

Increased glutathione levels in cortical and striatal mitochondria of the R6/2 Huntington's disease mouse model

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Huntington's disease (HD) is a progressive neurodegenerative disease characterized by a severe neuronal loss that occurs primarily in the neostriatum. It has been postulated that mitochondria dysfunction and oxidative stress may play significant roles in the etiology of the disease. Indeed, markers of oxidative stress damage have been detected in the brains of HD patients and in mouse models of HD. In this study, we evaluate the changes in the levels of the potent, endogenous antioxidant glutathione and enzymes involved in its metabolism or recycling in the cortex and striatum of an extensively studied HD mouse model (R6/2). In both cortex and striatum, the levels of cellular glutathione were not significantly different in the R6/2 mice when compared with littermate wild type controls. Remarkably, the levels of glutathione were significantly increased in mitochondria isolated from the cortex and striatum of R6/2 mice when compared with wild type control mice. This specific increase in the levels of glutathione in mitochondria suggests that a compensatory mechanism is induced in the R6/2 mice to protect against an increase in oxidative stress in mitochondria.

