## Introduction:

Joyce Gomes-Osman, an assistant professor in physical therapy and neurology at the University of Miami’s Millar School of Medicine states, “Exercise is a really, really great thing for the brain”[[1]](#footnote-1), it is one of the most promising non-pharmaceutical treatments to improve brain health[[2]](#footnote-2) and it has a significant impact on memory formation[[3]](#footnote-3), capability and long-term consolidation[[4]](#footnote-4). To gain these benefits, all that needs to be done is the physical act of exercising, which promotes neurogenesis[[5]](#footnote-5). Neurogenesis is the physiological change in the brain through the formation of nervous tissue[[6]](#footnote-6). Changes to the brain’s structure include[[7]](#footnote-7): An increase in cortex thickness; Increase in neurotransmitters, chemical substances that transmit nerve impulses across the synapse[[8]](#footnote-8); higher amount of synaptic connections; greater rate of angiogenesis, the formation and development of blood vessels[[9]](#footnote-9); an increase in growth factors, various proteins that promote the growth, organisation and maintenance of cells[[10]](#footnote-10). These growth factors are broadly known as neurotrophin polypeptides[[11]](#footnote-11) with specific examples being brain derived neurotrophic factor (BDNF) and Insulin-growth factor 1 (IGF-1)[[12]](#footnote-12). They are responsible for the growth and protection of neurons in the brain[[13]](#footnote-13), however, they particularly work in the hippocampus, the centre of memory in the brain[[14]](#footnote-14). All these factors contribute to the series of improvements in memory, mental processes and executive functions[[15]](#footnote-15).

## Neurogenesis and blood flow:

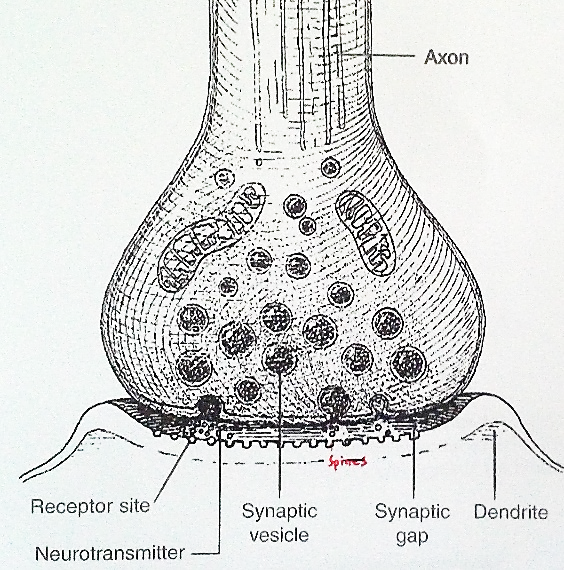
Jonathan Fields, the founder of The Good Life Project stated, “The physical state of our bodies [including the brain] can either serve or subvert the quest to create genius”[[16]](#footnote-16). Neurogenesis is the change in the brain’s anatomy, physiology and function that comes with exercise [[17]](#footnote-17). The process of neurogenesis consists of 4 essential components: proliferation, an increase in the number of cells; differentiation, where cells acquire specialist features; axonal path migration, the extension of neurons’ axons; maturation, becoming specialised for their specific job[[18]](#footnote-18). Studies conducted at the National Neuroscience Institute in Singapore revealed that aerobic exercise increased neuronal proliferation[[19]](#footnote-19) which inevitably indicates the rise of BDNF and serotonin levels[[20]](#footnote-20). BDNF correlates with an improved memory[[21]](#footnote-21) and serotonin links to an individual’s level of alertness[[22]](#footnote-22), indicating its relation to concentration. Thus, cognitive function improves when exercise is undertaken[[23]](#footnote-23), as well as protection from neuronal degeneration[[24]](#footnote-24). Neuroplasticity, changes in the brain’s structure in response to environmental stimuli, is closely A picture containing accessory, umbrella

Description generated with very high confidenceentwined with neurogenesis. It is also the most prevalent effect that exercise has on the brain, as seen in figure 1[[25]](#footnote-25), indicating just how much change exercise can induce in the brain[[26]](#footnote-26).

Figure 1: Effects of exercise on the brain

However, renewing the brain (neurogenesis)[[27]](#footnote-27) would not be as effective if it wasn’t for the exercise-induced change of maintaining efficient blood flow[[28]](#footnote-28),[[29]](#footnote-29). This is significant because increased cerebral blood flow does not happen globally across the brain but in specific regions such as the hippocampus. Extra blood flow to the brain allows for clearer thinking[[30]](#footnote-30) and the effect is immediate. John Medina who is the director of Seattle’s Pacific University’s Brain Centre for Applied learning states that research has consistently shown that those who exercise out perform non-exercisers in long-term memory, reasoning, attention and fluid intelligence[[31]](#footnote-31). This all starts with an increase in the blood flow to the brain[[32]](#footnote-32). Yet, the production of BDNF and Nerve growth factors (NGF) are also necessary for the stimulation and regulation of neurogenesis processes such as proliferation, differentiation and maturation[[33]](#footnote-33),[[34]](#footnote-34).

