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# Hopkins scientists find lasting positive impact of psilocybin-induced "All is One" experiences; publish ethical guidelines for hallucinogen research

More than a year after receiving the active agent in "sacred mushrooms" under rigorous scientific conditions, most of the volunteers in a Hopkins study looked back on their experience and rated it as the single, or one of the top five, most personally meaningful and spiritually significant of their lives.

The Hopkins research team reported today in the *Journal of Psychopharmacology* the impact of a day-long psilocybin session as assessed 14 or 16 months later. Remarkably, measures of the impact of the experience did not fade significantly from the scores collected two months after the session.

Most volunteers reported in their psilocybin session a key characteristic of "mystical experience": the perception that "All is One," which one volunteer called "the sense of unity." Said another, "I could see many spiritual beliefs that I hold/held and linked them – a more cohesive and comprehensive spiritual landscape became apparent to me." Fourteen months after the experience, more than 60% of participants reported substantial increases in life satisfaction and positive behavior. On no measure were participants worse off after the experience than they had been before, and no participant reported any lasting negative effect of participation.

The Hopkins scientists, led by Roland Griffiths, have already shown that the mushroom substance, psilocybin, can occasion mystical/spiritual experiences descriptively indistinguishable to the ones mystics and saints have reported for centuries.

Said Griffiths, "Today's report confirms, if it wasn't clear before, that psilocybin gives us a uniquely powerful tool to study primary spiritual experience and its short and long term effects. We've also gained confidence in what we think are a prudent set of 'best practices' to help to insure safety in this type of research."

Both at two months and at the year-later assessment, psychological tests and subjects' own reports showed no harm to study participants, though some reported periods of extreme anxiety or other unpleasant effects in the hours following the psilocybin capsule. The drug has not been observed to be addictive or physically toxic in animal studies or human populations. "In this regard," says Griffiths, a psychopharmacologist, "it contrasts with amphetamine, cocaine, heroin, and alcohol."

And yet, the research team cautions about substantial risks of taking psilocybin under inappropriate conditions or without adequate supervision. "Even in this study, where we carefully controlled conditions to minimize adverse effects, about a third of subjects reported significant fear, with some also reporting transient feelings of paranoia," says Griffiths. "Under unmonitored conditions, it's not hard to imagine those emotions escalating to panic and dangerous behavior."

The Hopkins team published another paper today in the *Journal of Psychopharmacology*

describing a set of guidelines to help insure the safety of volunteers in hallucinogen research. That paper's lead author, psychopharmacologist Matthew W. Johnson, commented, "Our experience confirms what has been found in decades of published research with hallucinogens: that with appropriately screened individuals, under prepared and supportive conditions, and with adequate supervision, hallucinogens can be given with a level of safety that compares favorably with many accepted human research and medical procedures. What we've published is our synthesis of the safety-related wisdom gained from earlier research with hallucinogens, from sacramental use by indigenous cultures, and from our own seven year-long track record."

As hallucinogens once again receive increased attention from scientists, the Hopkins team hopes that their published safety guidelines will help present-day researchers avoid the mistakes a small number of earlier researchers made, in either not appreciating the unique psychopharmacology of these substances, or not tailoring appropriate safeguards.

The guidelines describe how to screen potential study volunteers so that individuals can be excluded whose personal or family psychiatric histories indicate they may be at risk of averse reactions to hallucinogens. For volunteers who participate in hallucinogen research, the guidelines advise that two or more trained monitors meet with each volunteer on several occasions to prepare them for the possible effects of hallucinogens and to develop rapport and trust. When it comes time to administer a substance, the Hopkins team advises that two monitors be in the room for most of the session and that the volunteer is never left unattended. Finally, the team's "best practices" include having the monitors meet with the participant after the session and as needed to provide support in working through the thoughts and feelings encountered during or as a result of the session.

The Griffiths team broke new ground in 2006 when it published the first report of an experiment in which 36 healthy, well-educated volunteers with an active life no family history of psychosis or bipolar disorder were given psilocybin or methylphenidate (the chemical name for Ritalin), double-blind. All had active spiritual lives. "We thought a familiarity with spiritual practice would give them a framework for interpreting their experiences and so they'd be less likely to be confused or troubled by them," Griffiths says. Despite selecting spiritually inclined volunteers, subjects typically showed large increases in standardized measures of mystical experience following a psilocybin session but not after receiving methylphenidate.

