Drug addiction is clinically defined in behavioral terms. The Diagnostic and Statistical Manual-IV of the American Psychiatric Association defines “substance dependence” as a maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by three or more of the following criteria: tolerance, withdrawal, excessive use, inability to cut down, a great deal of time spent in procuring or recovering from its effects, important aspects of the individual’s life are reduced or ignored, and use continues despite ramifications. Examination of the neurobiological underpinnings of drug dependence and the consequences of drug dependence have been a constant focus of research for the past 70 years (in the case of opiate dependence). Initial studies focused on the ability to measure physical dependence on opiate drugs. Once it was determined that withdrawal syndromes could be reliably produced for opiates, alcohol, and other sedative-hypnotic drugs, dependence was often seen in physical terms although a second avenue of research, behavioral pharmacology, also emerged. The field of behavioral pharmacology developed to characterize the effects of drugs of abuse in human subjects and animal species. At this point, dependence was characterized as being of both physical and psychological natures, reflecting body-mind dualism. One of the global conclusions of the fields of behavioral pharmacology and neuroscience was that self-administration of drugs was a learned behavior with a biological basis.

A major tenet of neuroscience is that chronic administration of drugs of abuse produces long-term changes in brain function and that dependence is one of the potential consequences of such long-term administration. This concept has been studied at the molecular, cellular, brain system, and whole organism levels. Neuroimaging technologies have made unique, major contributions characterizing the effects of drugs of abuse and the consequences of such drugs on brain function. Studies using positron emission tomography (PET) have characterized the effects of acute administration of drugs of abuse (London et al., 1990); the effects of long-term polysubstance abuse on regional cerebral glucose utilization (Stapleton et al., 1995), and exposure to provocative stimuli associated with drug use in cocaine-dependent subjects (Grant et al., 1996) on regional cerebral glucose utilization. Acute administration of cocaine, for example, reduced glucose metabolism. Polysubstance abusers show a reduction in glucose metabolism in occipital areas. When metabolic rate for each region was normalized, higher glucose utilization was demonstrated in the prefrontal and temporal areas. Interestingly, magnetic resonance imaging showed reduced brain volumes in the prefrontal cortex in polysubstance abusers as compared with corresponding values in a comparison group of subjects who did not abuse drugs (Xiu et al., 1998). Stimuli associated with cocaine intake produced metabolic increases in the amygdala, parahippocampal gyrus, and dorsolateral prefrontal cortex in cocaine using subjects (Grant et al., 1996). The latter two structures are involved in explicit memory whereas the amygdala may subserve incentive-motivational aspects of drug craving. The metabolic increases were correlated to craving reported in the subjects. The results suggest activation of a medial temporal lobe/prefrontal circuit is associated with the processing of drug-related stimuli leading to a craving state.

Another major approach has used PET to evaluate changes in dopamine system following chronic cocaine exposure. These studies specifically assessed the effects of long-term cocaine abuse on changes in dopamine release following pharmacological challenge (Volkow et al., 1997), and dopamine receptor systems in abstinent cocaine-dependent subjects (Volkow et al., 1990). Dopamine release was compromised in cocaine-dependent subjects and reduced numbers of D2 dopamine receptors have been reported. Glucose metabolism in cocaine-abstinent subjects has been correlated to changes in dopamine receptor number in brain regions, which receive cortical projections of the dopamine system (Volkow et al., 1996).

Recently, functional magnetic resonance imaging has been used to determine brain regions involved in the high and craving that follows cocaine administration (Breiter et al., 1997). These results will be compared with those seen using PET technology.

References:


