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Letter to the Editor

Aerobic exercise and hippocampal change in youth at risk of serious mental illness

It is well accepted that exercise improves both physical and mental health. We previously published a pilot exercise study in youth at risk for serious mental illness (SMI) that would include for example schizophrenia, bipolar disorder, recurrent major depression. In this study, we demonstrated feasibility and observed significant improvements in aerobic fitness and body composition (Corbett et al., 2020). Previous research has found that higher levels of physical activity are also associated with larger hippocampal volumes in first episode schizophrenia patients (McEwen et al., 2015), however, this study was cross-sectional and based on self-reported exercise levels. Therefore, our aim in the present study was to extend these findings by examining longitudinal changes in hippocampal volume following a moderate to high intensity aerobic exercise intervention in a sample of youth at risk for SMI.

The sample include 26 young individuals who met criteria for being at risk for a serious mental illness (SMI) based on a clinical staging model (Hickie et al., 2013). The participants did not have any diagnoses of mental illness but were either experiencing low mood, or anxiety symptoms and were distressed (stage 1a) or were experiencing subthreshold symptoms for a SMI (stage 1b). This study was approved by the University of Calgary Conjoint Health Ethics Board and all participants signed a consent form.

Assessment of fitness before and after the fitness intervention involved an estimate of VO2max which was based on the maximum meters an individual could run and/or walk on a treadmill in 12 min. The exercise protocol was an aerobic activity executed at 12–14 RPE (Rate of Perceived Exertion) as a warm up for 10 min, followed by 45 min $\geq$15 RPE as the target intervention intensity, and cooling down with an additional 5 min at 10–12 RPE. The intervention was scheduled to be three times per week for 16 weeks (a total of 48 h). Aerobic activities included: skipping, calisthenics, running on a treadmill and on stairs, rowing on an ergometer, cycling on a stationary bike, and using an elliptical machine.

The MRI data was preprocessed using the ENIGMA protocol guidelines (http://enigma.ini.usc.edu), and the hippocampal segmentation was performed according to the EADC (European Alzheimer's Disease Consortium)-ADNI (Alzheimer's Disease Neuroimaging Initiative) Harmonized Protocol (HarP) for manual segmentation.

Complete details of the inclusion and exclusion criteria, including the staging model, sample demographics, the exercise assessment and intervention protocol and the preprocessing and segmentation fo the MRI data is available in the supplementary material.

Between baseline and post-intervention there was no volume change in the left hippocampus but there was a statistically significant increase in the right hippocampus ($t = 4.1$, $p<0.001$). We then explored possible changes in the anterior and posterior segments of the hippocampi. In the left hippocampus, neither the anterior nor the posterior portion showed a significant change in volume. The opposite pattern emerged in the right hippocampus whereby both anterior and posterior segments displayed significant increases in volume ($t = 3.7$, $p = 0.001$; $t = 3.3$, $p<0.01$, respectively). The mean intercranial volumes did not change significantly between baseline and post-intervention.

Interestingly, when we examined hippocampal volume changes with the improvement in aerobic fitness, significant correlations were observed between improvement in aerobic fitness and increased right total hippocampal volume ($r = 0.50$, $p<0.01$) and increased right anterior hippocampal volume ($r = 0.46$, $p<0.05$). Trend level significance was found in the relationship of change in aerobic fitness and right posterior hippocampal volume ($r = 0.39$, $p = 0.05$). All correlations between change in aerobic fitness and changes in left hippocampal volumes (total or segments) were non-significant. More detailed tables and figures of these results are in the Supplementary Material.

The results of this study suggest that physical exercise may help to increase hippocampal volumes in those at risk of SMI. However, these effects were only found in the right hippocampus. This increase in rightward hippocampal asymmetry is found in healthy adults, and increased asymmetry in the anterior portion of the hippocampus has been associated with verbal learning and verbal fluency (Woolard and Heckers, 2012), suggesting that exercise interventions may normalize volumes, and could have a downstream effect on cognitive function. Furthermore, change in aerobic fitness was positively correlated with changes in right hippocampal volume, both as a whole and when examining the anterior section. As reductions in hippocampal volume have been associated with early life adversity (Dahmen et al., 2018), aerobic exercise may play a role in ameliorating brain changes that have been linked to the development of mental illness.

Declaration of Competing Interest

The authors report no conflict of interest.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.pscychresns.2020.111199.

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