New study supports view that Lewy bodies are not the primary cause of cell death in Parkinson's Disease

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The pathology of Parkinson's disease is characterized by a loss of dopamine-producing neurons in the pars compacta of the substantia nigra (SN), an area of the brain associated with motor control, along with the development of α-synuclein (αS) protein in the form of Lewy bodies (LB) in the neurons that survive. The spread of LB pathology is thought to progress along with the clinical course of Parkinson's disease, although recent studies suggest that they are not the toxic cause of cell death. A new study published in The *Journal of Parkinson's Disease* finds no support for a primary pathogenic role of LBs, as neither their distribution nor density was associated with the severity of nigral cell loss.

"We investigated the relationship between nigral dopaminergic cell loss, distribution and density of α-synuclein immunoreactive LBs, and the duration of motor symptoms in 97 patients with Parkinson's disease," explains lead investigator Andrew J. Lees, MD, of Queen Square Brain Bank for Neurological Disorders and the Reta Lila Weston Institute for Neurological Studies, UCL Institute of Neurology, London, UK. "Despite the reasonably close correlation between neuronal density in SN and severity of bradykinesia and rigidity in Parkinson's disease, our results suggest that nigral cell loss is gradual and there is considerable variability, which may explain the clinical heterogeneity."

Researchers confirmed that both neuronal number and density in SN in

Parkinson's disease decrease over time. The density of nigral neurons was estimated to decrease by 2% each year after confirmation of the clinical diagnosis of Parkinson's disease, but showed marked heterogeneity across patients. Some patients with longer duration of illness still had a significant number of preserved nigral neurons at the time of death. An average of 15% of surviving nigral neurons contained LBs and the age-adjusted proportion of LB-bearing neurons appeared relatively stable through the disease duration. "This could be explained by a passive 'one-pass' phenomenon where the LBs appear at the beginning of the disease and then decrease at the same rate as nigral neurons are lost, or alternatively that a dynamic 'turnover' occurs with some LBs continuously produced and destroyed at the same rate," explains Dr. Lees.

Nigral neuron density was unrelated to the Braak PD stage of the disease (i.e. distribution of LBs in the brain) or to cortical LB densities. "In our view, the fact that neither the widespread regional distribution of LBs nor increased cortical LB densities were found directly linked with pars compacta nigral cell loss lends support to the view that they are not the primary cause of the pathological process leading to cell death in vulnerable regions in the brain in Parkinson's disease," concludes Dr. Lees.

More information: The article is "Disentangling the Relationship between Lewy Bodies and Nigral Neuronal Loss in Parkinson's Disease" by Laura Parkkinen, Sean S O'Sullivan, Catherine Collins, Aviva Petrie, Janice L. Holton, Tamas Revesz, and Andrew J. Lees. *Journal of Parkinson's Disease*. 1(2011) 277-286. DOI 10.3233/JPD-2011-11046

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