Summer 1998 Research Updates

The Janiger LSD Follow-up Project
The MAPS-funded and coordinated Janiger follow-up study, in which approximately 40 subjects were interviewed nearly forty years after initially ingesting a dose of LSD in a controlled study, is in the data analysis phase. The original research was conducted in Los Angeles from 1954 to 1962 by Dr. Oscar Janiger, a physician who was sent LSD by Sandoz Pharmaceuticals to explore its effects on psychologically normal human volunteers. This initial research was conducted before there was any great understanding of the effects of LSD or a language to describe the experience itself.

The goal of this follow-up research is to determine the role of an LSD experience in the context of each subject's life many years later. In the past year over forty audio-taped interviews have been completed and several meetings with Dr. Janiger have been conducted. Each interview has been included in an official log and assigned a confidential code number. A transcriber who analyzes data and the lead researcher are currently transcribing and qualitatively analyzing each interview. Analysts will constantly compare all transcribed interview data and findings agreed upon by the researchers will be considered valid and reliable only after they meet several criteria using constant comparisons: the findings are deemed qualitatively meaningful; researcher effects are examined; outliers and negative evidence are examined and determined not to change the finding; and spurious relations and rival explanations are excluded. With this in mind, researchers hope to gain an understanding of how participants interpreted their initial experience, and now situate that experience in the context of their lives.

Although it is far too early to draw any real conclusions, early results are indicating a significantly positive subject disposition toward their experience, both at the time and in the context of their lives, with apparently little harm resulting from the ingestion of LSD in the experiment.

Russia: Ketamine psychotherapy (KPT) with heroin addicts
Research Laboratory, Leningrad Regional Center for Alcoholism and Drug Addiction Therapy
Evgeny M. Krupitsky, M.D., Ph.D. and his research team have treated 34 patients as part of a three-year study of ketamine psychotherapy (KPT). Preliminary results seem promising, but the outcome won't be evaluated until the study is completed around the end of 1999. Post-treatment follow-up consists of a schedule of psychiatric evaluation, psychological tests and drug testing through urine analysis.

Dr. Krupitsky is currently one of two medical scientists in the world conducting clinical research into the therapeutic potential of a psychedelic drug. The other researcher is Dr. Deborah Mash, conducting a study in St. Kitt of the use of ibogaine in the treatment of heroin and cocaine addiction.

An $8,000 grant awarded to Dr. Krupitsky from MAPS in April 1998 is the second of three annual payments. In addition to support from MAPS, Dr. Krupitsky receives a grant of $5,000 a year from the Heffter Research Institute.

Why is this issue so short? See page 4.
Follow-up study of concentration camp survivors treated with LSD therapy

Addiction Research Institute, University of Utrecht

MAPS has pledged $5,000 to Nicole Maalsté and Hans Ossebaard, Addiction Research Institute, University of Utrecht, for a follow-up study to Dr. Jan Bastiaans’ research with LSD therapy and concentration camp survivors. This will be an efficacy outcome study that will not rely on pre-treatment/post-treatment comparison, since such data does not exist, but would simply be a self-report survey.

The investigators plan to contact several institutions which have already expressed their approval of a broader proposal (a process study to evaluate the methodology used by Dr. Bastiaans) and are specialized in the treatment of war survivors. The investigators will seek to publicize the study through the institutions’ publications, with a request that ex-patients contact the researchers. They will also request to check their databases, since people have often kept in contact with the clinic or center where they were treated for war-related trauma. If this does not yield enough study subjects, ads could be placed in national journals.

Ex-patients who contact the researchers will be sent a letter and a short questionnaire with about fifteen questions, which they can return to the university. They will be asked if they would like to participate in a bigger study later on, should funding become available. Both closed and open questions will be asked to give respondents the opportunity to tell their own stories, and to try to find out as precisely as possible which experiences could have resulted from LSD therapy and if they had positive or negative effects. The data will be assimilated into an article.

Israel: MDMA-Assisted Psychotherapy in Post-Traumatic Stress Disorder Patients (PTSD)

MAPS has pledged $50,000 to support the efforts of Dr. Moshe Kotler, University of Ben Gurion of the Negev, to design and conduct a study into the use of MDMA-assisted psychotherapy in Post-Traumatic Stress Disorder patients. This partnership with Dr. Kotler represents an important milestone in MAPS’ effort to catalyze MDMA/PTSD research. Dr. Kotler reports about the proposed research:

Post-Traumatic Stress Disorder (PTSD) is prevalent in Israel, a country with a high rate of war survivors and car accidents. Almost a third of the general population will be exposed to severe traumatic events during their lifetime. Ten to twenty percent of them will develop PTSD, a severe and highly distressful mental disorder. This disorder is relatively resistant to conventional psychological and biological therapies leading to many refractory chronic cases.

