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Prophylactic use of probiotics as an adjunctive treatment for ischemic stroke via the gut-spleen-brain axis

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ABSTRACT

A growing body of research has focused on the role of spleen in orchestrating brain injury through the peripheral immune system following stroke, highlighting the brain-spleen axis as a potential target for mitigating neuronal damage during stroke. The gut microbiota plays a pivotal role in the bidirectional communication between the gut and the brain. Several studies have suggested that probiotic supplements hold promise as a strategic approach to maintaining a balanced intestinal microecology, reducing the apoptosis of intestinal epithelial cells, protecting the intestinal mucosal and blood–brain barrier (BBB), enhancing both intestinal and systemic immune functions, and thereby potentially affecting the pathogenesis and progression of ischemic stroke. In this study, we aimed to clarify the neuroprotective effects of supplementation with *Lactobacillus*, specifically *Limosilactobacillus* reuteri GMNL-89 (G89) and Lacticaseibacillus *paracasei* GMNL-133 (G133) on ischemic stroke and investigate how G89 and G133 modulate the communication mechanisms between the gut, brain, and spleen following ischemic stroke. We explored the neuroprotection and the underlying mechanisms of *Lactobacillus* supplementation in C57BL/6 mice subjected to permanent middle cerebral artery occlusion. Our results revealed that oral treatment with G89 or G133 alone, as well as oral administration combining G89 and G133, significantly decreased the infarct volume and improved the neurological function in mice with ischemic stroke. Moreover, G89 treatment alone preserved the tight junction integrity of gut barrier, while G133 alone and the combined treatment of G89 and G133 would significantly decreased the BBB permeability, and thereby significantly attenuated stroke-induced local and systemic inflammatory responses. Both G89 and G133 regulated cytotoxic T cells, and the balance between T helper 1 cells and T helper 2 cells in the spleen following ischemic stroke. Additionally, the combined administration of G89 and G133 improved the gut dysbiosis and significantly increased the concentration of short-chain fatty acids. In conclusion, our findings suggest that G89 and G133 may be used as nutrient supplements, holding promise as a prospective approach to combat ischemic stroke by modulating the gut-spleen-brain axis.

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