



23A Shaler Lane
Cambridge, MA 02138
(617) 547-7271

**MAPS
Conference,
Bern,
Switzerland,
November/
December
1990**

Pages 2-4 of this newsletter summarize the highlights of the conference while pages 5-12 report on the conference in more detail. Feel free to contact MAPS if you have any further questions.

Multidisciplinary Association for Psychedelic Studies, Inc.

1991 New Year's Report from Rick Doblin, President of MAPS

This newsletter reports on the MAPS pharmacologically-assisted psychotherapy conference which was recently held in Bern, Switzerland from November 28 to December 1, 1990. Your support of MAPS enabled us to gather together psychiatrists, psychologists and researchers from the US, the USSR, Switzerland, Germany, and Czechoslovakia to discuss past studies and future research possibilities. The conference was successful beyond the expectations of most participants, myself included. Participants were left with a sense of optimism that has not existed for many years, which this newsletter explains. Your membership in MAPS was an essential element in making the conference a reality, and the following report will bring you up to date on the latest developments. ❖ **The primary outcome of the conference was a decision of psychiatrists from the US and USSR to work together to develop a protocol to research the use of MDMA in the psychotherapeutic treatment of patients with terminal illness.** ❖ A goal established at the conference was to work towards the development of a protocol that would be submitted to health authorities in both the US and the USSR. Such a protocol would be designed to gather scientific data both about the benefits to patients of such a treatment and about the physical risks, including neurotoxicity. It is hoped that researchers from other countries, particularly Czechoslovakia, will also seek to participate in this research effort. ❖ If the protocol is scientifically rigorous, it very possibly will gain the support of regulators. The possibility of FDA approval of an MDMA protocol has never been better, particularly if the FDA decides to give written approval, as they indicated they might, to a protocol investigating the use of LSD to treat substances abusers. ❖ The conference sought to find a research protocol acceptable to both the advocates of the psychotherapeutic use of MDMA and the MDMA neurotoxicity researchers. The patient population and dose schedule was specifically chosen both to minimize the risks of MDMA neurotoxicity and maximize the likelihood of demonstrable therapeutic benefits. ❖ The development of this protocol offers an excellent opportunity to move beyond the five year long prohibition of the scientific use of MDMA in humans. Your past financial support of MAPS enabled us to organize the conference. Future support will permit us to move forward with research.

The November
28 - December
1, 1990 MAPS
conference
in Bern,
Switzerland:
Research in
Pharmacologically-
Assisted
Psychotherapy

Purpose of the Conference

The conference was convened by MAPS with two purposes in mind. The first was to permit a small international group of psychiatrists, psychologists, neurologists, social scientists and drug policy practitioners to review and discuss the current state of knowledge concerning medical and non-medical risks and benefits of certain psychedelic drugs. Discussion focused primarily on MDMA and secondarily on LSD, psilocybin, and 2-CD. The second purpose of the conference was to review and discuss specific research proposals for the further investigation of these substances and to develop an integrated international research agenda and strategy.

Participants

P psychiatrists Aron Belkin, Lev Gertsik, Ivan Barkov and Nicholai Kharisov and psychologist/ translator Alla Malushina from Moscow, psychiatrists Zdenek Dytrych and Jan Prasko from Prague's Psychiatric Research Institute, psychiatrists Jorg Roth, Peter Bauman and Juri Styk of the Swiss Association for Psycholytic Therapy (SAPT) (five of whose members have been legally permitted for several years to use MDMA and LSD in psychotherapy), German psychiatrist Peter Hess, German psychologist and vice-president of the European Congress for the Study of Consciousness Michael Schlichting, German consultant to several Swiss pharmaceutical companies investigating the commercial potential of psychoactive drugs Andres Giger, US psychiatrists Charles Grob and Gary Bravo from the University of California at Irvine (who are preparing an application to the FDA to research the psychotherapeutic use of MDMA in terminal patients), US experts in MDMA neurotoxicity Lewis Seiden, Ph.D. and Dr. George Ricaurte,

US social scientists exploring MDMA's non-medical use, abuse potential, and medical use Deborah Harlow, M.A. and Jerome Beck, Ph.D., US LSD researchers psychologist Richard Yensen, Ph.D. and psychiatrist Donna Dryer, US drug policy expert Mark Kleiman, Ph.D., Swiss drug abuse physician Dr. Robert Hemmig, teacher of zen meditation Vanya Palmer, inventor of LSD Albert Hofmann, Ph.D., and representing MAPS, myself.

