Chronic Developmental Manganese Exposure Affects Behavioral Phenotypes in Dopamine Transporter Mutant Mice

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Overexposure to manganese (Mn) through contaminated water or occupational environment has been shown to result in dopaminergic dysfunction and overall neurotoxicity in the human brain [1]. The synaptic dopamine (DA) system primarily drives motivation, attention, and behavioral learning. Disruptions to dopaminergic signaling via the DA transporter (DAT) can play a causal role in autism spectrum disorder (ASD) and attention-deficit hyperactivity disorder (ADHD) development [2]. In mice, the DAT mutation T356M closely reflects behavioral indicators of autism and ADHD, such as repetitive behaviors, loss of social novelty, and hyperlocomotion [1]. Additionally, excess manganese intake in mice is positively correlated with dopamine dysfunction [2], and exposure to manganese during adolescence can drive expression of a hyperactive phenotype [3]. Groups of wild type and heterozygous DAT T356M mice were exposed to excess dietary manganese and compared to mice that received a control diet. Locomotor activity and spontaneous behavioral assessments were recorded and post-mortem brain levels of manganese, DAT, and tyrosine hydroxylase (TH) were analyzed [4]. Results from locomotor activity assessments show that male mice exposed to a high Mn diet become generally more hyperactive, while females become generally more hypoactive. Additionally, spontaneous behavior assessments demonstrated that the effects of high-Mn supplementation diminish over time, which could be attributed to age or homeostatic adaptations. Finally, these findings suggest that genotype effects may decrease with maturation.

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