

United States – Eastern Europe Regional Meeting on Methamphetamine and Ecstasy Research

March 31-April 2, 2000
Visegrád, Hungary

Cosponsored by



U.S. National Institute on Drug Abuse



Hungarian Ministry of Youth and Sports

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PREFACE

Abuse of methamphetamine and MDMA (Ecstasy), particularly by young adults, is a growing concern in Eastern Europe and the United States. During the *United States – Eastern Europe Regional Meeting on Methamphetamine and Ecstasy Research*, participants discussed scientific data from the United States and Eastern Europe about these drugs, sharing what we know about how they act on the brain, how they produce their behavioral effects, and strategies for prevention and treatment. By exchanging ideas on research, treatment practice, and service provider experience with these two drugs, the National Institute on Drug Abuse (NIDA) hopes to foster development of science-based strategies to address the dramatic increases in their abuse.

NIDA is the organization that supports more than 85 percent of the world's drug abuse research. The Institute's efforts to build collaboration in international drug abuse research begin with the exchange of scientific information, then proceed through capacity building and networking to full research collaboration. This meeting is an important step in that process. I was pleased to participate in the meeting and look forward to continuing our efforts to develop collaborations.

Alan I. Leshner, Ph.D.
Director
National Institute on Drug Abuse

PREFACE

The spread of synthetic drugs, especially among young adults, is becoming an increasingly alarming issue in the Eastern European countries. The region has only been facing the issues of drug abuse on a large scale for the past 10 years, and these societies were not prepared for the problems those issues present. By now there is growing concern over the trend of increase in methamphetamine and MDMA (Ecstasy) abuse and consequent damages in our geographic area.

At the moment, indicators of methamphetamine and MDMA (Ecstasy) use in our region are lower than those in the United States or Western Europe, and we are aiming to keep it that way. However, that does not mean that this is an issue we can ignore, as we are all very aware that prevention is the best cure. Thus, I was especially pleased that this conference took place, giving us the opportunity to learn from our colleagues in this region and overseas. It was a valuable chance to exchange ideas and discuss research with scientists, some of whom were in this field long before the problem arose in Eastern and Central Europe. I was pleased that the U.S. participants seemed to enjoy sharing their experiences with their European counterparts, who often had a different view of the issues.

This conference, with its high scientific standards, was a very exciting project and a promising source of cooperation. The Hungarian Ministry of Youth and Sports was delighted to have had the chance to take part in making it happen.

Ákos Topolánszky
Deputy State Secretary
National Anti-Drug Coordinator

ACKNOWLEDGMENTS

A number of individuals and institutions contributed to the success of the *United States – Eastern Europe Regional Meeting on Methamphetamine and Ecstasy Research*. As the organizing cosponsor, NIDA wishes to acknowledge the invaluable assistance of our cosponsoring institution, the Hungarian Ministry of Youth and Sports, particularly Deputy State Secretary Ákos Topolánszky. We thank the members of the scientific organizing committee for their contributions to setting the agenda, selecting the participants, and ensuring a successful meeting. In addition to Minister Topolánszky and myself, the scientific committee included Dr. Anna Borsodi, Hungarian Academy of Sciences, and Dr. Tibor Wenger, Semmelweis University. We gratefully acknowledge the support of four institutions whose support was instrumental in the success of the conference: Research and Development Division, Hungarian Ministry of Education; Department of Research Organization, Medical Scientific Council of Hungary; Hungarian Academy of Sciences; and Semmelweis University. Special thanks to the local organizing committee for their logistical support: Ágnes Ratalics, Motesz Travel Agency; Csaba Dávid and Gabriella Moldrich, Semmelweis University; Eszter Molnár, Hungarian Ministry of Youth and Sports; and Ildikó Szatmári, Biological Research Centre, Hungarian Academy of Sciences. Finally, we thank all of the attendees for their excellent preparation and participation. We appreciate your efforts to ensure a productive and enjoyable meeting.

M. Patricia Needle, Ph.D.
Director, International Program
Office of Science Policy and Communications
National Institute on Drug Abuse

MEETING HIGHLIGHTS

Executive Summary

During the March 31 to April 2, 2000, scientific meeting in Visegrád, Hungary, 45 drug abuse researchers from 9 Eastern European nations, the United Nations International Drug Control Programme (UNDCP), and the United States exchanged information about the growing abuse of methamphetamine and MDMA (Ecstasy) by young people and the potential for research cooperation in this area. The *United States – Eastern Europe Regional Meeting on Methamphetamine and Ecstasy Research* was cosponsored by NIDA and the Hungarian Ministry of Youth and Sports, with scientific organizing assistance from Semmelweis University, Budapest, and the Biological Research Centre of the Hungarian Academy of Sciences, Szeged. Meeting participants discussed scientific data about these drugs, sharing knowledge about how the drugs act on the brain, how the drugs produce their behavioral effects, and strategies for prevention and treatment.

Deputy State Secretary Ákos Topolánszky, Hungarian Ministry of Youth and Sports; Dr. Gyula Telegdy, President, Hungarian Academy of Sciences Medical Section; and NIDA Director Dr. Alan I. Leshner spoke at the welcoming session. The meeting was planned by an international organizing committee cochaired by Dr. Anna Borsodi, Hungarian Academy of Sciences; Dr. Tibor Wenger, Semmelweis University; and Dr. M. Patricia Needle, International Program Director, NIDA Office of Science Policy and Communications. In addition to Drs. Leshner and Needle, the U.S. delegation included Dr. Marianna K. Baum, University of Miami; Dr. Patricia Case, Harvard University; Dr. Richard Rawson, University of California, Los Angeles; Dr. George A. Ricaurte, The Johns Hopkins University; and Dr. Claire Sterk, Emory University.

Opening the scientific sessions, Rector Péter Sótonyi, Semmelweis University, called the scientific meeting a very important means of exchanging information about the social, medical, and legal consequences of drug abuse. Dr. Leshner updated participants on the December 1999 decision to substantially increase NIDA support for research into methamphetamine, MDMA (Ecstasy), and related drugs, focusing on the mechanisms of action, consequences of abuse, and development of effective prevention programs and treatment medications. Dr. Kálmán Szendrey, formerly of UNDCP and now with the University of Szeged, Hungary, used UNDCP data to report on international developments in methamphetamine abuse, focusing on the drug's rapidly changing chemical composition and geographic distribution. Dr. Needle and Dr. Alexandra Sulcová, Masaryk University, cochaired the session.

