

Abstract View**BIOCHEMICAL ANALYSES OF TYROSINE AND TRYPTOPHAN HYDROXYLASE IN THE R6/2 MOUSE MODEL OF HUNTINGTON'S DISEASE.**

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Previous studies have reported significant decreases in the levels of two biogenic amines, dopamine (DA) and serotonin (5-HT), in the brains of the R6/2 mouse model for Huntington's disease (HD). These results are in conflict with earlier post-mortem studies. In an attempt to elucidate the neurochemical aberrations in HD, the activities of tyrosine hydroxylase (TH) and tryptophan hydroxylase (TPH), the rate-limiting enzymes in the biosynthesis of DA and 5-HT respectively, were determined with radioenzymatic assays. Enzyme activity was measured in striatal and brain stem homogenates from 12 week old, symptomatic R6/2 mice compared with asymptomatic littermate control mice. We observed a 43% decrease in striatal TH activity in the R6/2 mice ($p < 0.001$), while no changes in TH immunoreactivity were seen. In the brain stem, TPH activity was decreased by 86% ($p = 0.005$) without a change in TPH immunoreactivity. Therefore, it appears that the loss of TH and TPH activities is not merely due to cell loss. Michaelis-Menten constants of TH and TPH for their co-substrate tetrahydrobiopterin (BH₄), revealed changes in the affinity of both enzymes for BH₄. These biochemical changes may help explain the functional consequences of HD and provide insights into new targets for pharmacotherapy.

Supported by: RO1 GM-38931 (to K.E.V.), NINDS NS-38106 (J-H.J.C), HDSA Coalition for the Cure, Glendorn Foundation)



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