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LETTER TO THE EDITOR

Kurt A. Jellinger

P25α immunoreactivity in multiple system atrophy and Parkinson disease

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Recently, Baker et al. [1] reported p25α and α-synuclein reactivity in glial cytoplasmic inclusions (GCI) in oligendroglia of multiple system atrophy (MSA) but p25α immunoreactivity in neuronal cytoplasmic inclusions (NCI) co-localized with α-synuclein labeling in only about 40%. These data can be largely confirmed by own studies in two cases each of MSA and Parkinson disease (PD), using formalin-fixed, paraffin-embedded slides and routine peroxidase immunohistochemistry for α-synuclein (monoclonal and polyclonal antibodies, Chemicon, Temecula, CA, USA) and p25α (purified polyclonal rabbit anti IgG, diluted 1:200 and 1:1000; gift of Prof. P. H. Jensen, Department of Medical Biochemistry, University of Aarhus, Denmark).

In MSA, anti-p25α labeled many GCI in oligodendroglia, virtually identical in localization and intensity with α-synuclein immunoreactivity, whereas it did not stain normal oligodendroglia [4]. In MSA, anti-p25α labeled only part of NCIs, virtually all of them being negative for α-synuclein [3].

In PD, the vast majority of cortical Lewy bodies showing intense α-synuclein immunoreactivity were negative for p25α, whereas subcortical Lewy bodies, consistently positive for α-synuclein, showed inconsistent p25α immunoreactivity.

While p25α-positive subcortical Lewy bodies in PD showed rather diffuse appearance, in MSA p25α-positive NCIs often displayed a punctate appearance of immunoreactive structures, as described by Baker et al. [1], suggesting that protein aggregation may occur, although p25α is folded and flexible without overt tendency for aggregation [5]. Brain-specific p25α was identified as a candidate that preferentially binds α-synuclein in its aggregated state [4]. Since p25α shares the property of heat stability with the aggregation-prone proteins tau and α-synuclein [4], these properties and the abnormal location of p25α suggest that aggregation of both p25α and tau-protein probably induced by additional co-factors may impair neuronal function, as suggested recently for Alzheimer disease (AD) neurons, showing co-localization of p25α and tau-positive pretangle structures [3], but not in other tauopathies. Since p25α-immunopositive neurons in both MSA and AD ultrastructurally show "twisted" and "straight" filaments [6], its abnormal expression may occur in a variety of neuronal types in diverse neurodegenerative disorders, in particular synucleinopathies, and may indicate some synergistic reaction with α-synuclein, as has been suggested for α-synuclein and tau [2, 7], which may also occur in PD.

K. A. Jellinger (✉)
Institute of Clinical Neurobiology,
Kenyongasse 18, 1070 Vienna, Austria
E-mail: kurt.jellinger@univie.ac.at
Tel.: +43-1-5266534
Fax: +43-1-5238634

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