



Past, present and future in exercise-cognition research

| Review

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Received 14 February 2017; Accepted 1 March 2017; Published 3 April 2017

Abstract: Early research into the effects of acute exercise on cognition were atheoretical and of poor design. In the 1990s and 2000s, cognitive-energetical theories and the catecholamines hypothesis have been developed as rationales for effects of acute exercise on cognition. It was claimed that acute exercise was a stressor and as such would affect cognition in an inverted-U manner, the same as other stressors. However, the inverted-U effect was rarely supported. Later research has somewhat consistently shown that moderate intensity, short to moderate duration exercise induces improved cognitive performance. However, the effects of heavy exercise and long-duration, moderate intensity exercise treatments remain somewhat equivocal, except for autonomous tasks which are facilitated. Recent research suggests that undertaking exercise, while simultaneously carrying out a motor task, is more beneficial than simply exercising before undertaking the cognitive tasks. Research examining the effect of chronic exercise on cognition was also originally atheoretical and poorly designed. Improved research designs have led to some consistency in findings and the evidence for chronic exercise having a facilitative effect on cognition is fairly consistent but only a small to moderate improvement has been demonstrated. Human studies provide a *prima facie* case for brain derived neurotrophic factor being a mediator in the chronic exercise-cognition interaction and evidence from animal studies strongly supports this. Recent work provides support for claims that exercise, while simultaneously undertaking a motor task, is more beneficial than simply exercising.

Key words: Exercise; cognition; arousal; catecholamines; central executive; BDNF; age.

1. Introduction

In this short review, I will attempt to present an outline of past, present and future research into the effect of exercise, both acute and chronic, on cognition. The review includes comment on underlying theories and mechanisms, as well as empirical studies. Moreover, it includes studies from a cognitive psychology perspective as well as those that are neuroscientifically-based.

2. Acute exercise

Early research into the effect of acute exercise on cognition was atheoretical and the nature of the exercise protocols left much to be desired. For example, Gutin

and DiGennaro [1] had participants undertake 1 min of step-ups, using the Harvard Step Test protocol. Meyers et al. [2] used a similar step-up protocol but had participants work for 5 min, while McAdam and Wang's [3] participants carried out a run-jog-walk protocol for 10 min. According to the authors, this was 'designed to work up a mild sweat, but not to fatigue' (p. 209). It is easy to criticize such protocols but we should remember that sports science, as we know it today, was only in its infancy. In fact, in most countries it was non-existent.

The first to provide a theoretical underpinning for hypothesizing that acute exercise would have an effect on cognition, was Davey [4]. He saw exercise as being a

stressor, which would affect arousal in the same way as other stressors. Davey [4], therefore, turned to Yerkes and Dodson's [5] arousal-performance theory to develop his hypotheses. Yerkes and Dodson [5] claimed that when arousal is low, performance will be poor but, as arousal rises to a moderate level, performance will become optimal. However, if arousal continues to rise, performance will return to a level equal to that shown during low levels of arousal. When plotted graphically, performance demonstrates an inverted-U curve. Based on this, Davey [4] claimed that at rest and during low intensity exercise, cognitive performance would be poor. When exercise intensity rose to a moderate level, performance would be optimal but continuing to increase the intensity would lead to a return to poor performance.

Davey's [4] research report was accompanied by a theoretical paper by Cooper [6], a neuropsychologist. In this paper, Cooper [6] proposed what my colleagues and I have called the 'catecholamines hypothesis' [7], in which he argued that exercise-induced circulating peripheral plasma catecholamines resulted in increases in concentrations of the neurotransmitters dopamine and noradrenaline in the brain. In turn, the brain catecholamines were responsible for increases in arousal by activating the reticular formation in the brainstem. However, behavioral neurochemistry was in its infancy and apart from one paper [8], it was not until 1994 that any development would be seen in neurochemical approaches. Instead, there was a slow move towards theoretical rationales becoming based in cognitive psychology.