*See www.csp.org/psilocybin for links to the report, published commentaries, and media reports about the original study.*

**The team's work has been widely praised by experts in the behavioral scientists.**

Cited as "landmark" in the commentary by former National Institute on Drug Abuse (NIDA) director, Charles Schuster, the research marks a new systematic approach to studying certain hallucinogenic compounds that, in the 1950s, showed signs of therapeutic potential or value in research into the nature of consciousness and sensory perception. "Human consciousness is a function of the ebb and flow of neural impulses in various regions of the brain-the very substrate that drugs such as psilocybin act upon," Schuster says. "Understanding what mediates these effects is clearly within the realm of neuroscience and deserves investigation."

The study isn't the first with psilocybin, the researchers say, though some of the earlier ones, done elsewhere, had notably less rigorous design, were less thorough in measuring outcomes, or lacked longer-term follow-up.

In the present study, thirty of the thirty-six subjects attended two separate 8-hour drug sessions, at two month intervals. On one they received psilocybin, on another, methylphenidate (Ritalin), the active placebo.

In designing the study, researchers had to overcome or at least, greatly minimize two hurdles: the risk of adverse side-effects and the likelihood that the expectations of getting the test drug or the placebo would influence subjects' perceptions.

To manage the risk of adverse side-effects, each subject met several times, before drug sessions began, with a reassuring "monitor," a trained professional experienced in observing drug study participants. Monitors stayed with them during the capsule-taking sessions. Actual trials took place in a room outfitted like a comfortable, slightly upscale living room, with soft music and indirect, non-laboratory lighting. Heart rate and blood pressure were measured throughout.

The researchers countered "expectancy" by having both monitors and subjects "blinded" to what substance would be given. For ethical reasons, subjects were told about hallucinogens' possible effects, but were also told they could, instead, get other substances-weak or strong-that might change perception or consciousness. Most important, a third "red herring" group of six subjects had two blinded placebo sessions, then were told they'd receive psilocybin at a third. Questionnaires later verified that this tactic kept participants and monitors in the dark at the first two sessions about each capsule's contents.

Nine established questionnaires and a new, specially created follow-up survey were used to rate experiences at appropriate times in the study. They included those that differentiate effects of psychoactive drugs, that detect altered states of consciousness, that rate mystical experiences and assess changes in outlook.

As for where the work could lead, the team has recently started a psilocybin study in patients suffering from advanced cancer-related anxiety or depression (http://www.cancer-insight.org/), following up suggestive research several decades ago. They're also designing studies to test a role for psilocybin in treating drug dependence.

Also of interest to the team are the non-medical implications of mystical-type experiences. As religion scholars and spiritual guides have long cautioned, experience is just that – it comes and it goes. At two-month followup and again a year later, most volunteers reported that the psilocybin session increased their sense of well-being or life satisfaction “moderately” or “very much” (and no volunteers reported decreases). Community observer ratings (family, friends, coworkers, etc.) tended to confirm this. But we need more sensitive measures of pro-social attitudes and behaviors, such as love, forgiveness, equanimity, and generosity, and we want to study factors that may help volunteers turn a transient peak experience into sustained good.

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Conduct of the psilocybin study was funded by grants from NIDA and the Council on Spiritual Practices. Preparation of the follow-up study reported today was supported by grants from the Council on Spiritual Practices and the Heffter Research Institute.

William Richards, Ph.D., Matthew W. Johnson, Ph.D., and Una McCann, M.D., of the Johns Hopkins Medical Institutions and Robert Jesse of the Council on Spiritual Practices, San Francisco, were co-researchers in today's report, *"Mystical-type experience occasioned by psilocybin mediate the attribution of personal meaning and spiritual significance 14 months later."*

Matthew W. Johnson, William A. Richards, and Roland R. Griffiths of the Johns Hopkins Medical Institutions authored the paper also published today, *"Human Hallucinogen Research: Guidelines for Safety."*

More information about the psilocybin study, including the 2006 report, concurrently published commentaries, the Hopkins press release, and links to various media reports may be found at www.csp.org/psilocybin

The 2006 commentaries were authored by

Hopkins neuroscientist and Professor of Neuroscience, Solomon Snyder, M.D.

Former NIDA head Charles Schuster, Ph.D., now Distinguished Professor of Psychiatry and Behavioral Neuroscience at the Wayne State University School of Medicine

Herbert Kleber, M.D., a professor of psychiatry at Columbia University and a former deputy director of the White House Office of National Drug Control Policy (ONDCP)

David Nichols, Ph.D., with the Purdue University School of Pharmacy and Pharmaceutical Sciences

Harriet de Wit, Ph.D., at the University of Chicago Department of Psychiatry. DeWit is the editor of *Psychopharmacology*.

