What Do We Know About Drug Addiction?

The National Institute on Drug Abuse (NIDA) is marking its 30th year of research in substance abuse. Over this period, significant advances have given us a better understanding of the neurobiology of drug addiction and of its treatment. To start with, scientific findings documenting long-lasting changes in the brain of individuals addicted to drugs have led to the conceptualization of drug addiction as a disease of the brain. Moreover, through the use of animal models and through imaging studies in human subjects, it has become possible to delineate neurotransmitter systems and neuronal circuits that are disrupted by the use of drugs. Ten studies in this issue exemplify some of these advances. This editorial discusses these papers within the framework of NIDA's top research priorities: prevention, treatment, and HIV/AIDS.

A challenging question is why, when exposed to drugs, some individuals become addicted while others do not. Compton et al. (p. 1494) used epidemiological studies to address this question, which examines the contribution of genetic, environmental, and developmental factors, and their interaction with one another, to facilitate or interfere with drug abuse and addiction. Genetic factors are estimated to contribute to 40%–60% of the variability in the risk of addiction, but this includes the contribution of combined genetic-environmental interactions. The neurobiological mechanisms by which environmental factors interact with genetic factors to affect vulnerability to addiction are just beginning to be investigated. An example of this is provided by Nader and Czoty (p. 1473), who focused on the influence that social environmental factors have on dopaminergic pathways and how these affect the propensity to take drugs.

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Brain developmental factors are important in drug abuse. For example, the relatively late development of brain circuits involved with emotion, judgment, and inhibitory control may explain the heightened propensity of adolescents to act impulsively and to ignore the negative consequences of their behavior, both of which increase the risk for substance abuse at this stage of development. Also, since drugs of abuse interact with some neurotransmitter systems that are essential for brain development (i.e., serotonin, acetylcholine), drug exposure during adolescence may be particularly harmful to the still developing brain.

Another major risk factor for drug abuse is the presence of a mental disorder. Children and adolescents suffering from depression, conduct disorder, attention deficit hyperactivity disorder, or schizophrenia are at a much higher risk of abusing drugs than unaffected youth. This can be viewed in two ways: as a high prevalence of drug abuse in the mentally ill or as a high prevalence of mental disorders in drug abusers. Both views suggest that there may be common neurobiological substrates for substance abuse and mental disorders. This is addressed by Brady and Sinha (p. 1483), who discuss how comorbidity has important implications for therapeutic intervention and prevention programs.

The identification of neurobiological substrates in addiction has provided new targets for treatment. Drug-induced increases in dopamine in the nucleus accumbens are considered to underlie the reinforcing responses to drugs of abuse, and repeated drug administration is believed to result in a series of adaptations involved in the loss of control and the compulsive drug administration that characterize addiction. Peter Kalivas

and I report on adaptations in the prefrontal-striatal glutamatergic pathway (p. 1403), which modulates the release of dopamine in the nucleus accumbens and thus regulates the magnitude of a response to a given reinforcer. Adaptations in this pathway could explain the enhanced saliency value of the drug and the decreased sensitivity to nondrug reinforcers in addicted subjects. Moreover, the magnitude of dopamine-induced increases could contribute to how the prefrontal cortex attributes and readjusts the value of a given reinforcer as a function of its context, so that disruptions in these regions may underlie the fixated high motivational value of the drug that leads to compulsive drug administration.

Steven Hyman elaborates on the theme of how learning and memory circuits may be involved in addiction (p. 1414). Since dopamine facilitates conditioned learning (a process mediated in part by the amygdala), the association of the drug-induced pleasurable experience with the increases in dopamine will result in strong conditioning, not only to the drug but to the stimuli that predict the drug (e.g., the house of the drug dealer, syringes). Through conditioning, initially neutral stimuli become highly salient and produce neural responses (e.g., dopamine increases) that trigger the motivation to procure the drug. This may account for the enhanced excitement for the drug and drug-related stimuli that overshadow the response to natural reinforcers.

The articles by Vocci et al. (p. 1432) and by O'Brien (p. 1423) review some of the advances in pharmacotherapy that have occurred over the past 10 years. The identification of common neurobiological substrates across various drug addictions suggests that, in some cases, it may be possible to develop medications that are beneficial for more than one type of addiction. In addition, advances in pharmacogenomics are helping identify genetic factors that may predict which individuals may have favorable responses to specific medications as treatments for addiction. An example of this for the treatment of nicotine addiction is provided by Berrettini and Lerman (p. 1441).

The complex behavioral consequences of addiction suggest that pharmacological and behavioral treatments with synergistic effects may be required for effective interventions. Significant advances in the behavioral treatments for drug addiction, reviewed by Carroll and Onken (p. 1452), have increased the options for combination treatments.

HIV/AIDS is also a major priority of NIDA, since drugs of abuse are a major vector in the transmission of HIV. This is due not just to sharing of contaminated syringes, which accounts for approximately 30% of new HIV cases, but to drug-induced changes in mental state during intoxication that favor risky sexual behaviors and to drug-induced physiological changes that may facilitate infection. Comorbid drug abuse and HIV can have deleterious effects on both neuronal and immunological function. Jernigan et al. (p. 1461) report on the consequences of comorbid HIV infection and methamphetamine dependence on brain morphological abnormalities. The findings are surprising in that they don't reveal a simple additive effect but what appears to be distinct consequences of the combination, highlighting the need to better understand the consequences of these interactions.

The chronic nature of drug addiction and the associated risks that it entails highlight the importance of prevention and early therapeutic interventions. Psychiatrists are in a unique position to be involved in the early recognition and treatment of drug abuse, which can positively impact not only the addiction process but also the course of other mental disorders.

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