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University of São Paulo

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University of São Paulo

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Commentaries on Viewpoint: A role for the prefrontal cortex in exercise tolerance and termination

IS IT THE BRAIN OR THE BODY?

TO THE EDITOR: Fatigue during exercise is a complex phenomenon and has historically been assigned to peripheral mechanisms. Recently more attention is paid to the “central” origin of fatigue, where failure of the motor cortex, changing neurotransmitter concentrations, decreased blood flow, etc., are put forward as underlying mechanisms (3). Both hypotheses (peripheral and central) contain the same “mistake” when isolating the head from the body and vice versa. In their Viewpoint, Robertson and Marino (4) link the prefrontal cortex (PFC) with exercise tolerance and possible fatigue. The PFC could play a role as switchboard during exhaustive exercise, taking part in “decision” making on exercise cessation (4). A declined EEG response to exercise was found in the PFC when exercise intensity increased (5), which confirms previous results with exhaustive exercise in the heat (2). This might indicate that electrocortical activity is diminished at exercise cessation or that other brain areas become more “active” (1). The important message of the recent paper (4) is that the authors clearly try to explain that the brain integrates several signals and emotions. However, the question remains if the brain really “thinks” and “makes decisions” to avoid catastrophe. It might also be that during exercise the disturbance of peripheral and central homeostasis are integrated and that several neurotransmitter systems influencing frontal and other brain regions overshoot or even become depleted at exhaustion (3). Also, temporary depletion of brain substrates (glucose, glycogen, lactate) could be involved. At this stage we probably don’t have the right tools (methods) available to confirm or reject this hypothesis.

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Romain Meeusen
Vrije Universiteit Brussel

PREFRONTAL CORTEX ACTIVATION AND AFFERENT FEEDBACK IN DIFFERENT EXERCISE MODES

TO THE EDITOR: The Viewpoint by Robertson and Marino (4) highlighted that the coordinative role of the PFC during exercise may depend on the exercise model under consideration. Although not exclusively, the ability to perform a particular exercise mode may be related to the capacity to tolerate unpleasant sensations triggered by afferents from peripheral organs and muscles (2). Previous study showed that the muscle recruitment for a given,

submaximal power output was greater in controlled-pace exercise than in self-paced exercise (3). This suggests that the muscle recruitment-produced bioproducts accumulation was higher in this former exercise mode, thus probably triggering a greater III/IV muscle afferents and cardiorespiratory response (1) toward interoceptive regions of the PFC areas (2, 4, 5). The PFC is suggested to integrate afferents from periphery into messages with emotional relevance when processing homeostatic adjustments to guide the decision making (4), so that the increased peripheral afferents during a controlled-pace exercise may impose a greater metabolic cost to PFC when integrating these afferents. As a result, controlled-pace exercise would further require higher cerebral (de)oxygenation, neurotransmitters depletion and temperature, with a concomitant higher effort sensation (3). Thus, a possible higher energy cost in PFC areas during controlled-pace exercise may implicate an unpleasant, less tolerable exercise mode, thereby limiting the capacity to maximally perform this exercise (when compared with self-paced exercise). Indeed, as reported to submaximal intensity, controlled-pace exercise is more psychologically and physiologically challenging than self-paced exercise (3). Future studies are required to confirm this hypothesis in maximal aerobic exercises performance.

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Flávio O. Pires
Fabiano A. Pinheiro
Exercise Psychophysiology Research Group
School of Arts, Sciences and Humanities
University of São Paulo, Brazil

COMMENTARY ON “A ROLE FOR THE PREFRONTAL CORTEX IN EXERCISE TOLERANCE AND TERMINATION”

TO THE EDITOR: The contribution of specific brain activities to (voluntarily or involuntarily) reduce muscle force/power (i.e., fatigue) or quit an exercise (task failure) is being more and more recognized. With the current paper (1), the authors present a model of how the brain forms the decision whether to terminate an exhaustive task. This model proposes one of several possible—and not mutually exclusive—mechanisms. Others include a change of serotonin concentration in the brain (2) or an insular processing loop proposed to regulate motor drive (3).

Eventually, these mechanisms may be combined into one model, as tentatively sketched in Fig. 1 of the present paper. However, we have to be clear about the concepts to be explained: motivation, effort, and pain should be understood as distinct factors influencing each other as well as supraspinal fatigue and task failure. It will be interesting to more specifically formulate hypotheses about how the proposed components of the system interact in different contexts. For example, many studies outside the field of exercise science link PFC to motivational processes. On the other hand, PFC modulates activity in regions like insula and thalamus known for sensory processing during placebo analgesia (4).

Thus, possibly, there are regulatory mechanisms of exercise tolerance on several hierarchical levels: more direct loops involving insular cortex analysis of interoceptive signals, and more indirect loops, involving PFC activities related to higher order cognition and motivation. The present paper provides an excellent starting point to investigate such possibilities.

