

Exercise Reduces DNA Damage, Inflammation and Apoptotic Markers in the Brain of High Fat Fed Animals

Paul J. Wisniewski, Laurie Joseph, Gabriella Composto, Sara C. Campbell.
Rutgers University, Piscataway, NJ

Obesity has become a worldwide pandemic. It is associated with many co-morbidities including decreases in neurogenesis and increased risk of Alzheimer's due to dysregulation of leptin, specifically in the hippocampus. Many prevention and intervention strategies have been developed, however exercise appears to be one of the more efficacious due to its many impacts on brain function. **PURPOSE:** Therefore, our study aimed to determine to what extent brain function was impacted by animals fed a high fat diet (HFD) that had free access to an exercise wheel. **METHODS:** Thirty-six mice were divided into four groups (n=9/group) as follows: 1) lean sedentary, 2) lean exercise, 3) HFD sedentary and 4) HFD exercise. During the 12-week study animals were monitored 3 times per week to measure food intake, body weights and exercise patterns. At the end of the 12 weeks animals were euthanized and brains were excised and immediately placed in a 3% paraformaldehyde, 2% sucrose solution for fixation so that immunohistochemistry could be performed. Our main outcome was to examine PCNA, a marker of DNA synthesis, and secondary measures related to inflammation, oxidative stress and apoptosis, which are known to increase with HFD and decrease with exercise. **RESULTS:** Pathology reports on the tissue indicated a significant increase in expression of PCNA in high fat animals, indicating DNA damage. In addition, expression of the apoptotic protein cleaved caspase-3 was also significantly elevated in HFD sedentary animals which was ameliorated by exercise. Finally, markers of inflammation (COX-2) and oxidative damage (iNOS) were damped by exercise even in the presence of a HFD. **CONCLUSION:** This indicates exercise may protect the brain from DNA damage and oxidative stress even when animals are consuming a HFD. Elucidation of mechanisms for this should be examined to continue to our understanding of the ways exercise promotes brain health.