

Gut microbe-derived metabolites regulate blood-brain barrier integrity

Lesley Hoyles
Matthew G. Pontifex
Ildefonso Rodriguez-Ramiro
M. Areeb Anis-Alavi
Khadija S. Jelane
Tom Snelling
Egle Solito
Sonia Fonseca
Ana L. Carvalho
Simon R. Carding
Michael Müller
Robert C. Glen
David Vauzour
Simon McArthur

Video Byte

Keywords: Microbiome, gut microbes, gut, blood-brain barrier, BBB, metabolites, cognition, methylamines, trimethylamine N-oxide, TMAO, trimethylamine, TMA, inflammation, inflammatory insult, tight junctions, epithelial cells

Posted Date: May 16th, 2022

DOI: <https://doi.org/10.21203/rs.3.rs-1662542/v1>

License:   This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Our gut microbiome has far-reaching effects on our bodies - including on our brain. Gut microbes primarily communicate with the brain via metabolites that are carried in the bloodstream. However, to influence neuronal cells, these metabolites must first interact with the blood-brain barrier (BBB). While diet influencing the brain has been well documented, the impacts of specific metabolites on the BBB are not. To close this gap, researchers combined cell culture and mouse models to examine two metabolites: trimethylamine N-oxide (TMAO) and its precursor trimethylamine (TMA). In humans, both TMAO and TMA are generated by the microbiota from dietary fish and seafood. At physiologically relevant concentrations, TMAO enhanced the integrity of the BBB and protected it from inflammatory damage. In fact, long-term exposure to TMAO in mice protected cognitive function from inflammatory challenge. In contrast, TMA impaired BBB function and disrupted the tight junctions between endothelial cells. Although more human research is needed, these results are consistent with the BBB being an interface in the gut-brain axis and contribute to our understanding of how individual microbial metabolites interact with the brain.