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Kai Lutz
Department of Neurology
University Hospital Zürich

BEHAVIOR AND EXERCISE TOLERANCE IN EXTREME ENVIRONMENTS

TO THE EDITOR: Robertson and Marino (4) present an interesting neural architecture linking the prefrontal cortex and its role in executive function and motivation, its integration of external and internal afferents, and ultimately the control of motor regions and exercise behavior. This parallels work on the neurological origins underlying human behavioral thermoregulation. Both streams can inform investigations into the determinants of exercise capacity in extreme environments. Dopamine reuptake inhibitors increases exercise tolerance only in hot but not in temperate conditions, primarily from elevated brain dopamine levels raising voluntary core temperatures in the heat but not in temperate environments (5). Higher core temperatures are also found at voluntary termination during uncompensable heat stress in highly fit compared with moderately fit individuals regardless of hydration or heat acclimation status, despite no differences in the rate of heat storage (1). In contrast, physiological capacity does not become degraded to a greater extent in untrained populations. Although low aerobic fitness and activity level are associated with a generally decreased tolerance to passive hyperthermia, maximum force production and voluntary activation were impaired to an equal level regardless of training status in those able to attain 39.0°C core temperature (2). Paulus et al. (3) provide insight into brain

activation during an aversive stimulus from increased breathing load, reporting that experienced adventure racers performed better on cognitive tasks and also had attenuated insular cortex activation compared with untrained controls. Future research should determine if manipulating the perceptual interpretation of homeostatic signals and motivation can influence exercise tolerance and cognition during environmental stress.

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Stephen S. Cheung
Department of Kinesiology
Brock University, Canada

EXERCISE TERMINATION IS A COGNITIVELY CONTROLLED DECISION

TO THE EDITOR: The possibility for the prefrontal cortex (PFC) to be involved in exercise tolerance and termination nicely postulated by Robertson and Marino (5) is timely. However, in the absence of compelling data, this hypothesis is currently based upon insufficient evidence from exercise studies. There remains uncertainty about how PFC accommodates to physical exertion by modulating cognitive control. Self-regulatory fatigue could occur due to either lack of increased PFC activity, heightened activity in subcortical structures, or both. Overcoming fatigue development likely requires the PFC to inhibit the anterior cingulate and insula activated in proportion to the degree of subjective fatigue (3). As suggested by the authors (5) the problem can be reduced to a trade-off between the costs and benefits of effort exertion, which has been extensively investigated in the decision-making literature (1). Fatigue as an increased accumulation signal (i.e., influence of afferent fibers' feedback on central motor output as a sensed perceived exertion) during exercise leads to high cost estimates compared with expected benefits and task difficulty. In this approach the decision whether to continue the exercise task is refined dynamically depending on cost and benefits until reaching upper bounds of the accumulation process that underpins effort allocation (4). At a brain level, current evidence supports a network of brain regions that are functionally connected with both the anterior cingulate and orbitofrontal cortices during an ongoing cost-benefit analysis (2). When cost exceeds benefits, PFC regions involved in an inhibitory process underlying cognitive control are disengaged, which quickly leads to the cessation of exercise.

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Stéphane Perrey
University of Montpellier

Rémi Radel
Jeanick Brisswalter
Université de Nice Sophia Antipolis

COMMENTARY ON “A ROLE FOR THE PREFRONTAL CORTEX IN EXERCISE TOLERANCE AND TERMINATION”

TO THE EDITOR: I agree with the gist of the authors' Viewpoint (5) but not that the PFC can “sustain exercise despite severe deficiencies in motor control.” PFC function is well described in the cognitive/emotional/behavioral literature (2), and we assigned a similar role to the PFC in our review, although focusing on feed-forward drive (3). Thus, although PFC pathways can be expected to “act in an integrated manner to choose a response” during cognitive tasks and more moderate exercise, it probably does not do so during peak sporting performance. For instance, crucial as PFC “task response selection” is for Stroop Task performance, it would be a liability when hitting a match winning serve at Wimbledon. Instead the PFC would be focused on one singular goal (1)—an awareness of optimal ball placement—which would be disrupted by any attempt at “task response selection” during the execution of movement. Ditto for endurance exercise. Clayton's famous “I'm going to smash you into the ground” statement at the start of the 1969 Antwerp Marathon helped him shatter the world record. Clayton's success was largely due to his extraordinary ability to remain goal directed, allowing him to “extend exercise tolerance in the face of afferent feedback,” presumably via midbrain dopamine release and stress induced analgesia (3). Instead of “exerting top down effects,” a more apt description would be *reduced PFC processing* at high exercise intensities (4). The authors allude to same in their “reinforced neural pathways” (hardwired rather than “choosing a response”) to explain increased exercise tolerance in athletes.

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H. G. Laurie Rauch
Division of Exercise Science and Sports Medicine
Department of Human Biology
University of Cape Town

EXTEROCEPTION IS AN IMPORTANT FACTOR IN EXERCISE TOLERANCE

TO THE EDITOR: We congratulate Robertson and Marino (3) for their prefrontal cortex model of exercise tolerance and termination, which is a welcome contribution to our broader understanding of the limits of human performance. The authors have constructed their model by bringing together neurocognitive evidence derived from their own and others' observations. Given the present methodological limitations of imaging whole brain activity during vigorous physical activity, particularly regarding functional interactions between various brain structures, their approach to model construction is warranted.

Nevertheless, we note that although their model is clear about interoceptive mechanisms of exercise tolerance, other than by the inclusion of the orbitofrontal cortex, exteroceptive pathways are understated. In this respect, we would like to stress the importance of incorporating human-environment interactions in models of human performance, especially given their relevance to real-life applications seen in sport, rehabilitation, or physical occupations. Recent work has found that situational and informational variations to the external environment influence exercise tolerance as measured through the perception of exertion (2, 5). In addition, the importance of natural, interactive behavior is demonstrated in a recent review on perception and action in pacing (4) and situational factors such as the presence of opponents appear to affect decision-based pacing and tactics in sports competition (1).

In summary, we think this is a very exciting paper explaining the interoceptive mechanisms of exercise tolerance and one that we hope will stimulate positive discussion and new research in this area. We would like to add that future research should also focus on including human-environment interactions.

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Dominic Micklewright
C. Beedie
F. Hettinga
Sport, Performance & Fatigue Research Unit
School of Biological Sciences
University of Essex