Neuronal and axonal loss in NAGM and subpial lesions in multiple sclerosis

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Research question and background

Multiple sclerosis (MS) is a demyelinating and neurodegenerative disease of the central nervous system. MS causes significant demyelination of the gray matter (GM), which is thought to importantly contribute to both physical and cognitive impairment. Of all demyelinated cortical lesions, subpial lesions are most common. The present study investigated neurodegenerative aspects of subpial lesion-containing cortex of 11 MS and 6 non-demented non-MS controls.

Methods and tissue used

Twenty-five tissue blocks from 11 clinically and neuropathologically confirmed MS patients and 6 tissue blocks from 6 non-demented controls were obtained from the Netherlands Brain Bank, Amsterdam, the Netherlands (http://www.brainbank.nl/). Cortical lesions were identified and characterized using anti-proteolipid protein (PLP) immunohistochemical stainings. Neurons and axons were stained using NeuN or SMI312 antibodies. Subsequently the neuronal density, neuronal size and axonal size were evaluated in NAGM, type III lesions and control cortex.

Results and conclusion

There were no significant differences in neuronal and axonal density between NAGM and type III lesions. Only in the cingulate cortex, neuronal size was 11.2% smaller in type III lesions than in NAGM. Compared to control cortex, type III lesions contained 25.4% fewer NeuN positive neurons. In addition, compared to control cortex, neuronal size was 13.6% smaller in normally myelinated cortex (normal-appearing GM; NAGM). Finally, the same regions showed a reduced axonal density in type III lesions (-31.4%) and in NAGM (-33.0%). In conclusion, compared to control cortex, NAGM and type III lesions showed significant neurodegenerative changes. However, there was no significant difference between NAGM and type III lesions in terms of neurodegenerative changes. This may suggest that neurodegeneration in MS cortex proceeds independently from cortical demyelination.