

Potential role of the microbiome-endocannabinoidome connection in the gut-brain axis after traumatic brain injury and its association with Alzheimer's disease.

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Traumatic brain injury (TBI) is the leading cause of death under the age 45 in the Western World and is followed by secondary brain damage leading to long-term consequences, such as increased prevalence of dementia, and Alzheimer's disease (AD). Moreover, TBIs represent a major health issue, especially for football players and soldiers who have frequent experiences of multiple brain injuries. The main challenge in this area is the development of new diagnostic and therapeutic approaches. However, recent evidence suggested that both TBI and AD have an alteration in the brain-gut microbiota axis that may significantly contribute to their pathogenesis and could be the missed link to understand their association. Furthermore, accumulating evidences in literature have showed that the endocannabinoid (eCB) system with the accompanying "endocannabinoidome" (eCBome), a complex system with key functions in the regulation of physiological and pathological conditions, have a key role in numerous physiological and pathological conditions. In particular, eCB system is increasingly emerging as a system of lipid mediators of the health-disease continuum and its strong connection with the gut microbiome has been so far suggested only in the context of inflammatory metabolic and intestinal disorders and has never been investigated in other disorders.

In this context, the aims and the preliminary results of project funded by "US Army Medical Research and Development Command" (USAMRDC) for the Peer Reviewed Alzheimer's Research Program (PRARP) – Funding leve I (Young investigators), will be presented. In particular, the objective of this research is to investigate the effects of a mild TBI on the subsequent development of AD-related neuropathology and cognitive impairments in an APP/PSI mice, the role of inflammation, the potential perturbation of the gut microbiome and how the potential alteration in gut microbiota composition may determine the severity of these disorders by regulating the activity of endocannabinoid and related mediators using a multidisciplinary approach.



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