

## **SMARTFit and Active Aging**

According to the Alzheimer's Association, the 2018 costs of Alzheimer's dementia in the US alone total approximately \$277 billion dollars. With a steadily increasing population of older adults, it has become critical to detect, manage, and prevent cognitive decline. Exercise and other lifestyle factors have been shown to be helpful in doing this, yet more aggressive and innovative solutions have yet to be popularized. Exercise specifically has garnered attention based on its positive effects on brain structure, function and cognition. Similarly, cognitive training has been highlighted as both a rich field of potential, but also one of false claims. A technology that effectively combines the two has yet to become widespread.

SMARTFit is a multi-target system that displays complex information that allows various cognitive processes to be trained while motor and aerobic demands may be simultaneously placed on the user. SMARTFit offers a solution to harnessing the synergistic effects of simultaneous cognitive and physical training,

This whitepaper examines the synergistic effects of engaging in physical and cognitive exercises simultaneously and dives into the proposed mechanisms by which these concurrent behaviors help to shape the body and sharpen the mind. Preliminary research suggests that engaging in these two types of exercise simultaneously may be more beneficial than merely the sum of their separate gains and that their combined effects can have a profound impact on both ameliorating and preventing cognitive decline in older individuals.

In order to understand the potential mechanisms in which cognitive-motor training may be helpful, it is first critical to understand the definitions from which it borrows from, and the neurobiology of how it may create beneficial adaptations.

### **The Science and Practice of Dual-Tasking**

Dual-tasking is the concurrent performance of two tasks that can be performed independently and have distinct and separate goals. Here, we examine the effects of dual-tasking using concurrent physical and cognitive challenges. One of the most interesting aspects of dual-tasking both physical and cognitive challenges at the same time is that one is, in fact, doing three difficult tasks simultaneously: engaging in physical exercise, working out cognitive challenges and multitasking by attending to both tasks at once and transferring attention between the two. Frequently, performance on one or both tasks at hand can deteriorate due to the high demands on the individual. Those high demands result in increased cognitive load, and the switching between these tasks requires a lot of effort and use of executive functions.

The classic dual-task one thinks of is walking and solving math equations or saying the alphabet. However, there are many more complex dual-task situations in everyday life. Dual-tasking has many real-world applications and is one cognitive ability that tends to deteriorate with age. In fact, a reduced ability to simultaneously divide attention between tasks (dual-tasking) has been linked to reduced reaction time and walking speed, more frequent run-ins with obstacles and an increased risk in falls <sup>[1]</sup>. Inability to successfully dual-task also creates

dangerous conditions when driving [2]. It seems that practicing dual-tasking can be hugely beneficial for older individuals, and may even prolong functional independence. Dual-tasking has also been shown to assess attentional resources and functional cognitive ability. Dual-tasking is even more useful when those two tasks at hand are specific to the cognitive goals and needs of the individual.

Dual tasking with aerobic exercise and cognitive challenges is a recently emerging and promising area of research. While cognitive exercise and physical exercise have unique benefits on the body and brain, several benefits are shared between the two. The primary ones are neurogenesis, synaptogenesis, and increased cerebral blood flow. Preliminary research in both animals and humans suggests that the simultaneous activation of these benefits may be larger than the additive properties of doing the two exercises sequentially or separately. Further research needs to be done to confirm some of these theories, but pilot studies on the subject are encouraging. [3]

SMARTFit allows this dual-task training to take place effectively, while maintaining engagement and practical applications to a variety of training environments. SMARTFit offers a multimodal set of cognitive stimuli that allows dual-tasking to be domain specific; meaning that instead of simply walking while reciting the ABC's, an individual may be perform a functional task (such as a lunge), while receiving a cognitive stimulus specific to the individuals needs (such as selective attention training; the process of filtering irrelevant stimuli while directing goal-oriented attention on the "correct" stimulus, as demonstrated in the SMARTFit category "Seek the Letter").

