

CHAPTER 3

PSILOCYBIN RESEARCH AT JOHNS HOPKINS: A 2014 REPORT

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Historically, currently, and cross-culturally, profound mystical experiences are often reported as beneficially life-changing, and certain plants and chemicals are reported as potent catalysts of those experiences. The research described here undertook to scientifically demonstrate a process using psilocybin that would occasion such events with high likelihood and reasonable safety. At least for individuals similar to those who have participated in the Hopkins psilocybin studies, we believe we can now confirm that such a process exists and that it can yield at least some of the surmised benefits.

This confirmation derives from experiments in our laboratory with over 200 volunteers to date, each of whom has received at least one day-long session involving a large dose of psilocybin. Two-thirds or more of the volunteers reported one of their sessions as among the most meaningful experiences of their lives and attributed to it positive changes in their mood, behaviors, and overall well-being. Most of the volunteers were psychologically and physically healthy, hallucinogen-naïve adults with some spiritual interest. Some were cancer patients seeking relief from psychological distress due to their diagnosis, and some were tobacco smokers, otherwise healthy, willing to try a cessation program including psilocybin sessions.

The team's work so far, listed in Table 3.1, comprises seven laboratory studies, completed or in progress, and two Internet-based survey studies.

The laboratory work has been conducted double-blind using methods intended to maintain the blind and to minimize expectancy effects, including obscuring design elements from the volunteers and most study staff. This research has been or will be reported in detail in scientific journal articles. In

Table 3.1 Psilocybin Research at Johns Hopkins, 1999 to date (2014)

Laboratory Studies	Size	Type	Status
Comparative psychopharmacology	N = 36	Nontherapeutic	Completed
Dose–effect	N = 18	Nontherapeutic	Completed
Novice meditators	N = 75	Nontherapeutic	Analysis under way
Cancer/anxiety	N = 44	Therapeutic	Under way
Smoking cessation	N = 25	Therapeutic	Under way
Experienced meditators	N = 10	Nontherapeutic	Under way
Religious leaders	N = 18	Nontherapeutic	In design; to be conducted at JHU & NYU
Internet Survey Studies			
Profound/meaningful experience	N = 1602	Survey	Completed
“Bad trips”	N = 1853	Survey	Completed, analysis under way

this chapter, we summarize some of its most salient findings, drawing from the data analyzed so far and our impressions of the program as a whole.

VOLUNTEER-RATED IMPORTANCE OF HIGH-DOSE PSILOCYBIN EXPERIENCES

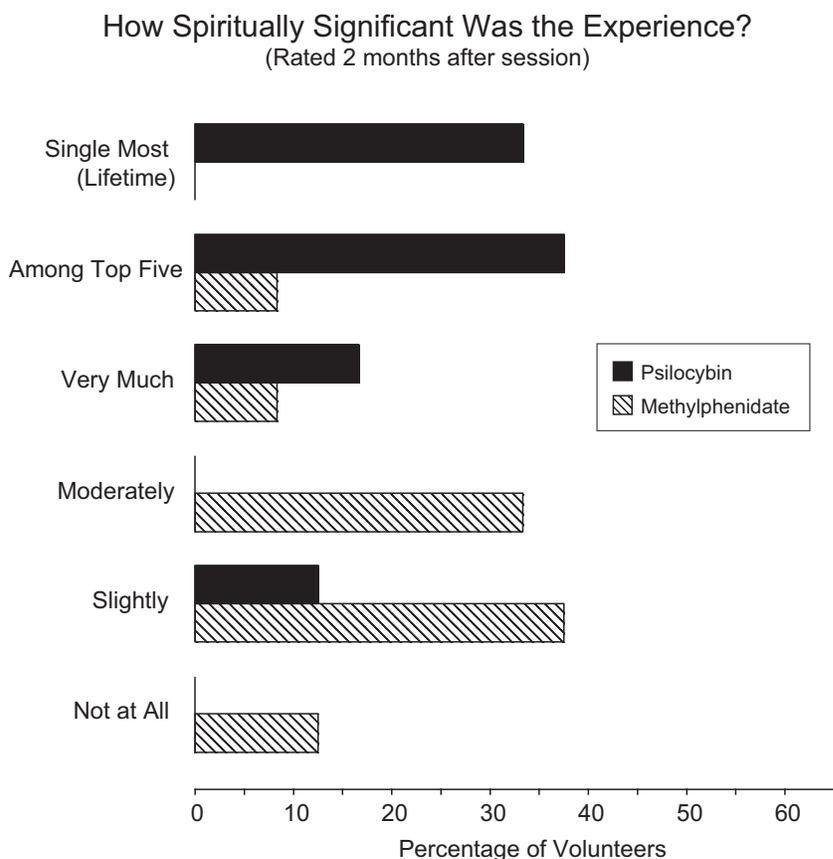
Early in the course of our first psilocybin experiment (Griffiths et al., 2006), we were struck by the profound effect some of the sessions appeared to have on volunteers, an impact that the measures we were using did not really convey. We added two questions that asked volunteers to rate on a multipoint scale how “personally meaningful” and how “spiritually significant” their sessions were. Each item’s top two rating options are “among the top five of my life” and “the single most of my life.” In the data collected with these scales, the ratings of “personally meaningful” and “spiritually significant” correlated highly ($r = 0.82$ in the 2006 data); we can think of a core construct underlying these two questions as subjective importance.

