The Effects of Psilocybin and LSD on Anxiety Associated with Life-Threatening Illnesses

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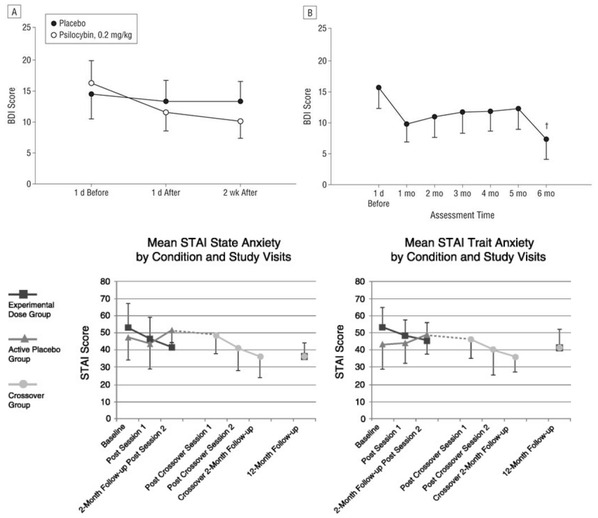
Introduction/Background

"Psychedelics", a class of hallucinogens, is derived from the Greek words meaning "soul-manifesting". Though historically reserved for cultural, spiritual, and recreational uses, the role of psychedelic drugs in psychotherapy has long been one of interest. Once a popular topic of research from the 1950's to the 1970's, the debate about the potential use of psychedelics in patient care has recently been reignited by the acceptance of medical marijuana. Similarly, another topic of growing awareness is palliative care, shifting the focus toward improving the quality of life and psycho-spiritual health in end-of-life patients. In this systematic review, we analyzed currently available research on the benefits, adverse effects, and potential use of psychedelics, specifically LSD and psilocybin, in the treatment of patients with life-threatening diseases, such as advanced-stage cancer or Parkinson's disease.

Psychedelics are psychoactive substances with strong dissociative and hallucinogenic effects. LSD exerts serotoninergic effects by activation of 5HT-2A, which primarily causes hallucinogenic activity, as well as significant modulation of 5HT-1A/5HT-2C receptors. Similarly, psilocybin is a selective agonist of 5HT-1A, 5HT-2A, and 5HT-2C receptors. It is found naturally in certain mushrooms and causes effects similar to, but less intense than LSD.



Outcomes of LSD in patients with life-threatening diseases

PICO

P= Anxious patients with severe, life-threatening diseases
I= Psychedelic drugs, specifically LSD and Psilocybin
C= Compared to Placebo
O= Subjective improvement in mood and psycho-spiritual well-being

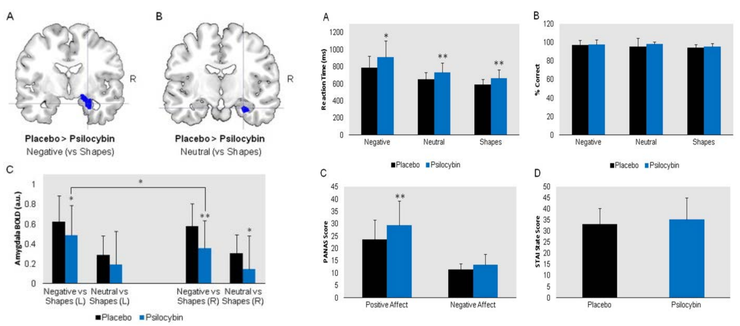
Methods

A literature search was conducted with the NCBI PubMed database using the search terms: Psilocybin, LSD, anxiety, and end-of-life. Additional filters include clinical trials only and English language. Of the 12 articles that met the search criteria, five were deemed most relevant, as they included patients with life-threatening illnesses and healthy patients with a wide range of ages.

Results

Reference	Study Design	Internal/External/Ecological Validity	Significance
Gasser et al. (2014)	Phase 2 double-blind, active placebo-controlled, randomized clinical trial	Procedure bias: 100% of control group participants were able to guess correctly that they were given the active placebo	For STAI trait and state, differences between the groups after treatment yielded p=0.033 (ES=1.1) and p=0. 021 (ES=1.2), respectively
Grob et al. (2011)	Pilot study, randomized, double-blind, placebo-controlled, cross-over design	Selection bias: all subjects had volunteered themselves, and 8/12 subjects had previous hallucinogen experience	BDI dropped by almost 30% from the first session to 1 month after second session (t11=−2.17, p=0.05), continuing for 6m (t7=2.71, p=0.03)
Schmid et al. (2014)	Phase 2, randomized, double-blind, placebo-controlled	Observer-expectancy bias: Despite placebo, therapists could guess correctly whether LSD or placebo had been given	Increased in many categories, most significantly "oceanic boundlessness" [F1,15=92.3, p<.001] and "experience of unity" [F1,15=60.2, p<0.001]
Kraehenmann et al. (2014)	Randomized, double-blind, placebo-controlled, cross-over design	Low ecological validity: subjects were placed in fMRI scans for assessment of the brain's blood-oxygen level	Psilocybin significantly increased positive affect (p=0.001) but not negative affect (p=0.87) or state anxiety (p=0.37). Observed effects lateralized to the right brain (p<0.05)
Griffiths et al. (2011)	Double-blind, between group, crossover design	Aptitude-treatment interaction: most volunteers were college grads reporting weekly spiritual/ religious activity	At 14 months follow-up, 94.4% of subjects rated the experience to be among their top 5 most meaningful and spiritually significant

