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WINNER

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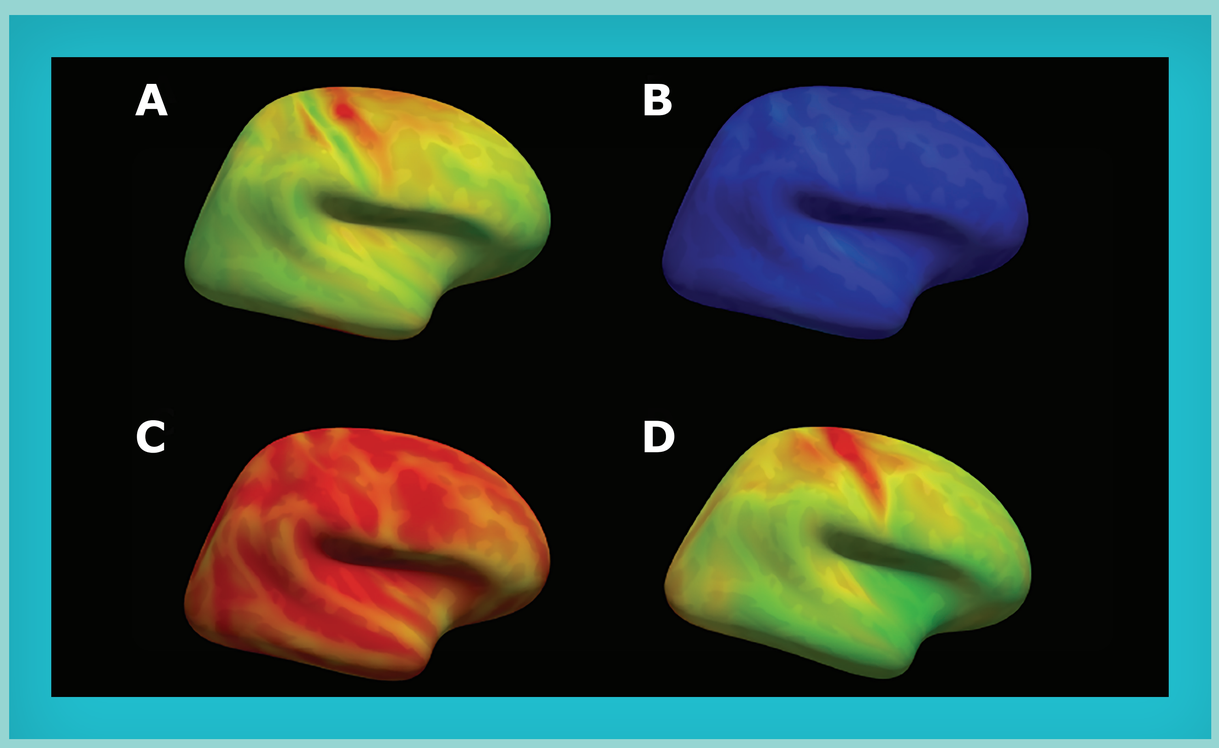
Rapid *in vivo* myelin and neurite density imaging: new promising quantitative and tissue-specific biomarkers for predicting disease progression and treatment response

Background

- The treatment of MS has been revolutionized in the past two decades; however, current treatments have mainly focused on modifying inflammatory disease activity
- New emerging MS therapies show promise in enhancing remyelination, which is likely to be protective for axons and preventative of long-term disability
- Studying the impact on demyelination and remyelination dynamics, and axonal integrity *in vivo*, requires robust and clinically feasible methods in order to monitor these physiological processes



Myelin imaging and NODDI in patients with MS analysed at mid-cortical depth and projected onto a common inflated cortical template. (A) Intracellular diffusion (neurite density); (B) Isotropic diffusion (oedema); (C) Orientation dispersion (organization of microstructure); (D) Myelin content
Adapted from Granberg T et al. Brain 2017;140:2912–26 with permission from Dr Mainero © the Author

NODDI, neurite orientation and dispersion density imaging; REMyDI, rapid estimation of myelin for diagnostic imaging

Hypothesis

- We hypothesize that application of a combination of two new MRI techniques (REMyDI and NODDI), which provide improved microstructural characterization of MS pathology *in vivo*, can be applied to better detect and understand disease heterogeneity at onset

Project synopsis

- The main objective of this project is to apply a combination of two new MRI techniques (REMyDI and NODDI) to better capture and characterize demyelinating MS pathology, as well as microstructural disruption of axons and dendrites
- To address our hypothesis, we will apply the following techniques:
  - Imaging will be performed on a 3 Tesla MRI scanner of 60 patients with MS who are newly diagnosed and treatment-naive, 40 patients with longstanding MS (>8 years) who received treatment since diagnosis and 20 healthy controls
  - Longitudinal clinical and neuroimaging follow-up will be performed over 2 years in combination with neurological, cognitive and patient-reported outcome measures
  - We will also determine comprehensive biofluid marker profiles collected longitudinally in blood and cerebrospinal fluid, including myelin- and neurite-related markers, to further our understanding of disease activity and progression
- The validation of novel quantitative imaging outcomes will be beneficial for early-stage clinical trials of novel therapeutic drugs aimed at enhancing remyelination, as existing standard imaging techniques have lower sensitivity in determining changes over short timespans in progressive forms of MS

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