Drug seeking specific molecular responses in mesocorticolimbic brain areas

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The development of drug addiction involves repeated drug taking, in which learned associations between the reinforcing effects of the drugs and environmental stimuli (cues) are established. Brain areas implicated in this learning process also mediate motivated behaviors towards natural reinforcer seeking and include the striatum and connected prefrontal cortical areas. It is well established that these areas undergo persistent neural adaptations as a consequence of repeated drug taking. There is increasing evidence that separate neuronal circuitries in these areas mediate processing of information regarding drug vs. natural reinforcers[1]. Therefore, formation of stimulus-reward associations involving drug reinforcers may result in unique neuronal reactivity in the aforementioned areas compared to stimulus-reward associations involving natural reinforcers. This study addresses whether unique forms of neuronal reactivity are associated with cue-induced (conditioned) drug (heroin) seeking as compared to natural reinforcer (sucrose) seeking. Molecular responses to a presentation of an identical heroin or sucrose cue will be investigated in major striatal and prefrontal cortical regions by tissue sampling and measuring immediate early gene (IEG) activity marker levels with real-time quantitative PCR (qPCR). So far, we have identified unique IEG expression patterns in the nucleus accumbens shell with regards to cue-induced heroin seeking compared to sucrose seeking, namely in the induction of c-fos transcripts, suggesting that heroin seeking is associated with enhanced and unique neuronal reactivity in that region. Investigation of other IEG transcripts, such as those whose products mediate neuronal signaling/structure, such as homer1a, arc, and mkp-1 are underway.

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