

Mystical-type experiences occasioned by psilocybin mediate the attribution of personal meaning and spiritual significance 14 months later

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Abstract

Psilocybin has been used for centuries for religious purposes; however, little is known scientifically about its long-term effects. We previously reported the effects of a double-blind study evaluating the psychological effects of a high psilocybin dose. This report presents the 14-month follow-up and examines the relationship of the follow-up results to data obtained at screening and on drug session days. Participants were 36 hallucinogen-naïve adults reporting regular participation in religious/spiritual activities. Oral psilocybin (30 mg/70 kg) was administered on one of two or three sessions, with methylphenidate (40 mg/70 kg) administered on the other session(s). During sessions, volunteers were encouraged to close their eyes and direct their attention inward. At the 14-month follow-up, 58% and 67%, respectively, of volunteers rated the psilocybin-occasioned experience as being among the five most personally meaningful and among the five most spiritually significant experiences of their lives; 64% indicated that the experience increased well-being or life

satisfaction; 58% met criteria for having had a 'complete' mystical experience. Correlation and regression analyses indicated a central role of the mystical experience assessed on the session day in the high ratings of personal meaning and spiritual significance at follow-up. Of the measures of personality, affect, quality of life and spirituality assessed across the study, only a scale measuring mystical experience showed a difference from screening. When administered under supportive conditions, psilocybin occasioned experiences similar to spontaneously occurring mystical experiences that, at 14-month follow-up, were considered by volunteers to be among the most personally meaningful and spiritually significant of their lives.

Key words

entheogen; hallucinogen; humans; mystical experience; psilocybin; psychedelic; religion; spiritual

Introduction

Although many have anecdotally claimed that psilocybin, the principal psychoactive component of various hallucinogenic mushroom species, can facilitate experiences providing sustained, positively valued impact, little is known scientifically about such effects. Psilocybin has been used as a sacrament for centuries, possibly millennia, in structured religious ceremonies (Wasson, 1980; Stamets, 1996; Metzner, 2004). Like

other classical hallucinogens [*d*-lysergic acid diethylamide (LSD), mescaline, *N,N*-dimethyltryptamine (DMT)], the effects of psilocybin are primarily mediated at 5-HT_{2A} receptor sites (Nichols, 2004), and the acute subjective effects include robust changes in perception, cognition, affect, volition and somaesthesia (Isbell, 1959; Wolbach, *et al.*, 1962; Rosenberg, *et al.*, 1964).

The degree to which responses to psilocybin are influenced by nonpharmacological variables was not understood by early

researchers (e.g. Isbell, 1959; Malitz, *et al.*, 1960; Rinkel, *et al.*, 1960; Hollister, 1961). By providing more preparation and interpersonal support during drug action, subsequent research described more positively valued experiences and fewer adverse effects (e.g. panic and paranoia) (Chwelos, *et al.*, 1959; Leary, *et al.*, 1963; Metzner, *et al.*, 1965; Pahnke, 1969). In response to the hallucinogen abuse of the 1960s, human hallucinogen research largely ceased and has only recently resumed. Notably, Vollenweider and colleagues in Switzerland and Gouzoulis-Mayfrank and colleagues in Germany have studied the neurocognitive, perceptual and psychosis-mimicking effects of psilocybin (e.g. Vollenweider, *et al.*, 1998; Gouzoulis-Mayfrank, *et al.*, 1999; Hasler, *et al.*, 2004; Carter, *et al.*, 2005, 2007).

Recently, we used rigorous double-blind methods to evaluate the acute (7 h) and longer term (2 months) psychological effects of a high dose of psilocybin (30 mg/70 kg) relative to an active comparison compound (40 mg/70 kg methylphenidate) in 36 hallucinogen-naïve volunteers (Griffiths, *et al.*, 2006). In contrast to the aforementioned recent psilocybin studies, the study optimized the potential for positively valued experiences by providing 8 h of preparation and by instructing volunteers to focus explicitly on the phenomenology of the drug experience rather than perform tasks. The results showed psilocybin to occasion experiences with substantial personal meaning and spiritual significance when evaluated 2 months after psilocybin. We have subsequently conducted a follow-up study evaluating effects at 14 months after their last drug session. Volunteers completed questionnaires that assessed personality, affect, quality of life, spiritual experience, and persisting changes in attitude and behaviour attributed to the blinded psilocybin session. This report analyses these 14-month follow-up results and the contribution of baseline characteristics and immediate drug effects to long-term persisting effects.

Methods

Participants

Participants were recruited through flyers announcing a study of states of consciousness brought about by a naturally occurring psychoactive substance used sacramentally in some cultures. The 36 study participants were medically and psychiatrically healthy and without histories of hallucinogen use. Sixteen participants were males [incorrectly reported as 14 in the previous publication (Griffiths, *et al.*, 2006)]. Participants had an average age of 46 years (range 24–64); 97% were college graduates and 56% had post-graduate degrees. All were employed full- or part-time. Fifty-three per cent indicated affiliation with a religious or spiritual community, such as a church, synagogue or meditation group. All volunteers indicated at least intermittent participation in religious or spiritual activities, such as religious services, prayer, meditation or study groups. Volunteers

did not receive monetary compensation for participation. Additional information about participant recruitment and demographics has been described previously (Griffiths, *et al.*, 2006).

Study design

The study compared the effects of orally administered psilocybin (30 mg/70 kg) and methylphenidate hydrochloride (40 mg/70 kg) using a double-blind 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 volunteers who received two sessions 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 third group ($n = 6$) received methylphenidate on the first two sessions and unblinded psilocybin on the third session. The purpose of having the possibility of a third session was to help control for expectancy effects (Griffiths, *et al.*, 2006).

