

The 2005 MAPS Conference in Israel

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The March 24, 2005 Israeli MAPS conference may have been the most “mainstream” psychedelic research conference in decades. Held under the auspices of the Israeli Ministry of Health and the Israeli Society of Addiction Medicine, the one-day event also brought representatives from the Israeli Anti-Drug Authority (equivalent to the Office of National Drug Control Policy), and even Israeli legislator Roman Bronfman’s office to learn about psychedelic research projects around the world.

MAPS organized the conference to educate Israeli researchers and regulators about the proposed MAPS-sponsored Israeli MDMA/PTSD pilot study (see page 3). The study would be under the direction of Dr. Moshe Kotler, Chair, Department of Psychiatry, Tel Aviv University, Sackler School of Medicine. The speakers included most of the few researchers in the world who have permission to give psychedelics to humans.

Here is a summary of the speakers’ presentations, in the order they were given. You can also watch videos of the talks at <http://www.maps.org/avarchive/>. In addition to the “usual gang” of MAPS-sponsored researchers, like Dr. Michael Mithoefer and Dr. John Halpern, we had the opportunity to hear from researchers in Israel, Spain, and Germany. All have exciting projects in the field of psychedelic or marijuana research.

Rick Doblin, Ph.D.

Opening the event, MAPS President Rick Doblin discussed MAPS’ seven-year effort to start MDMA/PTSD research in Israel. After meeting Dr. Moshe Kotler in 1998, MAPS organized two scientific conferences to pave the way for an Israeli study. In 1999, MAPS brought to Israel at least one person from every scientific team in the world that had permission to administer MDMA to human subjects. The second conference, in 2002, brought all the researchers who had conducted MDMA/PTSD research, as well as other scientists and researchers. Now that the U.S. MDMA/PTSD pilot study has generated promising results and the FDA has approved an MDMA/cancer anxiety study at Harvard, Doblin said he hoped that this third conference would be sufficient to start the formal protocol design and review process for an Israeli pilot study.

Michael Mithoefer, M.D.

The principal investigator of the MAPS-sponsored MDMA/PTSD study in South Carolina, Dr. Mithoefer discussed the preliminary results from the first five subjects who have completed the entire study, as well as two others who have completed everything but the final follow-ups. While no conclusions can be drawn from such a small sample, the data is extremely promising. There have been



Rick Doblin, June May Ruse, John Halpern, and Michael Mithoefer listen attentively during a meeting with the officials at the Israeli Anti-Drug Authority. Photo by Jose Carlos Bousou.

no adverse physiological responses or measurable neuro-cognitive problems. Five of these seven participants were given MDMA and two were given placebo; all five subjects who received MDMA and one who received placebo improved on scales that measure PTSD symptoms.

The fact that these subjects improved, particularly since all were resistant to conventional therapy and medications, is very promising. The fact that one placebo subject improved shows that the team’s approach can be beneficial, with or without the drug. If the rest of the data is similar to that already gathered, the pilot study will be a strong testament that MDMA can be used safely in this patient population and to the likelihood that MDMA-assisted psychotherapy is therapeutic.

Raphael Mechoulam, Ph.D.

Dr. Mechoulam is the Israeli scientist who identified THC as the psychoactive compound in marijuana, and decades later he discovered the brain’s endocannabinoid system and the endogenous neurotransmitter anandamide. He is one of the most respected Israeli neuroscientists and has been a senior advisor to the Israeli government on marijuana policy and the ethics of research with human subjects. He discussed his experiments demonstrating the neuroprotective effects of the endocannabinoid system in mice that have had traumatic injuries to the brain. He believes the neuroprotective effects of marijuana may eventually have applications for other neurological and psychiatric conditions, including Alzheimer’s and Parkinson’s disease.

Another fascinating discovery, one with implications for PTSD, is that the cannabinoid system is integrally related to memory, specifically to memory extinction. Memory extinction is the normal, healthy process of removing associations from stimuli. Dr. Mechoulam explained that an animal which has been administered an electric shock

after a certain noise will eventually forget about the shock after the noise appears alone for a few days. Mice without cannabinoid systems simply never forget—they continue to cringe at the noise indefinitely.

