VIEWPOINT

Reappraisal of the acute, moderate intensity exercise-catecholamines interaction effect on speed of cognition: role of the vagal/NTS afferent pathway

Terry McMorris
Department of Sport and Exercise Science, Institute of Sport, University of Chichester, College Lane, Chichester, West Sussex, United Kingdom

The hypothesis that circulating catecholamines induce improved cognitive functioning during moderate intensity exercise was first posited by Cooper (3) and subsequently developed first by Chmura et al. (2) and later by McMorris and colleagues (9–11). Based on the work of Samorajski and Marks (21), Cooper believed that during exercise, the blood-brain barrier would be compromised in the median eminence at the base of the hypothalamus and in the anterior pituitary gland. He also pointed to research demonstrating initiation of the sympathoadrenal system by the hypothalamus due to anticipation of undertaking exercise (20). Cooper pointed out that both of these actions would induce increased activation of the reticular formation and hence higher levels of arousal. Chmura et al. (2) added to the hypothesis by stating that the key issue, with regard to circulating catecholamines, was the point at which plasma concentrations show an exponential rise, known as the catecholamines threshold (CT) (17). We (9–11) elaborated on Chmura et al.’s ideas by pointing to animal studies that have shown that epinephrine and norepinephrine 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 solitarii (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 ceruleus (LC), to stimulate norepinephrine synthesis and release to other parts of the brain (15). Moreover, it has been shown that stimulation of the α1-adrenoceptor, by norepinephrine release from the LC, potentiates the firing of dopamine neurons in the ventral tegmental area, probably due to α1-adrenoceptor activation inducing enhanced glutamate release, which affects the excitability of dopamine neurons (5, 6).

Animal studies provide support for acute-exercise induced increases in norepinephrine and dopamine in the brain; however, results have been far from unequivocal. The effect of acute exercise on whole brain concentrations of norepinephrine in rodents has shown either a decrease in concentrations or no significant effect. Research has demonstrated increased dopamine concentrations, particularly in the brain stem and hypothalamus during and immediately after acute exercise (see Refs. 12 and 13 for reviews). Rodent studies have also shown increases in brain concentrations of the norepinephrine metabolites 3-methoxy 4-hydroxyphenylglycol (MHPG) and the dopamine metabolites 3,4-dihydroxyphenylacetic acid (DOPAC) and 4-hydroxy 3-methoxyphenylacetic acid, also known as homovanillic acid (HVA), suggesting increased turnover of dopamine and norepinephrine during exercise. Increased concentrations of MHPG have been found in most brain regions (12, 13), whereas increased concentrations of DOPAC and HVA have been shown, particularly in the brain stem and hypothalamus (7, 14). These studies and those using electrophysiological stimulation of the vagus nerve (19) support the previous research showing acute exercise-induced increases in brain catecholamines concentrations via the vagal/NTS pathway (15).

Given the above, it is not surprising to find that recent meta-analyses (3–5) have shown moderate to high mean effect sizes, g = 1.41, SE = 0.17 (9), g = 0.50, SE = 0.10 (10), and g = 0.55, SE = 0.10 (11) for acute, moderate intensity exercise-induced changes in speed of cognitive performance. [Results for accuracy have been shown to be nonsignificant, except for one study that showed a negative mean effect size, g = −0.44, SE = 0.16 (9). This is probably because most of the tasks used were designed to be assessed by speed of processing, which requires stimulus detection and identification, response selection, preparation, initiation, and activation. Speed is thought to be a measure of the efficiency of these processes.] However, when we (11) compared the mean effect size for studies at CT and the lactate and ventilatory thresholds, which occur at about the same time as CT (17, 23), with those where the exercise intensity was ≥40% maximum volume of oxygen uptake (VO2 max) but <80% VO2 max, we found no significant difference (g = 0.58, SE = 0.20 vs. g = 0.54, SE = 0.11). To explain this, we pointed to the fact that, during exercise at subthreshold intensities, plasma catecholamine concentrations begin to rise after ~30 min (8). In fact, a significant increase in plasma catecholamines at 20 min for a group who exercised at 75% lactate threshold was demonstrated (1). However, this did not apply to all of the studies, because several were only ~12 min duration. Below, we examine evidence from rodent studies, which we believe provide a viable explanation for an interaction between sub-CT acute exercise, vagal/NTS activation, and cognition. Rodent studies have shown that acute exercise below as well as above the lactate threshold (LT), which occurs about the same time as CT (17), activates A1 and A2 noradrenergic neurons in the NTS (16). Although the effect on A6 LC neurons was not measured, it would not be unreasonable to...
expect similar activation of these neurons, especially because A2 neurons project to the LC and are thought to modulate A6 activity (4, 18). This activation of the NTS can only have occurred because of vagus nerve activity, but the sub-LT/CT stimulation of the NTS cannot have happened via increased circulating plasma catecholamine activation of β-adrenoceptors. The vagus nerve, however, does not only contain chemoreceptors, such as β-adrenoceptors, but also includes mechanoreceptors, baroreceptors, and nociceptors. We should note that although sub-LT exercise induced increased c-Fos expression in A1 and A2 neurons, supra-LT exercise demonstrated significantly greater expression (16, 22).

Although this research does not unambiguously demonstrate acute exercise-induced stimulation of LC via the vagal/NTS pathway at or above CT, let alone sub-CT, it does provide strong circumstantial evidence for activation of the pathway via β-adrenoceptors, when exercise is at or above CT, but via activation of other receptors when exercise is below CT. Studies have shown that systemic administration of epinephrine stimulated norepinephrine activity in both the NTS and LC and that activation was attenuated by blockade of peripheral β-adrenoceptors (see Ref. 15), while Soya and associates (16, 22) found that supra-LT exercise activates noradrenergic neurons in the NTS. Taken together, these findings strongly support the claims that acute exercise at or above CT induces activation of β-adrenoceptors on the vagal/NTS pathway, which in turn activates the LC. It is therefore not surprising to see that exercise at or about CT results in improved speed of cognition (9–11).

That moderate intensity exercise below CT also facilitates speed of cognition can be accounted for if we accept that nonchémical receptors also affect activation of the NTS because of feedback concerning cardiovascular and muscular activity and feelings of pain. Although it is unlikely that this intensity of exercise will induce pain, it does result in cardio-respiratory and mechanoreceptor feedback, which may activate the vagal/NTS pathway. The use of heart rate variability after sub-CT exercise, in humans, could provide useful information concerning parasympathetic activity, which may allow extrapolation to vagal/NTS pathway affects in acute exercise-cognition research. This could be particularly useful if we are to determine whether post-CT exercise induces greater effects than sub-CT and maybe even allow us to determine the time at which exercise become so intense that negative effects begin to be seen, presumably nociceptive feedback would be increased at this stage. Similarly, we need to examine vagal/NTS activity during low intensity exercise to determine the intensity × duration needed for increased vagal/NTS-LC activation and hence improved cognition.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

Author contributions: T.M. conception and design of research; T.M. analyzed data; T.M. drafted manuscript; T.M. edited and revised manuscript; T.M. approved final version of manuscript.

REFERENCES