Using the new spiritual significance question two months after a high dose of psilocybin, about two-thirds of the volunteers rated the session as among the top five most spiritually significant experiences of their lives,

alongside, for example, the birth of a first child. One-third of the volunteers rated the session as the single most spiritually significant experience of their lives. When asked again at 14-month follow-up, the volunteer ratings of spiritual significance did not diminish significantly. From the view of psychopharmacology, it is remarkable that the impact of a single-day experience would be sustained for so long.

But was it the psilocybin? The laboratory sessions afforded volunteers a day in which to relax, listen to a program of music, and turn inward. That alone, amounting to a day-long contemplative retreat, could have significant effects. Indeed, volunteers tended to rate positively the personal meaning and spiritual significance of the sessions in which they received a comparison drug, methylphenidate. However, no methylphenidate session was rated as either the most personally meaningful or the most spiritually significant of a lifetime. Figure 3.1 shows the ratings of spiritual significance after a high

Figure 3.1 Percentage of volunteers endorsing different levels of spiritual significance after psilocybin versus after methylphenidate (N = 24) (adapted from Griffiths et al., 2006).



dose of psilocybin versus after a high dose of methylphenidate. Table 3.2 shows similar results using a no-dose comparison condition.

Volunteers in that study received only one psilocybin session, at a high dose. The next experiment, a dose-effect study (Griffiths et al., 2011), showed that the attributions of personal meaning and spiritual significance increase as a function of dose. In this study, volunteers received one placebo session and four psilocybin sessions, one each of a low dose, a medium dose, a medium-high dose, and a high dose. Ratings a month after each of the five sessions show that higher doses are more likely to occasion profound experiences (see Table 3.2). At 14-month follow-up, volunteers were asked

Table 3.2 Percentage of volunteers (N = 18) endorsing listed outcomes 1 month and 14 months after sessions (adapted from Griffiths et al., 2011)

