TESTIMONY

of

T. Celeste Napier, Ph.D.
Director, Center for Compulsive Behavior and Addiction
Professor, Departments of Pharmacology and Psychiatry
Rush University Medical Center
Chicago, IL

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Chairman Buschon, Ranking Member Lipinski, and distinguished members of the Subcommittee, thank you for the opportunity to provide testimony on methamphetamine addiction and how we can use science to explore solutions to problems associated with the abuse of this drug.

My name is T. Celeste Napier, and I am the Director of the Center for Compulsive Behavior and Addiction, and a Professor in the Department of Pharmacology and the Department of Psychiatry, at Rush University Medical Center in Chicago. I also serve as the Scientific Advisor for the Robert Crown Center for Health Education in Hinsdale, IL.

I will address three topics related to the abuse of methamphetamine. First, how basic brain research has informed us about methamphetamine abuse and has led towards promising treatments for addiction. Second, what scientific gaps remain in our knowledge of methamphetamine abuse, and what is needed to enable neuroscience to fill these gaps. Third, examples of prevention programs and the role that educational institutions can have in prevention will be discussed.

Methamphetamine is an insidious drug. Indeed, no other abused drug has such profound effects on the brain as methamphetamine, and modern neuroscience has deciphered many of the mechanisms that underlie its effects. Dopamine is a key chemical in the brain that mediates the sensation of pleasure. Its biological purpose is to provide rewards for behaviors that keep the individual and its species alive. For example, when given food, laboratory rats show an increase in dopamine of about 50% in a brain region called the nucleus accumbens, one of the brain's 'pleasure centers'. Sexual activity in laboratory rats is associated with about a 100% increase in accumbens dopamine. Abused drugs produce their effects by hijacking this natural reward system; for example, cocaine causes a 200% increase in accumbens dopamine. Methamphetamine increases dopamine in the nucleus accumbens by over 1,000%, completely swamping the ability of the brain to control this neurotransmitter. So while the user initially experiences an incredible sense of pleasure and euphoria when taking methamphetamine, the brain's natural brake system is overridden, and the consequences of this dopamine overload can be devastating.

Modern neuroscience research has revealed that the brain effects of methamphetamine extend beyond these temporary, albeit extraordinary, increases in brain dopamine. Methamphetamine causes inflammation in the brain and elsewhere in the body, it causes the breakdown of the brain's protective barrier, and it damages neuronal projections. Modern imaging studies of the human brain show biochemical and functional abnormalities even years after the methamphetamine-addicted individual stops using the drug. Because of the health ramifications and related costs to the abusing individual and society, understanding the driving mechanisms of methamphetamine-induced neuropathology is a critically important topic of neuroscience research.

Some highlights of my own research can underscore this point. One of the ways my laboratory studies the effects of methamphetamine on brain function is with laboratory rats. Laboratory rats can learn a task in which they can press a small lever in a test box in order to receive an infusion of methamphetamine into their blood stream. The rats will continue to press the lever sufficiently enough to maintain their desired dose for the duration of the test period. This illustrates that the feel-good sensations evoked by methamphetamine drive the rats to continue to use the drug for as long as it is available. If we let rats self-administer methamphetamine for a few hours each day for 2 weeks, and then leave them alone in their home cage for different periods of time, we find that by 3-4 weeks of abstinence, the rats' brain have degenerated to the point that the anatomy and neurobiology looks similar to the brain of a human with Parkinson's disease. These studies have helped identify the neurobiological constructs which support recent epidemiological studies showing that human methamphetamine abusers exhibit a 75% greater risk to develop Parkinson's disease than do non-abusing humans. Given that there are approximately a half a million methamphetamine-abusing individuals in the United States (National Survey on Drug Use and Health), the possibility that methamphetamine may promote such a devastating disease has enormous ramifications in terms of human suffering and medical costs required to treat Parkinson's disease. Consequently, our research is identifying viable biomarkers that hold promise as early detectors of Parkinson's disease-like pathology in the methamphetamine abuser, with the hope that presymptomatic detection will allow early therapeutic intervention to avoid developing Parkinson's disease. This example shows how basic neuroscience, using laboratory models of human methamphetamine abuse, can explain clinical observations about this condition, and in so doing, aid in identifying possible treatments.

