

The Effect of Oxidative Stress on Cytoskeletal Structures of Human Neuron Cells

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Oxidative stress is the major cause of injury that leads to a number of neurodegenerative diseases. Increasing number of studies suggest the involvement of multiple processes in the pathogenesis of cell injury during oxidative stress. Cytoskeleton disruption is known to be one such process by which oxidative stress disrupts cellular function. However we still do not have a detailed understanding of the mechanism by which the cytoskeletal disruption takes place. This study compares and contrasts the effect of oxidative stress on the three major cytoskeleton filaments, actin, microtubule and vimentin. Human cortical neuronal cell line (HCN2) was treated with 100 μ M tertiary butylhydroperoxide (a free radical generating neurotoxin) for 1, 3 or 6hrs. The cytoskeletal filament distribution and structure was studied by immunofluorescence studies and the protein levels were quantitated by SDS-PAGE and Western Blot studies. Under conditions of oxidative stress there was a loss of actin and microtubule filaments as compared to control cells. There was also some rearrangement and slight loss of vimentin filaments under similar treatment conditions. A loss in total amounts of actin, tubulin and vimentin was obtained by Western blot analysis when compared to control neurons. Further studies were done in order to understand if this loss in protein levels was directly modulated by down regulation at the gene level. DNA Microarray studies were done under similar treatment conditions and the gene levels of all three cytoskeletal proteins were down regulated. This study indicates that free radical generation in human neurons results in down regulation of cytoskeletal genes and results in disruption of the cytoskeletal filaments. Future studies will be done to understand the involvement of the other cytoskeletal-associated proteins so that we can design effective drug molecules to treat neurodegenerative diseases.