

## Review Article

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## Gut-Brain Axis Modulatory Effects of Mushrooms in Parkinson's Disease

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### ABSTRACT

Parkinson's Disease (PD) is the most common movement disorder. It is a form of neurodegenerative disorders characterized by imbalance, tremor, muscular rigidity, problem in speaking and cognitive impairments. Global PD burden is increasing alarmingly. Levodopa, currently used medication, is out of reach of the PD patients suffering from the developing and under-developed countries. Thus, search for cost-effective, easy to find, nutraceutical-based therapeutic approaches against PD, has reached momentum. In this aspect, therapeutic suitability of mushrooms, the edible macrofungi, has been explored in this article, focusing the "gut-brain axis" proposition of PD pathogenesis.

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### Introduction

Parkinson's Disease (PD) is the second leading neurodegenerative disorder that affects about 1% of people over 60 years globally [1-2]. Common symptoms of PD include motor neuronal dysfunctions including muscular tremor, rigidity, bradykinesia, difficulty in gait movement and posture [3]. Besides, gastrointestinal abnormalities such as constipation and some dysregulation of gastrointestinal microbiome have recently been noticed. Neuropathological hallmarks of PD entail loss of nigrostriatal dopaminergic neurons in the Substantia Nigra Pars Compacta (SNpc) along with accumulation of  $\alpha$ -synuclein dubbed as "Lewy bodies" in various regions of the brain [3]. Thus, both the Central Nervous System (CNS) and the Gastrointestinal (GI) tract harbor PD pathogenesis agents or consequences [3]. Treatment strategies aimed at both sites could provide extensive therapeutic support to the PD patients. However, hypotheses and theories as well as experience relating both the CNS and the GI tract or the "gut" prevail in PD research paradigm [4]. Present article critically articulates both the brain and/or gut relation as well as their segregation and cumulative effects in PD pathogenesis followed by suggestion of a common therapeutic agent against both of the pathogenetic milieu.

### Gut-Brain Axis/Braak Hypothesis

According to the "Braak hypothesis", PD originates when a pathogen or misfolded protein enters through the nose or digestive system and spreads step-by-step into the brain [5-6]. Clumping of misfolded  $\alpha$ -synuclein protein into Lewy bodies occurs in the enteric nervous system of the gut and in the olfactory bulb [5-6]. Through Vagus Nerve (VN), the pathology reaches to the lower brain stem en route to the midbrain and cortex. Prion-

like behavior of the misfolded proteins affect nearby neurons and PD pathogenesis spreads to the sensory and neocortex areas that manifest cognitive decline and other PD hallmarks [5-6]. Braak hypothesis has recently been intensified through the "gut-brain-axis" concept that facilitates bidirectional communicative networking through metabolic, endocrine, immune and neurological processes [5-6]. The "gut-brain-axis" encompass the gut microbiota with Autonomic Nervous System (ANS), Enteric Nervous System (ENS), Central Nervous System (CNS) and the Hypothalamic-Pituitary-Adrenal (HPA) axis [5-6]. ANS and vagus nerve directly while the ENS indirectly mediate the gut-brain communication [5-6]. This communication is substantiated by the gut microbiota and thus the gut has been christened as the "second brain" [7]. Gut is a reservoir of different microbes that play pivotal role in maintaining "healthy brain" and "healthy second brain" [7]. Gut microbiota confer significant impact on accumulation, distribution and dissipation of various neurobiochemicals [3]. Thus, present and absence of different gut microbiome acts as a gold standard for prognosing and assessing different neurological disorders [7]. Compared with those of the healthy individuals, PD manifestations have been correlated with increased level of Akkermansia, Bifidobacterium, Enterococcus and Lactobacillus [8]. The opposite occurrence has been aligned with Blautia, Coprococcus and Prevotellaceae [8]. Mechanism of action of the gut microbiome on healthy and neurodegenerative diseased brain such as of PD involve neurotransmitters, hormones and metabolites [8]. Gut microbiota produce several neurotransmitters such as acetylcholine, dopamine, epinephrine, norepinephrine and serotonin as well as corticotropin-releasing hormone (CRH) whose effect on the host (human) would aid in maintaining normal levels of the neurotransmitters [9]. Metabolites derived from the fermentation mediated by the gut microbiome act as chemical messenger in the bi-directional signaling cascades between the