Major Outcomes

1. The participants recognized the worldwide absence of any systematized pharmacologically-assisted psychotherapy research program involving both pre-clinical and clinical investigations and supported increasing the research effort.
2. Psychiatrists from the US and the USSR agreed to begin designing a protocol for the investigation of the use of MDMA in the psychotherapeutic treatment of patients with terminal illness. Their intention is to conduct the identical experiment in both countries in order to increase statistical validity and generalizability of the results.
3. US neurotoxicity researchers tentatively agreed that the neurotoxic risk to patients with terminal illness is balanced by potential psychotherapeutic benefits. If the protocol is rigorously designed to provide additional data about both neurotoxic risk and therapeutic efficacy, they may support the protocol before the FDA.
4. MAPS agreed to help assemble a small group of distinguished U.S. scientists and researchers to review, critique and endorse protocols prior to FDA submission.

Decisions by Psychiatrists

After two days of discussions, the US and the Soviet psychiatrists at the conference (Drs. Aron Belkin, Lev Gertsik, Ivan Barkov and Nicholai Kharisov from Moscow and Drs. Charles Grob and Gary Bravo from the US) decided to collaborate in the design of an experiment to scientifically explore MDMA as an adjunct in the psychotherapy of patients with terminal illness and to seek permission from their respective health authorities to conduct the experiment. Conducting the experiment in both countries will increase statistical validity and increase the generalizability of the study.

This study will permit data to be gathered about psychotherapeutic benefits in a population which often experiences high levels of fear and stress associated with impending mortality. In addition, long term adverse neurotoxic effects are of little significance with this population if such effects prove to be an empirical phenomenon. This experiment will also be specifically designed to test for neurotoxic risks. In addition to clinical evaluations, spinal taps can be performed before and after administration of MDMA and the brain can be examined post-mortem for signs of neurotoxicity.

The Czech psychiatrists (Drs. Zdenek Dytrych and Jan Prasko) also decided to seek permission from their health authorities to investigate the use of MDMA in psychotherapy but had not yet settled on whether to work with terminal patients or another patient group.

The German psychiatrist Dr. Peter Hess and psychologist Michael Schlichting indicated their primary interest was to research psychotherapeutic efficacy of altered states of consciousness, both with drugs and without. They are primarily interested in psilocybin and several newly discovered substances which are still legal in Germany. They have decided not to pursue MDMA due to political controversy and neurotoxic risk.

The Swiss psychiatrists (Drs. Jorg Roth, Juri Stryk and Peter Bowman) indicated their intention to continue working with MDMA and LSD as soon as permission is renewed. They voiced a relative lack of interest in researching psychotherapeutic efficacy and a total lack of interest in exploring MDMA neurotoxicity, but await word from the Swiss health authorities about new requirements.

In addition to therapeutic research, most psychiatrists voiced a need for personal training sessions to develop their ability to work with pharmacologically-assisted psychotherapy. These training sessions should involve sanctioned, supervised self-experiences with various compounds, beginning with MDMA. The process of training may eventually be formalized and could result in some form of certification limiting the use of these compounds to those psychiatrists who had completed the certification process. Hope was expressed that the members of the Swiss Association for Psycholytic Therapy (SAPT) would offer training sessions to psychiatrists from around the world.

There was general agreement that continued international collaboration on research and training offers the best opportunity for systematic scientific progress and also facilitates the political process of securing permission for research within each specific country. MAPS was encouraged to serve as an on-going communication channel for the participants in the conference and was requested by the Soviets to develop the capability for computer to computer data transfer via the San Francisco-USSR satellite-computer link-up. MAPS will also facilitate the development of the protocol for the use of MDMA in the psychotherapeutic treatment of patients with terminal illness and, if permission is granted from the appropriate governmental agencies, will seek to provide funding for the experiments themselves.

Psychiatrists from the US and USSR decided to join together to research MDMA!

Animal data demonstrates administration of Prozac completely blocks MDMA's neurotoxic effect, even when a single dose of Prozac is taken up to 6 hours after MDMA.

Conclusions of MDMA Neurotoxicity Researchers

Drs. Lewis Seiden and George Ricaurte expressed a deep reluctance to support the human use of MDMA in any patient population due to the uncertain and very narrow range of doses that would be both low enough to produce no neurotoxicity and high enough to produce a therapeutically desired outcome. The threshold level of MDMA in primates needed to cause some neurotoxicity was in the range of a single oral dose of 2.5 - 5.00 mg/kg. Due to the wide range of variability of response in humans, it is therefore possible that doses of 1.5 mg/kg (around the therapeutic dose) will cause some neurotoxicity in humans, however slight.

Dr. Ricaurte was also concerned by new evidence demonstrating that the previously observed recovery of damaged serotonin nerve terminals was only a temporary phenomenon, with gains in serotonin levels plateauing after four months and dissipating over the next year or so. Even though evidence demonstrates administration of fluoxetine (Prozac) completely blocks MDMA's neurotoxic effect, Dr. Ricaurte was generally uncomfortable with polypharmacy, especially in research contexts.