### **Research Findings on Cognitive-Motor Training**

One study examined the effects of cognitive-motor dual-task training on executive functions in a sedentary older adult population over 12 weeks and found that this combined training was more beneficial than single task training alone in improving broad domains of cognitive functions.[4] In another study participants engaged in a combination of a dual task training program as well as a mixed aerobic and resistance training program. While this particular study did not find synergistic effects of the two interventions, they did find that the dual task training program led to transfer effects in terms of executive performance on neuropsychological tests. This effect was not present in the exercise only or cognitive challenge only groups. [5]

Another study looked at an intervention using at Multicomponent Training (MCT) which consists of focusing on neuromuscular coordination, balance, agility, and cognitive executive control. This study found that the MCT intervention had a profound impact on improving inhibition in an older population.[6] Animal studies using novel combinations of physical and cognitive activities resulted in significant cognitive improvements when compared with control animals, specifically in the area of working memory.[7]

Lastly, a systematic review of all current studies examining the effects of motor and cognitive dual tasking to prevent or slow the age-related decline in cognition found that either simultaneous or subsequent combined cognitive physical training was more successful when compared with singular interventions alone. This landmark study, which examined over 20 peer-reviewed articles also noted that while some results should be interpreted with caution, there is clear evidence that there are effective training interventions using cognitive physical dual tasking, provided the interventions and tests are properly designed.[8]

### **Mechanisms of Cognitive-Motor Training: Cerebral Blood Flow, Angiogenesis and Neurotransmitters**

One shared benefit of both aerobic exercise and cognitive challenges is an increase in cerebral blood flow.<sup>[9]</sup> Cerebral blood flow is essential because while the brain does not have very much blood relative to the other organs in the body, the blood it does receive is vital to its function and overall health. Brain health, in turn, impacts the function of the body as a whole. Obviously, complete lack of blood flow to the brain deprives the brain of oxygen and results in death. Less evident is the damage that comes from inadequate cerebral blood flow in the form of oxidative stress. Oxidative stress can cause the death of brain cells and is implicated in the progression of diseases of the brain as well as in cognitive impairment and "brain fog."

While brain fog is not entirely due to oxidative stress or lack of oxygen to the brain it is certainly an important factor and the importance of healthy blood flow to the brain cannot be overstated. This steady flow of blood bathes the vital tissues of the brain with oxygen, glucose and other nutrients. Amazingly, both regular aerobic exercise and cognitive challenges amp up this flow of nourishing blood and increase the rate at which the brain receives these necessary ingredients. The combination of the two means one is engaging in two brain blood-boosting activities at once. In addition, the adding of cognitive challenges during exercise allows for the release of acetylcholine, dopamine, and other beneficial neurotransmitters that accelerate cortical plasticity, increase engagement, and facilitate faster learning. SMARTFit can provide additional cognitive challenges while allowing for the release of these beneficial neurotransmitters through the process of learning and novelty via new, randomized tasks in a gamified context, which in turn promotes engagement. The release of these neurotransmitters has been theorized to accelerate cortical plasticity, as highlighted by the work of Dr. Michael Merzenich.

Another way both physical exercise and cognitive challenges improve brain blood health is through the mechanism of angiogenesis in the cerebellum and the cortex of the brain<sup>[14]</sup>. Angiogenesis is the physiological process by which new blood vessels form from preexisting ones. Like increased blood flow, more blood vessels in the brain result in a healthier, more nutrient-rich brain tissue. These new capillaries aid the brain tissues in the critical exchange of oxygen and metabolites. Capillaries grow and regress due to metabolic demands all over the body. Engaging in repeated activities which foster this new blood vessel growth, especially simultaneously, is an excellent way to maintain a healthy blood supply to the vital tissues of the brain. Doing so keeps the vasculature of the brain healthy and active and helps to stave off atrophy. Fascinatingly, there is emerging evidence that the progression of cognitive decline and

