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High-resolution diffusion tensor spinal cord MRI measures as biomarkers of disability progression in a rodent model of progressive Multiple sclerosis

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Standard MRI sequences have been shown to be insensitive and non-specific in monitoring multiple sclerosis (MS) disease progression. This lack of reliability of spinal cord imaging in identifying significant disease is a major problem in the clinical management of MS patients. In the present study, we sought to address this gap by testing the hypothesis that diffusion tensor imaging (DTI), an advanced imaging technique, can reliably quantitate MS disease in the spinal cord, by using a well-characterized animal model of progressive MS, *i.e* Theiler's murine encephalomyelitis virus-induced demyelinating disease (TMEV-IDD). SJL mice with TMEV-IDD and varying levels of clinical disease were imaged using a 9.4 T horizontal bore small animal MRI scanner. Axial diffusivity (AD), radial diffusivity (RD), and fractional anisotropy (FA) were calculated. These DTI metrics were obtained for several regions-of-interest (ROIs) in the spinal cord, namely dorsal, dorsal-lateral, ventral and ventral-lateral white matter (WM) and gray matter (GM). Progressive disability in mice was assessed by the Rotarod performance test and disability data were expressed as a neurological function index (NFI). Correlation was then performed between DTI metrics and disability scores. TMEV-IDD mice displayed significant increased neurological deficits over time when compared with sham mice (two-way ANOVA $p<0.0001$). Concurrently, the values of FA and AD were both significantly decreased compared to sham controls (both $p<0.0001$), while RD was increased ($p<0.0001$). Overall, FA changes were greater in WM than in GM, and differences were more pronounced in the ventral region. Interestingly, lower NFI scores were associated with decreased FA values measured in the ventral ($r=0.68$; $p<0.0001$) and ventral-lateral ($r=0.70$; $p<0.0001$) regions of the WM, but not in the dorsal region of the WM ($r=0.08$; $p=0.625$) and the GM ($r=0.24$; $p=0.170$) In conclusion, these data demonstrate that improved DTI measures of the spinal cord contribute to strengthening the association between neuroradiological markers and clinical disability, and support the routine use of DTI measures in spinal cord imaging in MS patients.

Biography

Francesca Gilli, received her MS in Medical Biotechnology and PhD in Human Biology from the University of Torino (Italy). She then completed her postdoctoral research in neuroimmunology at University of Torino (Italy), University of Basel (Switzerland), and Geisel School of Medicine at Dartmouth (USA). She currently serves as Assistant Professor of Neurology at Geisel School of Medicine at Dartmouth, where she works as a basic scientist. Her research focuses on attempting to understand the basic biology of neuroinflammation, demyelination and neuronal injury in Multiple Sclerosis. She has published more than 37 papers in peer-reviewed journals including 23 as main author.

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