Target 'Cellular-Level' Activity in Dependence

BY RENÉE MATTHEWS

BETHESDA, MD. — Chemical dependence as a result of drug abuse occurs at the cellular level because of neurochemical dysregulation, and an evidence-based understanding of these chemical dynamics and of the circumstances that drive a person to abuse drugs could yield a more comprehensive and effective approach to treatment.

"Chemical dependence is a disease of the brain caused by genetic vulnerability as well as exposure to a drug, and possibly other environmental factors such as trauma and family influence," said Carlton Erickson, Ph.D., a researcher in addiction science at the University of Texas at Austin, at the annual conference of the Association for Medical Education and Research in Substance Abuse.

Specifically, dependence occurs because of a neurochemical dysregulation of the mesolimbic dopamine system (MDS), which also is called the medial forebrain bundle or the pleasure or reward pathway because of dopamine's association with mood regulation, motivation, and reward, he said.

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"We assume that a certain genetic propensity together with drug use can lead to dysregulation of the MDS neurotransmitter processes; that is, when people use a particular drug , it 'connects to' or 'matches' the transmitter system that is not normal" and disrupts the cellular-level functioning of the pathway. This connection occurs because drugs typically act on a single neurotransmitter system, and those systems are particularly vulnerable to the specific drugs.

Continued exposure of the MDS pathways to a drug leads to changes or adaptations in nerve function, which are known as neuroadaptations. These changes reach a threshold, leading to compulsive drug use over which the individual has impaired control, Dr. Erickson suggested. "The main symptom of chemical dependence is impaired control over the use of a drug, and the patient perceives this as a basic need for the drug."

The mesolimbic dopamine system is a grouping of axons that extends from the brain's amygdaloid region to the frontal, prefrontal, and anterior cingulate cortexes that regulate feelings of pleasure. The different regions of the brain along the route of the MDS are governed by certain neurotransmitters, for example, dopamine (pleasure) in the ventral tegmental area, amygdala, hippocampus, and nucleus accumbens; serotonin (cravings) in the hypothalamus; and gamma-aminobutyric acid (GABA; sleepiness), also in the nucleus accumbens. Some addictive drugs such as cocaine, LSD, or benzodiazepines match up with and target certain neurotransmitters (dopamine, serotonin, and GABA, respectively), which might explain why some people have a drug or drugs of choice, Dr. Erickson said. "Multiple dysregulation could explain a person's codependence on several drugs," he added.

Opioid Addiction Treatment Booklets

Three free booklets on medication-assisted treatment for opioid addiction are available from the Substance Abuse and Mental Health Services Administration. The booklets—two for patients and one for families and friends—provide information on medication options, proper use of medications, common side effects, and the recovery process. "The Facts About Naltrexone for Treatment of Opioid Addiction," "The Facts About Buprenorphine for Treatment of Opioid Addiction," and "Medication Assisted Treatment for Opioid Addiction: Facts for Families and Friends," can be ordered at http://ncadistore.samhsa.gov. ■

Other pairings between addictive drugs and neurotransmitters include heroin and endorphins, nicotine and acetylcholine, alcohol and glutamate and substance P, and marijuana and endocannabinoids.

If chemical dependence occurs at the cellular level, then it would make sense that the treatment should also work at the cellular level, Dr. Erickson said. "Drug abuse is seen as a problem that needs to be solved through education, coercion, punishment, environmental change, or maturation, whereas chemical dependence should be treated by positively affecting the abnormal brain function—dysregulation—to reduce the need for the drug that is being abused," Dr. Erickson said at the conference, which was sponsored by Brown Medical School.

Both abuse and dependence are serious conditions, and both need to be addressed, but they are not the same, he added. Drug abuse is volitional (person has control over drug use), but chemical dependence is an involuntary brain disease, so each requires a different treatment strategy.

Among the current options for initiating recovery are the traditional 12-step programs, which encourage abstinence; counseling for behavioral modification; cognitive-behavioral therapy (CBT) and primary care management; and medical treatment, which could include using detoxification medications or medications that enhance abstinence (at the cellular level), such as reward blockers, and anticraving medications such as methadone, buprenorphine, and vaccines.

One could argue, Dr. Erickson said, that behavioral therapies probably also change brain chemistry. "In other words, [during behavioral therapy] the MDS dysregulation begins to move back toward normal. It cannot be totally normalized, just "pushed back" toward normal, in much the same way that medications change brain chemistry."

Although there are no direct brain imaging studies that show that this happens in dependence treatment, plenty of imaging research shows that psychotherapeutic methods such as CBT change brain function. Thus, "talk therapies" probably change brain function in a positive manner to help overcome dependence, he explained. ■

Disclosures: *Dr. Erickson had no conflicts of interest to report.*