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ORIGINAL INVESTIGATION

Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance

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Abstract
Rationale Although psilocybin has been used for centuries for religious purposes, little is known scientifically about its acute and persisting effects.
Objectives This double-blind study evaluated the acute and longer-term psychological effects of a high dose of psilocybin relative to a comparison compound administered under comfortable, supportive conditions.
Materials and methods The participants were hallucinogen-naïve adults reporting regular participation in religious or spiritual activities. Two or three sessions were conducted at 2-month intervals. Thirty volunteers received orally administered psilocybin (30 mg/70 kg) and methylphenidate hydrochloride (40 mg/70 kg) in counterbalanced order. To obscure the study design, six additional volunteers received methylphenidate in the first two sessions and unblinded psilocybin in a third session. The 8-h sessions were conducted individually. Volunteers were encouraged to close their eyes and direct their attention inward. Study monitors rated volunteers' behavior during sessions. Volunteers completed questionnaires assessing drug effects and mystical experience immediately after and 2 months after sessions. Community observers rated changes in the volunteer's attitudes and behavior.
Results Psilocybin produced a range of acute perceptual changes, subjective experiences, and labile moods including anxiety. Psilocybin also increased measures of mystical experience. At 2 months, the volunteers rated the psilocybin experience as having substantial personal meaning and spiritual significance and attributed to the experience sustained positive changes in attitudes and behavior consistent with changes rated by community observers.
Conclusions When administered under supportive conditions, psilocybin occasioned experiences similar to spontaneously occurring mystical experiences. The ability to occasion such experiences prospectively will allow rigorous scientific investigations of their causes and consequences.

Keywords Psilocybin · Methylphenidate · Hallucinogen · Entheogen · Mystical experience · Spiritual · Religion · Anxiety · Humans

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Introduction

Psilocybin, a naturally occurring tryptamine alkaloid with actions mediated primarily at serotonin 5-$HT_{2A/C}$ receptor sites, is the principal psychoactive component of a genus of

mushrooms (*Psilocybe*) (Presti and Nichols 2004). Psilocybin, in the form of these mushrooms, has been used for centuries, possibly millennia, within some cultures in structured manners for divinatory or religious purposes (Wasson 1980; Stamets 1996; Metzner 2004). The psychological effects of psilocybin, which are similar to other classical serotonergically mediated hallucinogens [lysergic acid diethylamide (LSD), mescaline, and *N*,*N*-dimethyltryptamine (DMT)], include significant alterations in perceptual, cognitive, affective, volitional, and somatesthetic functions, including visual and auditory sensory changes, difficulty in thinking, mood fluctuations, and dissociative phenomena (Isbell 1959; Wolbach et al. 1962; Rosenberg et al. 1964).

Early clinical research with psilocybin in the 1950s and early 1960s attempted to study the effects of psilocybin without recognition of the powerful influences of set and setting (e.g., Isbell 1959; Hollister 1961; Malitz et al. 1960; Rinkel et al. 1960). Subsequent research, which included more preparation and interpersonal support during the period of drug action, found fewer adverse psychological effects, such as panic reactions and paranoid episodes, and increased reports of positively valued experiences (Leary et al. 1963; Metzner et al. 1965; Pahnke 1969). In response to the epidemic of hallucinogen abuse that occurred in the 1960s, clinical research with psilocybin and other hallucinogens largely ceased and has resumed only recently. Notably, Vollenweider and colleagues from Switzerland and Gouzoulis-Mayfrank from Germany have reported a series of studies that have characterized the acute subjective, physiological, and perceptual effects of psilocybin (e.g., Vollenweider et al. 1998; Gouzoulis-Mayfrank et al. 1999; Hasler et al. 2004; Carter et al. 2005).

In the present study, we sought to use rigorous double-blind clinical pharmacology methods to evaluate both the acute (7 h) and longer-term (2 months) mood-altering and psychological effects of psilocybin (30 mg/70 kg) relative to an active comparison compound (40 mg/70 kg methylphenidate). The study was conducted with 36 well-educated, hallucinogen-naïve volunteers.

Materials and methods

Participants

The participants were recruited from the local community through flyers announcing a "study of states of consciousness brought about by a naturally occurring psychoactive substance used sacramentally in some cultures." There were 135 individuals screened over the telephone and 54 were further screened in person. The 36 study participants (14 males) were medically and psychiatrically healthy, without histories of hallucinogen use, and without family histories of schizophrenia or other psychotic disorders or bipolar I or II disorder. The participants had an average age of 46 years (range 24 to 64) and were well educated; 97% (35 volunteers) were college graduates and 56% (20 volunteers) had post-graduate degrees. Eighty-three percent (30 volunteers) were employed full time, with the remainder employed part time. Fifty-three percent (19 volunteers) indicated affiliation with a religious or spiritual community, such as a church, synagogue, or meditation group. All 36 volunteers indicated at least intermittent participation in religious or spiritual activities such as religious services, prayer, meditation, church choir, or educational or discussion groups, with 56% (20 volunteers) reporting daily activities and an additional 39% (14 volunteers) reporting at least monthly activities. The volunteers did not receive monetary compensation for participation. Although most volunteers had very busy personal and professional schedules, they were interested in the study and made participation a priority. Based on interviews, their motivation for participation was curiosity about the effects of psilocybin and the opportunity for extensive self-reflection in the context of both the day-long drug sessions and the meetings with the monitors that occurred between sessions. The Institutional Review Board of the Johns Hopkins University School of Medicine approved the study, and all volunteers gave their informed consent before participation.

Study design

The study compared psilocybin (30 mg/70 kg) and methylphenidate hydrochloride (40 mg/70 kg) using a double-blind between-group, crossover design that involved two or three 8-h drug sessions conducted at 2-month intervals. Thirty-six volunteers were randomly assigned to receive either two sessions (N=30) or three sessions (N=6). The group of 30 volunteers were then randomly assigned to receive psilocybin or methylphenidate on the first session (15 per group), with the alternative drug administered on the second session. The other six volunteers received methylphenidate on the first two sessions and unblinded psilocybin on the third session. The purpose of this condition was primarily to obscure the study design to the participants and monitors (see "Expectancy" section), and data from the six participants were not used in the statistical analyses; however, those data were generally consistent with the results described in this report. Outcome measures obtained throughout the drug sessions included blood pressure and monitor ratings of participant mood and behavior. At about 7 h after drug ingestion (when the primary drug effects had subsided), the participants completed several questionnaires designed to assess various aspects of hallucinogen experience

(described below). The longitudinal measures assessed before and 2 months after each drug session included measures of psychiatric symptoms, personality measures, quality of life, and lifetime mystical experiences. A 1-year follow-up assessment is still underway.

Drug conditions

Psilocybin and methylphenidate were administered in identically appearing opaque, size 0 gelatin capsules with approximately 180 ml water. The dose of psilocybin (30 mg/70 kg) was selected as a high safe dose based on non-blind (Malitz et al. 1960; Metzner et al. 1965; Leuner 1981) and blind (Pahnke 1963, 1969) studies conducted with hallucinogen-naïve individuals in the 1950s–1960s. The methylphenidate dose (40 mg/70 kg) was selected for the comparison condition because it is a high, discriminable but safe dose, it has an onset and duration of subjective effects similar to psilocybin, and it produces some subjective effects (e.g., excitability, nervousness, and/or increased positive mood) overlapping with those of psilocybin (Chait 1994; Rush et al. 1998; Kollins et al. 1998).

Meetings with monitor before and after sessions

The primary monitor met with each participant on four occasions before his or her first session (for 8 h total) and on four occasions (for 4 h total) after each session. A major purpose of the participant-monitor meetings was to develop and maintain rapport and trust, which is believed to minimize the risk of adverse reactions to psilocybin (Metzner et al. 1965). During these meetings, the participant's life history and current life circumstances were reviewed. The preparation of participants by the monitors explicitly included the monitor's expectation that the drug session experiences could increase personal awareness and insight, however, avoided even mention of the criteria used to assess mystical experiences. A male clinical psychologist (W.R.) with extensive prior experience monitoring hallucinogen sessions and a female clinically trained social worker (M.C.) served as primary and assistant monitors, respectively, for all study participants.

