Regional brain atrophy in children with multiple sclerosis

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ABSTRACT

We used cross-sectional tensor-based morphometry to visualize reduced volume in the whole brains of pediatric patients with multiple sclerosis, relative to healthy controls. As a marker of local volume difference, we used the Jacobian determinant of the deformation field that maps each subject to a standard space. To properly assess abnormal differences in volume in this age group, it is necessary to account for the normal, age-related differences in brain volume. This was accomplished by using normalized z-score Jacobian determinant values at each voxel to represent the local volume difference (in standard deviations) between an individual subject and an age- and sex-matched healthy normal population. Compared with healthy controls, pediatric patients with multiple sclerosis exhibited significantly reduced volumes within the thalamus and the splenium of the corpus callosum and significant expansions in the ventricles. While T2-weighted lesion volume was correlated with reduced thalamic volume, no correlation was found between T2-weighted lesion volume and reduced thalamic volume. Reduced volumes of the optic pathways, including that of the optic tracts and optic radiations, correlated with disease duration. Our results suggest that focal inflammatory lesions may play an important role in tract degeneration, including transsynaptic degeneration.

Introduction

Atrophy of both gray matter (GM) and white matter (WM) has been detected in the brains of adults with multiple sclerosis (MS), with a faster development of GM atrophy compared with that of WM (Valsasina et al., 2005; Chard and Miller, 2009; Sastre-Garriga et al., 2005). Gray matter atrophy involves both cortical and deep GM and correlates with cognitive impairment and physical disability (Rudick et al., 2009; Khaleeli et al., 2007). Among deep GM structures, the thalamus and the basal ganglia seem to be more susceptible to atrophy (Chard and Miller, 2009).

To quantify GM and WM volumes on conventional magnetic resonance (MR) images, methods based on structure segmentation have been employed (Korteweg et al., 2009), as have voxel-based analyses. These techniques have the advantage of exploring the whole brain with no a priori assumptions about where atrophy may be occurring (Tao et al., 2009; Ceccarelli et al., 2008; Andreasen et al., 2010). One voxel-based method, voxel-based morphometry (VBM), spatially normalizes individual GM tissue maps to allow group analysis of specific tissue densities at the voxel level. Another voxel-based method, tensor-based morphometry (TBM), calculates the Jacobian determinant for each voxel of the deformation field warping an individual brain to a common template space, thus providing a measure of tissue growth or shrinkage for each voxel of the brain. Unlike VBM, TBM does not depend on tissue segmentation. Rather, it is calculated directly from the deformation field relating all the voxels of the brain in question to the target brain.

These methods have been widely employed with conventional MR images from adult MS populations. However, to our knowledge, only one study has reported the use of a voxel-based method on a pediatric MS group (Mesaros et al., 2008). Mesaros et al. used VBM to detect GM loss in a pediatric MS group compared with a matched control group and found decreased thalamic GM concentration in the MS group. They also found a significant correlation between thalamic GM loss and T2-weighted (T2w) lesion load, but no correlation with disease duration.

Our goal was to study the spatial distribution of reduced brain volumes in a pediatric MS group compared with healthy controls (HC). Because we are not analyzing longitudinal data, we cannot use the term atrophy (as a serial loss of tissue) in this cohort. Instead, we use the phrase ‘reduced volume relative to HC’ to underline that our cross sectional findings are comparing MS patients with HC. Since the brains of children grow as they get older and vary from one child to another, we used a novel approach, a z-score map, to represent the local volume difference between an individual subject and an age- and sex-matched healthy normal population. The z-score map indicated...
the number of standard deviations by which each subject's local Jacobian determinant was above or below the mean calculated for an age- and sex-matched normal population. The z-score was computed at each voxel by subtracting the mean Jacobian determinant for the age- and sex-matched normal population from the Jacobian determinant for each individual MS patient, and then dividing by the standard deviation of the Jacobian determinant for the age- and sex-matched normal population.

The investigation of group differences between MS subjects and healthy controls was performed using two-sample t-tests. To evaluate the relationship of the local volume change to T2w lesion volume and disease duration, we fit a linear model to the z-score values voxel by voxel across all individual z-score maps.