We propose to study implementing the use of MDMA-assisted psychotherapy in PTSD patients based on numerous previous reports where MDMA helped patients with severe mental pain following the exposure to traumatic events. Such a technique might help those patients to bring up painful repressed memories in the therapeutic encounter and also help them through the process of coping with traumatic memories.

The first stage in our proposed project will be designing a research protocol based on scientific grounds that will satisfy the local and state Review Boards. For this stage we will collaborate with a group of international scientists who have already gained rich experience in this field.

We hope that after the approval of the research protocol we will be able to proceed to the study phase where the use of MDMA in PTSD patients will be assessed and studied.

MAPS has pledged $5,000 to Nicole Maalsté and Hans Ossebaard for a follow-up study to Dr. Jan Bastiaans’ research with LSD therapy and concentration camp survivors.

MAPS has pledged $50,000 to support the efforts of Dr. Moshe Kotler to design and conduct a study into the use of MDMA-assisted psychotherapy in Post-Traumatic Stress Disorder patients. A grant of $12,500 given by Robert Barnhart in May 1998 will go towards this project.
The Safety of MDMA in Cancer Patients Protocol

Harbor-UCLA Medical Center

The research team is revising the protocol according to recommendations which resulted from the most recent FDA review. In March 1998, MAPS donated $5,500 to Dr. Russell Poland, Harbor-UCLA Medical Center, to support this protocol redesign process. The revised protocol will be resubmitted to the FDA before the end of Summer 1998.

Changes which are being considered are using a more homogeneous population of cancer patients, increasing the number of subjects at each dose level of the study, restricting the subject life expectancy range, excluding medically treated hypertensives, and creating formal stopping rules. The proposed dose range for this safety study is 0.25 mg/kg to 2.25 mg/kg.

Serotonin and dopamine system interactions in the reinforcing properties of psychostimulants: MDMA and d-amphetamine

Clinical Research Division on Substance Abuse, Department of Psychiatry and Behavioral Neurosciences, Wayne State University School of Medicine

To date, there are no well designed, double blind studies of MDMA compared to prototypical psychostimulants or 5-HT releasing drugs. The main goal of this study is to increase our understanding of the interaction between serotonin (5-HT) and dopamine systems in mediating subjective, discriminative stimulus, and reinforcing effects of psychostimulant drugs in humans. It will provide important information about the effects of MDMA (see “Serotonin and dopamine system interaction in the reinforcing properties of psychostimulants: A research strategy,” Manuel Tancer, M.D. and Charles R. Schuster, Ph.D., MAPS Bulletin Vol. VII No. 3, Summer 1997). This study has been approved for funding and is scheduled to begin in June 1998.

David Nichols, Ph.D., Purdue Department of Medicinal Chemistry and founder of the Heffter Research Institute, was able to provide ultrapure MDMA to the Wayne State research team from a supply of MDMA commissioned in 1985—by the organization that ultimately evolved into MAPS—for use in federally-approved research projects.

Two $1,000 research grants awarded to graduate students

In February 1998, MAPS awarded a $1,000 stipend to Marcus Lumbey, for travel to the Takiwasi Center in Tarapoto, Peru, in the context of his research into the biopsychosocial dynamics of the long-term attitude changes consequent to the ritualised near-death-type experience components of ayahuasca-based healing initiatives. Lumbey is completing a Ph.D. in Social Anthropology at Cambridge University, “Religions of the Twice-Born: Northwest Amazonian Ayahuasca Shamanism and Near-Death Experience.” His project will contribute to international multidisciplinary research initiatives investigating hallucinogenic plant-induced altered states of consciousness with a view to developing new therapeutic treatments in the West for a variety of mental disorders.

In March 1998, MAPS awarded a $1,000 grant to Roger Marsden, a Ph.D. student at the California Institute of Integral Studies. Marsden is completing a dissertation studying guided, structured group use of entheogenic medicines. The focus is on three groups with in-depth interviews of the guide and four participants in each group. Committee members are David Lukoff, Harrison Voigt and Richard Yensen.

The dissertation is now well past the half way point. The qualitative data will be worthy of a book after the completion of the dissertation stage. Marsden received a $6,000 grant from the Barnhart Foundation to support his work in 1997.

Dear MAPS Members:

We hope that you have been enjoying the first MAPS Bulletin of 1998, which was sent to you in March. This issue is much shorter than those to which you’ve become accustomed—we are experimenting with this new format for two reasons. First, many of you feel that the long issues take a while to read through (the last issue was 61 pages, the next one will about the same length).