Drug sessions

The participants were instructed to consume a low-fat breakfast before reporting to the research unit at 0800 hours, about 1 h before drug administration. A urine sample was taken to verify drug-free status, and the participants were encouraged to relax and reflect before drug administration. The 8-h drug sessions were conducted in an aesthetic living-room-like environment designed specifically for the study. Two monitors were present with a single participant throughout the session. For most of the time during the session, the participant was encouraged to lie down on the couch, use an eye mask to block external visual distraction, and use headphones through which a classical music program was played. The same music program was played for all participants in all sessions. The participants were encouraged to focus their attention on their inner experiences throughout the session. If a participant reported significant fear or anxiety, the monitors provided reassurance verbally or physically (e.g., with a supportive touch to the hand or shoulder). The sessions were videotaped and about 25% were reviewed by the first author to verify session procedures.

Expectancy

It is widely believed that expectancy plays a large role in the qualitative effects of hallucinogens (Metzner et al. 1965). Some expectancy effects are unavoidable because it would be unethical not to inform both the participants and the session monitors about the range of possible effects with hallucinogens. In addition, it is believed by many that ethical hallucinogen administration requires that sessions be monitored by individuals who are familiar with such altered states of consciousness (Masters and Houston 1966; Roberts 2001; Stolaroff 2001). Thus, the beliefs of the session monitors introduce another source of expectancy. While it was not possible to completely eliminate such expectancy effects, it was possible to significantly reduce such effects by studying participants without personal histories of hallucinogen use, by studying only a single participant at a time, and by using an experimental design and instructional sets that provided the expectation that sessions could involve not only the administration of a wide range of psilocybin doses but also a range of novel drugs, some of which could produce effects that overlap with those produced by psilocybin. Expectancy effects were also reduced because the experimental design was further obscured from both participants and monitors, who were not aware of which or how many participants would have a final unblinded psilocybin session (see "Instructions to participants and monitors").

Instructions to participants and monitors

The participants and monitors were informed that the participants would have either two or three sessions and that, in at least one session, they would receive a moderate or high dose of psilocybin. They were informed that an inactive placebo, a low dose of psilocybin or various doses of 11 other drugs that could produce various effects (dextromethorphan, nicotine, diphenhydramine, caffeine, methylphenidate, amphetamine, codeine, alprazolam, diazepam, triazolam, or secobarbital), could be administered in

sessions in which a moderate or high dose of psilocybin was not administered. After data collection 2 months after the second session, the six participants who received methylphenidate on the first and second session were informed that they would have a third session that would involve administration of a moderate or high dose of psilocybin. These six sessions were the only unblinded sessions. To help focus the participants on their experiences during the sessions, they were not asked to guess whether or not they received psilocybin. However, the monitors completed a rating form which recorded their guesses about the contents of capsules approximately 7 h after capsule administration but before the participant completed detailed questionnaires describing his or her experiences. The participants were given no information about these or any other monitor ratings.

Measures assessed throughout the session

Ten minutes before and 30, 60, 90, 120, 180, 240, 300, and 360 min after capsule administration, monitor ratings, blood pressure, and heart rate were obtained.

Blood pressure and heart rate Blood pressure (systolic, diastolic, and mean arterial pressure using oscillometric method with the blood pressure cuff placed on the arm) and heart rate were monitored using a Non-Invasive Patient Monitor Model 507E (Criticare Systems, Waukesha, WI, USA).

Monitor rating questionnaire At the same time-points at which the physiological measures were taken, the two session monitors completed the Monitor Rating Questionnaire, which involved rating or scoring 20 dimensions of the participant's behavior or mood (Table 1). The dimensions expressed as peak scores in Table 1 were rated on a five-point scale from 0 to 4. The dimensions expressed as total duration in Table 1 were rated as the estimated number of minutes since the last rating. The data were the mean of the two monitor ratings at each time-point.

Measures assessed 7 h after drug administration

At about 7 h after capsule administration, when the major drug effects had subsided, the participants completed three empirically derived (i.e., via factor analysis) questionnaires assessing subjective drug effects and two questionnaires assessing mystical experience, as described below. The participants typically completed these questionnaires in about 40 min.

Hallucinogen rating scale This 99-item questionnaire, which was designed to show sensitivity to the hallucinogen *N*,*N*-dimethyltryptamine (Strassman et al. 1994; Riba et al. 2001), consists of six subscales assessing various aspects of hallucinogen effects (intensity, somaesthesia, affect, perception, cognition, and volition).

APZ The APZ is a 72-item yes/no questionnaire designed to assess altered states of consciousness induced by drug (e.g., DMT or psilocybin) or non-drug (e.g., perceptual deprivation, hypnosis, and sensory overload) manipulations (Dittrich 1998). The three major scales on the APZ are the OSE (oceanic boundlessness, a state common to classic mystical experiences including feelings of unity and transcendence of time and space), the AIA (dread of ego dissolution, dysphoric feelings similar to those of some "bad trips" described by hallucinogen users), and the VUS (visionary restructuralization, which includes items on visual pseudo-hallucinations, illusions, and synesthesias). The data on each scale were expressed as a proportion of the maximum possible score.

Addiction research center inventory (ARCI) The ARCI was developed to differentiate subjective effects among several classes of psychoactive drugs including hallucinogens (Haertzen 1966). The short form of the ARCI consists of 49 true/false questions and contains five major scales: lysergic acid diethylamide (LSD, a hallucinogen-sensitive scale that is often interpreted as providing a measure of dysphoric changes); pentobarbital, chlorpromazine, and alcohol group (PCAG, a sedative sensitive scale); benzedrine group (BG); amphetamine (A) scales (amphetamine-sensitive scales); and morphine-benzedrine group (MBG, often interpreted as a measure of euphoria) (Martin et al. 1971; Jasinski 1977). The participants were instructed to answer the questions on the ARCI with reference to the effects they experienced after they received the capsules that morning.

States of consciousness questionnaire This 100-item questionnaire is rated on a six-point scale [0=none, not at all; 1=so slight, cannot decide; 2=slight; 3=moderate; 4=strong (equivalent in degree to any previous strong experience or expectation of this description); and 5=extreme (more than ever before in my life and stronger than 4)]. Forty-three items on this questionnaire comprised the current version of the Pahnke–Richards Mystical Experience Questionnaire (Pahnke 1969; Richards 1975), which was designed to assess mystical experiences, used as a primary outcome measure in the Good Friday Experiment (Pahnke 1963; Doblin 1991), and has been shown to be sensitive to other hallucinogens (Turek et al. 1974; Richards et al. 1977). This questionnaire is based on the classic descriptive work on mystical experiences and the psychology of religion by Stace (1960), and it provides scale scores for each of seven

domains of mystical experiences: internal unity (pure awareness; a merging with ultimate reality); external unity (unity of all things; all things are alive; all is one); transcendence of time and space; ineffability and paradoxicality (claim of difficulty in describing the experience in words); sense of sacredness (awe); noetic quality (claim of intuitive knowledge of ultimate reality); and deeply felt positive mood (joy, peace, and love). The specific items in each of the scales of the Pahnke–Richards Mystical Experience Questionnaire are available online as Electronic Supplementary Material, Table 1. The data on each scale were expressed as a proportion of the maximum possible score. Based on prior research (Pahnke 1969), the criteria for designating a volunteer as having had a "complete" mystical experience were that the scores on each of the following scales had to be at least 0.6: unity (either internal or external, whichever was greater), transcendence of time and space, ineffability, sense of sacredness, noetic quality, and positive mood. The remaining 57 items in the questionnaire served as distracter items.

