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Orally administered probiotics modulate gut microbiota and restore glucose homeostasis in a mouse model of Alzheimer's disease

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Abstract

Cerebral glucose homeostasis deregulation has a role in the pathogenesis and the progression of Alzheimer's disease (AD). Current therapiesdelay the decline in cognitive abilities and memory losswithout definitively curing AD.
Recent studies have focussed on the role of the gut microbiota in disorders associated with the central nervous system, with special interest in the modulation of the gut-brain axis.
Using 3xTg-AD triple transgenic AD mouse model, we have demonstrated that the oral administration of a formulation of lactic acid bacteria and bifidobacteria(namely SLAB51) counteracts cognitive decline, reduces Aβ aggregates and brain damages and partially restores the impaired neuronal proteolysis. Improvement of cognitive function is supported by enriched gut content of anti-inflammatory short chain fatty acids (SCFAs) and increased plasma concentrations of neuroprotective gut peptide hormones that play a role in modulating neuronal functions like learning and memory. In detail, probiotics oral administration influences energy metabolism and glycolysis-gluconeogenesis in AD mice, enhancing glucagon like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) plasma concentrations. Probiotics oral administration improves glucose uptake in 3xTg-AD mice by restoring the brain expression levels of key glucose transporters (GLUT3, GLUT1) and insulin-like growth factor I receptor β (IGF-IRβ), in accordance with the diminished phosphorylation of AMP-activated protein kinase (AMPK) and protein-kinase B (Akt). In parallel, phosphorylated tau aggregates decrease in treated mice. Probiotics counteract the time-dependent increase of glycated haemoglobin and the accumulation of advanced glycation end-products (AGE) in AD mice, consistently with memory improvement. Collectively, our data elucidate the mechanism through which gut microbiota manipulation ameliorates impaired glucose metabolism in AD, finally delaying the disease progression.

Keywords—*Alzheimer's disease, probiotics, glucose metabolism, AGEs*

Biography:

Laura Bonfili has completed her PhD in Ageing and Nutrition in 2014 at the School of Advanced Studies of the University of Camerino and she is currently a research fellow at the School of Biosciences and Veterinary Medicine of the University of Camerino. Her research has been mainly focused on the study of natural and synthetic modulators of proteolytic pathways in pathological conditions such as cancer and neurodegenerations and on the neuroprotective effects of gut microbiota modulation in a mouse model of Alzheimer's disease. She has published more than 40 papers in peer-reviewed journals (ORCID ID: http://orcid.org/0000-0002-9542-4310).

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