

Summary

MAPS Clinical Studies Summary

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MDMA-Assisted Psychotherapy for PTSD in Veterans of War

Charleston, South Carolina

Total cost: \$595,000 (\$16,000 still needed)

Clinical Investigators: Michael Mithoefer, M.D., and Annie Mithoefer, B.S.N.

Our current top priority project is our ongoing Phase 2 study of MDMA-assisted psychotherapy for 16 U.S. veterans with chronic, treatment-resistant PTSD. This study has now enrolled over a third of its subjects, all of whom suffer from PTSD as a result of military service, and is continuing to enroll and treat subjects. This study uses a sophisticated randomized, triple-blind, placebo-controlled protocol. During the three-month course of psychotherapy, all subjects receive weekly non-drug psychotherapy and three daylong MDMA-assisted psychotherapy sessions, scheduled three to five weeks apart. In addition to providing evidence for the safety and efficacy of MDMA-assisted psychotherapy for chronic, treatment-resistant PTSD, we are also using this study to develop techniques for standardizing both data collection and the therapy itself. Since our flagship study primarily involved female survivors of sexual abuse and assault, we hope this study will show that the benefits of MDMA-assisted psychotherapy extend to the population of veterans with war-related PTSD.

MDMA-Assisted Psychotherapy for PTSD (Flagship Pilot Study) (complete)

Charleston, South Carolina

Total cost: \$1,250,000

Clinical Investigators: Michael Mithoefer, M.D., and Annie Mithoefer, B.S.N.

Our flagship Phase 2 pilot study of MDMA-assisted psychotherapy for 20 veterans with chronic, treatment-resistant PTSD stemming from sexual abuse, violent crime, or war was completed in late 2008, and the outstanding results were published in July 2010 in the *Journal of Psychopharmacology*. Over 80% of the subjects who went through MDMA-assisted psychotherapy no longer qualified for a PTSD diagnosis, compared with 25% in the placebo group. The paper announcing these results was the journal's most downloaded article in 2010. This study was the first study ever to investigate a therapeutic application of MDMA under an FDA Investigational New Drug application. A long-term follow-up of subjects in this study (see next item) showed the benefits of MDMA-assisted psychotherapy were maintained an average of 3 and a half years later.

MDMA-Assisted Psychotherapy for PTSD (Flagship Long-Term Follow-Up Study)

Charleston, South Carolina

Total cost: \$10,000 (\$6,000 still needed)

Clinical Investigators: Michael Mithoefer, M.D., and Annie Mithoefer, B.S.N.

MAPS recently completed a long-term follow-up study of subjects who participated in our flagship Phase 2 pilot study of MDMA-assisted psychotherapy for PTSD. This study was intended to determine whether the outstandingly positive results of the original study persisted over time. The preliminary analysis shows that benefits from treatment with MDMA-assisted psychotherapy were maintained over time. An average of 41 months (about 3 and a half years) after completing the study, average scores on the Clinician-Administered PTSD Scale (CAPS) were statistically equivalent to those measured at the end of the treatment period. A few subjects did experience relapses, and these individuals will be eligible to enroll in our "relapse study" (see below). MAPS' clinical research team is currently preparing a manuscript detailing the results of the study. Once the manuscript is complete, it will be submitted for publication in a peer-reviewed scientific journal.

MDMA-Assisted Psychotherapy for PTSD (Relapse Study)

Charleston, South Carolina

Total cost: \$31,000 (\$16,000 still needed)

Clinical Investigators: Michael Mithoefer, M.D., and Annie Mithoefer, B.S.N.

Our long-term follow-up to our flagship Phase 2 clinical trial of MDMA-assisted psychotherapy for PTSD revealed that although over 80% of the subjects in our previous study no longer met criteria for PTSD two months after treatment, for several subjects symptoms did eventually return. Benefits from MDMA-assisted psychotherapy tended to persist over time during the long-term follow-up, conducted an average of 41 months after treatment. Our new "relapse study" will attempt to determine whether a single additional open-label MDMA-assisted psychotherapy session along with several non-drug psychotherapy sessions can enable these subjects to once again be free of a PTSD diagnosis. This study is now preparing to enroll subjects.

MDMA-Assisted Psychotherapy for PTSD (complete) Solothurn, Switzerland

Total cost: \$300,000

Clinical Investigators: Peter Oehen, M.D., and Verena Widmer, R.N.

In January 2011, the final long-term follow-up visit was completed in MAPS' Swiss study of MDMA-assisted psychotherapy for PTSD. The clinical research team has closed and locked the database, officially concluding the data collection portion of the study. A preliminary analysis suggests that the Clinician-Administered PTSD Scale (CAPS), which is the primary measure of PTSD symptom severity, showed a trend towards improvement after treatment, with CAPS reductions somewhat larger than in comparable studies of Zolof and Paxil. The Posttraumatic Diagnostic Scale (PDS), which is the secondary measure of PTSD symptoms completed by the subjects, also showed statistically significant improvements in symptoms after treatment. The clinical team is now preparing a paper describing the results for publication in a peer-reviewed scientific journal.