Mysticism scale This 32-item questionnaire was developed to assess primary mystical experiences (Hood et al. 2001; Spilka et al. 2005). The Mysticism Scale has been extensively studied, demonstrates cross-cultural generalizability, and is well regarded in the field of the psychology of religion (Hood et al. 2001; Spilka et al. 2005) but has not previously been used to assess changes after a drug experience. A total score and three empirically derived factors are measured: interpretation (corresponding to three mystical dimensions described by Stace (1960): noetic quality, deeply felt positive mood, and sacredness); introvertive mysticism (corresponding to the Stace dimensions of internal unity, transcendence of time and space, and ineffability); and extrovertive mysticism (corresponding to the dimension of the unity of all things/all things are alive). The items were rated on a nine-point scale (−4=this description is extremely not true of my own experience or experiences; 0=I cannot decide; and +4=this description is extremely true of my own experience or experiences). For the version of the questionnaire used 7 h after drug administration, the participants were instructed to complete the questionnaire with reference to their experiences after they received the capsules that morning.

Measures assessed 2 months post-session

At 7 to 8 weeks after each session and before any additional session, the participants returned to the research facility and completed a series of questionnaires to assess possible persisting changes in attitudes, mood, or behavior as well as possible changes in standardized measures of personality, mood, and spirituality. The participants typically completed these questionnaires in about 75 min.

At about this same time, community observer ratings of participants' attitudes and behavior were obtained by telephone. The outcome measures at this time-point are described below.

Persisting Effects Questionnaire This 89-item questionnaire sought information about changes in attitudes, moods, behavior, and spiritual experience that, on the basis of prior research (Pahnke 1963, 1969; Doblin 1991; Richards et al. 1977), would possibly be sensitive to the effects of psilocybin 2 months after the session. Eighty-six of the items were rated on a six-point scale (0=none, not at all; 1=so slight, cannot decide; 2=slight; 3=moderate; 4=strong; and 5=extreme, more than ever before in your life and stronger than 4). Sixty-six of the items were from Pahnke (1963, 1969) and 20 items were new. For purposes of summarizing the results before data analysis, 61 of the 86 items were judged as likely to be unambiguously divided into six categories: positive attitudes about life and/or self, negative attitudes about life and/or self, positive mood changes, negative mood changes, altruistic/positive social effects, and antisocial/negative social effects. Six raters independently sorted the 61 items into the six categories. Three items were excluded because fewer than five of the six raters agreed on the categories. For the remaining 58 items, at least five of the six raters agreed with the assignment of each item to each category, suggesting the appropriateness of the category descriptors. The category descriptors and the number of items associated with each category were: positive attitudes about life and/or self (17 items), negative attitudes about life and/or self (17 items), positive mood changes (four items), negative mood changes (four items), altruistic/positive social effects (eight items), and antisocial/negative social effects (eight items). Two additional categories were comprised of one item each: positive behavior change and negative behavior change. For scoring purposes, the eight category scores based on a total of 60 items were expressed as the percentage of the maximum possible score. The items in each of the categories of the Persisting Effects Questionnaire are available online as electronic supplementary material, Table 2. The remaining 23 items in the questionnaire that did not readily fit into the categories predominately reflected aspects of spirituality and mystical experience; these domains were characterized by other outcome measures.

The questionnaire also included these three questions: (1) How personally meaningful was the experience (rated 1= no more than routine, everyday experiences; 2= similar to meaningful experiences that occur on average once or more a week; 3=similar to meaningful experiences that

occur on average once a month; 4=similar to meaningful experiences that occur on average once a year; 5=similar to meaningful experiences that occur on average once every 5 years; 6=among the 10 most meaningful experiences of my life; 7=among the 5 most meaningful experiences of my life; and 8=the single most meaningful experience of my life)? (2) Indicate the degree to which the experience was spiritually significant to you (rated 1=not at all, 2=slightly, 3=moderately, 4=very much, 5=among the 5 most spiritually significant experiences of my life, and 6=the single most spiritually significant experience of my life). (3) Do you believe that the experience and your contemplation of that experience have led to change in your current sense of personal well-being or life satisfaction (rated +3=increased very much, +2=increased moderately, +1=increased slightly, 0=no change, −1=decreased slightly, −2=decreased moderately, and −3=decreased very much)?

This questionnaire was developed after the initiation of the study and was completed by all 24 of the 30 participants who thereafter received psilocybin and methylphenidate in counterbalanced order in the first two sessions (12 participants in each of the two drug orders).

Mysticism Scale-Lifetime The Lifetime version of this previously described questionnaire instructed the participants to answer questions with reference to their total life experiences. This questionnaire was completed at screening and at 2 months after each session.

Spiritual Transcendence Scale This 24-item questionnaire assesses a construct that reflects an individual's effort to create a broad sense of personal meaning in his or her life and has been shown to demonstrate cross-cultural generality (Piedmont 1999, 2005, 2006; Piedmont and Leach 2002). A total score and three empirically derived factors are scored: prayer fulfillment, universality, and connectedness. This questionnaire was completed at screening and at 2 months after each session.

NEO Personality Inventory (NEO PI-R) This 241-item questionnaire, which was completed on a computer, permits the assessment of five major personality factors: neuroticism, extraversion, openness, agreeableness, and conscientiousness (Costa and McCrae 1992). This questionnaire was completed at screening and at 2 months after each session.

PANAS-X (Positive and Negative Affect Schedule Expanded Form) This 60-item questionnaire permits the assessment of two broad general factors (positive affect and negative affect) accounting for most of the variance in self-rated affect (Watson and Clark 1994, 1997). The version of the questionnaire used instructed the participants to answer questions based on how they feel on the average. This questionnaire was completed at screening and at 2 months after each session.

Community observer ratings of changes in participants' behavior and attitudes After acceptance into the study, each participant designated three adults who were expected to have continuing contact with the participant (e.g., family members, friends, or coworkers/colleagues at work) such that they would be likely to observe changes in the participants' behavior and attitudes that might occur during the study. Ratings by the designated individuals were conducted via a structured telephone interview approximately 1 week after the participant had been accepted into the study and 7 to 8 weeks after each of the drug sessions. The interviewer provided no information to the community volunteer about the participant. Furthermore, most of the interviews (60%) were conducted by a research assistant who had never met the participant and had no knowledge about the participant's experiences during drug sessions. The structured interview consisted of asking the rater to rate the volunteer's behavior and attitudes using a ten-point scale (from 1=not at all to 10=extremely) on 11 dimensions that were identified from prior research (Pahnke 1963; Richards et al. 1977; Doblin 1991) as possibly sensitive to the effects of psilocybin. The rated dimensions were: inner peace, patience, good-natured humor/playfulness, mental flexibility, optimism, anxiety, interpersonal perceptiveness and caring, negative expression of anger, compassion/social concern, expression of positive emotions (e.g., joy, love, appreciation), and self-confidence. On the first rating occasion, which occurred soon after acceptance into the study, the raters were instructed to base their ratings on observations of and conversations with the participant over the past 3 months. On subsequent ratings, which occurred 7 to 8 weeks after each session, the raters were told their previous ratings and were instructed to rate the participant based on interactions over the last several weeks. The data from each interview with each rater were calculated as a total score, with anxiety and anger scored negatively. The changes in participants' behavior and attitudes after drug sessions were expressed as a mean change score from the preceding rating across the raters.

A failure to interview all three of the raters after one of the drug sessions resulted in elimination of 4 of the 30 participants who received psilocybin and methylphenidate in counterbalanced order on the first two sessions. Of the 52 rating occasions in the 26 participants, the majority (83%) involved interviews with all three raters on each rating occasion, with all of the remaining interviews conducted with two raters.

Data analyses

The data were statistically analyzed for the 30 participants who received psilocybin and methylphenidate in counterbalanced order on the first two sessions.

