Is Braak staging true for all Parkinson disease?

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Braak et al. [1] proposed that cases with Lewy pathology (LP) in peripheral nervous system, spinal cord and brain stem should be considered as prodromal Parkinson disease (PD), suggesting a hypothesized progression of PD pathology. While most studies assessing typical PD cases show that the vast majority (80–100%) fit the Braak staging scheme, a number of pathological studies argue against it. People with incidental Lewy body disease and PD can show LP in SN or other brain areas without involvement of the DMV [2]. The Braak staging is mainly valid for PD patients with young onset, long duration and predominant motor symptoms, but not for others, e.g., late onset and rapid course PD [3]. 10-15% of PD cases that are associated with genetic mutations show a pattern of LP that is quite distinct from that of idiopathic PD, fitting the Braak staging scheme [4]. The hypothesized cell-to-cell transmission [5] for PD has produced a paradigm shift in research into the propagation of the majority of late-life neurodegenerative conditions. In view of the currently discussed "prion-like" spreading of pathologic α-synuclein, the validity of Braak staging of LP and its relationship to neurodegeneration in various subtypes of PD warrants further study. Key references: Braak H, et al., Neurobiol Aging 2003;24:197-211, Jellinger KA, Biochim Biophys Acta 2009;1792:730-740; Rietdijk CD, et al., Front Neurol 2017;8:37; Surmeier DJ, et al., Nat Rev Neurosci 2017;18:101-113; Braak H, Del Tredici K, J Parkinsons Dis 2017;7:S73-S87.