Materials and methods

Subjects

The MS group consisted of 30 patients with relapsing–remitting (RR) MS who were younger than 17 years, 11 months at the time of the MRI scan (24 females and 6 males; mean age at MRI scan = 15.4 ± 2.1 years, range = 10.1 to 17.9 years; mean disease duration = 3.5 ± 2.6 years, range = 0.2 to 10.4 years). Patients were free of recent relapse or corticosteroid exposure for a minimum of 3 months prior to the MRI scan (24 females and 6 males; mean age at MRI scan = 15.4 ± 2.8 years). Patient details are given in Table 1.

Twenty-nine normal controls (NC) were recruited by local advertising (23 females and 6 males; mean age = 15.5 ± 2 years, range = 10.8 to 18.8 years) to be scanned on the same MRI scanner as the MS group. Subjects for the z-score normalization process described below.

From the 400+ subjects available in the NIHPD database, 302 subjects (154 females and 148 males) with multiple longitudinal scans were selected by age- and sex-matching, yielding a total of 488 acquisitions (mean age = 13.9 ± 2.8 years, (range = 9.8 to 18.8 years) used in our study to compute the z-score maps.

Table 1

<table>
<thead>
<tr>
<th>Patient</th>
<th>Disease duration (years)</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Lesion load (mm³)</th>
<th>EDSS</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3.27</td>
<td>17.61</td>
<td>F</td>
<td>89.65</td>
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<tr>
<td>2</td>
<td>2.52</td>
<td>10.08</td>
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<td>213</td>
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</tr>
<tr>
<td>3</td>
<td>4.19</td>
<td>13.15</td>
<td>F</td>
<td>6442</td>
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<tr>
<td>4</td>
<td>6.58</td>
<td>17.44</td>
<td>F</td>
<td>5212</td>
<td>1.5</td>
<td>Avonex</td>
</tr>
<tr>
<td>5</td>
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<tr>
<td>8</td>
<td>5.46</td>
<td>10.16</td>
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<td>95</td>
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<td>F</td>
<td>1346</td>
<td>nd</td>
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<tr>
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<td>F</td>
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<tr>
<td>13</td>
<td>7.94</td>
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<td>M</td>
<td>2204</td>
<td>4.5</td>
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</tr>
<tr>
<td>14</td>
<td>4.94</td>
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<tr>
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<tr>
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<tr>
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<td>F</td>
<td>940</td>
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<td>Copaxone</td>
</tr>
<tr>
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<td>3.96</td>
<td>14.9</td>
<td>F</td>
<td>556</td>
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<td>Copaxone</td>
</tr>
<tr>
<td>Median</td>
<td>2.9</td>
<td>15.72</td>
<td>F</td>
<td>3303</td>
<td>1</td>
<td>Copaxone</td>
</tr>
</tbody>
</table>

Supratentorial lesion load calculation

A pre-processing routine was run on all images to remove skull and scalp and to linearly register the PDw and T1w images to the T2w image to provide voxel-wise anatomical alignment across the modalities (Collins et al., 1994). The intensity range was normalized within each image using a two-piece linear transformation similar to that described by Nyul and Udupa (1999).

Magnetic resonance images of the 30 MS patients and 29 age- and sex-matched healthy controls were obtained using a single GE 1.5T TwinSpeed Excite 12.0 scanner (GE Healthcare, Waukesha, WI, USA) at the Hospital for Sick Children in Toronto, Canada. The standardized MRI protocol included a whole brain, three-dimensional (3D) T1w RF-spoiled gradient-recalled echo sequence. The parameters are detailed in Table 2. For lesion segmentation, we acquired a 2D multislice proton density-weighted (PDw)/T2w fast spin-echo sequence (2-mm thick consecutive slices, echo train length = 8, TR = 3500 ms, TE1/TE2 [effective] = 15/63 ms).

Scans of the NIHPD healthy controls were obtained at six pediatric study centers on GE and Siemens scanners. The standardized MRI protocol included a whole brain, 3D T1w RF-spoiled gradient echo sequence. The parameters are detailed in Table 2.

