

Update on MDMA-Assisted Psychotherapy for PTSD:

Building an International Research Program

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“The treatment manual we’ve created... conveys the essential elements of the therapy, while including enough flexibility to support each participant’s unique healing process and each therapist’s particular skills and intuition.”

As MAPS’ 25th anniversary approaches, we’re happy to report that MAPS-sponsored MDMA research is progressing in the US and other countries and is gaining increasing acceptance in the scientific community.

As we described a year ago in the *Bulletin*, the results of our first clinical trial of MDMA-assisted psychotherapy for PTSD (MP-1) were published in the *Journal of Psychopharmacology* in July 2010 (an online version can be found at <http://bit.ly/t3PSJZ>). The paper was subsequently chosen for review by the Faculty of 1000, an organization that “identifies and evaluates the most important articles published in Medicine” to recognize their “scientific merit and positive contribution...to the medical literature.” The reviews, written by prominent researchers from Emory University and the University of Chicago, were both favorable: one rated the paper as a “must read.” The *Journal of Psychopharmacology* also informed us that ours was the most frequently downloaded paper of 2010.

In November 2010, Dr. Mithoefer was invited by the American Medical Psychiatric Association’s journal *Psychiatric Times* to write an article about the future of MDMA in psychiatry. The article answered the question “Does MDMA Have a Role in Clinical Psychiatry?” (*Psychiatric Times*, Vol. 28 No. 5) with a resounding “yes”: MDMA is likely to have an increasingly important role, and much more research is still required.

We have also now completed a long-term follow-up of participants in our original flagship study. Our analysis shows that the substantial benefits resulting from MDMA-assisted psychotherapy were sustained for most participants from one to five years later (an average of 41 months). Dr. Mithoefer presented these long-term results at the 2010 meeting of the American Psychological Association in San Diego and the International Society for Traumatic Stress Studies (ISTSS) meeting in Montreal. We are now nearing completion of

a manuscript summarizing these results for submission to a medical journal.

Although the benefits of MDMA-assisted psychotherapy lasted a year or more for most participants in the original study, two of those individuals who responded well initially eventually had symptoms return. We recently received FDA, DEA, and Institutional Review Board (IRB) approval for a new protocol to offer one additional MDMA-assisted session to up to three people who experienced relapses with symptom scores at or above the level required for entry into the original study. We will begin this protocol in early 2012.

Our current main focus is our ongoing study of MDMA-assisted psychotherapy for veterans with PTSD (“A Randomized, Triple-Blind, Phase 2 Pilot Study Comparing 3 Different Doses of MDMA in Conjunction with Manualized Psychotherapy in 16 Veterans with Chronic Posttraumatic Stress Disorder”). These are veterans who have PTSD stemming from trauma during military service (either from combat or from sexual trauma while serving in the military) and who have not responded adequately to prior treatment with medications and/or psychotherapy. In this study, we are comparing three different doses of MDMA—low, medium, and full dose—rather than comparing full dose MDMA with an inactive placebo as we did in our original study. This design is intended to determine whether one of the lower doses could be an effective “active placebo,” making the subjects and investigators less likely to guess correctly which dose has been administered. Those who receive either a low or medium dose in the first three sessions are eligible to enroll in a second open-label portion (Stage 2) in which they receive three full-dose MDMA-assisted psychotherapy sessions.

Thus far, we have enrolled five participants in our U.S. veterans study: two women with military sexual trauma, and two men and one woman with combat related trauma. We

have been in contact with almost 100 veterans interested in participating, and 30 out of 37 potentially qualified subjects have passed the initial telephone screening. In addition to those already enrolled, two more have passed in-person screening and will be enrolled soon.

While it is still too early to report results, we are pleased with the way the study is progressing. We find it very gratifying to work with these veterans whose lives have been so severely affected by PTSD and who have not been adequately helped by treatments available at Veterans Administration hospitals and clinics. These men and women are acutely aware of the huge toll that PTSD exacts on veterans, and are not only highly motivated to do their own healing, but also very interested in new treatment methods that could eventually help their fellow veterans. We are also enjoying working with a fourth-year psychiatry resident from the Medical University of South Carolina who is getting credit for spending one day a week working with us on the protocol.

This and future MAPS studies of MDMA-assisted psychotherapy for PTSD represent important scientific advances in several ways. The first is that independent raters are watching videos of the study sessions and scoring them according to the manualized Adherence Measures that we have developed. This will enable us to evaluate whether both we and therapists in other studies are adhering to the Treatment Manual (<http://www.maps.org/treatmentmanual>) and using the same psychotherapeutic approach with each subject regardless of which dose of MDMA is administered. Highly qualified volunteers (psychiatrists, psychologists, and graduate students whom we have trained) are rating the sessions in the ongoing veterans study and will also be doing so for other studies.

Another way we are working to ensure that the same therapeutic approach is being used in all our studies is by developing a training program for additional independent raters, as well as continuing our existing training program for therapists working in other MAPS clinical trials. Although “manualizing” our largely non-directive approach to MDMA-assisted psychotherapy has been a challenge, doing so is necessary for the research

to move forward. We believe the Treatment Manual we’ve created (with the help of Dr. June Ruse and others) conveys the essential elements of the therapy, while including enough flexibility to support each participant’s unique healing process and each therapist’s particular skills and intuition. A consultant psychologist who is an expert in manualized therapy has also reviewed our Treatment Manual, and has determined that it is an effective manual for research purposes.



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In addition to our U.S. veterans and relapse studies, we have also initiated a study in which enrollment is limited to therapists who have completed our MDMA-assisted psychotherapy training program and who intend to work as therapist/investigators in future MAPS-sponsored clinical trials. Our therapist training protocol is designed to gather information about the psychological effects of MDMA in healthy volunteers in a therapeutic setting, adding to our knowledge of the effects of MDMA in the context of clinical research.

It will also provide an opportunity for therapists working in clinical trials to have their own MDMA-assisted psychotherapeutic experience (if they choose). We believe this experience is likely to expand therapists’ knowledge and practical skills and give them a more complete grasp of the study drug as experienced by research participants. One therapist has already completed this protocol and another is scheduled to enroll in December 2011.

MAPS’ clinical MDMA research program has definitely picked up speed in recent years. As we continue our research in Charleston, we have made exciting progress by collaborating with teams in other countries and other parts of the U.S. Dr. Peter Oehen and his wife Verena Widmer in Switzerland have now completed their own study of MDMA-assisted psychotherapy for PTSD using a protocol similar to our U.S. flagship study, but using low-dose MDMA as an active placebo. Another study has been approved in Israel, and similar studies are nearing approval in Vancouver and Jordan, while other protocols are being planned in Australia, Colorado, and (possibly) England. At the 25-year mark, our progress is accelerating fast. Although there’s still a great deal to be done, now there’s no question that it can be accomplished. •