Preparation and drug session procedures

Participants and monitors were informed that participants would have either two or three sessions, that in at least one session they would receive a moderate or high dose of psilocybin, and that an inactive placebo, a low dose of psilocybin, or various other drugs could be administered in the other session(s). Participants and monitors were unblinded to drug conditions after all participants had completed the 14-month follow-up. The primary monitor met with each volunteer on four occasions before the first session to develop rapport and trust.

The 8-h drug sessions were conducted in a living room-like environment. During the session, two monitors were present with a single participant. Participants were encouraged to focus their attention inward by lying down on the couch and wearing an eye mask and headphones through which a programme of classical music was played. Additional details of instructions to volunteers, volunteer–monitor meetings before and after sessions, and outcome measures have been described previously (Griffiths, *et al.*, 2006).

Measures of personality, affect, quality of life and spirituality assessed at screening, 2 months after each session, and at the 14-month follow-up

The following instruments were assessed: NEO Personality Inventory (NEO PI-R) (Costa and McCrae, 1992); Positive and Negative Affect Scale – Expanded Form (PANAS-X) for how one feels generally (Watson and Clark, 1994); Quality of Life Inventory raw score (Frisch, 1994); Measure of Actualization Potential (Leclerc, *et al.*, 1999); Mysticism Scale

(described below); Spiritual Transcendence Scale (Piedmont, 1999, 2007); Faith Maturity Scale – 12 item version (Benson, *et al.*, 1993); Functional Assessment of Chronic Illness Therapy – Non-Illness – Spiritual Well-Being Scale (FACIT-Sp-NI-12) (Peterman, *et al.*, 2002).

Measures assessed throughout the session

At 0.5–6 h after capsule administration, monitors rated several dimensions of participant behaviour and mood, including a rating of the overall drug effect on a 5-point scale from 0 = none to 4 = extreme. Data were the mean of the two monitors peak scores (i.e. the maximum value from 0.5 to 6 h after capsule administration for each monitor).

Measures assessed 7 h after drug administration

When the major drug effects had subsided, the participant completed two questionnaires assessing subjective drug effects: Hallucinogen Rating Scale (HRS) (Strassman, *et al.*, 1994) and APZ (assessing altered states of consciousness) (Dittrich, 1998).

Participants also completed two questionnaires assessing mystical experience. The Mysticism Scale (9-point version) has been extensively studied, demonstrates cross-cultural generalizability, and is well-regarded in the psychology of religion (Hood, *et al.*, 2001; Spilka, *et al.*, 2003). When administered 7 h after drug administration, participants were instructed to complete the questionnaire with reference to their experiences since they received the capsules that morning. For the lifetime version of the questionnaire, participants were instructed to answer with reference to their total life experiences.

As part of the States of Consciousness Questionnaire, volunteers completed the Pahnke-Richards Mystical Experience Questionnaire (Griffiths, *et al.*, 2006), which assesses 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, love). Ratings were made on a 6-point scale relative to the participant's overall life experience. Data on each scale were expressed as a proportion of the maximum possible score. A mean total score was calculated as the mean of the following six domains: unity (either internal or external, whichever was greater), transcendence of time and space, ineffability, sense of sacredness, noetic quality and positive mood. Based on prior research (Pahnke, 1969; Griffiths, *et al.*, 2006), criteria for designating a volunteer as having had a 'complete' mystical experience were that scores on each of the six domains were ≥ 0.6 .

Measures assessed two months post-session

For this assessment, participants completed the previously described standardized measures and the Persisting Effects Questionnaire, a measure of changes in attitudes, mood, and social and other behaviours (Griffiths, *et al.*, 2006). The questionnaire also included three questions: (I) How personally meaningful was the experience? (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 five most meaningful experiences of my life; 8, the single most meaningful experience of my life); (II) Indicate the degree to which the experience was spiritually significant to you? (1, not at all; 2, slightly; 3, moderately; 4, very much; 5, among the five most spiritually significant experiences of my life; 6, the single most spiritually significant experience of my life) and (III) 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 from +3 = increased very much to -3 = decreased very much). This questionnaire was developed after the initiation of the study and was completed by 29 of the 36 participants (approximately the same per cent within all three groups).

14-month follow-up

This assessment was conducted 14 months after the last session, which was 16 months after the psilocybin session in volunteers who received psilocybin in session 1, and 14 months after psilocybin in volunteers who received psilocybin in sessions 2 or 3. For this assessment, all 36 participants completed the Retrospective Questionnaire as well as the previously described standardized measures. At this same time, volunteers participated in an open-ended clinical interview reflecting on study experiences and current life situation.

For purposes of completing the Retrospective Questionnaire, volunteers were first asked to identify on which session they experienced the 'most pronounced changes in your ordinary mental processes'. All but one volunteer identified the psilocybin session. That volunteer, who reported having unusual experiences during both sessions, was asked to complete the questionnaire with regard to the psilocybin session. The remaining volunteers completed the questionnaire in reference to the identified session.

Forty-three items in this questionnaire comprised the previously described [doi:10.1016/j.sbsbs.2014.04.001](#) (ref7-417.E0-1.222Te)-709.7(the)-703.290

ratings were made relative to the participant's overall life experience, which could have changed over the intervening follow-up period. Eighty-nine items comprised the previously described Persisting Effects Questionnaire. For these items, volunteers were asked to rate any current persisting effects that they attribute to the experience. Within the Retrospective Questionnaire, volunteers were also asked to provide written descriptions of what was most memorable and what was most spiritually significant about the experience.

Statistical analysis

Inspection of the data indicated that the results from the 30 subjects, who received each drug once, were similar to results from the six subjects, who received methylphenidate twice followed by psilocybin once. Therefore, data from all 36 subjects are analysed below. Data from the first methylphenidate session were used for the six, who received it twice.

