

## **Brain Imaging: from Molecules to Behavior**

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It is estimated that approximately 50% of the vulnerability to addiction is accounted for by genetics. However, addiction is a complex disorder that involves interactions between a wide array of biological and environmental variables. From epidemiology data we have learned that addiction starts in childhood and adolescence, that is, it strikes a brain that is still under development. As an example, it is known that the anterior cingulate gyrus, a region responsible for inhibition, continues growing in humans through about age 21, in other words, as the person matures, his/her ability to say 'no' increases. In looking for the possible molecular determinants of the role of cingulate cortex in inhibition, Dr. Volkow and colleagues used fMRI to test the influence of the monoamine-oxidase A (MAO A) enzyme genotype in the response to the word "No" in normal controls, and found that compared with subjects with the allele for the higher concentration of MAOA, carriers of the allele encoding low concentrations of MAOA show reduced cingulate activity. As with many other polymorphisms, the functional relevance of these findings is to be determined, but is a good approach to understand the role of genes in cognitive control and vulnerability to addiction. Typically, addicted persons develop a stubborn craving for drugs, which is unrelated to their initial euphoric properties. Large, rapid increases in dopamine function are associated with those initial rewarding effects, while the addicted state is characterized by significant decreases in brain dopamine activity. Such decreases are associated with dysfunction of prefrontal regions including orbitofrontal cortex and cingulate gyrus. Imaging studies have also shown that the number of dopamine receptors in the brain reward circuits is decreased in addicts. Although it is still early and controversial data, two polymorphisms of the D2DR –Taq1A and C957T- have been implicated to D2 receptors availability in the striatum. These findings, along with abundant additional evidence, have helped researchers to identify the neurochemical and neuroanatomical regions subserving reward, motivation, memory and cognitive control, along with numerous neurotransmitters and neuropeptides involved in the serious social and medical problem of addictive behaviors.