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

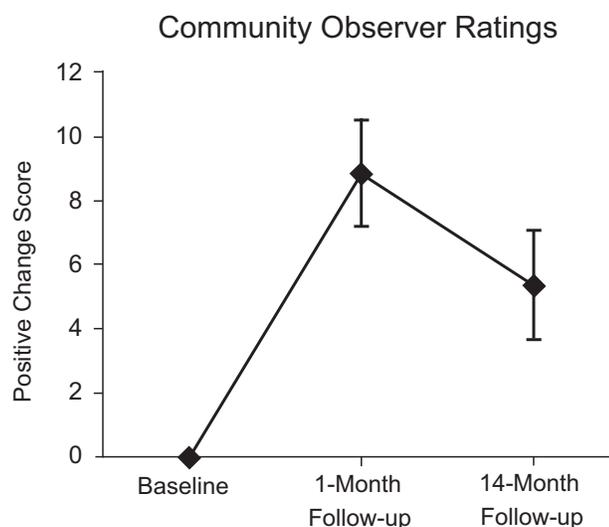
to rate the two highest-dose sessions together. Almost all the volunteers, 94 percent, rated at least one session as among the top five personally meaningful and as among the top five spiritually significant of their lives. Thirty-nine percent gave a rating of “single most personally meaningful of my life” and 44 percent gave a rating of “single most spiritually significant of my life.” These results also suggest that multiple sessions afford a greater chance of having a profound experience.

EFFECTS ON DAILY LIFE

Table 3.2 shows volunteer self-ratings of their “well-being or life satisfaction” and of positive behavior change throughout the dose-effect study. At the 14-month follow-up, 83 percent said well-being or life satisfaction was increased moderately or very much, and 90 percent reported moderate or more positive behavior change, with 44 percent reporting that change as “strong” or “extreme.”

A self-rating is one thing, while verifiable change—in behavior and well-being—can be quite another. In addition to self-reports, we sought third-party assessments of the volunteers’ attitudes and behavior. Upon enrollment, volunteers were asked to designate three adults with whom they expected to have continuing contact. Telephone interviews were conducted with these “community observers” close to the time of enrollment, about a month after the last session, and at 14-month follow-up. Each time, the

Figure 3.2 Community observer ratings of volunteers (N = 18, means and SEMs) (adapted from Griffiths et al., 2011).



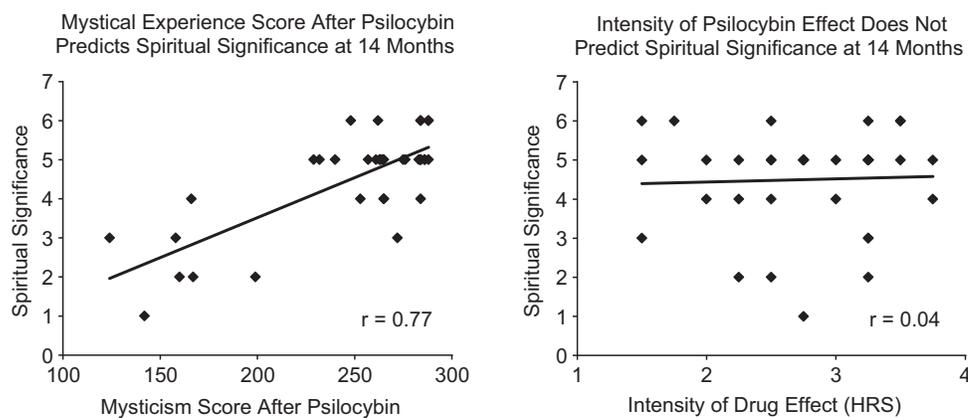
observers were asked to rate the volunteer using a 10-point scale on 11 items: inner peace, patience, good-natured humor/playfulness, mental flexibility, optimism, anxiety, interpersonal perceptiveness and caring, negative expression of anger, compassion/social concern, expression of positive emotions (e.g., joy, love, appreciation), and self-confidence. The raw composite change scores were significantly positive both at 1- and 14-month follow-up, though with some tendency to fade over time (see Figure 3.2).

MYSTICAL EXPERIENCE, NOT DRUG EFFECT INTENSITY, PREDICTS SPIRITUAL SIGNIFICANCE

The reputation of the classical hallucinogens as “recreational” drugs comes from their ability to produce effects such as colorful geometric patterns in the visual field, enhanced enjoyment of music and other sensory input, and reportedly novel or creative thinking.

