

Drug and sex specific alterations in dopamine receptor expression following adolescent exposure to methylphenidate

Sean D Clayton^a, Usry ME^a, White RH^a, Nazerian SD^a, Shanks RA PhD^a, SA Lloyd PhD^b

^a*Department of Biology, University of North Georgia, Dablonaga, GA, USA*

^b*Department of Psychological Science, University of North Georgia, Dablonaga, GA, USA*

Keywords: dopamine, methylphenidate, adolescent, plasticity, dopamine receptors, DAT, VMAT2

Abstract

The prevalence of ADHD diagnosis in pediatric patients increases every year, which leads to the misuse, diversion, and abuse of psycho-stimulant medications, especially Ritalin[®]. Methylphenidate (MPD), the active ingredient in Ritalin[®], increases dopamine (DA) release in synapses. DA and its receptors (D1-5) play essential roles in human physiology, including the regulation of reward-motivated behavior and neuroplastic events. Our lab previously demonstrated that adolescent MPD exposure leads to long-term behavioral sensitization, but only in females. This study investigates the mechanism by which these behavioral changes occur. Adolescent C57Bl/6J mice were treated with 10-mg/kg MPD or an equal volume of saline (SAL) for 10 days to model chronic abuse during adolescence. The prefrontal cortex (PFC) and striatum (STR) were micro-dissected, and the RNA was isolated. Real-time PCR was used to quantify MPD-induced mRNA expression changes in D1, D2, D3, D4, D5, DAT and VMAT2 using experimental samples standardized to an internal control (18S). No expression differences were seen in D2, D3, D4, D5, DAT or VMAT2 ($p > .05$). However, there was a treatment-dependent down-regulation in the PFC and a significant sex by treatment-dependent down-regulation in the STR in D1 expression ($p < .05$) with MPD-treated females showing the greatest down regulation. Our data suggests that reduced D1 expression alters DAergic signaling events, which may contribute to plasticity and subsequent changes in adult behavior indicative of addiction observed in adolescently MPD-exposed females. Therefore, this data may have important clinical implications in the treatment and diagnosis of adults with a prior history of MPD abuse.