Dr. Borsodi; Dr. Telegdy; Dr. Philip Lazarov, Bulgarian National Centre for Addictions; and Dr. Piotr Popik, Polish Academy of Sciences, chaired scientific sessions on the pharmacology of stimulants. Dr. Susanna Fürst, Semmelweis University, described the actions of amphetamine and related psychomotor stimulants that release monoamines from nerve terminals in the brain, particularly the noradrenaline and dopamine neurotransmitters. Dr. Sulcová presented studies of intravenous self-administration of methamphetamine by rats that indicate that both the serotonergic (5-HT) and cannabinoid receptor systems appear to play a role in the mechanism of action of methamphetamine. Dr. Sulcová also reported on studies that employed

chemiluminescence to measure metabolic activation of leukocyte phagocytic activity in mice treated with saline, methamphetamine, fluoxetine, or a combination of methamphetamine and fluoxetine. Dr. Malgorzata Filip, Polish Academy of Sciences, described research that indicated 5-HT_{1B} receptors are not involved in the locomotor, sensitization, and discriminative stimulus effects of cocaine in rats, but that pharmacological stimulation of these receptors counteracts the overall effects of cocaine. Dr. Julia Timár, Semmelweis University, presented the results of an investigation of short- and long-term behavioral consequences of methamphetamine- or MDMA (Ecstasy)-induced neurotoxicity. Dr. Popik discussed studies suggesting that the metabotropic group II glutamate receptors were involved in the development of antinociceptive morphine tolerance. Dr. Ryszard Przewlocki, Polish Academy of Sciences, described studies of the regulation of the PDYN and PENK gene expression in the nucleus accumbens as well as the opioid peptide and CRF gene expression in the central nucleus of the amygdala that suggest amphetamine and cocaine have different effects on the biosynthesis of opioid peptides in the mesolimbic system and amygdala, and that the changes they induce may play some role in the mechanism of addiction to psychostimulants.

Patterns and trends of methamphetamine and MDMA (Ecstasy) abuse in Eastern Europe and the United States were the topics for sessions chaired by Dr. Baum; Dr. Vlastimil Mayer, Slovakian National Programme on HIV/AIDS Prevention; Dr. Radu Vrasti, Romanian Psychiatric Hospital; and Dr. Rawson. Dr. Sterk presented information on U.S. trends in methamphetamine and MDMA (Ecstasy) abuse. She also discussed how data from national household surveys; school surveys; and law enforcement, drug treatment sites, and emergency rooms can be combined with targeted, cross-sectional, longitudinal, and ethnographic studies. Dr. Ladislav Csémy, Prague Psychiatric Centre, compared adolescent use patterns for methamphetamine and heroin, which he said imply that more attention should be devoted to prevention programs targeting adolescents and that treatment programs should be adapted to the needs of methamphetamine users. Dr. Zsolt Demetrovics, Eötvös Loránd University, stressed the importance of structural and dynamic family characteristics in explaining the onset and maintenance of addiction. Dr. Alojz Nociar, Slovakian Ministry for Drug Dependencies and Control, presented data demonstrating the marked increase of illicit drug abuse between 1994 and 1998 in the Slovak Republic, including the increased abuse of methamphetamine and MDMA (Ecstasy). Dr. Nociar compared responses from 1995 and 1999 school surveys to identify the following trends: drug use is increasing, particularly marijuana use; by 1999, drug use had spread to all areas of Slovakia; and MDMA (Ecstasy) and LSD use is increasing, as is consumption of alcohol and tobacco. Dr. Lubomir Okruhlica, Institute for Drug Dependencies, reported that based on treatment demand, Slovakia is not yet facing a crisis in methamphetamine use, but that lifetime prevalence of methamphetamine use and polydrug use is increasing. Dr. Vlastimil Mayer, Slovakian National Reference Center for HIV/AIDS Prevention, cited estimates that 75 percent of injection drug abusers in Bratislava share needles and engage in unsafe sexual practices, predicting that an epidemic of HIV infection is imminent among Slovakian drug users. Dr. Case discussed U.S. trends in methamphetamine and MDMA (Ecstasy) use, especially among men who have sex with men. She reported that methamphetamine use is associated with high-risk sexual behavior and high rates of HIV. Researchers do not know if MDMA (Ecstasy) use is a factor in high-risk sexual behaviors or increased HIV incidence. Dr. Case reported that because the drug use patterns are increasing so rapidly, researchers and surveillance systems often fail to include appropriate questions or classify drugs in different ways. Dr. Andrej Kastelic, Slovenian Center

for Treatment of Drug Addiction, discussed attitudes toward methamphetamine and MDMA (Ecstasy) use and described prevention and treatment activities. Dr. József Fürész, Hungarian Defense Forces Health Protection Institute, reported on an armed forces drug screening system that provides surveillance data, decreases general drug use, better identifies those soldiers who might benefit from interventions, and has decreased abuse of methamphetamine and methadone.

Dr. Wenger and Dr. Matej Sande, University of Ljubljana, Slovenia, chaired sessions on the neuropharmacology of methamphetamine and MDMA (Ecstasy). Dr. Ricaurte reported that those amphetamine derivatives, such as methamphetamine and MDMA (Ecstasy), which have high abuse liability for humans, produce particularly long-lasting and high neurotoxic activity in the brain, and that even a single dose of MDMA (Ecstasy) carries the risk of producing serotonin neuron cell injury in humans. Dr. Ricaurte also discussed advances in positron emission tomography (PET) that permit researchers to assess the status of brain dopamine and serotonin neurons in living humans. He called for additional research on the functional consequences of neuronal injury in the brain, and the mechanisms by which amphetamine derivatives damage brain cells.

Treatment options and the consequences of abuse were the topics of a session chaired by Dr. Ricaurte. Dr. Rawson reported on science-based methamphetamine treatment protocols funded by NIDA and developed jointly by researchers at the University of California and treatment providers at six Los Angeles-area clinics. He described treatment manuals which provide session-by-session guidelines for a 6-month outpatient treatment plan that includes cognitive behavioral therapy, education, positive reinforcement, classical conditioning, and family involvement. The manuals are available through the NIDA Web page, www.drugabuse.gov or www.nida.nih.gov. Dr. Miran Pustoslemšek, a Slovenian psychiatrist, described the diagnosis and treatment for a patient with acute MDMA (Ecstasy)-induced psychosis. Dr. Sándor Funk, Nyírö Gyula Hospital, Budapest, reported that most Hungarian methamphetamine or MDMA (Ecstasy) abusers seek treatment only as a result of legal mandates, family interventions, or drug-related medical emergencies. Dr. Baum reported that methamphetamine and MDMA (Ecstasy) are associated with high-risk injection and sexual behaviors that increase the risk for HIV infection and hepatitis. Toxicity and fatality are associated with drug-related cardiac arrhythmia and hypothermia.

Dr. Needle addressed funding mechanisms and professional development opportunities available to support the development of international collaborative research on drug abuse. Dr. Baum discussed the AIDS International Training and Research Program that is administered through the Fogarty International Center.

SCIENTIFIC PRESENTATIONS

Opening Plenary

Cochairs: M. Patricia Needle, *National Institute on Drug Abuse*
Alexandra Sulcová, *Masaryk University*

Methamphetamine and MDMA (Ecstasy): Confronting the Crises Through Research

Alan I. Leshner

National Institute on Drug Abuse

Dr. Leshner described NIDA research that has revealed how methamphetamine, MDMA (Ecstasy), and other drugs of abuse produce their effects. Through the use of advanced technologies such as imaging and molecular biology, researchers have documented that prolonged drug use actually changes the brain in fundamental and long-lasting ways, especially affecting behavior. Improving understanding of these changes in brain function may help explain addiction and is essential to the development of targeted treatments. Researchers know that each drug produces specific effects in the brain, but every drug of abuse produces a sharp increase in dopamine. As dopamine increases, it produces a pleasurable effect, which scientists think induces individuals to keep taking drugs.