Physiological and monitor rating questionnaire assessed throughout the session Two sets of analyses were conducted. For the first, a two-factor analysis of variance was used with drug (psilocybin and methylphenidate) and time (10 min before and 0.5, 1, 1.5, 2, 3, 4, 5, and 6 h after capsule administration) as within-subject factors. The mean square error term for the drug × time interaction was then used to conduct Tukey's honestly significant differences (HSD) post hoc tests comparing psilocybin and methylphenidate at each post-drug-administration time point. For the second set of analyses, the peak scores during the time-course were defined as the maximum value from 0.5 to 6 h after capsule administration, and temporally based measures (i.e., minutes sleeping and minutes speaking) were summed across the eight post-capsule time-points. Paired *t* tests were used to compare psilocybin and methylphenidate conditions.

Measures assessed 7 h after drug administration Paired *t* tests were used to compare psilocybin and methylphenidate conditions on the three measures of subjective drug effect (Hallucinogen Rating Scale, APZ, and Addiction Research Center Inventory) and the two questionnaires assessing mystical experience (States of Consciousness Questionnaire and Mysticism Scale).

Measures assessed 2 months post-session Paired *t* tests were used to compare psilocybin and methylphenidate conditions for the 24 participants who completed the Persisting Effects Questionnaire and the 26 participants for whom complete data were obtained for the community observer ratings of changes in participants' attitudes and behavior.

The remaining four questionnaires completed 2 months post-session (NEO, PANAS-X, Mysticism Scale-Lifetime, and Spiritual Transcendence Scale) provide general measures of personality, affect, and spirituality that could result in carry-over effects from post-session 1 to post-session 2. Accordingly, these data were analyzed using the following planned comparisons: (1) comparison (*t* test) of data obtained at screening for the group of participants that received psilocybin in session 1 (N=15) with that for the group that received methylphenidate in session 1 (N=15), (2) comparison (*t* test) of post-session 1 data for the group of participants that received psilocybin in session 1 (N=15) with the group that received methylphenidate in session 1 (N=15), and (3) comparison (paired *t* test) of data post-session 1 with data post-session 2 for the group of participants that received methylphenidate on session 1 and psilocybin on session 2 (N=15).

Results

Integrity of blinding procedures

The integrity of the blinding procedures was assessed by having the monitors complete a questionnaire after each session on which they guessed the capsule content and a questionnaire at the end of the study on which they provided their guesses about the study design. Overall, 23% of sessions were misclassified (methylphenidate identified as psilocybin or psilocybin identified as something other than psilocybin) by one or both of the monitors. The primary and most experienced monitor had an overall misclassification rate of 17%. Most misclassification errors involved rating a methylphenidate session as psilocybin. It is interesting to note that even the primary monitor, however, sometimes rated the psilocybin condition, which was a high dose, as being something other than psilocybin. On two of the three occasions on which this occurred, the participants subsequently rated their experiences as among the five most meaningful and spiritually significant experiences of their lives. These observations suggest that the experiences reported during psilocybin sessions were not merely artifacts of monitor expectation or suggestion.

At the conclusion of the study, the primary monitor and the assistant monitor completed a debriefing questionnaire in which they provided their guesses about the study design. Both monitors believed that a range of psilocybin doses had been administered as well as other active drugs and placebo. Caffeine, dextromethorphan, and diphenhydramine were thought likely to be the other drugs administered, and the primary monitor specifically guessed, based on his previous clinical experience, that methylphenidate had not been administered. Thus, we conclude that the blinding procedures overall were adequately maintained despite the differences in the pharmacological profiles of psilocybin and methylphenidate.

Blood pressure, heart rate, and monitor ratings throughout the session

Both psilocybin and methylphenidate produced significant and orderly time-related effects. For both drugs, the onset of significant blood pressure and monitor-rated effects occurred either at the 30- or 60-min assessment, with the effects generally peaking from 90 to 180 min and decreasing toward pre-drug-administration levels over the remainder of the session (Fig. 1). Heart rate increased by

about 10 bpm for both drugs and remained significantly elevated over the pre-drug value throughout the session. The volunteers were rated as showing very low sleepiness/sedation and restlessness during sessions, with no differences between the psilocybin and methylphenidate conditions (Table 1). The volunteers had a significantly greater number of minutes talking with the monitors after methylphenidate than psilocybin (72 vs 51 min, during the 6 h after capsule ingestion), although after psilocybin they had more physical contact (e.g., handholding) with the monitor (24 vs 58 min) and higher peak ratings of stimulation/arousal and spontaneous motor activity (Fig. 2; Table 1). It is noteworthy that, during psilocybin sessions, the participants were rated as being less responsive to questions, further from ordinary reality, and showing greater emotionality as reflected in peak ratings of tearing/crying, anxiety/fearfulness, joy/intense happiness, and peace/harmony (Fig. 2; Table 1).

Drug effect and mysticism measures assessed 7 h after drug administration

Hallucinogen-sensitive questionnaires The three questionnaires developed for sensitivity to hallucinogenic drugs showed differences between psilocybin and methylphenidate (Table 2). All six scales of the Hallucinogen Rating Scale, all three scales on the APZ Questionnaire, and the LSD scale of the ARCI were significantly higher after psilocybin than after methylphenidate. These differences reflect the fact that, after psilocybin, the participants experienced alterations in mood, affect, and cognition typical of hallucinogenic drugs. These included perceptual changes (e.g., visual pseudo-hallucinations, illusions, and synesthesias), labile moods (e.g., feelings of transcendence, grief, joy, and/or anxiety), and cognitive changes (e.g., sense of meaning and/or ideas of reference).

A mixed pattern of results occurred on the other scales of the ARCI. The PCAG subscale, which is sensitive to sedative drugs, was higher after psilocybin. It is interesting to note that the two stimulant scales showed opposite effects. The amphetamine scale (A), which was designed to show dose-related sensitivity to amphetamine, was significantly higher after psilocybin than after methylphenidate. However, the benzedrine group scale (BG), which measures amphetamine-induced increases in self-control, efficiency, and concentration, was significantly higher after methylphenidate than after psilocybin. Finally, the morphine-benzedrine group (MBG) scale, which is considered a

Table 1 Monitor ratings of volunteer behavior and mood throughout the session

Rated description	Methylphenidate	Psilocybin	*P* value
Peak effects (maximum score=4)			
Overall drug effect	1.10 (0.15)	3.13 (0.16)	<0.001
Sleepiness/sedation	0.17 (0.07)	0.10 (0.05)	N.S.
Unresponsive to questions	0.07 (0.05)	0.58 (0.20)	<0.05
Anxiety or fearfulness	0.42 (0.09)	1.05 (0.17)	<0.01
Stimulation/arousal	0.68 (0.12)	1.42 (0.26)	<0.001
Distance from ordinary reality	1.12 (0.16)	3.12 (0.14)	<0.001
Ideas of reference/paranoid thinking	0 (0)	0.17 (0.09)	N.S.
Yawning	0.05 (0.03)	1.18 (0.23)	<0.001
Tearing/crying	0.77 (0.13)	1.38 (0.21)	<0.001
Nausea	0.12 (0.06)	0.42 (0.11)	<0.01
Spontaneous motor activity	0.53 (0.17)	1.02 (0.23)	<0.05
Restless/fidgety	0.18 (0.07)	0.27 (0.08)	N.S.
Joy/intense happiness	0.63 (0.15)	2.03 (0.22)	<0.001
Peace/harmony	0.92 (0.15)	1.90 (0.20)	<0.001
Total duration in minutes (maximum score=360)			
Talking with monitor	72.0 (4.8)	50.9 (2.2)	<0.001
Total speech	122.2 (10.7)	106.0 (10.7)	N.S.
Non-speech vocalization[a]	2.2 (1.3)	16.1 (4.5)	<0.01
Physical contact with monitor[b]	23.7 (4.7)	57.6 (8.0)	<0.001
Sleep	0.5 (0.3)	0.2 (0.2)	N.S.
Strong anxiety	0.7 (0.3)	5.6 (2.7)	N.S.