The effects methamphetamine occur at all levels of neurobiology, including genes, proteins, cells, circuits and whole brain regions, and the profile of the damage changes with time. Such knowledge is informing modern day thinking about treatment, and this is critically important, as currently there are no FDA-approved treatments for methamphetamine addiction. Though dopamine plays a role in initiating the pathological effects of methamphetamine, we know that targeting treatments that act on the dopamine system is not clinically fruitful. Like the analogy that the train is already out of the station, treating addiction may have more to do with the progression of pathology that is subsequent to the excessive release of dopamine. This new view is directing current medication development where therapies being tested are better-suited to halt or slow down the chain of events that continue after drug-taking stops. For example, relapse to drug-taking by the withdrawn methamphetamine addict is hallmark to addiction, and identifying unique therapeutic targets that govern relapse has gained the spotlight in recent years. These endeavors span testing of vaccines for methamphetamine, as well as identification of targets that are involved in the intense urges for the drug that are thought to drive relapse. Research in our laboratory relates to this theoretical construct, and we have identified potential therapies that reduce relapse-like behaviors in laboratory rats that self-administer methamphetamine. Early clinical studies have indicated that these therapeutic agents may indeed be useful in humans. Embedded in this research endeavor are evaluations of therapies already used to treat humans for other diseases, and have pharmacological profiles we hold should also be useful in reducing relapse. As these therapies are already shown to be safe in humans, this should allow a more rapid translation of our laboratory findings with animal models back into humans. Moreover, as current estimates for developing clinically effective therapies from new chemical entities range from $4 to $11 billion (Forbes, March, 2012) and 12 years (US FDA) in the making, such rediscovery and repurposing of therapies provides a exceptionally expedited mechanism for developing effective, safe and affordable treatment solutions for addiction. To attract the interest of the pharmaceutical industry to addiction therapy, we are working with a innovative, international foundation based in Chicago named 'Cures Within Reach' to steward fundraising for repurposed treatments that we have identified for cocaine and methamphetamine addiction that present patent opportunities. We feel this approach of 'teaching old drugs new tricks' is a win-win model that should be explored to its greatest extent by academic biomedical researchers, government agencies and foundations like Cures Within Reach to work with pharmaceutical companies in implementing treatments for those that suffer from addictions.

Several other new paradigms are being explored by medication development researchers with the objective of expediting the implementation of treatments for methamphetamine addiction. We are challenging old normatives on what constitutes successful treatment. Current FDA guidelines for approving addiction therapeutics require the treatment to provide complete abstinence from the abused drug. This rubric differs from that applied to alcohol or nicotine abuse, where a significant reduction in the use of the drugs is sufficient, as it is known that such reductions are associated with positive health benefits for the patient. Thus, it is necessary for current research to verify the health benefits of reducing methamphetamine intake for those addicted to the drug. Spearheaded by NIDA, such research is now underway. Basic neuroscience research predicts that positive outcomes will be obtained, and it is our hope such empirical evidence will redirect FDA guidelines so we can rapidly put in place therapies that can provide relief from the ravages of methamphetamine addiction.

While the aforementioned research illustrates the forward momentum of the neuroscience of methamphetamine abuse, and how this research has informed medication development, several critical pieces remain before the puzzle of addiction can be completely assembled. To do so, may take a more bird's eye view of addiction and how abused drugs change the brain in such profound and enduring ways. The brain is extremely complex, more complex than the internet, traffic flow on metropolitan highways, or the weather. Thus, all of the tools that are at the disposal of modern science need to be utilized to understand the brain complexities associated with addiction. Like most genetically linked diseases where more than one gene is involved, there will not be a single cause to methamphetamine addiction. To best elaborate the complexities of addictions, this area of neuroscience would benefit greatly by more incorporation of mathematical models of reward-motivated behaviors, and by linking molecular neurobiology to function at the circuit and behavioral levels by utilizing shared data sets. This is a great opportunity for hand-shaking of efforts from NSF, DARPA and NIH as was so exquisitely discussed by this Subcommittee in a Hearing on July 31st of this year on the BRAIN Initiative.

