The Psychedelic Renaissance: Horizons, the Fifth Annual **Conference on Psychedelic Research**

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INTRODUCTION

In the spring of 1943, a 37-year-old Swiss chemist named Albert Hofmann had "a peculiar presentiment." He believed that he had missed something in 1938, the year when he first synthesized the twenty-fifth compound of the lysergic acid diethylamide series, LSD-25. For eight years at Sandoz Pharmaceuticals, Hofmann was in charge of the ergot project, which involved synthesizing ergotamine molecules for the treatment of migraines. On April 16, 1943, guided by a premonition, Hofmann synthesized and ingested a crystalline water-soluble batch of LSD-25. Shortly thereafter, Hofmann experienced "an uninterrupted stream of fantastic images of extraordinary plasticity and vividness . . . accompanied by an intense kaleidoscopic play of colors" (Stevens, 1987).

Less than thirty years after Hofman's discovery, the Drug Enforcement Agency (DEA) classified LSD and other related psychedelics, including psilocybin (the psychoactive component found in psilocybin mushrooms), as Schedule I, a category for drugs that have no known medical use and a high potential for abuse (DEA, 2011). As a result, nearly all research on psychedelics was placed on hold until the early 1990s, when several investigators received approval from the Food and Drug Administration (FDA) to conduct carefully designed research trials. In 1995, Rick Strassman, MD, a psychiatrist and graduate of Albert Einstein College of Medicine, completed a study at the University of New Mexico in which he administered N,N-dimethyltryptamine (DMT) to 60 volunteers. This was the first clinical research project involving a psychedelic drug that the United States government had approved and funded in more than twenty years (Strassman, 2001).

In the years following this study, with funding from nonprofit research and educational organizations such as the Multidisciplinary Association for Psychedelic Studies (MAPS), nearly a dozen more clinical research projects on psychedelic drugs have been initiated. Multiple investigations involving research questions ranging from the use of psilocybin as an end-of-life therapy for terminal cancer patients to the use of LSD for the treatment of cluster headaches have been completed or are under way at institutions such as the Johns Hopkins University and New York University (MAPS, 2011). On October 15, 2011, Horizons, the fifth annual national conference on psychedelic research, took place in New York City at Judson Memorial Church. Physicians, scientists, scholars, and artists gathered to learn about the latest research

projects from experts in the psychedelics field. The topics of that year's conference ranged from the treatment of post-traumatic stress disorder (PTSD) with the use of 3,4-methylenedioxymethamphetamine (MDMA) to the use of psilocybin as a treatment for depression and anxiety in terminal cancer patients.

SELECTED CONFERENCE PRESENTATIONS

MAPS' International Psychedelic Clinical Research: The Past, Present, and Future, by Berra Yazar-Klosinski, PhD

Berra Yazar-Klosinski, a clinical research associate at MAPS, provided an overview of the history of MDMA before describing two clinical research projects investigating potential therapeutic properties of the drug. In 1912, Merck & Co., Inc., first synthesized MDMA, commonly referred to as ecstasy, as a blood-clotting agent. However, no animal or human testing was conducted on MDMA until the early 1950s, when, it is believed, the U.S. Air Force tested it as a potential truth serum. MDMA did not appear again until the 1970s, when it was found in tablets seized in Chicago.

From 1980 to 1985, the physician George Greer synthesized MDMA in the lab of psychopharmacologist Alexander Shulgin and conducted more than a hundred therapeutic sessions with 80 individuals with the assistance of his wife, Requa Tolbert, a psychiatric nurse. They reported that their patients experienced a marked improvement in psychiatric disorders, as well as improved intimate communication with significant others. However, due to the increasing popularity of MDMA in underground raves and nightclubs across the United States, the DEA classified the drug as Schedule I in the spring of 1985.

