J Alzheimers Dis Parkinsonism 2015, 5:2
http://dx.doi.org/10.4172/2161-0460.S1.013

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Neuropathology and pathogenesis of multiple system atrophy: An update

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Multiple system atrophy (MSA) is a rare, rapidly progressive neurodegenerative disorder of uncertain aetiology, presenting with autonomic failure variably combined with parkinsonism, cerebellar dysfunction, and pyramidal signs. The pathological process affects central autonomic, striatonigral and olivopontocerebellar systems showing varying degrees of degeneration that underlie the stratification of the heterogenous disorder into two major clinical variants correlating to the morphological phenotypes of striatonigral degeneration (SND) (MSA-P) and olivopontocerebellar atrophy (MSA-C). The lesions are not limited to these most consistently and severely affected systems, but may involve other parts of the central, peripheral and autonomic nervous system, confirming the multisystem character of MSA. The histological core feature are distinctive glial cytoplasmic inclusions (GCI, Papp-Lantos bodies) containing misfolded α-synuclein (αSyn) within oligodendroglia cells that are required for the postmortem diagnosis of definite MSA. In addition to ectopic deposition of modified αSyn in oligodendroglia and other cells/tissues, oxidative stress, proteasomal and mitochondrial dysfunction, dysregulation of myelin lipids, impairment of oligodendrocyte progenitor cells, and energy failure are important contributors to the pathogenesis of this unique proteinopathy, as shown by various transgenic and other animal models. Although the basic mechanisms of αSyn-triggered gliopathy are not fully understood, neuron-to-oligodendrocyte transfer of αSyn and "prion-like" spreading of synucleinopathy inducing oligodendroglial and myelin dysfunction associated with chronic neuroinflammation. These lesions and recently described frequent occurrence of neuronal inclusions in many regions of MSA brain are finally leading to a system-specific pattern of neurodegeneration, which may act as an emerging template for cause-directed and disease-modifying therapies of MSA.

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Parkinson's disease and movement disorder: Development of a novel human cell model as a model for Parkinson's disease

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Although animal models of Parkinson's disease (PD) involving non-human primates, rodents, dogs, cats and goldfish are still the main approaches used in medical research, there is currently no available animal model that accurately reproduces the human disease. Whereas a range of symptoms might be understood, the causes of human illnesses and their progression are often impossible to identify in animals since the only human models available are post-mortem samples from PD patients. The initiation and progression of the disease in human still remain to be fully characterized. Therefore, there is an imperative need to go back to basics to investigate and understand the mechanism of the events happening prior to the dopaminergic cell death. To this aim, a human dopaminergic cell model was developed from a human neural progenitor ReNcells and to which a neurotoxin 6OHDA was applied to mimic ofthe different stages of human Parkinsonian dopaminergic cell.The aim of this study was to investigate the initiation and progression of the PD at the cellular level while monitoring the production of dopamine. This presentation includes the preliminaryresults of this study which validate our human cellular PD model and the effects of potential inhibitors of the loss of dopamine.

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