An important sector of our society that is in critical need of effective treatment, are those that are incarcerated. According to the Substance Abuse and Mental Health Services Administration, approximately 80% of incarcerated adults have a substance use problem. In recent years, I have had numerous opportunities to be involved in Continuing Legal Education for Criminal Defense Attorneys and Judges, speaking on the topic of the neuroscience of addiction and its impact on sentencing decisions. I am extremely impressed by the sincere desire of leaders within our judicial system to properly deal with substance abusing individuals. As Drug Courts mandate treatment, we need to do our best to assure that our judicial system has access to front line neuroscience. This is so important, particularly in methamphetamine cases, for which coerced treatment is often the only way an addict will access help. Studies show that coerced treatment yields the same, if not better treatment results, by motivating clients to stay in treatment longer. According to the National Association of Drug Court Professions, for methamphetamine-addicted people, Drug Courts increase treatment program graduation rates by nearly 80%. The savings offered by Drug Courts is substantial. The Office of National Drug Control Policy estimates that Drug Courts yield a savings of $21,000 per person annually, as the average cost per participant is $2000 and the cost of incarceration is $23,000. Clearly, a success.

However, our nation's courts are seeing an increase in the number of veterans with drug-related offenses, and this alarming trend deserves serious consideration. Substance use disorders are particularly high in returning warriors who have suffered traumatic brain injuries (TBI) and are experiencing post traumatic stress disorders (PTSD). We, as a nation, owe it to our warriors to figure out why this happens; therefore, this should be a topic of intense research efforts in the addiction field. I also believe that we need to establish clear educational links between scientists in the fields of TBI, PTSD and addiction with the nation's Drug Courts and do an even better job of informing our judicial system on the complexities of these disorders. Such efforts could be spearheaded by NSF, DARPA, and various institutes within NIH.

A particularly vulnerable population to the ravages of methamphetamine is our nation's youth. For example, according to the National Survey on Drug Use and Health, each day in the United States more than 4,500 children aged 12-17 years of age used an illicit drug for the first time. We must address this need, and I believe there is a role for neuroscience in this effort. Educational institutions typically include drug education in their health curriculum in grades 7 - 10th, and drug-related topics often focus on the legal consequences of illicit drug use, not health. As the striking epidemiological data suggest, the traditional approach to drug education is outdated and ineffective. New strategies that are initiated in earlier grades, involve yearly programming at regular intervals with up-to-date science-based curriculum and successful prevention methods, and include age-appropriate guidance are critically needed. Recent efforts by the Robert Crown Center for Health Education, a not-for-profit organization based in a suburb of Chicago, in conjunction with our Center for Compulsive Behavior and Addiction at Rush University Medical Center provides ,what I believe, is an excellent template for these goals. The Robert Crown Center is developing and implementing a completely new educational framework to interface with the school systems, based on what science tells us are the risk factors faced by youth and which contribute to experimenting with drugs. The primary prevention approach to this drug education program is a comprehensive, whole-school educational framework that integrates long-term, knowledge-building strategies for middle school and high school students, school personnel, and parents. The critical partnership with our Center for Compulsive Behavior and Addiction provides access to the cutting edge brain research that is then transferred to the classroom. The educational framework includes both the neuroscience-based knowledge of how abused drugs act on the adolescent brain as well as the social/emotional learning required to reverse the rising trends of drug abuse among our youth. Here again, is a critically important opportunity for active involvement of neuroscientists, both in terms of understanding how the adolescent brain differs from that of an adult, as well as, how drugs influence the brain. NSF and NIH have mechanisms to support these initiatives, and given the impact on the future of our nation's youth, new paradigms that expand these programs should be explored.

Understanding how the brain normally functions and how these functions go awry during methamphetamine abuse is a formidable challenge. The exciting advances we have made towards this challenge attests to the ingenuity and determination of addiction neuroscientists. To continue this trajectory, so that pharmacological treatments can be identified, will take careful consideration of where resources should be directed. Successful templates should be supported and promising new paradigms should be considered. Education programs need to be promoted to translate the wealth of empirically derived neuroscience to the public. By supporting the continuation of the impressive work in our academic research centers and government laboratories, in partnership with private foundations and the pharmaceutical industry, we will continue to make tremendous inroads into our nation's struggle with methamphetamine addiction. Funding from government agencies and leadership from our policy makers are critical components in the continued success of these initiatives. With concerted teamwork from all aspects of our society, I am confident that we can meet the challenge of controlling the abuse of methamphetamine, and reducing the suffering of those who suffer from its addiction.