## Neurotrophin polypeptides:

BDNF and Insulin-growth factor-1, a nerve growth factor, come under the family of neurotrophin polypeptides[[35]](#footnote-35). Both neurotrophin polypeptides exist to support the survival of mature neurons whilst encouraging the growth, regeneration and creation of new neurons and synapses[[36]](#footnote-36). BDNF also solidifies connections between neurons and nerve impulses to confirm reliable future firing[[37]](#footnote-37). It completes this through myelination, the process of forming a myelin sheath around a nerve to allow nerve impulses to move quickly across the synapse[[38]](#footnote-38). Figure 2 shows how neural impulses are carried across the synapse through synaptic vesicles. The outer coating is the myelin sheath, which assists the speed of this process[[39]](#footnote-39). Whilst BDNF is found in varied concentrations across the brain[[40]](#footnote-40), aerobic exercise physically starts the stimulation of producing BDNF[[41]](#footnote-41) increases BDNF expression[[42]](#footnote-42) particularly the hippocampus[[43]](#footnote-43). This occurs through the reduction of blood sugar levels during exercise, therefore β-hyroxybutyrate is used as an alternative source of energy. Whilst being used for energy, β-hyroxybutyrate also blocks enzymes that inhibit the production of BDNF, demonstrating that these physiological changes are designed to improve levels of BDNF in response to exercise[[44]](#footnote-44),[[45]](#footnote-45). Furthermore, BDNF can only be expressed if BDNF mRNA is being transcripted and translated. Studies have shown that after only a few days of aerobic exercise there is a significant increase of BDNF mRNA levels in the hippocampus which can be sustained for several weeks[[46]](#footnote-46),[[47]](#footnote-47) or longer if exercise is upheld[[48]](#footnote-48). To emphasise this, figure 3 shows an average of the amount of BDNF produced by rats according to the distance they ran each night. It is evident that a notable amount of exercise can dramatically increase BDNF levels[[49]](#footnote-49). An increase in BDNF mRNA leads to an increase in BDNF protein expression which is crucial for assisting the A close up of a map

Description generated with very high confidencecapability to learn and memorise[[50]](#footnote-50).

Figure 2: Transfer of nerve impulses across synapse

Figure 3: The amount of BDNF produced in relation to running distance

Once BDNF is expressed it can do numerous things, one of these is assisting in the consolidation of short-term memories into long-term memories[[51]](#footnote-51). The hippocampus holds both short-term and long-term memory[[52]](#footnote-52), so inevitably it plays a major role in fortifying learning by converting information from working memory, the limited- capacity memory used to process the present[[53]](#footnote-53), to long-term storage memory via electrical signals[[54]](#footnote-54). It does this by recalling and associating a memory with other information as it moves towards long-term storage[[55]](#footnote-55). BDNF is the factor which mediates this process, thus stating its importance in seeing the long-term benefits of exercise on the brain[[56]](#footnote-56).

NGF acts in a similar way to BDNF because it is a neurotrophin polypeptide which improves survival of neurons in the hippocampus, however NGF also increases serotonin producing cells[[57]](#footnote-57). A study conducted in measuring NGF showed that Olympic athletes have significantly higher levels than control individuals[[58]](#footnote-58) with associations also between higher neurotrophic factor levels and better memory performance[[59]](#footnote-59). Insulin growth factor-1 is a specific growth factor which also assists in BDNF gene regulation, neurogenesis and protection from injury. Together all factors contribute to the mediation of new neurons, through neurogenesis[[60]](#footnote-60), in the hippocampus which leads to a cascade effect of benefits[[61]](#footnote-61).

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Description generated with high confidenceThe development of neurons in the hippocampus is one of the limited number of places where the adult brain can generate new neurons on site[[62]](#footnote-62). Exercise can physically help grow new brain cells and activate the brain, as seen in figure 4[[63]](#footnote-63). One study saw exercising mice grow an average of 6,000 new brain cell in every millimetre of the hippocampus tissue which was sampled[[64]](#footnote-64). These 6,000 new brain cells gives millions of opportunities for new neuronal connections to be made, leaning to happen and memories to be formed. Dr Matias Ison at the University of Leicester describes how one neuron fires to two (or more) other neurons at the exact point of learning, creating new pathways[[65]](#footnote-65). John Medina, Director of Seattle Pacific University’s Brain centre for applied learning stated, “We have in our hands as close to a magic bullet for improving human health as exists in modern medicine, all we have to do is move”[[66]](#footnote-66), it is really that simple.