**Huston Smith Comments**

Huston Smith, holder of 12 honorary degrees, is an esteemed authority on comparative religion. His book *The World's Religions* has for forty years been the most widely used textbook on its subject, and in 1996 he was the focus of a five part Bill Moyers PBS program, "The Wisdom of Faith with Huston Smith." See hustonsmith.net for more.

Commenting on the study by Griffiths and colleagues, Smith said:

"Mystical experience seems to be as old as humankind, forming the core of many if not all of the

great religious traditions. Some ancient cultures, such as classical Greece, and some contemporary small-scale cultures, have made use of psychoactive plants and chemicals to occasion such experiences. But this is the first scientific demonstration in 40 years, and the most rigorous ever, that profound mystical states can be produced safely in the laboratory. The potential is great."

Smith also issued a caution and suggested that further research on the topic include social as well as neurological variables: "In the end, it's altered traits, not altered states, that matter. 'By their fruits shall ye know them.' It's good to learn that volunteers having even this limited experience had lasting benefits. But human history suggests that without a social vessel to hold the wine of revelation, it tends to dribble away. In most cases, even the most extraordinary experiences provide lasting benefits to those who undergo them and people around them only if they become the basis of ongoing work. That's the next research question, it seems to me: What conditions of community and practice best help people to hold on to what comes to them in those moments of revelation, converting it into abiding light in their own lives?"

**Questions and Answers about the 2006 Johns Hopkins Psilocybin Study with Roland Griffiths, the study's lead researcher.**

*Q 1: Why did you undertake this research?*

In the 1950s and 1960s, basic science and applied research studies were taking place with hallucinogens, offering hints that they might be of value in psychotherapy, addiction treatment, and creativity enhancement, and suggestions that the hallucinogens can occasion mystical-type experiences. Laws enacted in response to excesses of the "psychedelic 1960s" stopped almost all that work, leaving some promising threads dangling. Despite ongoing illicit and licit use, remarkably little is known, from the standpoint of modern psychopharmacology research, about the acute and long-term effects of the hallucinogens. Our study is among the first to re-open this field. Since the Hopkins psilocybin work began, researchers at other major universities, such as UCLA, the University of Arizona, and Harvard, have begun planning or are carrying out hallucinogen research.

*Q 2: Do you have any sign that the same brain "machinery" affected by psilocybin is identical to what people experience in spiritual epiphanies that occur without drugs?*

That work hasn't been done yet, though there is good reason to believe that similar mechanisms are at work during profound religious experiences, however they might be occasioned (for example, by fasting, meditation, controlled breathing, sleep deprivation, near death experiences, infectious disease states, or psychoactive substances such as psilocybin). The neurology of religious experience, newly termed neurotheology, is drawing interest as a new frontier of study.

*Q 3: Is this God in a pill? Does it render God or "revelation" irrelevant?*

The scientific method works with what can be observed in the physical realm, using tools such as atomic particle detectors, medical imaging devices, people's responses to psychological tests, interviews, and behavioral observations. We are attempting neither to validate nor to invalidate the truth of claims that some people have made about metaphysical realities as a consequence of their psilocybin experiences (or as a consequence of their meditation, fasting, or prayer experiences) - that's beyond our purview as scientists. It is within the purview of science to study the changes in mood, values, view of self, and behaviors that may follow such experiences.

Of course it would be a profound mistake to confuse the experience of something for the thing itself. We are not aware of study participants who felt their psilocybin experience devalued their own religious traditions; interviews suggested the opposite was more usually the case.

*Q 4: Are you trying to find a short cut to the spiritual journey that some people pursue for years?*

Our focus in this research was to study the effects of psilocybin using the methods of modern psychopharmacology. It's true that "transformative" changes in values, self-perception, and behaviors have been reported across cultures and eras as a consequence of mystical-type experience. This bears investigation.

*Q 5: Should religions feel threatened by this work?*

I can't see why.

The psychologist Walter Clark, in his 1958 book The Psychology of Religion, had this to say: "There is no more difficult word to define than 'religion'.... With full recognition that we are on ground where the experts disagree, we will venture our own definition. It is our feeling that religion 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."

Many of the volunteers in our study reported, in one way or another, a direct, personal experience of the "Beyond." Far from being threatened, the only thing we can imagine being of greater interest to religions is whether people live more wholesome, compassionate, and equanimous lives in consequence of such experiences.

