maps research update

MDMA/PTSD therapy study poised to begin in Spain

The Spanish research team has been joined by an American therapist experienced with MDMA in the treatment of post-traumatic stress disorder associated with rape. Marcela Ot'alora Roselli, bi-lingual therapist-in-training, currently lives in Boulder and is working on a masters degree at the Naropa Institute. Marcela decided to become professionally involved in MDMA therapy due to the contribution that MDMA therapy made to her own recovery from rape-associated PTSD. You can read her personal account on the MAPS website at www.maps.org/research/mdma/marcela.html. The projected cost of this study is $54,000 to $63,000. Nearly half of this amount has already been donated to MAPS by members.

We continue to seek additional support for this effort. Donors will be contributing to the first controlled study of the therapeutic use of MDMA ever conducted. For current updates on the MAPS website see www.maps.org/research/mdma/spain/mdmaspain.html.

Psilocybin in the treatment of obsessive-compulsive disorder

In May, MAPS sent a check for $10,527 to the University of Arizona Department of Psychiatry, to pay for the psilocybin for this historic study. Producing the psilocybin will probably take two to three months, then the study can begin. The research protocol and informed consent form are available on the MAPS website at www.maps.org/news/1099news.html.

This is the first FDA-approved study in over 25 years to examine the use of psilocybin in a patient population. The principal investigators, Dr. Pedro Delgado and Dr. Francisco Moreno, plan to study the use of psilocybin in ten patients suffering from obsessive-compulsive disorder (OCD). They want to determine if they can replicate in a clinical study several published case reports of patients whose OCD symptoms were reduced after self-experimentation with psilocybin mushrooms.

Review and summary of over 700 scientific papers on MDMA

Matt Baggott and associates are nearing completion of a MAPS-funded major review of over 700 scientific papers comprising all peer-reviewed articles reporting on basic and clinical research with MDMA. The review will be submitted to the FDA in conjunction with the MDMA research protocol being planned at Harbor-UCLA Hospital under the supervision of Dr. Charles Grob. The review will also be submitted to the Israeli Ministry of Health as part of the application for the MDMA/PTSD study in Israel.

German study of MDMA users published

At the MAPS symposium "Clinical Research with MDMA and MDE" held in Israel August 30-September 1, 1999, Dr. Efi Gouzoulis-Mayfrank presented data from a study comparing MDMA-using ravers with two control groups, one with subjects who had used cannabis but not MDMA and another with control subjects who did not use drugs. The mean estimated cumulative total dose of the MDMA-using group was 93 pills, the mean duration of regular use was 27 months.

Differences found were in certain subsets of memory and executive functions, with the MDMA-using group performing somewhat lower. These differences were statistically significant but clinically insignificant, meaning that neither the subjects nor the testers could tell the groups apart in normal social situations and the MDMA users' scores were still within the normal range.

Dr. Gouzoulis-Mayfrank's study was recently published in the *Journal of Neurology, Neurosurgery and Psychiatry.* The results have been sensationalized in the press with headlines such as "Study suggests even light use of Ecstasy might dull intelligence."

The memory findings in the studies of Drs. Bolla, Ricaurte and McCann are also statistically significant but clinically insignificant (*MAPS Bulletin* Vol. IX 3:6-8). Possibly confounding any causal role of MDMA in the memory findings is that these studies may be measuring effects of the Ecstasy raver lifestyle (lack of sleep, in some cases use of other drugs not matched by the control groups) or of possible preexisting factors such as subclinical depression and/or anxiety. However, the study of Dr. Gouzoulis-Mayfrank included no unusually heavy or poly-drug users.

As of yet, no study shows that one or a few doses of MDMA in a clinical research context results in any functional or behavioral consequences from possible neurotoxicity. Alex Gamma, Ph.D. candidate, University of Zürich, is reviewing all studies of MDMA and memory for a subsequent issue of the *MAPS Bulletin.* There is more that can be said about this topic, but we can't remember what it is.

MDMA study in Israel progressing as hoped

Protocol development for the $50,000 post-traumatic stress disorder study that MAPS is working to start at Ben Gurion University of the Negev is still underway. We hope to submit it for review to the Israeli Ministry of Health before the end of the year.

