

## Brain Foundation Final Report

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Title of Project: The effect of high-intensity exercise on Alzheimer's disease-related gene expression

*Summary: (approximately 1,000 words)*

The primary aim of the funded project is to evaluate changes in gene expression (i.e. whether a gene is turned 'on or off') following a six month high-intensity exercise intervention, compared with a moderate-intensity exercise intervention and control group. More specifically, we will be examining gene expression that is related to the development of Alzheimer's disease (AD), and thus hope to determine whether exercise plays a role in altering genes that may play a vital role in the development of Alzheimer's disease.

Blood samples from the Intense Physical Activity and Cognition (IPAC) study will be utilised for this study. These blood samples are collected pre-intervention (before the delivery of any exercise) and post-intervention (after 6 months of exercise intervention or control period). As a team, we have made the decision to conduct the gene expression analyses once all of the blood samples have been collected; this is vital in ensuring comparability of the results between subjects and across time points. Unfortunately a delay in recruitment contributed to a 6 month delay in all IPAC project related activities. Thus, we have not yet run the gene expression analyses on our samples. Nevertheless, the issue we were experiencing with recruitment has been overcome and, currently we have collected 90 baseline blood samples (target n = 105), and 20 post-intervention samples (target n = 105). We anticipate that all of our blood samples will be collected and analysed for Alzheimer's disease related gene expression by mid-2018. Following this analysis we will be able to share with you whether differing levels of exercise intensity are associated with changes in Alzheimer's disease-related gene expression in a group of adults aged 60 – 80. We will also be able to determine whether these changes in gene expression are reflected in improvements in memory and thinking, and other changes to the brain, such as increases in brain volume and/or brain network connectivity.

It is important to note that preliminary analyses of our fitness and exercise data suggests that our participants are reaching their required intensities of exercise (as per the study design) and are also receiving significant dose-dependent increases in fitness and functional capacity following their prescribed interventions. This

preliminary data is evidence that our exercise intervention is reaching the desired physiological outcomes that we had initially aimed for. This is vitally important in this field, as many previous studies have been criticised for being unable to provide evidence that their exercise interventions provided sufficient stimulus to significantly alter physical fitness.

#### *Hypotheses vs Findings*

Our hypotheses are:

1. A six month high-intensity exercise intervention will upregulate AD *protective* gene expression, and downregulate AD *risk* gene expression, compared with a low-intensity exercise intervention and control group.
2. Changes in AD-related gene expression will mediate any improvements observed in cognitive function and increased brain volume and activation, following a six month high-intensity exercise intervention.

As per the above, we have been unable to test our hypotheses until all blood samples are available for analysis (due mid-2018). We look forward to sharing these results with you.

#### *Unanswered questions*

As above.

#### *What these research outcomes mean*

Although a large amount of evidence exists suggesting that individuals that undertake higher levels of exercise are less likely to develop Alzheimer's disease, little is known about why this association exists. To date, nobody has evaluated the impact of exercise on AD-related gene expression; this project aims to fill this gap in current knowledge.