UPREGULATION OF ALZHEIMER-ASSOCIATED PROTEINS APOE AND LRP1 IN MELANIZED NEURONS COINCIDES WITH MICROGLIAL ACTIVATION IN SUBSTANTIA NIGRA IN INCIDENTAL LEWY BODY- AND PARKINSON´S DISEASE

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Altered lipid metabolism, endoplasmic reticulum (ER) stress and microglial activation are implicated in the pathology of Parkinson’s disease (PD). However, it remains unclear whether these phenomena are the result of the disease process or play a role earlier during disease development. Moreover, no information is available about the sequence of their occurrence in PD brain.

We aimed to answer these questions by using immunocytochemistry on tissue sections from the substantia nigra, pars compacta (SN) of well characterized control (n=6), Incidental Lewy Body Disease (ILBD; n=9) and clinical PD (n=5) cases.

Tissue sections were stained with antibodies against proteins representative of lipid metabolism (Apolipoprotein E, LRP1), ER stress and protein folding capacity (pPERK, pIRE1alpha, PDI, ERP57, calreticulin, tissue Transglutaminase) and microglial activation (MHC class I and II). ILBD was defined as alpha-synuclein pathology inside or outside the SN without clinical signs of brain disease, whereas PD was defined by alpha-synuclein pathology inside the SN together with a clinical diagnosis.

Irrespective of the presence of synuclein pathology in the SN, in ILBD consistent signs of microglial activation and induction of apolipoprotein E and LRP1 staining in melanized neurons were observed. In contrast, in only two of the ILBD cases weak signs of ER stress were detected. Besides neuronal loss, PD cases differed from ILBD cases by the consistent presence of synuclein pathology and signs of ER stress.

Our data suggest that altered lipid metabolism and immune activation occur early and precede ER stress and overt protein misfolding during PD pathogenesis.