Anatomical and functional MRI of Cocaine and Nicotine Addiction

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Drug abuse is characterized as the compulsive taking of a substance where its use results in potentially hazardous behavior or where continued use remains in the face of persistent negative consequences. It is a recurrent, relapsing brain disease with a complex etiology based on underlying neurobiological, genetic and environmental interactions. Preclinical data consistently implicate the mesocorticlimbic (MCL) dopaminergic system as the principal regions and pathways responsible for the initial actions of most abused drugs despite their very different pharmacological properties. However, the neuroplastic effects that occur as a consequence of chronic drug intake are much less well understood. Because of this, the pathophysiology of the disease in humans remains poorly understood and as such the field has relied on a series of behavioral symptoms checklist for diagnostic and treatment outcome prognosis. To this end, neuroimaging, specifically functional and structural MRI, would seem like an important tool to understand the ‘addicted’ brain and the complex actions of a drug on, and neuroplastic consequences to, various circuits and neurobiological mechanisms. Imaging can be used to identify state/trait phenotypic alterations within core neurobehavioral symptoms such as attention, inhibitory control and reward processes. Such phenotypes might be used as potential ‘indirect’ biomarker targets in drug discovery and smoking interventions. Further, key brain circuit(s)/networks that underlie addiction also remain to be defined.

In this lecture, data are presented from a series of task based and resting state studies in those addicted to nicotine and cocaine. A distinction is made between the acute effects of drug in dependent individuals (state-like) and those trait-like alterations that may or may not be modulated by acute intoxication. Deficits in reward processing have been found in the striatum, while response inhibition alterations are manifest with hypoactivity in dorsal anterior cingulate (dACC). Resting state functional connectivity studies implicate an impaired dACC - striatal circuit in nicotine addiction whose strength is inversely proportional to dependence severity. Further, this circuit is modulated by a specific alpha 5 nicotinic receptor polymorphism, is related to alterations in response inhibition striatal activation, and passes through an impaired white matter tract. Cocaine dependent individuals demonstrate impaired connectivity in specific MCL pathways compared with healthy matched control subjects, which may be related to impaired reward processing and striatal hypoactivity. Finally, cue-induced craving is well known to influence subsequent drug seeking and taking. These salient cues activate a medial frontal-limbic cortical circuitry that may serve as a biomarker of relapse.