

EXERBRAIN

Crosstalk between exercise and brain lipid metabolism in the protection against Alzheimer's Disease

Alzheimer's disease (AD) poses a huge emotional and financial burden on our aging population. While no effective disease-modifying drugs currently exist, physical exercise has been shown to protect from AD through unknown mechanisms. In EXERBRAIN we will test the hypothesis that the protective effect of exercise on AD is mediated by normalization of brain (lipid) metabolism in AD and subsequent reduction of lipid-induced AD pathogenesis. EXERBRAIN will for the first time test this hypothesis through an interdisciplinary and translational consortium, combining the unique expertise from three leading research groups from Germany, the Netherlands and Spain. The expertise of these groups includes the role of exercise on metabolism in mice, the role of brain lipid metabolism in AD pathogenesis in human induced pluripotent stem cell (iPSC)-derived brain cells and the relationship between exercise and AD biomarkers in a human cohort at risk for AD respectively.

The EXERBRAIN consortium will generate a highly detailed transcriptional and metabolic map of the effects of exercise on the mouse brain and validate these results in a human cohort at risk for Alzheimer's disease. In addition, EXERBRAIN will mimic brain-metabolic changes in human iPSC-derived neurons, astrocytes, and microglia to uncover the mechanisms that connect the effects of exercise on brain metabolism to key AD pathological processes including enhanced generation of Amyloid-beta, accumulation of hyperphosphorylated Tau and neuroinflammation. Together these data will provide a novel framework detailing the effect of exercise on the brain under normal and AD-conditions, while also connecting metabolic changes to the pathobiology of AD and providing novel brain metabolic biomarkers that can be used to monitor the effects of exercise on the brain in living human subjects.

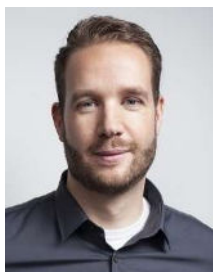
Overall EXERBRAIN will uncover the molecular pathways connecting exercise to brain metabolism and AD pathogenesis, thereby generating a novel understanding of the mechanisms underlying the protective effect of exercise as a non-pharmacological intervention for AD.

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