Drs. Lewis Seiden and George Ricaurte expressed a deepened understanding of the range and number of the anecdotal reports of MDMA's therapeutic potential and suggested a vigorous research effort to find compounds that lacked MDMA's neurotoxic potential yet retained its therapeutic qualities. Balancing the risks and benefits, Drs. Seiden and Ricaurte expressed fewer reservations about well designed human studies with patients with terminal illness. They recognized that there are still no cases in the literature of any individuals suffering from significant observable adverse neurological consequences from possible MDMA neurotoxicity. Non-subtle consequences of neurotoxicity, if there actually are going to be any, might take at least fifteen or twenty

years of use to develop. They indicated a strong possibility they would support a well designed study in terminal patients that limited MDMA to oral doses around 1.5 mg/kg and limited number and frequency to four or five exposures with two weeks or more between sessions.

Purpose of Protocol Review Committee

This volunteer group will be composed of psychiatrists, neurologists, brain researchers, psychologists, and past government regulators not all from the community of previous supporters of psychedelic research. This group would ideally but not necessarily convene in one location. They would evaluate the MDMA protocol for methodological shortcomings, suggest improvements, suggest outcome measures that were valid cross-culturally, and assist in the political process of securing permission to conduct such studies.

Since the FDA would probably assemble a similar advisory committee to review the protocol, it would be beneficial to have a committee of equal reputation review and improve the experimental design before submission. With a committee of sufficient expertise and reputation, the FDA may feel comfortable approving the protocol without the need of convening their own advisory committee. If this occurs, the use of MDMA in human studies may be able to begin up to a year sooner.

Since it is hoped that this area of research will grow substantially over the years, creating an expert committee experienced in reviewing protocols might also improve the overall quality of subsequent research and ensure the wise use of MAPS resources in the future. In the development of MDMA into an approved medicine, fiscal efficiency is of utmost importance.

Overall, the conference was successful beyond the expectations of most participants. A new-found sense of cautious optimism regarding the development of this field is at hand.

Brief Review of all the Presentations at the Conference

What follows is a summary of each talk and a discussion of some of the issues raised by the various speakers. The major outcomes of the conference can be more easily understood after a review of all the presentations at the conference. The review is given in the order of the presentations, an order which is logically only partially coherent due to the varying travel schedules of the participants.

Dr. Hofmann, talking about the War on Drugs, referred to it as Drugs Against War. MAPS seeks to develop Drugs Against War.

Albert Hofmann – An Opening Inspirational Talk

Wednesday night's opening talk was by Albert Hofmann, the discoverer of LSD. He spoke inspiringly about the potential of the psychedelics as tools for *personal growth and self-knowledge and as medicines* for those suffering from various psychological illnesses. The situation whereby the incautious use of these medicaments on the street and the fanaticism of the drug war had contributed to a worldwide prohibition of research for a generation was deplored. He encouraged us to persevere toward the aim of the conference which was to bring these substances once again into the research laboratories with full governmental approval.

Dr. Hofmann pointed us toward the extensive research literature that did exist and made a fundamental recommendation that this research be collected in one location and then computerized. Such a project has been begun by the Albert Hofmann Foundation in Los Angeles and is in the very early stages of development. The existence of such a data base would facilitate a meta-analysis of all the studies in hopes of generating new insights about therapeutic efficacy, solidifying or questioning old ones, and provide potential researchers with data useful in discussions with health authorities.

In a discussion after his talk, Dr. Hofmann stumbled in his use of English. Talking about the War on Drugs, he referred to it as Drugs Against War. This opened up a new line of thought for me, which is that MAPS is trying to develop drugs against war. Psychotherapy in general and psychedelics in particular are meant to be tools to reduce intrapsychic warfare. In addition, the introduction of the use of psychedelics into medical contexts may help to demonstrate that controlled use is both possible and beneficial and that the civil war against drug users need not be waged. Finally, psychedelics have historically facilitated experiences of psychological and mystical unity which can promote acceptance of others, even if they come from other cultures and countries. In all these ways, MAPS seeks to develop Drugs Against War.

