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Nicotine Addiction: Leading to a New Theory of Addiction

The latest issue of *Scientific American* provides us with new research and data, startling conclusions and a new avenue for exploration in the often-perplexing field of Addiction Medicine.

The key concept comes from new studies of adolescent smokers; they challenge accepted dogma that addiction symptoms, i.e. craving, withdrawal symptoms and failed attempts at quitting, take many years and/or heavy smoking to develop. Instead, these symptoms may occur within the first few weeks of starting to smoke, and sometimes with only the first few cigarettes.¹

The research and insights have been produced in the context of clinical research by a U. Mass. Medical School physician, Joseph DiFranza, M.D. His theories were funded by grants from the National Institute on Drug Abuse (NIDA) over a 10-year period. His initial idea focused on loss of autonomy, where stopping or quitting became a problem and where effort or some discomfort was involved. Dr. DiFranza was surprised to discover that signs of addiction showed up just weeks after adolescents began smoking, with as few as two cigarettes per week. He even had a few cases that showed addiction symptoms after only one or two cigarettes. By the way, DiFranza's studies have been replicated at Columbia University, McGill and a large research program in New Zealand. Symptoms of addiction were seen in 10% within two days of their first cigarette; and 25% showed symptoms after one to four cigarettes in the New Zealand studies.

The question is: how can one cigarette alter the brain sufficiently to produce addiction? The answer is in a fancy term called "up-regulation" of receptors. In animal research, it has been found that the equivalent of one cigarette produced enough nicotine to occupy 88% of the brain's nicotinic receptors - primarily in the hippocampus – the long-term memory center. Up-regulation means that the brain needs to produce significantly more additional nicotinic receptors to carry on its usual business, while so many of its nicotinic receptors are busy handling external nicotine.

The controversial model that Dr. DiFranza has postulated revolves around this point. One of the key functions of the nicotine system is to regulate hunger. Craving-generation (hunger) and craving-inhibition are usually in fine, healthy balance. When we are hungry, we eat. When we

feel sated, we stop (nicotinic inhibition). When we introduce cigarette nicotine to the brain, there is a rapid adaptation on the craving-generation side of the equation. One thing that will restore the brain balance is another cigarette or some other craving. However, in the earliest stages of addiction, a single cigarette can suppress the symptoms of withdrawal for weeks: sweating, irritability, sleep trouble, craving and failed attempts at quitting. Again, with animal studies, a single dose of nicotine triggers brain effects in most of the neurotransmitter systems for weeks afterwards, in GABA, glutamate, noradrenalin, dopamine, acetylcholine, opioid and serotonin systems.²

Another term to understand is: “dependence-related tolerance.” For the novice smoker, one cigarette every few weeks appears to keep withdrawal symptoms in check. However, tolerance develops with repeated use and the effect of each cigarette then diminishes over time. DiFranza’s conceptualization of cigarette addiction is that withdrawal symptoms cause the long-term heavy use instead of the reverse.

Rather than being addicted to pleasure, adolescents consistently report decreasing pleasure from smoking. Also, anyone who has smoked and stopped knows how awful the first few cigarettes taste when starting up again. The action of nicotine appears to provide a temporary suppression of craving. Withdrawal-related adaptations occur rapidly, while tolerance develops much more slowly. However, once tolerance emerges, DiFranza’s theory posits permanent brain changes so that the increases in tolerance become permanent. Even in abstinence, the “brain of a smoker is never restored to its original state.”

Dr. DiFranza has no illusions that his research and theories will change some of the prevailing viewpoints concerning origins and mechanisms of addiction. However, he believes that addiction is an “accident of physiology.” Because of a more recent understanding of brain plasticity, cigarettes specifically and drugs, in general, “trigger a remodeling of the brain.”

“The sensitization-homeostasis theory suggests that what is needed (in the addiction field) is a therapy that will suppress craving without stimulating compensatory responses that only make the craving worse in the long run. A better understanding of the addiction process may help researchers develop new treatments that can safely liberate smokers from nicotine’s deadly pull.” (Joseph R. DiFranza, M.D.)

Nicotine Glossary:

Nicotine Withdrawal: A cluster of symptoms that include craving, restlessness, nervousness, irritability, difficulty concentrating and difficulty sleeping.

Latency to Withdrawal: The symptom-free interval between the last cigarette and the onset of withdrawal symptoms. It can shrink from weeks to minutes over many years of tobacco use.

Dependence-Related Tolerance: The mechanism that causes the latency to withdrawal to shrink gradually over time.

Abstinence-Related Adaptation: A mechanism that mimics the action of nicotine by inhibiting craving. It develops in ex-smokers to counter the enduring effects of dependence-related tolerance.

References:

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2. A Sensitization-Homeostasis Model of Nicotine Craving, Withdrawal, and Tolerance: Integrating the Clinical and Basic Science Literature. DiFranza JR and Wellman RJ, "Nicotine & Tobacco Research," vol. 7, no.1, pps. 9-26, Feb. 2005.