Charcot Abstract 2021

Long title: Genetic and clinical risk factors for spasticity among people with MS

Short Title: Spasticity in MS: Genetic & clinical factors

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Background Spasticity is a common complication of MS, but information on specific genetic and other risk factors is lacking.

Methods People participating in Swedish MS studies genotyped with the MS Replication Chip were included. Data were linked to national registers and prevalent (pMS) or incident MS (iMS) patients were identified. First spasticity treatment was identified using ATC codes for first-line spasticity treatments. Genome wide association analysis (GWA) of ever vs never spasticity included all MS patients with GWA-genotypes (N=5065). People with spasticity prior to MS diagnosis or start of follow-up (1/Jul/2006) were excluded in cox regression models estimating hazard ratios (HR) and followed patients until spasticity, death, or 31/Dec/2014.

Results pMS patients (N=3519) had more spasticity than iMS (N=1826) (50% vs 33%). Among iMS, the highest magnitude association to spasticity was secondary progressive MS (HR 2.82 CI 2.06-3.87) and primary progressive MS (HR 2.34 CI 1.75-3.14) compared with relapsing remitting MS, and was similar for pMS. No sex differences were observed. Highest magnitude HRs were 0.5-3 years from MS diagnosis for both groups but reduced over time. HRs increased with increasing EDSS. Relapses, age at MS onset/diagnosis were not associated. Lower education, heart disease, type-1 diabetes, Parkinson's disease and depression were associated with spasticity among iMS, and to a lesser extent among pMS. Disease modifying treatments for MS reduced HRs only among iMS. GWA adjusting for PCAs identified 6 potentially associated loci at suggestive significance level ($p < 1.0x10^{-5}$). After adjusting further for PCAs, sex, birth year, disease course, education and depression, loci on chromosomes 3 (OR 1.42 CI 1.25-1.63) and 6 (OR 1.24 CI 1.13-1.35) remained.

Conclusions Spasticity is common among both iMS and pMS and is associated with greater MS severity, and comorbid diseases. Tentative indications that particular loci may be associated with spasticity should be confirmed.

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