Seven years later, the FDA agreed to accept proposals for the study of MDMA. From 1992 to 1995, Dr. Charles Grob conducted a Phase I safety study to investigate the drug's effects on the cardiovascular system. Subsequent efforts to obtain approval for a cancer study with MDMA were rejected by the FDA until the summer of 1999, when formal protests were addressed to senior FDA management, arguing that the potential therapeutic benefits of MDMA outweighed its potential for abuse. In 1999, the FDA approved the first proof-of-principle study with MDMA in which a specific potential use of the drug would be investigated. In 2003, a Johns Hopkins University research team retracted its report in Science speculating that ecstasy users face a greater risk of devel-

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oping Parkinson's disease, after the scientists realized they had mistakenly administered methamphetamine and not MDMA to all but one of the monkeys used in the study (Ricaurte et al., 2003). However, damage to the public's perception of MDMA had already been done.

After discussing the history of MDMA, Dr. Yazar-Klosinski explained current FDA recommendations for MAPSfunded pilot studies involving MDMA-assisted psychotherapy to treat patients suffering from PTSD. Current studies use two to three therapeutic sessions spaced three to five weeks apart in which the patient lies on a soft couch in a comfortable room. Investigators have found that spacing the sessions several weeks apart provides ample time for patients to process their experiences properly. This stands in contrast to most other treatment modalities, which require long-term and regular pharmaceutical intake. After the final therapy session, the subjects are monitored to assess lasting positive or negative effects and to determine if the patients feel compelled to seek MDMA illegally.

The degree of improvement in symptoms of PTSD following treatment with MDMA is measured using the Clinician-Administered PTSD Scale (CAPS). In a September 2008 Phase II U.S. pilot study involving 21 subjects with treatment-resistant PTSD resulting from sexual abuse, crime, or war, investigators found significant improvement in patients' CAPS scores after a single session with MDMA and psychotherapy versus psychotherapy and a placebo (Mithoefer et al., 2011). The subjects' CAPS scores continued to improve for two months after their second experimental session. In a similar study in January 2010 of 12 subjects in Switzerland with treatmentresistant PTSD, there was a clinically significant improvement in the experimental group's CAPS scores, equivalent to that of groups administered other drugs typically used for the treatment of PTSD (e.g., Zoloft). In these studies, 125 mg of MDMA was given to the experimental group and 25 mg of MDMA was given to the control group as the placebo. Participants in neither the U.S. nor the Swiss studies experienced any severe adverse events related to MDMA.

Research proposals are also being designed to investigate whether autism and Asperger's syndrome can be treated with MDMA. Dr. Yazar-Klosinski is hopeful that in the future, psychiatrists will be able to prescribe MDMA clinically to patients for the treatment of PTSD, depression, and other psychiatric disorders.

Recent Findings from the Johns Hopkins Hallucinogen Research Group, by Matthew W. Johnson, PhD

"I left the session animated and intellectually stimulated," said Clark Martin when describing his first session with psilocybin in the Johns Hopkins University pilot study for individuals suffering from anxiety and depression related to cancer. He noted, "Today, I don't have a sense of death like I used to. . . . I don't get too worked up about my illness anymore" (Zaitchik, 2011). Martin is a retired clinical psychologist who has undergone chemotherapy, counseling, and antidepressants in his battle against renal cancer.

Matthew Johnson, PhD, an assistant professor of behavioral pharmacology at Johns Hopkins, discussed seven ongoing or recently completed psychedelic research projects at the university, including the one in which Martin was enrolled. The initial Johns Hopkins clinical study on psilocybin investigated the effects of large doses of the drug on 36 high-functioning volunteers. The mean age of the participants was 46, and none of them had used hallucinogens prior to the study. Each volunteer received two sessions either with psilocybin or with the control drug, methylphenidate (Ritalin), which was selected for its ability to mimic the physical effects of psilocybin. Like the MDMA-assisted psychotherapy sessions described by Dr. Yazar-Klosinski, the psilocybin sessions took place in a comfortable room. Each session lasted eight hours and was conducted under the supervision of an "experienced guide" in case the volunteers became anxious or frightened (Griffiths et al., 2008).