Ayahuasca research in Spain

The ayahuasca research effort we described in a previous *MAPS Bulletin* article has been progressing slowly but surely. Obtaining ayahuasca was the first difficulty we encountered, but thanks to the help of several people we are indebted to, we were kindly sent two 10 litre batches of ayahuasca by CEFLURIS in Brazil. Our ayahuasca (Santo Daime) batches were freeze-dried and analyzed for beta-carboline and DMT contents. The former were determined at our HPLC facilities, while the latter was quantified by James C. Callaway in Finland. We would also like to express our gratitude to him. Once this was done, freeze-dried ayahuasca was encapsulated in gelatin capsules. The handling of the freeze-dried material was another unexpected difficulty, as the material proved extremely hygroscopic even within an environment controlled for humidity. This complicated the manipulation of the powder, which was done in special plastic bags under dry nitrogen, and the storage of the prepared capsules, which have since been kept in a freezer at -20 ℃ under dry nitrogen and protected from light.

Dosing subjects

Once we finally had the capsules ready, we began interviewing a number of local (Barcelona) ayahuasca users. We selected a group of six healthy male volunteers with previous experience with the tea, in order to conduct a pilot study. Even though we had first considered using 0.5 and 0.8 mg DMT/kg body weight doses, we decided to conduct a pilot study with three ayahuasca doses, containing respectively 0.5, 0.75 and 1.0 mg DMT/kg body weight. We administered the ayahuasca in a single-blind dose-escalating design. That is, subjects were told they would receive the doses in a randomized order. The investigator knew which doses were being given on each experimental day. They actually received the placebo on the first session, the lower dose on the second, the medium dose on the third and the higher dose on the fourth day of participation. This was done for safety reasons, in order to control for possible adverse reaction in the more stressing environment of a research lab. In this first pilot study the following measures were conducted: subjective effects were recorded by means of visual analogue scales (VAS), the Hallucinogen Rating Scale (HRS) and the Addiction Research Center Inventory (ARCI), a standard questionnaire used in the clinical evaluation of psychoactive drugs. Additionally, preliminary data on the prepulse inhibition of the startle response and the P50 event-related potential (both putative measures of sensorimotor gating) were also obtained.

After completion of the pilot study we analyzed the subjective reports and recorded cardiovascular measures. We are presently preparing a paper discussing the subjective effects reported by the subjects and the results of the preliminary tolerability analyses (cardiovascular measures, results from the biochemical and hematological determinations conducted after each experimental session). The pilot study developed without major problems, but one subject decided to withdraw after the second session, so we finished with only five volunteers. When the subjects were asked which doses they believed they had been given on each session, one subject mistook the lower dose with placebo. On the other hand, the higher dose was considered by all the remaining five participants as eliciting excessively intense effects. We decided thus to use a 0.6 DMT/kg body weight dose, that is a dose between the lower and medium doses of the pilot study, as the lower dose in the larger double blind study. As the higher dose of the final study, 0.85 mg DMT/kg body weight was chosen, between the medium and the higher doses administered in the pilot study. So the final ayahuasca doses employed were slightly different from those we reported in the MAPS article.

The experimental (clinical) part of the final double-blind trial is almost complete. Finding volunteers with experience in hallucinogen use and meeting the inclusion criteria set in the study protocol proved difficult. As many as 90 subjects reached the psychiatric interview stage, but a large number were excluded later for minor physical health problems or decided not to participate when they were told they would have to spend ten hours in the lab on four different days, if they entered the study. In the end, we have been able to include 18 volunteers as we had planned. As we described in the *MAPS Bulletin*, the final double-blind trial included a large number of study variables: the performance of 30 lead EEG recordings, blood sampling, urine collection, etc. at different time points. We also incorporated the PPI and P50 measures mentioned above, which were not ready at our lab until some time after we wrote the MAPS article. This has all been a considerable amount of work, but it is now done and the prospect of soon beginning to analyze the data gathered is again stimulating.

New study

As a final comment, we have now started working on a SPECT protocol in which ayahuasca will again be the center of our investigations. Before the protocol is sent to the Ethics Committee, we will concentrate on analyzing and publishing the data of the present study. This will doubtlessly facilitate the approval of a new ayahuasca project by the authorities.

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