

Effects of Probiotic Y and Probiotic Z Alone or in Combination on Sleep, Autonomic Nervous System, and Cognitive Function in APP/PS1 Mice

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Abstract

Background: Alzheimer's disease (AD), a common neurodegenerative disorder, is characterized by the accumulation of beta-amyloid (A β) and neurofibrillary tangles. Recent studies indicate that AD patients exhibit gut microbiota dysbiosis, anxiety, depression, sleep disturbances, and autonomic dysfunction before cognitive decline. Therefore, probiotics treatment is being explored to restore gut microbiota, thereby improving cognitive function. However, research on the role of sleep and autonomic function as potential pathways for improvement through probiotics is limited. Previous studies show that Probiotic Y (Y) improves depression and enhances sleep efficiency in humans, while Probiotic Z (Z) improves cognition and anxiety behavior in aged mice. **Hypothesis:** Long term consumption of Y and Z mixture can improve gut microbiota, sleep, and autonomic function, leading to greater cognitive improvements and reduced anxiety/depression-like behaviors in AD transgenic (APP/PS1) mice compared to either Y or Z alone. **Specific aims:** (1) To separately confirm the effects of Y, Z, and their mixture on APP/PS1 mice. (2) To compare the effects of feeding the Y and Z mixture on wild-type and APP/PS1 mice. **Materials and Methods:** After six weeks of probiotics treatment in WT and early-stage APP/PS1 mice, the sleep physiology signals will be recorded to analyze sleep and autonomic function. Behavioral tests will be conducted to assess cognitive and emotional behaviors. Additionally, fecal analysis will be performed to evaluate gut microbiota changes, and brain samples will be analyzed for A β and other cognitive-related biochemical markers. **Results:** First, we found that probiotic treatment can improve the borrowing behavior in APP/PS1 mice. Second, the Y and Z probiotic mixture can better ameliorate the anxiety behavior in marble burying test than Y or Z alone. Furthermore, Y and Z mixture can also better improve the spatial learning and memory ability. **Conclusions:** Probiotic treatment can improve the instinctive behavior, and the probiotic mixture of Y and Z can better ameliorate the anxiety behavior and the cognitive function in APP/PS1 mice. **Significance:** This study will provide a strategy for early prevention and delay the progression of AD for potential patients.

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