

Effects of Adolescent Exposure to Methylphenidate and Amphetamine on Conditioned Place Preference in Adulthood

There is a steady increase in prescription misuse and abuse of ADHD medications in adolescence. Adolescence is a time of continued, but sexually dimorphic, brain maturation, especially in the mesocorticolimbic dopaminergic pathways. Since ADHD medications directly affect these pathways, exposure to them may cause neural alterations manifested as long-term behavioral alterations in adulthood. In previous studies, our lab uncovered drug by sex effects in adult behavioral cross-sensitization after adolescent methylphenidate (MPD) or amphetamine (AMPH) exposure. Behavioral sensitization is a hallmark of neuroplasticity, while conditioned place preference (CPP) directly assesses shifting reward values and neuroplasticity. We hypothesize that adolescent exposure to MPD and AMPH during early adolescence will induce drug- and sex-specific effects in CPP in adulthood, indicative of alterations in the rewarding value of future drug use. Adolescent male and female C57Bl/6J mice ($n = 72$) received daily i.p. injections of 1mg/kg AMPH, 10mg/kg MPD, or saline. In adulthood, place preference was induced to 1mg/kg METH over 10 days to establish a pairing between the drug and a distinct environment. Increases in time spent in the drug-paired environment at post conditioning in the absence of the drug demonstrates CPP, while subsequent measurements of CPP assess the extinction and strength of this learned association towards a model of relapse susceptibility. Preliminary results suggest adolescent drug exposure by sex interaction effects on both the establishment of and extinction of CPP. These data will determine the extent of shifting reward values of stimulant drugs after abusive, adolescent ADHD drug exposures.

Key words: neuroplasticity, methylphenidate, amphetamine, adolescence, addiction, conditioned place-preference