

U.S.–Netherlands Workshop on Binational Research Collaboration on Drug Abuse and Addiction

Executive Summary

Celebrating a decade of progress through a uniquely successful binational agreement, officials from the National Institute on Drug Abuse (NIDA) and the Dutch Addiction Programme (DAP) heard from jointly funded research teams at the U.S.–Netherlands Workshop on Binational Research Collaboration on Drug Abuse and Addiction, which was held October 22 and 23, 2009, in Washington, DC. Workshop participants met with White House Office of National Drug Control Policy (ONDCP) Deputy Director Dr. A. Thomas McLellan, who described the Obama Administration’s priorities for drug control strategies, suggested ways that research can inform policy development, and congratulated NIDA and DAP for their “long and fruitful collaboration.”

NIDA and DAP representatives reviewed the factors contributing to what NIDA Deputy Director Dr. Timothy P. Condon called the Institute’s “most successful international collaboration” and identified priority areas for future collaboration. Researchers from both countries described preliminary findings from binational projects funded in 2007 and outlined plans for newly funded projects. NIDA International Program Director Dr. Steven W. Gust and DAP Chair Dr. Sineke ten Horn chaired the workshop. Dutch Ministry of Health, Welfare, and Sport Senior Policy Officer Wil M. de Zwart stressed the unique and successful collaboration and discussed the drug policy review currently underway in The Netherlands, explaining that final statements are expected in spring 2010 to address drug abuse-related prevention, treatment, health care, and criminal justice. Noting that U.S. and Netherlands drug policies have differed on significant points, she reported that those policy considerations have not negatively impacted research inquiries and that five consecutive Dutch ministers of health have adopted evidence-informed drug policies.

Welcoming participants to Washington, DC, Dr. Gust reported on the history of the binational agreement, which was signed October 19, 1999, by NIDA, The Netherlands Organisation for Health Research and Development (ZonMw), and The Netherlands Organization for Scientific Research (NWO) and has resulted in 16 jointly funded research projects and six binational workshops. He described how the binational research teams are independent but linked, permitting researchers to assemble teams with complementary skills; expand their individual research portfolios; and examine the effect of national differences in such areas as policies, drug-using populations, abused drugs, patterns of abuse, special populations, prevention programs, and treatment protocols. Proposals are evaluated independently and jointly to ensure that projects both meet the individual nation’s research criteria and scientific priorities and address topics of mutual interest that require binational collaboration.

The U.S.–Netherlands Binational Agreement research projects are jointly funded, which permits the funding partners to expand the impact of scarce financial resources. Since 1999, NIDA has awarded \$2.35 million to U.S. researchers, and DAP has awarded a similar amount to the Dutch researchers. Projects are funded for 1 or 2 years, depending on the research needs, and receive an average of about \$100,000 per year from each country. Both Dr. Gust and Dr. ten Horn noted that the arrangement has been especially cost-effective for the two funding agencies, resulting in a much larger impact than would normally be expected from such small grants: the 13 projects funded between 1999 and 2007 have produced nearly 100 peer-reviewed journal articles or presentations at scientific meetings.

Dr. Condon told participants that NIDA is delighted with the results of the 1999 agreement and determined to ensure that such a productive partnership continues. He identified pressing research needs, including drug abuse and HIV among criminal justice populations; substance use disorders and comorbidities among veterans, military personnel, and their families; outreach to health care professionals to improve drug abuse screening, brief interventions, and treatment; and blending research and practice. Dr. Condon noted that more research is needed about the increasing abuse of

prescription drugs, especially by young adults, and how effective treatment protocols for prescription drug abuse will differ from those that address abuse of illicit drugs.

Research Reports and Future Directions

Binational teams funded in 2007 reported on research investigating the pharmacotherapy varenicline to treat cocaine addiction, ecological momentary assessment (EMA) to measure implicit cognition in nicotine and heroin addiction, the role of dopamine in reinforcing drug use, and decisionmaking in marijuana users. Discussing their studies of relapse vulnerability, Dr. Anna Rose Childress, University of Pennsylvania, and Dr. Wim van den Brink, University of Amsterdam Academic Medical Center, reported that varenicline can blunt the limbic response to drug reward cues even before patients are consciously aware of the cues, suggesting that varenicline could normalize the cocaine-dependent decrease in dopamine receptor D₂ activity. Reporting on their experiments using EMA to measure mood, craving, and context in abstinent smokers (United States) or heroin users (The Netherlands), Dr. Andrew Waters, Uniformed Services University of the Health Sciences, and Dr. Ingmar Franken, Erasmus University Rotterdam, documented how both implicit and explicit cognitions increase prior to relapse, suggesting that EMA can be used to track when patients are vulnerable to relapse so that a brief intervention could be delivered in a timely manner. Exploring the role of dopamine in reinforcing drug use, Dr. Paul Phillips, University of Washington, and Dr. Matthijs Feenstra, Netherlands Institute for Neuroscience, reported that habit formation in adult rats is correlated with risk-taking in adolescent rats, and that as habits are formed, behavior control shifts from the prefrontal cortex to the dorsal striatum. The pair developed a new type of microsensor for *in vivo* dopamine detection, which is being adapted for use in humans. Summarizing imaging studies to assess the cognitive performance of marijuana users, Dr. Linda Porrino, Wake Forest University, and Dr. Anneke Gourdriaan, University of Amsterdam, reported that at-risk marijuana users appeared to employ different brain circuits than control subjects did but achieved similar results on tests of working memory, impulse control, and decisionmaking.