Mark Kleiman – A Risk/Benefit Analysis

Dr. Mark Kleiman, lecturer in criminal justice and drug policy at Harvard's Kennedy School of Government, concluded the opening session. He strongly encouraged *researchers and regulators to review potential research projects through the lens of a risk-benefit analysis.* Taking MDMA research in humans as a case in point, Mark subjected the scientific evidence to a risk-benefit analysis focused more broadly than on simply medical questions of therapeutic and neurotoxic potential and incorporated explicit consideration of the effects of medical research on non-medical use. He concluded with the opinion that the current data on MDMA's medical and non-medical risks and benefits suggests a decision in support of human research involving permitting selected patients to receive several low doses of MDMA. A special caution was expressed that researchers be circumspect regarding press coverage so as not to create a situation whereby media attention promotes non-medical use or makes health authorities permitting research vulnerable to increased levels of political pressure.

Drs. Richard Yensen and Donna Dryer – LSD Protocol Submitted to FDA

The conference got down to details on Thursday morning with a report by Drs. Richard Yensen and Donna Dryer on the protocol they submitted to the FDA for the investigation of the use of LSD-assisted psychotherapy in the treatment of substance abusers. Their protocol, designed with Dr. Albert Kurland, was thoroughly discussed and critiqued. Strong suggestions were made by Dr. Zdenek Dytrych of Prague to reduce the heterogeneous nature of their patient population which involved individuals between the ages of 21-60, male or female, who fit the DSM-3-R criteria of substance abusers. Zdenek made the observation that there might be so many different types of patients that it could be virtually impossible for observations to reach levels of statistical significance. There was also widespread concern that a non-drug control group was needed despite the impossibility that such a control group would

remain double-blind. Without such a control group, any therapeutic gains might easily be attributed to normal recovery processes. In addition, the one year follow-up was felt to be too short since many substance abusers suffer relapses after that period.

The protocol, if it is approved, will be the first one involving LSD in many years. Richard and Donna expressed an interest in establishing a small expert committee to review the protocol from the perspective of the safety of the volunteers, in effect creating an Institutional Review Board (IRB) specifically constituted to review their protocol. Such a committee may be established under the auspices of the Albert Hofmann Foundation. If the protocol is approved by the FDA, it will undergo review by the special IRB, and then be submitted for funding to the National Institute on Drug Abuse or the National Institute on Mental Health, foundations, and individuals.

Vanya Palmer – MDMA and Meditation

Zen meditation teacher Vanya Palmer reported on the use of low doses of MDMA in the area of 50 mg. as an adjunct to meditation. This use was reported to have been explored by a small group of individuals from a variety of religious contexts and found to have exceptional value. Vanya indicated that occasional use served to deepen the meditative experience and to create an internal guidepost to direct subsequent meditative sessions. He thought such use could be valuable both to beginners and also to experienced meditators. While such applications are not likely to be scientifically explored in the near future, they are an intriguing counterpoint to both the medical and the recreational use of MDMA and offer fascinating possibilities for future study.

The use of low doses of MDMA as an adjunct to Zen meditation was reported to be of great value.

Swiss Experiences with Pharmacologically-Assisted Psychotherapy

Swiss psychiatrist Dr. Peter Bauman discussed the history of the development of the use of MDMA and LSD by some members of the Swiss Association for Psycholytic Therapy (SAPT), of which he is president, and the events that led to the current hiatus in their work. Dr. Bauman was subjected to some very difficult questioning about his patient who received a dose of ibogaine and subsequently died. This particular patient had experienced ibogaine once before without negative effects and her death still remains a mystery. The French autopsy has not yet been released and until that occurs all psychedelic psychotherapy in Switzerland remains on hold. Appreciation was expressed to Dr. Bauman for coming to the conference to tell of the difficulties in person.

Drs. Jorg Roth and Juri Styk, both psychiatrist members of SAPT, discussed their work with a wide variety of patients. They enthusiastically endorsed the use of pharmacologically-assisted psychotherapy, in particular with MDMA. Dr. Roth worked with patients within an internalized session model with patients reclining on a couch listening to music and wearing eyeshades. Dr. Roth would treat several patients at a time by locating each patient in a separate room and moving between them throughout the day. Dr. Styk and his wife, also a psychiatrist and a member of SAPT, treated patients using a group therapy model. Patients would be gathered together in a large room and would be able to focus on their internal experience or interact with other patients. The two Drs. Styk found MDMA to be especially useful in working with couples on their relationships.

Discussion of possible Swiss research efforts

None of the members of the SAPT were particularly enthusiastic about formal scientific research. They felt research would require the use of placebos and control groups and possibly spinal taps and that the quality of care they could offer their patients would be significantly diminished. They resisted the idea that because they had been the only

psychiatrists in the world who could use MDMA and LSD in treatment that they had a responsibility to the rest of the world to conduct research. They felt their primary responsibility was to their patients and that their development of case histories demonstrating the benefits that resulted from use of these substances in treatment expanded the opportunities of others around the world. The Swiss psychiatrists explained that the neurotoxicity risk was of little concern to them due to the relatively small doses they used, the infrequent number of treatments each patient received (usually 1-5), and the complete lack of any observable harmful neurological consequences experienced by any of their patients or published anywhere in the literature.

