ATTC Messenger – August 2013
Feature Article

Neuroscience and Addiction

Drug addiction research has made exciting advances over the last couple of decades, particularly in the area of neuroscience. The initial molecular sites of action of virtually all the major drugs of abuse, including cocaine, heroin, amphetamine, nicotine and alcohol have been identified. The main components of a "reward system," and how it connects to brain areas involved in motivation and emotion, are now defined, and much has been discovered about the chemical messenger systems such as dopamine and noradrenaline that are fundamental to the mechanism of addiction. Yet, much is still unknown. Where is this research going to take us in the future? Hopefully to more effective treatment and prevention. This article will provide a few highlights related to how the brain is affected by substances such as drugs, take a look at just a few of the emerging research areas, and offer resources for more information on this exciting subject.

Some key points on the addicted brain

The Harvard Mental Health Letter *(*http://www.health.harvard.edu/newsletters/Harvard_Mental_Health_Letter/2011/July/how-addiction-hijacks-the-brain*)* provided an excellent, understandable overview of how drugs affect the brain, excerpts of which follow. Other resources for this same kind of overview are provided in the *Resources* section.

- In nature, rewards usually come only with effort and after a delay. Addictive drugs provide a shortcut. Each in its own way sets in motion a biological process that results in flooding the nucleus accumbens with dopamine. The pleasure is not serving survival or reproduction, and evolution has not provided our brains with an easy way to withstand the onslaught. In a person who becomes addicted through repeated use of a drug, overwhelmed receptor cells call for a shutdown. The natural capacity to produce dopamine in the reward system is reduced, while the need persists and the drug seems to be the only way to fulfill it. The brain is losing its access to other, less immediate and powerful sources of reward. Addicts may require constantly higher doses and a quicker passage into the brain. It's as though the normal machinery of motivation is no longer functioning; they want the drug even when it no longer gives pleasure.
- Many addicts go through long periods without taking the drug, but they risk relapse even after years of abstinence, when the dopamine reward circuit has had plenty of time to recuperate. They are victims of conditioned learning, which creates habitual

responses. Drug-induced changes in the links between brain cells establish associations between the drug experience and the circumstances in which it occurred. These implicit memories can be retrieved when addicts are exposed to any reminder of those circumstances — moods, situations, people, places, or the substance itself. A heroin addict may be in danger of relapse when she sees a hypodermic needle, an alcoholic when he passes a bar where he used to drink or when he meets a former drinking companion. Any addict may resume the habit on falling into a mood in which he used to turn to the drug. A single small dose of the drug itself is one of the most powerful reminders. "It's the first drink that gets you drunk," as they say in Alcoholics Anonymous.

- Internal or external stress is another cause of relapse. The nucleus accumbens sends signals to the amygdala and hippocampus, which register and consolidate memories that evoke strong feelings. When asked why they relapse, addicts may say, "My job was not going well," or even, "The traffic was so heavy that day." These answers suggest that they are hypersensitive to stress, either congenitally or as a result of past addiction. Levels of corticotropin releasing hormone (CRH), the brain chemical that regulates the stress hormone system, often rise in addicts just before a relapse, while the amygdala becomes more active. Mice bred without receptors for CRH are less susceptible to drug addiction.
- In the last few years, research has suggested that addiction involves many of the same brain pathways that govern learning and memory. Addiction alters the strength of connections at the synapses (junctions) of nerve cells, especially those that use the excitatory neurotransmitter glutamate. Underlying these changes are drug-induced activation and suppression of genes within nerve cells, another process scientists are beginning to explore.
- The reward system may be more vulnerable, responses to stress more intense, or the formation of addictive habits quicker in some people, especially those suffering from depression, anxiety, or schizophrenia, and those with disorders like antisocial and borderline personality.
- Individuals also differ in their capacity to exercise judgment and inhibit impulses. The brain's prefrontal cortex helps to determine the adaptive value of pleasure recorded by the nucleus accumbens and checks the urge to take the drug when it would be unwise. If the prefrontal cortex is not functioning properly, an addictive drug has more power to monopolize the reward circuit. Recent research shows that the prefrontal cortex is not fully developed in adolescence, which could explain why we so often develop addictions at that time of life. Antisocial personalities also have deficiencies in prefrontal functioning. (1)

Emerging Research

What follows is by no means a comprehensive list, nor are the studies mentioned the only ones underway for each focal area; rather, these are just a few examples of what is being done to broaden our understanding of the neuroscience of addiction, and to increase the effectiveness of treatment.

