Feeding the Aging Brain: Diet, Microbiome, and Cognitive Health

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Age-related cognitive decline represents a growing public health concern as the global population ages. Although its causes are multifactorial, impaired metabolic function in both the brain and periphery plays a central role. Aging is also associated with shifts in the gut microbiota—characterized by reduced diversity and compositional changes—that likely contribute to systemic and cerebral metabolic dysfunction. Dietary strategies such as ketogenic diets (KD) and time-restricted feeding (TRF) offer promising avenues to counteract these effects. KDs, high in fat and low in carbohydrates, provide an alternative energy substrate to glucose and have been shown to enhance mitochondrial function, improve metabolic flexibility, reduce inflammation, and reshape the gut microbiome. TRF similarly improves peripheral metabolic health and has demonstrated benefits for cognitive performance in aged subjects. Both diets illustrate the potential for peripherally-acting interventions to improve brain health through gut–brain axis modulation. Emerging evidence supports the microbiome as a key mediator of these effects, opening the door for more targeted interventions. Probiotic therapies, which introduce beneficial live microbes, may mimic some of the positive outcomes of dietary modulation. In a recent study, we administered Lactobacillus paracasei three times weekly to TgF344-AD rats, a transgenic model of progressive Alzheimer's disease. This intervention ameliorated cognitive deficits in a biconditional association task, highlighting the potential of microbiome-targeted strategies. Together, these findings emphasize the therapeutic promise of diet and microbiome-based interventions to preserve cognitive function during aging and suggest that probiotics may offer a practical, non-invasive approach to mitigating neurodegenerative decline.

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