

**AFTERWORD:**  
**THE PSYCHEDELIC RESEARCH RENAISSANCE —**  
**A REVIEW OF RECENT PSYCHEDELIC**  
**PSYCHOTHERAPY RESEARCH**

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*By: L. Jerome, Ph.D., Valerie Mojeiko, Rick Doblin, Ph.D.*

IT IS NOW 2008, and this is the fourth time that *LSD Psychotherapy* by Dr. Stanislav Grof has gone to press. Since the third edition was published seven years ago, more progress has been made in the field of psychedelic therapy than in the previous twenty-one years since its original publication. There are currently patients being treated around the globe with psilocybin, MDMA, ibogaine, and soon LSD, as part of legitimate “above-ground” research investigations. The renewal of LSD-assisted psychotherapy research marks the culmination of the initial period of the renaissance of psychedelic research. Indeed, LSD is perhaps the most controversial of all the psychedelics due to its widespread non-medical use in the 1960s and its association with political protest groups, most notably the anti-Vietnam War movement. This afterward aims to summarize the tremendous accomplishments that have enabled the pioneering research of Dr. Grof and many others to return to the laboratory in mainstream Western society.

Three American organizations have been instrumental in sponsoring and funding the resurgence of research: the Multidisciplinary Association for Psychedelic Studies (MAPS; [www.maps.org](http://www.maps.org)) (the publisher of this book), the Heffter Research Institute (HRI; [www.heffter.org](http://www.heffter.org)), and the Council on Spiritual Practices ([www.csp.org](http://www.csp.org)). All three organizations are located and sponsor research in the United States. MAPS also sponsors research in Europe, Israel, Canada, and Mexico, and HRI sponsors research in Switzerland. In Switzerland, the Swiss Association for Psycholytic Therapy (SAePT) has also played over the years, and continues to play, a role in keeping the torch burning and in co-sponsoring research.

After thousands of psychedelic research studies were conducted from the 1940s to the late 1960’s, nearly all human studies of LSD, psilocybin, and other psychedelics ceased in 1972 in the US and around the world as a result of political suppression. However, after almost twenty-years of hiatus, with the approval of a new generation of regulators, a new generation of researchers began cautiously studying psychedelic drugs and MDMA in the context of research into the correlates of consciousness and basic psychopharmacology, and the potential of these substances as psychotherapeutic agents. Kicking off this new paradigm in 1990, Dr. Rick Strassman investigated the physiological and subjective effects of N,N-5,5-dimethyltryptamine (DMT), assessing subjective and physiological effects after injections of up to 0.4

mg/kg DMT (Strassman 1994; Strassman 1996; Strassman and Qualls 1994).

There are currently seven basic areas of clinical research into the uses of psychedelics that will be discussed in more detail below:

- 1) Psychedelic (psilocybin, LSD, and MDMA)-assisted psychotherapy in subjects with anxiety associated with end-of-life issues
- 2) Psilocybin in the treatment of obsessive-compulsive disorder (OCD),
- 3) LSD, lysergic acid amide (LSA), and psilocybin in the treatment of cluster headaches (CH),
- 4) Psilocybin in catalyzing spiritual experiences,
- 5) MDMA-assisted psychotherapy in subjects with posttraumatic stress disorder (PTSD)
- 6) Ketamine-assisted psychotherapy and ibogaine use in the treatment of alcoholism and opiate dependence
- 7) Basic scientific studies with various psychedelics

Many of the psychotherapy studies described below involve psychotherapy that is either directly based upon or borrows elements from the psychotherapeutic methods of Dr. Grof. These elements include: performing therapy in a setting specifically designed for comfort and introspection, treatment by a male/female pair of co-therapists, the use of musical programs, and encouraging patients to confront whatever feelings arise while the therapists serve as supportive guides in the experience. Even when not seeking to replicate Grof's techniques, people studying psychedelic-assisted psychotherapy have been influenced by the LSD-assisted psychotherapy performed by Dr. Grof.

#### PSILOCYBIN/LSD/MDMA PSYCHOTHERAPY IN SUBJECTS WITH END-OF-LIFE RELATED ANXIETY

Researchers interested in studying this therapeutic potential of psychedelic drugs began conducting studies during the early 2000s. Many of these studies are based on at least some features of Dr. Grof's original format for LSD therapy. In April 2004, Charles S. Grob, M.D. began a pilot study at the Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center examining psilocybin-assisted psychotherapy as a potential treatment for anxiety in 12 subjects diagnosed with advanced-stage cancer (Grob 2005). The study aims to test whether psilocybin might be effective in reducing anxiety, depression, and physical pain, thereby improving the quality of life for these patients. Dr. Grob wished to follow the model and research first laid down by Grof (Grob 2007 (personal communication)). At the time of this writing, 11 of 12 subjects in this study, sponsored by HRI, have completed the treatment. Study results have not yet been published.