Methamphetamine and similar drugs (MDMA, GHB, Rohypnol, ketamine, and LSD) are often referred to as “club drugs” because of their prevalence at all-night parties and “rave” dance clubs and bars. Uncertainties about club drugs’ sources, pharmacologic agents, chemicals used to manufacture them, and possible contaminants make it difficult to determine toxicity, consequences, and symptoms. Treatment and prevention efforts are also complicated by the use of club drugs in combination with one another and with alcohol. Methamphetamine is a toxic, addictive stimulant, and its use can contribute to higher transmission rates of infectious diseases, especially hepatitis and HIV/AIDS. Methamphetamine abuse is associated with serious health consequences, including memory loss, aggression, violence, psychotic behavior, and potential cardiac and neurological damage. Methamphetamine abusers may have significant reductions in dopamine transporters.

MDMA (Ecstasy) can produce both stimulant and psychedelic effects that last approximately 3 to 6 hours, although adverse effects have been reported to occur even weeks after the drug was taken. MDMA (Ecstasy) can produce a significant increase in heart rate and blood pressure and may also lead to dehydration, hypertension, and heart or kidney failure. It can be extremely dangerous in high doses and may lead to hyperthermia, heart attacks, strokes, and seizures. Chronic use of MDMA (Ecstasy) appears to produce long-lasting, perhaps permanent, damage to the neurons that release serotonin, and it is likely that MDMA (Ecstasy) use can impair memory and cause a variety of behavioral and cognitive consequences.

In the United States, methamphetamine use has progressed from the west coast to the Midwest, but is used less frequently on the east coast. NIDA research efforts have been designed to stop

the public health epidemic spread of methamphetamine use. In December 1999, as part of a national initiative to combat the increasing use of club drugs, NIDA substantially raised its funding for research relating to these substances, focusing on epidemiology, mechanisms of action, consequences of abuse, effective prevention programs, and treatment medications. Medications are being tested to treat stimulant addiction, and a new antibody is being tested to provide an effective treatment for methamphetamine overdose. In addition to increased research funding, NIDA and four other national organizations launched a multimedia public education strategy to increase awareness of the dangers of using club drugs and to disseminate recent scientific advances on club drugs to the public and health care practitioners.

Amphetamine Abuse: Recent Regional and International Developments

Kálmán Szendrey

University of Szeged

Dr. Szendrey, formerly of UNDCP, used United Nations data to report on international developments in methamphetamine abuse, focusing on the drug's rapidly changing chemical composition and geographic distribution. Historically, abuse of amphetamine-type stimulants has been observed for nearly 50 years primarily in the United States, Japan, and Sweden. Each epidemic had a characteristic root, onset phases, and periodic recurrences. Amphetamine abuse was practically unknown in Central Eastern Europe until the 1990s. Recently, production and manufacturing of illicit amphetamine-type stimulants has been diversified, accompanied by a rapid geographic diffusion. Researchers have documented three major characteristics of the new amphetamine epidemics:

- C The number of amphetamine-type substances available on the illicit market is steadily changing, and their chemical structure is increasingly diverse. Abuse of newly introduced variations of methamphetamine, amphetamine, MDMA (Ecstasy), and methcathinone (ephedrone) is reported to be increasing.
- C Consumption patterns have changed considerably throughout Europe, Asia, and the Far East, with a steady increase in the number of countries reporting growing abuse of amphetamine and related drugs. For example, MDMA (Ecstasy) is widely used in Eastern Europe; methamphetamine abuse is reported increasing in the Far East; and methcathinone is reported most often in the independent states of the former Soviet Union, but may be moving into Eastern Europe.
- C These drugs became popular very quickly among young consumer groups and that rapid adoption, combined with flexibility in production and distribution, has created serious challenges for affected nations and the international community. Initiatives to address the issue have included those sponsored by the United Nations and the World Health Organization as well as more focused regional collaborations in Asia, Europe, and North America.

Pharmacology of Amphetamines

Cochairs: Anna Borsodi, *Hungarian Academy of Sciences*
Philip Lazarov, *Bulgarian National Centre for Addictions*
Gyula Telegdy, *Semmelweis University*
Piotr Popik, *Polish Academy of Sciences*

The Pharmacology of Central Nervous System Stimulants

Susanna Fürst
Semmelweis University

Dr. Fürst described the actions of amphetamine and related psychomotor stimulants that release monoamines from nerve terminals in the brain, particularly the noradrenaline and dopamine neurotransmitters. She outlined their primary pharmacologic effects, including euphoria and excitement, locomotor stimulation, decrease of mental and physical fatigue, hyperexcitability, hypothermia, increased wakefulness, insomnia, stereotyped behavior, anorexia, and peripheral sympathomimetic activity in the cardiovascular system. Chronic use of amphetamines results in amphetamine psychosis, with hallucinations, delusions, aggression, paranoia, and stereotyped behavior. Dr. Fürst reported that amphetamine psychosis is similar to a schizophrenic attack and is sensitive to the actions of antipsychotic drugs.

Changes of Methamphetamine Intake in Rats at Pharmacological Manipulation on Serotonergic and Cannabinoid Receptor Systems

and

Influence of Fluoxetine Coadministration on Methamphetamine Suppression of Leukocyte Phagocytosis in Mice

Alexandra Sulcová
Masaryk University

Dr. Sulcová described studies of intravenous self-administration of methamphetamine by rats that indicate that both the serotonergic (5-HT) and cannabinoid receptor systems appear to play a role in the mechanism of action of methamphetamine. Methamphetamine-dependent rats were pretreated with serotonergics or cannabinoids 15 minutes before being permitted to self-administer methamphetamine. Pretreatment with the serotonin reuptake inhibitor fluoxetine, the 5-HT_{1A/1B} agonist RU 249-69, and the 5-HT_{1B} agonist CGS-12066B dose-dependently decreased the rats' methamphetamine self-administrations, but the 5-HT_{1A} agonist 8-OH DPAT had no effect on methamphetamine intake. Dr. Sulcová reported that the effects were most noticeable with CGS-12066B. In followup studies, withdrawal of fluoxetine caused the rats to return to previous levels of methamphetamine self-administration. Pretreatment with the cannabinoid receptor agonists anandamide and methanandamide increased methamphetamine self-administration, but not significantly, while pretreatment with the cannabinoid receptor agonist AM 251 significantly suppressed methamphetamine self-administration.

Dr. Sulcová also reported on studies that employed chemiluminescence to measure metabolic activation of leukocyte phagocytic activity in mice treated with saline, methamphetamine, fluoxetine, or a combination of methamphetamine and fluoxetine. All doses of methamphetamine significantly suppressed phagocytosis. Fluoxetine alone significantly increased leukocyte phagocytic activity and reversed the suppressant effects of methamphetamine when administered in conjunction with methamphetamine.