MDMA-Assisted Psychotherapy for PTSD

Vancouver, Canada

Total cost: \$310,000 (\$231,000 still needed)

Clinical Investigators: Ingrid Pacey, M.D., and Andrew Feldmár, M.A.

The goal of our 12-person Canadian study, designed similarly to our Swiss study, is to learn if we can replicate the outstanding results of our U.S. study. Our Canadian study will be conducted in a similar cultural context as our U.S. study. Ingrid Pacey, M.D., a psychiatrist and certified Grof Holotropic Breathwork practitioner, and Andrew Feldmár, M.A., a Hungarian-Canadian psychologist and disciple of R.D. Laing, are the male/female co-therapists conducting this study. Both of these experienced and highly trained therapists worked with MDMA-assisted psychotherapy prior to its criminalization and share a theoretical orientation with our U.S. and Swiss teams. We're using two senior therapists in Canada to give us the best chance to replicate the outstanding U.S. results. We are currently awaiting final approval from Health Canada following a security inspection of the pharmacy that will be used to store the MDMA. Once approved, this will be the first clinical psychedelic study in Canada since the mid-1970s.

MDMA-Assisted Psychotherapy for PTSD Tel Aviv, Israel

Total cost: \$260,000 (\$212,000)

Clinical Investigator: Moshe Kotler, M.D.

Building on our experience with previous studies, MAPS has determined that pairing traditionally trained psychiatrists with others with more direct experience working with altered states of consciousness may help produce a more effective therapeutic team. For this reason, our new Israeli study of MDMA-assisted psychotherapy for PTSD will employ three (rather than two) male/female co-therapist teams in order to increase enrollment rates and provide more opportunities for therapists to learn from each other. The variety of expertise brought to the therapeutic sessions by these co-therapist teams should make them more effective at achieving positive treatment outcomes. The study has the full approval of Israeli regulatory bodies including the Israeli Ministry of Health and an Ethics Committee. The protocol will also be submitted to the US FDA, which must prospectively approve the study before we can start enrolling subjects since it is being conducted under a US Investigational New Drug application.

MDMA-Assisted Psychotherapy for PTSD

Amman, Jordan

Total cost: \$141,000 (\$56,000 still needed)

Clinical Investigator: Nasser Shuriquie, M.D.

MAPS is working to conduct an MDMA/PTSD pilot study in Jordan as part of our efforts to explore whether MDMA-assisted psychotherapy can be successfully conducted in a range of cultural contexts. These cultural differences will require us to think ever more carefully about the core elements of our therapeutic approach and how we teach them to our therapist teams. The study will explore the safety and effectiveness of three MDMA-assisted psychotherapy combined with traditional therapy for 12 subjects with chronic, treatment-resistant PTSD. The first two subjects in the study will participate in a full-dose open-label lead-in portion in order to train our Jordanian co-therapists in our manualized treatment method. This study also uses a slightly higher active placebo dose (40mg MDMA) than our other studies to help gather more data on the relative effectiveness of a range of doses. The study is currently awaiting clearance from the Jordanian Food and Drug Administration (JFDA).

MDMA-Assisted Psychotherapy for PTSD Australia

Total cost: \$125,000 (\$50,000 still needed)

**Clinical Investigator: Stuart Saker, M.D.,
and Fiona MacKenzie, M.Psych**

MAPS is now working with a group of researchers in Australia to plan a new study of MDMA-assisted psychotherapy for subjects with chronic, treatment-resistant PTSD. This study is in the protocol development process. Planning for Phase 3 of our MDMA-assisted psychotherapy for PTSD research program involves determining which study sites and which cultural contexts are most likely to produce the most significant results. Conducting our ongoing series of Phase 2 clinical trials in a variety of international contexts helps us determine whether and to what extent the effectiveness of MDMA-assisted psychotherapy for PTSD depends on language and culture, as well as subject demographics and independent rater variables.

MDMA-Assisted Psychotherapy for PTSD (Intern Study) Boulder, Colorado

Total cost: \$265,000 (\$164,000 still needed)

Clinical Investigator: Marcela O'Alora, M.A.

MAPS is currently planning a Phase 2 "intern study" to investigate the effectiveness of MDMA-assisted psychotherapy for PTSD when one member of the standard male/female co-therapist team is a healthcare intern (being trained in therapy, social work, or nursing). The other member of the team will be a professional therapist trained in our treatment method. As interns work for free in exchange for fulfilling required training hours under professional supervision, this approach would reduce costs and train the next generation of psychedelic therapists. Subjects will be U.S. veterans with chronic, treatment-resistant PTSD, mostly from the Iraq, Afghanistan, or Vietnam wars, along with survivors of childhood sexual abuse, assault, rape, and others.

