Exercise induces cerebral VEGF and angiogenesis via the lactate receptor HCAR1.


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Recommendations:

Very Good 04 Jul 2017

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Interesting Hypothesis | New Finding

DOI: 10.3410/f.727641638.793533771

This paper demonstrates a novel mechanism through which intense exercise increases cerebral angiogenesis. They provide compelling data suggesting that the lactate receptor HCAR1 is necessary for exercise-induced increases in angiogenesis in the brain but not skeletal muscle.

Disclosures
None declared

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Very Good 07 Jul 2017

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Interesting Finding | Novel Drug Target

DOI: 10.3410/f.727641638.793533813

Although the beneficial effect of exercise for brain health is well established, the molecular mechanisms involved are as yet incompletely understood. This paper provides insight into a novel mechanism based on lactate production in muscle. Intense bouts of exercise (or subcutaneous lactate injections producing a similar increase in lactate levels) are shown to enhance cerebral angiogenesis via the lactate receptor HCAR1. This receptor is found to be strategically localized in pial cells lining meningeal vessels as well as in pericytes in intracerebral microvessels. The effect, which is completely lost in mice lacking HCAR1, appears to be mediated by an increase of vascular endothelial growth factor A. The results open up new avenues to benefit from the positive influence of exercise on brain health.

Disclosures
None declared

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Abstract:

Physical exercise can improve brain function and delay neurodegeneration; however, the initial signal from muscle to brain is unknown. Here we show that the lactate receptor (HCAR1) is highly enriched in pial fibroblast-like cells that line the vessels supplying blood to the brain, and in pericyte-like cells along intracerebral microvessels. Activation of HCAR1 enhances cerebral vascular endothelial growth factor A (VEGFA) and cerebral angiogenesis. High-intensity interval exercise (5 days weekly for 7 weeks), as well as L-lactate subcutaneous injection that leads to an increase in blood lactate levels similar to exercise, increases brain VEGFA protein and capillary density in wild-type mice, but not in knockout mice lacking HCAR1. In contrast, skeletal muscle shows no vascular HCAR1 expression and no HCAR1-dependent change in vasculogenesis induced by exercise or lactate. Thus, we demonstrate that a substance released by exercising skeletal muscle induces supportive effects in brain through an identified receptor.

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