



Mini Review

The Relationship between Perioperative Gut Microbiome and POCD

Tianyao Zhang^{1,2} and Peng Liang^{1*}

¹Department of Anesthesiology, Laboratory of Anesthesia and Critical Care Medicine, Translational Neuroscience Center, West China Hospital of Sichuan University, Chengdu, Sichuan, China

²Department of Anesthesiology, The First Affiliated Hospital of Chengdu Medical College, Chengdu, Sichuan, China

Abstract

Intestinal microbiome could have an impact on the function of cognition. It might alter the neuroinflammation in the central nervous system via the gut-brain axis. Perioperative antibiotics application is a major factor of gut dysbiosis, which might be effective to postoperative cognitive dysfunction. However, because of the antiinflammation of antibiotic, it could have a double-side effect on cognition. Therefore, this review basically focused to explore the underlying relationship between gut microbiome and postoperative cognition deficits.

Keywords: Microbiome; POCD; Perioperative dysbiosis; Neuroinflammation

Microbiome-gut-brain axis is an extremely crucial bidirectional signaling communication between the intestinal flora and the central nervous system. The two-way interaction may play an important role for our physical and mental health, which mainly based on the vagus nerve, and circulatory system [1,2], in which signaling molecules could transmit through the blood and across the brain blood barrier. Vast majority of researches, based on several animal models with antibiotic administration [3], feces transplantation [3,4], germ-free animal [5], probiotic use [6] and synthetic microbiome colonization [7], showed that microbiota disruption may result in intestinal inflammation so that lead to neuroinflammation through the gut-brain interaction, even progressing to neurodegenerative diseases. It was observed that antibiotics-induced gut dysbiosis decrease neurogenesis of

*Corresponding author: Peng Liang, Department of Anesthesiology, Laboratory of Anesthesia and Critical Care Medicine, Translational Neuroscience Center, West China Hospital of Sichuan University, Chengdu, Sichuan, China, Tel: 8618980602201; Email: liangpeng_world@foxmail.com

Citation: Zhang T, Liang P (2019) The Relationship between Perioperative Gut Microbiome and POCD. J Alzheimers Neurodegener Dis 5: 025.

Received: July 22, 2019; **Accepted:** July 31, 2019; **Published:** August 07, 2019

Copyright: © 2019 Zhang T and Liang P, This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

hippocampus with the same declination of cognitive function [7]. Further, intestinal microflora had also been proven some contributions to perioperative cognition by Jiang et al, which applied compound antibiotics to eliminate the gut colonization, and found that mice showed an improved cognition without gut microbiota after anesthesia/surgery [8,9]. Timothy et al. made a transplantation of gut microorganism from PD patients to mice, and found an enhanced motor dysfunction in mice. Therefore, the relationship between gut microbiome and cognition was increasingly prominent. These results were recently confirmed and extended by [10], who transplanted fecal microbiome from SAMP8 or SAMR1 mice into germ-free mice. In this separate study, obtaining the feces, GF mice had significantly lower cognitive function compared with non-transplantation. Received bacteria of SAMR1 mice, GF mice showed higher advancements in cognition than those from SAMP1 mice [10].

In contemporary researches, the mechanism of POCD mainly focus on neuroinflammation [11,12], Abeta [13] and cholinergic neuron [14], etc. The relationship between neuroinflammation and POCD has been proven and extended in a great number of studies. Zuo et al illustrated that NLRP3/caspase-1 pathway may be involved in isoflurane-induced impaired cognition, which was related to the effect of improved hippocampal neuroinflammation in aged mice [15]. Additionally, the INTUIT study conducted by Miles Berger et al. revealed an increasing neuroinflammation underlying POCD, which based on an investigation including 200 patients older than 60 years of age [16]. Therefore, neuroinflammation might contribute to big proportions of pathogeny of POCD.

