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The impact of ketone bodies on microglial sensitivity to inflammation induced by energy starvation

The premise of this project is to further explore the relationship between energy availability and microglial function established by Churchward et al. in which glucose deprivation causes cells to become primed to activation thus resulting in a stronger and longer inflammatory response when exposed to an inflammatory agent (2018). Taking this into consideration with the matter that neural inflammation induced by microglia has been found to contribute to the pathogenesis of a number of neurodegenerative and psychiatric disorders and glucose deprivation of cells with a high energy need can occur naturally in individuals despite adequate caloric intake - determining if this effect can be remedied is of crucial importance. Therefore, this project seeks to examine if supplying glucose deprived cells with an alternative energy source, ketone bodies, will remedy the sensitization caused by energy deprivation.

To study this relationship, immortalized mouse microglial cells were be grown in media with no glucose and then treated with the inflammatory agent Interferon gamma as well as the ketone body β-hydroxybutyrate (BHB) to mimic a switch from a glucose deprived state to a state of ketosis. Following treatment, nitrite levels were measured as an indicator of inflammation and cells were examined under fluorescent microscopy to assess morphological changes indicative of a pro-inflammatory state.

The results revealed a statistically significant decrease in Nitrite produced by BHB treated cells supporting the hypothesis that ketone bodies could possess an anti-inflammatory effect on energy starved cells. These results aid in the understanding of the interplay between metabolism and microglia function as ketone bodies are the only energy source besides glucose able to cross the blood brain barrier thus possessing the potential for therapeutic application in remedying the effect of energy starvation.

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