

Lactobacillus gasseri NK109 and Its Supplement Alleviate Cognitive Impairment in Mice by Modulating NF- κ B Activation, BDNF Expression, and Gut Microbiota Composition

Presented by: Huang, Ching-Tang, Advised by: Michael Chan, Date: 2023/3/24

論文的概要與重大發現

老化相關的腸道菌叢生態失衡會致使腸道發炎並誘發包括失智症等的身心疾病，益生菌可減輕腸道菌叢生態失衡並被認為可減輕認知功能障礙的症狀。本篇論文研究 *Lactobacillus gasseri* NK109 及含有 NK109 的營養補充品 (NS) 對 *aged mice*, *5XFAD transgenic mice*, and *mildly cognition-impaired adult fecal microbiota (MCF)-transplanted mice* 的認知功能影響。研究發現給予 NK109 或 NS 可減少 *aged mice/ 5XFAD transgenic mice/ MCF-transplanted mice* 認知功能障礙的行為，它們的補充抑制了下視丘及大腸 *TNF-alpha* 及 *p16* 的表現以及 *NF-kB* 活化細胞，但卻增加了 *brain-derived neurotrophic factor (BDNF)*; 同時也部分改變了腸道菌叢的組成及多樣性。

對論文內容的疑問




論文中發現某些腸道菌種和老鼠認知功能的測試表現正相關，而某些腸道菌種則是負相關，但沒有再說明這些正負相關的發現背後的原理。

論文的缺點與評論

益生菌百百種，是不是每種益生菌或是大多數益生菌還是只有少數幾種益生菌能改善老鼠的認知功能？本篇只實驗了一種益生菌，其他的益生菌呢？單一種益生菌的補充會有功效，如果合併使用兩種各自有效的益生菌，甚至是三種以上的益生菌，是不是也有一樣的效果甚至會有 加乘的效果就不得而知了，另外，同樣的發現是不是也適用於人類的治療，又是另一個需要研究的課題了。

Article

Lactobacillus gasseri NK109 and Its Supplement Alleviate Cognitive Impairment in Mice by Modulating NF- κ B Activation, BDNF Expression, and Gut Microbiota Composition

Soo-Won Yun ¹, Hee-Seo Park ², Yoon-Jung Shin ², Xiaoyang Ma ², Myung Joo Han ^{1,*} and Dong-Hyun Kim ^{2,*}¹ Department of Food and Nutrition, Kyung Hee University, Seoul 02447, Republic of Korea² Neurobiota Research Center, College of Pharmacy, Kyung Hee University, Seoul 02447, Republic of Korea

* Correspondence: mjhan@khu.ac.kr (M.J.H.); dhkim@khu.ac.kr (D.-H.K.); Tel.: +82-2-961-0553 (M.J.H.); +82-2-961-0374 (D.-H.K.)

Abstract: Aging-related gut microbiota dysbiosis initiates gut inflammation and microbiota dysbiosis, which induce the occurrence of psychiatric disorders including dementia. The alleviation of gut microbiota dysbiosis by probiotics is suggested to be able to alleviate psychiatric disorders including cognitive impairment (CI). Therefore, to understand how probiotics could alleviate CI, we examined the effects of anti-inflammatory *Lactobacillus gasseri* NK109 and its supplement (NS, mixture of NK109 and soybean embryo ethanol extract) on cognitive function in aged (Ag), 5XFAD transgenic (Tg), or mildly cognition-impaired adult fecal microbiota (MCF)-transplanted mice. Oral administration of NK109 or NS decreased CI-like behaviors in Ag mice. Their treatments suppressed TNF- α and p16 expression and NF- κ B-activated cell populations in the hippocampus and colon, while BDNF expression was induced. Moreover, they partially shifted the β -diversity of gut microbiota in Ag mice to those of young mice: they decreased Bifidobacteriaceae, Lactobacillaceae, and Helicobacteriaceae populations and increased Rikenellaceae and Prevotellaceae populations. Oral administration of NK109 or NS also reduced CI-like behaviors in Tg mice. Their treatments induced BDNF expression in the hippocampus, decreased hippocampal TNF- α and A β expression and hippocampal and colonic NF- κ B-activated cell populations. NK109 and NS partially shifted the β -diversity of gut microbiota in Tg mice: they decreased Muribaculaceae and Rhodospiraceae populations and increased Helicobacteriaceae population. Oral administration of NK109 or NS decreased MCF transplantation-induced CI-like behaviors in mice. NK109 and NS increased hippocampal BDNF expression, while hippocampal and colonic TNF- α expression and NF- κ B-activated cell populations decreased. These findings suggest that dementia can fluctuate the gut microbiota composition and NK109 and its supplement NS can alleviate CI with systemic inflammation by inducing BDNF expression and suppressing NF- κ B activation and gut microbiota dysbiosis.

Keywords: *Lactobacillus gasseri*; aging; dementia; fecal microbiota transplantation; gut microbiota dysbiosis; gut inflammation



check for updates

Citation: Yun, S.-W.; Park, H.-S.; Shin, Y.-J.; Ma, X.; Han, M.J.; Kim, D.-H. *Lactobacillus gasseri* NK109 and Its Supplement Alleviate Cognitive Impairment in Mice by Modulating NF- κ B Activation, BDNF Expression, and Gut Microbiota Composition. *Nutrients* **2023**, *15*, 790. <https://doi.org/10.3390/nu15030790>

Academic Editor: Elvira Verduci

Received: 23 December 2022

Revised: 24 January 2023

Accepted: 29 January 2023

Published: 3 February 2023



Copyright: © 2023 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

1. Introduction

Aging is a progressive, degenerative process tightly associated with chronic inflammation, which can develop complex diseases such as dementia, sarcopenia, gut inflammation, and gut microbiota dysbiosis [1–3]. Moreover, patients with a psychiatric disorder have co-morbid inflammatory bowel disease and gut microbiota dysbiosis [4,5].

A variety of stressors including pathogen infections, antibiotics, and ageing cause the loss of beneficial gut microbiota and overexpression of gut bacterial endotoxins, resulting in gut microbiota dysbiosis, which can cause gut inflammation [6–9]. Gut microbiota-mediated gut inflammation is closely connected with the occurrence of dementia through the down-regulation of NF- κ B activation-involved brain-derived neurotrophic factor (BDNF) expression [8,10,11]. Thus, psychiatric disorders can cause gut inflammation and gut