JONLA
Journal of the National Library of Addictions
Publisher and Editor-in-Chief: Punyamurtula Kishore, MD

Volume 5, Issue 8 August 2008
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Cocaine and the Brain

One of the important unresolved problems in the field of Addiction Medicine is the high rate of relapse, even in well-treated, highly motivated patients. Using animal models and cocaine addiction as a template, we are learning more every day about what happens to the brain during the unfolding of full-blown addiction. This understanding may have implications for all addictions and specifically lead to better approaches for dealing with one of the most vexing problems in addiction treatment, namely relapse.

Since the decade of the '90's (the "Decade of the Brain" – NIMH), we have new understanding of brain plasticity. The old understanding was, "You can't teach old dogs new tricks." The new understanding is, "If you're not learning and growing, you'll be left behind." The human brain is exquisitely equipped for this task. And brain plasticity is the primary mechanism for it. What this means is that the brain has circuitry and neural brain centers responsible for learning and memory that drive motivated behavior. We are all familiar with natural motivators which we return to again and again: our favorite ice cream flavor, vanilla or chocolate etc., or our favorite vacation get-away, the mountains or the ocean, etc. Chronic drug use, however, produces maladaptive behavioral patterns where there is a strong drive to seek and consume the drug of choice, often to the exclusion of other activities, even in the face of severe negative consequences.

The key neurotransmitter involved in both natural motivation and drug-induced motivation is dopamine. In the natural situation, neuroplasticity determines that once a reinforced behavior gets locked in, other brain centers take over in the learning and memory process and dopamine decreases. Cocaine, in fact, blocks this process and the brain keeps on producing synaptic dopamine but no longer under natural regulation. The animal experiments inform us that the excessive release of dopamine produces a kind of "super-learning" of all factors associated with the drug, the set and the setting, including all the environmental stimuli and circumstances associated with the drug use. In this way, drugs "over-power" other motivators in the person's life that may have been important before.

There is a neural relay center called the Nucleus Accumbens (NA), which connects the limbic/memory circuitry, the decision-making circuitry and the motor output. The NA, in turn, is divided into the shell section and the core – both sub regions are mediated by dopamine, and involved in drug addiction. As a behavior becomes well-learned and habit-like, the activated part of the brain moves from the shell (cognitive, decision-making) to the core (automatic, less impacted by thinking and planning). To reiterate, the shell of the NA is responsive to the

rewarding effects of cocaine; however, as the use of the drug becomes more habitual and chronic, it is the core of the NA that becomes more activated.

It turns out, with information derived from our animal models[1], that dopamine synapses, known to be involved in the early on, inductive aspects of drug addiction, are not important for reinstatement, or relapse. Several different brain centers are now known to be involved with the relapse phenomenon including those that are activated by cue triggers, Pavlovian associations, context triggers, and stress triggers. It appears that once the brain is an "addicted" brain, the dopamine release comes from the "habit" centers of the brain with little involvement of the decision-making or frontal part of the brain. This is a vitally important insight into the rehabilitation process that is often fraught with multiple relapses, and frustrations and disappointments among treaters and patients alike. In addition to the important biopsychosocial interventions that must be addressed, behavioral approaches that address cues, triggers and urges that are outside of conscious control are critical. Self-help programs such as AA, NA or Smart Recovery are well-positioned to provide the behavioral support that becomes so important to address: mood states, desires, urges and impulses that derive from deeper, more primitive and non-thinking, or reflex, or "habit" centers in the brain. In addition to deeper centers of the brain involved in the addiction process, there is evidence, once again from animal models, that it is glutamate rather than dopamine that is primarily involved. In the animal studies, with long-term cocaine self-administration, followed by detoxification, when glutamate levels are stabilized by administration of glutamate precursors, the reinstatement of cocaine "addiction" (relapse) is significantly reduced.

These studies[2] also give us another diagnostic tool for assessing and treating patients, even given the fact that we have a long way to go to discover the pathophysiology of addiction precisely. This research describes the relapse process as occurring along a spectrum with three modes going from left to right: 1. Little or no relapse; 2. Regulated Relapse; 3. Compulsive Relapse. Number 1 is the social drug user with less intense or enduring damage to the neural circuitry. Drug-seeking behavior depends upon the "reward" circuitry and dopamine.

The other end of the spectrum, #3, occurs after sufficient neural damage; and drug taking is mediated by deeper brain centers, and glutamate is involved. In this state, decision-making has little or no effect on drug-seeking behavior; this person is now a chronic drug user, facing compulsive drug use and frequent relapse. Our treatment options have offered little relief to this population. The ray of sunshine in this gloomy picture is that once a person seeks treatment, they have moved themselves to the left of the spectrum from #3, to #2, from Compulsive Relapse to Regulated Relapse, i.e., they have begun a cognitive struggle, activating the thinking, decision-making parts of their brain and diminishing denial. Therapy helps these patients move from Pre-contemplation[3] (they want a change) to Contemplation (focus on what to change and why). And as they prepare for action steps, they begin to realize that they need to change, and make changes in their life-style, social networks, and particularly, their way of handling psychoactive substances.

Summary:

The key modern insight is neuroplasticity, the process whereby the human brain is in a continual state of growth and renewal – not the old-fashioned idea of static lump of brain tissue where you are born with "x" billion brain cells and "y" million die off each day. The process is mediated by new learning and memory. In the natural reward state (something novel; an exciting new learning experience), dopamine spikes and then diminishes. In response to ingested drugs, the dopamine is not shut down as in the natural state. And learning moves from the cognitive portion of the brain to deeper "habit" centers, where damage to the neuroplasticity system leaves the decision-making ineffective, while the "habit-centers" (drug-seeking, drug acquiring, addictive behaviors) become stronger and take over the majority of motivated behavior. Simply making the decision to seek treatment is a beginning and an action of the cognitive, decision-making portion of the mature brain to reassert itself. The patient has begun the process of moving from dysfunction to healthy function; from pre-contemplation in the cycle of change to contemplation and so on.

References:

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