How do mitochondrial dynamics shape responses to stressful & dietary interventions in high anxiety?

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ABSTRACT

A third of the world population will suffer from an anxiety disorder throughout their lifetime. Highly anxious individuals are prone to the effects of modern, fast-paced lifestyle which is stressful and also influences dietary habits. Accumulating data implicate mitochondria in the regulation of anxiety, eating disorders and stress [1,2]. However, the modulatory role of mitochondrial dynamics, i.e. mitochondrial biogenesis, fusion, fission and mitophagy, on dietary interventions and stress responses in a high anxiety background remains elusive.

In this project, we investigate how lifestyle interventions, including food restriction and stress exposure shape brain mitochondrial dynamics in a mouse model of high anxiety-related behavior (HAB). HAB mice were exposed either to a limited food access (LFA) or to an acute restraint stress (ARS) protocol. Changes in their anxiety- and depression-related behavior were then assessed by a behavioral test battery. Mitochondrial dynamics changes upon LFA or ARS were investigated in relevant brain regions to identify expression differences in key players of the mitochondrial dynamics machinery using biochemical and molecular biology methods.

Our data reveal that female HAB mice exposed to LFA showed increased depression-like behavior compared to control HAB females. Importantly, hippocampal levels of the mitochondrial fusion protein mitofusin 2 (Mfn2) significantly correlated with % weight loss in these mice. Additionally, male HAB mice subjected to ARS had significantly decreased mRNA levels of genes involved in mitochondrial biogenesis, fission and mitophagy and increased mRNA levels of a key fusion regulator compared to control HAB mice.

Taken together, these results point towards an emerging role of mitochondrial dynamics in dietary and stress interventions in highly anxious organisms. Elucidating the underlying mechanisms of brain mitochondrial dynamics will pave the way for identifying candidate biomarkers and novel therapeutic targets of eating and stress-related disorders.

REFERENCES

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