What is Bad for the Heart is Bad for the Brain?

Dear Editor,

We have read with great interest the most recent issue of *Heart and Mind* addressing the relationship between exercise, heart, and cognition.[1,2] Dr. Jenna Taylor excellently summarized the intertwine between cardiovascular and brain health and how regular moderate and vigorous exercises positively impinge the cardiovascular-cognition connection.[1] The growing core of evidence supporting exercise as a promising tool to blunt cardiovascular risk factors, but also cognitive impairment, is exhaustively reviewed. However, while the benefits of regular moderate exercise are undoubted and convincingly supported by preclinical and clinical data, the consequences of long-term strenuous exercise are still uncertain. In fact, emerging evidence shows that the relationship between training load and cardiovascular and brain health is not linear (*the more exercise, the more benefit*), but rather U-shaped. In recent years, long-term strenuous exercise has shown to increase the risk of cardiovascular disease, particularly cardiac arrhythmias , in certain populations. Atrial fibrillation risk is heightened in male endurance athletes, exercise is central to the pathophysiology of the arrhythmogenic cardiomyopathy in some patients, and the (formerly considered) physiological athlete's bradycardia could evolve into clinically relevant sinus node dysfunction.[3] Moreover, recent data also suggest aortic tunica media damage in heavily trained animals[4] and more intense coronary atherosclerosis in male master marathon runners.[5] Could these negative effects extend to the brain?

The robustness of clinical trials assessing long-term exposures is jeopardized by confounding factors and the lack of control groups. Although caution is needed when translating the conclusions of animal work to humans, preclinical studies restrict confounding factors and enable a more precise comparison between exercise loads. In an animal model, we have recently shown that high-intensity exercise could not replicate many of the moderate exercise-induced benefits on cerebrovascular and connectivity efficiency enhancement, both underlying improved learning capacity.[6] These results suggest that the maximal benefit of exercise in brain health is obtained at moderate doses while very high loads yield limited effects, thereby supporting the existence of a "*sweet spot*" for exercise intensity and duration on cognition.[7] Clinical studies confirm this notion, including a large epidemiological trial in which former professional athletes (i.e., soccer players) had a higher risk of neurodegenerative disease than the general population.[8]

The pathophysiology behind many of the deleterious effects of strenuous exercise is only partially understood. The reduced cerebral blood flow occurring in an animal model after long-term strenuous training[6] would link the unexpected cognitive effects to recently demonstrated exercise-induced vascular damage.[4,5] Each strenuous bout of exercise superimposes a hemodynamic and biochemical stress on the cardiovascular system, which may result in transient right ventricular dysfunction.[9] Similarly, transient oxidative stress and altered mitochondrial energetics in the brain could mediate the observed reversal of benefits at high-intensity exercise.[6] Experiments conducted in human just after strenuous exercise support transient cognitive decline and impaired brain flow regulation. Finally, factors other than exercise itself may explain these deleterious effects. Repetitive concussion could not only contribute to deteriorate brain health in heavy contact sports, but also in sports such as football, as recently suggested.[10]

Altogether, animal models and human trials suggest that the cognitive benefits promoted by regular exercise may be highly dependent on exercise intensity and duration; strenuous and long-term forms of exercise may paradoxically show deleterious. These data need to be confirmed, though, in large and well-designed studies.

O'Keefe *et al*. appropriately state in their editorial[2] that "what is good for the heart is good for the brain." Should we also claim that "what is bad for the heart is bad for the brain?"

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Conflicts of interest

Dr. Eduard Guasch is an Editorial Board member of Heart and Mind. The article was subject to the journal's standard procedures, with peer review handled independently of Dr. Eduard Guasch and the research group. There are no conflicts of interest.

Gemma Sangüesa[1,2], Montserrat Batlle[3,4], Eduard Guasch[3,4,5]

[1]Department of Basic Sciences, Faculty of Health Sciences at Manresa, University of Vic - Central University of Catalonia (UVic-UCC), Manresa, Catalonia, Spain, [2]Tissue Repair and Regeneration Laboratory (TR2Lab), Institute for Research and Innovation in Life and Health Sciences in Central Catalonia (IRIS-CC), Vic, Catalonia, Spain, [3]Arrhythmia and Physical Activity Group, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Catalonia, Spain, [4]CIBERCV, Madrid, Spain, [5]Cardiovascular Institute, Clinic Barcelona, University of Barcelona, Barcelona, Catalonia, Spain

Address for correspondence: Dr. Eduard Guasch, Cardiovascular Institute, Clinic Barcelona, Villarroel, 170, Barcelona, Catalonia 08036, Catalonia, Spain.
E-mail: eguasch@clinic.cat

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