

Is Use of Psychedelic Drugs a Risk or Protective Factor for Late-Life Cognitive Decline?

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Abstract

Objectives: Common age-related health conditions can lead to poor mental health outcomes and deteriorate cognition. Additionally, commonly prescribed medications for various mental/physical health conditions may cause adverse reactions, especially among older adults. Psychedelic therapy has shown positive impacts on cognition and has been successful in treating various mental health problems without long-lasting adversities. The current study examines the association between psychedelic drug usage and cognitive functions in middle-aged and older adults. **Methods:** Data were from wave 3 (2013–2014) of the Midlife in the United States (MIDUS) study. We used multiple linear regression models examining associations between psychedelic usage and cognitive functions, controlling for covariates of sociodemographic and health factors. **Results:** We included 2,503 individuals ($M_{age} = 64 \pm 11$). After controlling for covariates, the finding revealed that psychedelic usage was independently associated with more favorable changes in executive function ($\beta = .102$, $SE = 0.047$, $p = .031$) and less depressive symptoms ($\beta = -.090$, $SE = 0.021$, $p < .001$). The same effect was not found for episodic memory ($\beta = .039$, $SE = 0.066$, $p = .553$). **Discussion:** Addressing the mental health implications of physical health conditions in older adults are vital for preventing neurocognitive deterioration, prolonging independence, and improving the quality of life. More longitudinal research is essential utilizing psychedelics as an alternative therapy examining late-life cognitive benefits.

Keywords

psychedelics (hallucinogens [MeSH]), older adults (aged [MeSH]), MIDUS, quality of life, cognition

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Introduction

Advancements in medicine and sanitation have caused an increase in life expectancy (Rahman et al., 2022). Although people are living longer, many older adults are experiencing chronic illnesses that cause disability and psychological distress. Often, chronic illnesses come with a tremendous emotional burden that can lead to poor mental health outcomes like depression. Earlier research considered that depression is a prodrome of developing dementia (i.e., an early detectable symptom before the emergence of major signs/symptoms) in older adults (Bennett & Thomas, 2014). Further, the increasing older adult population requires additional economic and healthcare support. Improving the overall health of the older population is important for reducing the healthcare and economic strain associated with aging.

Additionally, improving the neurocognitive health of older adults can prolong independence. Unfortunately, most age-related neurocognitive disorders have no definite curative intervention and treatment options through modern medical management; available drugs for managing neurocognitive disorders can only temporarily

delay the disease progression, but do not treat the underlying causes of the disease (Bhattacharyya et al., 2022; Crous-Bou et al., 2017; Zheng et al., 2020). Thus, finding alternative and cost-effective therapy options for neurocognitive disorders are essential for improving the quality of the aging process. Psychedelic therapy has the potential to improve neurocognitive functioning (Yehuda & Lehrner, 2023) and manage mental health problems associated with the development of depression and subsequent dementia (Magaraggia et al., 2021). Studies suggest that psychedelic consumption can reduce cognitive decline, prevent deteriorative neurocognitive disorders (Yehuda & Lehrner, 2023), and ultimately increase healthy life expectancy. Increasing healthy life expectancy would reduce the economic

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burden and healthcare strain caused by age-related diseases and improve the quality of life of older adults (W. Zhang et al., 2018).

Cultural Perspective

Psychedelics have an extensive history of cultural and ritual use (Nichols, 2016). Psilocybin mushrooms have been consumed by humans for thousands of years. In ancient India, a hallucinogenic substance called “soma” (a plant extract) was consumed in rituals and praised frequently throughout Rigveda, the oldest sacred book of Hinduism (Britannica, 2020; Nichols, 2016). In an ancient village outside of Athens, there was an annual ceremony involving the ingestion of a hallucinogenic brew for more than 2,000 years (Nichols, 2016). Aztec shamans used psilocybin mushrooms for healing and divinatory rituals (Nichols, 2016). “Mescaline” derived from peyote cacti has been consumed by Native Americans during church services for millennia (Nichols, 2016). There are many other examples of the historical usage of psychedelics throughout various cultures. The historical consumption of psychedelics indicates that there are benefits to consuming psychedelics.

Although history and various studies indicate that psychedelics have positive impacts on well-being, psychedelic research lacks government support and funding from agencies, such as the National Institute of Health and the National Institute of Mental Health (Nichols, 2016). This is primarily due to political influences in the 1960s and 1970s because lysergic acid diethylamide (LSD) and marijuana users (often referred to as hippies) rejected social norms by protesting the Vietnam War, which was thought to be caused by drug use (Nichols, 2016). Mainstream culture thought that psychedelic use resulted in younger people rejecting social norms and war, and these substances have no established medical value (Tupper et al., 2015). This widespread false belief about psychedelics quickly led to the passage of the Controlled Substances Act of 1970, which placed all known psychedelics into Schedule 1, the most restrictive category of drugs (Nichols, 2016). This Act made clinical research on psychedelics impossible and terminated ongoing research regarding the useful properties of psychedelics (Nichols, 2016).