A MAPS-funded study under development will examine the safety and efficacy of psilocybin-assisted psychotherapy in treating nine subjects with anxiety associated with Stage IV melanoma. This investigation will take place at the Mt. Sinai Comprehensive Cancer Center (MSCCC) in Miami, Florida, and the principal investigator is Sameet Kumar, Ph.D., Clinical Psychologist in MSCCC's Department of Psychosocial Services. The FDA has reviewed the protocol favorably, which at the time of this writing is under review with the Institutional Review Board (IRB) at MSCCC. The study is expected to commence in early 2008.

MAPS and SAePT are co-sponsoring a similar study of illness-related anxiety using LSD rather than psilocybin, studying people with any life-threatening diagnosis in addition to diagnoses of advanced-stage cancer. This study is to take place in Solothurn, Switzerland, under the direction of Peter Gasser, M.D. (Gasser 2007). Though there has been prior research with LSD in cancer patients with anxiety that demonstrated safety and some degree of efficacy (Grof et al. 1973; Kast 1967; Kast and Collins 1964; Pahnke et al. 1971), no researchers have been able to follow up on these findings during the past 35 years. Dr. Gasser's study has been approved by both a Swiss Ethics Committee and SwissMedic. This study is also expected to commence in early 2008.

MAPS was instrumental in initiating a study at Harvard Medical School's McLean Hospital investigating MDMA-assisted psychotherapy in the treatment of anxiety associated with a diagnosis of advanced-stage cancer (Halpern 2006). Principal investigator John H. Halpern, M.D. plans to enroll 12 participants and has begun to recruit people for this study. This is the first clinical study of any psychedelic to take place at Harvard Medical School since 1965.

#### PSILOCYBIN IN SUBJECTS WITH OBSESSIVE COMPULSIVE DISORDER

Beyond the indications that Dr. Grof outlined in this seminal text, anecdotal reports have led researchers to examine the potential applications of psychedelics to the treatment of other conditions. Dr. Francisco Moreno and colleagues recently investigated psilocybin as a potential treatment for nine patients suffering from OCD (Moreno et al. 2006). Dr. Moreno's team conducted their research on the basis of previous medical case reports of efficacy (Hanes 1996; Leonard and Rapoport 1987; Moreno and Delgado 1997). Subjects in the study received four different doses of psilocybin ranging from sub-psychedelic to frankly psychedelic. Marked decreases in OCD symptoms of variable degrees were observed in all subjects during one or more of the treatment sessions.

#### LSD, LSA, AND PSILOCYBIN IN SUBJECTS WITH CLUSTER HEADACHE

CH is an extremely painful and often treatment-resistant type of headache. However, a group of individuals suffering from cluster headaches discovered a potential application of psychedelics in the treatment of this debilitating disorder. Clusterbusters ([clusterbusters.com](http://clusterbusters.com)), an organization founded by people with CH, is sponsoring research with some support from MAPS that will examine the safety and efficacy of using LSD, psilocybin, or LSA-containing "morning glory" seeds to interrupt CH cycles or to prevent future CH attacks from occurring. This research grew out of the experience of Clusterbuster members, and is supported by a case series (Sewell et al. 2006). All three psychedelic compounds seem to help people with CH, with preliminary evidence suggesting that LSD is the most effective treatment. Research will also be important to confirm safety from ergotism, which is a potential complication from repeated and/or high-dose exposures to most botanical sources of LSA as a result of containing other ergolines (Chao and Der Marderosian 1973). Protocols to study the use of LSD and psilocybin in the treatment of CH are currently in the protocol development and approval stage at McLean Hospital, Harvard Medical School, under the direction of principal investigator Dr. Halpern.

## PSILOCYBIN IN CATALYZING SPIRITUAL EXPERIENCES

Research examining the effects of psilocybin and other psychedelics has provided the basis for a recent study investigating spiritual experiences arising from the use of psilocybin. A study supported by the Council on Spiritual Practices showed psilocybin to be a catalyst for peak or spiritual experiences when administered to people with established religious or spiritual practices (Griffiths et al. 2006). This study garnered significant media attention, and that attention has made it easier for other studies to take place, most notably the study of psilocybin-assisted psychotherapy under development with Dr. Kumar at MSCCC.

