A sharper image of dementia with Lewy bodies

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English abstract

Dementia with Lewy bodies is a common, but relatively understudied cause of dementia. Early diagnosis and disease mechanisms are relevant topics. In this thesis we studied several aspects of neurophysiological and imaging techniques that are commonly used in the diagnostic process of DLB.

The main findings of this thesis are:

- A normal ^{123}I-FP-CIT SPECT does not exclude the diagnosis DLB, and can become abnormal over time with as disease progresses
- EEG shows good diagnostic performance to discriminate between DLB and AD, also in the prodromal (MCI) stage of the disease
- EEG characteristics are related to progression from MCI to dementia in DLB
- Concomitant AD-pathology in DLB probably worsens disease manifestation by more severe atrophy, especially in the hippocampus
- Global and posterior cortical atrophy is seen in 'pure' DLB
- Concomitant AD-pathology does not influence ^{123}I-FP-CIT DAT-binding and EEG
- EEG theta/alpha ratio may be predictive of cholinesterase inhibitor response

With this thesis we aimed to contribute to 'a sharper image' of DLB, to help the clinician with interpretation of diagnostic test results and patients to be diagnosed early and accurately. Despite the absence of disease-modifying therapy, early diagnosis is of great importance to patients and caregivers in order to understand and receive recognition for their complaints and to receive appropriate care and symptomatic treatment. Several new research questions have arisen and been mentioned in the separate chapters and throughout the discussion. Development of a reliable alpha-synuclein biomarker (e.g. blood, csf or PET) would be a large contribution to the field of the Lewy body diseases. Until then, the indirect biomarkers are of value for diagnostic and research purposes. Multimodal and/or automated analysis may be of additional aid. Biomarkers for neurotransmitter deficiencies or synaptic function (e.g. EEG,

nuclear imaging) are of importance in relation to clinical symptoms and (symptomatic) treatment response.

Further pre-clinical and pathological research will be needed to unravel the contributions and interactions of different proteinopathies. AD-pathology has effects on the disease course of DLB and when disease-modifying therapy for AD is available, this medication should also be studied in DLB-patients with concomitant AD-pathology. Next to alpha-synuclein, preservation or regeneration of synapses may be a focus for future therapy in DLB.