Since the 1960s, recreational psychedelic use in Western societies has been increasing regardless of the drug classification. Over 30 million people in the United States have consumed classic psychedelics, such as psilocybin, LSD, or mescaline (Krebs & Johansen, 2013). Research suggests some other substances also produce similar hallucinogenic effects and considered as atypical psychedelics, such as marijuana/cannabis (Wolinsky et al., 2024). Further, it is evidenced that some antidepressants, such as St John’s wort (Ferrara et al., 2017; Gurok et al., 2014) and Fluoxetine (Webb & Cranswick, 2003), and some

tranquilizers (Kadriu et al., 2021) also produce some hallucinogenic effects. Psychedelic therapy for treating various mental health disorders is gaining popularity, and people are beginning to become more open-minded about psychedelic therapy. For example, in Canada, many people support legal access to psilocybin therapy, and the Canadian government recently began allowing physicians to use psilocybin therapy in patients with terminal medical conditions (Canadian Psychedelic Association, 2021). The increasing championship for psychedelic therapy from governments and societies may promote human longevity by benefiting individuals’ cardiometabolic health (Simonsson et al., 2021).

Psychedelic Therapy

Current treatment options for neurocognitive and mental health disorders are limited to some medications and psychotherapies, such as antidepressants and cognitive-behavioral therapy, respectively (Craighead & Dunlop, 2014). Medications are typically the preferred treatment, but these drugs are usually prescribed for longer periods and often cause adverse health effects (Craighead & Dunlop, 2014). When medications and psychotherapy are not effective in treating neurocognitive and mental health disorders, alternative therapeutic options should be taken into consideration. Psychedelic therapy is the clinical administration of psychoactive compounds in a controlled setting. Psilocybin and LSD are two psychoactive compounds being increasingly researched regarding their health benefits (Yehuda & Lehrner, 2023). *Psilocybin* is a chemical compound produced naturally by hundreds of fungi species. LSD is a synthetic chemical compound discovered and synthesized by Albert Hoffman in 1938 (Pallardy, 2022).

Multiple studies have shown that classic psychedelics (e.g., psilocybin and LSD) and atypical psychedelics (e.g., cannabis) may be useful in treating mental and neurocognitive disorders due to their ability to stimulate neurogenesis, produce neuroplastic changes, and reduce neuroinflammation (Vann Jones & O’Kelly, 2020; Vollenweider & Preller, 2020; Wolinsky et al., 2024). Neuroinflammation is significantly associated with the development of Alzheimer’s disease and is considered the most common form of dementia (F. Zhang & Jiang, 2015). In this context, neurogenesis is the formation of neurons in the brain, which is important for learning and memory (Maharjan et al., 2020; The University of Queensland, 2021), and neuroplasticity refers to the brain’s ability to adapt to new stimuli and control how neurons communicate (Maharjan et al., 2020; The University of Queensland, 2018). *Neurotransmitters* are chemicals that communicate signals between neurons and from neurons to muscles (The University of Queensland, 2017) and are essential for maintaining homeostasis and adequate brain functioning. Psychedelics, also called

serotonergic hallucinogens, are non-addictive substances that affect the central nervous system by acting as agonists on serotonin (5-HT_{2A}, 5-HT_{1A}, and 5-HT_{2C}) receptors (Psiuk et al., 2021). Serotonin (5-HT) is a key neurotransmitter that affects mood, emotion, sexuality, breathing, stress, addiction, sleep, and digestion (Watson, 2021).

Cognitive Health and Psychedelic Therapy in Late Life

Although aging is an individualized process, some degree of cognitive decline is considered to be a normal aspect of aging. Older adults typically experience some decline in receiving, interpreting, transmitting, and processing information (Saxon et al., 2014, p. 85). Relatedly, episodic memory and executive function are two major cognitive domains that have been studied extensively (Glisky et al., 2022). Older adults experiencing normal age-related cognitive declines are still able to perform activities of daily living and instrumental activities of daily living. However, often, older adults experiencing progressive deterioration in their memory, communication, reasoning, judgment, and attention end up with some type of dementia (Bhattacharyya, Ansel, & Small, 2021; Lee et al., 2013). Dementia is an umbrella term for neurocognitive disorders that impair a person's ability to think, remember, and perform activities of daily living (Duong et al., 2017). Dementia is not a normal aspect of aging. The number of dementia cases is increasing significantly due to population aging, which is worrisome because of its expensive management options and non-curable nature. The prevalence of dementia is expected to quadruple by 2050 (Rocca et al., 2011). Persons with dementia require extensive formal and informal support. However, there is a dearth of adequately trained healthcare professionals caring for persons living with dementia (Surr et al., 2017). Globally, dementia costs \$1.3 trillion annually and causes a significant decrease in life quality; thus, it is essential to find effective treatment and therapy options for dementia (Alzheimer's Disease International, 2015, 2020). Ideally, people should aim to preserve their cognitive functions early on by doing mentally stimulating activities, such as meditation, yoga, reading, physical exercise, socializing, and learning a new language. Focusing on the prevention of health conditions can combat the increasing prevalence of age-related diseases like dementia. Health interventions after disease progression are not as effective as preventing diseases altogether.

Purpose of the Study

Nevertheless, there is an urgent need to find effective prevention, treatment, and alternative therapy options for late-life cognitive decline and dementia. Not much clinical research has been conducted considering the

impact of classic psychedelics and other hallucinogenic compounds on cognitive functions, particularly episodic memory and executive function, and depression in middle aged and older adults; the current study will examine the above associations in a publicly available national dataset, the Midlife in the United States (MIDUS). In line with the earlier research, we hypothesize that the use of classic psychedelics and other hallucinogens would improve cognitive functions and reduce depressive symptoms in middle-aged and older adults.