The members of SAPT did recognize that the Swiss health authorities might require some sort of formal evaluation of their work if and when permission to use these substances was renewed. Dr. Roth expressed his intention to conduct only that research that was required. He thought they would not be asked to research neurotoxicity nor would they be asked to conduct controlled experiments. Most likely, they will need to report on their case histories in a systematic manner.

In an effort to gather useful data for the international research community, discussion focused on methods that would interfere as little as possible with the treatment of patients yet still gather valuable information. The basic concern is that case histories, even if gathered in a systematic manner, are only collections of anecdotal reports and can easily be dismissed. The main request to the members of SAPT was that they administer some quantitative psychological tests to their patients before therapy begins and at intervals after the treatment. Most of these tests require an hour or less to complete and do not interfere with treatment. Which tests to use depends of course on the patient populations. The main challenge will be to choose appropriate instruments that are valid both scientifically and cross-culturally. Results of such tests would at least begin to address the question of the benefits of such treatment and would be of use to health authorities in other countries considering whether or not to permit research. The actual determination of tests and procedures was left for after the Swiss authorities issue their specific new conditions regarding the work with psychedelics.

German Research – Michael Schlichting

Michael Schlichting of Germany then reported that it is not possible to research MDMA because of the political controversy and the problems with neurotoxicity. He discussed his research with a substance known as 2-CD, in conjunction with Dr. Leuner of the University of Göttingen. The 2-CD research was conducted in 1985, as part of Michael's work on a Ph.D. The work began in the hopes of finding a substance that would be more controllable than LSD, and also legal. Michael indicated that this work was not a model for MDMA research but might serve as a point of departure. The patient population involved 14 healthy volunteers and 4 neurotic outpatients with a variety of diagnosis. Measures were used which characterized both the pharmacological and psychological effects of 2-CD and also the effects on the subjects.

At the time of the study, no prior animal toxicity studies had been conducted. A year later when information was published that MDMA might cause neurotoxicity, the Ph.D. committee at the University became concerned about the lack of toxicity data for 2-CD. They declined to award a Ph.D. degree to Michael out of concern that an ethical mistake was made by initiating human trials prior to obtaining animal toxicity data. Dr. George Ricaurte informed Michael that research with 2-CB, a compound similar to 2-CD, found no evidence of neurotoxicity. Michael was very interested in this finding but felt that the basic criticism of the Ph.D. committee was still valid. Whether they will ever award him a Ph.D. for the work with 2-CD remains in doubt.

Discussion of the Requirement that Animal Studies Precede Human Studies

Michael's discussion raised the complicated issue of the value of animal toxicity studies prior to human studies and the difficulties in funding that research. Pre-clinical animal studies sufficient for the FDA would cost about \$100,000 for each new compound, assuming the research raises no questions. Dr. Lewis Seiden pointed out that

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the pharmaceutical companies routinely spend this money on any compound they research for use in humans and that there is a need to conscientiously investigate the toxicity of compounds that may be taken by humans. He pointed out that a major social issue is raised since this amount of money is not easily available to MAPS or to other interested researchers. It is available to pharmaceutical companies and to governments but they are not currently interested in conducting a search for the development of compounds that can facilitate psychotherapy.

A requirement that \$100,000 be spent on new compounds before determination of whether or not they might have therapeutic potential effectively halts this field of research. With the current designer drug law in the US, even researchers who decide to test their own compounds on themselves are committing a criminal offense. One possible solution discussed would be for the government to allocate \$20 million or so for the search for compounds useful to psychotherapy, with promising leads to be developed by pharmaceutical companies, perhaps under the auspices of the Orphan Drug Act. Faced with these obstacles to research, the case for proceeding with efforts to research MDMA is strengthened. The National Institute on Drug Abuse has already funded millions of dollars of pre-clinical research and the neurotoxic risk is becoming clearer. Also, the therapeutic potential of MDMA is well-reported and there are no substances of its type known to be more therapeutically efficacious.

Soviet Research

Dr. Aron Belkin, with Dr. Lev Gertsik translating, reported that in the Soviet Union at the present time there is no research in process with MDMA. The Soviet psychiatrists had come to the meeting as official representatives of the Ministry of Health and were going to make recommendations about whether or not the Soviets should investigate MDMA-assisted psychotherapy. LSD had been researched in the Soviet Union in the past and had been stopped around the same time as in the US. There is interest in the Soviet Union in psychoactive substances. For example, Dr. Belkin reported that in the

eastern part of the Soviet Union, the Koryak culture has a history of mushroom use. These mushrooms are highly prized, with one worth two deers. They have the peculiar effect of being inactive to the first person who consumes them but become active in the urine, which is then drunk by mentally ill members of the community with reportedly good results.