To characterize the study sample on measures of personality, affect, quality of life and spirituality relative to the general population, individual subject data at screening were converted to *T*-scores using norms for: the five factors of the NEO PI-R (Costa and McCrae, 1992); the Positive and Negative Affect factors of the PANAS-X (Watson and Clark, 1994); raw score on the Quality of Life Inventory (Frisch, 1994); the overall mean on the Measure of Actualization Potential (Leclerc, *et al.*, 1999); total score on the Mysticism Scale-Lifetime (Hood and Williamson 2000; Ralph W. Hood Jr, 2007, personal communication) and total score of the Spiritual Transcendence Scale (Ralph L. Piedmont, 2007, personal communication). *T*-scores below 45 or above 55 were considered low or high, respectively, on that dimension.

Repeated measures analysis of variance (ANOVA) was conducted to examine changes in the measures of personality, affect, quality of life and spirituality that were assessed at screening, 2 months after the psilocybin session, and 14 months after the last session ($N = 36$). Bonferroni-corrected *t*-tests were used to assess differences among the three time-points. ANOVA with Bonferroni-corrected *t*-tests were also conducted with the Persisting Effects Questionnaire data ($n = 29$) assessed at 2 months post-methylphenidate and post-psilocybin, and again retrospectively for psilocybin at the 14-month follow-up, and with the Pahnke-Richards Mystical Experience Questionnaire data ($N = 36$) assessed 7 h post-methylphenidate and post-psilocybin, and again retrospectively for psilocybin at the 14-month follow-up.

To examine differences in the proportion of subjects endorsing specific answers on the Persisting Effects Questionnaire, *z*-tests of proportions compared data at 2 months post-methylphenidate, 2 months post-psilocybin and again retrospectively for psilocybin at the 14-month follow-up. For ratings of personally meaningful and spiritually significant, endorsement was defined as rating either 'among the top 5' or 'the single most'. For ratings of increased well-being or life satisfaction, endorsement was defined as rating 'increased moderately'

or 'increased very much'. For ratings of positive behavioural change, endorsement was defined as rating 'moderate', 'strong' or 'extreme'.

Pearson's correlations were calculated to examine the relationships between: (1) volunteer's ratings of personal meaning and spiritual significance at the 14-month follow-up and (2) the following screening measures: scores on the five factor subscales of the NEO PI-R, total scores on the Mysticism Scale, Spiritual Transcendence Scale, Faith Maturity Scale, and FACIT-Sp-NI, and mean overall score on the Measure of Actualization Potential Questionnaire.

Pearson's correlations were calculated between: (1) volunteer's ratings of personal meaning and spiritual significance at the 14-month follow-up and (2) data obtained on the psilocybin session day. The psilocybin session data used for these calculations were: peak monitor ratings of six dimensions of participant's behaviour during sessions (overall drug effect, anxiety or fearfulness, distance from ordinary reality, tearing/crying, joy/intense happiness, and peace/harmony); the six subscales of the HRS; the three subscales of the APZ questionnaire; total scores on the post-session Mysticism Scale and mean score on the post-session Pahnke-Richards Mystical Experience Questionnaire. The follow-up data used for these calculations were the volunteer ratings of personal meaning and spiritual significance attributed to the psilocybin session experience.

Significant correlations between the total scores on the Mysticism Scale and follow-up measures of personal meaning or spiritual significance were further examined using a multiple regression model to control for any confounding by intensity of drug effect. Three separate measures of drug effect intensity were examined: peak monitor ratings of overall drug effect; subject-rated intensity as measured by the Intensity subscale of the HRS and subject-rated intensity from the single item rating 'Intensity' in the HRS. In separate analyses for each intensity measure, the intensity measure was entered into the regression first and the post-session Mysticism Scale score was entered second to assess its effect on the follow-up measures independently of intensity.

For statistical tests, $p < 0.05$ was considered significant except for correlations (for which a more conservative $p < 0.01$ was used) and for the Bonferroni-corrected *t*-tests.

Results

Measures of personality, affect, quality of life and spirituality assessed at screening, 2 months after the psilocybin session, and at the 14-month follow-up

The measures of personality, affect, quality of life, and spirituality assessed at screening indicated that the volunteers were generally well-adjusted, outgoing, open and high in spirituality. More specifically, relative to adult norms, the mean *T*-score for

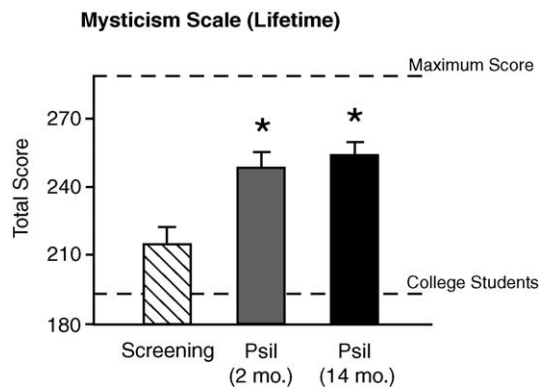


Figure 1 Total score on lifetime version of the Mysticism Scale at screening, 2 months following psilocybin, and at the 14-month follow-up. Bars are mean scores with brackets showing 1 SEM ($N = 36$). Asterisks show significant differences from the screening assessment. For comparison, lower dashed line shows mean score for college students (Hood, *et al.*, 2001; Ralph W. Hood Jr, 2007, personal communication); upper dashed line show maximum possible score.

the group of volunteers on the NEO PI-R were low on Neuroticism (T -score, 41.8) and high on Extroversion, Openness, and Agreeableness (55.3, 65.7, and 55.7 respectively); low on Negative Affect on the PANAS-X (44.4); and high on the Measure of Actualization Potential (59.2), Mysticism Scale-Lifetime (55.6), and Spiritual Transcendence Scale (63.1).

