**Title: Initial cross-sectional MR spectroscopy analysis of a cohort of secondary progressive MS patients enrolled in the MS-SMART trial**

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## Abstract

**Background:** Proton MR spectroscopy (MRS) is able to detect and quantify different metabolites in the central nervous system, and has been widely studied in multiple sclerosis (MS). These include: N-acetyl aspartate (NAA) and N-acetylaspartylglutamate (NAAG) (both markers of neuronal integrity); myoinositol (mI, a marker of glial proliferation); glutamate and glutamine (Glx, representing a mixture of aminoacids acting as excitatory and inhibitory neurotransmitters); creatine and phosphocreatinine (Cr+PCr, suggested marker of gliosis); and glycerophosphocholine+phosphocholine (GPC+PCh, markers of membrane phospholipids, highly suggestive of ongoing inflammation when elevated). Normalization of metabolite levels to Cr+PCr has several advantages, including the reduced influence of inhomogeneities and relaxation parameters.

**Aim:** To examine metabolite concentrations using MRS, in 120 secondary progressive MS (SPMS) patients, and to correlate them with clinical and demographic measures.

**Method:** 120 SPMS patients, enrolled in the MS-SMART trial (NCT01910259) were studied at baseline by 1H-MRS. The mean values of GPC+PCh/Cr+PCr; NAA+NAAG/Cr+PCr; Glx /Cr+PCr; mI/Cr were calculating by considering one single voxel of normal appearing white matter (NAWM) in each hemisphere. Kendall's tau-b coefficients were used to test the correlations between the variables. Two sample t-tests were performed to test for differences between gender groups and EDSS band.

**Results:** There were no significant associations between any of the metabolites studied and: age, EDSS, total disease duration, SPMS duration and time since diagnosis. NAA+NAAG/Cr+PCr was significantly higher in females ($p = 0.02$) and mI/Cr was significantly higher in males ($p < 0.01$).

**Conclusion:** Our initial cross-sectional results show that the metabolic processes underlying the progression of the disease may differ between males and females, and ultimately could affect clinical course.

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