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Measuring spontaneous remyelination in a longitudinal multiple sclerosis cohort

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Introduction:
Remyelination trials are in need of a functional outcome measure. We propose that longitudinal measurement of oculomotor function may be used to measure and quantify spontaneous and therapeutic remyelination.

Objectives/Aims:
We aimed to measure spontaneous remyelination with infrared oculography in a longitudinal multiple sclerosis (MS) cohort.

Methods:
In a prospective, longitudinal, cohort study from the MS Center Amsterdam oculomotor function was measured and analysed using a validated standardized infrared oculography protocol (DEMoNS) at baseline, 3 months and 1 year follow-up. Presence of an internuclear ophthalmoplegia (INO) was defined by previously published cut-off levels of the versional dysconjugacy index (VDI). All subjects were also assessed for clinical function, including Expanded Disability Status Scale (EDSS), Nine Hole Peg Test (NHPT) and the visual functioning questionnaire (VFQ) and checklist individual strength (CIS).

Results:
Among 80 individuals with MS, INO was persistent in 14 individuals and resolved in 7 individuals after a year of follow-up. Resolution of INO was consistent over time and occurred within 3 months in 3 participants and after 3-12 months in 3 participants. Compared to participants with persistent INO participants with resolved INO showed a 5.7% (95% CI 2.3-9.1%) reduction in VDI area under the curve (AUC) and a 10.7% (95% CI 5.0-16.0%) reduction in VDI peak velocity (pV/Am). Participants with resolved INO showed improved oculomotor function resulting in improved pro-saccadic latency (-33.3 ms; 95% CI [-66.2, -0.4]), fixational horizontal gaze stability (standard deviation -34%; 95% CI [-53%, -6%]), EDSS brainstem functional system (-0.75, 95% CI [-1.49, -0.02]), mental health symptoms due to vision (VFQ mental health +12, 95% CI 2-23) and driving difficulties (VFQ mental health +15, 95% CI 4-25) compared to participants with persistent INO. Participants with resolved INO also showed more improvement in NHPT (-3.47 sec, 95% CI [-6.68, -0.33]) and fatigue during physical activity (CIS activity -5; 95% CI [-1, -9]), compared to participants with persistent INO. There was no statistically significant difference in the presence of radiological disease activity among participants with resolved INO compared to participants with persistent INO (OR 0.24, 95% CI 0.004 - 2.878).

Conclusion:
Spontaneous remyelination appearing as resolution of INO on longitudinal infrared oculography coincides with
improvement of oculomotor function, clinical and subjective functioning.

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