Ilaria Trezzi et al., J Neurol Disord 2018, Volume 6
DOI: 10.4172/2329-6895-C11-056

Early changes in astrocytes are associated with neurodegeneration in Parkinson's disease

Ilaria Trezzi, MD, Central Clinical School, University of Sydney, Sydney
Glenda Halliday, PhD, Central Clinical School, University of Sydney, Sydney

Background and aim: Neuroinflammation is a well-known contributor to the alpha-synucleinopathy in Parkinson's disease (PD), in which astrocytes appear to be key mediators and collaborate with activated microglia. The main function of astrocytes is to support neurons. Animal and cell culture studies indicate that astroglia dysfunction may trigger the pathogenesis of PD, particularly, the demise of dopaminergic neurons. The aim of this study was to investigate specific astrocytes changes related to early stage PD in post mortem human tissue. Materials and Methods: The study has been conducted on formalin-fixed paraffin-embedded anterior cingulate cortex sections of 10 PD cases and 5 controls. Ethics was approved by Human Research Ethics Committee at the University of Sydney. Three astrocytic markers (GFAP, Aldh1l1 and S100B) and one pathology marker (S129 phosphorylated alpha-synuclen) were used to study astroglial morphology, reactivity, function and pathology load using immunohistochemistry and immunofluorescence methods. Results: Immunofluorescence revealed no phenotype change in astrocytes in PD, with Aldh1l1 labeling astrocytic cell bodies and GFAP their processes in all cases and controls. In the brainstem stage of PD when biochemical changes occur in limbic regions, astrocytes (S100B and GFAP) appear to be quiescent, whereas when neuronal alpha-synuclein structural pathology appears in limbic cortices, they display a reactive morphology. Quantification of Aldh1l1 immunoreactive astrocytes revealed a loss of astrocytes prior to obvious structural pathology compared to controls. Conclusions: The early loss of certain astrocytes may facilitate structural pathology that stimulate a neuroinflammatory reaction in remaining astrocytes.

Biography

Ilaria Trezzi is a young neurologist with recent neuropathological research experience due to an internship training program. She has completed one year under the supervision of Prof. G. Halliday in her Dementia and Movement Disorders Group at the University of Sydney. During this training she has learnt histological techniques, and acquired microscopy and image analyses skills. The Dementia and Movement Disorders Group investigates the role of inflammation in neurodegeneration, among other topics. This project focusses on astrocytes because they have an under-recognised role in neurodegeneration which is not fully understood. The results from this study indicate that their dysfunction is a key contributor early and prior to the structural pathologies observed in PD.

Ilaria.trezzi@sydney.edu.au

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