Alzheimer's disease itself may be due, at least in part, to an age-related decline in angiogenesis. Researchers call this theory the Angiogenesis Hypothesis.<sup>[15]</sup> In a nutshell, it suggests that Alzheimer's and dementia symptoms are due to these age-related decreases in new blood vessel formation which in turn diminishes blood flow and reduced cerebral microcirculation. This reduction in cerebral capillary density, due to several growth factors in the blood, leads to cognitive decline. This is a burgeoning and exciting new area of research with lots of data in animal studies to support the angiogenesis hypothesis.<sup>[16]</sup> It is also interesting, of course, because it suggests that with increased blood flow and neuroangiogenesis we might be able to stave off or even reverse some age-related cognitive decline.

### **Trophic Factors**

In addition to these shared benefits, aerobic exercise and increased cardiovascular activity can increase bioenergetic factors like Brain-Derived Neurotrophic Factor (BDNF) insulin-like growth factor -1 (IGF-1) and Vascular Endothelial Growth Factor (VEGF).<sup>[10]</sup> These growth factors are putative mechanisms by which cardiovascular activity benefits cognitive function. Changes in serum concentrations of these important markers are linked to changes in functional connectivity and brain growth. Specifically, researchers found exercise-induced increases in functional connectivity in the temporal lobe of older adults after a one-year aerobic exercise program<sup>[11]</sup>

### **Subjective Cognitive Decline and Dual-Tasking**

In addition to brain fog, many older adults report suffering from subjective cognitive decline. Subjective cognitive decline (SCD) is the subjective interpretation of cognitive decline with no diagnosis of dementia. Oftentimes this impairment in cognition can progress to Mild Cognitive Impairment (MCI) and in some cases SCD can be the first signs of the progression of Alzheimer's Disease (AD). Some researchers refer to the symptoms of SCD as "senior moments". There is a range of severity in of these symptoms, from trivial forgetfulness like walking into a room and forgetting why you went there, to more severe and potentially dangerous types of memory impairment. There is preliminary evidence that engaging in challenging cognitive exercises and a variety of physical activity can help to combat SCD and may even help to reverse it.<sup>[12]</sup>

Interestingly, dual-tasking may work both as a tool to prevent cognitive decline and as an early detection mechanism. This has been seen in the dual-tasking "timed up and go" (TUG) test in which a traditional physical assessment adds a layer of cognitive assessment in order to add some more real-world functionality to it. In these assessments, individuals with early-stage cognitive decline do more poorly on the dual task parts of the assessment than neurocognitively normal controls.<sup>[13]</sup> While normative data has yet to be collected, SMARTFit offers promising potential as one of these combined cognitive-physical assessment strategies. In the absence of normative data to be able to compare performance on SMARTFit tasks to similar age groups, demographics, and clinical conditions, it is possible to assess and demonstrate relative improvements in individual performance on cognitive-motor tasks.

## **The Aging Brain and Neurogenesis**

Another hypothesis relating to the aging brain is the frontal lobe hypothesis. This hypothesis theorizes that the atrophy and decreased functional activity in the prefrontal cortex of older adults leads to decreases in executive functions. Executive functions are a set of cognitive processes that are necessary for the cognitive control of behavior. They include selecting and successfully monitoring behaviors that facilitate the attainment of chosen goals. By integrating cognitive demands into our exercise plan we can adhere to both the angiogenesis hypothesis (increasing blood flow through both cognitive and physical challenges) and providing engaging prefrontal cortex stimulation by incorporating cognitive challenges that specifically work on improving executive functions.

One of the most profound ways that both exercise and cognitive challenges can improve brain and body health is through complementary processes of neurogenesis. Neurogenesis is the adult production of new neurons in the brain. Every day, thousands of new neurons are produced in the adult brain.<sup>[17]</sup> However, unlike the highly plastic and flexible brains of infants and children, adult brains are thought to only grow new neurons in two distinct regions of the brain: the olfactory bulb (area of the brain pertaining to smell) and the hippocampus (an area of the brain specific to learning and memory).

