

Abstract View

CHRONIC L-DOPA ADMINISTRATION IN VMAT2 +/- KNOCKOUT MICE

[M.E. Reveron*](#); [K. Savelieva](#); [J. Tillerson](#); [G.W. Miller](#)

Pharmacology and Toxicology, University of Texas at Austin, Austin, TX, USA

It is unclear whether L-DOPA therapy exacerbates dopaminergic damage in Parkinson's disease. In this study, we examined the effects of chronic L-DOPA in an animal model that exhibits an impaired ability to sequester dopamine and an increased vulnerability to dopaminergic toxins (VMAT2 heterozygote knockout mice, VMAT2 +/-). VMAT2 +/- mice have been shown to be more sensitive to the neurotoxic effects of MPTP and methamphetamine. In this study, we subjected these mice to long-term and repeated administration of L-DOPA (L-DOPA (50mg/kg) and carbidopa (5mg/kg) i.p., t.i.d. for 28 days) and examine neurochemical and behavioral changes. An increase in locomotor activity (movement and climbing) was observed 20 minutes following a single injection in the VMAT2 +/- mice but not in the VMAT2 +/+ mice. Biochemical analysis revealed an increase in striatal dopamine transporter (DAT) protein expression in the VMAT2 +/- mice, while VMAT2 levels (an index of terminal integrity) remained unchanged. These data indicate that chronic L-DOPA therapy in a model of impaired dopamine storage leads to sustained increases in striatal dopamine, an appropriate compensatory response, and a lack of overt neurotoxicity. (Supported by NIH NS-37031 and ES-07784)