2.1. Cognitive psychology rationales

Following Davey's [4] example, some researchers (e. g. [9-11]) examined the hypothesis that acute exercise would affect cognition in an inverted-U fashion. However, it was not until the publication of a seminal paper by Tomporowski and Ellis [12] that research generally became theoretically based. Moreover, Tomporowski and Ellis' [12] critique led to a tightening of research designs. While some researchers stuck with Yerkes and Dodson's [5] unidimensional theory, others favored more multidimensional theories. It is not the purpose of this review to delve deeply into the particular arousal-performance interaction theories used as rationales for an acute exercise-cognition interaction effect, rather I will briefly outline the most commonly used of the theories (for more detailed reviews see [13,14]). The allocation of resources or cognitive-

energetic theories that were and, indeed, still are the most popular, were developed from Kahneman's [15] theory.

Kahneman [15] believed that individuals have a limited amount of resources. The amount is not fixed but flexible. He claimed that as arousal rises, the number of resources available within the brain increases. Like Yerkes and Dodson [5], he argued that this increase is beneficial for performance up to a certain point, after which there will be a return to baseline levels. It is here that Kahneman disagrees with Yerkes and Dodson [5]. To Kahneman increases in arousal are not the only factor affecting performance. The increase in the number of resources, as arousal rises to a moderate level, will only result in improvements in performance if the person allocates the resources to the task in hand. The allocation of resources to task relevant information is said to be undertaken by cognitive effort (more often just referred to as effort). Kahneman [15] believed that during moderate levels of arousal, effort can easily allocate resources to the task. This does not differ from Yerkes and Dodson [5]. However, Kahneman [15] claimed that even at low levels of arousal, performance can be optimal if cognitive effort allocates resources to task relevant information and the task is not too demanding. Demanding tasks would require an amount of resources that are not available when arousal is low. However, during high levels of arousal, Kahneman [15] believed that the individual would not be able to allocate resources to the task. In these circumstances, evaluation of task demands will tend to lead to the perception that the task cannot be successfully completed.

Sanders [16] took a similar approach to Kahneman [15] but there were some differences. Sanders argued that the different stages of cognitive processing needed to be energized by different energetical mechanisms. He termed these arousal, activation, the evaluation mechanism and effort. Arousal is seen as a readiness to process input, while activation is a motor readiness to respond. The role of the evaluation mechanism is to provide effort with information concerning performance outcome and, perhaps more importantly, the physiological states of the arousal and activation mechanisms. This is vital because effort is responsible for energizing response choice but also has the job of controlling and coordinating arousal and activation.

2.2. Catecholamines hypothesis

As we saw above, Cooper [6] posited the hypothesis that acute exercise-induced increases in circulating

catecholamines result in improved cognitive functioning during moderate intensity exercise but inhibit cognition during heavy exercise. This he claimed was because increases in brain catecholamines increase arousal by activating the reticular system (see [17] for a detailed account of Cooper's [6] theory and its development). Chmura et al. [18] and later my colleagues and I [7] elaborated on Cooper's [6] original work. We pointed out that during exercise, animal studies have shown that peripherally circulating adrenaline and noradrenaline (NA) activate β -adrenoceptors on the afferent vagus nerve, which runs from the abdomen through the chest, neck and head, and terminates in the nucleus tractus solitarius (NTS) within the blood-brain barrier. The excitatory neurotransmitter glutamate mediates synaptic communication between the vagal afferents and the NTS, allowing noradrenergic cells in the NTS, which project into the locus coeruleus (LC), to stimulate NA synthesis and release to other parts of the brain [19]. Moreover, it has been shown that stimulation of α_1 -adrenoceptors, by NA release from the LC, potentiates the firing of dopamine neurons in the ventral tegmental area, probably due to α_1 -adrenoceptor activation inducing enhanced glutamate release, which affects the excitability of dopamine neurons [20].

Animal studies provide support for acute exercise-induced increases in NA and dopamine in the brain, however results have been far from unequivocal. The effect of acute exercise on whole brain concentrations of NA in rodents has shown either a decrease in concentrations or no significant effect. Research has demonstrated increased dopamine concentrations particularly in the brainstem and hypothalamus during and immediately following acute exercise (see [21,22] for reviews). Rodent studies have also shown increases in brain concentrations of the NA metabolite 3-methoxy-4-hydroxyphenylglycol (MHPG) and the dopamine metabolites 3,4-dihydroxyphenylacetic acid (DOPAC) and 4-hydroxy-3-methoxyphenylacetic acid (homovanillic acid, HVA), suggesting increased turnover of brain dopamine and NA during exercise. Increased concentrations of MHPG have been found in most brain regions [21,22], while increased concentrations of DOPAC and HVA have been shown, particularly in the brainstem and hypothalamus [23,24].

