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Letter to editor

Effects of exercise on cognition, hippocampal neurogenesis, and learning: Muscle–brain crosstalk in health and diseases

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Dear Editor-in-Chief

Based on recent studies, it is now clear that there is a muscle–brain endocrine loop that can be partly mediated by myokine signaling. There are also other metabolites as mediators which can affect circulating compounds (Rai & Demontis, 2016) and these include noncoding RNAs (Makarova et al., 2014), hormone-associated responses, as well as, muscular enzymes (Pedersen, 2019). Brain-Derived Neurotrophic Factor (BDNF) is considered to be a key role in helping to mediate the impacts of exercise on the hippocampus (Loprinzi & Frith, 2019). Studies conducted on laboratory rats showed an increase in BDNF mRNA and BDNF protein in the hippocampus of these animals when wheel running exercise was performed for 1 to 8 weeks (Adlard, Perreau, & Cotman, 2005; Farmer et al., 2004; Liu & Nusslock, 2018; Neeper, Góauctemez-Pinilla, Choi, & Cotman, 1995; Oliff, Berchtold, Isackson, & Cotman, 1998; Van Hoomissen, Chambliss, Holmes, & Dishman, 2003). In terms of cognitive functions, i.e. memory and learning, BDNF has also been demonstrated to be effective in the improvement of such functions (Vaynman, Ying, & Gomez-Pinilla, 2004; Vaynman, Ying, & Gómez-Pinilla, 2004).

Research on humans indicates that their brains can release BDNF while cycling (Rasmussen et al., 2009; Seifert et al., 2010), also in another study in healthy people as well as people with schizophrenia who had been training in aerobic exercise for three months, the level of BDNF increased in their hippocampus by 12% and 16%, respectively (Pajonk et al., 2010). As a growth factor for the hippocampus, BDNF plays a significant role in learning and improving cell survival (Wrann et al., 2013). Interestingly enough, research findings show that BDNF can also be expressed in skeletal muscle tissues during exercise in humans; nonetheless, it is not clear whether muscle-derived BDNF can get into the bloodstream from the muscle to create a direct interaction between muscle and brain (Matthews et al., 2009).

Some fascinating studies indicate that irisin and myokines cathepsin-B might cross the (BBB) blood-brain barrier, and consequently, BDNF levels may increase. In recent a study conducted by Moon et al. (Moon et al., 2016) a novel myokine, cathepsin B (CTSB) was identified. Other work also demonstrated that exercise can increase CTSB systemic level, therefore, BDNF expression will be promoted in the hippocampus and lead to the formation of nerve tissue as well. Running on a treadmill for four months increased CTSB plasma levels, as well as CTSB gene expression in humans, mice, and rhesus monkeys. In addition, it was indicated that CTSB could cross BBB in mice. In studies by Moon et al. (2016) on CTSB knockout mice, it was made clear that mice without CTSB refused to do voluntary exercise regarding hippocampal growth and cognitive development. It is not clear whether myokine CTSB can lead to cognitive function development in humans regarding exercise training or not (Moon et al., 2016; Suzuki, 2016).

The PGC-1α-dependent myokine irisin, which is famous for its browning impacts (Boström et al., 2012), can play a role in the intervention of the brain's physical activity (Wrann et al., 2013). An excessive expression of irisin in the primary cortical neurons can cause a higher BDNF expression, while FNDC5 knockdown mediated by RNAi can cause a lower BDNF expression. Furthermore, irisin delivery to the mice's liver by adenoviral vectors will raise the systemic irisin level, consequently resulting in a higher level of BDNF in the hippocampus. Whether doing exercise can increase irisin plasma concentration in humans (Albrecht et al., 2015; Wrann, 2015), and whether irisin is affected by a muscle–brain endocrine loop is a disputable issue.

References

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Adlard, P. A., Perreau, V. M., & Cotman, C. W. (2005). The exercise-induced expression of BDNF within the hippocampus varies across life-span. Neurobiology of aging, 26(4), 511-520. Doi: https://doi.org/10.1016/j.neurobiolaging.2004.05.006

Albrecht, E., Norheim, F., Thiede, B., Holen, T., Ohashi, T., Schering, L., . . . Drevon, C. A. (2015). Irisin–a myth rather than an exercise-inducible myokine. Scientific reports, 5(1), 8889. Doi: https://doi.org/10.1038/srep08889

Boström, P., Wu, J., Jedrychowski, M. P., Korde, A., Ye, L., Lo, J. C., . . . Long, J. Z. (2012). A PGC1-α-dependent myokine that drives brown-fat-like development of white fat and thermogenesis. Nature, 481(7382), 463-468. Doi: https://doi.org/10.1038/nature10777

Farmer, J., Zhao, X., Van Praag, H., Wodtke, K., Gage, F., & Christie, B. (2004). Effects of voluntary exercise on synaptic plasticity and gene expression in the dentate gyrus of adult male Sprague–Dawley rats in vivo. Neuroscience, 124(1), 71-79. Doi: https://doi.org/10.1016/j.neuroscience.2003.09.029

Liu, P. Z., & Nusslock, R. (2018). Exercise-mediated neurogenesis in the hippocampus via BDNF. Frontiers in neuroscience, 52. Doi: https://doi.org/10.3389/fnins.2018.00052

Loprinzi, P. D., & Frith, E. (2019). A brief primer on the mediational role of BDNF in the exercise-memory link. Clinical physiology and functional imaging, 39(1), 9-14. Doi: https://doi.org/10.1111/cpf.12522

Makarova, J. A., Maltseva, D. V., Galatenko, V. V., Abbasi, A., Maximenko, D. G., Grigoriev, A. I., . . . Northoff, H. (2014). Exercise immunology meets MiRNAs. Exercise Immunology Review, 20.