*Q 6: Why did you use volunteers who have active spiritual practices? Didn't that help assure the results you got?*

Psilocybin and similar compounds have been reported to sometimes bring about experiences called spiritual, religious, mystical, visionary, revelatory, etc. Such experiences may be difficult psychologically and emotionally. We felt that volunteers who had some engagement with prayer, meditation, churchgoing, or similar activities would be better equipped to understand and consolidate any mystical-type experiences they might have in the study.

You might think that the volunteer's spiritual orientation would have them naturally interpret any drug experience as spiritual. And yet, using standardized measures, these volunteers typically

reported mystical experience upon receiving psilocybin, but not upon receiving methylphenidate, the comparison drug. This finding, using our double-blind experimental design, lets us attribute the spiritual effects specifically to psilocybin.

*Q 7: Aren't hallucinogens dangerous? How can you give them to human volunteers?*

No mind-affecting drug is absolutely safe. But the risks of the hallucinogens can be managed in appropriate research settings.

Unlike drugs of abuse such as alcohol and cocaine, the classic hallucinogens are not known to be physically toxic and they are virtually non-addictive, so those are not concerns.

The primary effect of psilocybin, in medium to large doses, is strong alteration of consciousness. It is possible that such experiences can trigger latent schizophrenia in susceptible individuals. Thus in our study we disqualified potential volunteers whose personal or family psychiatric histories indicate that they may be at increased risk of that disorder.

Our study confirms that some individuals, during some or all of the hours of the drug's action, may experience paranoia, extreme anxiety, or other unpleasant psychological effects. It is not difficult to imagine such stresses leading to dangerous or inappropriate behaviors, which may constitute the substance's most prominent risk. We managed that in our study through a short course of psychological preparation and through careful and interpersonally sensitive monitoring of each drug session. The monitors were trained to provide reassurance (e.g., supportive words or gentle touch to a hand) if needed.

*Q 8: What kind of substance is psilocybin?*

Psilocybin is one of a class of compounds whose primary activity is known to be on 5-HT-2a/c serotonin receptors. Their effects include changes in perception and cognition. In the pharmacology literature, this class of drugs is called "hallucinogens, " though they rarely cause "hallucinations" in the sense of seeing or hearing things that are not there. Within other academic fields, the term 'entheogen,' roughly meaning "spirit-facilitating," is coming into prominence for this class of substances.

*Q 9: Studies at Hopkins have shown the potential for brain damage from MDMA ( "ecstasy"). How do you know psilocybin doesn't have the same risk?*

Some studies have shown that MDMA can damage certain nerve cells. There is no experimental or clinical evidence in animals or humans that psilocybin, even in very high doses, is similarly neurotoxic. Enough research has been done with psilocybin, starting in the 1950s, that we can be reasonably confident that it is not physically toxic in doses humans ordinarily use. This is consistent with the fact that psilocybin-containing mushrooms have not, in millennia of use, acquired a reputation of being physically harmful. Traditions that use psilocybin mushrooms do, however, caution about psychological and spiritual risks of using them haphazardly.

*Q 10: Isn't your work similar to what Timothy Leary did?*

We are conducting rigorous, systematic research with psilocybin under carefully monitored conditions, a route which Dr. Leary abandoned in the early 1960s.

*Q 11: Isn't there a risk that a study like this could encourage abuse of psilocybin or similar substances?*

Our report explains the substantial risks that could easily follow from use without the psychiatric screening, preparation, and monitoring we provided in this study.

Herbert D. Kleber, M.D., addressed this question in a commentary published concurrently with our paper. Dr. Kleber is Professor of Psychiatry at the Columbia University College of Physicians & Surgeons and the Director of Division on Substance Abuse of the New York State Psychiatric Institute. He previously served as a deputy director of the White House Office of National Drug Control Policy (ONDCP).

Dr. Kleber wrote, "The positive findings of the study cannot help but raise concern in some that it will lead to increased experimenting with these substances by youth in the kind of uncontrolled and unmonitored fashion that produced casualties over the past three decades?

"Any study reporting a positive or useful effect of a drug of abuse raises these same concerns. In this Internet age, however, where youth are deluged with glowing personal reports in chat rooms and web sites as well as detailed information about the various agents and how to use them, it is less likely that a scientific study would move the needle much.

"Psychedelic drug use has remained in a relatively constant range over the past three decades as various fads have come and gone and enthusiastic personal accounts are balanced by negative reports about casualties.

Discovering how these mystical and altered consciousness states arise in the brain could have major therapeutic possibilities, e.g., treatment of intolerable pain, treatment of refractory depression, amelioration of the pain and suffering of the terminally ill, to name but a few, as well as the already noted and needed improvement in treatment of substance abuse and dependence states so that it would be scientifically shortsighted not to pursue them."

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