Obviously, there was an important connection among dysbiosis and neuroinflammation and cognition. In a study of our team, 6-8-week-old CD-1 mice were administrated cefazolin or saline after laparotomy once per day for 5 days. One week later, gut microorganism disrupted and gut inflammation enhanced. Nevertheless, the concentrations of IL-1 β in cortex in mice with surgery and cefazolin were lower than that with only surgery, and at the same time, IL-1 β in mice with cefazolin alone, also showed a higher level than the former one, which means that cefazolin could lead to gut inflammation and inhibit the neuroinflammation from anesthesia/ surgery. As a result, cefazolin advanced memory and learning in mice after laparotomy, as well as might impair these abilities in mice without surgery [17]. A newly research from Jiang et al. demonstrated the same trend. In his research, compound antibiotics treatment had been used for 4 weeks before surgery. From the perspective of Jiang, the elimination of microbiota by compound antibiotics could improve reference memory in Morris water maze, so that intestinal dysbacteriosis mediated anesthesia/surgery-induced deficits [18]. However, there was a controversy in these two studies. Liang et al. described a declination of memory at group cefazolin only, on the opposite, Jiang et al. illuminated an increasing trend in memory at group antibiotics only. Maybe it is because that the former research is the application of only one kind of antibiotics for just 5 days, and the latter one is the administration of compound antibiotics for 4-week period. Time of utilization and quantity of antibiotics may contribute to the main reason for this difference.

Additionally, Jiang et al. found that there were two types of bacteria (Lachnospiraceae and Ruminococcaceae) displaying the highest likelihood of contributing to learning and memory impairments after anesthesia/surgery [18]. Another research from Zhan, et al. (2019) [10], the effect of anesthesia/surgery-induced cognition dysfunction was elucidated. A total of 24 types of gut microbiota have been shown to be altered in the POCD phenotype. In the fecal samples of POCD mice, Firmicutes phylum and Tenericutes phylum was significantly decreased while the abundance of *E. coli* and Chlamydiae phylum showed an increasing tendency [19]. A research on the population of dementia [20], Saji et al. demonstrated a strong relativity between a lower prevalence of Bacteroides and demented patients. These associations might be stronger than those for traditional dementia biomarkers. Further study could focus on finding out the specific types of microbiome which are the most relative to anesthesia/surgery-induced deficits.

For the application of perioperative antibiotics, there are several benefits and harm. Although antibiotics could improve cognitive impairments after anesthesia/surgery, it disturbed the regular colonization in gut. In Liang's experiment, he indicated that there was still dysbacteriosis in mice with surgery and cefazolin, when stopping the administration of cefazolin for 2 weeks, while the gut dysbiosis had been rebalanced in mice with cefazolin alone. That means surgery could prolong the recovery of gut dysbiosis, which is a very interesting phenomenon [17]. Further study could be conducted for the relative behavior in animal model on this outcome.

Furthermore, the result of Jiang et al. also indicated an improvement of reference memory by oral gavage VSL#3, a strains of compound probiotics, in mice after anesthesia/surgery. It was indicated that VSL#3 could alleviate the negative effects on reference memory of anesthesia/surgery [18]. Meanwhile, it was observed that 3-week application of galacto-oligosaccharide (B-GOS) could alleviate neuroinflammatory and cognition deficits in rat after abdominal surgery. In their study, Yang et al. found that B-GOS downregulated the expression of SOCS3 after operation, which would be a gene marker of M2b/c microglia, a negative regulator of IL-6 signaling [21].

Intestinal dysbacteriosis is known to be relative to neuroinflammation and cognition dysfunction. Although the relationship between the gut microbiome and human health has been known for a few years, Liang, et al. [17] now have suggested a novel linking of perioperative gut microbiosis to postoperative cognition dysfunction. Antibiotics is one of the most commonly applied perioperative medicine for preventing from infection, while gut microbiota disorder is inevitable for a long time of antibiotics using. It is a complicated question that antibiotics-induced dysbacteriosis could lead to perioperative cognition alteration. More studies need to be done to confirm this finding and extend how dysbacteriosis lead to cognition deficits. In addition, it is necessary that clinical researches should be designed to confirm this result in human body.