With this shorter Bulletin, we would like to give readers an opportunity to catch up with current research in a short, easily-readable format. The longer issues will continue to include more in-depth and thought-provoking articles. Secondly, we would like to commit more staff time to the MAPS website over the next six months. See page 8 for a preview of the next issue...
Marijuana Research

In May 1998, MAPS donated $1,000 to Dr. Ethan Russo, University of Montana, for the preparation of a grant application to the National Institutes of Health for a study investigating the use of smoked marijuana and oral THC in the treatment of migraine headaches. Dr. Russo is currently the only researcher in the United States (of whom we are aware) trying to obtain an NIH grant to study the medical use of marijuana in a patient population. Dr. Russo's previous NIH grant application was rejected and he is submitting a revised application for the July 1 deadline. This latest $1,000 grant is for a statistician to do study sample size calculations for the revised protocol. MAPS has previously awarded Dr. Russo two grants for the preparation of the NIH applications: $1,500 in March 1998 and $3,500 in 1997.

The medical marijuana research of Dr. Donald Abrams, UC San Francisco, has finally begun. Dr. Abrams' protocol, "Short-term Effects of Cannabinoids in HIV Patients," was approved and awarded a $978,000 NIH grant in September 1997; a supply of marijuana will be provided by NIDA in conjunction with this grant. This study will take about two years to conduct. Subjects taking protease inhibitors will be hospitalized for almost a month, administered either smoked marijuana, oral THC or placebo, and extensively evaluated. An article by Dr. Abrams about the five and a half year effort to obtain approval for this study appears in the Journal of Psychoactive Drugs Vol. 30, No. 2, April-June 1998. (To obtain a copy of this issue, you can contact the JPD at 415-565-1904.) A comprehensive MAPS report on this effort with links to supporting documents, including the approved protocol, is online at www.maps.org/mmj/.

In other marijuana research news, MAPS and California NORML have co-sponsored an analysis of samples of marijuana used by medical marijuana patients around the country. Samples are being tested for levels of THC, CBD and CBN. Details will be reported in an upcoming MAPS Bulletin.

New on ketamine

[submitted by Matthew Baggott, Research Associate, Drug Dependence Research Center, University of California]

The following article is likely to be of interest to MAPS readers:

Browle TA; Radant AD; Cowley DS; Kharasch ED; Strassman RJ; Roy-Byrne PP. Psychedelic effects of ketamine in healthy volunteers: relationship to steady-state plasma concentrations. Anesthesiology, 1998 Jan, 88(1):82-8. Here is the abstract:

BACKGROUND: Ketamine has been associated with a unique spectrum of subjective "psychedelic" effects in patients emerging from anesthesia. This study quantified these effects of ketamine and related them to steady-state plasma concentrations.

METHODS: Ketamine or saline was administered in a single-blinded crossover protocol to 10 psychiatrically healthy volunteers using computer-assisted continuous infusion. A stepwise series of target plasma concentrations, 0, 50, 100, 150, and 200 ng/ml were maintained for 30 minutes each. After 20 minutes at each step, the volunteers completed a visual analog (VAS) rating of 13 symptom scales. Peripheral venous plasma ketamine concentrations were determined after 28 minutes at each step. One hour after discontinuation of the infusion, a psychological inventory, the Hallucinogen Rating Scale, was completed.

RESULTS: The relation of mean ketamine plasma concentrations to the target concentrations was highly linear, with a correlation coefficient of R=0.997 (P=0.0027). Ketamine produced dose-related psychedelic effects. The relation between steady-state ketamine plasma concentration and VAS scores was highly linear for all VAS items, with linear regression coefficients ranging from R=0.95 to 0.99 (P<0.024 to P<0.0005). Hallucinogen Rating Scale scores were similar to those found in a previous study with psychedelic doses of N,N-dimethyltryptamine, an illicit LSD-25-like drug.

CONCLUSIONS: Subanesthetic doses of ketamine produce psychedelic effects in healthy volunteers. The relation between steady-state venous plasma ketamine concentrations and effects is highly linear between 50 and 200 ng/ml.

One interesting aspect of the paper is the brief descriptions of the subjective effects of ketamine:

Volunteers also had the opportunity to make written comments on the HRS form. Several of them described altered physical sensations or body image: "tingling sensation in the limbs, followed by numbness"; "floating, very carefree feelings throughout entire body"; "felt so different. Wasn't able to describe the way I was feeling"; "floating in space"; "almost complete annihilation of physical self, shrunken"; "dizzy, shaky lightheaded." One subject wrote the following summary: "The experience seems to be a mystical experience, an incomprehensible comprehension of the universe. There seemed to be no past, present or future, no time, just existence. Life and death at the same time."

It is a shame that psychopharmacology research (indeed, science in generally) so seldom attempts to measure religious or mystical experience.