brain and the gut [9]. These chemical messengers include Short Chain Fatty Acids (SCFA) such as acetate, propionate and butyrate [9]. SCFAs intensify gut barriers, provide nutritive support to the colon cells, prevent leakage of toxins to the blood stream, anti-inflammatory support to both the gut and the brain and influence neurobiochemical activities as the SCFAs can cross the Blood Brain Barrier (BBB) [10]. On the other hand, hippuric acid and trimethylamine-N-oxide, two metabolites of gut microbiota, confer PD pathogenesis [10]. However, some schools of thought do not fully agree with “Braak hypothesis” and opine for much complex pathogenic routes rather than the single straight forward one proposed by the “Braak hypothesis” [11].

### Mushrooms As Prebiotics for Parkinson's Disease Treatment

According to the International Scientific Association for Probiotics and Prebiotics (ISAPP), a “prebiotic” is “a substrate that is selectively utilised by host microorganisms conferring a health benefit” [12]. They are non-digestible foods that promote the growth of beneficial microorganisms especially in the gut [12]. Mushrooms fulfill the criteria of prebiotics fully [13-15]. Mushrooms possess complex carbohydrates including beta-D-glucans, hemicellulose and chitin that are indigestible in the stomach and promote growth of beneficiary microbes like *Bifidobacterium* and *Lactobacillus* in the large intestine [13-15]. Fermentation of mushroom-derived complex carbohydrates produce SCFAs that maintain healthy gut lining along with anti-inflammatory defense [13-15]. Prebiotic roles of the mushrooms, once combined with those of the probiotics (live microorganisms that, when administered in adequate amounts, confer a health benefit on the host-ISAPP), turns into heightened PD modulating agents [16-18]. This occurs due to enhanced production of postbiotics (inanimate microorganisms and/or their components that confers a health benefit on the host-ISAPP) through combined support of the pre- and post-biotics that ultimately become beneficiary to the host (human). In this aspect, mushrooms as prebiotics, promote growth of probiotic microorganisms (bacteria) and release of postbiotics (neurotransmitters, vitamins, amino acids, metabolites) in the gut of human (host) and thus aid in maintaining “healthy brain” and “healthy second brain (the gut)” that ultimately provide PD and other neurodegenerative amelioration [12]. Mushrooms (*Agaricus blazei*, *Flammulina velutipes*, *Ganoderma lucidum*, *Grifola frondosa*, *Hericium erinaceus*, *Lentinula edodes*, *Lingnospus rhinocersu*, *Pleurotus ostreatus*) improve both motor (tremors, stiffness) and non-motor (depression, anxiety, cognitive decline) symptoms associated with PD [16-18]. Psychedelic mushrooms (*Psilocybe cubensis*) have been found having anti-depression and anxiety-relieving effects [19-20]. In addition, anti-oxidative (through various phenolics), anti-inflammatory (through triterpenoids) and neurite outgrowth promoting potentiality of mushrooms make them ideal as PD therapeutic agents [21]. Self-medication of reishi mushroom (*Ganoderma lucidum*) provided immense improvement in PD symptoms [22]. *In silico*, cell lines and animal model studies also provide support to beneficiary effect of mushrooms on PD and other neurodegenerative diseases [23-26]. Constipation, a prominent hallmark of “brain-gut” nexus relating PD, had been reported to be relieved through edible and medicinal mushroom (*Auricularia auricula*, *Flammulina velutipes*, *Pleurotus citrinopileatus*) intake [27-30]. Constipation relieving mechanism had been reported as the mushroom-derived dietary fibers that rather provide fermentation promoting microenvironment in the gut to the beneficiary gut microbiome [27-30]. In these ways, mushrooms, through their prebiotics efficiency, support the growth of the probiotics microorganisms that ultimately aid in PD pathogenesis amelioration [31-32].

