

THE DEMENTIA OF PARKINSON'S DISEASE IS MAINLY DUE TO CHOLINERGIC DEFICIENCY

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From the neuropathological point of view, the Lewy body pathology is not singular in PD dementia (PDD) brains, but often associated with plaques, tangles and cholinergic deficit. There is an association between longer duration of parkinsonism prior to dementia and less severe cortical alpha-synuclein pathology and lower CERAD plaque scores, but not tangle Braak staging. An unexpected correlation between more pronounced cortical cholinergic deficits and longer duration of parkinsonism prior to dementia was also noted in the same study (Ballard et al., 2006). Furthermore, the cortical cholinergic denervation in PD is associated with depressive symptoms (Bohnen et al., 2007) and depression seems to be a risk factor for dementia (Geerlings et al., 2008). According to Braak's staging of Parkinson's disease, the nucleus basalis of Meynert, where the majority of the cholinergic cortical projections originate, is affected early, in stage III – at the same time with substantia nigra (Braak et al., 2003). However, in a majority of PD cases to which Braak's staging seems to apply, the cognitive impairment is detected significantly later than motor signs. There could be at least two explanations for this clinical evolution: either the cholinergic deficit is longer compensated as compared to the dopaminergic deficit or some other pathology is necessary to arise beside the cholinergic deficit in order to trigger the cognitive decline. Meanwhile, the increase of cholinergic signalling obtained with cholinesterase inhibitors is the only significant therapy of PDD, even though the size of the effect on cognition is small, probably due to the fact that at this time of the disease evolution many of the cholinergic neurons are already lost, so the total amount of acetylcholine that can be preserved is low.

In conclusion, there are many data, from basic studies to clinical effects, supporting the importance of cholinergic deficiency in PDD pathogenesis. Nevertheless, other pathologic factors seem to play an additive role in triggering the cognitive decline in PD on the background of an already existing decreased cholinergic cortical signalling, which can be considered a prerequisite for PDD.

References

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