Do higher doses merely produce stronger versions of those effects, so strong that people would rate them as among life’s most important experiences? Our research suggests a different story. The peak intensity of drug effect, as measured by staff ratings during sessions and participant ratings after sessions, did not correlate significantly with the reported spiritual significance 14 months later. What did correlate was the post-session score on the Hood Mysticism Scale (see Figure 3.3). Regression analysis showed that post-session mysticism scores also predicted personal well-being, life satisfaction, and positive behavior change at 1-month and 14-month follow-up assessments.

Figure 3.3 Post-session mysticism scores, but not drug effect intensity scores, predict ratings of spiritual significance 14 months later. Data points show individual volunteer data (adapted from Griffiths et al., 2008).



Mystical experience is one name for a cluster of experiences noted in diverse cultures and disciplines, and thus given many other names, among them unitive consciousness, experience of nonduality, satori, samadhi, cosmic consciousness, and primary religious experience. Our research shows that experiences of this type can have positive consequences. We suspect this is particularly true for experiences that are strong in the noetic quality and so are regarded as authoritative. Such experiences may have the potential to treat some forms of psychological distress or addictions and, in healthy individuals, to heighten personal well-being and inclination to care about others.

CHARACTERIZING THE MYSTICAL-TYPE EXPERIENCE

A large body of philosophical and scientific work has described and characterized mystical-type experiences (e.g., James, 1902; Huxley, 1945; Stace, 1960), and psychometric tools have been developed to measure them. In our research, we have used two such instruments, the well-studied Mysticism Scale (Hood, 1975), which has been shown to have a three-factor structure (Hood et al., 1993), and a previously unvalidated, 43-item instrument called the Pahnke-Richards Mystical Experience Questionnaire (Griffiths et al., 2006, 2008).

To investigate the validity, reliability, and factor structure of questionnaire items assessing mystical experience, our team conducted an anonymous Internet-based survey (MacLean et al., 2011). The survey method yielded a large sample ($N = 1602$) of individuals who reported having had a profound, personally meaningful experience after taking psilocybin mushrooms. Exploratory and confirmatory factor analysis of the data confirmed the validity and reliability of a 30-item questionnaire termed the Mystical Experience Questionnaire (MEQ). The analysis demonstrated a four-factor structure for psilocybin-occasioned mystical experience: (1) mystical, comprised of items assessing internal and external unity, noetic quality, and sacredness; (2) positive mood; (3) transcendence of time and space; and (4) ineffability.

FEAR, ANXIETY, AND PARANOIA

The classical hallucinogens can produce a remarkably wide range of effects, including fear, anxiety, paranoia, and ideas of reference. Such negative effects were seen not infrequently in our laboratory, despite careful screening and preparation before receiving psilocybin and despite a comfortable living-room-like setting and the presence of supportive monitors during the sessions.

In the first study, 33 percent of volunteers after psilocybin and none after methylphenidate reported strong or extreme ratings of fear sometime during the session. Intervals of fear or anxiety had unpredictable times of onset and durations. In the dose–effect study, such challenging effects occurred in 39 percent of volunteers, but almost exclusively at the highest dose (only 1 of 18 volunteers at the second-highest dose and none at lower doses). Between the two highest doses used in this study, it may be that a “sweet spot” dose is available, trading the likelihood of complete mystical experience against the likelihood of acute negative effects.

In all of our laboratory work, acute negative effects were managed as needed with reassurance from the monitors and did not persist beyond the session. Curiously, these occurrences did not affect the overall rate of having “complete” mystical experiences as assessed at the end of the session and did not show a relationship with later ratings of personal meaning or spiritual significance.