Role of Serotonin (5-HT_{1B}) Receptors in the Cocaine-Evoked Locomotor, Sensitizing, and Discriminative Stimulus Effects in Rats

Malgorzata Filip

Polish Academy of Sciences

Dr. Filip described research that indicated 5-HT_{1B} receptors are not involved in the locomotor, sensitization, and discriminative stimulus effects of cocaine in rats, but that pharmacological stimulation of these receptors counteracts the overall effects of cocaine. The researchers used the 5-HT_{1B} receptor ligands CP 94,253, an agonist, and GR 127935, an antagonist. In locomotion studies, CP 94,253 potentiated the effect of a challenge dose of cocaine unless the rats had been pretreated with GR 127935. When given alone, GR 127935 had no effect on the expression of cocaine sensitization but blocked the effects of CP 94,253, which increased sensitization in a dose-related manner. Alone or in combination with cocaine, CP 94,253 affected the rats' discriminative responses. Pretreatment with GR 127935 failed to modulate the dose-effect curve for cocaine, but reversed the enhancement of cocaine discrimination evoked by the combination of CP 94,253 and cocaine.

Behavioral Consequences of Methamphetamine- or MDMA-Induced Neurotoxicity in Rats

Julia Timár

Semmelweis University

Dr. Timár presented the results of an investigation of short- and long-term behavioral consequences of methamphetamine- or MDMA (Ecstasy)-induced neurotoxicity. In studies of general activity, cognitive function, sensitivity of postsynaptic dopamine and 5-HT receptors, and the function of the 5-HT neurons, MDMA (Ecstasy)-treated rats exhibited a significantly reduced effect of presynaptically acting compounds, indicating long-term impairment of the 5-HT neuron function. The researchers found no detectable changes in cognitive function or in the sensitivity of postsynaptic receptors.

Group II Glutamate Metabotropic Receptor Agonist LY354740 Inhibits Morphine Tolerance in Mice

Piotr Popik

Polish Academy of Sciences

Dr. Popik discussed studies of LY354740, the first systemically active agonist of presynaptic metabotropic group II glutamate receptors. Coadministration of morphine and either 1 mg/kg or 10 mg/kg of LY354740 inhibited morphine tolerance, suggesting that the metabotropic group II glutamate receptors were involved in the development of antinociceptive morphine tolerance.

Effects of Psychostimulants on the Opioid Peptide and CRF Expression in the Nucleus Accumbens and Central Nucleus of the Amygdala

Ryszard Przewlocki

Polish Academy of Sciences

Dr. Przewlocki described studies of the regulation of the PDYN and PENK gene expression in the nucleus accumbens as well as the opioid peptide and CRF gene expression in the central nucleus of the amygdala after acute and chronic amphetamine and cocaine administration. The researchers concluded that amphetamine and cocaine have different effects on the biosynthesis of opioid peptides in the mesolimbic system and amygdala, and that the changes they induce may play some role in the mechanism of addiction to psychostimulants. Amphetamine evokes long-lasting changes in the PDYN system activity in the nucleus accumbens, but has little effect on the gene expression in the central nucleus of the amygdala. Cocaine has a profound effect on PDYN biosynthesis in both the nucleus accumbens and the central nucleus of the amygdala, as well as on the CRF expression in the central nucleus of the amygdala.

Patterns and Trends of Methamphetamine and MDMA (Ecstasy) Abuse in Eastern Europe and the United States

Cochairs: Marianna Baum, *University of Miami*
Vlastimil Mayer, *Slovakian National Reference Center for HIV/AIDS Prevention*
Radu Vrasti, *Psychiatric Hospital of Romania*
Richard Rawson, *University of California, Los Angeles*

A View of Use Among Heterosexual Adolescents and Adults

Claire Sterk
Emory University

Dr. Sterk stressed that drug users are the best source of information about drug use patterns and trends, and that the terminology, use, and actual chemical composition of methamphetamine varies widely. Methamphetamine and MDMA (Ecstasy) users report ingesting, smoking, inhaling, or injecting these varied substances, and the different routes of administration change the drugs' pharmacologic and behavioral impacts. Thus, it is very important for researchers to ask drug users why, how, and with whom they use a particular drug. Users also report that they like methamphetamine and MDMA (Ecstasy) because the drugs produce a mild high and the coming down process is gradual. Dr. Sterk discussed how national household surveys; school surveys; and data from law enforcement, drug treatment sites, and emergency rooms provide valuable information about who is using what type of drug, but must be combined with other types of research to avoid the biased perspective of a single source. She recommended combining these surveys with targeted, cross-sectional, and longitudinal studies as well as with small, indepth ethnographic studies. Qualitative data are extremely useful for placing quantitative findings in the larger context, for developing research questions and study hypotheses, and for evaluating the wording of questions and response categories in a close-ended format. Qualitative research methods facilitate both process evaluation and community-based approaches that actively involve members of the community under study while quantitative research methods facilitate outcome evaluations and statistical exploration of trends. Treatment and prevention programs must address the various stages of drug use (which range from experimentation to occasional use, regular use, and dependence), as well as polydrug use—which is especially prevalent among methamphetamine and MDMA (Ecstasy) users—and the medical and social consequences of the drugs and drug-associated behaviors.

Methamphetamine Use in Czech Adolescents: Prevalence, Patterns, and Consequences

Ladislav Csémy
Prague Psychiatric Centre

Dr. Csémy discussed the similarities and differences in adolescent use patterns for methamphetamine and heroin. Data indicate that methamphetamine is the most frequently misused substance in the Czech Republic, and abuse of methamphetamine is increasing most rapidly. Dr. Csémy also presented data from the European School Survey Project on Alcohol, Tobacco, and Other Drugs indicating that adolescent use of marijuana and methamphetamine

increased dramatically between 1995 and 1999. Factors associated with increased drug use included attending a vocational school, poor school performance, living in an urban area, living in a single-parent family, increased availability of drugs, decreased social disapproval of drug use, and decreased perception of drug-related consequences. Polydrug use was very common, particularly among methamphetamine users, but heroin users reported a higher frequency of daily drug use. Comorbid childhood disorders were reported higher among methamphetamine users. Patients entering treatment for methamphetamine abuse rarely complete the treatment program. The epidemiological and treatment program data imply that more attention should be devoted to prevention programs targeting adolescents and that treatment programs should be adapted to the needs of methamphetamine users.

The Family Dynamics of Opiate and Stimulant Users: A Comparison

Zsolt Demetrovics

Eötvös Loránd University

Dr. Demetrovics stressed the importance of structural and dynamic family characteristics in explaining the onset and maintenance of addiction. Three primary family characteristics for opiate addiction are broken homes; an overprotective mother who coexists with an absent, aggressive, or negligent father; and drug-induced changes in the family that reinforce the addiction. He noted that the child's drug use reinforces his role in the family. The interpersonal relationships among family members of opiate users show consistent, specific developmental patterns, while families of amphetamine users do not, Dr. Demetrovics said. Methamphetamine users report they use drugs to avoid emptiness and search for internal and external stimulation.