## MDMA RESEARCH

The renewal of formal psychedelic research began primarily with MDMA, which was legal until 1985 and which is milder and shorter-acting than the traditional psychedelics such as LSD and psilocybin.

George Greer, M.D. and Requa Tolbert, R.N., M.S.N. (1986) conducted an uncontrolled study of then legal MDMA-assisted psychotherapy. This work was inspired in part by attending a seminar that Dr. Grof conducted at Esalen on psychedelic psychotherapy in 1975 (Greer 2007). Greer and Tolbert used psychotherapeutic methods largely adapted from those found in *LSD Psychotherapy*. After MDMA was criminalized in the US in 1985, the FDA initially refused to permit clinical research.

In 1985, the World Health Organization (WHO) Expert Committee on Drug Dependence issued its 22nd Report, in which MDMA was recommended for criminalization around the world. This recommendation was made over the objection of the Chairman, Dr. Paul Grof (Stan Grof's brother), who managed to persuade the Committee to conclude its recommendation with a statement urging "countries to use the provisions of article 7 of the Convention of Psychotropic Substances to facilitate research on this interesting substance."

In 1988, based in part on the justification provided by this sentence, the Swiss Ministry of Health authorized a small group of psychiatrists to administer MDMA and LSD to their patients. No formal research was required but permission was withdrawn in 1993. In order to gather some data, self-report questionnaires were mailed to patients asking them to evaluate the outcomes of their therapy (Gasser, 1994).

In 1992, the FDA approved the first human research with MDMA, permitting Dr. Charles Grob to conduct a MAPS-sponsored Phase I dose-response study. In 1996, Dr. Grob and colleagues published their results (Grob et al. 1996).

Interest in the effects of MDMA and psychedelic drugs continued to grow throughout the 1990s. Franz Vollenweider, M.D. and colleagues at the University of Zurich took up two programs of research in the mid-1990s, one studying psilocybin and the other MDMA. The Zurich team conducted brain imaging and reported on the metabolism and subjective effects of psilocybin (Hasler et al. 1997; Vollenweider et al. 1998a; Vollenweider et al. 1997; Vollenweider et al. 1998b). They continued this research with a number of studies into the effects of psilocybin on brain function and some of the receptor systems involved in producing these effects (Umbricht et al. 2003; Vollenweider et al. 1999). The Zurich team also conducted studies on the subjective, physiological, and neuroendocrine effects of MDMA in humans

(Vollenweider et al. 1998a), and they performed imaging and EEG studies, as well (Frei et al. 2001; Gamma et al. 2000). This team conducted studies with 74 participants and included evaluation of neurotransmitter systems involved in the acute effects of MDMA (Liechti et al. 2001; Liechti and Vollenweider 2001). Euphrosyne Gouzoulis-Mayfrank, M.D. and colleagues at the University of Aachen, Germany began performing studies with psilocybin and the MDMA relative, 3,4-methylenedioxyethylamphetamine (MDE) at approximately the same time as the Zurich team (Gouzoulis et al. 1992; Spitzer et al. 1996), culminating in studies comparing these drugs with the psychostimulant methamphetamine (Gouzoulis-Mayfrank et al. 1999a; Gouzoulis-Mayfrank et al. 1999b).

Only a few years later, a team of researchers in Barcelona, Spain began studying the effects of MDMA in male volunteers (Cami et al. 2000; Mas et al. 1999). In 2000, a MAPS-sponsored Spanish researcher, José Carlos Bouso, Ph.D., began a pilot study of MDMA-assisted psychotherapy in women with PTSD related to sexual assault; his studies were halted in 2002 for political reasons after media coverage of the study (Bouso 2003). With the exception of the work of Greer and Tolbert and this preliminary work in Spain, which remains unpublished to date (Bouso et al. 2008), these initial studies did not consider the therapeutic potential of psychedelic drugs, but their findings supported the safety of human trials.

Researchers at the University of California-San Francisco studied the physiological, subjective, and neuroendocrine effects of MDMA (Harris et al. 2002; Lester et al. 2000), with funding from the US National Institute on Drug Abuse (NIDA). Around the same time, addiction researchers at Wayne State University began NIDA-funded studies on MDMA that included investigations of desirable drug effects ("reinforcing effects") and neurotransmitter systems involved in producing MDMA effects (Tancer and Johanson 2001; Tancer and Johanson 2003).