Method

Study Sample

We used data from the third wave of the MIDUS study. The MIDUS 3 study was conducted in 2013 to 2014, with 3,294 English-speaking participants from the U.S. households in the 48 contiguous states (Bhattacharyya, Hueluer, et al., 2021; Hughes et al., 2018). In wave 3, participants were aged between 42 to 92 years ($M=64 \pm 11$, 55% women) (Lachman et al., 2014). MIDUS 3 was conducted through the phone, along with a mailed self-administered questionnaire (SAQ).

Measures and Procedure

Key Independent Variable. The usage of LSD/other hallucinogens (as psychedelics) was used as the key independent variable. Participants responded to the question, whether during the past 12 months did they ever use any of the following substances on their own—Marijuana, LSD, or other hallucinogens (e.g., PCP, Angel dust, Peyote, Ecstasy (MDMA), Mescaline, Prozac)? Responses were coded as a binary variable (0=no, 1=yes).

Dependent Variables. We used episodic memory and executive function, measured at wave 3 with the Brief Test of Adult Cognition by Telephone (BTACT), as dependent variables (Lachman et al., 2014). Episodic memory was measured with two tests (immediate and delayed free recall of 15 words, Rays-O). Executive function was measured by inductive reasoning (measured by number series completion), category verbal fluency (measured by verbal ability and fluency in 60 s), working memory span (measured by backward digit span), processing speed (measured by 30-second and Counting Task, or 30-SACT), and attention switching and inhibitory control (measured by Stop and Go Switch Task, or SGST, calculating reaction times) (Lachman et al., 2014). The results of factor analysis for cognitive tests in MIDUS were reported by Lachman et al. (2014). The tests were *z*-scored ($M=0$; $SD=1$) according to the means and standard deviations of the entire wave 3 sample. Lachman et al. (2010) calculated a composite score for both episodic memory and executive function as the mean of the *z*-scored measures.

Table 1. Demographic Characteristics of US Adults in MIDUS Wave 3 (n=2,503).

Variables	Overall	Psychedelic user n = 205 (8.2%)	Psychedelic non-user n = 2,298 (91.8%)	p-Value
Age in year <i>M</i> (<i>SD</i>)	64.8 (11.0)	61.5 (9.2)	65.1 (11.1)	.017
Female (%)	55.5	55.1	55.6	.015
Race/ethnicity (%)				
White	90.2	90.1	90.2	.198
African American	3.1	4.9	3.0	
Other	6.7	5.0	6.8	
Marital status (%)				
Married	66.7	55.1	67.8	<.001
Separated/divorced	14.6	26.8	13.5	
Widowed	11.8	8.8	12.0	
Never married	6.9	9.3	6.7	
Education (%)				
No/some school	5.4	7.3	5.3	.201
Graduated from school/in college	42.2	44.4	42.0	
Graduated from college	33.9	34.6	33.8	
Master's/professional degree	18.5	13.7	18.9	
Employment (%)				
Working	49.5	45.3	49.9	.035
Self-employed	12.3	14.5	12.1	
Retired	29.5	28.5	29.6	
Unemployed	1.8	3.9	1.6	
Other	6.9	7.8	6.8	
Tobacco user (%)	8.5	15.6	7.9	<.001
Alcohol user (%)	59.1	75.1	57.7	<.001
Chronic conditions (%)	82.1	85.4	81.8	<.001

Note. *M* = mean; *SD* = standard deviation; values are in *M* (*SD*) or column %. Bold numbers highlight the significant *p* values.

We also considered depressive symptoms that persisted for two/more weeks in the past 12 months based on a mean score on the 7-item DEPCON scale in MIDUS that was administered by telephone (Cutler & Lleras-Muney, 2010). Responses were entered as a binary variable (0 = no, 1 = yes).

Covariates. We considered the following sociodemographic variables, including age (continuous), gender (0 = male, 1 = female), race (1 = White, 2 = other), marital status (1 = married, 2 = separated/divorced, 3 = widowed, 4 = never married), education (1 = no/some school, 2 = high school graduate/in college, 3 = graduated from college, 4 = having master's/professional degree), and employment (1 = currently working, 2 = self-employed, 3 = retired, 4 = unemployed, 5 = other). We also considered participants' chronic condition/s in the past 12 months (0 = no, 1 = yes) and tobacco and alcohol use (1 = regular tobacco/alcohol user, or 0 = not).

Statistical Analysis

We conducted statistical analyses using Stata 18.0 SE (College Station, TX) software. To examine the association between the usage of psychedelic agents and the cognitive functions of individuals, we estimated multiple linear regression models by predicting executive

function, episodic memory, and depressive symptoms (dependent variables) in separate models while controlling for covariates (sociodemographic factors and health status). These models only included predictor variables that showed significant group differences associated with psychedelic use. Statistical significance was evaluated at $p < .05$ (two-sided). We reported unstandardized regression coefficients (β) and standard errors (*SE*).

Results

Descriptive statistics of the dependent and independent variables, including demographic variables and health status at wave 3, are shown in Table 1. A total of 2,503 individuals aged 42 to 92 years ($M = 65$, $SD = 11$) were included in the analysis. Women made up 56% of the sample, 49% were employed. The respondents' educational levels were high, with 52% having graduated from college and 19% having a master's or professional degree. Table 1 also stratified participants based on psychedelic use; 205 participants (8.2%) used LSD/other hallucinogens in the last 12 months. Psychedelic use was found to be higher in younger and women participants, those who were separated/divorced and never married, unemployed, tobacco and alcohol users, and participants with more chronic conditions.