Dopamine and NA work together to control cognition but their efficiency is affected by stress levels, with regard to this review that is exercise-induced stress levels. When stress levels are low, performance is comparatively poor because, as Cooper [6] pointed out,

at low levels of arousal the appropriate sequence of neuronal activation cannot be obtained as neurons cannot be stimulated to an adequate level of summation. This would be the case when at rest and during low intensity exercise (<40% volume of oxygen uptake, VO_{2max}). When exercise increases to a moderate level ($\geq 40\%$ VO_{2max} to 79% VO_{2max}), brain catecholamines concentrations rise and there is increased firing of the high affinity α_{2A} -adrenoceptors by NA [25], which increases the strength of neural signaling in the preferred direction by inhibiting cyclic adenosine monophosphate (cAMP) activation [26]. Similarly, the high affinity D1-receptors are activated by dopamine, which dampens the 'noise' by inhibiting firing to non-preferred stimuli [27]. Thus, dopamine and NA working together improve the signal to 'noise' ratio. This is what we would expect during moderate intensity exercise and should lead to optimal performance. However, during heavy exercise (>80% VO_{2max}) or during long-duration (≥ 45 min), moderate intensity exercise, NA and dopamine concentrations become excessive. The excess NA activates the lower affinity α_1 - and β -adrenoreceptors [25]. Activation of α_1 -adrenoreceptors results in reduced neuronal firing in the prefrontal cortex, while excessive stimulation of D1-receptors and β -adrenoreceptors induces excess activity of the secondary messenger cAMP, which dampens all neuronal activity, thus weakening the signal to 'noise' ratio [28]. Thus, working memory tasks which depend on activation of the prefrontal cortex are inhibited by heavy exercise and long-duration, moderate intensity exercise. On the other hand, tasks which activate the sensory cortices and their association areas can benefit during heavy exercise. Animal studies have shown that high concentrations of NA activating α_1 - and β -adrenoceptors can positively affect signal detection [29, 30]. Moreover, research has also shown that the effect can be stimulated by exercise-induced increases in brain corticotropin releasing factor (CRF) acting on the LC-NA system. CRF causes tonic firing of LC-NA neurons, which results in suppression of somatosensory signal transmission within the somatosensory thalamus and cortex [31]. This appears to reduce detectability of low-intensity stimuli without affecting high-intensity stimuli [32,33].

Learning and memory also benefit from heavy exercise and long-duration, moderate intensity exercise. Consolidation of declarative information appears to be primarily undertaken by the hippocampus and requires the process of long-term potentiation (LTP), i.e. the strengthening of synaptic connections between neurons.

High concentrations of NA in the hippocampus activate β -adrenoceptors, which are guanosine triphosphate-binding proteins and stimulate cAMP activation. Acute exercise also results in increases in serum or plasma brain derived neurotrophic factor (BDNF) concentrations in humans [34-36], while animal studies have demonstrated strong evidence for acute exercise inducing increased BDNF and/or BDNF messenger ribonucleic acid (mRNA) expression in the brain, in particular in the hippocampus [37-39]. It is the interaction between BDNF and NA via cAMP activity that is vital for LTP. The synaptic actions of BDNF are 'gated' or regulated by cAMP, as it modulates the signaling and trafficking of the BDNF receptor tropomyosin-related kinase B (Trk B) [34,35]. The binding of BDNF to Trk B initiates a number of intracellular signaling cascades, including calcium/calmodulin kinase II and mitogen-activated protein kinase, resulting in the phosphorylation of cAMP-response element binding protein (CREB) [40, 41]. The whole process modulates synaptic transmission in a lasting manner by modifying synaptic protein composition via local protein synthesis [41], thus facilitating synaptic transmission.