Dr. Belkin discussed research being conducted in the USSR on psychotropic effects of all known hormonal and hormonally active substances. They found that the human body produces a full range of naturally produced psychoactive drugs, many mediated through neuropeptides. These substances can be isolated and then explored for their efficacy in the treatment of various mental illnesses. They reported on the use of synthetic enkephalen in drug abusers, particularly of hashish, and alcoholics.

Also discussed was thyroid releasing hormone, which seemed to facilitate the expression of emotion in patients who found that to be difficult. Therapists who were sympathetic to the needs of their patients were able to get better results than those who were not. Oxytocin, which seemed to prevent hallucinations in schizophrenic patients and is a reputed aphrodisiac, was also mentioned.

MDMA Neurotoxicity Research

Dr. Lewis Seiden presented animal data demonstrating that MDMA causes damage to serotonergic neurons. Since most of his presentation was illustrated with slides and quite technical so I'll summarize his conclusions rather than his data.

1) The primary conclusion is that MDMA is toxic to a certain portion of 5HT (serotonin) neurons in the brains of mice, rats, guinea pigs and rhesus and squirrel monkeys. 2) By extrapolation, it may also be toxic to human neurons containing 5HT. 3) Therefore, there is potential risk in administering MDMA. Massive serotonin neurotoxicity is just beginning to be associated with clinical significance, in the form of reduced time sense in rats. 4) Reasoned and ethical considerations would require that the potential benefits of MDMA substantially outweigh the potential hazards.

Dr. George Ricaurte presented data from studies with rats, squirrel monkeys and human MDMA users. He found that the threshold level of MDMA in primates needed to cause some neurotoxicity was in the range of a single oral dose of 5.00 mg/kg. Due to the wide range of variability of response in humans, it is therefore possible that doses of 1.5 mg/kg (around the therapeutic dose) will cause some neurotoxicity in some humans, however slight.

There is evidence demonstrating that a single dose of Prozac completely blocks the neurotoxic effect of MDMA, even when administered six hours after the MDMA. This suggests that MDMA is not itself neurotoxic. Dr. Ricaurte speculates that a metabolite of MDMA may be neurotoxic while Dr. Seiden thinks excess levels of serotonin itself may be neurotoxic. The evidence for recovery of nerve terminals is unclear. While some researchers have shown that the damaged serotonin system in rats completely recovers after one year, these findings are being reexamined as a result of some of George's studies in primates. The newest data shows a temporary recovery of serotonin levels after 4 months which plateaus for some time and then begins to decline again so that after about a year and a half all the recovery has faded and the serotonin levels are back to their low post treatment levels. No functional effects were observed in primates after serotonin levels were reduced by 80%, climbed back to 50% of baseline, and fell again to 80% below normal.

The evidence from human studies is still very preliminary. Controlled studies at Johns Hopkins are about one and a half years from completion. Previous studies at Stanford explored the serotonin levels of MDMA users who were exposed to an average of 125 doses of roughly 1.7 mg/kg. These people show roughly 25% lower levels of serotonin metabolites than the control group, a finding of no observable functional or behavioral significance. Since the levels of serotonin metabolites in the spinal fluid are likely to understate the levels of serotonin in the brain, it is possible that the MDMA users have 50% less serotonin on average than the control group. There are many factors which could influence this result other than MDMA neurotoxicity, which the Johns Hopkins

studies will help sort out. None of the Stanford subjects demonstrated observable negative neurological effects and most felt MDMA use had improved their lives.

Discussion of the neurotoxic risk to humans focused on research indicating that the currently approved prescription drug fenfluramine causes more serotonin neurotoxicity in primates than MDMA. Fenfluramine has prescribed on a daily basis to millions of patients for over twenty years yet it has not been associated with harmful neurological effects. MDA, widely used non-medically in the 1960's and twice as neurotoxic as MDMA, has also not been associated with any harmful neurological effects. If neurotoxicity does occur in humans, its effects remain unnoticed and must be extremely subtle.

A worst case analysis of the neurotoxic risk assumes that the differences in the Stanford study between the control group and the MDMA group are completely due to MDMA use only. An estimate can be made of the neurotoxic effect of one average dose, assuming effects are linear. With the Stanford group averaging 125 doses of about 1.7 mg/kg. and 25% fewer serotonin metabolites, each dose may reduce serotonin metabolites 0.2%. Since reductions in CSF serotonin metabolites understates reductions in brain serotonin levels, each dose may cause a 0.4% reduction in brain serotonin. Five doses of MDMA taken in the course of a research protocol may thus reduce serotonin metabolites 1% and serotonin levels 2%. With assumed reductions of 50% resulting in no observable harmful effects, the risk to terminally ill experimental subjects of 2% reductions may be considered relatively slight.