Figure 4: Effect of exercise on the brain

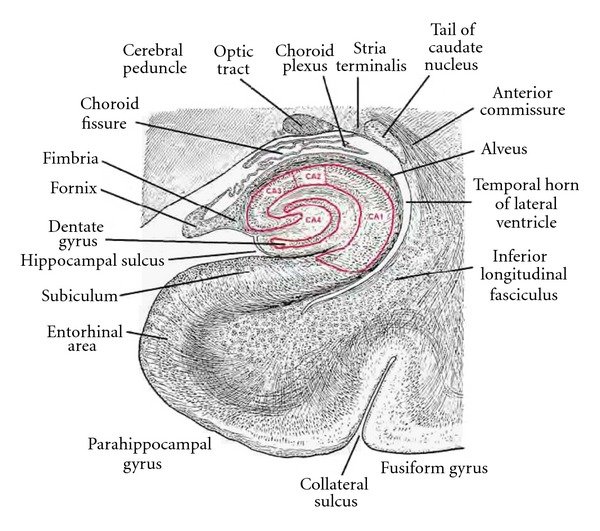
## The hippocampus:

The hippocampus is the area of the brain which responds most strongly to aerobic exercise[[67]](#footnote-67) as it physically increases its volume by producing more brain cells (already discussed) by up to 2 percent in one year[[68]](#footnote-68). Exercise-induced production of more brain cells in the hippocampus leads to an increase in volume, an increase in volume results in better long-term memory formation and recall[[69]](#footnote-69),[[70]](#footnote-70). Typically, brain volume decreases with age[[71]](#footnote-71), however, in a study conducted at the University of British Columbia, regular aerobic exercise appears to boost the physical size of the hippocampus[[72]](#footnote-72). Many other studies have also seen that other parts of the brain that are involved with control thinking and memory are larger in volume in those who exercise compared to those who don’t[[73]](#footnote-73). Dr McGinnis, an instructor in neurology at Harvard Medical school who observed these studies, declared that engaging in regular exercise of moderate intensity over a six to twelve-month period increases the volume of other selected brain regions too[[74]](#footnote-74).

Cognition is thoroughly benefitted through an increase in oxygen and blood flow in the brain[[75]](#footnote-75) as well as chemicals which assist the health and growth of blood vessels in helping them to survive and multiply too[[76]](#footnote-76). However, a reason why this is so prominent in the hippocampus is that exercise is the crucial factor in hyper-glycogen storage in the hippocampus[[77]](#footnote-77). The brain goes through supercompensation allowing it to store 29-60% more glycogen than it is normally able to within 6 hours of exercise and these levels remain for up to 24 hours after exercise[[78]](#footnote-78). The increase in glycogen comes from an increase in oxygen and can also help with the reduction of A screenshot of a cell phone

Description automatically generatedinsulin resistance and inflammation in the blood stream[[79]](#footnote-79). As seen in figure 5, a key reason why aerobic exercise is best for increasing memory function is because of the significant oxygen intake that aerobic exercise has compared to other forms of exercise[[80]](#footnote-80). This increase of oxygen leads to the cascade of benefits already considered. Resistance exercise also requires a greater intake of oxygen than normal, however, it doesn’t lead to as good blow flow of oxygen. Therefore, the hippocampus is not impacted and benefitted as much as it is with aerobic exercise.

A more specific area of the hippocampus which is heavily involved with neural growth and therefore increased volume and therefore assisting to progress memory is the dentate gyrus[[81]](#footnote-81). It is the central aspect of the hippocampus, as seen in figure 6, so is inescapably involved[[82]](#footnote-82). Following significant evidence, it is also the most prominent area in the hippocampus for neurogenesis[[83]](#footnote-83). When BDNF stimulates the dentate gyrus, it causes chronic net neurogenesis[[84]](#footnote-84).



## Conclusion:

Since it is evident that exercise can have a profound effect on the brain but particularly on the formation and long-term factor of memory, through increasing the production of neurons and assisting in the protection and health of the present ones, exercise should be a priority. It has also been noted that there is a strong positive correlation between physical exercise and academic achievement[[85]](#footnote-85). Those who exercise have better attention control[[86]](#footnote-86), as well as more fluid ability to respond to sensory, cognitive and motor events which are neuroelectric signals that assist with the allocation of attention[[87]](#footnote-87). This has also been backed up with studies which show that students’ aerobic fitness relates to academic achievement, with those who exercised doing better on tests including reading, spelling and maths[[88]](#footnote-88). As well as concluding a high BMI (low aerobic fitness) has a negative relation to academic achievement[[89]](#footnote-89). Charles Hillman, director of the Neurocognitive Kinesiology Laboratory in Illinois and leader of these studies stated that the effect of exercise on achievement isn’t statistically significant, yet it is a meaningful difference[[90]](#footnote-90). But exercise doesn’t just help the young, it also protects and reduces the risk of Parkinson’s and Alzheimer’s diseases for the older generation[[91]](#footnote-91) by up to 32%[[92]](#footnote-92). Although, memory isn’t the only benefit from exercise, further benefits include: greater energy[[93]](#footnote-93), mood[[94]](#footnote-94) and concentration[[95]](#footnote-95). The importance of exercise is expressed by Mr. Hillman who said, “There’s no medicine or other intervention that appears to be nearly as effective as exercise in maintaining or even bumping up a person’s cognitive capabilities.”

Word count: 1986

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