Of the eight questionnaires assessed, only the Mysticism Scale-Lifetime showed significant changes across the study. For the Mysticism Scale-Lifetime, the total score (Figure 1) and the scores on each of the three factors (Interpretation, Introvertive Mysticism, and Extrovertive Mysticism) were significantly greater than screening at both the 2-month and 14-month assessments.

Pahnke-Richards Mystical Experience Questionnaire assessed immediately after sessions and at the 14-month follow-up

The psilocybin session experience, when rated immediately post-session and when rated retrospectively at the 14-month follow-up, produced significant elevations compared with the methylphenidate experience in each of seven domains of mystical experience and the mean total score on the Pahnke-Richards Mystical Experience Questionnaire (Table 1). The 14-month retrospective rating for psilocybin did not differ significantly from the immediate post-session rating. Based on *a priori* criteria, 22 of the 36 volunteers had a 'complete' mystical experience based on immediate post-session ratings; at follow-up, 21 volunteers continued to fulfil these criteria.

Measures of persisting effects assessed 2 months after drug sessions and at the 14-month follow-up

Compared with methylphenidate, the psilocybin session experience produced significant increases in ratings of positive attitudes, mood, social effects and behaviour when rated retrospectively at both 2 months and at the 14-month follow-up (Table 2). The ratings at the 14-month follow-up did not differ significantly from those at 2 months. The ratings of negative changes on these same dimensions were very low and not significantly different across conditions.

Table 2 also shows that the psilocybin session was associated with significant increases in ratings of the personal meaning of the experience, the spiritual significance of the experience, and well-being or life satisfaction due to the experience. No volunteer rated the experience as having decreased his or her sense of well-being or life satisfaction at either 2 months or the 14-month follow-up. Figure 2 shows ratings from these three questions plus a question on positive behaviour change expressed as the percentage of the

Table 1 Volunteer Ratings on the Pahnke-Richards Mystical Experience Questionnaire section of the State of Consciousness Questionnaire completed at the end of methylphenidate and psilocybin sessions, and again retrospectively for psilocybin at the 14-month follow-up^a

Scale description	Methylphenidate (post-session) ^b ($N = 36$)	Psilocybin (post-session) ($N = 36$)	Psilocybin (14 months) ($N = 36$)
Internal unity	0.26 (0.04)	0.73 (0.05)*	0.71 (0.05)*
External unity	0.22 (0.04)	0.64 (0.05)*	0.67 (0.05)*
Sacredness	0.38 (0.04)	0.80 (0.04)*	0.78 (0.04)*
Intuitive knowledge	0.32 (0.05)	0.74 (0.05)*	0.73 (0.04)*
Transcendence of time and space	0.27 (0.04)	0.75 (0.04)*	0.75 (0.04)*
Deeply felt positive mood	0.39 (0.04)	0.75 (0.04)*	0.70 (0.05)*
Ineffability and paradoxicality	0.33 (0.04)	0.80 (0.04)*	0.78 (0.05)*
Mean total score	0.33 (0.04)	0.76 (0.04)*	0.75 (0.04)*

^aData were mean scores with 1 SEM shown in parentheses; data were expressed as a proportion of the maximum possible score.

^bFor the six subjects, who received methylphenidate on two sessions, the data were from the first session.

*Significant difference from the post-methylphenidate condition ($P < 0.05$); there were no significant differences between the psilocybin post-session condition and the psilocybin 14-month follow-up.

Table 2 Volunteer ratings on the Persisting Effects Questionnaire completed 2 months following the methylphenidate and psilocybin sessions, and again retrospectively for psilocybin at the 14-month follow-up^{a,b}

Scale or question description	Methylphenidate (2 months) (<i>n</i> = 29) ^c	Psilocybin (2 months) (<i>n</i> = 29)	Psilocybin (14 months) (<i>n</i> = 29)	Psilocybin (14 months) (<i>n</i> = 36) ^d
Positive attitudes about life and/or self	23.4 (4.0)	53.1 (4.6)*	53.5 (5.4)*	53.6 (4.7)
Negative attitudes about life and/or self	0.3 (0.1)	0.6 (0.3)	0.5 (0.3)	0.7 (0.3)
Positive mood changes	16.6 (3.1)	37.4 (4.7)*	36.0 (5.5)*	37.9 (4.8)
Negative mood changes	0.5 (0.4)	1.4 (0.6)	1.6 (0.9)	1.7 (0.8)
Altruistic/positive social effects	19.0 (4.1)	44.5 (5.3)*	45.5 (6.3)*	46.3 (5.4)
Antisocial/negative social effects	0.3 (0.2)	0.7 (0.4)	0.7 (0.4)	0.6 (0.4)
Positive behaviour changes	29.7 (6.1)	56.6 (5.0)*	58.3 (5.4)*	58.1 (4.9)
Negative behaviour changes	1.4 (1.0)	0.0 (0)	0.7 (0.7)	0.6 (0.6)
How personally meaningful was the experience?	3.6 (0.3)	6.4 (0.2)*	6.3 (0.3)*	6.1 (0.2)
How spiritually significant was the experience?	2.7 (0.2)	4.8 (0.2)*	4.5 (0.3)*	4.5 (0.2)
Did the experience change your sense of well-being or life satisfaction?	+0.9 (0.2)	+1.9 (0.2)*	+1.9 (0.2)*	+1.8 (0.2)

^aData were mean ratings with 1 SEM shown in parentheses.

^bData on attitudes, mood, social, and behaviour changes were expressed as percentage of maximum possible score; data for the three questions were raw scores.

^cFor the five subjects who received methylphenidate on two sessions and who completed this questionnaire, the data are from the first session.

^dData for the full group of 36 were not available for the 2-month assessments, but is presented here for comparison.

