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KetoResi

Ketogenic signaling in resilience promotion

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Stress-related mental disorders are often comorbid with metabolic dysregulation, e.g., hyperglycemia, insulin resistance and low-grade inflammation. Furthermore, epidemiological studies have shown that high glycemic diets can promote the occurrence of depression. Thus, stress-related and metabolic disorders appear to be highly intertwined. Individual responses are commonly observed to stressor impact, coining the term stress resilience for those subjects that stay mentally healthy despite high stressor load. In this translational study involving (i) two rodent stress resilience models and (ii) human cohorts from a longitudinal stress resilience study, we will assess the hypothesis that ketone body signaling is a promising strategy to boost stress resilience. This hypothesis is substantiated by the current knowledge on candidate stress resilience mechanisms and also on data showing that ketogenic signaling is able to positively modulate many of the potential resilience mechanisms. Here, we aim at investigating several of these underlying mechanisms and identifying potential molecular and behavioral predictors of stress resilience. In a multidisciplinary approach, this consortium will implement a broad range of state-of-the-art techniques including behavioral analyses, cell type-specific transcriptomics, chromatin analysis, cell-type viral strategies to perform chemogenetic interventions, metabolic studies, in vivo imaging in rodents (fMRI, calcium imaging, neurotransmitter sensors) and in humans (fMRI).

We explore the link between stress resilience and metabolism. The suggested interventions are easily applicable, self-determining, and affordable, and importantly without ethical dilemmas. Thus, in the current times of high stressor load, this project will decisively contribute to improve the general health and to alleviate stress-related disorders.