Reducing the risk estimate is the possibility of serotonin nerve terminal recovery, which may be more likely after small insults rather than the massive ones given to the primates in the recovery study, and the likelihood that the doses in question will cause no neurotoxicity.

If neurotoxicity occurs in humans, its effects remain unnoticed and must be extremely subtle.

Volunteers are still needed for Dr. Ricaurte's MDMA neurotoxicity research project at Johns Hopkins. Volunteers, who have either never taken MDMA or taken it ten times or more, spend four days in the hospital giving blood and spinal fluid and taking psychological tests. For more information, call Dr. Ricaurte at (301) 550-0993.

Czechoslovakian Research Possibilities

Dr. Zdenek Dytrych, who formerly researched LSD with Dr. Stanislav Grof, expressed a strong interest in conducting MDMA research at the Psychiatric Research Center in Prague and presented a plan for the initiation of this research. The main advantages he sees are that the Center was associated with LSD research in the past and they

currently have people with excellent training in methodology. The main disadvantages are that they have no experience with MDMA, some associates think that MDMA neurotoxicity is so strong that MDMA should only be used as a form of brain surgery in patients who have an excess of serotonin, and there is a strong biological orientation at the Center which views psychotherapy itself with suspicion.

Zdenek suggested that the first step is for a group of Czech psychiatrists to

experience a training session with MDMA so that they can judge for themselves the therapeutic potential. After that has occurred, they will be in a better position to choose with which patient populations to begin MDMA research. He suggested that the political process of securing research would be much easier after the Swiss have been given permission to resume their work and that the training sessions should probably take place in Switzerland. After the therapeutic research with the first patient population has concluded, a second patient population would be administered MDMA. After the second study had concluded, a determination could be made about how to regulate the use of MDMA by psychiatrists. Only after the psychiatric use had been thoroughly explored could some determination be made about the proper regulation for the non-medical use of MDMA.

Dr. Dytrych will seek permission to conduct MDMA research from the appropriate authorities with success uncertain.

**Dr. Zdenek Dytrych,
who formerly
researched LSD
in association with
Dr. Stanislav Grof,
would like to conduct MDMA
research in Prague.**



**Non-Medical Use of MDMA in the US –
A NIDA Study by Dr. Jerome Beck**

Dr. Jerome Beck reported on a recently completed two-year study funded by the National Institute on Drug Abuse exploring the non-medical use of MDMA in the US. Extensive interviews were conducted with 100 MDMA users. The results of the study suggested that the recreational use of MDMA has not resulted in a significant public health problem and was not likely to become one in the future. MDMA was found to have a low to moderate abuse potential with self-limiting pharmacological properties serving to minimize abusive use patterns.

**Survey of Therapeutic Use of
MDMA in the US and Switzerland –
Deborah Harlow**

US researcher Deborah Harlow reported on a survey conducted with all 5 members of the SAPT with clinical experience with pharmacologically-assisted psychotherapy as well with 9 psychiatrists and 3 clinical psychologists from the US with clinical experience with MDMA prior to its DEA scheduling. Respondents reported on over 6000 sessions with over 1800 patients. The use of MDMA in patients suffering from depression, terminal illness, post-traumatic stress syndrome and various phobias was particularly recommended. The use of MDMA in the treatment of cocaine addiction seemed promising though the success of MDMA in the treatment of alcoholism was reported to be less dramatic. The use of MDMA in marital therapy was also reported to be very effective. There was strong support for using MDMA in the training of psychotherapists.

Caution was expressed at the potential for abuse of the powerful affect that can be generated with the use of empathogenic substances such as MDMA. A strong recommendation was made that all therapists work as part of a clinical team in which careful supervision be provided. Ideally, the actual treatment sessions should ideally be conducted by two-person teams, one male and one female.

Soviet Research Possibilities – Ivan Barkov

Ivan Barkov spoke as a psychiatrist who recently spent a year as a bureaucrat in the Soviet Ministry Of Health. After listening to all the discussions, he and his colleagues were very interested in seeking official permission to conduct MDMA research. He saw a widespread and strong interest in Moscow in the role of altered states in psychotherapy coupled unfortunately with an increasing unwillingness of bureaucrats to make any sort of a controversial decision. The political system is in such a state of flux that it is very difficult to get anything done.

