

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: 24 May 2006 / Accepted: 27 May 2006
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The decade of the 1960s began the current era of heavy drug use in America, beginning perhaps with Timothy Leary's Pied Piper invitation to, "Turn On, Tune In, Drop Out" (with psychedelic drugs). While fortunately most youths who experimented did not suffer lasting damage, those of us on the mental health front lines at the time saw a number of casualties (Kleber 1967). Eventually, the hippies and the LSD-fueled "Summer of Love" in San Francisco were replaced by motorcycle gangs, amphetamines, and gratuitous violence. Psychedelic drugs receded into a permanent background of US drug use, never going away altogether, but not reaching the same penetration.

Unfortunately, one of the lasting casualties of the street use of these agents was research. Sandoz, the manufacturer of LSD, discontinued supplying it to researchers around 1965, concerned that the company's reputation was being tainted by the illicit use. Even though street chemists supplied the vast majority of the illicit use, the licit supply for research more or less disappeared and so did research funding. Prior to the cessation, research with LSD and other psychedelics was active in a variety of areas: as a potential producer of a model psychosis (it has significant limitations); the nature of hallucinations (it produces more illusions); as a therapeutic agent for trauma and the dying (inadequate data); and as a way to study altered reality states, e.g., Huxley's *The Doors of Perception*, Pahnke's

Good Friday Experiment, and Blum's *Utopiates: The Use and Users of LSD-25*. Some of the research was carefully done; in most, the researchers seem to be carried away by the effects of the agents.

This category of agents has many names, each reflecting a different point of view as noted above: psychotomimetics (mimicking psychosis), hallucinogens (producing hallucinations), entheogens (revealing the God within), and psychedelics (mind-manifesting). It is in these last two domains that the findings of the study of Griffiths et al. belong to even though they did not use either term.

The authors should be commended for the way they designed and carried out the double-blind project. The design involved using 30 mg/70 kg of psilocybin as the active experimental agent and 40 mg/70 kg of methylphenidate as an active control. All subjects received at least one session with each agent in a counterbalanced method. Great care was taken both to minimize risk to subjects, who were all naïve to this category of drugs, and to be able to separate drug effects from expectancy and possible suggestion bias by the monitors. The blinding was done so carefully that even the experienced monitors misidentified the administered agent approximately one quarter of the time. The extensive time with the monitors both before and after the sessions kept adverse effects such as fear and panic to a minimum although 8 of the 36 subjects described all or most of the psilocybin sessions to be dominated by anxiety or dysphoria. These effects did not persist beyond the session, were handled by reassurance, and apparently were of no lasting negative consequence. None of the methylphenidate subjects reported this response. As far as positive effects were concerned, psilocybin increased measures relating to mystical experiences: 22 of the 36 volunteers had a "complete" mystical experience after psilocybin compared to only 4 of the 36 after methylphenidate. At

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the 2-month follow-up, 67% rated the psilocybin experience to be either “The single most meaningful experience” of their lives or among the top five most meaningful “experiences.” After methylphenidate, 8% of the volunteers rated the experience to be “among the top five most meaningful experiences,” with none rating it as the single most meaningful experience. Thus, psilocybin significantly increased subjective reports of such experiences while methylphenidate was associated with them only occasionally and to a much lesser effect.

As far as future research is concerned, this study suggests a number of possibilities, both basic and translational, that should merit NIH support. More information is needed on dose effects, subject differences, and the actions of various selective antagonists. Neuroimaging may shed light on sites and mechanisms of action. It would be interesting to see whether the positive responders to methylphenidate activated similar brain sites as the positive psilocybin responders or different ones, as well as what was happening in the brains of the psilocybin nonresponders. From a translational perspective, experienced clinicians are well aware of the profound role that spiritual reawakening experiences, whether achieved through Alcoholics Anonymous, traditional religious venues, or some life experience, can have on successful outcomes from addictive disorders. Increased knowledge about the neuroscience underpinnings of such transformational events could improve drug abuse treatment. It is necessary to keep in mind, however, that drug-induced states are unlikely to have lasting effects in inadequately prepared individuals, as LSD studies on alcoholism in the 1960s suggested.

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. Such a concern, in view of history, is

not unwarranted. Even a proponent of such research, Humphry Osmond, who coined the term “psychedelic,” noted, “Psychedelics are instruments and like most of our artifacts are capable of being used well or ill. Unluckily, misuse is at least as likely as good use...”

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 type states arise in the brain could have major therapeutic possibilities, e.g., treatment of intolerable pain, treatment of refractory depression, amelioration of 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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