

**Abstract View****FUNCTIONAL NEUROGENOMIC AND BIOCHEMICAL ANALYSES OF ENZYMATIC DIFFERENCES IN DOPAMINE TRANSPORTER KNOCKOUT MICE**

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Previous studies have reported significant decreases in the levels of tyrosine hydroxylase in the brains of the dopamine transporter knockout (DAT KO) mouse model. In an attempt to elucidate the neurochemical adaptations in these knockout mice, the activity and protein levels of tyrosine hydroxylase (TH), the rate-limiting enzyme in the biosynthesis of DA, were determined. Enzyme activity was measured in caudate/putamen homogenates from wild-type (n=6) and knock-out mice (n=6). We observed a decrease in caudate TH activity in the DAT KO mice, that corresponded to a decrease in TH immunoreactivity. These data support previous observations on TH regulation in a chronic pharmacological blockade of the DAT (Freeman *et al.*, *Drug Alcohol Depend.* 2000 61:15-21.) and supplement the findings in the DAT KO itself (Jaber *et al.*, *Eur J Neurosci.* 1999 11:3499-511).

To illuminate global compensatory changes in mice lacking the dopamine transporter, hybridization array analysis was performed in duplicate on the caudate/putamen of wild-type and knockout mice. Mitogen activated protein kinase 1, NMDA receptor 2B, regulator of G-protein signaling 4, GABA transporter 1, and shab family potassium channel were induced by greater than 50% on both sets of arrays. These genes may represent mechanisms to compensate for the inability to reuptake dopamine.

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