A potential protective role of Nurr1 in multiple sclerosis motor cortex

Jonathan Pansieri[1], Marco Pisa[1], Richard Yates[1], Sydney Yee[1], Margaret Esiri[1], Gabriele DeLuca[1]

1 Nuffield Department of Clinical Neurosciences, University of Oxford, Level 6 West Wing, 6 John Radcliffe Hospital, Oxford, UK

Main author: Jonathan Pansieri

ABSTRACT

Cerebral cortical inflammation and neurodegeneration are hallmark pathological features of multiple sclerosis (MS) that contribute to irreversible neurological disability. While the reason for nerve cell death is unknown, the pathogenic inflammatory role of infiltrating lymphocytes is likely an important contributor. The transcription factor Nurr1 counteracts inflammation in animal models of MS, and protects against neuronal loss in other neurodegenerative disorders, but its role in MS is not known. We investigated Nurr1 expression in MS motor cortex and evaluated its relationship with motor cortical pathology. To accomplish this, an autopsy cohort of pathologically confirmed MS (n=46) and control (n=11) cases was used, where Nurr1 expression was related to neuronal, microglial, astrocytic and lymphocytic densities. Motor cortical Nurr1 was overexpressed in MS compared to control cases. Increased Nurr1 expression positively associated with neuronal densities, especially when expressed in neuronal nuclei, and associated with decreased CD8+ cytotoxic lymphocyte density and activated astrocytes. Additionally, we found that Nurr1 was expressed in microglia and astrocytes, but no relationship between microglia and Nurr1 was found. Our findings expand the current knowledge on Nurr1 in neurological diseases, and support the hypothesis that Nurr1 may play a dual protective role in MS by influencing inflammatory and neurodegenerative processes. Future studies elucidating the influence of Nurr1 on these processes in MS may cast light onto novel targets that may be modulated to alter clinical outcome.

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UNIVERSITY OF OXFORD