Data are mean scores with one SEM shown in parentheses (N=30)
N.S. not significant
[a]For example, humming, sighs, laughter
[b]For example, reassuring touch

Table 2 Volunteer ratings on three drug-sensitive questionnaires completed 7 h after drug administration

Questionnaire	Subscale description	Methylphenidate	Psilocybin	*P* value
Hallucinogen Rating Scale (4=maximum)	Intensity	1.38 (0.14)	2.79 (0.12)	<0.001
	Somaesthesia	0.91 (0.10)	1.92 (0.11)	<0.001
	Affect	1.16 (0.10)	2.16 (0.10)	<0.001
	Perception	0.54 (0.11)	2.07 (0.14)	<0.001
	Cognition	1.03 (0.14)	2.54 (0.15)	<0.001
	Volition	1.39 (0.06)	1.77 (0.07)	<0.001
APZ Questionnaire	OSE (oceanic boundlessness)	3.30 (0.50)	8.00 (0.45)	<0.001
	AIA (dread of ego dissolution)	1.03 (0.21)	5.03 (0.74)	<0.001
	VUS (visionary restructuralization)	3.70 (0.59)	8.87 (0.47)	<0.001
Addiction Research Center Inventory (ARCI)	PCAG (sedative)	4.83 (0.41)	7.27 (0.58)	<0.001
	BG (amphetamine/self-control)	5.83 (0.38)	4.57 (0.32)	<0.05
	A (amphetamine)	3.80 (0.44)	5.13 (0.41)	<0.05
	MBG (euphoria)	6.77 (0.73)	8.60 (0.67)	N.S.
	LSD (hallucinogen/dysphoria)	4.33 (0.37)	7.33 (0.40)	<0.001

Data are mean ratings with one SEM shown in parentheses (*N*=30)
N.S. not significant

measure of drug-induced euphoria, did not differ significantly between the drug conditions.

Measures of mystical experience At 7 h after capsule administration, the volunteers also completed two questionnaires designed to assess primary mystical experiences based on classic phenomenological descriptions from the psychology of religion (Table 3). The total score and all three empirically derived factors of the Mysticism Scale and all seven scales on States of Consciousness Questionnaire were significantly higher after psilocybin than after methylphenidate. Based on a priori criteria, 22 of the total group of 36 volunteers had a "complete" mystical experience after psilocybin (ten, nine, and three participants in the first, second, and third session, respectively) while only 4 of 36 did so after methylphenidate (two participants each in the first and second sessions).

Measures assessed 2 months post-sessions

Persisting Effects Questionnaire As shown in Table 4, compared to methylphenidate, psilocybin produced significantly greater elevations in ratings of positive attitudes, mood, social effects, and behavior; the negative ratings of these same dimensions were very low and did not differ across the drug conditions. This questionnaire also included ratings of the personal meaningfulness and spiritual significance of the experience and whether the experience changed their sense of well being or life satisfaction. Table 4 shows that these ratings were significantly higher after psilocybin than after methylphenidate. It is remarkable that 67% of the volunteers rated the experience with psilocybin to be either the single most meaningful experience of his or her life or among the top five most meaningful experiences of his or her life (Fig. 3). In written

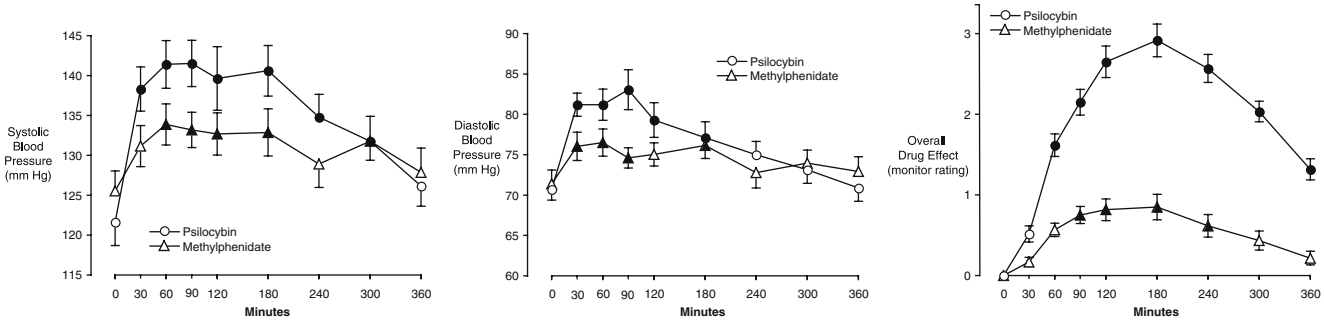

Fig. 1 Within-session time-course of psilocybin and methylphenidate effects. Blood pressure (systolic and diastolic) and monitor ratings (mean of overall drug effect) as a function of time since capsule ingestion (time 0=before drug administration). *Data points* are means with *brackets* showing ±1 SEM (N=30) *Filled data points* indicate a significant difference (Tukey HSD) from pre-administration of the drug (time 0). The figure shows that, compared to methylphenidate, psilocybin produced modestly higher elevations in blood pressure but substantially higher monitor rating of overall drug effect

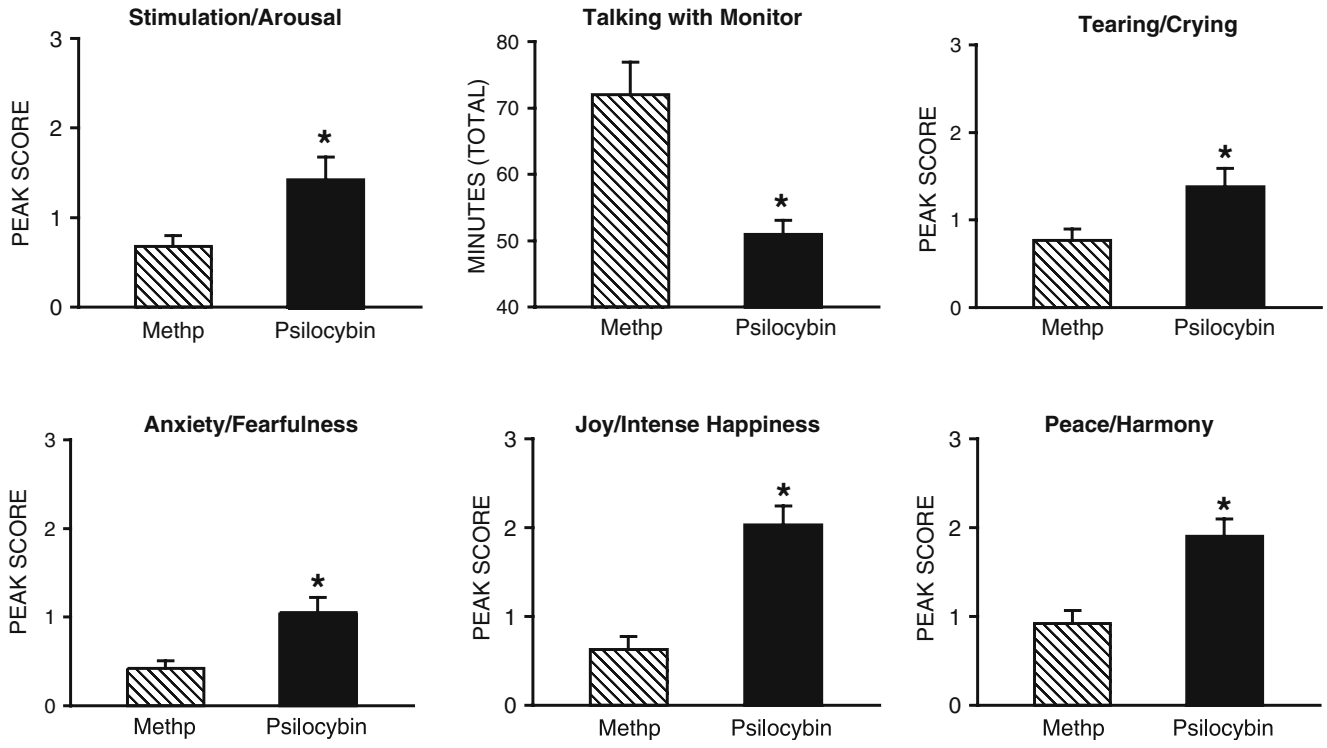

Fig. 2 Monitor ratings during sessions. *Bars* are mean ratings with 1 SEM shown in *brackets* (*N*=30). *Asterisks* indicate a significant difference between the methylphenidate (*Methp*) and psilocybin conditions. Maximum possible rating=4