### Conclusion

Mushrooms, as prebiotics, confer support to growth of probiotic microorganisms in the gut. Microbes aid in PD amelioration of the human hosts through secretion of beneficiary metabolites to the host gut that later on acts on the brain. Through maintenance of the “healthy gut-brain” relationship, mushrooms provide PD amendment effects.

### References

1. (2023) Parkinson disease <https://www.who.int/news-room/fact-sheets/detail/parkinson-disease>.
2. Su D, Cui Y, He C, Yin P, Bai R, et al. (2025) Projections for prevalence of Parkinson's disease and its driving factors in 195 countries and territories to 2050: modelling study of Global Burden of Disease Study 2021. *bmj* 388: e080952.
3. Morris HR, Spillantini MG, Sue CM Williams-Gray CH (2024) The pathogenesis of Parkinson's disease. *The Lancet* 403: 293-304.
4. Foltynie T, Bruno V, Fox S, Kühn AA, Lindop F, et al. (2024) Medical, surgical, and physical treatments for Parkinson's disease. *The Lancet* 403: 305-324.
5. Porwal M, Malviya R, Chandra P, Sridhar SB, Shareef J, et al. (2026) Microbiome-gut-brain axis modulation for the management of Parkinson's disease: Emerging mechanisms and translational insights. *Journal of Neuroimmunology* pp: 579099.
6. Jin X, Wei J, Min X, Fan Y, Yuan Z, et al. (2026) Gut microbiota and Parkinson's disease: exploring pathogenesis and potential therapeutic strategies from a gut-brain axis perspective. *Iscience* 29: 289- 297.
7. Oliver J, Civitelli L, Hu MT (2025) The gut-brain axis in early Parkinson's disease: From prodrome to prevention. *Journal of neurology* 272: 413.
8. Carrossa G, Misenti V, Faggini S, Giron MC, Antonini A, (2025) Gut-Brain Axis and Parkinson's Disease: The Role of Small Intestinal Microbiota from Symptom Onset to Therapeutic Perspectives. *Biomedicine* 13: 1769.
9. Menozzi E, Schapira AH, Borghammer P (2025) The gut-brain axis in Parkinson disease: emerging concepts and therapeutic implications. *Movement Disorders Clinical Practice* 12: 904-916.
10. Ran Z, Mu BR, Wang DM, Ma QH, Lu MH (2025) Parkinson's disease and the microbiota-gut-brain axis: metabolites, mechanisms, and innovative therapeutic strategies targeting the gut microbiota. *Molecular Neurobiology* 62: 5273-5296.
11. Lionnet A, Leclair-Visonneau L, Neunlist M, Murayama S, Takao M, et al. (2018) Does Parkinson's disease start in the gut?. *Acta neuropathologica*, 135: 1-12.
12. Salminen S, Collado MC, Endo A, Hill C, Lebeer S, et al. (2021) The International Scientific Association of Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of postbiotics. *Nature reviews Gastroenterology & hepatology*, 18: 649-667.
13. Ajibola OO, Nolasco-Hipólito C, Thomas R (2026) Fermented mushroom beverages: Exploring probiotic, prebiotic, and synbiotic properties through nanoscience for enhanced health benefits. *Future Foods* 13: 100890.
14. El-Maradny YA, Abouakkada AS, Abbass AAG, Abaza AF, El-Fakharany EM (2025) Prebiotic properties and antioxidant effect of crude extracts and polysaccharides from *Agaricus bisporus* and *Pleurotus ostreatus* mushrooms. *Scientific Reports* 15: 31113.
15. Ayimbila F, Keawsompong S (2025) Unveiling the prebiotic properties of mushrooms in improving gut health and related

