Medicinal Mushrooms for Cognition and Mood: A review of human clinical trials

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Abstract

Medicinal mushrooms have been used since ancient times to treat disease and promote general health and well-being. Various health-promoting properties have since been confirmed with studies demonstrating immunomodulatory, anti-cancer, anti-viral, anti-bacterial, anti-inflammatory, neuroprotective, and cardioprotective activity among other properties. An additional interest in the use of mushroom nutraceuticals for mental health and cognition enhancement has also developed with various dietary supplement companies advertising their mushroom products with claims of improved memory, focus, and mood. However, research is still in its early stages with few human clinical trials to support these claims. The purpose of this review is to compile and examine the evidence for beneficial effects on the mind by medicinal mushrooms, specifically regarding the domains of cognition and mood, by reviewing human clinical trials. This review reveals trends of improvement in well-being by *G. lucidum in* the context of taxing disease states, improvement in cognitive function *H. erinaceus* in the context of cognitive decline, and general improvement in depression and anxiety by *H. erinaceus*. Potential mechanisms and limitations due to research design are also discussed. This review provides further clarity on the validity of health claims made by supplement companies and calls for future research in these areas.

Methods

A search was conducted through the PubMed database. Only available, full-text, human clinical trials on the selected mushrooms which also measured at least one cognition-related outcome were included. The following mushrooms and their common names were searched: Hericium erinaceus, lion's mane, and monkey head mushroom; Ganoderma lucidum, reishi, and lingzhi; Ophiocordyceps sinensis, Cordyceps sinensis, Cordyceps militaris, and caterpillar fungus; Inonotus obliquus, and chaga; Trametes versicolor, Coriolus versicolor, Polyporus versicolor, and turkey tail. The following terms were used to search for cognition-related outcome measures: cognit*, mind, mental, memory, attention, focus, executive function, brain, mood, anxiety, depression, dementia, Alzheimer's, psych*, and well-being. Additional available studies referenced in other articles that met the inclusion criteria were also included.

Results

- The search yielded 11 studies on 4 mushrooms species. One study was found for *Cordyceps militaris*, one for *Coriolus versicolor*, 4 for *Ganoderma lucidum*, and 5 for *Hericium erinaceus*.
- ***Cordyceps militaris***: no evidence was found supporting the efficacy of *C. militaris* for improving insomnia or depression in patients with depression taking duloxetine.
- ***Coriolus versicolor*** *(Trametes versicolor)*: improvements in mood related to Meniere's disease (MD) was observed in patients with MD treated with *C. versicolor* in addition to significant improvements in oxidative stress status, tinnitus severity, and auditory function. This was not observed in the control group.
- ***Ganoderma lucidum***: "cognitive functioning" improved significantly in patients with breast cancer but not in patients with Alzheimer's disease (AD). In populations of patients with breast cancer and fibromyalgia, reductions in depression and anxiety were observed following *G. lucidum* supplementation. Increased well-being was also observed in the population with fibromyalgia and in another population of adults with lung cancer.
- ***Hericium erinaceus***: improvements in cognitive function were observed following *H. erinaceus* intake in adults with mild cognitive impairment, mild AD, and in healthy adults, though the point difference in MMSE score was miniscule in the healthy population. Trends of improvement in depression and anxiety were observed in females and adults with overweight or obesity with at least one mood or sleep disorder or with binge eating behavior.

Table 1. Summary of Studies (modified)