Table 2

<table>
<thead>
<tr>
<th>Field (T)</th>
<th>Scanners</th>
<th>Sequence</th>
<th>TR (ms)</th>
<th>TE (ms)</th>
<th>Excitation pulse</th>
<th>Refocusing pulse</th>
<th>Orientation</th>
<th>Thickness, gap (mm)</th>
<th>Field of view (mm²)</th>
<th>Matrix (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NIHPD</td>
<td>GE and Siemens</td>
<td>3D RF-SPCG</td>
<td>22–25</td>
<td>10–11</td>
<td>30</td>
<td>180</td>
<td>Sagittal</td>
<td>1.0</td>
<td>AP:256 LR:160–180</td>
<td>250</td>
</tr>
<tr>
<td>HSTC</td>
<td>GE</td>
<td>3D RF-SPCG</td>
<td>22</td>
<td>8</td>
<td>30</td>
<td>180</td>
<td>Sagittal</td>
<td>1.5</td>
<td>AP:256 LR: for 1 mm isotropic</td>
<td>256*256</td>
</tr>
</tbody>
</table>

Voxel size (mm³) | 1*1*1 | 0.98*0.98*1.5
An initial segmentation was performed using a locally developed automated Bayesian classifier (Francis, 2004; Ghassemi et al., 2008). The T2w lesion label outputs by the initial segmentation were superimposed on the T1w, T2w, and PDw images, reviewed carefully, and if necessary, corrected manually. Manual corrections were performed at the McConnell Brain Imaging Centre by trained staff blinded to clinical data.

Tensor-based morphometric analysis

All data from the three groups (MS, NC, and NIHPD) were submitted to the same processing steps defined below: pre-processing, spatial normalization, and Jacobian calculation. We used the MNI Talairach-like ICBM152 stereotaxic 18.5–43.5 template as the standard space (Fonov et al., 2010). The pre-processing step detailed below is slightly different from that detailed in the lesion calculation, as each pipeline was optimized for its own purpose, namely, lesion calculation for one and TBM analysis for the other.

Image pre-processing

The original acquired images were corrected for intensity inhomogeneity due to RF coil variations (Sled et al., 1998) and normalized to have an intensity range between 0 and 100 with linear scaling by using histogram matching with the ICBM152 18.5–43.5 template.

Spatial normalization

To aid registration, the skull and scalp were removed from all MR images (Smith, 2002). T2-weighted lesions in the MS patients were masked to avoid matching healthy tissue to lesions. Spatial normalization was used to transform the T1w MR images of each subject to match the ICBM152 18.5–43.5 template: First, a nine-parameter linear registration based on intensity cross-correlation as a similarity measure was performed. Second, a nonlinear registration algorithm ANIMAL (Collins et al., 1995) was applied, using a coarse-to-fine approach by registering subsampled and blurred T1w MR images to the stereotaxic target, with the resulting deformation field defined on a regular grid with a 2 × 2 × 2 mm³ resolution.

Jacobian calculation

In the spatial normalization step, we computed the deformation \( d \) such that the subject \( S \) was mapped to the template \( T \) when deformed by \( d \) (i.e., \( d(S) \)). To be able to compare all subjects in the common (template) space, we computed the inverse mapping \( h \) of \( d \) to map the template \( T \) to the subject \( S \). If \( v \) denotes the voxel location \((x, y, z)\), then \( h(d(v)) = v \) for all \( v \).

The Jacobian matrix of the deformation \( h \) is defined by:

\[
J_h = \begin{bmatrix}
\frac{\partial h_x}{\partial x} & \frac{\partial h_x}{\partial y} & \frac{\partial h_x}{\partial z} \\
\frac{\partial h_y}{\partial x} & \frac{\partial h_y}{\partial y} & \frac{\partial h_y}{\partial z} \\
\frac{\partial h_z}{\partial x} & \frac{\partial h_z}{\partial y} & \frac{\partial h_z}{\partial z}
\end{bmatrix}
\]

The Jacobian map is defined as the determinant of the Jacobian matrix \( |J_h| \). It is one of the simplest and most common features of TBM: A positive Jacobian determinant value indicates a local volume increase, while a negative determinant value indicates a local volume decrease in the subject’s T1w images relative to the template.

As all the Jacobian maps were computed in the template’s coordinate system, group statistics could be computed at each voxel to identify localized group local volume differences (Chung et al., 2001). It is important to note that the Jacobian maps are estimated on the
deformation fields after the nine parameter linear transformation to stereotaxic space has been applied. In this way, no global brain volume variable is required as a covariate in the analysis below.

**Z-score calculation**

To account for age expected growth, normal variability and sex differences, each subject of the MS and NC groups was compared with all NIHPD normal subjects of the same sex and the same age (±3 months) to compute a z-score-normalized Jacobian map. The number N of age- and sex-matched subjects available in the NIHPD database depended on the age and sex of the subject and ranged from 8 to 22 (mean = 14). Fig. 1 shows the histogram of subject ages in the NIHPD population.

