GUT MICROBES
2024, VOL. 16, NO. 1, 2316533
https://doi.org/10.1080/19490976.2024.2316533

Taylor & Francis
Taylor & Francis Group

RESEARCH PAPER

OPEN ACCESS Check for updates

Probiotic *Lactobacillus* spp. improves *Drosophila* memory by increasing lactate dehydrogenase levels in the brain mushroom body neurons

Shuk-Man Ho[a*], Wan-Hua Tsai[b*], Chih-Ho Lai[a,c,d,e,f*], Meng-Hsuan Chiang[a], Wang-Po Lee[a], Hui-Yu Wu[a], Pei-Yi Bai[a], Tony Wu[g], and Chia-Lin Wu[a,g,h]

[a]Department of Biochemistry, Department of Microbiology and Immunology, Graduate Institute of Biomedical Sciences, Department of Biomedical Sciences, College of Medicine, Chang Gung University, Taoyuan, Taiwan; [b]Research and Development Department, GenMont Biotech Incorporation, Tainan, Taiwan; [c]Molecular Infectious Disease Research Center, Department of Pediatrics, Linkou Chang Gung Memorial Hospital, Taoyuan, Taiwan; [d]Department of Medical Research, School of Medicine, China Medical University and Hospital, Taichung, Taiwan; [e]Department of Nursing, Asia University, Taichung, Taiwan; [f]Research Center for Emerging Viral Infections, Chang Gung University, Taoyuan, Taiwan; [g]Department of Neurology, New Taipei Municipal TuCheng Hospital, Chang Gung Memorial Hospital, New Taipei City, Taiwan; [h]Brain Research Center, National Tsing Hua University, Hsinchu, Taiwan

ABSTRACT

Probiotics are live microorganisms that offer potential benefits to their hosts and can occasionally influence behavioral responses. However, the detailed mechanisms by which probiotics affect the behavior of their hosts and the underlying biogenic effects remain unclear. Lactic acid bacteria, specifically *Lactobacillus* spp. are known probiotics. *Drosophila melanogaster*, commonly known as the fruit fly, is a well-established model organism for investigating the interaction between the host and gut microbiota in translational research. Herein, we showed that 5-day administration of *Lactobacillus acidophilus* (termed GMNL-185) or *Lacticaseibacillus rhamnosus* (termed GMNL-680) enhances olfactory-associative memory in *Drosophila*. Moreover, a combined diet of GMNL-185 and GMNL-680 demonstrated synergistic effects on memory functions. Live brain imaging revealed a significant increase in calcium responses to the training odor in the mushroom body β and γ lobes of flies that underwent mixed feeding with GMNL-185 and GMNL-680. Quantitative reverse transcription polymerase chain reaction (qRT-PCR) and whole-mount brain immunohistochemistry revealed significant upregulation of lactate dehydrogenase (LDH) expression in the fly brain following the mixed feeding. Notably, the genetic knockdown of *Ldh* in neurons, specifically in mushroom body, ameliorated the beneficial effects of mixed feeding with GMNL-185 and GMNL-680 on memory improvement. Altogether, our results demonstrate that supplementation with *L. acidophilus* and *L. rhamnosus* enhances memory functions in flies by increasing brain LDH levels.

ARTICLE HISTORY
Received 21 September 2023
Revised 21 January 2024
Accepted 5 February 2024

KEYWORDS
Probiotics; *Lactobacillus*; Brain; Olfactory memory; Lactate dehydrogenase; *Drosophila melanogaster*

Introduction

A well-balanced gut microbiota is important for human health, and altering the composition of the gut microbiota could potentially impact the physiological responses of the host, leading to neural and behavioral changes.[1–3] Gut microbiome is influenced by the dietary preferences and innate immune system of the host.[4,5] Gut microbes can produce and utilize various neurotransmitters, including norepinephrine, dopamine, serotonin, and gamma-aminobutyric acid (GABA),[6] which affect the physiological responses of the hosts.[7] Accumulated evidence suggests that the gut microbiome is intricately involved in virtually all aspects of nutrient metabolism within the host; however, the precise interactions between the gut microbiota and host physiology remain poorly understood.[8,9] Probiotics are either single or combined live beneficial microorganisms, such as bacteria or yeast, that naturally inhabit the human body. Probiotic consumption is associated with several benefits, and it has been reported that probiotics could alleviate the symptoms of lactose intolerance, promote intestinal health, and reduce the risk of the development of various diseases.[10–13]

Previous studies investigating the benefits of the gut microbiota on host health predominantly employed mammalian models. Numerous studies

CONTACT Chia-Lin Wu clwu@mail.cgu.edu.tw Department of Biochemistry, Department of Microbiology and Immunology, Graduate Institute of Biomedical Sciences, Department of Biomedical Sciences, College of Medicine, Chang Gung University, Taoyuan, Taiwan
*Equal contribution to this work.
Supplemental data for this article can be accessed online at https://doi.org/10.1080/19490976.2024.2316533
© 2024 The Author(s). Published with license by Taylor & Francis Group, LLC.
This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. The terms on which this article has been published allow the posting of the Accepted Manuscript in a repository by the author(s) or with their consent.