for the effect of physical activity on brain plasticity

IGF-1 and VEGF

IGF-1 is a factor produced mainly in the liver, despite cartilage, muscles and other organs can also produce IGF-1. IGF-1 induce mitosis and differentiation, on the opposite side, suppress apoptosis. Physical activity can increase IGF-1 gene expression which can be associated with BDNF, protein kinases and calcium-calmodulin complex. It has been indicated that the inhibition in IGF-1 receptors, may eliminate the effect of the above mentioned factors.

VEGF is a homodynamic glycoprotein which can be produced in response to hypoxia and can induce angiogenesis. Moreover, it can help vascular recovery. Physical activity can induce angiogenesis due to increase in VEGF expression. In the brain, this angiogenesis in regions especially hippocampus which can lead to neurogenesis and brain plasticity along with its effect on adiponectin level, Irisin, lactate, beta-hydroxy-butyric acid.<sup>18</sup>

Which physical activity type, is the most effective?

There is still remained unknown that which type of physical activity may have more effect on brain plasticity. Some studies, have suggested that physical activities with higher intensities are the most effective type for improving brain plasticity, despite other studies indicated that activities with moderate intensities are the best type. It is well known that physical activities with moderate to higher intensities can improve cardio-vascular endurance and capacity, manifested as VO<sub>2</sub>max, although it seems that activities with moderate intensities on brain plasticity. Aerobic activities with intensity below the voluntary threshold, can bring beneficial effect on hippocampus, whereas, acute activities in higher intensities, may not have the similar effect on the hippocampus. Physical activities with higher intensities, can increase the risk of physiological stress and cortisol hormone with can have detrimental effect on brain plasticity.<sup>19–21</sup>

It is approved that adaptation is a result of regular exercise, so it can be concluded that brain plasticity resulted from physical activity, require time and can be considered as an adaptation. Studies have suggested that the beneficial effects on brain plasticity, can be about 6 weeks with the intensity of 70–80% of rest heart rate.<sup>22</sup> According to the in consistent result from studies, researchers have assessed the athletes' brain in function and structure using fMRI and have suggested that in response to regular training, adaption will occur and performance will improve which can be associated with brain plasticity. These changes seems to be accompanied by changes in different regions of brain and improvement in network connection in brain, as, different regions in brain, will change in response to different tasks which make athletes able to predict and meke better decisions in response to unpredicted events along with better and faster information transfer and improvement in gray matter in some especial regions in the brain.<sup>23,24</sup>

## Discussion and conclusion

Physical activity can improve brain plasticity. There are several suggested mechanisms which physical activity can improve brain plasticity including increase in BDNF, IGF-1, VEGF, Irisin and acetylation of histones.

Cellular cascade will be activated in response to physical activity and increase in mentioned factors which can lead to brain plasticity. There are several hypotheses regarding the most effective type of physical activity on brain plasticity and it is not clear yet which type of activity is more effective than other. Although, the beneficial effects of physical activity on health such as mental health, has been approved. Further research is needed to investigate the effect of physical activity and the most effective type on brain flexibility.

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## Conflicts of interest

The authors declare no conflicts of interest.

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