The experiences of the volunteers were evaluated using the Lifetime Mysticism Scale (LMS), a 32-item guestionnaire that assesses primary mystical experiences. The LMS has been extensively studied and shows cross-cultural reliability, as well as sensitivity to psilocybin-based experiences. Of the volunteers, 35% claimed that their sessions with psilocybin could be classified as the most significant spiritual experience of their lives, and 40% reported that the sessions were within their top five most significant lifetime experiences. According to self-reported questionnaires assessing changes in attitudes, mood, and social and other behaviors, these changes were still considered significant 2 and 14 months after the sessions.

In a second clinical study, volunteers underwent five sessions with psilocybin, spaced one month apart, but half of the volunteers received progressively increasing doses of psilocybin while the other half received progressively decreasing doses. Three weeks after the sessions ended, the effects were assessed; the group that received increasing doses of psilocybin responded more favorably than the group that received decreasing doses. Seven participants (39%) experienced elements of a "bad trip" for a brief period of time during one of the sessions, and six of these subjects experienced these effects at the highest dose of psilocybin. The researchers noted that the chance of having a mystical experience at the highest dose of psilocybin is only 10% greater than at the next lower dose, although the chance to experience adverse effects is much greater. The subjects also reported dosedependent headaches (Griffiths et al., 2011).

A third study was similar to the first two, but its purpose was to measure changes in the personality dimension of

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"openness" in subjects who had a "complete mystical experience" as defined by the LMS. Openness, as defined by the 240-item NEO Personality Inventory used in contemporary psychology to describe human personality, is based on an examination of various specific facets. These facets include fantasy (e.g., "I have a very active imagination"), aesthetics (e.g., "I am intrigued by patterns I find in art and nature"), feelings (e.g., "I experience a wide range of emotions and feelings"), ideas (e.g., "I often enjoy playing with theories or abstract ideas"), values (e.g., "I consider myself broad-minded and tolerant of other people's lifestyles"), and actions (e.g., "I think it's interesting to learn and develop new hobbies"). Each item was rated on a five-point scale ranging from "strongly disagree" to "strongly agree" (MacLean et al., 2011). The results of this study showed that participants who had a mystical experience during a psilocybin session had remained significantly more open compared to the control group more than a year later. This suggested to the Johns Hopkins researchers that psilocybin could be used for chronic conditions, such as the treatment of addiction and end-of-life issues in patients with terminal

An ongoing study at Johns Hopkins is measuring the effects of five psilocybin sessions on smoking cessation. While the data are preliminary, they demonstrate a significant decline in smoking addiction among participants after the fifth session. Another psilocybin clinical study at Johns Hopkins was the one in which Martin, the retired clinical psychologist, was enrolled. Its aim was to determine whether treatment with psilocybin helps terminal cancer patients cope with end-of-life issues. The results were promising and suggest that psilocybin may play an important role in reducing the amount of anxiety experienced by patients with late-stage cancer (Grob 2011).

The results of these psilocybin studies have far-reaching implications and pose many questions about the nature of consciousness. For their next psilocybin project, researchers at Johns Hopkins are planning to investigate the similarities and differences in states of consciousness between individuals in deeply meditative states and those who are under the influence of psilocybin. At the conclusion of his presentation, Matthew Johnson left the audience with an important question to ponder: "If psilocybin can help terminal cancer patients accept death and find new meaning in their lives, what should its role be in healthy individuals?"

POTENTIAL NEW HORIZONS?

For the current resurgence of psychedelic research to continue successfully, scientists and physicians must not become overly zealous and make the same mistakes that brought psychedelic research to a halt in the late 1960s. Designing safe and carefully controlled research protocols under strict regulation by the FDA is critical for the continuing investigation of the potential therapeutic applications of these drugs. As reliable and verifiable data continue to be generated by both basic science and clinical research studies, more questions will arise about the potential healing properties of psychedelics. The more questions that researchers can safely and ethically answer, the more treatments may become available for treating conditions ranging from PTSD to anxiety. If the research projects discussed at Judson Memorial Church during the fifth annual Horizons conference provide any indication of the promising ideas at work in the minds of today's researchers and clinicians, then the future of psychedelic research is sure to be an interesting one.

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Conflict of Interest Disclosures: The author has completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. No conflicts were

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