*Significant difference from methylphenidate 2-month assessment ($p < 0.0001$); there were no significant differences between the psilocybin 2-month condition and the psilocybin 14-month follow-up ($n = 29$).

participants endorsing specific answers. Even at the 14-month follow-up, 58% of 36 volunteers rated the experience on the psilocybin session as among the five most personally meaningful experiences of their lives and 67% rated it among the five most spiritually significant experiences of their lives, with 11% and 17%, respectively, indicating that it was the single most meaningful experience, and the single most spiritually significant experience. Furthermore, 64% of the 36 volunteers indicated that the psilocybin session experience increased their sense of well-being or life satisfaction either moderately or very much, and 61% rated that the experience was associated with moderate to extreme positive behaviour change.

Relationships between screening data and the 14-month follow-up data on volunteer ratings of personal meaning and spiritual significance

Because attribution at follow-up of sustained high personal meaning and spiritual significance to the psilocybin session experience was so striking, correlations were used to examine the relationships between data obtained at screening and the 14-month follow-up data on volunteer's ratings of personal meaning and spiritual significance. Ratings of personal meaning at follow-up were significantly correlated (Pearson's r , $df = 34$, two-tailed $p < 0.01$) with negative affect on the PANAS-X ($r = -0.51$), raw score on the Quality of Life Inventory ($r = +0.47$), total score on the Faith Maturity Scale ($r = +0.41$) and mean score of the Mea-

sure of Actualization Potential questionnaire ($r = +0.44$). There were no significant correlations between any of the outcome measures and the subscales of the NEO PI-R (Neuroticism, Extroversion, Openness, Agreeableness and Conscientiousness) or the total scores on the Mysticism Scale, Spiritual Transcendence Scale or FACIT-Sp-NI.

Relationships between psilocybin session data and the 14-month follow-up data on volunteer ratings of personal meaning and spiritual significance

To further understand the sustained ratings of high personal meaning and spiritual significance, correlations were used to examine the relationships between data obtained on the psilocybin session day and the 14-month follow-up data of volunteer's ratings of personal meaning and spiritual significance. Rating of the experience as personally meaningful correlated significantly (Pearson's r , $df = 34$, two-tailed $p < 0.01$) with the HRS subscales somaesthesia, affect, perception and cognition ($r = 0.35$, 0.49 , 0.42 , and 0.46 , respectively), the APZ questionnaire subscales OSE-oceanic boundlessness ($r = 0.55$) and VUS-visual restructuralization ($r = 0.54$), total score on Mysticism Scale ($r = 0.65$), and total score on Pahnke-Richards Mystical Experience Questionnaire ($r = 0.65$). Rating of spiritual significance showed a significant correlation with the APZ questionnaire subscales OSE ($r = 0.56$) and VUS ($r = 0.48$), total score on Mysticism Scale ($r = 0.77$), and total score on Pahnke-Richards

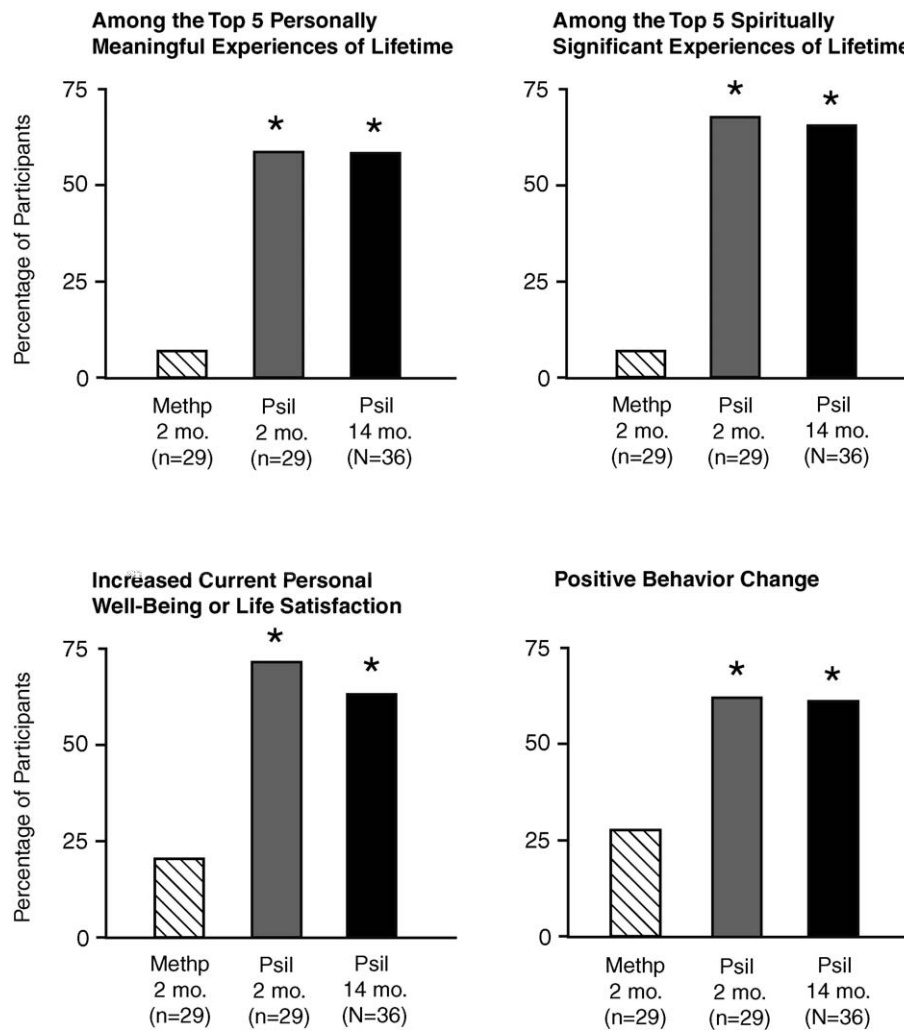


Figure 2 Percentage of volunteers endorsing specific answers on the Persisting Effects Questionnaire completed 2 months following the methylphenidate (Methp) and psilocybin (Psil) sessions ($n = 29$), and again retrospectively for psilocybin at the 14-month follow-up ($N = 36$). For ratings of personally meaningful and spiritually significant (top two panels), the data are the percentage rating ‘among the top 5’ or ‘the single most’. For ratings of increased well-being or life satisfaction, the data were the percentage rating ‘increased moderately’ or ‘increased very much’. For ratings of positive behavioural change, the data were the percentage rating ‘moderate’, ‘strong’ or ‘extreme’. Asterisks show significant differences ($p < 0.05$, z-test of proportions, $n = 29$ at each assessment) from the methylphenidate 2-month assessment; there were no significant differences between the psilocybin 2-month condition and the psilocybin 14-month follow-up assessment. For the methylphenidate results, the data presented are from the first methylphenidate session for the five subjects who received methylphenidate on two sessions and who completed this questionnaire.