For each voxel \((x,y,z)\) of the Jacobian determinant map \(J_i\) of each subject from the NC and MS groups, its z-score \(z(x,y,z)\) was computed as follows:

\[
z(x,y,z) = \frac{\log J_i(x,y,z) - \mu}{\sigma}
\]

where

\[
\mu = \frac{1}{N} \sum_{i=1}^{N} J_i(x,y,z)
\]

and

\[
\sigma = \sqrt{\frac{1}{N} \sum_{i=1}^{N} \left(\frac{J_i(x,y,z) - \mu}{N-1}\right)^2}
\]

and where \(J_i\) is the Jacobian map of an age- and sex-matched NIHPD subject \(i (i = 1, \ldots, N)\).

**Statistical analysis**

Statistical analysis was performed with Glim Image, a generalized linear modeling program developed at the Montreal Neurological Institute. Two-sample parametric t-tests for unpaired data were performed voxel by voxel to compare the z-score values of the two groups (MS and NC). Linear regression was applied to determine the correlation between z-scores and disease duration and between z-scores and supratentorial lesion loads in the MS group.

Clusters were considered significant at the \(p < 0.05\) cluster level, corrected for multiple comparisons. Corrected p-values were based on the smallest value between non-isotropic random field theory correction, Bonferroni correction, and discrete local maxima correction (Worsley, 2005).

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**Results**

**Z-score map**

Fig. 2 shows an example z-score map of a 12-year-old female and the images from which it was calculated: the Jacobian map computed in the template space showing the deformation field of the 12-year-old female brain and the mean and standard deviation Jacobian maps for the age- and sex-matched normal controls in the NIHPD population (i.e., all girls aged between 11.75 and 12.25 years old).

Fig. 3 displays the mean z-score maps of the MS and NC groups. Negative values (blue colors) represent regions with volume loss in the MS subjects relative to the age- and sex-matched NIHPD subjects. Positive values (red colors) represent regions with volume expansion in the MS subjects relative to the age- and sex-matched NIHPD subjects. The z-score values for the NC group are near zero (green), confirming that the NC group is comparable to the NIHPD population and that our z-score normalization method is justified. In the MS group, the significant changes are seen centrally, with the greatest extent of volume loss occurring in central structures, particularly the thalamus, and the greatest extent of volume increase in the lateral ventricles.

**Supratentorial lesion volume probability distribution**

For the 30 MS subjects, the supratentorial lesion volume varies from 0.089 cm\(^3\) to 37.7 cm\(^3\), with a mean of 7 cm\(^3\). To determine the impact of T2w supratentorial lesions on local volume change, we computed the percent probability of a lesion being present at any voxel (i.e., the fraction of patients with lesions at a given location, multiplied by 100). The T2w lesion distribution maps are shown in Fig. 4. The highest probabilities were located in the occipital periventricular WM (32%) followed by the frontal periventricular WM (around 16%). No lesions were detected in the deep GM structures.

**Group comparison**

The significant clusters (\(p < 0.05\)) of volume reduction and expansion in the MS group compared with the NC group are listed in Table 3. Compared with the NC group, volume loss in the MS group was significant in the left and right thalamus, more precisely, the pulvinar (both sides) and anterior nuclei (right side) (see Fig. 5), as well as in the splenium of the corpus callosum and a small part of the globus pallidus.
(both sides). Volume expansion was significant in the foramen of Monro and near the posterior horn of the left lateral ventricle.

As for sex, no significant difference in terms of volume change was found between males and females in the MS group.

Regression against lesion load and disease duration

Regression against T2w lesion load showed a region of significantly correlated volume reduction in the splenium of the corpus callosum (see Fig. 6). However, the regression against T2w lesion load showed no regions of significantly correlated expansion ($p<0.05$, corrected for multiple comparisons).

Regression against disease duration showed significantly correlated volume reductions in the left and right globus pallidus and within the optic tract, from the optic chiasm to the lateral geniculate nucleus and then to the anterior part of the optic radiations ($p<0.05$, corrected for multiple comparisons). Fig. 7 shows transverse slices of the brain with clusters found in different regions of the visual pathway. The reduced lateral geniculate nucleus volume does not seem to be associated with lesions in the optic tracts. Lesions are present in the optic radiations, but the regression against total T2w lesion volume was not significant.