Overview of Drug Epidemiology in Slovakia and First Signs for HIV Introduction Among Injection Drug Users

Alojz Nociar

Slovakian Ministry for Drug Dependencies and Control

Lubomir Okruhlica

Institute for Drug Dependencies

Vlastimil Mayer

Slovakian National Reference Center for HIV/AIDS Prevention

Dr. Nociar presented data demonstrating the marked increase of illicit drug abuse between 1994 and 1998 in the Slovak Republic, including the increased abuse of amphetamines and MDMA (Ecstasy). Intravenous heroin is the predominant drug of abuse, although heroin and methamphetamine have recently been used in combination. He estimated that there are approximately 1,333 drug abusers per 100,000 population in the capital city of Bratislava. The country has 2,800 registered addicts, a number that has been increasing by 500 persons annually. Average age at first use is 17.5 years, and average age at first treatment is 20. Dr. Okruhlica

reported that based on treatment demand, Slovakia is not yet facing a crisis in methamphetamine use, but that lifetime prevalence of methamphetamine use is increasing, particularly among young people in Bratislava. Polydrug use is increasing rapidly, especially among patients already enrolled in drug treatment programs for abuse of other drugs. Dr. Mayer cited estimates that 75 percent of injection drug users in Bratislava share needles and engage in unsafe sexual practices, predicting that an epidemic of HIV infection is imminent among Slovakian drug users. He called for expansion of prevention efforts, which currently include limited street-based outreach counseling and education, needle exchange programs, methadone maintenance treatment, hepatitis B immunization, and monitoring infections in drug abusers who seek treatment.

Patterns and Trends in MDMA (Ecstasy) and Methamphetamine Use Among Men Who Have Sex with Men

Patricia Case

Harvard University

In the United States, methamphetamine use has been observed among men who have sex with men since the 1940s. MDMA (Ecstasy) use is emergent in this population, but little is known about its prevalence, context of use, or sexual and injection risk behavior related to its use. Methamphetamine is used in particular geographic locations, primarily the west coast, the rural Midwest, and major cities on the eastern seaboard. Travel appears to be an important vector in these drug use patterns, with users reporting that they purchase drugs on trips to high-use regions. Qualitative data reveals that methamphetamine use is frequent in particular social contexts, such as “circuit” parties, local clubs and bars, and in public sex venues. Users report choosing methamphetamine for a particular purpose, such as to reduce inhibition, provide an escape from stress (users call this a “drug vacation”), and to cope with post-traumatic stress. Methamphetamine use is particularly high among refugees, the poor, and gay men in locations where AIDS deaths have been especially high. Its use is associated with high-risk sexual behavior and high rates of HIV.

Dr. Case added that much of what individuals consume as MDMA (Ecstasy) is adulterated or a placebo. In a recent study of drugs available at “rave” party sites, half of the drugs tested contained only MDMA (Ecstasy). Of the remaining drugs, some contained no active ingredients. A significant portion were adulterated with other drugs, primarily dextromethorphan, a serotonin reuptake inhibitor used in cough syrup that is extremely dangerous if used in conjunction with MDMA (Ecstasy). Researchers do not know if MDMA (Ecstasy) use is a factor in high-risk sexual behaviors or increased HIV incidence among men who have sex with men, but the precursor drug MDA has been related to a 30 percent increase in high-risk sexual behavior and HIV incidence.

Dr. Case reported that because the drug use patterns are increasing so rapidly, researchers and surveillance systems often fail to include appropriate questions or classify drugs in different ways. For example, Federal drug enforcement officials, State police, and drug treatment providers do not classify methamphetamine and MDMA (Ecstasy) use consistently, so researchers cannot compare or track data from publicly available surveillance data. Dr. Case

called for more research in four areas: 1) core questions for surveillance systems that track emerging drug trends; 2) rapid assessments; 3) drug-specific effects on HIV risk and behavior; and 4) development of targeted interventions to prevent drug abuse and HIV transmission.

Comparison of 1995 and 1999 School Surveys in Slovakia with Respect to Use of Synthetic Drugs by Risk Groups of Students Aged 15 to 18

Alojz Nociar

Slovakian Ministry for Drug Dependencies and Control

The Slovak Republic was one of 25 nations to participate in the European School Survey Project on Alcohol, Tobacco, and Other Drugs. Dr. Nociar compared responses from 8,179 secondary school students in 1995 with those from 7,975 students in 1999 to identify the following trends: drug use is increasing, particularly marijuana use; drug use in 1999 had spread to all areas of the country from the 1995 concentration in the western portion; relatively new drugs, such as MDMA (Ecstasy) and LSD, are gaining acceptance; and consumption of alcohol and tobacco is also increasing, particularly among girls. Lifetime prevalence of marijuana use increased from 12.4 percent to 23 percent; MDMA (Ecstasy), 0.1 percent to 1.8 percent; LSD, 0.8 percent to 3.3 percent; and amphetamine, 1 percent to 1.6 percent. The 1999 data showed lifetime prevalence increased with age (18-year-olds were 3 times more likely to have used marijuana than were 15-year-olds) and gender (boys used all classes of illicit drugs more frequently than girls). Family characteristics, such as low socioeconomic status and divorce, were also relevant to use of alcohol, tobacco, and other drugs. Country-specific questions in the Slovak Republic mapped tobacco dependence and estimated growth of alcohol tolerance. Age at first use of tobacco correlated strongly with a similar age at first use of marijuana. Students who were identified as very high risk for alcohol tolerance were far more likely to use illicit drugs than those who drank without exhibiting tolerance. For example, lifetime prevalence of marijuana was 57.1 percent in alcohol-tolerant students and 10.9 percent in nontolerant students.

Use of Amphetamines in Populations Seeking Help in Public Network

Andrej Kastelic

Slovenian Center for Treatment of Drug Addiction

Dr. Kastelic reported that 30 percent of Slovenian 15- and 16-year-olds reported a lifetime prevalence of illicit drug use; most used marijuana as their first illicit drug. Although only 5 percent of the students reported using MDMA (Ecstasy), 40 percent said the drug was “easy to obtain.” In 1995, one-third of the students reported knowing about MDMA (Ecstasy); by 1999, that figure was 90 percent. Dr. Kastelic added that methamphetamine and MDMA (Ecstasy) abuse are not taken seriously by drug users, parents, teachers, or officials in Slovenia. Individuals who seek treatment for methamphetamine or MDMA (Ecstasy) abuse are usually polydrug users who also abuse alcohol, benzodiazepines, or opiates. Some injection drug users try to prevent or treat opiate overdoses by injecting methamphetamine. Individuals who seek treatment only for methamphetamine or MDMA (Ecstasy) use usually do so only after

experiencing an overdose or drug-related psychosis. Reviewing data from drug treatment centers and emergency rooms, Dr. Kastelic reported a small but growing incidence of methamphetamine-related admissions. Prevention activities include special training for emergency room and drug treatment center professionals and stationing health care professionals at venues such as dance clubs where methamphetamine use is common.