Mystical Experience Questionnaire ($r = 0.66$). Ratings of personally meaningful and spiritual significance did not significantly correlate with peak monitor ratings during the session of overall drug effect, anxiety or fearfulness, distance from ordinary reality, tearing/crying, joy/intense happiness, or peace/harmony. Figure 3 illustrates the robust correlation between the score on the Mysticism Scale (completed 7 h after psilocybin administration and with reference to the experience during the session) and ratings of the spiritual significance of the experience at the 14-

month follow-up. For contrast, the figure also shows the relative lack of relationship between the subject-rated Intensity (of drug effect) HRS scale completed 7 h after psilocybin administration and ratings of the spiritual significance of the experience at the 14-month follow-up.

To further examine the contribution of mystical experience (as measured immediately post-session by the Mysticism Scale) to these follow-up measures, regression analysis controlling for intensity of drug effects was undertaken. Three separate

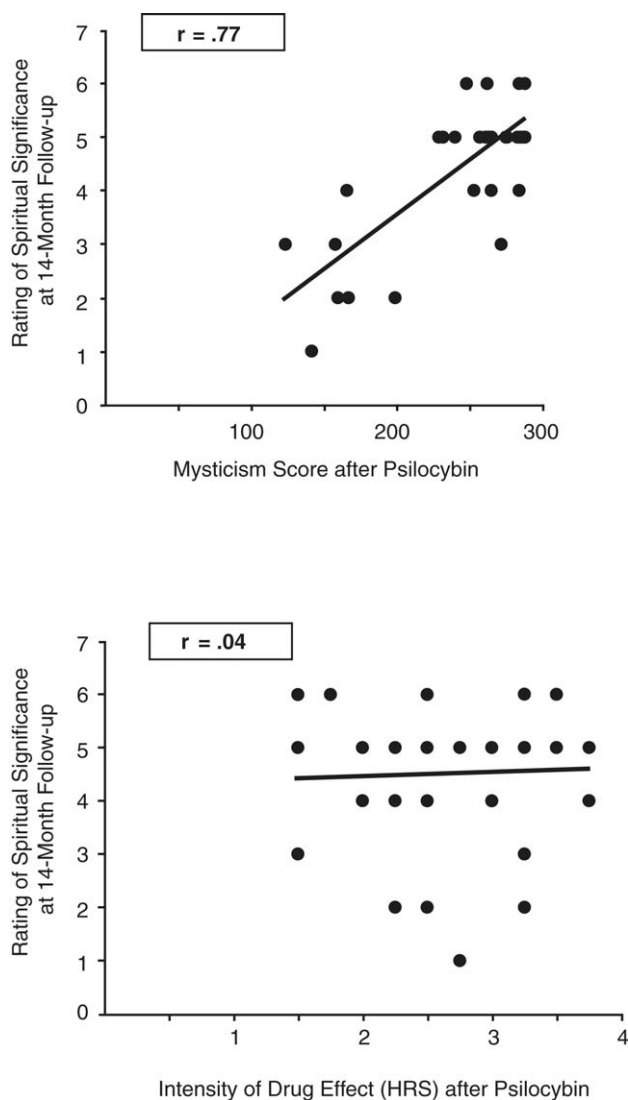


Figure 3 Ratings of the spiritual significance of the psilocybin session experience at the 14-month follow-up as a function of subject ratings complete 7 h after psilocybin administration on the Mysticism Scale (upper panel) and the Intensity subscale of the Hallucinogen Rating Scale (HRS). Data points represent individual subject data ($N = 36$); slope and correlation coefficients are shown.

measures of intensity of drug effect were used: peak monitor ratings of overall drug effect; subject-rated intensity as reflected in the Intensity subscale of the HRS questionnaire and subject-rated intensity as assessed by the single item rating 'Intensity' in the HRS questionnaire. For both the rating of personally meaningful and the rating of spiritual significance, the measures of intensity contributed only small non-significant effects. The resulting r -values for scores on Mysticism Scale remained highly significant ($p < 0.0001$): personally meaningful (0.65, 0.61, and 0.61 controlling for the three measures of intensity, respectively); spiritually significant (0.77, 0.78 and 0.74 controlling for the three measures of intensity, respectively).

