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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Background:

Traumatic brain injury (TBI) is the leading cause of death under the age 45 in the Western World and could lead to long-term consequences, such as Alzheimer's disease (AD). In this context, both the microbiota gut-brain axis and the endocannabinoid (eCB) system, which is part of a wider signaling system known as the "endocannabinoidome" (eCBome), seem to play a decisive role in the pathogenesis of, and may represent the missing link to understand the association between, TBI and AD.

Methods and Results:

Our data show significant alterations in the behavioral and biochemical phenotype of these mice induced by the trauma, in both WT and APP/PS1. Interestingly, in WT mice, *Enterobacteriaceae* and *Desulfovibrio* decreased significantly after mTBI, whereas in APP mice, *Cyanobacteria* increased in the mTBI group. Additionally, the levels of the β-amyloid (1-42) peptide increased significantly in the cortex of APP mice subjected to mTBI. Targeted lipidomics analysis by LC-MS-IT-TOF and MALDI-MS imaging showed significant alterations of the eCBome and neurotransmitters in the brain and intestine of these mice, as well as in the metabolome of their fecal microbiome.

Conclusions and Significance:

Given their proposed neuroprotective role, both eCBome and gut microbiome mediators whose concentrations were shown here to be modified following trauma, might be partly responsible for the pathological, behavioral and biochemical alterations observed in this condition.

Keywords:

Traumatic brain injury, Alzheimer, endocannabinoidome, gut microbiome

References

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Thematic Area:

- Frontiers in Microbiome Research