Experience with Drug Screening Systems in the Hungarian Defense Forces

József Fürész

Hungarian Defense Forces Health Protection Institute

Dr. Fürész reported on a 1996 effort that used urinalysis and questionnaires to determine the extent of drug use by Hungarian soldiers. The initial screening involved 250 soldiers from 5 areas; 17 percent reported that they had used drugs recently, but urinalysis documented that as many as 52 percent tested positive for illicit drugs. Methamphetamine was the most commonly abused drug. Researchers were surprised to discover that methadone was also abused, because it is available in Hungary only as a treatment for opiate dependence and surveillance systems had not indicated it was emerging as a drug of abuse. Risk factors, such as socioeconomic status and family characteristics, were similar to those reported for civilian drug abusers. The results prompted military officials to create a drug screening system that tests soldiers when they join the military, during basic training, and randomly during their enrollment. Dr. Fürész described how the drug screening program provides surveillance data on the incidence, type, and geography of drug abuse trends; decreases general drug use; and better identifies those soldiers who might benefit from interventions. He added that abuse of methamphetamine and methadone has declined since the screening program was implemented.

Neuropharmacology of Methamphetamine and MDMA (Ecstasy)

Cochairs: Tibor Wenger, *Semmelweis University*
Matej Sande, *University of Ljubljana*

Neurotoxicology of Methamphetamine and MDMA (Ecstasy)

George A. Ricaurte
Johns Hopkins University School of Medicine

Those amphetamine derivatives such as methamphetamine and MDMA (Ecstasy) that have high abuse liability for humans produce particularly high neurotoxic activity in the brain, affecting dopamine, serotonin, or both depending on the drug's chemical structure. Serotonin is implicated in cognition, memory, mood regulation, impulse control, appetite, and sleep. Animals given MDMA (Ecstasy) develop toxic changes in brain serotonin cells, developing long-term deficits in virtually every chemical marker unique for brain serotonin cells. Toxicity of MDMA (Ecstasy) occurs in every animal species considered, at a dose of approximately 5 mg/kg. Brain studies of animals treated with MDMA (Ecstasy) 2 weeks, 18 months, and 7 years previously have documented that virtually every region of the forebrain is denervated of its serotonergic axonal input.

U.S. researchers and treatment providers are concerned that MDMA (Ecstasy) has become a very popular recreational drug among high school students, college students, and young adults because the drug is such a potent toxin toward brain serotonin cells. Adjusting the known animal toxicity rate of 5 mg/kg for cross-species differences, body mass, route of administration, and frequency of administration, researchers determined that a toxic dose of MDMA (Ecstasy) in humans falls precisely within the range required to produce the drug's desired subjective effects (approximately 1.7 to 2.7 mg/kg). Thus, Dr. Ricaurte has concluded that even a single dose of MDMA (Ecstasy) carries the risk of producing serotonin neuron cell injury in humans.

Dr. Ricaurte discussed advances in positron emission tomography (PET) that permit researchers to assess the status of brain dopamine and serotonin neurons in living humans. Animal studies have documented dose-related destruction of dopamine and serotonin axon terminals by methamphetamine and MDMA (Ecstasy). Initial studies were conducted with baboons and then with healthy, abstinent humans who had previously abused either methamphetamine or MDMA (Ecstasy), using PET radioligands that selectively bind the dopamine and serotonin transporters to monitor drug-induced neurotoxicity. Dr. Ricaurte reported that both baboon and human subjects who had experienced neurotoxic regimens of methamphetamine showed significant reductions in binding of the PET radioligand [¹¹C] WIN-35,428 to the dopamine transporter. MDMA (Ecstasy) abusers had reduced binding of the radioligand [¹¹C] McN5652 with the serotonin (5-HT) transporter that was directly related to the level of previous MDMA (Ecstasy) exposure. Similar experiments with methcathinone users indicated that nigral striatum dopamine damage was similar to that for methamphetamine users but not as severe as that for individuals with Parkinson's Disease. The human data is being duplicated by other researchers in the United Kingdom, The Netherlands, and the United States.

Researchers are investigating whether drug-related dopaminergic neuronal damage combined with normal, age-related attrition of dopaminergic neurons will contribute to higher risks of

developing Parkinsonian syndrome later in life. Dr. Ricaurte called for additional research on the functional consequences of neuronal injury in the brain, and the mechanisms by which amphetamine derivatives damage brain cells. By studying the mechanisms of neurotoxicity for amphetamine derivatives, he predicted that researchers can learn more about neurodegenerative diseases like Parkinson's Disease and about the function of serotonin.

Research on MDMA (Ecstasy) and Dance Drugs in Slovenia: A Knowledge Base for Prevention

Matej Sande

University of Ljubljana

Dr. Sande reported on quantitative and qualitative research that was used to shape prevention programs in Slovenia. Using the methodology of the European School Survey Project on Alcohol, Tobacco, and Other Drugs, researchers determined that 15-year-olds in Ljubljana most frequently abused marijuana and MDMA (Ecstasy), with 7 to 15 percent reporting lifetime prevalence of MDMA (Ecstasy) use. The relative popularity of cocaine, methamphetamine, and MDMA (Ecstasy) depends upon availability and price. For some segments of drug users, MDMA (Ecstasy) is replacing marijuana as the first illicit drug. Using snowball sampling, field interviews, questionnaires, and Web-based questionnaires, the researchers obtained qualitative data about the drug supply network; users' knowledge of drug consequences, harm reduction techniques, or prevention programs; and users' desire for treatment programs. One-fourth of the respondents reported that drug use changed their life. Marijuana users were more likely to report that they did not attend college and experienced negative consequences from drug use. Methamphetamine or MDMA (Ecstasy) users were more likely to report that they did attend college and were more socially successful. Prevention programs were neither sought nor remembered, but users conducted their own informal cost-benefit-risk analyses. Some MDMA (Ecstasy) users reported that they stopped using the drug after developing a tolerance. Dr. Sande described the multimedia educational campaign that included flyers; outreach work at "rave" parties; workshops for young people, professionals, and parents; peer education programs; and Web-based advice lines, drug identification information, and chat rooms.

Significance of MDMA (Ecstasy) and Methcathinone Manufacturing Impurities

Gábor Nagy

University of Szeged

Clandestine synthetic drugs are seldom pure chemical entities, a function of their varied ingredients, manufacturing processes, and producers. The European Nordic Countries Amphetamine Profiling project and the United Nations-sponsored International Methamphetamine Profiling project use synthetic impurities to characterize synthetic drugs, identify drug sources, and catalog common impurities. Very little accurate information exists about the pharmacological or toxicological impact of synthetic drug impurities and byproducts. Dr. Nagy described two interrelated projects that are investigating the significance of

manufacturing impurities on sample analysis and toxicity of MDMA (Ecstasy) and methcathinone. Researchers hope to identify those manufacturing impurities that might indicate where and how the drugs were synthesized or that would be useful in further toxicity studies. Dr. Nagy outlined the common impurities identified so far, and asked participants to evaluate the potential for practical use of pharmacological and toxicological research in limiting drug-related morbidity or in developing effective prevention programs.

