One pathway involves L-DOPA directly entering the cells to convert dopamine through AADC activity; in this step, TH activity is inhibited. The other pathway involves L-DOPA activating TH to enhance dopamine biosynthesis by second-messenger signaling pathways such as the D1 receptors–cAMP–PKA system.

P.76

THE INFLUENCE OF α-SYNUCLEIN ON SH-SY5Y CELLS TREATED WITH ROTENONE

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α-Synuclein is the primary structural component of the Lewy bodies and has been postulated to play a central role in the pathogenesis of Parkinson's disease (PD). Although the etiology of PD is still not fully understood, epidemiologic studies showed that environmental factors shared with the common mechanisms of resulting in α-synuclein aggregation by inhibiting complex I of mitochondria and leading to oxidative stress. To investigate the effects of α-synuclein, we used human dopaminergic SH-SY5Y cells transfected with α-synuclein-enhanced green fluorescent protein (EGFP) and treated with rotenone. Cell viability and oxidative stress were detected with MTT assay and DCF assay. Superoxide dismutase (SOD) activity was assessed with xanthine peroxidase method. Cell apoptosis was detected with flow cytometry. Results showed that α-synuclein gene was constantly over-expressed in these cells. After treatment with rotenone, both cell viability and complex I activity in these cells were reduced in a concentration-dependent manner and oxidative stress was also found in these cells. Compared with SH-SY5Y cells, SOD activity in α-synuclein overexpression cells were increased distinctly ($P<0.05$) and α-synuclein overexpression significantly attenuated rotenone-induced cell apoptosis. These results suggest that the α-synuclein overexpression in SH-SY5Y cells has a tendency to partially resist oxidative stress induced by rotenone and this response may assist cell survival.

P.77

STERYL GLYCOSIDE AS A NOVEL ENVIRONMENTAL TOXIN INVOLVED IN THE ETIOPATHOGENESIS OF %0BALS-PDC

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There is increasing evidence that suggests environmental toxins are involved in the pathogenesis of neurodegenerative diseases. Epidemiological studies have correlated the cluster of the Guamanian neurological disorder, ALS-PDC to consumption of seeds from cycad plant. Fractionation of cycad seeds suggested that steryl glycosides may be the neurotoxic component. Steryl glycosides are common in the environment and can be acquired from plants, various bacteria, and mammalian self synthesis. *In vivo* studies with dietary exposure of sterol glucosides to mice showed reduction in neuronal numbers accompanied by gliosis. To further characterize the toxic effects of steryl glycosides, we treated cholesterol glucosides (CG) to NSC34 cells, a motor neuron derived cell line. NSC34 cells treated with increasing doses of CG for up to 7 days showed a dose- and time-dependent decrease in cell viability. CG treatment for 3 days at 250 μM induced over 50% cell loss. Among the dying cell, we observed that some cells lay out long, sustained processes that are not observed in the control cells. These processes stained positively with β-tubulin III and the heavy subunit of the neurofilament protein. Furthermore, these processes exhibit axonal beading and are immunoreactive for phosphorylated tau. The axonal beading did not colocalize with a DNA-binding protein, TDP-43, which has been found to translocate to the cytoplasm during neurodegeneration in frontotemporal-dementia and sporadic ALS. Our finding suggests that steryl glycoside, such as those derived from plants and bacteria, have neurotoxic properties and may potentially be involved in the etiopathogenesis of age-related neurodegenerative diseases.

P.78

CYTOTOXICITY OF PARAQUAT IN MICROGLIAL CELLS: INVOLVEMENT OF THE PKC- AND ERK 1/2-DEPENDENT NADPH OXIDASE

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Parkinson's disease (PD) is a movement disorder characterized by a progressive loss of dopaminergic neurons in the substantia nigra. Excess reactive oxygen species production has been implicated as a crucial mechanism underlying the pathogenesis of PD. Exposure to paraquat, a widely used herbicide with structure similar to the dopaminergic neurotoxin, 1-methyl-4-phenylpyridinium (MPP^+), has been shown to produce PD-like symptoms. Despite previous focus on the dopaminergic neurons and signaling pathways involved in their cell death, recent studies have implicated microglial cells as a source of ROS production leading to damage to neighboring neurons. In this study, we examined the source of ROS and the underlying signaling pathway for paraquat-induced cytotoxicity to BV-2 microglial cells. Paraquat-induced ROS production in BV-2 cells was accompanied by translocation of p67phox, the cytosolic subunit of NADPH oxidase, to the membrane. Paraquat-induced ROS production was inhibited by NADPH oxidase inhibitors, apocynin and diphenylene iodonium (DPI). Apocynin and DPI also rescued cells from paraquat-induced