comments, the volunteers judged the meaningfulness of the experience to be similar, for example, to the birth of a first child or death of a parent. Thirty-three percent of the volunteers rated the psilocybin experience as being the single most spiritually significant experience of his or her life, with an additional 38% rating it to be among the top five most spiritually significant experiences. In written comments about their answers, the volunteers often described aspects of the experience related to a sense of unity without content (pure consciousness) and/or unity of all things. After methylphenidate, in contrast, 8% of volunteers rated the experience to be among the top five (but not the single most) spiritually significant experiences. Seventy-nine percent of the volunteers rated that the psilocybin experience increased their current sense of personal well being or life satisfaction "moderately" (50%) or "very much" (29%), in contrast to 17 and 4%, respectively, after methylphenidate. No volunteer rated either the psilocybin or methylphenidate experience as having decreased their sense of well being or life satisfaction.

Table 3 Volunteer ratings on two mystical experience questionnaires completed 7 h after drug administration

Questionnaire	Subscale description	Methylphenidate	Psilocybin	*P* value
Mysticism Scale	Interpretation	70.6 (4.5)	96.1 (3.3)	<0.001
	Introvertive	66.9 (4.4)	96.3 (2.8)	<0.001
	Extrovertive	37.2 (3.2)	59.7 (2.9)	<0.001
	Total	174.7 (11.3)	252.1 (8.5)	<0.001
States of Consciousness Questionnaire[a]	Internal unity	0.25 (0.05)	0.73 (0.05)	<0.001
	External unity	0.21 (0.05)	0.66 (0.06)	<0.001
	Sacredness	0.36 (0.05)	0.80 (0.04)	<0.001
	Intuitive knowledge	0.30 (0.05)	0.72 (0.05)	<0.001
	Transcendence of time and space	0.27 (0.05)	0.76 (0.04)	<0.001
	Deeply felt positive mood	0.38 (0.04)	0.77 (0.05)	<0.001
	Ineffability	0.29 (0.05)	0.81 (0.05)	<0.001

Data are mean scores with one SEM shown in parentheses (*N*=30)
N.S. not significant
[a]For States of Consciousness Questionnaire, data are expressed as a proportion of the maximum possible score

Table 4 Volunteer ratings and community observer ratings completed 2 months after sessions

Outcome measures	Description	Methylphenidate	Psilocybin	*P* value
Persisting Effects Questionnaire (volunteer ratings)[a]	Positive attitudes about life and/or self and/or self	22.8 (4.5)	55.0 (5.0)	<0.001
	Negative attitudes about life and/or self	0.3 (0.1)	0.5 (0.3)	N.S.
	Positive mood changes	16.0 (3.5)	39.2 (5.3)	<0.001
	Negative mood changes	0.6 (0.5)	1.5 (0.7)	N.S.
	Altruistic/positive social effects	17.3 (4.4)	46.6 (5.5)	<0.001
	Antisocial/negative social effects	0.3 (0.2)	0.7 (0.5)	N.S.
	Positive behavior changes	29.2 (6.5)	60.0 (4.8)	<0.001
	Negative behavior changes	1.7 (1.2)	0 (0)	N.S.
	How personally meaningful was the experience?	3.42 (0.35)	6.54 (0.22)	<0.001
	How spiritually significant was the experience?	2.63 (0.22)	4.79 (0.26)	<0.001
	Did the experience change your sense of well being or life satisfaction?	+0.79 (0.18)	+2.04 (0.17)	<0.001
Community observer ratings of changes in participants' behavior and attitudes[b]	Positive change score	−0.03 (0.68)	2.42 (0.70)	<0.01

Data are mean ratings with one SEM shown in parentheses
N.S. Not significant
[a]For Persisting Effects Questionnaire, data on attitude, mood, social, and behavior changes are expressed as percentage of maximum possible score, and data for the last three questions are raw scores; for volunteer ratings, *N*=24 (cf., "Materials and methods")
[b]For ratings by community observers, data are mean positive change scores; for observer ratings, *N*=26 (cf., "Materials and methods")

Personality and affect None of the factors on the two widely used questionnaires assessing five factors of personality (NEO and PI-R) and measures of general positive and negative affect (PANAS-X) was differentially affected by psilocybin. At screening and at 2 months after session 1, there were no significant differences between the group that received psilocybin on the first session (*N*=15) and the group that received methylphenidate on the first session (*N*=15). Furthermore, within the latter group, there were no significant changes from post-session 1 to post-session 2.

Lifetime assessment of mystical experience and spirituality Two additional questionnaires completed 2 months after each session provided lifetime measures of mystical experiences (Mysticism Scale) and spirituality (Spiritual Transcendence Scale). As with the measures of personality and affect, there were no significant differences at screening between the group that received psilocybin on the first session (*N*=15) and the group that received methylphenidate on the first session (*N*=15). As shown in Fig. 4, at 2 months after the first session, lifetime mystical experience and spiritual transcendence scores were significantly higher in the group that received psilocybin on the first session than the group that received methylphenidate on the first session. At 2 months after the second session, the scores in the group that received psilocybin on the second session increased significantly on both measures. As expected, because these scores reflect *lifetime* measures, these scores did not decrease after the second session in the group that received psilocybin on the first session.

Community observer ratings of changes in participants' and behavior and attitudes Table 4 shows that, compared to methylphenidate, psilocybin sessions were associated with small but significant positive changes in the participants' behavior and attitudes.

Fear, anxiety/dysphoria, and ideas of reference/paranoia

According to monitor ratings, post-session ratings and written comments by the monitors and the participants, and post-session interviews with the participants, many participants reported mild or moderate anticipatory anxiety at the beginning of sessions. In post-session ratings, 11 of the 36 total volunteers after psilocybin and none after methylphenidate rated on the States of Consciousness Questionnaire their "experience of fear" sometime during the session to be "strong" or "extreme." Four volunteers (all of whom had high post-session fear ratings) reported that their entire session was dominated by anxiety or unpleasant psychological struggle (i.e., dysphoria). Four others (again, all of whom had high post-session fear ratings) reported that a significant portion of their session was characterized by anxiety/dysphoria. Although the onset of episodes of notable anxiety/dysphoria was most likely to occur shortly after onset of drug effect, there were occasions on which onset occurred later in the session when drug effects were