#### MDMA-ASSISTED PSYCHOTHERAPY IN SUBJECTS WITH POSTTRAUMATIC STRESS DISORDER

Researchers are also picking up where Greer and Tolbert left off with respect to MDMA-assisted psychotherapy. Not long after Dr. Grob had begun the study of psilocybin-assisted psychotherapy, the FDA reviewed and the IRB approved the first study of MDMA-assisted psychotherapy. In March 2004, Michael Mithoefer, M.D. and Ann Mithoefer, B.S.N. became the first legal MDMA psychotherapy researchers in the United States when they began using MDMA in survivors of sexual or other physical assault with treatment-resistant PTSD (Mithoefer 2004; 2006). The study, which is taking place in Charleston, South Carolina, recently recruited its 20th subject, and the investigators will be analyzing final results in the middle of 2008. Study criteria were expanded over the course of the recruitment period to include subjects with war and terrorism-related PTSD, and there are two veterans of the war in Iraq enrolled in the study. The second vet (Subject #21, the final subject in the study) required FDA and IRB approval prior to enrollment. Though classified as disabled by the VA, he was not offered individual psychotherapy and was thus not a treatment failure. Results from this Phase II study will be submitted to the FDA as the basis for a larger Phase III study that will be designed to generate data under an investigational new drug application (IND) seeking eventual approval

of MDMA-assisted psychotherapy as a legal pharmaceutical treatment.

This was the flagship study for several more of its kind, all sponsored by MAPS in an effort to develop MDMA as a prescription medicine. A Phase II, MDMA/PTSD pilot study taking place in Switzerland under the direction of Peter Oehen, M.D. and Verena Widmer, R.N. began in 2006 and has currently treated four (one dropped out) out of an eventual 12 subjects, under a similar protocol and subject population as the study in the US (Oehen 2006). The data from this Swiss study will be submitted to the European Medicines Agency (EMA) in addition to the US FDA. A study is also underway in Israel at Beer Yaakov Mental Health Center investigating MDMA's efficacy in treating subjects with war and terrorism-related PTSD (Mojeiko 2006). Principal investigator Moshe Kotler, M.D. is former chief psychiatrist of the Israeli Defense Forces and is the current chair of the Department of Psychiatry at Tel Aviv University's Sackler School of Medicine. This data will also go toward approval by both the US FDA and EMA.

#### IBOGAINE RESEARCH IN SUBJECTS WITH OPIATE DEPENDENCE

A myriad of ibogaine clinics have sprung up all over North America and Europe to treat people with addictions. This work is in line with anecdotal reports and research findings in non-human subjects suggesting that ibogaine is effective at eliminating or reducing the signs of opiate withdrawal (Alper 2001). MAPS is currently sponsoring two observational case series, one now underway and another in development, that will study the long-term effectiveness of ibogaine in treating dependence to opiates and other drugs. These observational studies will survey people who are already receiving treatment from existing clinics for up to 12 months after being administered ibogaine. Along the line of Dr. Grof's work in the use of LSD to treat addictions, these studies will pay particular attention to the content of the psychedelic experience and how it relates to recovery rates.

#### KETAMINE-ASSISTED PSYCHOTHERAPY IN ALCOHOLICS AND OPIATE DEPENDENT SUBJECTS

Evgeny Krupitsky, M.D., a Russian researcher, has reported promising findings from treating people with dependence to alcohol and heroin through the use of the dissociative psychedelic ketamine (Krupitsky et al. 2002; Krupitsky et al. 2001; Krupitsky and Grinenko 1997). In a MAPS and HRI co-sponsored study, Dr. Krupitsky found that the subjects in the experimental group who received a high, psychedelic dose of ketamine had a significantly greater rate of abstinence in a two year follow-up period than people who received a low, sub-psychedelic dose of ketamine. He has also found that multiple ketamine-assisted psychotherapy sessions are more effective than a single session, demonstrating that the one-dose miracle cure model needs to be replaced by the more realistic model of repeated sessions over time (Krupitsky et al. 2007). Unfortunately, Dr. Krupitsky has been blocked from conducting further studies due to the rise of the non-medical use of ketamine in Russia and the heavy-handed refusal of the Russian authorities to permit continued scientific research into ketamine's therapeutic uses in the treatment of addiction.

