Adolescent Atomoxetine Treatment in a Rodent Model of ADHD: Effects on Cocaine Self-Administration and Dopamine Transporters in Frontostriatal Regions.

Somkuwar SS, Jordan CJ, Kantak KM, Dwoskin LP.

Department of Pharmaceutical Sciences, College of Pharmacy, University of Kentucky, Lexington, Kentucky, USA.

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Cocaine abuse and attention deficit/hyperactivity disorder (ADHD) are often comorbid. Preclinical research indicates that medial prefrontal (mPFC) and orbitofrontal (OFC) cortices are important neural substrates for both disorders. Using the spontaneously hypertensive rat (SHR) model of ADHD, we reported that adolescent treatment with the stimulant methylphenidate, a dopamine (DAT) and norepinephrine (NET) transporter inhibitor, enhanced cocaine self-administration during adulthood, and was associated with increased DAT function in mPFC. The current study investigates the effects of atomoxetine treatment, a selective NET inhibitor, during adolescence on cocaine self-administration and on DAT function and cell-surface expression in mPFC and OFC during adulthood. SHR acquired cocaine self-administration faster than Wistar-Kyoto and Wistar. Across cocaine doses, SHR earned more cocaine infusions and had higher progressive-ratio breakpoints than Wistar-Kyoto and Wistar, demonstrating that the SHR phenotype models comorbid ADHD and cocaine abuse. Prior atomoxetine treatment did not augment cocaine self-administration in SHR, but acquisition was enhanced in Wistar-Kyoto. No strain differences were found for DAT kinetic parameters or cellular localization in the vehicle controls. Atomoxetine did not alter DAT kinetic parameters or localization in SHR mPFC. Rather, atomoxetine decreased Vmax and DAT cell surface expression in SHR OFC, indicating that inhibition of NET by atomoxetine treatment during adolescence indirectly reduced DAT function and trafficking to the cell surface in OFC specifically in the ADHD model. Thus, atomoxetine, unlike methylphenidate, does not enhance vulnerability to cocaine abuse in SHR and may represent an important alternative for teens with ADHD when drug addiction is a concern.