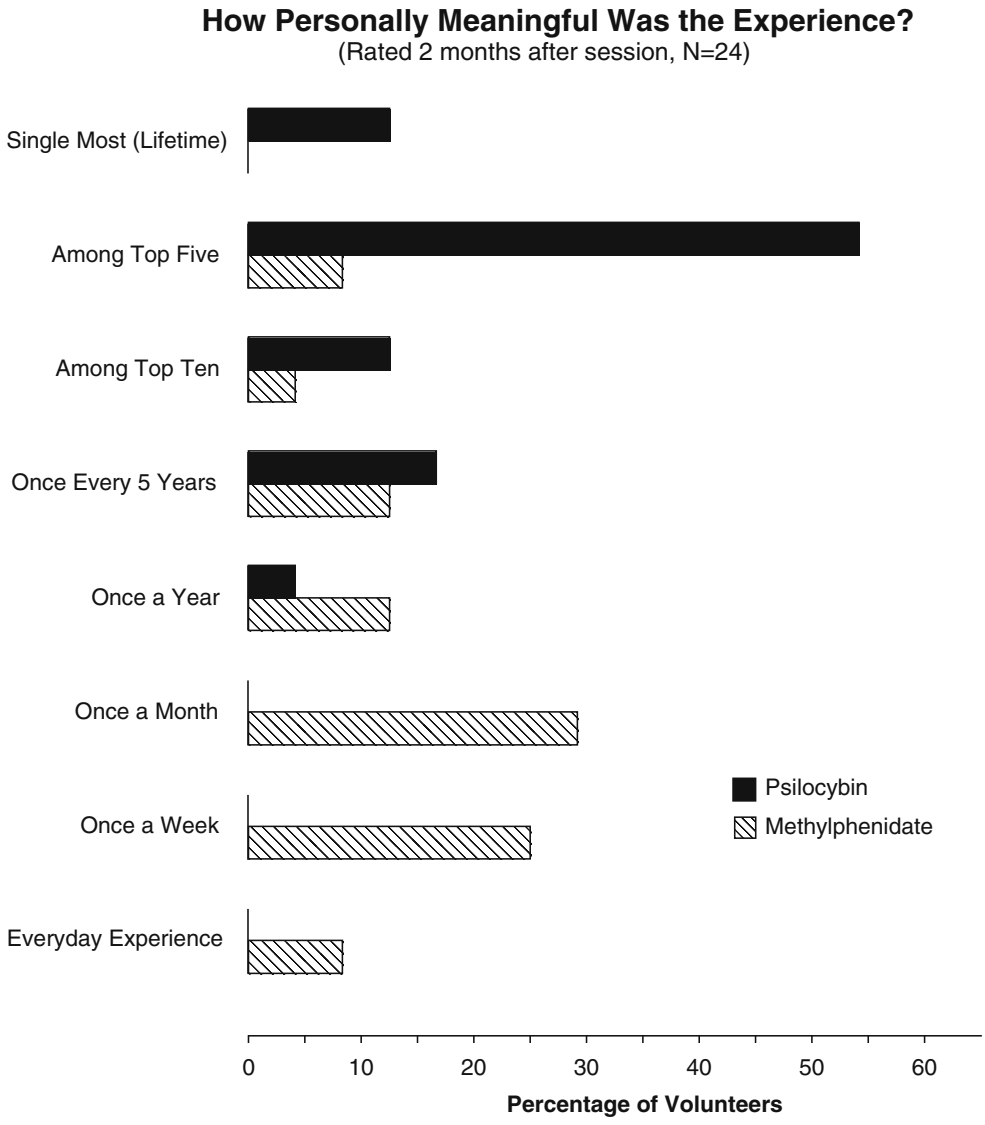

Fig. 3 Percentage of volunteers who endorsed each of eight possible answers to the question "how personally meaningful was the experience?" on a questionnaire completed 2 months after the session (*N*=24)

subsiding. Anxiety/dysphoria occurred when psilocybin was administered on the first (two participants), second (four participants), and third (two participants) sessions, suggesting that longer preparation time and being unblinded to psilocybin administration were not protective. Six of the eight volunteers with a notable anxiety/dysphoria response had mild, transient ideas of reference/paranoid thinking sometime during the 6 h after psilocybin administration. These effects were readily managed with reassurance and did not persist beyond the session. Two of the eight volunteers compared the experience to being in a war and three indicated that they would never wish to repeat an experience like that again. Despite these psychological struggles, most of these participants rated the overall experience as having personal meaning and spiritual significance and no volunteer rated the experience as having decreased their sense of well being or life satisfaction.

Discussion

The present double-blind study shows that psilocybin, when administered under comfortable, structured, interpersonally supported conditions to volunteers who reported regular participation in religious or spiritual activities, occasioned experiences which had marked similarities to classic mystical experiences and which were rated by volunteers as having substantial personal meaning and spiritual significance. Furthermore, the volunteers attributed to the experience sustained positive changes in attitudes and behavior that were consistent with changes rated by friends and family.

The present study advances the empirical analysis of mystical experience. From a scientific perspective, most of what is known about mystical or religious experience is based on descriptive characterization of spontaneously occurring experience (Stace 1960; Spilka et al. 2005).

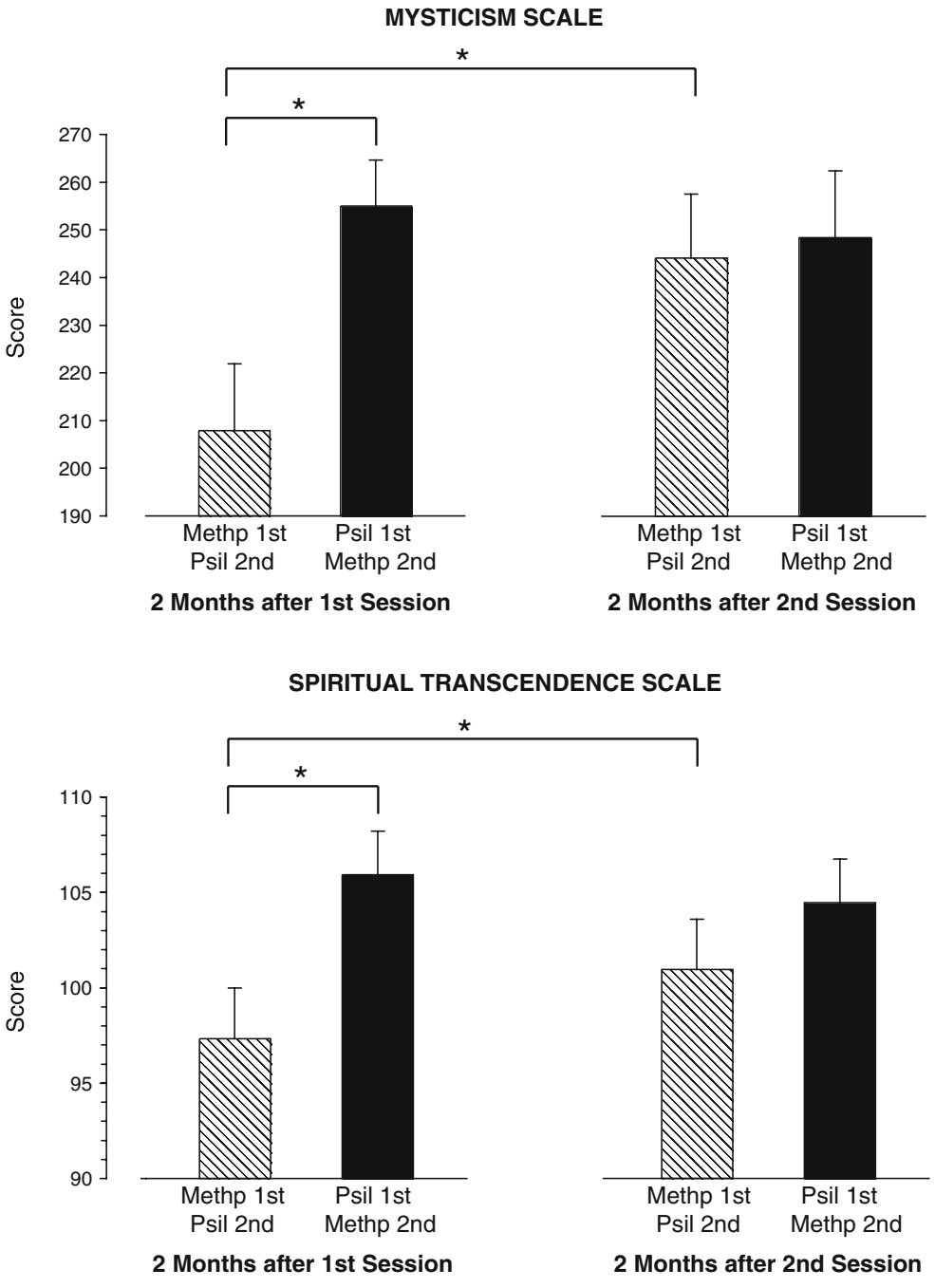

Fig. 4 Lifetime mystical experience (Mysticism Scale) and spirituality (Spiritual Transcendence Scale) scores 2 months after the first session (*left two columns*) and 2 months after the second session (*right two columns*) in two groups of participants. One group (*N*=15) received methylphenidate on the first session and psilocybin on the second session (*Methp 1st*, *Psil 2nd*) and the other group (*N*=15) received the reverse order (*Psil 1st*, *Methp 2nd*). *Bars* are means with *brackets* showing one SEM. *Asterisks* indicate a significant difference between the conditions