2.2.1. Summary

The cognitive psychology theories and the catecholamines hypothesis suggest a possible inverted-U effect of acute exercise on cognition but one that might be moderated by task type. Moderate intensity, short to moderate duration exercise should have facilitating effects on all types of task. However, heavy exercise and long-duration, moderate intensity exercise may affect differing task types differentially. Central executive tasks would be expected to be inhibited by the effects of high concentrations of brain catecholamines in the prefrontal cortex during heavy exercise and long-duration, moderate intensity exercise. However, perceptual and attention tasks may benefit from dampening of neural noise in the sensory cortices and their association areas. The interaction between β -adrenoceptors, cAMP and BDNF stimulates LTP in the hippocampus thus improving long-term memory and learning. In the next sub-section, we examine the empirical data to see if this is what really happens.

2.3. Empirical research results

Based on the findings of three recent systematic reviews combined [14,42,43], we find that during moderate intensity exercise carried out for a short to moderate duration, accuracy and speed results differ somewhat,

with speed showing greater effects than accuracy. We believe that this is due to the nature of the tasks that are most commonly used. The majority were designed to be measured primarily by speed and, in fact, few errors ever occur. However, there are tests which could be used in which accuracy is targeted. More research using such tasks is required (see [42] for more detail). Moreover, there are still a quite substantial amount of studies in which results are non-significant. However, in the two meta-analyses [42,43], moderate to large mean effect sizes were demonstrated. This supports the notion that many of the non-significant results are due to small sample sizes, which have a negative effect on the power of the statistics. Despite this, we could say that for moderate intensity, short to moderate duration exercise, when speed is the dependent variable, results tend to show support for a facilitative effect.

For heavy exercise and long-duration moderate intensity exercise, the situation is far less clear. Results demonstrate very mixed effects but this is not unexpected given that we believe that task type will be a moderating variable. We need, therefore, to examine this factor. McMorris et al. [14] reported that for autonomous tasks, none of the studies demonstrated any significant effect of heavy exercise when accuracy was the dependent variable. However, when speed was the dependent variable, there was 100% facilitation. For attention/perception tasks, with accuracy as the dependent variable, 50% showed no significant effect, 33.3% demonstrated inhibition and 16.7% facilitation. When speed was the dependent variable, inhibition was shown by 47.1%, non-significance by 35.3% and facilitation by 17.6%. The authors reported only two studies examining accuracy of central executive tasks, one demonstrated no significant effect but the other showed a negative effect. The position was identical with speed as the dependent variable, one task demonstrating no significance and one inhibition. Only one study examined long-term memory, and it showed a facilitative effect. A more recent study [44] has also demonstrated a beneficial effect of heavy exercise on long-term memory.

2.4. Current trends

Several researchers are focusing on areas of research which have tended to be neglected. The effect of heavy exercise on long-term memory [44] is creating some interest but we need more research on the effects of heavy exercise on all types of task. Attempts to examine possible underlying mechanisms are also being

undertaken [45]. The use of studies in which the participants undertake physical and/or mental tasks while simultaneously exercising are also being examined, with researchers looking at underlying mechanisms and translational factors [46]. These are all areas that need research and will help us better understand the acute exercise-cognition interaction.

3. Chronic exercise

As most schoolchildren know, the ancient Greeks and Romans saw a link between chronic exercise and cognition. Despite this, there has been little research into the topic until the beginning of the 21st century [47]. As with acute exercise, early research was atheoretical. In fact, one might argue that until very recently, attempts to examine underlying mechanisms have been very weak. Elsewhere [48], I have reported that Colcombe and Kramer [49] listed the first theories as being the speed hypothesis [50], the visuospatial hypothesis [51], the controlled-processing hypothesis [52] and the central executive hypothesis [53], all of which concern the effect of chronic exercise on cognition in the elderly. These hypotheses were based on the argument that tasks requiring these processes are most likely to benefit from chronic exercise. They are more descriptions of the types of tasks rather than attempts to provide real theories or describe mechanisms. In a similar vein, Etnier described the cardiovascular fitness hypothesis [54,55], the cognitive reserve hypothesis [56,57] and the frontal lobe (or executive control) hypothesis [58]. The cardiovascular fitness hypothesis, which proposes that the increases in cardiovascular fitness that occur in response to physical activity are responsible for the changes in cognitive performance observed [47]. However, the mechanisms by which this occurs are not described. Moreover, Etnier et al. [59] used meta-regression techniques to specifically test the cardiovascular fitness hypothesis. Results failed to support the hypothesis. According to the cognitive reserve hypothesis, individuals who have a greater cognitive reserve are able to maintain their cognitive abilities better with advancing age and have a lower risk of dementia [56,57]. Again, no mechanisms are reported and Etnier [47] pointed out that “because of the lack of clarity in operationalizing cognitive reserves” (p. 34), no empirical studies have been carried out which specifically assess the role of cognitive reserve as a mediator of the effects of chronic physical activity on cognitive performance. The frontal lobe (or executive control) hypothesis is like the theories outlined by Colcombe and

Kramer [49], merely stating the types of task that are most beneficially affected by chronic exercise.

