Patients with progression independent of relapse activity show increased white matter degeneration on diffusion tensor imaging maps of major white matter tracts

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Background

- Progression independent of relapse activity (PIRA) has been described to occur in multiple sclerosis (MS) patients even in the earliest disease stages.
- PIRA patients show increased atrophy rates in multiple brain regions compared to stable patients.
- PIRA is the most frequent manifestation of disability accumulation across the full spectrum of traditional MS phenotypes.
- Whether increased degeneration of major white matter (WM) tracts is also associated with PIRA, is currently unknown.

Methods

Patients cohort
258 patients with RRMS, with clinical follow up (median follow-up: 4 years)

PIRA: ≥ 90 days ≥ 6 months
EDSS increase:
- 21.5 points if baseline EDSS 0;
- 21.0 point if baseline EDSS 1.0-5.5;
- 20.5 points if baseline EDSS >5.5.

- 39 RRMS patients with PIRA (74.4%; Age: 50.3±12.0y; EDSS: 3.5 [2.75, 4.25])
- 219 stable patients (63.9% female; 48.0±11.2y; EDSS: 2.0 [1.5, 3.0])

Propensity-score matching
(age, sex, disease duration, lesion volume, relapses in last 2 years, treatment)

Linear model, adjusted for multiple comparisons with the false-discovery rate

Diffusion Tensor Imaging (DTI) measures [wms-DTI, 1.8 mm iso, 3 min AT]

**JHU DTI white matter atlas**

Results

DTI alterations of patients with PIRA vs stable patients

**Corpus callosum**

<table>
<thead>
<tr>
<th>Fractional anisotropy</th>
<th>Mean diffusivity</th>
<th>Radial diffusivity</th>
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**Motor tracts**

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Conclusions and perspectives

- Patients with PIRA showed increased degeneration in white matter regions of the corpus callosum and in motor tracts compared to stable patients.
- Hereby suggesting that white matter damage is associated with the development of PIRA (Wallerian degeneration?)

Future work

- Increase the sample size and explore other diffusion metrics to assess neurodegeneration
- Explore the relation between white matter damage & specific lesion types

References


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Swiss MS Cohort study

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