Three newly funded binational teams also discussed their research plans. Dr. George F. Koob, The Scripps Research Institute, and Dr. Judith R. Homberg, Radboud University Nijmegen, will explore the motivation and etiology of cocaine dependence by investigating the interaction of inherited differences in the serotonin and cortisol stress systems that increase extracellular serotonin levels and lead to neuroadaptations. Dr. Chris Pierce, University of Pennsylvania, and Dr. Louk Vanderschuren, Utrecht University, will use pharmacological modulation of striatal circuits, deep brain stimulation to attenuate reinstatement, and optogenetics to inhibit or enhance neuronal activity to examine the roles of striatal subsystems in cocaine reinforcement and the reinstatement of cocaine seeking. Dr. Raymond Booth, University of Florida, and Dr. Wim van den Brink, University of Amsterdam Academic Medical Center, will test (1R,3S)-(-)-trans-1-phenyl-3-dimethylamino-1,2,3,4-tetrahydronaphthalene (PAT) to investigate the neuropharmacology of cocaine addiction. PAT may be a potential pharmacotherapy for cocaine addiction without abuse liability in humans.

Drs. Gust and ten Horn led a spirited discussion of potential avenues for future research collaboration. Participants pointed out that the current system of joint funding for investigator-driven projects has resulted in exceptionally high-quality research and encouraged both funding agencies to continue to bring together experts from the two countries to leverage financial support and demonstrate the value of research to addicts, caregivers, and policymakers. Participants suggested that funding targeted to specific areas of research supplement the current system, not supplant it. Among the suggestions for future research topics were translation of basic science findings to treatment and policy, the roles of comorbidity and trauma in drug use, pharmacogenetics, vulnerable populations, nicotine, and natural experiments on differences in sociopolitical environments and the availability and potency of illicit drugs.

U.S. Office of National Drug Control Policy Priorities

Dr. McLellan discussed five ONDCP priorities for U.S. drug control strategies: (1) develop a national prevention system; (2) engage primary care; (3) close the addiction treatment gap; (4) expand special care for offenders; and (5) develop timely, useful performance measures. He said that ONDCP was particularly interested in research to identify practical systems that could combine treatment and supervision to help the 700,000 Americans released from jail annually, 30 percent to 40 percent of whom return to jail within 1 year of initial release, often because of a single positive urine test for drug use. Dr. Terry Zobeck, ONDCP Research and Data Analysis Unit, described a pilot drug court system that is showing some efficacy in managing drug use among newly released offenders by imposing less stringent sanctions for positive urine tests. Dr. McLellan said that ONDCP was particularly interested in research on: (1) the characteristics of patients for whom drug courts work; (2) developing community support for drug-free housing for ex-offenders; and (3) evaluating treatment protocols where re-entering offenders agree to comply with a predetermined treatment program, gaining privileges for treatment compliance and losing privileges for failure to comply with the treatment program. Dr. Wim van den Brink, University of Amsterdam Academic Medical Center, suggested that Dutch stepped-care/matched-care treatment protocols might be adapted by future binational research teams to help develop programs that would address the ONDCP goals.

Dr. McLellan also discussed ONDCP priorities for research on the effect of broad, community-based, early interventions that address risk factors for substance use disorders (SUD). He cited research findings that: (1) young people between the ages of 10 and 20 are most at risk for developing SUD; (2) common risk factors such as dropping out of school, bullying, depression, and teen pregnancy are predictive for development of SUD; (3) preventing any one of the risk factors can improve drug abuse prevention outcomes; and (4) implementation of more than one prevention program leads to more robust responses to all the prevention programs. Dr. McLellan suggested that researchers investigate programs that target young people early and move from isolated, single interventions to broader, more coordinated approaches that combine resources from education, justice, and mental health services that address the common multiple risk factors. Dr. van den Brink recommended that U.S.–Netherlands research teams adapt coordinated, school-community-family early interventions that address a range of existing problems in The Netherlands.

Addressing research needs to close the addiction treatment gap and engage the primary care system, Dr. McLellan reported that between 23 million and 25 million Americans meet diagnostic criteria for alcohol or other drug dependence but only 1 in 10 are in treatment because the current drug treatment system is designed for the most chronic, complicated patients, not the majority of those with SUD. Less than 3 percent of drug abuse treatment referrals come from the medical care system; the balance comes from the criminal justice system. Nearly one-third of the 11,600 specialty treatment programs treat fewer than 200 individuals each year, and the Federal Government funds 80 percent of that treatment. Dr. McLellan said that ONDCP is interested in research that will help identify effective treatment protocols for individuals diagnosed with less severe forms of SUD and mimic those for other chronic illnesses (such as diabetes, asthma, or heart disease), where primary care providers screen patients, provide standard interventions, refer patients to specialists only when standard interventions fail, and monitor the ongoing treatment plan developed by the specialists. Services research priorities include investigating cost-effective ways to add comprehensive addiction treatment services at federally qualified health centers and Indian Health Service facilities; programs to train primary care physicians in SUD screening and brief interventions; and a prescription monitoring system to help address prescription drug abuse.