Studies on the effects of psilocybin and LSD on anxiety in patients with life-threatening illnesses were chosen based on the evaluation of their safety and efficacy. Other sources on the effects of psilocybin and LSD on healthy subjects were cited in order to further illuminate the potential effects and side effects of these substances. Finally, the remaining source further answered the question of the usefulness of LSD in translational psychiatric research.



Questionnaire Items	1 Month after Sessions Psilocybin Dose (mg/70 kg) 0‡	5‡	10‡	20‡	30‡	20 or 30‡	14 Month Follow-up (20 or 30 mg/70 kg)‡‡
How personally meaningful was the experience?							
Single most meaningful experience of life	0.0	0.0	5.6	16.7	**33.3**	**44.4**	**38.9**
Top 5 most meaningful, including single most	0.0	11.1	**33.3**	**77.8**	**61.1**	**77.8**	**94.4**
How spiritually significant was the experience?							
Single most spiritually significant experience of life	0.0	0.0	5.6	**27.8**	**44.4**	**61.1**	**44.4**
Top 5 most spiritually significant, including single most	11.1	11.1	**44.4**	**66.7**	**77.8**	**83.3**	**94.4**
Did the experience change your sense of well-being or life satisfaction?							
Increased well-being/life satisfaction (very much)	5.6	**27.8**	**38.9**	**72.2**	**55.6**	**77.8**	**61.1**
Increased well-being/life satisfaction (moderately or very much)	38.9	55.6	**72.2**	**83.3**	**88.9**	**94.4**	**83.3**
Your behavior changed in ways you would consider positive since the experience.							
Positive behavioral change (strong or extreme)	22.2	16.7	**50.0**	38.9	**55.6**	**55.6**	**44.4**
Positive behavioral change (moderate, strong or extreme)	33.3	50.0	61.1	61.1	**88.9**	**88.9**	88.9

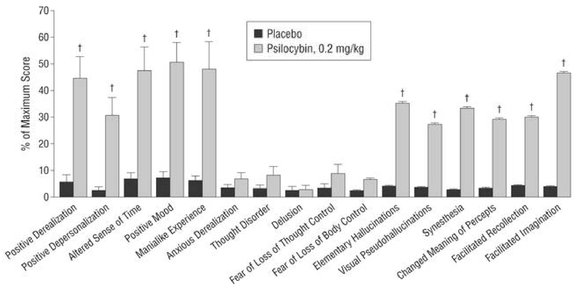
Conclusions

Psilocybin and LSD, since the 1950s, have attracted considerable attention as potential treatments in psychiatric therapy. From the 1950s to 1970s they showed promise in the treatment of multiple psychological disorders. Recently, the interest has been rekindled and new studies have preliminarily shown them to be effective in improving mood in both patients with serious diseases as well as healthy individuals.

These drugs are also well-known to have serious adverse side effects in many cases of recreational use. Even in a controlled, therapeutic setting they frequently can cause hypertension and induce fear, for example. These side effects in most cases go away after the effects of the drugs wear off. Nonetheless, they are significant and important to minimize. Through these studies, researchers have come closer to finding the "sweet spot" in dosing these drugs, further maximizing their positive effects on mood, while minimizing their negative effects.

With this in mind, the results of these pilot studies are promising. In a clinically controlled setting, both psilocybin and LSD are reasonably safe and efficacious in treating anxiety in seriously ill patients. Participants received significant, long-lasting benefits with primarily mild to moderate, short-lasting side effects. This outcome warrants further research into psilocybin and LSD as treatments for anxiety in patients with life-threatening illnesses.

Two larger studies exploring the effects of psilocybin on anxiety in cancer patients are currently ongoing at NYU and Johns Hopkins. The outcomes of these trials will be important in further elucidating this question.



A Word of Caution: The use of hallucinogens is not without serious side effects. In Griffiths et al, during the largest dosage session, four subjects reached hypertensive crisis, and almost half the subjects experienced extreme fear and paranoia despite being carefully screened and prepared before sessions, and closely monitored during the experiment. The purpose of this literature review is to elucidate the potential benefits of hallucinogens in patients with advanced diseases when administered in a controlled setting under the surveillance of a knowledgeable physician, rather than to encourage recreational use.