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Letter to the Editor

Parkinson's Disease and Dementia with Lewy Bodies: One and the Same?

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Dear Editors,

Borghammer et al. [1], in their recent review "Parkinson's Disease and Dementia with Lewy Bodies: One and the Same" emphasize that, when comparing PDD and DLB, neuropathologists generally conclude that no pathologic substrate found at postmortem can reliably differentiate these clinically defined disorders and ultimately finding them indistinguishable. These statements need some serious discussion, based on personal and other recent data about the complex neuropathology of LB diseases, some of which have not been cited by the authors. In an autopsy study of 110 PPD and 78 DLB patients, the latter being significantly younger and showing shorter disease duration (age at death 79.8 vs 83.9 yrs; disease duration 6.7 vs 9.2 yrs), Braak LB stages were significantly higher in the DLB group (mean 5.2 vs 4.4), as were Braak NFT stages (mean 5.3 vs 4.4); Thal Aβ phases were significantly higher in DLB (mean 4.0 vs 3.0) with striatal Aβ plaques in 55% of DLB and less than 10% in PDD. The most significant differences concerned the frequency and severity of CAA (98.7% vs 50% and 2.9 vs 0.73) [2]. In a larger autopsy study of 290 PD patients (100 PDND, 110 PDD and 80 DLB), PDD cases were significantly older at death than both PDND and DLB (mean 83.9 vs 77.9 vs 80.0 yrs), with longest disease duration (mean 14.5 vs 9.2 vs 6.7 yrs). Braak DLB scores increased from PDND to DLB (mean 4.0 vs 4.2 vs 5.2), the same in Braak NFT stages (mean 2.3 vs 4.4 vs 5.2) as well as Aβ phases (mean 1.8 vs. 3.0 vs 4.1); and striatal Aβ pathology stage 3+ (zero in PDND, 5% PDD and 70% DLB). CAA frequency and severity increased from PDND via PDD to DLB (2.4% vs 50% vs 97%; severity 0.3 vs 0.7 vs 2.9) [3]. These and other autopsy cohorts of PDD and DLB patients [4] have shown significant differences between PDD and DLB, most frequently increased striatal Aβ load [5], and significantly more severe both cortical LB and tau load in DLB. The most significant difference between DLB and PDD were the higher CAA frequency and severity in DLB ($p < 0.001$ and $p < 0.01$, respectively) supporting the notion that the morphological distinction between the two phenotypes is not restricted to Aβ deposition in cortex and particularly in striatum, but specifically by the impact of CAA [3, 4]. This showed different pattern of severity, mostly affecting the frontal cortex in DLB and AD, and occipital cortex in DLB [6]. Further differences between PDD and DLB are more severe αSyn load in hippocampal subareas CA 2/3 and entorhinal cortex in DLB, implicating the role of these specific areas in the pathogenesis of DLB [7]. Furthermore, there is different involvement of substantia nigra, with more severe loss of dopaminergic neurons in ventrolateral cell groups in PD but predominant involvement of dorsolateral ones in DLB [8], causing less severe postsynaptic dopaminergic upregulation, while significant preservation of serotonin transporter re-uptake sites in parietal cortex was seen in DLB [9]. Although there is general agreement that both PDD and DLB share both clinical and pathological features and increasing co-pathologies with rising age, there are essential differences as shown above. These facts should be considered despite the recent proposals for a biological re-definition of Lewy

body diseases [10, 11]. On the other hand, many of the neuropathological changes in DLB more closely resemble AD rather than PDD and PD [6] and should be taken into consideration when stratifying patients for clinical trials or designing disease-modifying therapies.

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CONFLICT OF INTEREST

The author declares that he has no conflict of interest.

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