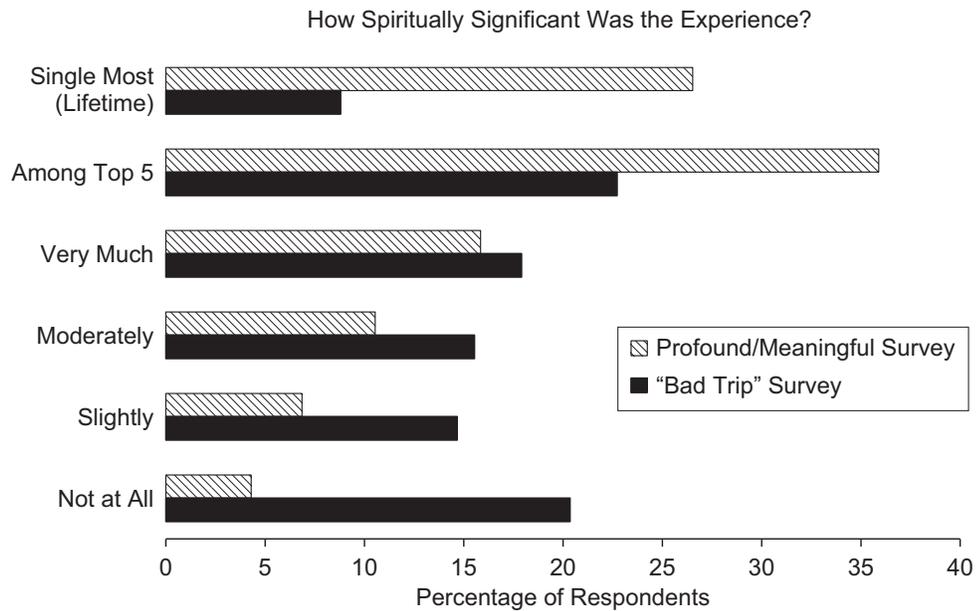
An anonymous, Internet-based survey of “bad trips” on psilocybin mushrooms provided another means of studying acutely challenging psilocybin experiences. This completed but as yet unpublished study asked volunteers about their most challenging experience after ingesting psilocybin mushrooms. Although almost 40 percent of participants rated the experience as among the five most challenging experiences of their lives, more than 30 percent rated it as among the five most meaningful experiences of their lives. The survey also afforded an opportunity to develop a new scale, the Challenging Experience Questionnaire. Its scores correlated reasonably highly, as expected, with an independent measure of experience difficulty, but not with ratings of spiritual significance.

Figure 3.4 compares the spiritual significance ratings from the two Internet-based surveys. More than a few survey participants gave high ratings of personal meaning to their challenging mushroom experience, mirroring Walter Houston Clark’s paradoxical observation (1976): “‘Bad trips’ may be the best trips.”

But that was often not the case. In a preliminary analysis, nearly 11 percent of “bad trip” survey respondents said they had put themselves or others at risk of physical harm during the experience, and nearly 3 percent said they had behaved in a physically aggressive or violent manner during the experience. Nearly 3 percent said that after the experience they sought treatment for fear, anxiety, or depression. Seventy-five percent said there had been no guide or sitter present during their experience.

These numbers come from a subset of mushroom users who saw a public call for information about “bad trips” and took the time to respond to it. We cannot extrapolate from them to mushroom use overall. Nonetheless, the

Figure 3.4 Percentage of respondents endorsing different levels of spiritual significance in Internet-based surveys of profound/meaningful experiences (N = 1602) and of “bad trips” (N = 1853) on psilocybin mushrooms.



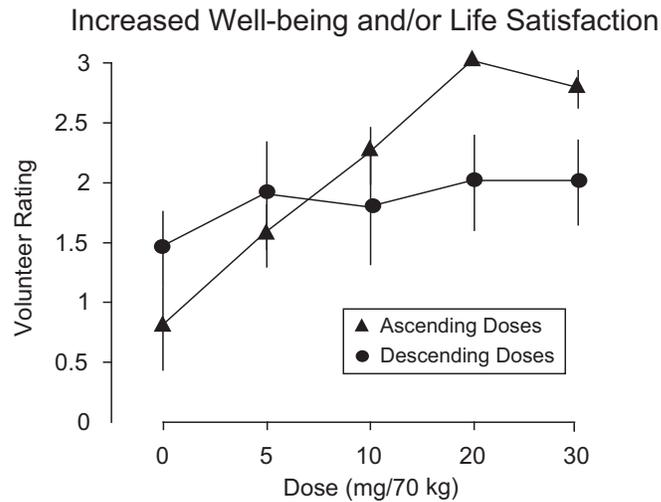
findings underscore the importance of precautions (Johnson et al., 2008), particularly the importance of competent supervision during the hours of psilocybin action.