Verbatim comments at the 14-month follow-up about the nature of the psilocybin-occasioned spiritual experience

Although the patterns of responses on the various subscales of questionnaires provide an empirical representation of the nature of the psilocybin session experiences, unstructured comments from volunteers are helpful to further understand the sustained high ratings of spiritual significance at the 14-month follow-up. Table 3 presents verbatim written comments about the nature of the spiritual experience for all 24 volunteers, who rated the experience at the 14-month follow-up as being among the top five

Table 3 Verbatim written comments about the nature of the spiritual experience for all 24 volunteers who rated the experience at the 14-month follow-up as being among the top five (including the single most) spiritual experiences of their lives. These comments were excerpted from the Retrospective Questionnaire that asked open-ended questions about what was most memorable and what was most spiritually significant about the experience

Volunteer	Verbatim comments
02	The understanding that in the eyes of God – all people...were all equally important and equally loved by God. I have had other transcendent experiences, however, this one was important because it reminded and comforted me that God is truly and unconditionally loving and present.
03	Freedom from every conceivable thing including time, space, relationships, self, etc... It was as if the embodied 'me' experienced ultimate transcendence – even of myself.
04	A non-self self held/suspended in an almost tactile field of light.
05	That in every horrible experience or frightening experience, if you stay with it, enter into it, you will find God. That the horror is in reality only an illusion and God lies beneath it all. It has become a guiding principal in my life.
07	The utter joy and freedom of letting go – without anxiety – without direction – beyond ego self
08	Collapse of ordinary space and time sense. Realization of unity of existence and relativity of ordinary consciousness... I have had glimpses of this before – but this was profound and sustained.
09	The 'knowing' was so powerful and yet personal. Experiencing the Beloved and falling in love.
13	The sense that all is One, that I experienced the essence of the Universe and the knowing that God asks nothing of us except to receive love.
17	I became like a point of awareness able to travel inside myself, others and the outside world. No reference to time or space... The feeling of joy and sadness at the same time – paradoxical.
21	The experience of death, which initially was very uncomfortable, followed by absolute peace and being in the presence of God. It was so awesome to be with God that words can't describe the experience.
23	To cease to 'BE', as I understand it, was not frightening. It was safe and much greater than I have words for or understanding of. Whatever is larger than the state of being is what was holding me.
27	'Surrender' is intensely powerful. To 'let go' and become enveloped in the beauty of – in this case – music – was enormously spiritual.
28	The feeling of no boundaries – where I didn't know where I ended and my surroundings began. Somehow I was able to comprehend what oneness is.
29	The profound grief I experienced as if all of the pain and sadness of the world were passing through me cell by cell tearing apart my being.
32	The breath of God/wind/and my breath are all the same... I really enjoy the deep knowings or truths and laughing about them with 'God'.
36	It opened my third eye – I could see many spiritual beliefs that I hold/held and linked them – a more cohesive and comprehensive spiritual landscape became apparent to me.
37	The experience expanded my conscious awareness permanently. It allows me to let go of negative ideas faster. I accept 'what is' easier.
39	[I experienced] a reality that was clear, beautiful, bright and joyful... In short, this experience opened me up (gave me a tangible vision) of what I think is attainable every day.
40	I felt as if tons of information about 'what is' was being downloaded quickly into my knowing/understanding.
43	The part that continues to stick out for me was 'knowing' and 'seeing' and 'experiencing' with every sense and fiber of my being that all things are connected.
45	When I confronted my shadow and yelled 'What do you want?' and it disappeared in a puff of smoke.
46	The complete and utter loss of self... The sense of unity was awesome... I now truly do believe in God as an ultimate reality.
47	My conversation with God (golden streams of light) assuring me that everything on this plane is perfect; but I do not have the physical body/mind to fully understand.
50	I remember feeling a profound sense of loss of [my family]... I remember after I resolved my fears, the shift then went to joy.

spiritual experiences of their lives. Although not easily summarized, several themes from these unstructured comments include a sense of the unity of all things, a separate 'self' ceasing to exist, and merging and/or an encounter with ultimate reality (or God).

Open-ended clinical interview at the 14-month follow-up

An open-ended clinical interview at the 14-month follow-up provided a clinical context conducive to the spontaneous reporting of study-associated adverse events. There were no

reports of persisting perceptual phenomena sometimes attributed to hallucinogen use or of recreational abuse of hallucinogens. Overall, all participants appeared to continue to be well-adjusted, high-functioning and productive members of society.

Comment

The most striking finding from this 14-month follow-up evaluation of the effects of psilocybin and methylphenidate

administered to hallucinogen-naïve volunteers is that a large proportion of volunteers rate their 'psilocybin experience'¹ as among the most personally meaningful and spiritually significant of their lives. Fifty-eight per cent and 67% of volunteers, respectively, rated the experience as being among the five most personally meaningful experiences of their lives, and the five most spiritually significant experiences of their lives; 11% and 17%, respectively, indicated that it was the single most meaningful experience, and the single most spiritually significant experience. Furthermore, 64% of the volunteers also indicated that the psilocybin experience increased their sense of well-being or life satisfaction moderately or very much, and no volunteer rated the experience as having decreased well-being or life satisfaction. The magnitude of these effects was undiminished from similar ratings completed 2 months after the psilocybin session and were substantially and significantly greater than ratings completed 2 months after the methylphenidate session. Compared with methylphenidate, attributions to the psilocybin experience also included positive changes in attitudes, mood, altruism, and other behaviour. Although the generalizability of the findings is limited by the study population (hallucinogen-naïve, well-educated, spiritually active, middle-aged adults), it is remarkable that a 8-h laboratory-based intervention could have such large and sustained personally and spiritually significant effects in such a large proportion of volunteers. The findings of sustained reports of positive effects after psilocybin are consistent with a 25-year follow-up study (Doblin, 1991) of seven theological seminary students, who received psilocybin in the context of a religious service (the Good Friday Experiment: Pahnke, 1963, 1967).

