GENDER EFFECTS ON ATROPHY IN MS: COGNITIVE IMPLICATIONS

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Introduction: Multiple sclerosis displays clear gender effects in female predisposition, as well as male negative clinical prognosis. Previous studies on atrophic brain changes in MS have mostly focused on group-based differences, using gender simply as a covariate. There are few studies, however, looking at specific gender effects on atrophy. In this study, therefore, we investigated atrophy in MS separately for male and female patients, as well as the cognitive impact of these effects.

Methods: Structural scans and cognitive evaluations were performed on 32 RRMS patients (14 male, 17 female) and 22 healthy controls (10 male, 12 female). All groups were matched for age, education, disability and disease duration. Imaging was performed using a 3T-MR system (GE Signa HDXT, V15M), using a 3D-T1 sequence (TR 7.8ms, TE 3.0ms, TI 450ms), as well as dual echo PD/T2 (TR 9680ms, TE 22/112ms) and spin echo T1 (TR 475ms, TE 9.0ms) sequences. SIENAX, part of FSL4.0 (FMRIB, Oxford, UK), was used to calculate grey matter (NGMV), white matter (NWMV) and whole-brain (NBV) volumes, corrected for head size, using the 3D-T1 sequence. Lesion volumes were measured using a local thresholding technique (Alice, PII Inc.). Neurocognition was assessed in six domains: executive function, verbal memory, working memory, information processing, attention and psychomotor speed. All data was analyzed in SPSS 15.0 for Windows. ANCOVA was used to investigate group*gender interactions, correcting for age, using post-hoc LSD confident interval adjustments to compare main effects. Pearson's correlation coefficient was used to calculate correlations between cognition and brain volumes.

Results: SIENAX analyses revealed a significant interaction between gender and group for NBV ($F=4.1$, $p=0.05$), with a trend for NGMV ($F=3.8$, $p=0.06$). White matter volume showed no such interaction effect. Female patients showed no reduction in any brain volume compared to female controls. Male patients, however, showed significant reductions compared to male controls in all three brain volumes (NGMV: $p=0.001$; NWMV: $p<0.01$; NBV: $p=0.001$).

Cognitive domains also showed an interaction between gender and group for verbal memory ($F=7.6$, $p<0.01$), with a trend for psychomotor speed ($F=3.7$, $p=0.06$). Both showed lower performance in male patients only ($p=0.004$ and $p=0.006$ respectively). Male patients also showed lower scores in working memory ($p=0.04$) attention ($p=0.04$) and psychomotor speed ($p=0.03$), although these domains showed no significant interaction between gender and group. There were no cognitive domains impaired in female patients.

In the patient group NGMV correlated significantly with verbal memory ($r=0.4$, $p=0.03$), working memory ($r=0.4$, $p=0.04$), information processing ($r=0.4$ $p=0.03$) and psychomotor speed ($r=0.4$, $p=0.04$). NBV correlated significantly with verbal memory ($r=0.4$, $p=0.04$), working memory ($r=0.4$ $p=0.02$) and information processing ($r=0.4$, $p=0.04$). In the healthy control group no correlations were found between brain volumes and cognitive domains.

No gender effect was found in lesion volume measurements.

Conclusions: A significant gender effect was found for NGMV, NBV and verbal memory. Male patients were found to be impacted more severely in all three measures. A significant correlation was also found between cognition and atrophy in the patient group only, revealing a clinically relevant gender effect in MS. This underlines the need for future research to investigate gender effects in MS more thoroughly, with possible therapeutic implications as well.

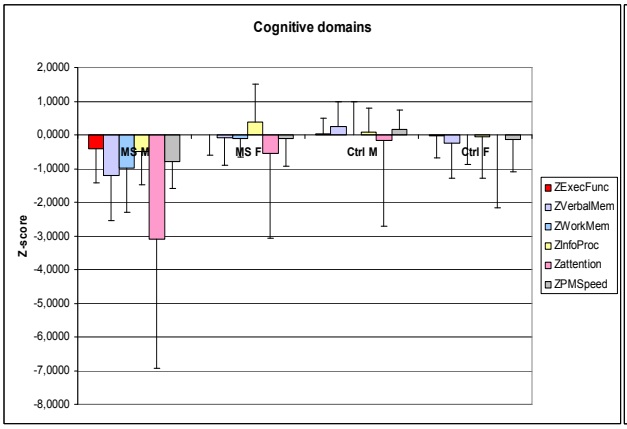

Figure 1. Cognitive domains

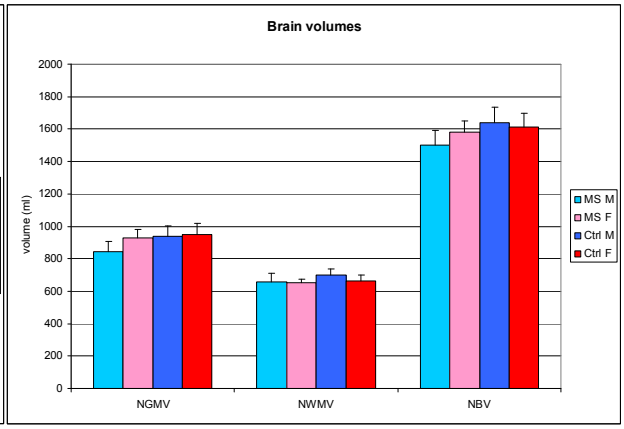

Figure 2. Normalized brain volumes

This study was supported by the Dutch MS Research Foundation (grant no. 08-650)