

Different patterns of regional subcortical and cortical atrophy in patients with multiple sclerosis. A case control study.

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Objective

To assess the relationship between regional subcortical and cortical atrophy, and disease severity.

Background

Both subcortical and cortical atrophy are observed in multiple sclerosis (MS) and are associated with clinical outcomes. FreeSurfer software, a set of voxel-based automated tools for brain reconstruction, offers an opportunity to investigate the characteristics of regional- and tissue-specific subcortical and cortical atrophy.

Methods

We examined 21 normal controls (NC) [mean age 35.1 ± 11.4 ; Caucasian 81.0%; female 47.6%], 71 MS patients [40 relapsing-remitting (RR), 14 secondary-progressive (SP) and 17 primary-progressive (PP) with mean age 46.9 ± 9.0 ; mean disease duration 11.3 ± 8.6 ; median EDSS 3.0; Caucasian 85.9%; female 74.6%], and 17 patients with clinically isolated syndrome (CIS) [mean age 37.8 ± 10.1 ; mean disease duration 1.94 ± 2.0 ; median EDSS 1.5; Caucasian 41.2%; female 94.1%]. Brain segmentation was performed on high-resolution 3D-T1 weighted SPGR MRI images on 1.5T. Region-specific subcortical (Figure 1.) and cortical (Figure 2.) volumes in mm³ were obtained by FreeSurfer.^{1,2} Logistic regression and general linear model (GLM) analyses, adjusted for age, sex and race were conducted to investigate differences between NC, MS and CIS patients. Intra cranial volume was included to correct for head size variation.

Results

GLM analysis revealed significantly lower volumes for ventral diencephalon (VDC), right ($p=0.001$) and left ($p=0.002$) thalamus ($p<0.0001$), right pallidum ($p=0.008$), right hippocampus ($p=0.01$), left putamen ($p=0.05$), lateral ventricles bilaterally ($p<0.0001$), third ventricle ($p=0.001$), and fourth ventricle ($p=0.04$) in MS patients compared to NC. Different patterns of regional subcortical atrophy were observed in MS group when compared to NC. While RRMS had significantly lower thalamic volumes ($p<0.0001$), ventral diencephalon, putamen and pallidum bilaterally ($p<0.01$) with enlargement of lateral ($p<0.0001$), third ($p<0.0001$) and fourth ventricles ($p=0.01$), SPMS group had significantly lower volumes in thalamus bilaterally, right hippocampus ($p=0.02$), right caudate ($p=0.04$) with bilateral increase in lateral ventricles ($p=0.01$). PPMS group had significantly lower volumes in right hippocampus ($p=0.01$), right amygdala ($p=0.03$), right caudate ($p=0.05$) with significant increase in third ventricle ($p=0.04$). No significant subcortical atrophy was observed in CIS group when compared to NC. Significant regions from GLM analysis were entered to regression model. Logistic regression yielded left thalamus ($p=0.001$) to be predictive of MS group. The right lateral ventricle (R square=0.119, $p=0.002$) predicted disease severity as measured by EDSS. Third ventricle (R square=0.226) and right thalamus (R square=0.312) were significantly correlated to disease duration at $p<0.0001$. GLM analysis of cortical volumes yielded significantly lower volumes only for right posterior cingulate ($p=0.01$) for MS group when compared to NC.

Conclusions

Regional subcortical atrophy is more prominent than regional cortical atrophy in MS patients, particularly more pronounced in progressive groups, and is accompanied with significant increase in ventricle volumes. Subcortical atrophy is also related to higher disability.

Figure 1. Representative 3D SPGR T1-weighted image showing regional subcortical atrophy in a single patient with multiple sclerosis (50 years of age, female, 13 years of disease duration, EDSS-6.5, secondary-progressive).

Color legend: pink - gray matter; white - left cerebral white matter; neon green - right cerebral white matter; gray - brain stem; yellow - hippocampus; rose pink - putamen; blue - pallidum; green - thalamus, violet - lateral ventricles; light blue - caudate

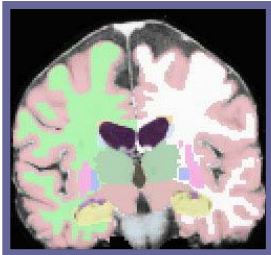
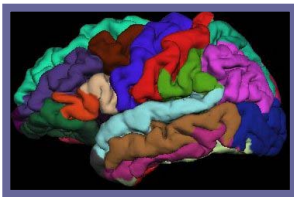


Figure 2. Representative 3D SPGR T1-weighted image showing regional cortical volume of left cerebral hemisphere in a patient with multiple sclerosis (50 years of age, female, 13 years of disease duration, EDSS-6.5, secondary-progressive).

Color legend: light turquoise - superior frontal; violet - rostral middle frontal; dark brown - caudal middle frontal; dark green - lateral orbitofrontal; orange - parstriangularis; skin tone - parsopercularis; blue - pre central; crimson red - post central; parrot green - suupramarginal; dark turquoise - superior parietal; light blue - superior temporal; light pink - inferior parietal; light brown - middle temporal; dark blue - lateral occipital; dark pink - inferior temporal.



References

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