Table 2. Multiple Linear Regression Models Examining Associations of Cognitive Functions and Depressive Symptoms with Psychedelic Use in Mid and Later Life ($n = 2,503$).

Variables	Executive function			Episodic memory			Depressive symptoms		
	β	SE	p	β	SE	p	β	SE	p
Intercept	1.111	0.146	<.001	1.251	0.202	<.001	0.474	0.065	<.001
<i>Key independent variable</i>									
Psychedelic user (ref. non-user)	0.102	0.047	.031	0.039	0.066	.553	-0.090	0.021	<.001
<i>Covariates</i>									
Age (years)	-0.024	0.002	<.001	-0.027	0.002	<.001	-0.004	0.001	<.001
Female (ref. male)	-0.062	0.028	.026	0.546	0.039	<.001	0.035	0.012	.005
<i>Marital status (ref. married)</i>									
Separated/divorced	-0.108	0.038	.004	-0.188	0.052	<.001	0.050	0.017	.003
Widowed	-0.191	0.044	<.001	-0.146	0.061	.017	0.079	0.020	<.001
Never married	-0.148	0.051	.004	-0.092	0.071	.199	0.066	0.023	.004
<i>Employment (ref. other)</i>									
Working	0.285	0.038	<.001	0.237	0.053	<.001	-0.096	0.017	<.001
Self-employed	0.283	0.050	<.001	0.291	0.070	<.001	-0.063	0.022	.005
Retired	0.167	0.037	<.001	0.122	0.051	.017	-0.066	0.016	<.001
Unemployed	0.106	0.111	.338	0.202	0.154	.190	0.065	0.050	.194
Tobacco user	-0.158	0.046	.001	-0.072	0.064	.265	0.051	0.021	.014
Alcohol user	0.110	0.027	<.001	0.022	0.038	.563	0.000	0.012	.988
Chronic conditions	-0.048	0.034	.153	-0.027	0.047	.561	0.057	0.015	<.001

Note. Values are measured in wave 3 of MIDUS. Bold numbers highlight the significant p values.

Table 2 shows the results of multiple linear regression models estimating the associations of psychedelic usage and cognitive functions in wave 3. After controlling for sociodemographic factors and health characteristics, psychedelic usage was independently associated with a more favorable change in executive function ($\beta = .102$, $SE = 0.047$, $p = .031$) and less depressive symptoms ($\beta = -.090$, $SE = 0.021$, $p < .001$). However, the same effect was not found for episodic memory ($\beta = .039$, $SE = 0.066$, $p = .553$).

Discussion

The current findings revealed that psychedelic use was associated with improved cognitive function, assessed by executive function, partially supporting our hypothesis; however, the same association was not evident with episodic memory. Further, psychedelic use was associated with a reduction in depressive symptoms. Although our participants were limited, the results corroborated earlier findings in a lesser-explored area of research.

Studies show that psilocybin and LSD are useful in treating mental health disorders, such as depression and anxiety (Raison et al., 2023; Yehuda & Lehrner, 2023). Raison et al. (2023) showed that a single dose of psilocybin remarkably reduced depressive symptoms after 6 weeks; our result corroborates that. This result is significant because depression is often associated with mild cognitive impairment and dementia (Bennett & Thomas, 2014). The current medications used to treat depression are associated with various adverse effects. Some adverse

effects of commonly prescribed antidepressants (serotonin reuptake inhibitors, serotonin-noradrenaline reuptake inhibitors) are diarrhea, constipation, abdominal pain, insomnia, sexual dysfunction, anxiety, and headaches (National Health Service [NHS], 2021). Further, age-related biological changes make older adults more vulnerable to the adverse side effects of antidepressants. Older adults taking antidepressants may experience hyponatremia (a significant drop in sodium levels), which can cause reduced appetite, confusion, seizures, agitation, psychosis, tiredness, and coma (NHS, 2021). A good alternative option for treating depression without the risk of numerous adverse side effects may be psychedelic therapy (Davis et al., 2021). After one to two doses of psychedelics, people experience sustained relief from the symptoms of major depressive disorder without long-lasting adverse effects (Psiuk et al., 2021). Treating depression before it progresses to further cognitive impairment may reduce the risk of developing dementia. Enhancing neurological health with psilocybin and LSD therapy sessions can improve cognition and prolong independence in older age.

The current findings corroborate the existing literature establishing mixed effects concerning why psychedelic use revealed differences in episodic versus executive cognitive functions (Barrett et al., 2020). Perhaps our finding regarding better scores on executive functioning versus episodic tasks suggests that executive functioning is more hard-wired into the aging process; a self-selection bias should also be considered as a potential confounding evidence to show that it may help

some individuals perform better in some specific cognitive dimensions (Roth et al., 2015). Multiple studies established the negative effects of stress on cognitive performance (Bhattacharyya et al., 2022; Chen et al., 2018; Goda et al., 2020). Individuals' sympathetic nervous system is triggered in the stress process, releasing various neurotransmitters, which may have adverse and beneficial effects on cognition. One of the beneficial neurotransmitters is serotonin, which mediates satisfaction, happiness, and optimism (Dfarhud et al., 2014). While excessive stress may be detrimental to cognitive functions, milder stress may help better cognitive performance (O'Sullivan et al., 2019), supporting why even small doses of psychedelic benefits cognitive performance.

