Research Proposal

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Mens Sana in Corpore Sano

INTRODUCTION:

Epidemiological studies have highlighted that lifestyle and metabolic factors can drive the risk of developing neurodegenerative diseases such as Alzheimer's and other dementias (Popa-Wagner et al., 2020; Muddapu et al., 2020). This is because well-known unhealthy lifestyle choices change the levels of blood metabolites that have adverse effects on our physiology (Beuchel et al., 2019). The present research aims to explore how aberrant levels of metabolic factors can damage neurons, which set the scene for the progression to dementia. To do this, I will use advanced microscopy and intracellular imaging techniques to look at the integrity of key intracellular structures, specifically the mitochondria, and how these metabolic factors affect their function. As mitochondrial dysfunction is one of the earliest steps on the pathway to dementia, this will allow me to piece together the pathway of metabolic disturbance to neurodegeneration.

RESEARCH DESIGN AND METHODOLOGY:

This research will involve preparing slides of neuronal cell line, SH-SY5Y and HT-22, that have been treated with metabolites commonly overexpressed in Alzheimer's Disease which are linked to poor diet and lifestyle choices, such as homocysteine, copper, and amyloid beta. Triiodothronine, commonly referred to as *thyroid hormone (T3)*, will also be used as a potential enhancer of metabolic activity to allow me to explore changes in mitochondrial morphology and numbers. The techniques used in this process will include cell staining, fluorescent imaging, and determination of the impact of the metabolites on cellular wellbeing. Additional imaging software packages like Zeiss Imager and Fiji will also be used. To analyse these, I will measure the fluorescent intensity and organelle morphology to develop a fuller picture of how metabolic disturbances affect mitochondrial health.

EXEPECTED RESULTS RESEARCH IMPLICATIONS:

From this research, it is expected that if thyroid is helpful, there will be differences in mitochondrial morphology compared to the controls. Comparatively, if the thyroid hormone does not enhance metabolic activity, there would be similar results to the cells treated with the metabolites. It is expected that the cells treated with these metabolic

stressors will have significantly fewer mitochondria and changes in mitochondrial morphology, compared to the untreated cells.

The findings of this research will contribute towards understanding why a risk factor leads to disease at a cellular level, which will open new pathways in drug discovery and inform future drug design avenues. Crucially, this project also has public health implications as it allows for a more targeted approach to the precise lifestyle modifications that can be made to reduce the probability of developing dementia and improve brain health.

REFERENCES:

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