This has implications for patients with PTSD, who respond to stimuli that remind them of their initial trauma even when it is no longer appropriate. By aiding in memory extinction, marijuana could help patients reduce their association between stimuli (perhaps loud noises or stress) and the traumatic situations in their past. Working with Army psychiatrists, Dr. Mechoulam has obtained the necessary approvals for a study on PTSD in Israeli veterans, and hopes to begin the study soon.

This theoretical model is in some senses the opposite of the one underpinning MDMA research, as people report remembering their trauma more clearly with MDMA. By processing painful emotions that were too difficult without the MDMA, people can move past the trauma. This is not through forgetting, but through accepting and realizing that the present moment carries with it the scars of the past but that the past trauma does not necessarily have to be repeated in the present.

Dr. Mechoulam also obtained permission from the Israeli Ministry of Health for some hospitals to administer marijuana to patients under limited circumstances. The patient's doctor must submit a request to a hospital committee, and usually within 24 hours the patient can receive the medication. Marijuana has so far been used for cancer-related nausea, eating disorders, Tourette's syndrome, and depression.

Jose Carlos Bouso, Ph.D. candidate

Jose Carlos Bouso is a Ph.D. candidate at the Autonomous University of Madrid, and the principal investigator for the MAPS-sponsored MDMA/PTSD dose-response study in Spain, which was the first legal MDMA psychotherapy study in the world. The Madrid Anti-Drug Authority, after favorable media reports about the initial subjects treated in the study, pressured the hospital hosting the study to shut it down. MAPS is working with Bouso to submit a new protocol with several changes to the Ministry of Health.

The new study will be at a private hospital, making it easier to resist political pressure than at the public hospital at which the initial study took place. It will also use higher doses of MDMA, since appropriate dosing (one of the questions in the earlier dose-response study) has been determined by other projects.

June May Ruse, Psy.D.

Dr. Ruse is the director of MAPS' MDMA/PTSD treatment manual project. The treatment manual serves not only as a teaching guide for therapists, but also as a way to formalize and standardize the treatment method for the FDA, the National Institute of Mental Health (NIMH), and the scientific community. This is a necessary step to obtain

federal funding for future MDMA-assisted therapy studies and particularly if MDMA is to become a prescription medicine.

The manual (available at <http://www.maps.org/research/mdma>, look under "Clinical Research") covers all stages of treatment, including initial assessment, establishing a therapeutic relationship, creating a safe space, preparation, facilitating the MDMA-assisted sessions, and following-up to help the subject integrate insights from the process.

MAPS submitted a grant application on June 1, 2005 to NIMH seeking \$50,000 a year for two years for the development of our treatment manual, and for the creation of a standardized system to evaluate compliance of therapists to the principles set out in the manual. NIMH was a major funder of psychedelic psychotherapy research in the 1960s but hasn't funded any such research for over 35 years.

Valerie Mojeiko

MAPS staffer and Clinical Research Associate Valerie Mojeiko discussed her proposed outcome study of the use of ibogaine in treating substance abusers. She described different ibogaine treatment options and explained the necessity of an evaluation component of ibogaine treatment programs. After explaining the measures used to evaluate patients' recovery, she reported on promising preliminary data gathered from patients of the Iboga Therapy House in Vancouver.

The Addiction Severity Index will be the primary outcome variable in the study. While many outcome studies on substance abuse report only whether patients have maintained abstinence or not, the proposed MAPS-sponsored study would measure relapsed patients' quality of life and substance use patterns, avoiding the "zero tolerance" approach and examining whether the treatment was helpful even if patients have returned to use. In some cases, patients may have moved to less destructive patterns or improved other aspects of their lives. The study will also employ the Peak Experience Profile, to show whether a more intense psychedelic experience (whether pleasant or unpleasant) is more beneficial or not.

Udi Bastiaans, M.D.

Dr. Bastiaans is a clinical researcher who recently moved to Israel from the Netherlands. His thesis for medical school, "Life after Ibogaine," is the first longitudinal study of ibogaine treatment's effects. He also used a variation on the Addiction Severity Index, examining both drug use patterns and other factors of healthy living in the 21 patients he surveyed. The study found that 24% of the participants were drug free at the time they filled in the questionnaire, with an average abstinence period of over three years. Another 43% of the participants were not using their primary and secondary drugs (which they were treated for), but were using other substances (often marijuana or alcohol). The remaining 33% of the sample

were using either primary or secondary drugs. All participants reported using less of their substances of abuse than before the study.