Findings on covariates indicate that increasing age is negatively associated with cognitive functions. Age is a major risk factor for the development of multiple chronic health conditions, such as cancer, hypertension, diabetes, and dementia (Niccoli & Partridge, 2012). Chronic health conditions are associated with a psychological burden that can further deteriorate health if not addressed adequately. Healthcare professionals must ensure they manage the emotional aspects of their patient's chronic illnesses. Utilizing therapies that help patients cope with their chronic health conditions can improve the treatment process. An experimental study involving advanced cancer patients found that two psilocybin therapy sessions improved their outlook on life with cancer, spiritual well-being, and quality of life (Psiuk et al., 2021). Older adults with persisting health conditions are benefiting from therapies that improve their mental well-being. Addressing the mental health implications of chronic health conditions can prolong independence and improve the quality of life of older adults. In line of earlier research (Bhattacharyya, Hueluer, et al., 2021), the current findings also suggest that married (compared to their non-married counterparts) and working participants (compared to others) showed better cognitive functions.

Limitations

Multiple limitations should be considered in interpreting the current result. First, psychedelic therapy requires longer time than other therapies (up to 12 hr per session), a properly prepared environment for the therapy session, and monitoring throughout the session (Psiuk et al., 2021). Because of its cross-sectional nature, our study did not consider longer follow-up. Another issue with psychedelic therapy is that the hallucinations caused by psychedelic compounds may be too overwhelming for some patients (Psiuk et al., 2021). Although from the nature of the MIDUS questionnaire it seems that much of the use was as off-label recreational purposes, with little understanding of dosage or safety, side effects and high dosages of certain psychedelics may outweigh the benefits. The most common side effects of psychedelic

therapy are short-term anxiety, psychological discomfort, headache, nausea, and vomiting (Psiuk et al., 2021). Micro-dosing (small, reoccurring doses that do not alter perception) psilocybin or LSD may be a useful option for those who want to prevent the hallucinogenic effects. However, from the existing MIDUS data, it is impossible to find out the exact form, frequency, and dosing of psychedelics used by the participants, inducing generalizability concerns. Additionally, given the broad age range of participants, from middle-aged to older adults, a potential generalizability bias in the results may arise from variations in baseline cognitive functions. Finally, even after growing scientific interest in psychedelic medicines in recent years, their usage is limited even by physicians, probably due to hesitancy from its scientific evidence of risks and limited latest knowledge about psychedelics. For example, only a little over 8% of participants used psychedelics (including both classical and atypical psychedelics), as a key limitation of our analysis, posing some concern about our result; however, many participants were hesitant (around 1.5% refused to answer the question) to respond about psychedelic usage, reducing the chance of achieving stronger findings.

Conclusion

In conclusion, population aging is causing a significant increase in mental and physical health problems that negatively impact the quality of life of older adults. Many current treatment options have proved to be ineffective and lead to even worse health outcomes. Alternative therapies for age-related diseases are necessary because there are ramifications of consuming various prescription medications. Polypharmacy is common in older adults, and many current drug treatments for age-related illnesses cause adverse side effects and interact poorly with each other. Adverse drug reactions contribute to disability and the increasing need for care in older adults. For example, long-term use of immunosuppressants can lead to health ramifications like diabetes, infections, hypertension, and osteoporosis (Lallana & Fadul, 2011; Ruiz & Kirk, 2015); this is concerning because various age-related illnesses such as rheumatoid arthritis, inflammatory bowel disease, multiple sclerosis, and lupus are treated with immunosuppressants (Lallana & Fadul, 2011). Furthermore, many of these age-related illnesses are an emotional burden to live with, which leads to hopelessness, isolation, and depression.

Depression can lead to cognitive impairment and, ultimately, dementia. Although research on long-term psychedelic usage is limited, recent evidences suggest benefits of serotonergic psychedelics in depression (Husain et al., 2023; Nutt et al., 2023), particularly among middle-aged and older adults (Carhart-Harris et al., 2018). Utilizing alternative therapies like psilocybin therapy, due to its potential antidepressant but

minimal adverse effects, may increase healthy life expectancy by treating mental health disorders and improving cognition (Husain et al., 2023). The federal and state governments should de-criminalize psychedelics so that research can be conducted in a manner that ensures reliability and validity. More longitudinal research, including clinical and community samples, is essential utilizing psychedelics as an alternative therapy examining benefits in late-life cognitive functions. The increasing public support for pharmaceutical companies conducting psychedelic therapy clinical trials is also necessary to improve mental health management in later life. Mental and physical health are interrelated; therefore, good mental health is essential for maintaining good physical health. Overall, improving the neurocognitive and mental health of older adults using psychedelic therapy is beneficial for improving quality of life, healthcare systems, and the economy.