Matthews, V. B., Åström, M.-B., Chan, M., Bruce, C. R., Krabbe, K., Prelovsek, O., . . . Mortensen, O. H. (2009). Brain-derived neurotrophic factor is produced by skeletal muscle cells in response to contraction and enhances fat oxidation via activation of AMP-activated protein kinase. Diabetologia, 52, 1409-1418. Doi: https://doi.org/10.1007/s00125-009-1364-1

Moon, H. Y., Becke, A., Berron, D., Becker, B., Sah, N., Benoni, G., . . . Mattison, J. A. (2016). Running-induced systemic cathepsin B secretion is associated with memory function. Cell metabolism, 24(2), 332-340. Doi: https://doi.org/10.1016/j.cmet.2016.05.025

Neeper, S. A., Góauctemez-Pinilla, F., Choi, J., & Cotman, C. (1995). Exercise and brain neurotrophins. Nature, 373(6510), 109-109. Doi: https://doi.org/10.1038/373109a0

Oliff, H. S., Berchtold, N. C., Isackson, P., & Cotman, C. W. (1998). Exercise-induced regulation of brain-derived neurotrophic factor (BDNF) transcripts in the rat hippocampus. Molecular Brain Research, 61(1-2), 147-153. Doi: https://doi.org/10.1016/s0169-328x(98)00222-8

Pajonk, F.-G., Wobrock, T., Gruber, O., Scherk, H., Berner, D., Kaizl, I., . . . Meyer, T. (2010). Hippocampal plasticity in response to exercise in schizophrenia. Archives of general psychiatry, 67(2), 133-143. Doi: https://doi.org/10.1001/archgenpsychiatry.2009.193

Pedersen, B. K. (2019). Physical activity and muscle–brain crosstalk. Nature Reviews Endocrinology, 15(7), 383-392. Doi: https://doi.org/10.1038/s41574-019-0174-x

Rai, M., & Demontis, F. (2016). Systemic nutrient and stress signaling via myokines and myometabolites. Annual review of physiology, 78, 85-107. Doi: https://doi.org/10.1146/annurev-physiol-021115-105305

Rasmussen, P., Brassard, P., Adser, H., Pedersen, M. V., Leick, L., Hart, E., . . . Pilegaard, H. (2009). Evidence for a release of brain-derived neurotrophic factor from the brain during exercise. Experimental physiology, 94(10), 1062-1069. Doi: https://doi.org/10.1113/expphysiol.2009.048512

Seifert, T., Brassard, P., Wissenberg, M., Rasmussen, P., Nordby, P., Stallknecht, B., . . . Nielsen, H. B. (2010). Endurance training enhances BDNF release from the human brain. American Journal of Physiology-Regulatory, Integrative and Comparative Physiology. Doi: https://doi.org/https://doi.org/10.1152/ajpregu.00525.2009

Suzuki, W. A. (2016). How body affects brain. Cell metabolism, 24(2), 192-193. Doi: https://doi.org/10.1016/j.cmet.2016.07.022

Van Hoomissen, J. D., Chambliss, H. O., Holmes, P. V., & Dishman, R. K. (2003). Effects of chronic exercise and imipramine on mRNA for BDNF after olfactory bulbectomy in rat. Brain research, 974(1-2), 228-235. Doi: https://doi.org/10.1016/s0006-8993(03)02584-8

Vaynman, S., Ying, Z., & Gomez-Pinilla, F. (2004). Hippocampal BDNF mediates the efficacy of exercise on synaptic plasticity and cognition. European Journal of neuroscience, 20(10), 2580-2590. Doi: https://doi.org/https://doi.org/10.1111/j.1460-9568.2004.03720.x

Vaynman, S., Ying, Z., & Gómez-Pinilla, F. (2004). Exercise induces BDNF and synapsin I to specific hippocampal subfields. Journal of neuroscience research, 76(3), 356-362. Doi: https://doi.org/10.1002/jnr.20077

Wrann, C. D. (2015). FNDC5/Irisin–their role in the nervous system and as a mediator for beneficial effects of exercise on the brain. Brain plasticity, 1(1), 55-61. Doi: https://doi.org/10.3233/BPL-150019

Wrann, C. D., White, J. P., Salogiannnis, J., Laznik-Bogoslavski, D., Wu, J., Ma, D., . . . Spiegelman, B. M. (2013). Exercise induces hippocampal BDNF through a PGC-1α/FNDC5 pathway. Cell metabolism, 18(5), 649-659. Doi: https://doi.org/10.1016/j.cmet.2013.09.008