One mechanism underlying these effects appears to be that psilocybin occasioned an experience having features similar to spontaneously occurring classical mystical or religious experiences. Of the eight questionnaires measuring personality, affect, quality of life, and spirituality assessed before the study and at follow-up, only the Mysticism Scale-Lifetime showed significant differences (Figure 1). This extensively studied, empirically derived scale is based on the dimensions of mystical experience originally described by William James in 1902 in his classic book 'The Varieties of Religious Experience' (James, 1902) and further elaborated by Stace (1960). Because the version of the scale shown in Figure 1 assesses mystical experience over the entire life-time, it is not possible to attribute the increases observed at both the 2-month and 14-month assessments to the psilocybin experience *per se*. However, the original study (Griffiths, *et al.*, 2006) showed that the version of this questionnaire that assessed experience

at the end of the session was significantly increased after psilocybin compared with methylphenidate, suggesting that the increases at 2 and 14 months were probably due to the psilocybin experience. Eight dimensions of the mystical experience were also assessed by the Pahnke-Richards Mystical Experience Questionnaire, which documented robust increases on all dimensions after psilocybin (Table 1). Based on *a priori* criteria, almost 60% of the volunteers at the 14-month follow-up continued to fulfil the criteria for having had a 'complete' mystical experience during the psilocybin session. Correlation and regression analyses provided further evidence suggesting a central role of this mystical-type experience in the sustained high ratings of personal meaning and spiritual significance at follow-up, with *r*-values from regression analyses ranging from 0.74 to 0.78 for the analyses between Mysticism Scale scores immediately after psilocybin sessions and the follow-up ratings of the spiritual significance of the experience. Finally, unstructured written comments in a retrospective questionnaire completed at follow-up asked what was most memorable and spiritually significant about the experience. Responses were suggestive of a sense of the unity (e.g. the unity of all things and merging and/or an encounter with ultimate reality), which is a core aspect of mystical experiences as described by James and Stace, and as assessed by the Mysticism Scale. Thus, the domain(s) of experience assessed by the Mysticism Scale appear to be closely related to later attributions of spiritual significance and personal meaning.

Notably, none of the assessments of personality, affect, quality of life, or spirituality conducted at screening were predictive of (i.e. correlated with) ratings of spiritual significance at follow-up, and only a few of these measures significantly correlated with ratings of personal meaning. Given the large number of correlations conducted and the seeming inconsistency across different types of measures that presumably assess similar domains (e.g. openness as a personality trait was assessed by both the NEO and by the Measurement of Actualization Potential; spirituality as assessed by four separate measures), there do not appear to be any strong predictors of these sustained effects of psilocybin. Future research should explore the replicability of the observed negative correlation of ratings of personal meaning with negative affect and positive correlation with quality of life. Finally, it should be noted that, by design, the volunteer group of this study was relatively homogeneous, with screening measures showing low neuroticism and negative affect and high extroversion, openness, agreeableness and spirituality. It is possible that predictive relationships with such screening measures might emerge in a group showing more variability on such measures.

A limit to the generality of the study is that all of the participants reported at least intermittent participation in religious or spiritual activities before the study. It is plausible that such interests increased the likelihood that the psilocybin experience would be interpreted as having substantial spiritual significance and personal meaning. A systematic replication of the study comparing groups having different levels of spiritual/religious dispositions or interests could be informative.

¹ Use of the phrase 'psilocybin experience' is not intended to imply that a single type of psilocybin experience exists. Qualitative features of the 'psilocybin experience' may vary widely. The experience is best understood as formed of many factors, including psychological state (i.e. set) and environment (i.e. setting), in addition to the drug.

Although the 14-month follow-up provided no evidence of adverse effects of the psilocybin exposure, it is important not to underestimate the potential risks of hallucinogen exposure. These risks include: (1) panic or fear reactions resulting in dangerous behaviour during the time of drug action; (2) precipitation or exacerbation of enduring psychiatric conditions; (3) long-lasting perceptual disturbances and (4) development of a pattern of abuse of hallucinogens (Abraham, *et al.*, 1996; Halpern and Pope, 1999; Johnson, *et al.*, in press). In the original report of this study (Griffiths, *et al.*, 2006), we reported that 11 of the 36 volunteers experienced a period of significant fear during the psilocybin session, with six having transient ideas of reference/paranoia. These effects did not persist beyond the session. Given the extensive screening, preparation and supportive monitoring in the study protocol, this rate of difficult experience is notable and underscores the possible risk of under-supervised use escalating to panic or dangerous behaviour. Elsewhere, we provide a detailed discussion of the risks of human hallucinogen administration and safety guidelines for minimizing these risks in the context of human research (Johnson, *et al.*, in press).

The high personal meaning and spiritual significance ascribed to the psilocybin-occasioned mystical-type experience prompts consideration of whether such effects could be used to facilitate treatment of some psychiatric and behavioural disorders. Descriptive research suggests that naturally occurring instances of dramatic positive behavioural change are sometimes associated with spontaneously occurring, transformative psychological experiences, frequently of a mystical-type variety (Miller and C'de Baca, 2001; C'de Baca and Wilbourne, 2004; Forchimes, 2004). Consistent with this, observations in early studies with classical hallucinogens that examined treatment of drug and alcohol dependence (Chwelos, *et al.*, 1959; Kurland, *et al.*, 1971; Savage and McCabe, 1973) and psychological distress associated with advanced cancer (Pahnke, *et al.*, 1969; Richards, *et al.*, 1977) suggested that the occurrence of a mystical-type (i.e. transcendent or peak) experience played a key role in positive therapeutic outcome. Unfortunately, many of the early studies of therapeutic use of hallucinogens used sub-optimal procedures for supporting the experience and/or lacked modern methodological controls now expected of rigorous clinical trials (Mangini, 1998). The present demonstration that mystical experiences having sustained meaning can be occasioned in a high proportion of volunteers suggests that there may be value to re-initiating therapeutic trials with classical hallucinogens.

When administered under supportive conditions, psilocybin occasioned experiences similar to spontaneously occurring mystical experiences that, over a year later, were considered by volunteers to be among the most personally meaningful and spiritually significant experiences of their lives and to have produced positive changes in attitudes, mood, altruism, behaviour and life satisfaction. In addition to possible therapeutic applications, the ability to prospectively produce mystical-type experiences should permit rigorous scientific investigations about their causes and consequences, and may

provide novel information about the biological bases of moral and religious behaviour.

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