To better understand the basis for reduced optic radiation volume and its relation to disease duration, we checked for a history of optic neuritis (ON) in each patient. Fourteen of the MS patients had a history of ON, whereas the other 16 did not. Disease duration at the time of MRI was 4.1 ± 2.7 years for the patients with a history of ON and 2.9 ± 2.5 years for those without. Thus, the increased probability of developing ON over time in MS may underlie at least part of the regression against T2w lesion load and disease duration.

Table 3

Regional volume reductions and expansions in MS group compared to NC.

<table>
<thead>
<tr>
<th>Clusters</th>
<th>Main area</th>
<th>Center of mass stereotaxic (x,y,z)</th>
<th>Size (cm$^3$)</th>
<th>Corrected $p$-value</th>
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</thead>
<tbody>
<tr>
<td><strong>Volume reductions</strong></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Left pulvinar</td>
<td>$-18.4, -26.3, 0.7$</td>
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<td>.0003</td>
</tr>
<tr>
<td>2</td>
<td>Right pulvinar and splenium of CC</td>
<td>$16.4, -29.5, 3.0$</td>
<td>2.5</td>
<td>.002</td>
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<tr>
<td>3</td>
<td>Right lateral ventral thalamus</td>
<td>$35.2, -32.2, 20.0$</td>
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<td>.003</td>
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<tr>
<td>4</td>
<td>Right anterior nuclei of the thalamus</td>
<td>$8.9, -1.4, 1.3$</td>
<td>0.6</td>
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<td><strong>Volume expansions</strong></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Left posterior lateral ventricle</td>
<td>$-30, -50.7, 10.3$</td>
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<td>.0002</td>
</tr>
<tr>
<td>2</td>
<td>Foramina of Monro</td>
<td>$0.4, -4.3, -5.3$</td>
<td>0.8</td>
<td>.0041</td>
</tr>
</tbody>
</table>

Discussion

It is difficult to assess morphometric differences between groups of subjects in the pediatric age range. For example, is a volume difference due to atrophy or to lack of age-expected growth? To properly assess abnormal changes in the brain volumes of MS patients in this age group, it is necessary to account for the normal, age-related changes in brain volumes. Therefore, we explored volume changes in the brains of children with MS by computing z-score maps of the Jacobian determinant of the deformation field with respect to age- and sex-matched control subjects in the NIHPD. In so doing, we addressed the issue of growth-related variability in pediatric patients with MS.

We utilized two control populations for our study, the NIHPD and a locally-enrolled normative control (NC) population. Due to its size (and great cost), a dataset similar to the NIHPD would be nearly impossible to acquire from a single site; thus one is forced to face the issues of variability due to multi-site data. To mitigate this concern, the NIHPD normative data was acquired with a protocol that was designed to yield similar data across sites and subject selection was balanced across sites. We modeled the MRI protocol for our study using a similar acquisition protocol (see Table 2). Nonetheless, we could not absolutely exclude a scanner-related impact on our analyses. The near-zero values of the voxel-by-voxel z-score mean map of the NC group (left in Fig. 3) confirm that our NC group scans are a good representation of normal pediatric scans and that the data we acquired on the GE scanner at the Hospital for Sick Children is comparable to the NIHPD data. The mean z-score normalized data from the MS group highlights morphological differences between the patient group and the normative NIHPD population. These differences represent regions with parenchymal loss (or ventricular enlargement) in the MS subjects relative to the age- and sex-matched NIHPD subjects.

One possible limit of this technique is the relatively small numbers of comparison subjects for some age groups: while a mean of 14 subjects was used over all sub-groups, 5 sub-groups (14.5 year old males, 15 year old females, 15.5 year old males, 16.5 year old males and 17 year old females) had less than 10 subjects. While this is perhaps not ideal for a group matching, this is much more powerful than most study designs that use only single-subject age- and sex-matching, enabling us to account for anatomical variability across different ages. While it would be possible to increase the size of the age window to include more subjects for normalization, we would lose age specificity because age-related variability would increase. Practically, our use of a z-scaled normalization takes maximum advantage of data available, and yields a conservative estimate to evaluate population differences because the power to reject the null hypothesis (i.e., both groups similar) is inversely proportional to the square root of the number of samples. Therefore, we are minimizing Type I errors (false positives) at the expense of Type II errors (false negatives).