Ivan identified two primary areas of research they were interested in exploring. One was in the use of MDMA in the psychological treatment of terminal patients. He felt that MDMA might be particularly effective with that group and that permission would be most easily secured for such patients. He also felt that it was necessary to obtain training sessions for the therapists who might work on this project, perhaps in Switzerland.

Interest was expressed in a possible collaboration on animal studies. The costs of conducting research is likely to be much less in the Soviet Union than in the US. There are excellent animal research labs in Georgia and they would probably be most interested in exploring issues of MDMA neurotoxicity in the primate.

A Request from a MAPS Member

The 20 year old son of Sherry Atri has been arrested, convicted and sentenced to 12 years in prison for sale of LSD. He would appreciate correspondance and can be reached at:

Walter Premchand Atri
 FCI-McKean, PO Box 8000
 Bradford, PA 16701-0980

MAPS would appreciate comments from members regarding the criminalization of the non-medical use of psychedelics.

German Psychedelic Research Possibilities - Michael Schlichting

Michael Schlichting emphasized that his priority and that of his co-workers in Germany was the investigation of the clinical use of altered states of consciousness, both with and without drugs. He favors controlled clinical trials with placebos and is a strong supporter of the need to conduct psychotherapeutic research to add to the already sufficient number of case histories. He preferred to work in a discrete manner with substances that were not as controversial as MDMA and for the near future plans to concentrate on psilocybin.

The Personal Use of MDMA by 20 US Psychiatrists – An Intriguing Study

Dr. Charles Grob, in collaboration with Drs. Bravo, Leister and Walsh, presented the results of a study on the personal use of MDMA by 20 US psychiatrists. None had administered MDMA to their patients. All subjects, 18 males and 2 females, were given semi-structured interviews to assess the phenomenology and sequelae of their MDMA experiences. They had used MDMA an average of 4.2 times at about 150 mgs. per dose. Over half thought that MDMA had a high or very high potential as an adjunct to psychotherapy. The most commonly reported long term effects involved improved interpersonal and occupational functioning. Long term negative effects were not reported.

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The protocol which seems to offer the greatest possibility of succeeding scientifically to gather important new information about both the risks and the benefits of MDMA-assisted psychotherapy is also the protocol that is more likely to succeed politically both in the US and in the USSR.

**US MDMA Research Possibilities –
Drs. Grob and Bravo**

A protocol for the use of MDMA in the treatment of terminal patients and AIDS patients was presented by Drs. Charlie Grob and Gary Bravo. The protocol called for the use of an active placebo, an inactive placebo, and MDMA. In addition to psychological tests, subjects were to receive a series of spinal taps after each session.

The use of more than two spinal taps was considered too disruptive of the fragile state of health of terminal patients, and also to be unnecessary, and was strongly discouraged. Furthermore, the use of spinal taps at all with only one administration of MDMA was questioned. Dr. Ricaurte felt that the normal variation in serotonin levels would probably cloud the neurotoxic effect of one oral dose of 1.5 mg/kg if indeed it had such an effect. Suggestions were made to increase the exposures to MDMA to four so as to ensure a greater likelihood of finding a neurotoxic effect if one did indeed exist.

The value of an active placebo was also questioned since the experimenters would not remain blind to which substance had been administered. Some sort of control was desired but psychotherapy alone might serve as an active placebo, to compare with psychotherapy plus MDMA.

The recommendation was also made to prepare two distinct protocols, one with terminal patients and the other with AIDS patients. AIDS' known neurological effects would confound the effort to determine the neurotoxic effects of MDMA in that population. The effects of MDMA on the immune system are also unknown, although anecdotal evidence suggests that there might be both positive effects mediated by psychological factors and negative effects mediated by physiological factors.

**A Collaborative US-USSR
Research Project with MDMA and
Terminal Patients**

The discussion of the Grob/Bravo protocol led directly to the central outcome of the conference. The protocol which seems to offer the greatest possibility of succeeding scientifically to gather important new information about both the risks and the benefits of MDMA-assisted psychotherapy is also the protocol that is more likely to succeed politically both in the US and in the USSR. Once we all realized this confluence, the idea of mutually designing one experimental protocol to be carried out in both countries began to be developed. Problems centered on finding outcome measures that would be valid cross-culturally and on training therapists so that the same sort of treatment would be provided to patients in both countries. Advantages centered on the additional data to be gathered, on the additional scrutiny that the protocol would receive from researchers in both countries, on the possibility of also conducting the experiment in other countries, and on the political advantages with national health authorities that may result from the internationalization of the research effort.

The conference ended with feelings of great excitement about future research. If any of your friends or associates would like to join MAPS, or if you care to make another donation, the research would be closer to actually happening.

**“Since wars begin in the minds of men,
it is in the minds of men that the
defenses of peace must be constructed.”**

UNESCO Charter