

1. **Record Nr.** TD18044521
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Titolo Ketogenic diet impacts Blood-Brain Barrier physiology: implications for Alzheimer's disease [Tesi di dottorato]

Lingua di pubblicazione Inglese

Formato Tesi di dottorato

Livello bibliografico Monografia

Note diritti: none
In relazione con info:eu-repo/semantics/altIdentifier/hdl/11573/1110752

Sommario Given the current absence of an effective pharmacologic treatment for Alzheimer's disease (AD), the development of alternative therapeutic approaches (such as the ketogenic diet, KD) might be considered. The KD is a low-carbohydrate, high-fat diet based on the production of ketone bodies (KBs) in the blood. In view of the KD's beneficial effects on the central nervous system and the lack of published data on the blood brain barrier (BBB), we used an in vivo/in vitro approach to investigate the effect of the KD and KBs on the BBB. For the in vivo study, blood from 129Sv mice was assayed for beta-hydroxybutyrate and glucose dosage. Brain capillaries were isolated from mouse cortices, and RT-qPCR assays were used to evaluate the mRNA expression of transporters/receptors involved in the synthesis and transport of KBs, glucose and beta-amyloid peptide. The mRNA assays were also performed in an in vitro BBB model, based on brain-like endothelial cells (BLECs). After a ketotic state had been established and the BLECs' integrity had been confirmed, we evaluated the mRNA expression of KB-, glucose- and amyloid-beta-related genes. Lastly, the transport of fluorescently labelled beta-amyloid peptide across the BBB was studied after treatment with KBs. Our results showed that KBs modulate the physiology of the BBB by regulating the expression of certain beta-

amyloid peptide transporters/receptors and amyloid peptide-synthesizing enzymes. These data suggest that it is possible to modulate key molecular players in beta-amyloid peptide transport and synthesis at the BBB, and thus open up new perspectives for studying KB-related therapeutic approaches.

Localizzazioni e accesso

http://memoria.depositolegale.it/*/http://hdl.handle.net/11573/1110752