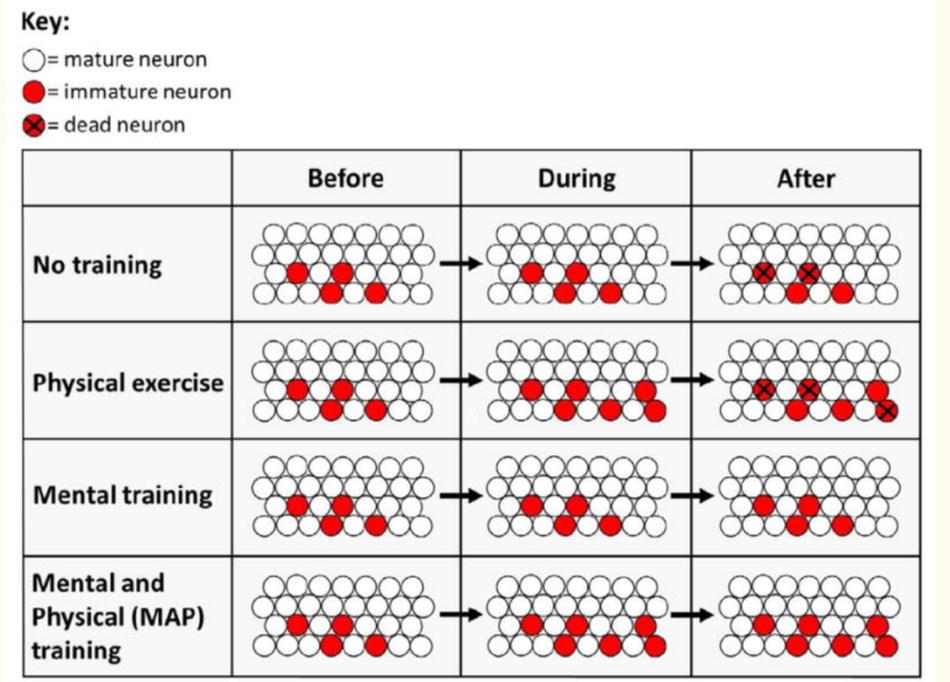
Unfortunately, rates of neurogenesis can decline rapidly with age; however, several behaviors can foster and promote neurogenesis, specifically in the hippocampus. Two of those behaviors are aerobic exercise and effortful learning. Interestingly, these two behaviors affect the process of neurogenesis in distinct but interconnected ways. New cells undergo two crucial phases of existence: proliferation (literally the birth of new cells) and survival (integration into existing neural networks). Merely making new cells is not enough, they must incorporate into the existing brain tissue to survive. Due to this feature, many people describe hippocampal neurogenesis as a kind of "use it or lose it" scenario. The new cells can be made abundantly through specific activities, but if they are not used, by doing some activity that recruits them to stay, they undergo apoptosis and die in a relatively short period of time.

Luckily, exercise and cognitive challenges in tandem seem to be a perfect recipe for the guaranteed survival of at least some of these precious new cells. Aerobic exercise helps to increase the proliferation of the cells<sup>[18]</sup> and effortful learning helps integrates them<sup>[19]</sup>! Combination of increased proliferation from the aerobic exercise and increased survival from the cognitive challenges is a putative neurobiological explanation for how the combined simultaneous exercise and cognitive challenge paradigm manifests itself and delivers benefits greater than the sum of its parts. The diagram below explains the process in further detail: (Figure from Curlik & Shors, 2013)

These newly proliferated neurons have a relatively small window of time during which they must be stimulated (by effortful learning or cognitive challenges) in order to survive. The "sweet spot" seems to be about 7 to 14 days after proliferation. That is to say that the cells that are proliferated today, will atrophy and die if they are not recruited or engaged in the coming

week. This is due to the functional maturing of the cell and the normal lifespan of new neurons. The best way to ensure these new neurons are recruited is to keep up a consistent pattern of aerobic exercise and cognitive challenges. SMARTFit allows this to occur through either the simultaneous incorporation of physical activity during cognitive challenges, sequential cognitive stimulation amidst physical activities, or as a platform for cognitive stimulation with a significant aerobic or motoric load.