Mushroom	Citation	Study Population	Sample Size[a]	Duration of Supplementation	Dosage (per day)	Cognitive Outcomes
Ganoderma lucidum	Zhao et al., 2012	Adult females with breast cancer	Treatment: 25 Control: 23	4 weeks	3 g spore powder	• Significant improvement in "emotional well-being" and "emotional functioning" (measured by FACT-F and EORTC QLQ-C30 respectively) in treatment group only, and significant difference between groups favoring the treatment group. • Significant improvement in anxiety and depression (measured by HADS) in treatment group only, and significant difference between groups favoring the treatment group. • No significant change in "social/family well-being" or "social functioning" (measured by FACT-F and EORTC QLQ-30 respectively) in either group, nor significant difference between groups. • Significant improvement in "cognitive functioning" (measured by EORTC QLQ-C30) in treatment group only and significant difference between groups favoring the treatment group
	Wang et al., 2018	Adults with Alzheimer's disease	Treatment: 21 Control: 21	6 weeks	3 g spore powder	• No significant difference between groups in cognition, dementia-related neuropsychiatric symptoms, and quality of life (measured by the ADAS-Cog, NPI, and WHOQOL-BREF respectively)
	Liu et al., 2020	Adults with non-small cell lung cancer	Treatment: 61 Control: 21	6 weeks	0.45 g spore powder[b]	• Greater improvements in "social/family well-being," "emotional well-being," and "functional well-being" contributing to a higher quality of life (measured by FACT-G) in treatment group, but no significant difference between groups.
	Pazzi et al., 2020	Adult females with fibromyalgia	Treatment: 26 Control: 24	6 weeks	6 g fruiting body	• Significant improvements in happiness, satisfaction with life, and depression (measured by SHS, SWLS, and GDS respectively) from baseline in treatment group but not placebo group with a significant difference between groups favoring the treatment group in happiness. • Significant improvement in "social functioning," "emotional role" of health and "mental health" (measured by the SF-12) from baseline in treatment group and an improvement in only "mental health" in placebo, but no significant difference between groups.
Hericium erinaceus	Mori et al., 2009	Adults (50-80 y/o) with mild cognitive impairment	Treatment: 14 Control: 15	16 weeks	1 g fruiting body powder	• Significant improvement in cognitive function (measured by modified HDS-R) from baseline in treatment group and compared to placebo group
	Nagano et al., 2010	Adult females	Treatment: 12 Control: 14	4 weeks	2 g fruiting body powder	• Significant improvement in depressive symptomatology (measured by CES-D) from baseline in treatment group, but no significant difference between group outcomes. • Significant improvements in "incentive" and "concentration" subscores relevant to depression (measured by ICI) from baseline in treatment group with improvement in "incentive" significantly greater compared to placebo. • Significant improvement in subscore of "irritating" (measured by ICI) from baseline in the treatment group, but no significant difference between groups. • Significant improvement in "anxious" subscore (measured by ICI) from baseline in the treatment group, but no significant difference between groups.
	Saitsu et al., 2019	Healthy adults over 50 years old	Treatment: 16 Control: 15	12 weeks	3.2 g fruiting body powder	• Significant improvement in cognitive function (measured by MMSE) from baseline in only the treatment group with a significant difference between groups favoring the treatment group • No significant difference in visual cognitions (measured by Benton Visual Retention Test) between groups • No significant difference in short-term memory (measured by S-PA) between groups
	Vigna et al., 2019	Adults with overweight/obesity and at least one mood/sleep disorder or with binge eating behavior	Treatment (low-calorie diet + *H. erinaceus*): 35 Control (low-calorie diet): 35	8 weeks	1.2 g mycelium + 0.3 g fruiting body	• No significant improvement in depression (measured by Zung's Depression Scale) from baseline in either group nor difference between groups, but in patients selected for depression symptomatology, only the treatment group showed significant improvements from baseline. • Significant improvement in anxiety (measured by Zung's Anxiety Scale) from baseline in only the treatment group with even greater significance in patients selected for anxiety symptomatology in the treatment group but not control group. • Significant improvement in "depression" and "anxiety" domains (measured by SCL-90) from baseline in the treatment group test with greater significance in patients selected for symptomatology.
	Li et al., 2020	Adults over 50 years old with Mild Alzheimer's Disease	Treatment: 20 Control: 21	49 weeks	1.05 g mycelia (enriched with 5 mg/g erinacine A)	• No significant improvement in dementia-related neuropsychiatric symptoms (measured by NPI) in either group nor difference between groups. • Trend of improvement in cognitive abilities (measured by CASI) from baseline in treatment group with a trend of deterioration in placebo group reaching significance at week 25, but no significant difference between groups • Significant improvement in cognitive function (measured by MMSE) from baseline in treatment group only, but no significant difference between groups. • Significant difference in ability to perform instrumental activities of daily living (measured by IADL) between groups at the end of the intervention favoring the treatment group. • No change in monocular or binocular BCVA (measured by Snellen eye chart) from baseline in either group. • No change in monocular or binocular CS (measured by Pelli-Robson chart) from baseline in either group with the exception of a significant change in binocular CS in placebo from baseline and a significant difference in left-eye CS between groups favoring the treatment group.

[a]number included in final analysis

[b]Part of a Reishi & Privet Formula containing 0.45 g dried sporederm-broken Ganoderma lucidum spores + 0.33 g glossy Privet fruit extract (3.36g total weight, standardized for >1% polysaccharide and > 2.0 mg oleanolic acid)

Conclusion

- Modern research increasingly supports the **therapeutic utility** of medicinal mushrooms
- These studies reveal trends of improvement in **well-being** by *G. lucidum* in the context of taxing disease states, improvement in **cognitive function** by *H. erinaceus* in the context of cognitive decline, and general improvement in **depression and anxiety** by *H. erinaceus*
- These studies demonstrate the low-risk and general **safety** of the consumption of these mushrooms.
- Medicinal mushrooms hold great potential as complements to the limited conventional treatments. This calls for future rigorous clinical trials and further research to identify the mechanisms behind the effects.

Hericium erinaceus

Ganoderma lucidum

Discussion

- The studies reviewed show trends of improvement in **cognition** from *H. erinaceus* and in **mood** from both *H. erinaceus* and *G. lucidum.*
- The bioactive compounds in *H. erinaceus*, which include hericenones and erinacines, stimulate neurotrophin-synthesis. These neuropeptides play key roles in neuronal growth, maintenance, and protection. Low levels of neurotrophins, which include nerve growth factor (NGF) and brain-derived neurotrophic factor (BDNF) are associated with both neurodegenerative diseases and mood disorders. It is possible that the benefits of *H. erinaceus* are related to its neurotrophin-stimulating abilities.
- The effects of *G. lucidum* on mood may be explained by its benzodiazepine-like activity demonstrated in rats via GABAergic mechanisms, or the neurotrophin-like activity of *G. lucidum* triterpenoids (promoting neuronal survival and inducing neuronal cell differentiation by MAPK activation *in vitro*). The potent antioxidant activity of *G. lucidum* may also contribute to reductions in neuroinflammation which is implicated in the development of mood disorders.
- Due to the context of disease states, such as fibromyalgia and cancer, in most of the studies, it is difficult to isolate the impact on mood without considering that improvements in one's physical condition may also improve one's affect.
- Future research may benefit from greater consistency in the measurement tools used between studies and consideration of frequency of cognitive function test administration to avoid the learning effect. Greater consistencies in the form, dose, and duration of supplementation would also reduce the variables between studies, allowing for more insightful comparisons and stronger evidence for use.