Psychopharmacology
DOI 10.1007/s00213-006-0458-4

COMMENTARY

Commentary on: *Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance* by Griffiths et al.

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Received: 3 May 2006 / Accepted: 27 May 2006
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The article by Griffiths et al. in this issue of Psychopharmacology should make all scientists interested in human psychopharmacology sit up and take notice. It is the first well-designed, placebo-controlled, clinical study in more than four decades to examine the psychological consequences of the effects of the hallucinogenic (psychedelic) agent known as psilocybin. In fact, one would be hard-pressed to find a single study of psychedelics from any earlier era that was as well-done or as meaningful. Perhaps more importantly, despite the notion by many people that psychedelics are nothing more than troublesome drugs of abuse, the present study convincingly demonstrates that, when used appropriately, these compounds can produce remarkable, possibly beneficial, effects that certainly deserve further study.

Although many people seem to believe that "psychedelics" simply appeared during the turbulent 1960s, in fact the use of these materials spans back through many millennia of human history. Ancient substances with names such as *Soma* (India), *Kykeon* (Greece), and *Teonanacatl* (South America) served for thousands of years as psychopharmacological catalysts in a variety of sacred religious and magical rituals (Nichols 2004; Schultes and Hofmann 1979). Peyote, the ceremonial use of which is now thought by anthropologists to date back at least 5,000 years, is revered as a sacrament by the Native American Church. Ayahuasca, a decoction made from plants that grow in the Amazon basin, is a sacrament used by a syncretic church in Brazil. This church has a small following in the US that has just received a favorable decision by the US Supreme Court allowing them continued use of this material.

The parallel between mystical states and the effects of psychedelic drugs is well-known among those familiar with the literature. Aldous Huxley, in his classic but controversial 1954 book, *The Doors of Perception*, (Huxley 1970) noted the similarity of his own mescaline-induced state to experiences described by mystics and visionaries from a variety of cultures. Perhaps it is not surprising then that the name "entheogen," with the connotation that these materials reveal god within, is becoming increasingly popular among those who continue to use these substances for purposes that are neither medical nor "recreational."

We must, therefore, take note of what has come to be known as the "Good Friday Experiment," carried out by Walter Pahnke for his Ph.D. studies at a small private chapel in Boston. His 1963 Ph.D. dissertation was titled *Drugs and Mysticism. An analysis of the relationship between psychedelic drugs and the mystical consciousness*. He described in an experiment with 20 student volunteers from a local Christian theological seminary. Subjects were given either 30 mg of psilocybin or 200 mg of nicotinic acid as a "placebo." The experiment was carried out in a religious setting during a Good Friday service. Pahnke concluded, "Under the conditions of this experiment, those subjects who received psilocybin experienced phenomena which were indistinguishable from, if not identical with, certain categories defined by our typology of mysticism."

Clearly, these substances have profound effects on human consciousness, and in the 1950s and 1960s, the drug known as LSD was hailed as a revolutionary new technology for psychiatry. LSD was intensively investigated for its medical potential and for possible use as an adjunct to psychotherapy until clinical research was

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abruptly halted by laws passed in response to concerns over widespread recreational use. Despite studies that involved tens of thousands of patients, using "therapeutic" approaches that employed LSD in a variety of ways, little of clear significance resulted, at least partly due to faulty experimental design and data analysis. As a consequence, a conventional wisdom seems to have developed that psychedelic drugs are generally pretty worthless. But medical technology has advanced in the past four decades; we know quite a bit more about the brain now than we did then, and human experimental methods are certainly much better.

All that being said, there was one indication for the use of psychedelics, particulary LSD, that was reasonably well-documented. Chicago internist Eric Kast first reported in 1964 that some "gravely ill" patients treated with LSD obtained mood elevation and reductions in the need for pain medication that lasted for nearly 2 weeks after the drug, and that some patients "displayed a peculiar disregard for the gravity of their situations" (Kast and Collins 1964). In a subsequent study, he further noted that, "Patients who had been listless and depressed were touched to tears by the discovery of a depth of feeling they had not thought themselves capable" (Kast 1966).

Kast's findings served as the foundation for a series of groundbreaking studies into the value of LSD in the treatment of terminal cancer patients. That work was carried out at the Maryland Psychiatric Research Center in Baltimore, Maryland by Drs. Stanislav Grof, Al Kurland, Walter Pahnke, Sanford Unger, and their colleagues (Grof et al. 1973; Pahnke et al. 1969, 1970a,b). Significantly reduced need for analgesics and improved mood and quality of life were observed in 60–70% of patients treated with LSD. The treatment response appeared to be correlated with the extent to which the patients experienced a mystical or transcendental state. That is, those who experienced the most profound LSD-induced states seemed to gain the most improvement. The basis for this benefit appeared to be related to a reduced or abolished fear of death, with an attendant reduction in anxiety, which we know affects subjective pain.

What Griffiths et al. have done in their present work represents an important extension of Pahnke's "Good Friday" experiment. They have used proper controls, better experimental design, and have provided a better analysis of the experience using more modern instruments. The experiments were not conducted in a church, or in a venue that would lead to a strong expectation of some sort of religious experience. The subjects in the Griffiths et al. study were not theology students, but were simply ordinary people with an interest in spiritual things. The work by Griffiths et al. demonstrates that, under appropriate experimental conditions, psilocybin occasioned experiences similar to spontaneously occurring mystical states. Most importantly, some of the persisting positive changes in attitudes and behavior reported by subjects were confirmed by independent ratings from community observers such as family members or friends.

The prospects for far-ranging scientific advancement are exciting. We know that psychedelics have powerful effects in many areas of the brain that are critically important for cognition and awareness. Our present understanding is that they act principally by activating serotonin 5-HT_{2A} receptors, especially those densely expressed on the apical dendrites of cortical pyramidal cells, the quintessential computational units within the cortex of the brain. In that respect, psychedelics depolarize these cortical cells, leading one to speculate that they may become more sensitive to low-level signals. That is, perhaps they can do more with less, potentially amplifying processes that are normally running, but which are not generally apparent in everyday awareness.

The science of pharmacology involves perturbing biological systems with chemical modulators (i.e., drugs), the results of which have had profound effects on our understanding of both normal and disease state physiology. Rigorous research with psychedelics may hold the key to understanding the very nature of consciousness, self-awareness, the ability to introspect, and the properties of mind that set us apart from other species.

With such a huge potential impact, is there any good reason why a well-done study like the one reported here by Griffiths et al. should appear only once in half a century? Until a related compound, DMT, was studied by Rick Strassman at the University of New Mexico in the mid-1990s (Strassman and Qualls 1994; Strassman et al. 1994; Strassman 1996), no significant work on the clinical effects of psychedelics had appeared in the scientific literature for more than a generation. Perhaps the time has now come to reinvestigate the psychopharmacological properties of psychedelics. Thus, the study by Griffiths et al. in this issue could be a watershed event.

Finally, Griffiths et al. conclude, "The ability to occasion such experiences prospectively will allow rigorous scientific investigations of their causes and consequences." Indeed.

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