References

- Crumeville-Arias M, Jaglin M, Bruneau A, Vancassel S, Cardona A, et al. (2014) Absence of the gut microbiota enhances anxiety-like behavior and neuroendocrine response to acute stress in rats. *Psychoneuroendocrinology* 42: 207-217.
- Gasperotti M, Passamonti S, Tramer F, Masuero D, Guella G, et al. (2015) Fate of microbial metabolites of dietary polyphenols in rats: is the brain their target destination? *ACS Chem Neurosci* 6: 1341-1352.
- Bercik P, Denou E, Collins J, Jackson W, Lu J, et al. (2011) The intestinal microbiota affect central levels of brain-derived neurotrophic factor and behavior in mice. *Gastroenterology* 141: 599-609.
- Collins SM, Kassam Z, Bercik P (2013) The adoptive transfer of behavioral phenotype via the intestinal microbiota: Experimental evidence and clinical implications. *Curr Opin Microbiol* 16: 240-245.
- Sudo N, Chida Y, Aiba Y, Sonoda J, Oyama N, et al. (2004) Postnatal microbial colonization programs the hypothalamic-pituitary-adrenal system for stress response in mice. *J Physiol* 558: 263-275.
- Bravo JA, Forsythe P, Chew MV, Escaravage E, Savignac HM, et al. (2011) Ingestion of Lactobacillus strain regulates emotional behavior and central GABA receptor expression in a mouse via the vagus nerve. *Proc Natl Acad Sci U S A* 108: 16050-16055.
- Desai MS, Seekatz AM, Koropatkin NM, Kamada N, Hickey CA, et al. (2016) A dietary fiber-deprived gut microbiota degrades the colonic mucus barrier and enhances pathogen susceptibility. *Cell* 167: 1339-1353 e21.
- Mohle L, Mattei D, Heimesaat MM, Bereswill S, Fischer A, et al. (2016) Ly6C(hi) monocytes provide a link between antibiotic-induced changes in gut microbiota and adult hippocampal neurogenesis. *Cell Rep* 15: 1945-1956.
- Sampson TR, Debelius JW, Thron T, Janssen S, Shastri GG, et al. (2016) Gut microbiota regulate motor deficits and neuroinflammation in a model of Parkinson's Disease. *Cell* 167: 1469-1480.
- Zhan G, Yang N, Li S, Huang N, Fang X, et al. (2018) Abnormal gut microbiota composition contributes to cognitive dysfunction in SAMP8 mice. *Aging (Albany NY)* 10:1257-1267.
- Hu J, Feng X, Valdearcos M, Lutrin D, Uchida Y, et al. (2018) Interleukin-6 is both necessary and sufficient to produce perioperative neurocognitive disorder in mice. *Br J Anaesth* 120:537-545.
- Li N, Zhang X, Dong H, Hu Y, Qian Y (2017) Bidirectional relationship of mast cells-neurovascular unit communication in neuroinflammation and its involvement in POCD. *Behav Brain Res* 322:60-69.
- Zhang B, Tian M, Zheng H, Zhen Y, Yue Y, et al. (2013) Effects of anesthetic isoflurane and desflurane on human cerebrospinal fluid Abeta and tau level. *Anesthesiology* 119:52-60.
- Su D, Zhao Y, Wang B, Xu H, Li W, et al. (2016) Isoflurane-induced spatial memory impairment in mice is prevented by the acetylcholinesterase inhibitor donepezil. *PLoS one* 6:e27632.
- Wang Z, Meng S, Cao L, Chen Y, Zuo Z, et al. (2018) Critical role of NL-RP3-caspase-1 pathway in age-dependent isoflurane-induced microglial inflammatory response and cognitive impairment. *Journal of Neuroinflammation* 15:109.
- Berger M, Oyeyemi D, Olurinde MO, Whitson HE, Weinhold KJ, et al. (2019) The INTUIT study: Investigating neuroinflammation underlying postoperative cognitive dysfunction. *J Am Geriatr Soc* 67:794-798.
- Liang P, Shan W, Zuo Z (2018) Perioperative use of cefazolin ameliorates postoperative cognitive dysfunction but induces gut inflammation in mice. *Journal of Neuroinflammation* 15:235.
- Jiang XL, Gu XY, Zhou XX, Chen XM, Zhang X, et al. (2019) Intestinal dysbacteriosis mediates the reference memory deficit induced by anesthesia/surgery in aged mice. *Brain Behav Immun* 80: 605-615.
- Zhan G, Hua D, Huang N, Wang Y, Li S, et al. (2019) Anesthesia and surgery induce cognitive dysfunction in elderly male mice: The role of gut microbiota. *Aging (Albany NY)* 11:1778-1790.
- Saji N, Niida S, Murotani K, Hishida T, Tsudiki T, et al. (2019) Analysis of the relationship between the gut microbiome and dementia: A cross-sectional study conducted in Japan. *Sci Rep* 9:1008.
- Yang XD, Wang LK, Wu HY, Jiao L (2018) Effects of prebiotic galacto-oligosaccharide on postoperative cognitive dysfunction and neuroinflammation through targeting of the gut-brain axis. *BMC Anesthesiol* 18:177.



