

MDMA-Assisted Psychotherapy for Posttraumatic Stress Disorder

MAPS' top priority is developing MDMA-assisted psychotherapy into a legal, Food and Drug Administration (FDA) and European Medicines Agency (EMA)-approved treatment for chronic, treatment-resistant PTSD caused by sexual assault, war, violent crime, or any other trauma.

Principal Investigator Michael Mithoefer, M.D., is leading our ongoing Phase 2 study in veterans, firefighters, and police officers in Charleston, South Carolina. His preliminary studies, in mostly women survivors of childhood sexual abuse or adult rape and assault, have shown that MDMA in conjunction with psychotherapy can help people overcome chronic, treatment-resistant PTSD.

MDMA (3,4-methylenedioxymethamphetamine) is a semi-synthetic compound patented by Merck in 1914 and now in the public domain. MDMA decreases activity in the left amygdala (associated with fear and traumatic memories); increases activity in the frontal cortex; and promotes the release of oxytocin and prolactin, hormones associated with love and bonding. MDMA can decrease fear and defensiveness while increasing trust and empathy.

In MDMA-assisted psychotherapy, MDMA is administered only a few times, in the context of a several month process of non-drug psychotherapy, unlike most medications for mental illnesses which are often taken daily for years.

MDMA-Assisted Therapy for Social Anxiety in Autistic Adults

MAPS is sponsoring an exploratory pilot study into MDMA-assisted therapy for the treatment of social anxiety in autistic adults, with **Principal Investigators Charles Grob, M.D.**, and **Alicia Danforth, Ph.D.**

Autistic individuals frequently experience difficulty in the realm of social interaction. There are currently no FDA-approved pharmacological treatments for autistic adults with social anxiety, and conventional anti-anxiety medications lack clinical effectiveness in this population. Based on numerous anecdotal reports, MDMA-assisted therapy may be a suitable intervention for the treatment of social anxiety in autistic adults and warranted further investigation in a randomized controlled clinical trial.

MAPS' randomized, double-blind, placebo-controlled study with dose escalation is assessing the safety and feasibility of MDMA-assisted therapy to treat social anxiety in 12 MDMA-naïve adults on the autism spectrum. This study will obtain estimates of effect size based on two experimental MDMA-assisted therapy sessions and associated non-drug preparatory and integrative sessions, in comparison to an inactive placebo control group with the same non-drug preparatory and integrative sessions.

MDMA-Assisted Psychotherapy for Anxiety Associated with Life-Threatening Illness

MAPS' randomized, double-blind, placebo-controlled Phase 2 study, located in Marin, California, is gathering preliminary data about the safety and efficacy of MDMA-assisted psychotherapy for anxiety in 18 subjects diagnosed with a life-threatening illness.

Outcomes will include treatment-related changes in anxiety, depression, sleep quality, quality of life, self-reported and observer-reported changes in attitudes, attitudes toward death and the prospect of death, and changes in self-compassion and self-reported mindfulness. Results from this study, if promising, will inform the dose, end points, and treatment regimen for subsequent studies. This study is also intended to develop a manualized psychotherapeutic approach to this potential treatment.



Principal Investigator Phil Wolfson, M.D., published an article on MDMA-assisted psychotherapy in the *Journal of Psychoactive Drugs* titled "Meetings at the Edge with Adam: A Man for All Seasons?" (1986, 18(4):329–33.) He is also the author of *Noe: A Father-Son Song of Love, Life, Illness, and Death*.

Medical Marijuana for Symptoms of Posttraumatic Stress Disorder

MAPS is the only organization working to demonstrate the safety and efficacy of whole-plant marijuana as a prescription medicine. Our upcoming study will be the first controlled study ever conducted to explore whether smoking marijuana can help reduce PTSD symptoms in 76 U.S. veterans with chronic, treatment-resistant PTSD. The study will investigate four varieties of marijuana: (a) placebo, (b) high THC/low CBD, (c) high CBD/low THC, and (d) high THC/high CBD. There will be a three-week dosing period with patient self-titration up to 1.8 grams/day, a two week washout, and another three-week dosing period.

The Colorado Department of Public Health and Environment has fully funded the study with a \$2.15 million grant awarded to MAPS. The study has been approved by the FDA, IRBs, and the Public Health Service/NIDA and was featured in the CNN documentary by Dr. Sanjay Gupta, *Weed 3: The Marijuana Revolution*, broadcast on Sunday, April 19, 2015.

Principal Investigator Sue Sisley, M.D., was honored with the Americans for Safe Access Researcher of the Year Award at the National Medical Marijuana Unity Conference in Washington, D.C., on March 30, 2015.



Developing MDMA into a Prescription Medicine

Timeline for regulatory approval of MDMA-assisted psychotherapy for PTSD



Current Phase 2 Studies

- US Study in 24 veterans, firefighters, and police officers (Charleston, South Carolina)
- US Study in 23 subjects with PTSD from any cause (Boulder, Colorado)
- Israeli Study in 10 subjects with mostly war- and terrorism-related PTSD (Beer Yaakov Mental Health Center)
- Canadian Study in 12 subjects with PTSD from any cause (Vancouver, British Columbia)

Phase 3 Studies

- US Study in 300 subjects/10 sites (2016–2020)
- European Study in 100 subjects/4 sites (2017–2021)

For more information, see maps.org/research/mdma.



