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Title: Cortical grey matter ratio differentiates relapsing remitting multiple sclerosis from secondary progressive multiple sclerosis

Background: Relapsing remitting multiple sclerosis (RRMS) and secondary progressive multiple sclerosis (SPMS) are differentiated solely on clinical grounds. Therapeutic strategies differ considerably between these phenotypes. Non-clinical measures to support clinical differentiation, such as MRI, could contribute to improved patient management.

Objective: Primary objective is to compare Cortical Grey Matter volumes (CGMv) and Deep Grey Matter volumes (DGMv) across RRMS and SPMS patients. Based on outcomes of the primary objective, secondary objective is to test a regression model fitted to predict clinical phenotype.

Methods: Fully-automated segmentation (MSmetrix; icoMetrix NV) was applied to 108 RRMS and 30 SPMS patient brain MRI scans (acquired at Antwerp University Hospital, Belgium) to quantify CGMv and DGMv. Acquired volumes were compared to MSmetrix healthy control volumes (HCv's), by expressing patient volume in ratio of its respective age, gender and intracranial volume normalized HCv, resulting in CGM-ratio (CGMr) and DGM-ratio (DGMr). EDSS ≥ 4.0 was applied as SPMS cut-off.

Results: Mean CGMr differed significantly between phenotypes (RRMS 1.0240, SPMS 1.0016, P=.006). Differences in CGMr were not attributable to active therapy. DGMr mean did not differ (RRMS 0.8767, SPMS 0.8533, P=.209). CGMr correlated with DGMr (RRMS: r=0.308, P=.001) (SPMS: r=0.324, P=.080). Log-transformed CGMr (logCGMr) and disease duration emerged as predictors of phenotype (P=.038, P=.002 respectively). Disease duration predicted RRMS and SPMS correct in 98,1% and 16,7% of cases respectively. Addition of logCGMr increased accuracy to 99,1% for RRMS and to 26,7% for SPMS.

Conclusion: CGMr's are significantly higher in RRMS compared to SPMS, DGMr's however do not differ. logCGMr improves a predictive model based on disease duration. Surprisingly, mean CGMr is >1 in both RRMS and SPMS, possibly indicating a conceivable pseudo-hypertrophy effect secondary to cortical edema and remodelling.