- Journal of Anesthesia & Clinical Care
- Journal of Addiction & Addictive Disorders
- Advances in Microbiology Research
- Advances in Industrial Biotechnology
- Journal of Agronomy & Agricultural Science
- Journal of AIDS Clinical Research & STDs
- Journal of Alcoholism, Drug Abuse & Substance Dependence
- Journal of Allergy Disorders & Therapy
- Journal of Alternative, Complementary & Integrative Medicine
- Journal of Alzheimer's & Neurodegenerative Diseases
- Journal of Angiology & Vascular Surgery
- Journal of Animal Research & Veterinary Science
- Archives of Zoological Studies
- Archives of Urology
- Journal of Atmospheric & Earth-Sciences
- Journal of Aquaculture & Fisheries
- Journal of Biotech Research & Biochemistry
- Journal of Brain & Neuroscience Research
- Journal of Cancer Biology & Treatment
- Journal of Cardiology: Study & Research
- Journal of Cell Biology & Cell Metabolism
- Journal of Clinical Dermatology & Therapy
- Journal of Clinical Immunology & Immunotherapy
- Journal of Clinical Studies & Medical Case Reports
- Journal of Community Medicine & Public Health Care
- Current Trends: Medical & Biological Engineering
- Journal of Cytology & Tissue Biology
- Journal of Dentistry: Oral Health & Cosmesis
- Journal of Diabetes & Metabolic Disorders
- Journal of Dairy Research & Technology
- Journal of Emergency Medicine Trauma & Surgical Care
- Journal of Environmental Science: Current Research
- Journal of Food Science & Nutrition
- Journal of Forensic, Legal & Investigative Sciences
- Journal of Gastroenterology & Hepatology Research
- Journal of Gerontology & Geriatric Medicine
- Journal of Genetics & Genomic Sciences
- Journal of Hematology, Blood Transfusion & Disorders
- Journal of Human Endocrinology
- Journal of Hospice & Palliative Medical Care
- Journal of Internal Medicine & Primary Healthcare
- Journal of Infectious & Non Infectious Diseases
- Journal of Light & Laser: Current Trends
- Journal of Modern Chemical Sciences
- Journal of Medicine: Study & Research
- Journal of Nanotechnology: Nanomedicine & Nanobiotechnology
- Journal of Neonatology & Clinical Pediatrics
- Journal of Nephrology & Renal Therapy
- Journal of Non Invasive Vascular Investigation
- Journal of Nuclear Medicine, Radiology & Radiation Therapy
- Journal of Obesity & Weight Loss
- Journal of Orthopedic Research & Physiotherapy
- Journal of Otolaryngology, Head & Neck Surgery
- Journal of Protein Research & Bioinformatics
- Journal of Pathology Clinical & Medical Research
- Journal of Pharmacology, Pharmaceutics & Pharmacovigilance
- Journal of Physical Medicine, Rehabilitation & Disabilities
- Journal of Plant Science: Current Research
- Journal of Psychiatry, Depression & Anxiety
- Journal of Pulmonary Medicine & Respiratory Research
- Journal of Practical & Professional Nursing
- Journal of Reproductive Medicine, Gynaecology & Obstetrics
- Journal of Stem Cells Research, Development & Therapy
- Journal of Surgery: Current Trends & Innovations
- Journal of Toxicology: Current Research
- Journal of Translational Science and Research
- Trends in Anatomy & Physiology
- Journal of Vaccines Research & Vaccination
- Journal of Virology & Antivirals
- Archives of Surgery and Surgical Education
- Sports Medicine and Injury Care Journal
- International Journal of Case Reports and Therapeutic Studies

Submit Your Manuscript: <http://www.heraldopenaccess.us/Online-Submission.php>