Although the study's conclusions are based on a relatively small number of subjects who completed a self-reported Internet questionnaire, the project serves to support the need for more controlled studies into ibogaine's potential for treating drug dependence.

Dr. Bastiaans' grandfather, Dr. Jan Bastiaans, was the first physician to work with ibogaine for drug dependence. He was also the therapist who pioneered the use of LSD in the psychotherapeutic treatment of concentration camp survivors. He worked with Ka-Tzetnik, the Holocaust survivor who describes his LSD psychotherapy in the autobiographical *Shivitti*. (*Shivitti* may be ordered from MAPS: see page 23 for more information.)

John Halpern, M.D.

The Assistant Director of Substance Abuse Research at Harvard Medical School's McLean Hospital, Dr. Halpern spoke about two research projects with MDMA. The first is his study on the neurocognitive profile of moderate and heavy MDMA users. Unlike previous studies, this one compares a population of non-drug using young people who attend raves with a population of MDMA users who also attend raves, and who do not use other drugs or alcohol. Participants must have taken MDMA 20 or more times.

MAPS provided the initial \$15,000 for this study, and based on the pilot data on over 40 subjects, the National Institute on Drug Abuse (NIDA) provided a five-year \$1.8 million grant for its completion. The study will eventually include 200 participants, a much larger group than has been used in most studies of MDMA users.

The data from the pilot study indicates no differences between the control group and the moderate user group (20-55 exposures to MDMA), and only slight differences in the heaviest users (60 or more exposures). These differences are not in verbal memory deficits, as some studies have shown, but in strategic thinking. These users' scores, however, remain in the normal range. It remains to be seen whether this difference will be significant in the larger study.

Dr. Halpern is also the principal investigator for the proposed MAPS-sponsored research on MDMA for anxiety in patients with advanced-stage cancer. The research is already approved by the FDA and two institutional review boards (IRB), and awaits DEA registration.

Jordi Riba, Ph.D.

A pharmacologist at the Autonomous University of Barcelona, Dr. Riba studied ayahuasca users for his Ph.D. dissertation. While not directly related to therapy, Dr. Riba's research paves the way for studies on beneficial uses of ayahuasca by providing information about its safety and mode of action. He discussed the chemical composition of ayahuasca, noting that three basic alkaloids are present—harmine, harmaline, and DMT. His first study was a single-blind pilot study of six males, given placebo then three doses in increasing size, leading to 1 mg/kg. After this pilot study, a second study included eighteen participants in a double-blind, placebo controlled, randomized design.

Dr. Riba's team is studying a number of different factors, including cardiovascular effects, cerebral blood flow, hormone levels, and immune system effects. Future studies will include a repeat dose to test tolerance.

Interestingly, only one volunteer in the study experienced vomiting as a side effect. The study employed encapsulated, freeze-dried preparations of the ayahuasca brew, indicating that the common side effect may be closely related to the taste and smell of the tea.

Torsten Passie, M.D.

Dr. Passie is a German researcher who studies psilocybin, ketamine, and other psychoactive substances. He first talked about a current study on psilocybin intended to measure subjective effects of psilocybin, and visual effects in particular. It is a double-blind study in which participants spend their experience lying on a couch with little outside intervention.

Dr. Passie also discussed his plans for an upcoming study using MDE (methylenedioxyethylamphetamine, a substance similar to MDMA) and/or MDMA as an adjunct to couples therapy. Dr. Passie noted that the World Health Organization considers troubled relationships to be a significant health problem, and studies have found that a satisfying relationship is the strongest marker for a high quality of life. The study is still in the design phase and MAPS has pledged \$25,000 to this project.

Outcomes

The conference was a success. Soon after the event, Dr. Kotler submitted the study protocol to the local ethics committee at Beer Yaakov Mental Health Center, and on June 6, 2005, the hospital's committee approved it, sending it on for review to the national ethics committee. The conference also sparked a favorable article in a prominent Israeli newsmagazine (see page 7). In fact, the article concluded with the endorsement of the study by Dr. Rachel Bar-Hamburger, chief scientist of the Israeli Anti-Drug Authority.

We now hope that the next MAPS conference in Israel will include the presentation of data from an Israeli MDMA/PTSD pilot study.