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References

- Alzheimer's Disease International. (2015). *World Alzheimer's report: The global impact on dementia. An analysis of prevalence, incidence, cost, and trends*. Retrieved August 7, 2023, from <https://www.alz.co.uk/research/WorldAlzheimerReport2015.pdf>
- Alzheimer's Disease International. (2020). *Dementia facts & figures*. Retrieved August 7, 2023, from <https://www.alzint.org/about/dementia-facts-figures/>
- Barrett, F. S., Krimmel, S. R., Griffiths, R. R., Seminowicz, D. A., & Mathur, B. N. (2020). Psilocybin acutely alters the functional connectivity of the claustrum with brain networks that support perception, memory, and attention. *NeuroImage*, *218*, 116980. <https://doi.org/10.1016/j.neuroimage.2020.116980>
- Bennett, S., & Thomas, A. J. (2014). Depression and dementia: Cause, consequence or coincidence? *Maturitas*, *79*(2), 184–190. <https://doi.org/10.1016/j.maturitas.2014.05.009>
- Bhattacharyya, K. K., Andel, R., & Small, B. J. (2021). Effects of yoga-related mind-body therapies on cognitive function in older adults: A systematic review with meta-analysis. *Archives of Gerontology and Geriatrics*, *93*, 104319. <https://doi.org/10.1016/j.archger.2020.104319>
- Bhattacharyya, K. K., Dobbs, D., & Hueluer, G. (2022). Mind-body practice, personality traits, and cognitive performance: A 10-years study in US adults. *Gerontology & Geriatric Medicine*, *8*, 1–12. <https://doi.org/10.1177/23337214221083475>
- Bhattacharyya, K. K., Hueluer, G., Meng, H., & Hyer, K. (2021). Movement-based mind-body practices and cognitive function in middle-aged and older adults: Findings from the Midlife in the United States (MIDUS) study. *Complementary Therapies in Medicine*, *60*, 102751. <https://doi.org/10.1016/j.ctim.2021.102751>
- Britannica, T. (2020). *Rigveda*. Retrieved August 7, 2023, from <https://www.britannica.com/topic/Rigveda>
- Canadian Psychedelic Association. (2021). *Strong majority of Canadians would support or somewhat support a government that legalized mushroom-based psilocybin-assisted psychotherapy to improve the quality of life for terminally ill patients*. Retrieved August 7, 2023, from <https://ml.globenewswire.com/Resource/Download/25e79f36-ab1d-4a7f-b897-e51ccaa60f97>
- Carhart-Harris, R. L., Bolstridge, M., Day, C. M. J., Rucker, J., Watts, R., Erritzoe, D. E., Kaelen, M., Giribaldi, B., Bloomfield, M., Pilling, S., Rickard, J. A., Forbes, B., Feilding, A., Taylor, D., Curran, H. V., & Nutt, D. J. (2018). Psilocybin with psychological support for treatment-resistant depression: Six-month follow-up. *Psychopharmacology*, *235*(2), 399–408. <https://doi.org/10.1007/s00213-017-4771-x>
- Chen, Y., Wang, J., Liang, Y., Sun, F., & Dong, X. (2018). Perceived stress and cognitive functions among Chinese older adults: The moderating role of health status. *Gerontology & Geriatric Medicine*, *4*, 1–8. <https://doi.org/10.1177/2333721418778390>
- Craighead, W. E., & Dunlop, B. W. (2014). Combination psychotherapy and antidepressant medication treatment for depression: For whom, when, and how. *Annual Review of Psychology*, *65*, 267–300. <https://doi.org/10.1146/annurev.psych.121208.131653>
- Crous-Bou, M., Minguillón, C., Gramunt, N., & Molinuevo, J. L. (2017). Alzheimer's disease prevention: From risk factors to early intervention. *Alzheimer's Research & Therapy*, *9*(1), 71. <https://doi.org/10.1186/s13195-017-0297-z>
- Cutler, D. M., & Lleras-Muney, A. (2010). Understanding differences in health behaviors by education. *Journal of Health Economics*, *29*(1), 1–28. <https://doi.org/10.1016/j.jhealeco.2009.10.003>
- Davis, A. K., Barrett, F. S., May, D. G., Cosimano, M. P., Sepeda, N. D., Johnson, M. W., Finan, P. H., & Griffiths, R. R. (2021). Effects of psilocybin-assisted therapy on major depressive disorder: A randomized clinical trial. *JAMA Psychiatry*, *78*(5), 481–489. <https://doi.org/10.1001/jamapsychiatry.2020.3285>
- Dfarhud, D., Malmir, M., & Khanahmadi, M. (2014). Happiness & health: The biological factors-systematic review article. *Iranian Journal of Public Health*, *43*(11), 1468–1477.
- Duong, S., Patel, T., & Chang, F. (2017). Dementia: What pharmacists need to know. *Canadian Pharmacists Journal*, *150*(2), 118–129. <https://doi.org/10.1177/1715163517690745>

