CHAPTER 2

The Pain of Pleasure—The Neurobiology of Opioid Use Disorders

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The next time you have a pleasurable experience, ask yourself: *how is this feeling possible? What's going on in my brain right now?* Then ask: *how does this feeling of pleasure affect my choice to do it again?* We have all had the experience of having a second dessert when we were trying to stick to a diet or drinking one beer too many. ***How does the brain construct a moment of enjoyment and can that process break down?***

To create a pleasurable experience, the brain brings reward together with learning and even past memories. Genetic and epigenetic influences play their role. The stress system becomes involved. All of these things combine to create enjoyment so we can savor a delicious piece of chocolate cake or the warmth of alcohol or a favorite song. These feelings of enjoyment and pleasure drive our decision making and even our social and emotional capacities.

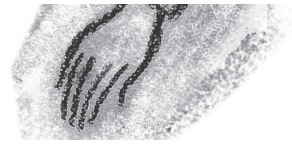
Substance use disorder (SUD) is all of this becoming unraveled. It is a disorder in the brain's ability to properly perceive pleasure that leaves an individual vulnerable to problematic substance misuse. At its heart, SUD is a defect in the brain's dopamine system, but dopamine is only the first of several neurochemicals involved in the construction of a hedonic experience—what is often called the hedonic cascade.[1,2] This disruption of hedonic processing then impairs motivation, emotions, and self-awareness.[3]

Controversial as this idea may be, there is no scientific reason why hedonic perception and volition could not be part of a neurologic disease. Pleasure and free will are capacities realized in the brain, and the brain can suffer pathology like any other organ or physiologic system in the body. That is what disease is: a defect in an organ or organ system leading to signs and symptoms.[4] SUD is a stress-induced, genetically-mediated defect in the limbic brain's reward learning areas that impairs the frontal cortex's decision making and self-awareness.[5] Research into the neurophysiology of SUD reveals the areas of the brain involved, its genetic and environmental causes, and how their interaction leads to the symptoms of SUD. That is why most neuroscientists and clinicians who make SUDs their area of study contend that it is, in fact, a disease.[6]

Knowing the neuroscience of SUD not only opens a fascinating area of contemporary science, it also allows the ability to help a group of patients who are very misunderstood and have traditionally been ignored. In the midst of a terrible, unprecedented, and largely iatrogenic epidemic, this knowledge is quite essential.

PRACTICE POINT

SUD is characterized by impairment of control over intoxicant use, an inability to abstain from intoxication, and craving to become intoxicated.



SUD PATHOPHYSIOLOGY

The discovery of the pathophysiology of SUD closely parallels the evolution of ways to investigate the brain. Early brain research involved careful observation of the disabilities associated with specific brain lesions in humans and animals. These lesions allowed scientists to construct a basic map of anatomical locations and functions. Next came experiments involving stimulation of specific brain areas. Electrodes implanted into these areas in laboratory animals and of patients during neurosurgery confirmed, denied, or expanded the knowledge obtained from lesion studies.[7]

The neuroscience of SUD can trace its origin to a brain stimulation experiment published in 1954. Two Canadian researchers, James Olds and Peter Milner, demonstrated that electrical stimuli delivered to the septal areas of the brains of laboratory rats produced dramatic reinforcement behaviors—animals readily and avidly pressed levers to self-administer stimulation via electrodes placed in these areas and did so for long periods of time even to the exclusion of food and water, and in some cases leading to death.[8] These septal areas, specifically the ventral tegmentum area (VTA) in the midbrain and the nucleus accumbens (NAc) in the striatum, were often referred to as the pleasure centers of the brain. The pathway of neurons that connected them, known as the median forebrain bundle, became known as the reward circuit.

Later studies showed that substances associated with SUD administered to these same areas produced the same strong reinforcing effects as electrical stimulation. The technique of in vivo microdialysis gave researchers the ability to measure extracellular fluid in these brain areas, and substances were found to cause increases of the neurotransmitter dopamine from neurons traveling from the VTA to the NAc and frontal cortex.[9]

The central concept of SUD neuroscience is: all substances of misuse release the neurotransmitter dopamine in brain reward structures.[10] This is especially true for stimulants, which directly release dopamine in the reward structures of the basal gan-