The image below explains the interesting phenomenon of the lifespan of newly proliferated hippocampal neurons and their survival intervention window in greater depth:



**Figure 3**  
 Physical exercise greatly increases the number of new neurons produced during training (van Praag, et al., 1999; van Praag, 2009), and mental training increases the numbers that survive after training (Gould et al., 1999; Shors et al., 2011). In principle, a combination of both mental and physical (MAP) training should be more effective than either training approach alone, increasing the overall number of neurons that survive to become mature functioning neurons in the adult brain (Fabel et al., 2009).

(adapted from Shors article in Scientific American)

Preliminary studies in animals and humans seem to support this hypothesis that combined physical and cognitive training is more effective at recruiting and maintaining new neurons than either intervention alone. In fact, in one study wherein aerobic exercise was combined with an enhanced environment (similar to a cognitive challenge for rodents) researchers found as much as a 30% greater increase in new neurons than was found with either of the singular interventions alone<sup>[20]</sup>!

**Synaptogenesis**

In addition to neurogenesis, exercise and cognitive challenges also aid in synaptogenesis or birth of new synapses. Synapses are spaces between neurons and link the activity of one neuron to another. Neurons can have many synapses and link to one another an almost limitless number of configurations. There is an old adage in neuroscience that "neurons that fire together wire together" meaning that the neural patterns that one engages in reinforce on a physiological level. This process is called Hebbian Law, after its founder, Donald Hebb. In short, an increase in synaptic efficacy results from the presynaptic cells' persistent and repeated stimulation of the postsynaptic cell. Through repeated activation of this link, the link is strengthened. This persistent strengthening of the synaptic connections through activity is just one of many ways that behavior and physiology are directly linked. The circuits you frequently engage are strengthened and those which get little or no use atrophy and wither. In this sense, synaptogenesis (like neurogenesis) is genuinely a "use it or lose it" process. Like neurogenesis and angiogenesis, synaptogenesis is rampant during early brain development and slows later in life. Robust increases in synaptogenesis and neurogenesis can lead to an overall increase in brain volume, specifically in the gray matter areas of the cortex and cerebellum. Thus, both aerobic exercise and cognitive challenges have also been shown to increase brain volume through the mechanisms described.<sup>[21]</sup>

## **Conclusion**

The benefits of robust brain volume in old age are enormous. The boost in neural plasticity from neurogenesis and synaptogenesis is thought to have a direct positive impact on cognition. While some of the exact benefits of neurogenesis are still in research, we know new neural growth can help to enhance learning and memory as well as to act as a protective factor against neurodegenerative diseases. Other areas of cognition that can improve with these interventions include verbal memory, executive functioning, processing speed and visuospatial memory. There is even some evidence that improvements in these areas can lead to improved mood and declines in rates of some forms of mental illness. SMARTFit offers a variety of programming that may be able to specifically address these cognitive deficits that occur with age, as well as deliver the multi-domain benefits of exercise sequentially and/or simultaneously.

In short, a brain that engages in increased levels of angiogenesis, synaptogenesis, and neurogenesis is more efficient, plastic and adaptive. This physiological improvement translates behaviorally into better performance and imparts protective factors against further decline and disease. During a critical period in life, when typically cognitive function declines and brain volume shrinks, it is significant to recognize that innovative technological solutions, such as SMARTFit, can be implemented in addition to exercise and lifestyle modifications to hopefully improve the cognitive trajectory over the lifespan.

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