- Ferrara, M., Mungai, F., & Starace, F. (2017). St John's wort (*Hypericum perforatum*)-induced psychosis: A case report. *Journal of Medical Case Reports*, *11*(1), 137. <https://doi.org/10.1186/s13256-017-1302-7>
- Glisky, E. L., Woolverton, C. B., McVeigh, K. S., & Grilli, M. D. (2022). Episodic memory and executive function are differentially affected by retests but similarly affected by age in a longitudinal study of normally-aging older adults. *Frontiers in Aging Neuroscience*, *14*, 863942. <https://doi.org/10.3389/fnagi.2022.863942>
- Goda, A., Shimura, T., Murata, S., Kodama, T., Nakano, H., & Ohsugi, H. (2020). Psychological and neurophysiological effects of robot assisted activity in elderly people with cognitive decline. *Gerontology & Geriatric Medicine*, *6*, 1–7. <https://doi.org/10.1177/2333721420969601>
- Gurok, M. G., Mermi, O., Kilic, F., Canan, F., & Kuloglu, M. (2014). Psychotic episode induced by St. John's wort (*Hypericum perforatum*): A case report. *Journal of Mood Disorders*, *4*(1), 38–40. <https://doi.org/10.5455/jmood.20131230123539>
- Hughes, M. L., Agrigoroaei, S., Jeon, M., Bruzzese, M., & Lachman, M. E. (2018). Change in cognitive performance from midlife into old age: Findings from the Midlife in the United States (MIDUS) study. *Journal of the International Neuropsychological Society*, *24*(8), 805–820. <https://doi.org/10.1017/S1355617718000425>
- Husain, M. I., Ledwos, N., Fellows, E., Baer, J., Rosenblat, J. D., Blumberger, D. M., Mulsant, B. H., & Castle, D. J. (2023). Serotonergic psychedelics for depression: What do we know about neurobiological mechanisms of action? *Frontiers in Psychiatry*, *13*, 1076459. <https://doi.org/10.3389/fpsy.2022.1076459>
- Kadriu, B., Greenwald, M., Henter, I. D., Gilbert, J. R., Kraus, C., Park, L. T., & Zarate, C. A. (2021). Ketamine and serotonergic psychedelics: Common mechanisms underlying the effects of rapid-acting antidepressants. *The International Journal of Neuropsychopharmacology*, *24*(1), 8–21. <https://doi.org/10.1093/ijnp/pyaa087>
- Krebs, T. S., & Johansen, P. Ø. (2013). Psychedelics and mental health: A population study. *PLoS One*, *8*(8), e63972. <https://doi.org/10.1371/journal.pone.0063972>
- Lachman, M. E., Agrigoroaei, S., Murphy, C., & Tun, P. A. (2010). Frequent cognitive activity compensates for education differences in episodic memory. *The American Journal of Geriatric Psychiatry*, *18*, 4–10. <https://doi.org/10.1097/JGP.0b013e3181ab8b62>
- Lachman, M. E., Agrigoroaei, S., Tun, P. A., & Weaver, S. L. (2014). Monitoring cognitive functioning: Psychometric properties of the brief test of adult cognition by telephone. *Assessment*, *21*(4), 404–417. <https://doi.org/10.1177/1073191113508807>
- Lallana, E. C., & Fadul, C. E. (2011). Toxicities of immunosuppressive treatment of autoimmune neurologic diseases. *Current Neuropharmacology*, *9*(3), 468–477. <https://doi.org/10.2174/157015911796557939>
- Lee, P. L., Hsiao, C. H., & Wang, C. L. (2013). Physical activity and memory complaints in middle-age Americans: Results from the MIDUS study. *American Journal of Alzheimer's Disease and Other Dementias*, *28*(6), 600–605. <https://doi.org/10.1177/1533317513494744>
- Magaraggia, I., Kuiperes, Z., & Schreiber, R. (2021). Improving cognitive functioning in major depressive disorder with psychedelics: A dimensional approach. *Neurobiology of Learning and Memory*, *183*, 107467. <https://doi.org/10.1016/j.nlm.2021.107467>
- Maharjan, R., Diaz Bustamante, L., Ghattas, K. N., Ilyas, S., Al-Refai, R., & Khan, S. (2020). Role of lifestyle in neuroplasticity and neurogenesis in an aging brain. *Cureus*, *12*(9), e10639. <https://doi.org/10.7759/cureus.10639>
- National Health Service (NHS). (2021). *Side effects—Antidepressants*. Retrieved August 7, 2023, from <https://www.nhs.uk/mental-health/talking-therapies-medicine-treatments/medicines-and-psychiatry/antidepressants/side-effects/>
- Niccoli, T., & Partridge, L. (2012). Ageing as a risk factor for disease. *Current Biology*, *22*(17), R741–R752. <https://doi.org/10.1016/j.cub.2012.07.024>
- Nichols, D. E. (2016). Psychedelics. *Pharmacological Reviews*, *68*(2), 264–355. <https://doi.org/10.1124/pr.115.011478>
- Nutt, D. J., Peill, J. M., Weiss, B., Godfrey, K., Carhart-Harris, R. L., & Erritzoe, D. (2023). Psilocybin and other classic psychedelics in depression. *Current Topics in Behavioral Neurosciences*. Advance online publication. https://doi.org/10.1007/7854_2023_451
- O'Sullivan, M., Brennan, S., Lawlor, B. A., Hannigan, C., Robertson, I. H., & Pertl, M. M. (2019). Cognitive functioning among cognitively intact dementia caregivers compared to matched self-selected and population controls. *Aging & Mental Health*, *23*(5), 566–573. <https://doi.org/10.1080/13607863.2018.1428937>
- Pallardy, R. (2022). *Albert Hofmann*. Retrieved August 7, 2023, from <https://www.britannica.com/biography/Albert-Hofmann>
- Psiuk, D., Nowak, E., Cholewa, K., Łopuszańska, U., & Samardakiewicz, M. (2021). The potential role of serotonergic hallucinogens in depression treatment. *Life*, *11*(8), 765. <https://doi.org/10.3390/life11080765>
- Rahman, M. M., Rana, R., & Khanam, R. (2022). Determinants of life expectancy in most polluted countries: Exploring the effect of environmental degradation. *PLoS One*, *17*(1), e0262802. <https://doi.org/10.1371/journal.pone.0262802>
- Raison, C. L., Sanacora, G., Woolley, J., Heinzerling, K., Dunlop, B. W., Brown, R. T., Kakar, R., Hassman, M., Trivedi, R. P., Robison, R., Gukasyan, N., Nayak, S. M., Hu, X., O'Donnell, K. C., Kelmendi, B., Sloschower, J., Penn, A. D., Bradley, E., Kelly, D. F., . . . Griffiths, R. R. (2023). Single-dose psilocybin treatment for major depressive disorder: A randomized clinical trial. *JAMA: Journal of the American Medical Association*, *330*(9), 843–853. <https://doi.org/10.1001/jama.2023.14530>
- Rocca, W. A., Petersen, R. C., Knopman, D. S., Hebert, L. E., Evans, D. A., Hall, K. S., Gao, S., Unverzagt, F. W., Langa, K. M., Larson, E. B., & White, L. R. (2011). Trends in the incidence and prevalence of Alzheimer's disease, dementia, and cognitive impairment in the United States. *Alzheimer's & Dementia*, *7*(1), 80–93. <https://doi.org/10.1016/j.jalz.2010.11.002>
- Roth, D. L., Fredman, L., & Haley, W. E. (2015). Informal caregiving and its impact on health: A reappraisal from population-based studies. *The Gerontologist*, *55*(2), 309–319. <https://doi.org/10.1093/geront/gnu177>
- Ruiz, R., & Kirk, A. D. (2015). Long-term toxicity of immunosuppressive therapy. In R. W. Busuttil & G. B. G. Klintmalm (Eds.), *Transplantation of the liver* (3rd ed.,

