

# Imaging Diseases of Addiction



## Yesterday

- Substance abuse and addictive disorders were largely attributed to moral weakness or lack of character. This view was fueled by the lack of understanding of how brain function is disrupted by drugs and leads to the compulsive behaviors of people addicted to drugs.
- Until very recently, studies that evaluated the effects of drugs in the human brain were limited to laboratory analyses of post-mortem samples. The lack of tools to investigate the living human brain left huge gaps in our understanding of drug addiction.

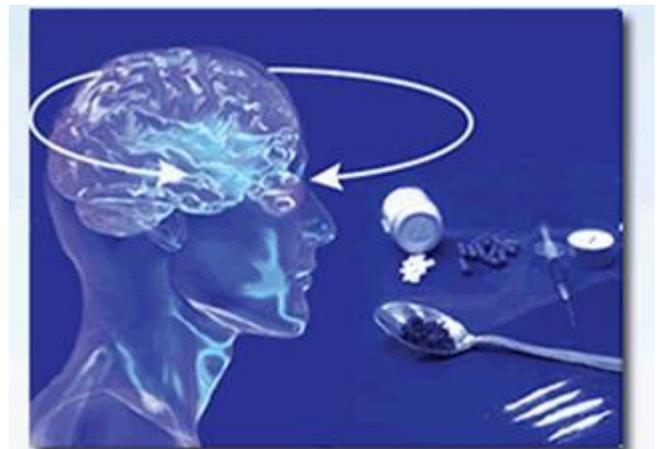
## Today

- The advent of noninvasive brain imaging technologies allows the study of the human brain in real-time, at ever finer temporal and spatial resolutions and chemical sensitivity. These tools allow us to assess many different brain responses under diverse conditions and at different stages of development.
- This constantly evolving suite of imaging tools has let us see directly the harmful effects of chronic drug abuse on multiple brain circuits, revealing the complexity of the brain systems (beyond dopamine and the reward system) that contribute to addiction.



**PET scans showing glucose metabolism in healthy and cocaine-addicted brains. Even after 100 days of abstinence, glucose metabolism has not returned to normal levels. Courtesy NIDA**

- An innovative application using a technique known as functional magnetic resonance imaging, or fMRI, permits assessment of the normal functional connections in a “resting” brain, offering a baseline for comparing healthy vs. diseased brains (see figure above). NIH-supported studies in drug abusers show enhanced connectivity of regions related to reward, memory, craving, and motivation, but reduced connections within regions associated with cognitive control, craving, and behavioral guidance.
- We are beginning to catch the first glimpses of the



potential of real-time imaging technologies as adjuncts to therapies for brain disorders. For example, an fMRI study revealed that cocaine abusers may retain some ability to voluntarily inhibit craving and that strengthening the ability of the pre-frontal cortex, or the brain’s main decision-making center, may be possible and beneficial in treating addiction. We have also learned through a technique called neurofeedback (symbolically represented above) that giving patients a live view of regional brain activation enables them to voluntarily dial the activity of that region up or down and gain a measure of volitional control over, for example, the perception of pain. Recently published, NIH-funded studies include:

- Control over brain activation and pain learned by using real-time functional MRI. (In Proceedings of the National Academy of Sciences, 2005)

- Learned regulation of spatially localized brain activation using real-time fMRI. (In NeuroImage, 2004)
- Imaging techniques and genetic databases are slowly merging into a more comprehensive approach to tackling many diseases, including addiction. Linkages are emerging, for example, between particular genetic variations and distinct properties of specific brain regions.

## Tomorrow

- The emerging understanding of addiction afforded by brain imaging technologies has exposed a host of new targets at the molecular and system levels for the development of next-generation addiction treatments. For example, a deeper knowledge of addiction-related changes in resting-state brain connectivity will open up powerful new avenues for safely and non-invasively diagnosing and monitoring the efficacy of addiction treatments.
- We also envision the arrival of a truly multimodal psychotherapy that harnesses the real-time and high-resolution properties of imaging technologies for use in combination with established pharmacological and behavioral approaches.
- Imaging genetics, a new but evolving field that combines the identification of particular genes with particular brain structures and activity patterns, will one day be used routinely to personalize disease diagnosis and clinical treatment, as well as better investigate how the environment influences disease risk and progression.
- Combined, these advances will dramatically enhance our ability to detect the signs of drug-induced brain changes that can increase a person's risk of addiction. This in turn will allow clinical researchers to develop better strategies to counter these alterations and prevent addiction from ever developing.

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