Michael Mithoefer, M.D., is a psychiatrist practicing in Charleston, SC, where he divides his time between clinical research and outpatient clinical practice. He and his wife, Annie Mithoefer, are currently conducting a MAPS-sponsored Phase 2 clinical trial testing MDMA-assisted psychotherapy for PTSD in

veterans, firefighters, and police officers who have PTSD resulting from their service. Before going into psychiatry in 1995 he practiced emergency medicine for ten years, served as medical director of the Charleston County and Georgetown County Emergency Departments, and holds a clinical faculty position at the Medical University of South Carolina (MUSC). He is currently board certified in Psychiatry, Emergency Medicine, and Internal Medicine.

Publications

Michael C Mithoefer, *et al.* "Durability of improvement in PTSD symptoms and absence of harmful effects or drug dependency after MDMA-assisted psychotherapy: a prospective long-term follow-up study." *Journal of Psychopharmacology*. 2013; 27(1): 28–39. Epub 2012 Nov 20.

Michael C Mithoefer, *et al.* "The safety and efficacy of MDMA-assisted psychotherapy in subjects with chronic, treatment-resistant PTSD: the first randomized controlled pilot study." *Journal of Psychopharmacology*. 2010; 1–14. Epub 2010, July 19.

Mithoefer *et al.* "MDMA ("Ecstasy") and Neurotoxicity." *Science*, 2003; 300: 1504.



"This is serious research addressing pressing public health problems. My hope is that our work will lead to FDA approval for MDMA-assisted psychotherapy to be widely available to patients who suffer from PTSD."—Co-therapist Annie Mithoefer, B.S.N.



Charles Grob, M.D., is a professor of psychiatry and pediatrics at the UCLA School of Medicine and the Director of the Division of Child and Adolescent Psychiatry at the Harbor-UCLA Medical Center. He and Alicia Danforth, Ph.D., are currently leading an exploratory MAPS-sponsored pilot study on MDMA-assisted therapy for social

anxiety in adults on the autism spectrum. His research has included the first FDA-approved Phase 1 study of the physiological and psychological effects of MDMA; a multi-national, collaborative study of the Amazonian plant hallucinogen decoction, ayahuasca, in Brazil; and a pilot investigation of the safety and efficacy of psilocybin in the treatment of anxiety in adult patients with advanced-stage cancer.

Publications

Danforth, A.L., Struble, C.M., Yazar-Klosinski, B., and Grob, C.S. "MDMA-assisted therapy: A new treatment model for social anxiety in autistic adults." *Progress in Neuropsychopharmacology and Biological Psychiatry*. 2015, March 25.

Grob, C.S., Danforth, A.L, Chopra, G.S., Hagerty, M.C., McKay, C.R., Halberstadt, A.L., and Greer, G.R. "Pilot study of psilocybin treatment for anxiety in patients with advanced-stage cancer." *Archives of General Psychiatry* 2011 Jan; 68(1):71–8. Epub 2010 Sep 6.

Grob, C.S., Poland, R.E., Chang, L, Ernst, T. "Psychobiologic effects of 3,4-methylenedioxymethamphetamine in humans: methodological considerations and preliminary observations." *Behavioural Brain Research* 1996; 73(1–2):103–7.

Grob, C.S., *et al.* "The MDMA-neurotoxicity controversy: implications for clinical research with novel psychoactive drugs." *The Journal of Nervous and Mental Disease* 1992; 180(6):355–6.

About MAPS

Founded in 1986, the Multidisciplinary Association for Psychedelic Studies (MAPS) is a 501(c)(3) non-profit research and educational organization that develops medical, legal, and cultural contexts for people to benefit from the careful uses of psychedelics and marijuana.

MAPS furthers its mission by:

- Developing psychedelics and marijuana into prescription medicines
- Training therapists and working to establish a network of treatment centers
- Supporting scientific research into spirituality, creativity, and neuroscience
- Educating the public honestly about the risks and benefits of psychedelics and marijuana.

All MAPS-sponsored research is conducted by the MAPS Public Benefit Corporation (MPBC), a wholly owned subsidiary of MAPS. The special purpose of MPBC is to serve as a vehicle for conducting MAPS' research, and to balance social benefits with income from the eventual legal prescription sale of MDMA, other psychedelics, and marijuana.

Phase 3 Researchers Needed

MAPS encourages clinicians interested in conducting research as part of our Phase 3 MDMA-assisted psychotherapy for PTSD research to contact Shannon Pettitt at shannon@maps.org.

Join the Conversation

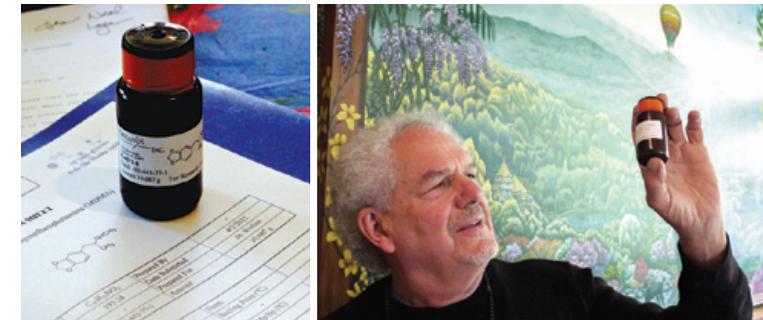
Learn more about our research and education programs at maps.org.

MAPS
1115 Mission Street
Santa Cruz, CA 95060
maps.org • mdmmaptsd.org
askmaps@maps.org
831.429.6362



MAPS

Clinical Research with Psychedelics



MAPS is close to completing Phase 2 of our \$20 million clinical research plan to develop MDMA-assisted psychotherapy for PTSD into an FDA-approved prescription treatment by 2021.

maps.org