## BASIC SCIENCE WITH PSILOCYBIN, DMT, AYAHUASCA, MDMA

Scientists studying perception, attention, and cognition continue to examine the effects of psilocybin, ayahuasca (the South American psychedelic brew and its constituent DMT) and MDMA in humans. Working with Dr. Vollenweider's research team at the University of Zurich, Dr. Olivia Carter and colleagues have studied and published findings on the effects of psilocybin on visual perception (Carter et al. 2005; Carter et al. 2007; Carter et al. 2004; Wittmann et al. 2007). The Zurich team has also continued publishing papers on the subjective and physiological effects of different doses of psilocybin (Hasler et al. 2004). In Spain, Jordi Riba, Ph.D. and colleagues have studied the physiological, electroencephalographic, and subjective effects of freeze-dried ayahuasca (Riba et al. 2004; Riba et al. 2002a; Riba et al. 2002b; Riba et al. 2001). Continuing in the vein of her earlier research, Dr. Gouzoulis-Mayfrank and colleagues are now comparing and contrasting the acute subjective, and cognitive effects of DMT with those of ketamine, using within-subject designs (Gouzoulis-Mayfrank et al. 2006; Gouzoulis-Mayfrank et al. 2005; Heekeren et al. 2007). Meanwhile, in the Netherlands, Kim P.C. Kuypers, Ph.D. and colleagues are studying the acute effects of MDMA upon skills employed in driving vehicles, including visual attention, perception, and impulsivity (Kuypers and Ramaekers 2005; 2007; Kuypers et al. 2007; Ramaekers and Kuypers 2006). Only now are these studies taking up the promise that psychedelic compounds offer in understanding perception, cognition, and the correlates of consciousness.

## CONCLUSION

After over thirty years of quiescence, psychiatric and psychological research has rediscovered the potential of psychedelic compounds. The current group of studies is more sophisticated than its predecessors, and some have even taken up the challenge of investigating psychedelic-assisted psychotherapy. In a climate where the US Supreme Court recently ruled to stay the hand of the federal government in further prosecuting a religion for using ayahuasca tea (*Gonzales v. O Centro Espirita Beneficente União Do Vegetal*, 2006), research into the therapeutic uses of psychedelics is finally thriving. Western culture is once again opening up to the idea of using psychedelics as medicines and beginning the healing of the deep traumas of our society, a fitting tribute to the power of the ideas and data presented by Dr. Stanislav Grof in *LSD Psychotherapy*.

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Founded in 1986, the Multidisciplinary Association for Psychedelic Studies (MAPS) is a membership-based, IRS-approved 501 (c) (3) non-profit research and educational organization. We assist scientists to design, fund, obtain approval for, conduct, and report on studies evaluating the risks and benefits of MDMA, psychedelic drugs, and marijuana. MAPS' mission is to sponsor scientific research designed to develop psychedelics and marijuana into FDA-approved prescription medicines and to educate the public honestly about the risks and benefits of these drugs.

For decades, the government was the biggest obstacle to research. Now that long-awaited research is finally being approved, the formidable challenge is funding it. At present, there is no funding available from governments, pharmaceutical companies, or major foundations. That means, for the time being, the future of psychedelic and marijuana research rests in the hands of people like you.

Can you imagine a cultural reintegration of the use of psychedelics and the states of mind they engender? Please join MAPS in supporting the expansion of scientific knowledge in this promising area. Progress is only possible with the support of individuals who care enough to take individual and collective action.

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- Sponsored the first US FDA-approved study evaluating MDMA's therapeutic applications, for subjects with chronic posttraumatic stress disorder (PTSD), as well as MDMA/PTSD pilot studies in Switzerland, Israel and Spain.
- Waged a successful lawsuit against DEA in support of Professor Lyle Craker's proposed MAPS-sponsored medical marijuana production facility at the University of Massachusetts-Amherst; led campaigns to gain support from over 50 members of the US House of Representatives.
- Supported long-term follow-up studies of pioneering research with LSD and psilocybin from the 1950s and 1960s.
- Sponsored Dr. Evgeny Krupitsky's pioneering research into the use of ketamine-assisted psychotherapy in the treatment of alcoholism and heroin addiction.
- Assisted Dr. Charles Grob to obtain permission for the first human studies in the United States with MDMA after it was criminalized in 1985.
- Sponsored the first study to analyze the purity and potency of street samples of "Ecstasy" and medical marijuana.

- Funded the successful effort of Dr. Donald Abrams to obtain permission for the first human study into the therapeutic use of marijuana in 15 years, and to secure a \$1-million grant from the National Institute on Drug Abuse.
- Obtained orphan-drug designation from the FDA for smoked marijuana in the treatment of AIDS Wasting Syndrome.
- Funded the synthesis of psilocybin for the first FDA-approved study in a patient population in twenty-five years.
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