Abuse, Consequences, and Therapy of Methamphetamine and MDMA (Ecstasy)

Chair: George A. Ricaurte, *Johns Hopkins University School of Medicine*

The Treatment of Methamphetamine-Related Disorders: State of Current Knowledge

Richard Rawson

University of California Los Angeles

Dr. Rawson described science-based methamphetamine treatment protocols funded by NIDA and developed jointly by researchers at the University of California and treatment providers at six Los Angeles-area clinics. Unlike cocaine, heroin, or alcohol abusers, methamphetamine abusers in the United States usually are employed and are frequently forced into treatment by workplace or legal system mandates. Individuals experiencing a methamphetamine-induced psychotic episode present with well-formed delusions and extreme paranoid ideation; confronting them precipitates violence. The withdrawal syndrome includes anhedonia, fatigue, anxiety, inertia, appetite suppression, and cognitive deficits. The acute cognitive deficits worsen initially and strongly impact treatment in the first 2 weeks. Methamphetamine abusers recognize that their brains are not functioning properly and are very receptive to information about what they are experiencing and how long their recovery is expected to take. Educational material must be presented in very simple terms because the methamphetamine abusers cannot process complex information at this stage of treatment. Outpatient treatment has proven to be more effective than residential treatment in helping stimulant abusers cope with high sensitivity to conditioned cues and strong drug cravings. Outcomes improve with retention in treatment. Controlled, randomized clinical trials are underway for treatment manuals that provide session-by-session guidelines for a 6-month outpatient treatment plan including cognitive behavioral therapy, education, positive reinforcement, classical conditioning, and family involvement. The manuals are available through the NIDA Web page, www.drugabuse.gov or www.nida.nih.gov.

Diagnosis and Treatment of MDMA (Ecstasy) Toxicosis

Miran Pustoslemšek

Psychiatrist

Dr. Pustoslemšek described the diagnosis and treatment for a patient with acute MDMA (Ecstasy)-induced psychosis. The patient was disoriented about time and place, had no recollection of the previous week, and presented with agitation, intense fear, confusion, hallucinations, and delusions. Physical examination and laboratory tests were normal with no signs of trauma, although the electrocardiogram revealed sinus bradycardia. A subsequent history documented that the patient had used MDMA (Ecstasy) regularly for the previous 12 months, and had possibly experienced shorter psychotic episodes during that time. After 5 days, a slight hemiparesis developed in the left hand; a computed tomography (CT) scan diagnosed cerebral edema, possibly a result of drug-induced hyperthermia. Dr. Pustoslemšek reported that MDMA (Ecstasy) abuse is unique in causing simultaneous delirium, psychosis, and organic

symptoms such as the cerebral edema. He outlined the types of diagnostic tests that should be conducted immediately when MDMA (Ecstasy) abuse is suspected.

Addiction and Methamphetamines

Sándor Funk

Nyíró Gyula Hospital

Dr. Funk described the influence of illicit drugs on affect, cognition, alertness, psychomotor coordination, sensitivity, and consciousness. The Department of Addictology is most concerned with drugs that cause great euphoria, have a high abuse liability, and are illicit, such as heroin. Individuals who become dependent upon heroin first experience the euphoria, then develop tolerance and mild drug craving, and finally experience drug craving that exceeds their tolerance. This third stage leaves drug users at high risk for overdose, which they attempt to counteract by combining heroin with stimulants such as methamphetamine and MDMA (Ecstasy). Recent experiences with methamphetamine and MDMA (Ecstasy) abuse may change the benign way those drugs have been considered by healthcare professionals in Eastern Europe. Dr. Funk reported that most Hungarian methamphetamine or MDMA (Ecstasy) abusers seek treatment only as a result of legal mandates, family interventions, or drug-induced medical emergencies.

Health Consequences of Designer Drugs

Marianna Baum

University of Miami

Dr. Baum reported on the interaction of methamphetamine, MDMA (Ecstasy), and MDA (a precursor to MDMA) with infectious diseases and behaviors that increase risks of acquiring viral infections. Users report that MDA reinforces emotions and empathy, while MDMA (Ecstasy) decreases inhibitions. All three drugs are associated with high-risk injection and sexual behaviors (such as sharing needles and syringes, trading sex for drugs, having unprotected sex, and engaging multiple sexual partners) that increase the risk for HIV infection and transmission of hepatitis B and C. Methamphetamine use is also associated with cardiac complications. MDMA (Ecstasy) generates life-threatening interactions with protease inhibitors in HIV-positive individuals, is associated with polydrug use, and has been reported to reduce resistance to infections. A higher frequency of bronchial infections and an increase in urinary tract infections has been described in Dutch female MDMA (Ecstasy) users. Toxicity and fatality are associated with cardiac arrhythmia and hyperthermia.

Building A Cross-National Research Agenda: United States - Eastern Europe Cooperation

NIDA Funding Mechanisms and Professional Development Opportunities

M. Patricia Needle

National Institute on Drug Abuse

Dr. Needle described professional development opportunities sponsored by NIDA for international researchers:

- C *INVEST Research Fellowships* are competitive, 1-year fellowships for scientists from outside the United States to conduct postdoctoral research with a NIDA-funded researcher. Fellows receive an orientation program at NIDA and travel support to attend scientific meetings. Fellows and their mentors jointly develop a collaborative research proposal for implementation in the Fellows' home countries.
- C *NIDA Hubert H. Humphrey Drug Abuse Research Fellowships* are competitive, 10-month fellowships for mid-career professionals from eligible countries that combine academic course work at The Johns Hopkins University with professional development activities, including travel support for attendance at scientific meetings and a professional research affiliation with a NIDA grantee.
- C *NIDA Distinguished International Scientist Collaboration Program Awards* are competitive 1-to 3-month professional visits to the United States for experienced drug abuse researchers from any other country to stimulate development of innovative collaborative research. This program gives senior international researchers the opportunity to propose projects that can potentially advance the scientific agenda in both countries as well as offer the ability to apply enhanced research skills and mechanisms in the non-U.S. scientist's home country.

Dr. Needle also addressed U.S. National Institutes of Health (NIH) funding mechanisms available to support the development of international collaborative research on drug abuse, the NIH peer review process, NIH grant review criteria, and human subject protections. Several sources of funding are available to international researchers through the NIH grants process, including:

- C *Administrative supplements* to existing grants can be proposed by NIDA grantees for a maximum of \$100,000 per year or 25 percent of the direct costs of the grant (whichever is less). The added component must be related to the purpose and integrity of the original grant. The proposal is not scored competitively through NIH, but approval and budgetary signoff within NIDA are required.
- C *Domestic grants with a foreign component* enable U.S.-based principal investigators to conduct cooperative international studies. The foreign component is part of the original grant; the entire application is scored competitively.

- C *Foreign grants* allow researchers from outside the United States to compete for funding within the NIH system. The actual research is conducted outside the United States. For a grant to be awarded to a foreign institution, the principal investigator must demonstrate a special opportunity to further drug abuse research through the use of expertise, resources, populations, or environmental conditions not readily available in the United States.

