

# MDMA-Assisted Psychotherapy in the Treatment of Posttraumatic Stress Disorder (PTSD): Fifth Update on Study Progress



By Michael Mithoefer, MD  
(mmit@bellsouth.net)

Since my last update in the Spring of 2004 our study has progressed smoothly and we've gotten permission to expand the protocol in some significant ways.

At this point seven subjects have completed the study, one more has been enrolled and is currently participating in the protocol and several others will soon be screened. A brief chronology of recent events is as follows:

- 8/10/04 Site visit by our Institutional Review Board (IRB) to review documentation and compliance with the protocol
- 9/3/04 Approval from IRB to continue the study—this is routinely required every 6 months
- 11/15/04 Data Safety Monitoring Board (DSMB) met as scheduled to review the records of the first five subjects to complete the study. The DSMB (a psychiatrist, a psychologist and a PharmD pharmacologist not otherwise involved in the study) reported no safety concerns
- 11/16/04 Based on our experience with the first five subjects, who had completed the study safely and with promising results, we wrote the FDA requesting five modifications in the protocol. These requests were approved by the FDA in December and by the IRB in January. These changes have now been incorporated in the protocol and are as follows:
  1. At the final (17<sup>th</sup>) visit of the existing protocol the blind is broken and subjects who received placebo during their experimental sessions are offered inclusion in a second stage of the study (Stage 2) in which MDMA is given in an open label fashion (subjects and researchers know ahead of time that MDMA is being administered in both experimental sessions of this stage). This occurs during the same kind of eight-hour MDMA-assisted psychotherapy session as in Stage 1. There are 6 follow-up therapy sessions in stage 2 and outcome measures are repeated approximately 2 months after the second MDMA-assisted therapy session. In order to protect the blind in Stage 1, the blind will not be broken for the last five of the subjects until they have all completed the study. Any placebo subjects in this group will be offered participation in Stage 2 at that point.
  2. In addition to subjects with crime related PTSD we may now also include people with war related PTSD of less than five years duration.
  3. The upper age limit is increased from 65 to 70 years. Before this change we had been obligated to turn away some subjects over 65 who were in good physical health and had no reason for exclusion other than the age limit.
  4. We are able to use more clinical judgment about how often we must measure blood pressure and pulse in certain situations. We are still required to take these measurements at least every 15 minutes for 4 hours and every 30 minutes for 2 more hours.
  5. Although subjects are required to be off all psychotropic medications, we may now make an exception for gabapentin (Neurontin) in a subject who needs it for pain related to traumatic nerve injury.

We are now in the process of sending out another round of recruitment letters to psychiatrists, psychologists and other therapists giving an update on the progress of the study and informing them about these protocol changes. The IRB has now also given us permission to use newspaper advertising for recruitment. This is expensive so it will be used sparingly but we hope it will be helpful with ongoing recruitment. We're in competition for subjects with several PTSD studies going on at the Medical University in Charleston (not using MDMA!) that appear to have large advertising budgets from drug companies or government grants. Pending these additional recruitment methods, some new subjects have been referred by therapists already familiar with the study; some have called because they learned about it by word of mouth from previous subjects or from media coverage of MDMA research. There's been another upsurge in this coverage recently with the approval of John Halpern's MAPS sponsored MDMA study at Harvard. His approval is not only great news in general, it's helpful because it demonstrates that we're not the only ones crazy enough to think the therapeutic potential of MDMA is worth studying.

We're very pleased with the recent adjustments in the protocol. The fact that we can now offer MDMA-assisted sessions to subjects who got placebo is likely to help with recruitment, and it will add valuable data, as these subjects will serve as their own placebo controls. In addition, the preliminary results are encouraging and, most importantly, there has been no indication of harm to the subjects.