"Resetting" the addicted brain: Targeted stimulation of the brain's prefrontal cortex is being explored as a promising treatment for addiction. A study in rats has found that stimulating a key part of the brain reduces compulsive cocaine-seeking and suggests the possibility of changing addictive behavior generally. "This exciting study offers a new direction of research for the treatment of cocaine and possibly other addictions," said NIDA Director Dr. Nora Volkow. "We already knew, mainly from human brain imaging studies, that deficits in the prefrontal cortex are involved in drug addiction. Now that we have learned how fundamental these deficits are, we feel more confident than ever about the therapeutic promise of targeting that part of the brain." "We are planning clinical trials to stimulate this brain region using non-invasive methods," said Dr. Antonello Bonci, NIDA scientific director and senior author of the study. "By targeting a specific portion of the prefrontal cortex, our hope is to reduce compulsive cocaine-seeking and craving in patients." (2)

Neural basis of memory and habit: This area of inquiry focusses on whether drug addiction may entail a form of habit learning controlled by the dorsal striatum, a brain structure related to the nucleus accumbens. One of the predictions is that drug cravings arise in part from memories for cues that have become associated with the drug. By focusing on the neural basis of these memories, neuroscientists hope selectively to disrupt their formation and break the drug-addiction cycle. (3)

Brain signaling: Looking into the brain biology of nicotine relapse, researchers showed that when they used a compound to block glutamate receptors, or a compound to prevent the large release of glutamate, rats were no longer motivated to seek nicotine, even when given the sound and light cues that signaled nicotine availability. "In this study, we were able to prevent this increased sensitivity of the nucleus accumbens by pretreating the animal with a drug, and it blocked the whole thing. The animal didn't relapse and show this big expansion in synaptic strength" noted Dr. Peter Kalivas of MUSC's Department of Neurosciences. The team is working on a pilot clinical trial to test one of these compounds, N-acetylcysteine, in cigarette smokers. They will use N-acetylcysteine in combination with varenicline to treat smoking relapse, hoping for an additive effect that will prove to be a more effective way to stop smoking. Kalivas said varenicline acts to suppress nicotine cravings, whereas the compound in their study targets the more fundamental neural circuitry that his team thinks underlies the basic pathology of the addiction. "By fixing the neuropathology as well as suppressing craving,

the combination of drugs might help turn the key and be a very useful combination in treating cigarette addiction and possibly other addictions, as well, he notes." (4)

Neural synchronization patterns: The introduction and restriction of drugs over time causes neurons to lose their ability to engage supervisory control over brain function and behavior. Researchers noticed that these short periods of desynchronization were much more prevalent and caused changes in neurobiology and behavior**. "**A better understanding of the dynamics of neural synchrony could have very important implications for understanding the addicted brain and may provide a physiological target to understand persistent neural changes that contribute to the probability of relapse," said Christopher Lapish, Ph.D., assistant professor of psychology at IUPUI**.** Synchrony has long been considered to play an important role in how the brain processes data, so any disruption of this pattern could hold significant research value. (5)

One of the greatest challenges in addiction research remains how to translate research findings to practical clinical use. Recently (June 2013) the *Psychology of Addictive Behaviors* published a special issue on "Neuroimaging Mechanisms of Change in Psychotherapy for Addictive Behaviors" (available for free at http://psycnet.apa.org/index.cfm?fa=browsePA.volumes&jcode=adb), which focused on NIH-funded research aimed at integrating brain science and addiction treatment research. The authors address a range of addictive behaviors, such as alcohol, cigarettes, marijuana, cocaine, and pathological gaming. Reviewing this special issue, and checking some of the recommended resources which follow, will give you a more in-depth overview of this important and evolving field of inquiry.

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Sources

1. "How Addiction Hijacks The Brain." Harvard Mental Health Letter 28.1 (2011): 1-3. Retrieved 7/13/13 from http://www.health.harvard.edu/newsletters/Harvard_Mental_Health_Letter/2011/July/how-addiction-hijacks-the-brain.

2. ”NIH study sheds light on how to reset the addicted brain” National Institutes on Health News and Events webpage: Wednesday, April 3, 2013; retrieved online on 7/14/13 from http://www.nih.gov/news/health/apr2013/nida-03.htm.

3. “Breaking ground in understanding the neurochemical and molecular aspects of addiction” University of Cambridge-Cambridge Neuroscience**;** retrieved online on 7/11/13 from http://www.neuroscience.cam.ac.uk/research/cameos/AddictedBrain.php.

4. Brazell, D. MUSC Office of Public Relations. “Nicotine addiction: Neuroscience lab pushes treatment frontier” May 21, 2013; retrieved online on 7/15/13 from http://academicdepartments.musc.edu/pr/newscenter/2013/kalivas.html#.UdScj6w08f4.

5. IUPUI neuroscience project researches neural synchronization patterns during addiction, June 10, 2013. IUPUI Newsroom**;** retrieved online on 7/16/13 from http://news.iupui.edu/releases/2http://www.the-scientist.com/?articles.view/articleNo/32039/title/Dopamine--Duality-of-Desire/013/06/neuroscience-research.shtml.