Neurodegenerative Disorders: GSH Prevention of Neuronal Death.

GSH is an important protector of energy metabolism (mitochondrial function) during periods of oxidative stress.⁵⁴ Dopaminergic neurons are very sensitive to changes in the internal oxidant buffering capacity of the cell caused by reductions in GSH levels that can lead to disruption of calcium homeostasis and cell death.⁵⁵ GSH, but not vitamins C or E, protects human neural cells from dopamine-induced apoptosis.⁵⁶ Notably, dopamine treatment during GSH depletion is documented to produce defects in psychomotor behavior in a laboratory animal model.⁵⁷

Oxidative stress has been implicated in various neurodegenerative disorders and may be a common mechanism underlying various forms of cell death including excitotoxicity, apoptosis and necrosis. Bains and Shaw⁵⁸ present evidence for a role of oxidative stress and diminished GSH in Lou Gehrig's disease (ALS), Parkinson's disease, and Alzheimer's disease. GSH modulation may prove to be beneficial in spinal cord injury,⁵⁹ multiple sclerosis⁶⁰ and stroke.^{61,62} Since cysteine supplementation increases GSH it may hold promise as a method to modulate neurodegenerative diseases.

- Zeevalk, G.D., Bernard, L.P., Nicklas, W.J. Role of oxidative stress and the glutathione system in loss of dopamine neurons due to impairment of energy metabolism. J. Neurochem. 70(4): 1421-1430, Apr. 1998.
- 55. Jurma, O.P., Hom, D.G., Andersen, J.K. Decreased glutathione results in calcium-mediated cell death in PC12. Free Radic. Biol. Med. 23(7): 1055-1066, 1997.
- 56. Gabby, M., Tauber, M., Porat, S., Simantov, R. Selective role of glutathione in protecting human neuronal cells from dopamine-induced apoptosis. Neuropharmacology 35(5): 571-578, May 1996.
- 57. Shukitt-Hale, B., Denisova, N.A., Strain, J.G., Joseph, J.A. Psychomotor effects of dopamine infusion under decreased glutathione conditions. Free Radic. Biol. Med. 23(3): 412-418, 1997.
- 58. Bains, J.S., Shaw, C.A. Neurodegenerative disorders in humans: the role of glutathione in oxidative stress-mediated neuronal death. Brain Res. Brain Res. Rev. 25(3): 335-358, Dec. 1997.
- 59. Lucas, J.H., Wheeler, D.G., Emery, D.G., Mallery, S.R. The endogenous antioxidant glutathione as a factor in the survival of physically injured mammalian spinal cord neurons. J. Neuropathol. Exp. Neurol. 57(10): 937-954, Oct. 1998.
- Singh, I., Pahan, K., Khan, M., Singh, A.K. Cytokine-mediated induction of ceramide production is redox-sensitive. Implications to proinflammatory cytokine-mediated apoptosis in demyelinating diseases. J. Biol. Chem. 273(32): 20354-20362, Aug. 7, 1998.
- Weisbrot-Lefkowitz, M., Reuhl, K., Perry, B., Chan, P.H., Inouye, M., Mirochnitchenko, O. Overexpression of human glutathione peroxidase protects transgenic mice against focal cerebral ischemia/reperfusion damage. Brain Res. Mol. Brain Res. 53(1-2): 333-338, Jan. 1998.
- Skaper, S.D., Ancona, B., Facci, L., Franceschini, D., Giusti, P. Melatonin prevents the delayed death of hippocampal neurons induced by enhanced excitatory neurotransmission and the nitridergic pathway. FASEB J. 12(9): 725-731, June, 1998.