PREBIOTIC SUPPLEMENTATION INDUCE MICROGLIAL MORPHOLOGICAL CHANGES IN HIGH-FAT DIET MODEL IN AGED MICE

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Consumption of a chronic high-fat diet (HFD) and ageing are both associated with metabolic dysfunction and increased neuroinflammation. It contributes to the loss of gut microbiota diversity and the development of neurodegenerative diseases. Microglia are highly sensitive to metabolic and inflammatory signals, and their morphology is closely linked to its functional state. These molecular signals can derive from gut microbiota and influence microglia activation and disease progression. Gut microbiota-focused interventions have the potential to reduce the chronic inflammation and have a protective effect on microglia.

In this study, we examined how prebiotic supplementation with galactooligosaccharides and fructooligosaccharides (GOS+FOS) modulates microglial morphology in aged mice exposed to long-term HFD. The C57BL/6J mice were assigned to four dietary conditions for 18 months: control diet (CD), CD - GOS+FOS, HFD, and HFD - GOS+FOS. We utilized immunohistochemical staining to quantify three-dimensional branching architecture and two-dimensional shape descriptors.

Compared with CD, microglia in HFD-fed conditions exhibited measurable morphological changes consistent with a metabolically primed microglia phenotype. HFD supplementation with GOS+FOS reduced those HFD-induced structural alterations: average branch length decreased toward CD levels, and projected soma area was significantly smaller than in HFD, indicating partial structural recovery. In the CD - GOS+FOS group, microglial morphology were similar to CD group, indicating that the effects of GOS+FOS are specific to reducing HFD-associated microglial alterations rather than modifying baseline microglial structure.

Collectively, these findings suggest that prebiotic supplementation with GOS+FOS can modulate microglial structural remodeling in the aged brain under metabolic challenge, highlighting a protective role of gut microbiota-targeted interventions in diet-induced neuroinflammatory conditions.

Keywords: microglia, microglia morphology, gut-brain axis, high-fat diet, ageing