Online Proceedings

POSTER SESSION 3

Balcony, Easel 105

2:30 PM to 4:00 PM

Examining Differences in Neuron Manganese Sensitivity when Co-Cultured with Regional Astrocytes

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Exposure to manganese (Mn) causes a neurodegenerative syndrome with clinical manifestations of Parkinsonism (PS) similar to Parkinson's disease (PD). Although both PD and Mn-induced PS feature movement dysfunction resulting from decreased striatal dopamine, pathologically, Mn-induced PS is thought to be related to striatal degeneration, while in PD, dopaminergic neuron bodies residing in the substantia nigra pars compacta are largely affected. Recent evidence has suggested that astrocytes, glial cells that play a vital role in maintaining homeostasis such as uptake and release of important molecules like precursors for neurotransmitters, may play a vital role in neuronal survival in PD and PS. In order to determine whether the regional differences in sensitivity to Mn are conferred by inherent differences in astrocytes from these brain regions I examined the role of such astrocytes in neuron survival. Contact co-cultures of two neuron-like immortalized cell lines, MES and SH-SY5Y cells, were made with astrocytes from the ventral mesencephalon (vm), striatum (str), and cortex (ctx). These were treated with 10μM and 100μM of Mn and stained for the markers MAP2, TH, and GFAP, imaged, and neurons were counted. Based on previous results, MES cells grown with str astrocytes are expected to have a lower survival rate when treated with Mn, versus those plated with vm and ctx astrocytes. If this trend is observed in the separate SH-SY5Y cell line, this would suggest other neuron-like cell lines and dopaminergic neurons respond similarly to Mn. By examining if Mn affects astrocytes, and in turn neuron survival, this could not only elucidate the pathogenesis of Mn-induced PS, but also elucidate the region specific astrocyte-neuron relationships in the brain.

POSTER SESSION 3

Balcony, Easel 104

2:30 PM to 4:00 PM

Interaction Between Astroglial Mortalin and α-Synuclein: A Potential Interaction Involved in the Pathogenesis of Parkinson's Disease and Manganese-Induced Parkinsonism

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Exposure to high levels of manganese (Mn) causes a form of Parkinsonism (PS) with clinical features similar to, but distinguishable from, Parkinson's disease (PD). Though the clinical phenotype of Mn-induced PS is similar to PD, PD is characterized by neurodegeneration in the substantia nigra, whereas Mn-induced PS features striatal neurodegeneration. Mortalin, an important mitochondrial chaperone protein involved with the response to oxidative stress, has shown to be downregulated in PD. Moreover, in recent studies we found mortalin expression to be decreased in striatal astrocytes of Mn exposed miners and in astrocytes of the substania nigra of PD patients. Additionally, we found that in vitro, a reduction in mortalin expression impairs astrocytic protection of neurons. Importantly, Mn-induced astrocyte dysfunction is substantially reduced in cells lacking expression of α-Synuclein (α-Syn), suggesting that their interaction modulates astrocyte function, potentially affecting their neuro-protective role in PS. The interaction between α-Syn and mortalin was investigated in astrocytes isolated from brain regions associated with PD and of Mn-induced neurotoxicity. We employed an animal model of cultured astrocytes from the ventral mesencephalon, striatum, and cerebral cortex to examine this interaction. The cells were treated with 0, 10, or 100 μM Mn, then examined using western blotting and immunofluorescence microscopy. The relative levels of mortalin and α-Syn were then quantified and analyzed. We saw a decrease in the availability of functional astrocytic mortalin with increasing Mn in striatal cells compared to other regions and substantial aggregation of α-Syn, reflecting the astrocytic dysfunction. This study helps bring light to the potentially critical association between mortalin and α-Syn in motor-impaired neurodegenerative diseases and can have important implications for understanding the pathogenesis of α-Syn aggregation and ultimately, PS related neurodegeneration.