One could ask if it would be better to compare the MS group to the NIHPD group directly to potentially find greater differences. Even though our comparison of the NC and NIHPD groups showed no significant differences, we decided to err on the side of caution since some slight scanner-bias may remain. Therefore, instead of comparing the MS group directly to the NIHPD group, we decided to compare the MS and NC groups (after the z-normalization) procedure. In this manner, any scanner-specific bias should affect both groups similarly, and thus increase the chance that the changes found between these two groups are real.
We found reduced volume of the splenium of the corpus callosum in MS patients relative to HC that was related to T2w lesion volume and reduced volume of the optic radiations related to disease duration (but not to T2w lesion volume). We also found reduced volume of deep GM structures, including the thalamus and the globus pallidus, with the reduction of the globus pallidus volume correlating with disease duration. The lack of significant abnormalities in the cortex is expected, as the normal anatomical variability of this region renders the standard deviation of deformations high (Fig. 2) and the detection of significant findings unlikely. In addition, the regional variability in cortical atrophy between patients could also explain the lack of significant atrophy in cortical regions.

The reduction of the splenium volume in MS patients relative to HC was not associated with co-localized lesions, but was associated with total lesion volume, the majority of which was located in occipital WM. Taken together, these data suggest the volume loss in the splenium of the corpus callosum results from Wallerian degeneration in nerve fiber tracts transected by WM lesions in the hemispheres. This is consistent with the pathological observations of Evangelou et al. (2000) relating axonal loss in the corpus callosum to T2w lesion volume.

Thalamic volume loss has been described in relapsing–remitting, benign and progressive forms of adult MS (Sepulcre et al., 2006; Khaleeli et al., 2007; Tao et al., 2009) and in pediatric MS by Mesaros et al. (2008). However, in the Mesaros et al. study, thalamic volume loss correlated strongly with T2w lesion volume, whereas in ours it did not. This difference is of noticeable consequence, as it has implications for the pathogenesis of this volume loss. We believe that the explanation for the discrepancy may be due to a processing step in Mesaros’ study, where “To avoid MS lesion misclassification, lesions were masked out from the GM maps and reassigned to WM maps, after each segmentation was run.” This remapping could potentially mislabel GM voxels of the thalamus as WM when lesions are present. Given that 9 of the 28 patients in Mesaros’ study had lesions in the thalamus, it is not surprising that they found 1) reduced gray matter concentration in the thalamus in pediatric MS patients compared to controls and 2) high correlation between gray matter concentration and T2-visible lesion load. In the method used in our study, T2 lesions were masked to avoid matching healthy tissue with lesions and therefore, the non-linear registrations and the resulting Jacobian maps could not be impacted by the presence of lesions. It is possible that a relation exists between T2-visible lesion load and thalamic atrophy, however our study was not able to detect it. In our case, the explanation for the thalamic atrophy would appear to be less directly related to white matter lesions.

We speculate that volume loss of the thalamus may be determined by pathology that was not visualized in our study, such as that in cortical GM or normal-appearing WM. The mechanisms responsible for this are unclear and could include Wallerian degeneration, trans-synaptic effects, or immune-mediated cytotoxicity. The importance of transsynaptic effects is supported by the observation of atrophy of the lateral geniculate nucleus and the optic radiations. However, our failure to detect a difference in the pattern of volume loss between patients with a history of optic neuritis and those without should not be over-interpreted, as many patients have subclinical involvement of the optic nerves and other factors, such as retrograde degeneration from lesions in the optic radiations, may be playing a role. Although we found no correlation between volume loss of the lateral geniculate nucleus and total T2w lesion volume, we did not assess the volume
specifically in the optic radiations. By contrast, Sepulcre et al. (2006) did perform this assessment and found that lesions in the optic radiations could explain 28% of the volume reduction they observed in the lateral geniculate nucleus.

Conclusion

The onset of MS during childhood is associated with significant losses of volume in key brain structures, suggesting that young age-expectated resiliency to injury to the central nervous system or capacity for enhanced neural repair is insufﬁcient for protecting pediatric MS patients from the degenerative aspects of MS, even early in the disease. These ﬁndings raise considerable concern about the long-term impact of the onset of MS during childhood.

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References