- diseases. *Food Bioscience* 70: 107040.
16. Poluektova EU, Stavrovskaya A, Pavlova A, Yunes R, Marsova M, (2025) Gut Microbiome as a Source of Probiotic Drugs for Parkinson's Disease. *Int J Mol Sci.* 26: 9290.
  17. Envenuti L, Di Salvo C, Bellini G, Seguela L, Rettura F, et al. (2024) Gut-directed therapy in Parkinson's disease. *Front. Pharmacol* 15: 1407925.
  18. Magistrelli L, Contaldi E, Visciglia A, Deusebio G, Pane M, et al. (2024) The Impact of Probiotics on Clinical Symptoms and Peripheral Cytokines Levels in Parkinson's Disease: Preliminary In Vivo Data. *Brain Sciences* 14: 1147.
  19. Bradley ER, Sakai K, Fernandes-Osterhold G, Szigeti B, Ludwig C, et al. (2025) Psilocybin therapy for mood dysfunction in Parkinson's disease: an open-label pilot trial. *Neuropsychopharmacology* 50: 1200-1209.
  20. Fleury V, Tomkova E, Catalano Chiuvé S, Penzenstadler L (2025) Psilocybin-assisted psychotherapy for Parkinson's disease without depression: a case-report. *Journal of Parkinson's Disease* 15: 440-444.
  21. Cordaro M, Modafferi S, D'Amico R, Fusco R, et al. (2022) Natural compounds such as *Hericium erinaceus* and *Coriolus versicolor* modulate neuroinflammation, oxidative stress and lipoxin A4 expression in rotenone-induced Parkinson's disease in mice. *Biomedicines* 10: 2505.
  22. Kuypers KP (2021) Self-medication with *Ganoderma lucidum* ("Reishi") to combat Parkinson's disease symptoms: a single case study. *Journal of medicinal food* 24: 766-773.
  23. Rai SN, Mishra D, Singh P, Vamanu E, Singh MP (2021) Therapeutic applications of mushrooms and their biomolecules along with a glimpse of in silico approach in neurodegenerative diseases. *Biomedicine & Pharmacotherapy* 137: 111377.
  24. Yang PP, Lin CY, Lin TY, Chiang WC (2020) *Hericium erinaceus* mycelium exerts neuroprotective effect in Parkinson's disease-in vitro and in vivo models. *J Drug Res. Dev* 6: 1-6.
  25. Ren ZL, Wang CD, Wang T, Ding H, Zhou M, et al. (2019) *Ganoderma lucidum* extract ameliorates MPTP-induced parkinsonism and protects dopaminergic neurons from oxidative stress via regulating mitochondrial function, autophagy, and apoptosis. *Acta Pharmacologica Sinica* 40: 441-450.
  26. Lee W, Fujihashi A, Govindarajulu M, Ramesh S, Deruiter J, et al. (2019) Role of mushrooms in neurodegenerative diseases. *Medicinal Mushrooms: Recent Progress in Research and Development* pp: 223-249.
  27. Gao Y, Deng L, Chen Y, Qin P, Zhao Y, et al. (2025) Therapeutic efficacy of a galactoglucan from *Pleurotus citrinopileatus* in constipation: modulation of aquaporin signaling and intestinal barrier. *Frontiers in Nutrition* 12: 1635487.
  28. Bellini M, Tonarelli S, Barracca F, Rettura F, Pancetti A, et al. (2021) Chronic constipation: is a nutritional approach reasonable?. *Nutrients*, 13: 3386.
  29. Yu C, Dong Q, Chen M, Zhao R, Zha L, et al. (2023) The effect of mushroom dietary fiber on the gut microbiota and related health benefits: A review. *Journal of Fungi* 9: 1028.
  30. Hobbs C (2023) The health and clinical benefits of medicinal fungi. In *Biochemical engineering and biotechnology of medicinal mushrooms*. Cham: Springer International Publishing pp: 285-356.
  31. Kulshreshtha S (2024) Mushroom as prebiotics: A sustainable approach for healthcare. *Probiotics and Antimicrobial Proteins* 16: 699-712.
  32. Liu X, Yu Z, Jia W, Wu Y, Wu D, et al. (2020) A review on linking the medicinal functions of mushroom prebiotics with gut microbiota. *International Journal of Medicinal Mushrooms* 22: 943-951.

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