Rigorous attempts to prospectively experimentally manipulate such experiences have generally been associated with only modest effects (e.g., Hood et al. 1990; Spilka et al. 2005). Although there are anecdotal reports from the clinical research in the 1960s of hallucinogens occasioning religious experiences, even when administered in a secular setting (Smith 1964; Masters and Houston 1966; Dobkin de Rios and Janiger 2003), a systematic study of such effects has been almost nonexistent. The most relevant study was one in which theological seminary students received either 30 mg psilocybin (ten participants) or 200 mg nicotinic acid (ten participants) in a group setting during a religious service (the Good Friday Experiment, Pahnke 1963; 1967; Doblin 1991). The participants who received psilocybin showed significant elevations on the Pahnke Mystical Experience Questionnaire and reported positive changes in attitudes and behavior at 6 months and at 25-year follow-up. Those results are consistent with the present study, which also demonstrated sustained increases on two closely related outcome measures (Pahnke–Richards Mystical

Experience Questionnaire and Persisting Effects Questionnaire). Significant limitations of the Pahnke study were that the participants were explicitly told that some would receive psilocybin and some would be controls, and that it was conducted in a group setting. These features resulted in the double-blind being quickly broken during the session, which presumably contributed to the assessed differences between the groups (Doblin 1991; Wulff 1991; Smith 2000). The present study represents an important extension of the Pahnke study using better blinding and comparison control procedures, assessment of effects in individual participants unconfounded by group interactions, empirically validated measures of mystical experience (the Mysticism Scale and the Spiritual Transcendence Scale), and assessment of effects by community observers. The credibility of the blinding procedure is reflected in the facts that the debriefing interviews with the monitors at the end of the study indicated that they remained unaware of the study design and that some volunteers rated their experience during the methylphenidate session as being among the most personally meaningful experiences of their lives (Fig. 3).

The proportion of volunteers who fulfilled Pahnke's criteria for having a "complete" mystical experience (61%, 22 of 36) is somewhat higher than the 30–40% reported by Pahnke in the Good Friday Experiment (cf. Pahnke 1967, p 67). It seems likely that the greater preparation time (at least 8 versus 3 h in the Pahnke study) and the differences in context (individual sessions with an eye mask and music in an aesthetic room verses the Pahnke study conducted in a group setting with 30 individuals, some of whom were acting bizarrely) likely contributed to this difference. The present study provides no evidence that preparation beyond that given before the first session produced an increase in the incidence of a mystical experience (i.e., on the first, second, and third session, respectively, 67, 60, and 50% of participants who received psilocybin met the criteria for a complete mystical experience) or a decrease in the incidence of anxiety/dysphoria.

The extent to which the study population limits the generalizability of the results is unknown. The participants in this study were hallucinogen-naïve, well educated, psychologically stable, and middle-aged adults, who reported regular participation in religious or spiritual activities. In particular, it seems plausible that the religious or spiritual interest of the participants may have increased the likelihood that the psilocybin experience would be interpreted as having substantial spiritual significance and personal meaning. It is also unknown how the hallucinogen-naïve status of the participants affected either the intensity or qualitative interpretation of the experience. Recruiting volunteers without histories of use avoided the problem of participant selection bias in which individuals who had previously had positive experiences with hallucinogens would have been most likely to participate. However, it is also possible that the novelty of the experience in hallucinogen-naïve individuals enhanced both the intensity and the personal and spiritual significance of the experience.

An important finding of the present study is that, with careful volunteer screening and preparation and when sessions are conducted in a comfortable, well-supervised setting, a high dose of 30 mg/70 kg psilocybin can be administered safely. It is also noteworthy that, despite meetings and prior sessions with monitors ranging from 8 h (when psilocybin was administered on the first session) up to 24 h (when psilocybin was administered on the third session) of contact time, 22% (8 of 36) of the volunteers experienced a period of notable anxiety/dysphoria during the session, sometimes including transient ideas of reference/paranoia. No volunteer required pharmacological intervention and the psychological effects were readily managed with reassurance. The primary monitor remained accessible via beeper/phone to each volunteer for 24 h after each session, but no volunteer called before the scheduled follow-up meeting on the next day. The 1-year follow-up is ongoing but has been completed by most volunteers (30 of 36). In that follow-up, an open-ended clinical interview reflecting on the study experiences and current life situation provides a clinical context conducive to the spontaneous reporting of study-associated adverse events. To date, there have been no reports of persisting perceptional phenomena sometimes attributed to hallucinogen use or of recreational abuse of hallucinogens, and all participants appear to continue to be high-functioning, productive members of society.

The results of the present study have implications for understanding the abuse of hallucinogens. Although psilocybin is regulated by the federal government under the most restrictive category (Schedule I) of the Controlled Substances Act, the National Institute on Drug Abuse (2001, 2005) does not consider psilocybin and the other classical hallucinogens to be drugs of "addiction" because they do not produce compulsive drug-seeking behavior as do classic addicting drugs such as cocaine, amphetamine, heroin, and alcohol. This conclusion is consistent with observations that psilocybin and other classic hallucinogens do not maintain reliable drug self-administration in animal laboratory models of drug abuse (Griffiths et al. 1980; Fantegrossi et al. 2004) and that most recreational users of classical hallucinogens decrease or stop their use over time (National Institute on Drug Abuse 2001). In the present study, psilocybin did not produce a classic euphorigenic profile of effects: measures of anxiety and dysphoria (monitor ratings of anxiety: AIA scale on the APZ Questionnaire, LSD scale on the ARCI) were significantly greater after psilocybin than after methylphenidate. However, the present study also shows that, in some people under some conditions, psilocybin can occasion experiences that are rated as highly valued. This seems a likely

mechanism underlying the long-term historical use of psilocybin and other hallucinogens such as DMT within some cultures for divinatory or religious purposes.

While there is no indication that carefully monitored clinical exposure of psilocybin to hallucinogen-naïve volunteers results in subsequent abuse (present study; Gouzoulis-Mayfrank, personal communication; Yensen and Dryer, (1992)[1]; Leuner 1981), the epidemic of hallucinogen abuse in the 1960s raises an important cautionary note. Abuse of hallucinogens can be exacerbated under conditions in which hallucinogens are readily available illicitly and the potential harms to both the individual and society are misrepresented or understated. It is important that the risks of hallucinogen use not be underestimated. Even in the present study in which the conditions of volunteer preparation and psilocybin administration were carefully designed to minimize adverse effects, with a high dose of psilocybin 31% of the group of carefully screened volunteers experienced significant fear and 17% had transient ideas of reference/paranoia. Under unmonitored conditions, it is not difficult to imagine such effects escalating to panic and dangerous behavior. Also, the role of hallucinogens in precipitating or exacerbating enduring psychiatric conditions and long-lasting visual perceptual disturbances should remain a topic of research (Abraham et al. 1996; Halpern and Pope 1999).

In conclusion, the present study showed that, when administered to volunteers under supportive conditions, psilocybin occasioned experiences similar to spontaneously occurring mystical experiences and which were evaluated by volunteers as having substantial and sustained personal meaning and spiritual significance. The ability to prospectively occasion mystical experiences should permit rigorous scientific investigations about their causes and consequences, providing insights into underlying pharmacological and brain mechanisms, nonmedical use and abuse of psilocybin and similar compounds, as well as the short-term and persisting effects of such experiences.

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