ASCENDING DOSE SEQUENCE HELPS

In the dose–effect study, unbeknownst to the volunteers and the session monitors, the four different doses were given in either an ascending or a descending order. To help obscure the ordering, the no-dose placebo session was quasi-randomly inserted in the sequence of five sessions.

With the ascending sequence, measures of mystical experience, personal meaning, and spiritual significance, and persisting positive effects were generally greater at the two highest dose levels and lower at the two lowest levels, relative to the descending sequence (see Figure 3.5). This suggests that the ascending dose sequence is more likely than the descending sequence to

Figure 3.5 Ratings of increased well-being or life satisfaction by volunteers receiving psilocybin doses in either an ascending or descending dose sequence (means and SEMs, N = 9 for each group) (adapted from Griffiths et al., 2011).

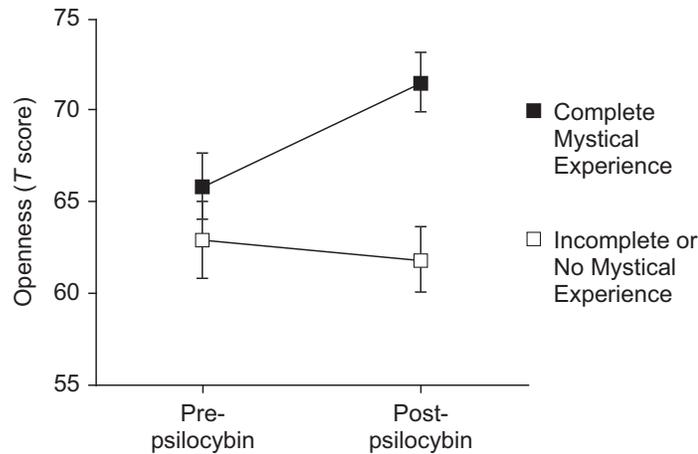


produce long-lasting positive changes in attitudes and behavior. We incorporated this finding into the design of the novice meditator study (now undergoing data analysis), giving one group of volunteers a medium-high-dose session followed by a high-dose session.

THE PERSONALITY TRAIT OF OPENNESS

The persisting changes in attitudes and behaviors observed in the study volunteers prompted us to wonder if psilocybin sessions were changing personality. This is a provocative question because personality is usually considered to be a set of characteristics that are mostly stable after maturity, changing thereafter only slowly if at all. Examining data across our first two studies, MacLean et al. (2011) showed that psilocybin increased the personality domain of openness. Specifically, individuals who had complete mystical experiences after psilocybin showed increases in openness at follow-up (see Figure 3.6). This finding is intriguing because openness encompasses esthetic appreciation and sensitivity, fantasy and imagination, and broad-minded tolerance of others' viewpoints and values. Openness predicts creativity in a wide range of domains such as the arts, sciences, and humanities.

Figure 3.6 Change in the personality domain of Openness from before to after psilocybin in volunteers who did ($N = 30$) and did not ($N = 22$) have a complete mystical experience (means and SEMs) (adapted from MacLean et al., 2011).



ONGOING AND PLANNED STUDIES

Cancer Patient Study

Continuing a line of research dating at least back to the early 1960s (Kast and Collins, 1964), the Hopkins laboratory is conducting a clinical trial in which cancer patients with anxiety or depression due to their cancer diagnosis are given psilocybin sessions (Grob et al., 2013). A supportive context is provided that encourages these psychologically distressed individuals to explore whatever thoughts and feelings arise. The study extends a promising pilot study with psilocybin (Grob et al., 2011) by testing a higher dose in a larger patient group. The present Hopkins study administers an amount of psilocybin we believe more likely to occasion unitive consciousness and its potentially beneficial therapeutic consequences.