- pp. 1354–1363). Elsevier. <https://doi.org/10.1016/B978-1-4557-0268-8.00097-X>
- Saxon, S. V., Etten, M. J., & Perkins, E. A. (2014). *Physical change and aging: A guide for the helping professions* (6th ed., p. 85). Springer.
- Simonsson, O., Osika, W., Carhart-Harris, R., & Hendricks, P. S. (2021). Associations between lifetime classic psychedelic use and cardiometabolic diseases. *Scientific Reports*, *11*(1), 14427. <https://doi.org/10.1038/s41598-021-93787-4>
- Surr, C. A., Gates, C., Irving, D., Oyeboode, J., Smith, S. J., Parveen, S., Drury, M., & Dennison, A. (2017). Effective dementia education and training for the health and social care workforce: A systematic review of the literature. *Review of Educational Research*, *87*(5), 966–1002. <https://doi.org/10.3102/0034654317723305>
- The University of Queensland. (2017). *What are neurotransmitters?* Retrieved August 7, 2023, from <https://qbi.uq.edu.au/brain/brain-physiology/what-are-neurotransmitters>
- The University of Queensland. (2018). *What is synaptic plasticity?* Retrieved August 7, 2023, from <https://qbi.uq.edu.au/brain-basics/brain/brain-physiology/what-synaptic-plasticity>
- The University of Queensland. (2021). *What is neurogenesis?* Retrieved August 7, 2023, from <https://qbi.uq.edu.au/brain-basics/brain-physiology/what-neurogenesis>
- Tupper, K. W., Wood, E., Yensen, R., & Johnson, M. W. (2015). Psychedelic medicine: A re-emerging therapeutic paradigm. *CMAJ: Canadian Medical Association Journal*, *187*(14), 1054–1059. <https://doi.org/10.1503/cmaj.141124>
- Vann Jones, S. A., & O’Kelly, A. (2020). Psychedelics as a treatment for Alzheimer’s disease dementia. *Frontiers in Synaptic Neuroscience*, *12*, 34. <https://doi.org/10.3389/fnsyn.2020.00034>
- Vollenweider, F. X., & Preller, K. H. (2020). Psychedelic drugs: Neurobiology and potential for treatment of psychiatric disorders. *Nature Reviews. Neuroscience*, *21*(11), 611–624. <https://doi.org/10.1038/s41583-020-0367-2>
- Watson, S. (2021). *Serotonin: The natural mood booster*. Retrieved August 7, 2023, from <https://www.health.harvard.edu/mind-and-mood/serotonin-the-natural-mood-booster>
- Webb, A., & Cranswick, N. (2003). Fluoxetine induced auditory hallucinations in an adolescent. *Journal of Pediatrics and Child Health*, *39*(8), 637–638. <https://doi.org/10.1046/j.1440-1754.2003.00254.x>
- Wolinsky, D., Barrett, F. S., & Vandrey, R. (2024). The psychedelic effects of cannabis: A review of the literature. *Journal of psychopharmacology (Oxford, England)*, *38*(1), 49–55. <https://doi.org/10.1177/02698811231209194>
- Yehuda, R., & Lehrner, A. (2023). Psychedelic therapy—A new paradigm of care for mental health. *JAMA: Journal of the American Medical Association*, *330*(9), 813–814. <https://doi.org/10.1001/jama.2023.12900>
- Zhang, F., & Jiang, L. (2015). Neuroinflammation in Alzheimer’s disease. *Neuropsychiatric Disease and Treatment*, *11*, 243–256. <https://doi.org/10.2147/NDT.S75546>
- Zhang, W., Liu, S., & Wu, B. (2018). Defining successful aging: Perceptions from elderly Chinese in Hawai’i. *Gerontology & Geriatric Medicine*, *4*, 2333721418778182. <https://doi.org/10.1177/2333721418778182>
- Zheng, L., Li, G., Gao, D., Wang, S., Meng, X., Wang, C., Yuan, H., & Chen, L. (2020). Cognitive frailty as a predictor of dementia among older adults: A systematic review and meta-analysis. *Archives of Gerontology and Geriatrics*, *87*, 103997. <https://doi.org/10.1016/j.archger.2019.103997>