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Modulation of Beta-Amyloid Peptide Transporters on Brain-Blood Barrier by Ketogenic Diet

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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 amyloid-beta (Aβ) 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 Aβ-related genes. Lastly, the transport of fluorescently labelled Aβ-peptide across the BBB was studied after treatment with KBs. Our results showed that KBs regulate the expression of certain Aβ-peptide transporters/receptors and amyloid peptide-synthesizing enzymes. These data suggest that it is possible to modulate key molecular players in Aβ-peptide transport and synthesis at the BBB, and thus open up new perspectives for studying KB-related therapeutic approaches.

Biography:

Rita Businaro, MD, PhD is a Professor of Human Anatomy in Faculty of Pharmacy and Medicine at Sapienza University of Rome, Italy. She is a Director of the II level Master in "Stress, Sport, Nutrition: New Diagnostic and Therapeutics Tools for Wellness, Fitness and Rehabilitation". She is Vice-president of AIF (Italian Fulbright Association) and Member of ISNIM (International Society for NeuroimmunoModulation). She is also Coordinator of Erasmus Plus program. His main research topics is Study of comorbidity of Alzheimer's disease and cerebrovascular disorders: a multidisciplinary approach to identify cellular proteins and mechanisms involved in the accumulation of amyloid aggregates in the central nervous system, Cross-talk Central Nervous System-Immune System and Diet role in delaying Alzheimer's disease progression.