DOES LEVODOPA ACCELERATE THE PATHOLOGICAL PROCESS IN PARKINSON'S DISEASE BRAIN?

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Introduction: Several in vitro studies have suggested that levodopa (L-dopa) might be toxic to dopaminergic neurons and that it can modulate the aggregation process of alpha-synuclein (AS).

Aims: To investigate the relationship between cumulative life-time dose of L-dopa, nigral dopaminergic cell loss and AS-immunoreactive Lewy body (LB) pathology in Parkinson's disease (PD).

Methods: 96 cases of PD with well-documented clinical records relating to antiparkinsonian drug treatment were identified from the Queen Square Brain Bank. Density of pigmented neurons was measured unilaterally in a single section of substantia nigra (SN) with delineation of the dorsal and ventral tiers. Cortical and nigral LB densities were determined using a morphometric approach.

Results: Mean cumulative life-time dose of L-dopa correlated significantly (p< 0.001) with duration of PD in the entire study population (n=96) and it was not possible to disentangle their individual influence on neuropathological findings. This was not the case in a subgroup analysis of younger onset patients with a longer duration of PD (n=40) who showed no significant association between L-dopa and total SN neuronal density (p=0.07), after adjustment for duration of illness. There was, however, an inverse association between L-dopa and neuronal density in the ventral (p=0.02) but not in the dorsal (p=0.27) tier. We found no difference in the L-dopa dose between Braak PD stages (p=0.58). Furthermore, the subgroup analysis showed no relationship of L-dopa dose to either cortical (p=0.47) or nigral (p=0.48) LB density.

Conclusions: Chronic use of L-dopa in PD does not enhance progression of PD pathology.