MDMA-Assisted Psychotherapy Training Study Charleston, South Carolina

Total cost: \$85,000 (\$25,000 still needed)

**Clinical Investigators: Michael Mithoefer, M.D.,
and Annie Mithoefer, B.S.N.**

This protocol is in healthy subjects, rather than in subjects with PTSD. This protocol is a placebo-controlled, double-blind, randomized, cross-over study in which we administer a single MDMA-assisted psychotherapy session to up to 20 therapists as part of their training to conduct MAPS' MDMA-assisted psychotherapy for PTSD studies, while also conducting a series of evaluations of the psychological effects of MDMA administered to healthy volunteers in a therapeutic context. This study has full clearance both from the FDA and an independent Institutional Review Board, and is now enrolling and treating subjects.

LSD-Assisted Psychotherapy for Anxiety Associated with Advanced-Stage Illness (complete)

Solothurn, Switzerland

Total cost: \$200,000

Clinical Investigator: Peter Gasser, M.D.

MAPS is proud to have completed the first study of the therapeutic use of LSD in humans in more than 35 years. The twelfth and final subject in our Swiss study of LSD-assisted psychotherapy for anxiety associated with advanced-stage illness was treated in May 2011, and half have now completed the long-term follow-up portion. In 30 treatment sessions, not a single subject experienced a severe negative reaction (serious adverse event, or SAE) such as a psychotic experience, suicidal crisis, flashback, or severe anxiety ("bad trip"). According to Clinical Investigator Peter Gasser, M.D., all 12 patients reported benefits from the treatment—however, it is too early to say whether the results will be statistically significant. Regardless of statistical significance, however, the preliminary results indicate that the risk of administering LSD in carefully controlled clinical settings is acceptably low, and that there is a promising future for LSD research.

Marijuana for Symptoms of PTSD in Veterans of War Phoenix, Arizona

**Total cost: \$20,000 for protocol development and
approval (\$10,000 still needed)**

Clinical Investigator: Sue Sisley, M.D.

MAPS' proposed pilot study of marijuana for 50 veterans with chronic, treatment-resistant PTSD is at a standstill, following a refusal by the US Department of Health and Human Services (HHS) to sell us marijuana for the study. Despite the fact that the FDA cleared the study in April 2010, the monopoly held by the National Institute on Drug Abuse (NIDA) (a division of HHS) on the supply of marijuana for medical research allows it to deny researchers permission to purchase marijuana regardless of FDA clearance. We are now preparing a detailed response to the reviewers' concerns, though the contradictory and misinformed nature of their critiques reveals their basic unwillingness to allow research into the possible beneficial uses of marijuana for suffering veterans. MAPS, in collaboration with Professor Lyle Craker of the University of Massachusetts-Amherst, the American Civil Liberties Union, and pro bono support from prestigious Washington, D.C., law firm Covington & Burling LLP, are also suing the Drug Enforcement Administration in the First Circuit Court of Appeals for refusing to let us break the NIDA monopoly by starting our own medical marijuana farm. If approved, this study would be the first clinical outpatient study of marijuana for PTSD.

Ibogaine Treatment for Addiction and Dependence Playas de Tijuana, Mexico

Total cost: \$32,000

Principal Investigator: Thomas Kingsley Brown, Ph.D.

All 30 subjects have now been enrolled in our ongoing observational study of ibogaine treatment for addiction, taking place at an independent ibogaine clinic in Mexico. Given the increasing numbers of people around the world seeking ibogaine treatment for drug addiction, this study aims to gather evidence about the safety and effectiveness of the treatment and to compare different approaches to that treatment.

Ibogaine Treatment for Addiction and Dependence New Zealand

Total cost: TBD

Principal Investigator: Geoff Noller, Ph.D.

Researchers are developing a new protocol to explore the safety and effectiveness of ibogaine treatment for addiction to take place at an independent ibogaine treatment center in New Zealand. This new observational study will provide additional data to complement our recently completed observational ibogaine treatment study in Mexico. This study will follow 20 to 30 subjects already enrolled in an ibogaine treatment program and evaluate the long-term effects of ibogaine treatment on addictive behaviors and overall quality of life. The protocol is currently under development, and the study will begin once it has been cleared by an independent Ethics Committee. This is an investigator-sponsored study with assistance from MAPS, and has been made possible by a generous \$25,000 grant for ibogaine research from Matt and Kristi Bowden of Stargate International.

Ayahuasca Treatment for Addiction and Compulsive Behaviors

British Columbia, Canada

Total cost: TBD

Principal Investigator: Gerald Thomas, Ph.D.

Sponsored by MAPS Canada, this observational study is investigating the safety and long-term effectiveness of ayahuasca treatment for individuals suffering from addiction and dependence. Combining Western psychotherapeutic techniques with South American shamanic (Vegetalista) healing practices, this study is gathering preliminary evidence about the safety and effectiveness of ayahuasca-assisted therapy. Treatment consists of participation in a five-day retreat (facilitated by independent psychiatrist Gabor Maté, M.D.) including ayahuasca-assisted therapy, which may help reduce problematic substance use as well as addictions, compulsive behavior, and self-harming thought patterns. The study is being conducted in cooperation with a British Columbia First Nations band. All treatment sessions have now been completed, and the research team is collecting follow-up data from 15 study participants. •

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