Smoking Cessation Pilot Study

Our laboratory is conducting a pilot study, led by Matthew Johnson, to explore whether psilocybin experiences can facilitate smoking cessation in treatment-seeking, nicotine-dependent smokers. The treatment approach integrates high-dose psilocybin sessions with cognitive-behavioral therapy and guided imagery. The unpublished results to date look very promising, showing higher abstinence rates than those achieved through established cessation programs.

Nicotine addiction is considered a model addiction for laboratory research because it is not uncommon for users to be psychologically healthy, allowing study of the addiction without confounding comorbidities. If psilocybin-assisted treatment for nicotine addiction is confirmed as effective, it will increase the motivation to explore hallucinogen-assisted treatments for other addictions as well (see Krebs and Johanson, 2012).

Other Psilocybin Research in Progress at Hopkins

Three other studies are in development or in progress, all with healthy volunteers. One, with novice meditators, seeks to understand the interactions between psilocybin sessions and more conventional spiritual practices, such as meditation or mantra repetition, and social support. The experimental phase of this work is complete. Another study, our first to use brain imaging, will explore the effects of psilocybin in long-term meditators. In the third study, a joint effort of Hopkins and New York University, religion professionals such as ministers and rabbis will receive psilocybin sessions. We will examine the effects of the sessions on the individuals personally, including any deepening or other changes in their relationship to their tradition, and on their vocational lives.

QUANTUM CHANGE

The apparent ability of mystical-type experience to bring about rapid and lasting change is curious. We believe it may connect with what has been termed “quantum change” (Miller, 2004). Naturalistically, this phenomenon seems to occur spontaneously at low rates, sometimes under circumstances one would not want to precipitate, such as near-death experience. A reasonably reliable means of occasioning quantum-change experiences, which psilocybin appears to afford, could enable new lines of prospective experimental research.

As Abraham Maslow wrote about the hallucinogens,

It looks as if these drugs often produce peak-experiences in the right people under the right circumstances, so that perhaps we needn't wait for them to occur by good fortune. Perhaps we can actually produce a private personal peak-experience under observation and whenever we wish under religious or non-religious circumstances. We may then be able to study in its moment of birth the experience of illumination or revelation. Even more important, it may be that these drugs, and perhaps also hypnosis, could be used to produce a peak-experience, with core-religious revelation,

in non-peakers, thus bridging the chasm between these two separated halves of mankind. (Maslow, 1964)

CLOSING THOUGHTS

The psilocybin process used at Hopkins (Johnson et al., 2008) extends some of the research and clinical practices developed decades ago, before hallucinogens were prohibited and research went dormant. The Hopkins process can no doubt be improved. At the same time, some informed observers, such as Huston Smith, have cautioned that even a successful means of occasioning mystical or non-dual experience must be evaluated with respect to larger contexts:

[T]he goal (it cannot be stressed too often) is not religious experiences, but the religious life. And with respect to the latter, chemically occasioned “theophanies” can abort a quest as readily as they can further it. (Smith, 2000)

Today, the term “religious life” may connote conformity or demonstrative piety. Clark’s understanding of religion offers a more spacious interpretation:

[R]eligion can be most characteristically described as the inner experience of the individual when he senses a Beyond, especially as evidenced by the effect of this experience on his behavior when he actively attempts to harmonize his life with the Beyond. (Clark, 1958)

More work is needed to understand the benefits and the hazards of any chemically quickened spiritual path and to learn ways of enhancing the gains and minimizing the risks. Work also remains to identify and highlight factors that can help an individual retain and develop the fruits of a unitive experience. A variety of religious and cultural traditions assert the value of contemplative practices, teachers, and the presence of a community vessel. We expect that, in time, thoughtful laboratory research and naturalistic study will bring all of these matters into sharper scientific focus.