3.1. Brain derived neurotrophic factor hypothesis

The discovery by van Praag et al. [60] that in rodents, chronic exercise results in the release of BDNF in the brain, has proven to be very important to explaining the mechanisms underlying the effect of chronic exercise on cognition (see [48] for a fuller critique of the BDNF hypothesis). BDNF is a protein and a member of the neurotrophic family. It is widely distributed throughout the brain but is particularly well represented in the hippocampus, neocortex, cerebellum, striatum and amygdala [40,61]. BDNF is initially encoded by the BDNF gene to pro-BDNF which is either proteolytically cleaved intracellularly by pro-convertases and secreted as mature BDNF; or secreted as pro-BDNF and then cleaved by extracellular proteases to mature BDNF [62]. BDNF plays a major role in neurogenesis and synaptic transmission, and hence learning and memory. Its activity is initiated when it binds with one of its receptors, the high-affinity Trk-B. Binding to Trk-B results in receptor dimerization and trans-autophosphorylation of tyrosine residues in the cytoplasmic domains of the receptor, which initiates a number of intracellular signaling cascades, including calcium/calmodulin kinase II and mitogen-activated protein kinase, resulting in the phosphorylation of CREB [40,63]. Activation of these signaling pathways is essential for neurogenesis and neuroplasticity, and hence learning and memory.

3.2. Empirical results

Etnier et al. [47], reviewing empirical, meta-analytical and narrative reviews, concluded that studies with random controlled trials (RCTs), supported small-to-moderate positive effects of chronic physical activity on cognitive performance in the elderly. She also found support for a positive relationship between regular physical activity and cognitive performance in children. However, the majority of this evidence came from cross-sectional studies. With participants of diverging age, Smith et al. [64] demonstrated only small mean effect sizes (Hedges' $g < 0.20$), although they were significant. On the other hand, Pesce and Ben Soussan [65] reported the findings of 11 studies, all of which demonstrated some advantage of undertaking physical activity. Moreover, studies examining the interaction between physical activity, BDNF and cognition also show some mixed results [48].

Griffin et al. [36] demonstrated a significant improvement in memory performance following 5 weeks of training but not after 3 weeks. This improvement coincided with post-exercise increases in serum BDNF concentrations. There were no significant effects on the Stroop color test. Erickson et al. [66] showed an increase in hippocampal volume, which was related to serum BDNF concentrations. There were improvements in spatial memory, which were related to increased hippocampal volume but not to Δ BDNF concentrations. Whiteman et al. [67] showed that a BDNF x fitness interaction was a strong predictor of long-term memory performance. They found that for active participants, serum BDNF concentrations and memory were positively correlated but for sedentary individuals they were negatively correlated. However, BDNF serum concentrations were not correlated with fitness level (see [48] for more detail). Weinstein et al. [68] showed that fit individuals had greater gray matter volume in several regions, including the dorsolateral prefrontal cortex, which is particularly active during the performance of several central executive tasks [69, 70], while Chaddock and colleagues [71] have demonstrated greater basal ganglia volumes in fit compared to unfit children.

3.3. Summary and current trends

To summarize, we could say that at the moment, there is only support for a small to moderate effect of chronic exercise on cognition but studies that have included long periods of exercise, e.g. over one year [66], do suggest that chronic exercise does have an effect. Moreover, the studies measuring changes in BDNF and/or metamorphic changes also lead one to think that we need to undertake longer periods of exercise. A recent innovation that is showing great promise is the use of physical activity plus cognition or playing active games, which also require the person to think while exercising. This may be more beneficial than simply exercising (see [65]). In a similar vein to this, activities such as dance [72], resistance training [73] and yoga [74] are demonstrating promising results.

Declaration of interests

The author declares no competing interests.

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