Duration of Parkinsonism Prior to Dementia is Associated with a Different Pattern of Neuropathological and Neurochemical Substrates in DLB and PDD

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Background: Dementia associated with Parkinson's disease (PDD) and dementia with Lewy bodies (DLB) are common and debilitating syndromes characterized by cortical Lewy bodies. An arbitrary distinction is made between patients presenting with more than a year of Parkinson's disease prior to the onset of dementia (PDD), and those developing parkinsonism and dementia concurrently (DLB). This is the first study to compare neuropathological and neurochemical changes in patients with Lewy body disease and different durations of PD prior to dementia.
Methods: Fifty seven subjects with autopsy confirmed DLB or PD received prospective clinical evaluation during life, including standardized clinical histories and assessments of cognition and parkinsonism. DLB and PD were diagnosed clinically and neuropathologically according to operationalized criteria. Dementia in PD was diagnosed according to the DSM-IIIR dementia criteria based on a clinical interview and cognitive tests.

The severity of plaques was determined using the CERAD guidelines. Braak staging was performed to quantify tangle pathology. Lewy body score, using the principles outlined in the DLB consensus criteria, were assigned in brainstem, limbic and neocortical utilizing α-synuclein staining. To emasure choline acetyltransferase (CHAT), snap frozen blocks of tissue, maintained at -70ºC from the temporal cortex (BA 36, 20) and thalamus were analyzed according to established methods..

Results: 57% were female, mean age (SD) 76.2 (5.7), MMSE closest to death 12.2 (9.2). Significant correlations were evident between plaque severity (CERAD score) , α-synuclein pathology and ChAT (BA36) and the duration of PD prior to dementia, but there was no relationship with Braak staging . Patients with the longest duration of PD prior to dementia had less plaques and less severe α-synuclein pathology, but more severe cortical cholinergic deficits.
Conclusions: In the largest reported cohort of prospectively studied, autopsy conformed DLB and PDD patients, the data strongly support a "continuum" model, and indicate that any arbitrary clinical distinction between DLB and PDD does not reflect the pattern of neuropathological and neurochemical changes.