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REFERENCES

- Clark, Walter Houston. (1958). *The Psychology of Religion*. New York: Macmillan.
- Clark, Walter Houston. (1976). "Bad trips" may be the best trips. *FATE Magazine*, April 1976.
- Griffiths, Roland R., William A. Richards, Una McCann, and Robert Jesse. (2006). Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance. *Psychopharmacology*, 187(3): 268–283.
- Griffiths, Roland R., William A. Richards, Matthew W. Johnson, Una D. McCann, and Robert Jesse. (2008). Mystical-type experiences occasioned by psilocybin mediate the attribution of personal meaning and spiritual significance 14 months later. *Journal of Psychopharmacology*, 22(6): 621–632.
- Griffiths, Roland R., Matthew W. Johnson, William A. Richards, Brian R. Richards, Una D. McCann, and Robert Jesse. (2011). Psilocybin occasioned mystical-type experiences: Immediate and persisting dose-related effects. *Psychopharmacology*, 218(4): 649–665.
- Grob, C. S., A. L. Danforth, G. S. Chopra, M. Hagerty, C. R. McKay, A. L. Halberstadt, and G. R. Greer. (2011). Pilot study of psilocybin treatment for anxiety in patients with advanced-stage cancer. *Archives of General Psychiatry*, 68(1): 71–78.
- Grob, Charles S., Anthony P. Bossis, and Roland R. Griffiths. (2013). Use of the classic hallucinogen psilocybin for treatment of existential distress associated with cancer. In: B. I. Carr and J. Steel (Eds.), *Psychological Aspects of Cancer*. New York: Springer.
- Hood, Ralph W. (1975). The construction and preliminary validation of a measure of reported mystical experience. *Journal for the Scientific Study of Religion* 14(1): 29–41.
- Hood, Ralph W., Ronald J. Morris, and P. J. Watson. (1993). Further factor analysis of Hood's mysticism scale. *Psychological Reports*, 73(2): 1176–1178.
- Huxley, Aldous. (1945). *The Perennial Philosophy*. New York: Harper & Bros.
- James, William. (1902/2002). *The Varieties of Religious Experience: A Study in Human Nature*. New York: Random House.
- Johnson, Matthew W., William A. Richards, and Roland R. Griffiths. (2008). Human hallucinogen research: Guidelines for safety. *Journal of Psychopharmacology*, 22(6): 603–620.
- Kast, Eric C., and Vincent J. Collins. (1964). Lysergic acid diethylamide as an analgesic agent. *Anesthesia & Analgesia*, 43: 285–291.
- Krebs, Teri S., and Pål-Ørjan Johansen. (2012). Lysergic acid diethylamide (LSD) for alcoholism: Meta-analysis of randomized controlled trials. *Journal of Psychopharmacology*, 26(7): 994–1002.
- MacLean, Katherine A., Matthew W. Johnson, and Roland R. Griffiths. (2011). Mystical experiences occasioned by the hallucinogen psilocybin lead to increases in the personality domain of openness. *Journal of Psychopharmacology*, 25(11): 1453–1461.

- MacLean, Katherine A., Matthew W. Johnson, Jeannie-Marie S. Leoutsakos, and Roland R. Griffiths. (2012). Factor analysis of the mystical experience questionnaire: A study of experiences occasioned by the hallucinogen psilocybin. *Journal for the Scientific Study of Religion*, 51(4): 721–737.
- Maslow, Abraham H. (1964). *Religions, Values, and Peak Experiences*. Columbus: Ohio State University Press.
- Miller, William R. (2004). The phenomenon of quantum change. *Journal of Clinical Psychology*, 60(5): 453–60.
- Smith, Huston. (2000). *Cleansing the Doors of Perception: The Religious Significance of Entheogenic Plants and Chemicals*. San Francisco: Council on Spiritual Practices.
- Stace, Walter Terence. (1960). *Mysticism and Philosophy*. New York: Macmillan.