Other NIH programs are administered through the Fogarty International Center and support professional development opportunities or international research collaborations:

- C *Fogarty International Research Collaboration Awards (FIRCA)* provide up to \$32,000 per year, for up to 3 years, for international research partnerships between NIH-supported scientists and collaborators' eligible countries. The FIRCA goal is to extend and enhance the research of the U.S. investigators while benefiting the scientific interests of international scholars.
- C *AIDS-FIRCA* grants support cooperative studies by NIH grant recipients and foreign institutions on HIV/AIDS and on new and reemerging infectious diseases. AIDS-FIRCA grants are available for collaborative research in all countries. Support is similar to that available through the FIRCA grants.
- C *Specific country grants*. Research funds occasionally become available through sources targeted to a specific country or region. One example is the Japan Society for the Promotion of Science.
- C *International Training and Research Program in Emerging Infectious Diseases (ERID)* enables U.S. universities and nonprofit research institutions to support international training and research programs for foreign scientists and public health workers from eligible nations in research, control, and prevention strategies related to emerging and reemerging infectious diseases. The ERID award is an institutional training grant.

The AIDS International Training and Research Program

Marianna Baum

University of Miami

Dr. Baum reported on the AIDS International Training and Research Program (AITRP) that develops research infrastructure within eligible countries so that U.S. and foreign researchers can collaborate on biomedical and behavioral research related to AIDS. NIH has awarded 15 grants to U.S. institutions to train international health professionals in clinical trials, prevention, and related research, including research on HIV infection among drug-using populations. Training programs send international researchers to the United States for short-term training, conduct in-country training programs, and support pilot research projects in other countries.

APPENDIX A: AGENDA

March 31 (Friday)

- 16:00-17:30 Arrival at Visegrád
16:00-19:00 Registration (The registration desk closes at 19:15 and reopens April 1 at 8:00)
- 19:30 Welcome greetings:
Ákos Topolanszky, Deputy State Secretary, Ministry of Youth and Sport, Hungary
Alan I. Leshner, Director, National Institute on Drug Abuse, United States
Gyula Telegdy, President, Medical Section of the Hungarian Academy of Sciences, Hungary
- 20:00 **Opening Reception**

April 1 (Saturday)

Chairpersons: M.P. Needle, (United States) and A. Sulcová (Czech Republic)

- 8:45 **Opening Address**
P. Sótonyi, Rector, Semmelweis University, Budapest, Hungary
- Introductory Lectures**
- 8:50 Methamphetamine and MDMA (Ecstasy): Confronting the Crises through Research
A.I. Leshner, NIDA, United States
- 9:15 Amphetamine Abuse: Recent Regional and International Developments
K. Szendrey, Department of Pharmacognosy, University of Szeged, Hungary

PRESENTATION OF PAPERS

(The allowed time includes short discussion, there will be general discussion at the end of each session)

PHARMACOLOGY OF AMPHETAMINES

Chairpersons: A. Borsodi (Hungary) and P. Lazarov (Bulgaria)

- 9:40 The Pharmacology of Central Nervous System Stimulants
S. Fürst, Hungary

April 1 (Saturday)

10:00 I. Changes of Methamphetamine Intake in Rats at Pharmacological Manipulation on Serotonergic and Cannabinoid Receptor Systems
II. Influence of Fluoxetine Coadministration on Methamphetamine Suppression of Leukocyte Phagocytosis in Mice
A. Sulcová, Czech Republic

10:25 Role of Serotonin (5-HT_{1B}) Receptors in the Cocaine-Evoked Locomotor, Sensitizing, and Discriminative Stimulus Effects in Rats
M. Filip, Poland

10:40 **Coffee Break**

Chairpersons: G. Telegdy (Hungary) and P. Popik (Poland)

11:00 Behavioral Consequences of Methamphetamine- or MDMA-induced Neurotoxicity in Rats
J. Timár, Hungary

11:20 Group II Glutamate Metabotropic Receptor Agonist, LY354740 Inhibits Morphine Tolerance in Mice
P. Popik, Poland

11:40 Effects of Psychostimulants on the Opioid Peptide and CRF Expression in the Nucleus Accumbens and Central Nucleus of the Amygdala
R. Przewlocki, Poland

12:00 **General Discussion**

12:30 **Lunch**

PATTERNS AND TRENDS OF METHAMPHETAMINE AND MDMA (ECSTASY) ABUSE IN EASTERN EUROPE AND THE UNITED STATES

Chairpersons: M. Baum (United States) and V. Mayer (Slovakia)

14:00 A View of Use Among Heterosexual Adolescents and Adults
C.E. Sterk, United States

April 1 (Saturday)

- 14:20 Methamphetamine Use in Czech Adolescents: Prevalence, Patterns, and Consequences
 L. Csémy
- 14:40 The Family Dynamics of Opiate and Stimulant Users: A Comparison
 Z. Demetrovics, Hungary
- 15:00 Overview of Drug Epidemiology in Slovakia and First Signs of HIV Introduction Among Injection Drug Users
 V. Mayer, L. Okruhlica, A. Nociar, Slovakia
- 15:20 **Coffee Break**

Chairpersons: R. Vrasti (Romania) and R. Rawson (United States)

- 16:00 Patterns and Trends in MDMA (Ecstasy) and Methamphetamine Use Among Men Who Have Sex with Men
 P. Case, United States
- 16:20 Comparison of 1995 and 1999 School Surveys in Slovakia with Respect to Use of Synthetic Drugs by Risk Groups of Students Aged 15 to 18
 A. Nociar, Slovakia
- 16:40 Use of Amphetamines in Population Seeking Help in Public Network
 A. Kastelic, Slovenia
- 17:00 Experience with Drug Screening Systems in the Hungarian Defense Forces
 J. Fárész, Hungary
- 17:20 **General Discussion**
- 19:30 **Gala Dinner (hosted by National Institute on Drug Abuse)**

April 2 (Sunday)

NEUROPHARMACOLOGY OF METHAMPHETAMINE AND MDMA (ECSTASY)

Chairpersons: T. Wenger (Hungary) and M. Sande (Slovenia)

- 9:00 Neurotoxicology of Methamphetamine and MDMA (Ecstasy)
George Ricaurte (United States)
- 9:20 Research on MDMA (Ecstasy) and Dance Drugs in Slovenia: A Knowledge Base
for Prevention
Matej Sande, Slovenia
- 9:40 Significance of MDMA (Ecstasy) and Methcathinone Manufacturing Impurities
G. Nagy, Hungary
- 10:20 **Coffee Break**

**ABUSE, CONSEQUENCES, AND THERAPY OF METHAMPHETAMINE AND MDMA
(ECSTASY)**

Chairpersons: G.A. Ricaurte (United States)

- 10:40 The Treatment of Methamphetamine-Related Disorders: State of Current
Knowledge
R. Rawson, United States
- 11:00 Diagnosis and Treatment of MDMA (Ecstasy) Toxicosis
Miran Pustoslemšek, Slovenia
- 11:20 Addiction and Methamphetamines
S. Funk, Hungary
- 11:40 Health Consequences of Designer Drugs
M.K. Baum, United States
- 12:00 **General Discussion**
- 12:30 **Lunch**

April 2 (Sunday)

- 14:00 Building a Cross-National Research Agenda: United States – Eastern European
Cooperation
 M.P. Needle, United States
The AIDS International Training and Research Program
 M.K. Baum, United States
- 16:45 **Closing Remarks:**
 A.I. Leshner, United States; Á. Topolánszky, Hungary; M.P. Needle,
United States

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