



The Potential Role of Psychedelic Therapy in Alzheimer's Dementia

Madeline Jones, PA-S



Background

Alzheimer's disease (AD) is the most common cause of cognitive impairment or dementia in people 65 years and older, currently with no disease-modifying treatment options.¹

Purpose

To explore the role that psychedelic therapy, specifically psilocybin and lysergic acid diethylamide (LSD), could play in the prevention and treatment of AD. This research aims to determine the effects of psychedelics on neurodegenerative and neuropsychiatric conditions and relate their outcomes to the pathophysiology of AD.

PICOT

In patients with Alzheimer's dementia, does psychedelic therapy promote positive disease modification and improvement of symptoms compared to current medication options?

Design & Methods

- Keywords:** psychedelic therapy, LSD, psilocybin, Alzheimer's Disease, AD, dementia, neuroinflammation, neuroplasticity
- Inclusion:** over 18, published in the past 5 years, direct effects of psychedelic therapy on receptors in the brain, secondary effects on mood and cognition
- Exclusion:** previous recreational psychedelic drug use, psychedelic drug use within 5 years, publications over five years, studies with patients under the age of 18.

Summary of Evidence Search

Database	Yielded	Reviewed	Included
Cochrane Library	223	10	1
Google Scholar	2,260	32	4
PubMed	541	17	2
Medline via EBSCO	85	13	1
PsycInfo	18	3	1
Total:	3,127	75	9

Synthesis of Evidence

Level of Evidence	Included in Analysis
Meta-analysis	1
Systematic Review	3
Randomized Control Trial	3
Open-label pilot study	1

- ❖ The efficacy of psychedelic therapy was then determined based on neuroplastic changes determined by positron emission testing and functional magnetic resonance imaging.
- ❖ Further benefits were explored including cognitive and psychiatric behavioral improvement.

Results:

Primary Outcomes

- Disease-modifying effects: Lasting neuroplastic changes
- ❖ Psilocybin increases global brain glucose metabolism, primarily in the frontal and medial temporal cortex.³
 - ❖ Increased global functional brain connectivity a month after psilocybin administration.⁶
 - ❖ Increased functional connectivity in areas with high concentrations of 5HT2A receptors, suggesting their ability to reorganize dysfunctional circuits.^{3, 4}

Secondary Outcomes

- Symptomatic effects:
- ❖ Anti-inflammatory effects may be therapeutically applicable.²
 - ❖ Improved mood and cognition in relation to cognitive decline associated with AD.²
 - ❖ Higher mean global positive change score of the Persisting Effects Questionnaire (PEQ) four months after psilocybin administration.⁷
 - ❖ LSD increased Rey-Osterrieth Complex Figure (ROCF) immediate recall points ($p = 0.044$) and percentage ($p = 0.018$), demonstrating improved spontaneous visuospatial memory encoding and recall.⁸
 - ❖ Increased Object-Location Memory Task (OLMT) consolidation in the LSD group ($p = 0.022$), showing improved memory consolidation overnight compared to recall before drug administration.⁸

Discussion:

- ❖ Lasting neuroplastic changes that were found suggest neuroprotection and cognitive enhancement in prodromal AD. The increased brain glucose metabolism is encouraging in relation to the pathophysiology of AD.
- ❖ Increased global functional brain connectivity found on fMRI a month after administration of psilocybin promotes the theory that psychedelic therapy stimulates neuroplasticity that can last a prolonged period.
- ❖ Improvement of mood and cognition found in older adults who used psilocybin demonstrates that psychedelics may have a role of symptomatic treatment in AD.

Limitations/Further study:

More studies are needed to directly assess the effects of psychedelic therapy on patients with diagnosed AD as well as studies with larger population groups in order to further conclude how effective psychedelic treatment can be. Studies currently in the works include research through Johns Hopkins which is looking at the efficacy of psychedelic therapy for various conditions such as opioid addiction and AD.⁹

Conclusion:

Results are consistent with the hypothesis that psychedelic therapy can not only help symptomatic treatment of AD but may also have a role in disease modification and there are proven positive neurologic benefits to psychedelic therapy that suggest a role in the treatment and management of AD

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