ADC evaluations of the hippocampus and amygdala in multiple sclerosis

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Abstract

Background & Objective: Diffusion-weighted MR imaging and apparent diffusion coefficient (ADC) values provide significant structural information about tissues in multiple sclerosis (MS). The goal of this study was to evaluate the ADC values in the hippocampus and amygdala in MS. Methods: Thirty-eight patients with MS and 41 healthy individuals were included in the study. ADC values were measured bilaterally from three different points in the hippocampus and amygdala in MS patients and were compared with those of the controls. An analysis of variance posthoc test was used to analyse the differences among mean ADC values between MS and control groups. Results: The mean ADC values of both sides of the hippocampus and the left amygdala in MS patients were lower than the control group. The mean ADC values of the right amygdala in MS patients were lower than the control group, but the difference was not statistically significant. Conclusion: We observed restricted diffusion in the hippocampus and amygdala in MS patients contrary to information in the literature.

INTRODUCTION

Multiple sclerosis (MS) is a chronic inflammatory, demyelinating, and neurodegenerative disease of the central nervous system and the most common cause of non-traumatic disablement in young adults. Patients with MS frequently develop psychiatric disorders, and the hippocampus, which plays a basic role in memory processing, has been implicated through a retrospective discovery of a correlation between psychosis in MS patients and temporal lobe pathology. There is evidence of selective atrophy within the hippocampus in MS that is associated with impaired performance on a cognitive test of verbal memory. These findings implicate distinct disease mechanisms leading to grey matter loss in MS and are consistent with emerging evidence of an early neurodegenerative process affecting the grey matter in MS patients.

The literature lacks adequate information on the apparent diffusion coefficient (ADC) values of the hippocampus and amygdala in MS patients. Therefore, we aimed to compare the ADC values of hippocampus and amygdala in MS patients with an age-matched control group.

METHODS

Thirty-eight MS patients (8 male and 30 female, age range 23–48 years, mean 35.9±6.4 years) diagnosed as relapsing-remitting multiple sclerosis (RRMS) according to the McDonald criteria were included in the study. All patients in the study were MS patients. Magnetic resonance (MR) examinations obtained from the patients evaluated in the study were taken after an average of 8.7 ± 6.9 (r = 1-25) days from the most recent relapse episode. The control group consisted of 41 healthy individuals (15 male, 26 female, age range 22–57 years, mean 35.8 ± 9.6 years) with no neurologic disability or intracranial pathology found upon MR examination. The study was approved by the hospital ethics committee.

All experiments were performed by using a head coil in conjunction with a 1.5-T whole-body imager (Infinion; Philips Medical Systems, Cleveland, OH) with a maximum gradient amplitude of 50 mT/m and a maximum gradient slew rate of 100 mT/m/s. The head coil had an inner diameter of 27 cm.

ADC values were measured bilaterally from three different points in the amygdala and hippocampus in MS patients and were compared with those of the controls.

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Conventional magnetic resonance examinations

Before diffusion-weighted MR imaging (DWI), T1-weighted images were acquired in the transverse plane by using the following parameters: TR/TE, 407/10; bandwidth, 20.83 kHz; matrix size, 256 × 256; field of view (FOV), 22 × 22 cm; number of sections, 20; section thickness, 5 mm; and gap, 1 mm. T2-weighted fast spin-echo images were acquired with the following parameters: TR/TE, 4555/125; bandwidth, 20.83 kHz; matrix size, 256 × 256; FOV, 22 × 22 cm; number of sections, 20; section thickness, 5 mm; and gap, 1 mm.

Diffusion-weighted images

DWI was performed by using a diffusion-weighted, single echo-planar, MR-imaging sequence. During the MR studies, the two experienced radiologists evaluated the quality of the diffusion-weighted images and selected by consensus those images that had a minimum of distortion from susceptibility artefacts and ghosting for further analysis. We selected b values of 0 and 1000 s/mm² for the calculation of ADCs in this study. Diffusion-weighted images were obtained over 43 s. DWI was performed with the following parameters: TR/TE, 7216/122.8; flip angle, 90°; FOV, 24 × 24 cm; and matrix size, 128 × 128 mm. Between 20 and 24 axial sections were obtained, with a section thickness of 5 mm and an intersection gap of 2.5 mm.

The reconstructed magnitude images were transferred from the MR system to an independent workstation for the calculation of the trace images and ADC values.

Apparent diffusion coefficient measurements

All measurements were performed by one radiologist. To ensure accurate localization and consistency of measurements, radiologist independently placed region of interest (ROI) areas on the right and left side of the brain in different characteristic localisations (hippocampus, amygdala) on the images obtained with a b value of 1000 s/mm². At each pre-specified site, three ADC values were obtained by using three different-sized ROI areas. Each measurement was repeated by using three ROI areas (average areas of regions of interest were 18± 2 mm²).

The ADC values were noted according to each location, which were the right and the left sides of the hippocampus (three different measurements per side) (Figure 1) and the right and left amygdala (three different measurements per side). Mean values were used for statistical comparisons.

Statistical analysis

Statistical analyses were performed with SPSS 16.0 using one-way descriptive to calculate mean and standard deviation values, upper and lower bounds, and minimum and maximum values. An analysis of variance (ANOVA) post-hoc test was used to analyse the differences among ADC values between patients and control groups and to calculate p values in different localisations. Cross-tabulation and chi-square tests were used to calculate compliance with gender; one-way descriptive and ANOVA tests were used to calculate age compliance between patients and control groups.
Table 1: The study group descriptive

<table>
<thead>
<tr>
<th></th>
<th>Multiple sclerosis n = 38</th>
<th>Control group n = 41</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>35.9 ± 6.4</td>
<td>35.8 ± 9.6</td>
<td>0.9</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>8/30</td>
<td>15/26</td>
<td>0.145</td>
</tr>
</tbody>
</table>

RESULTS

Descriptive statistics of the study group are summarized in Table 1. The gender distribution and the mean age of the MS patients were similar to those of the control group (p=0.145, p=0.9, respectively). Mean duration of illness of the patients in the study was 4.1 ± 4.2 (r = 1-16) years. Two male and six female patients showed cerebral atrophy and there were no lesion in the targetted area of amygdala and hippocampus.

The ADC values of both groups are summarised in Table 2. ADC values observed in the left and right amygdala were lower than the ADC values observed in the right and left sides of the hippocampus in both the MS group and the control group. In the control group, the mean ADC values of the right amygdala and left amygdala did not differ statistically from each other (p = 0.648), nor was there any difference in the mean ADC values between the left and right sides of the hippocampus (p = 0.233). In the MS patients, the mean ADC measurements of the right amygdala were slightly higher than those of the left amygdala but with no difference statistically (p = 0.345). ADC measurements of the right side of the hippocampus were slightly lower than the left side in the MS patients, but again there was no statistical difference (p = 0.151). The mean ADC values of the right amygdala in the MS patients were lower than those of the control group but not significantly (p = 0.149); however, the mean ADC values of the left amygdala and the right and left sides of the hippocampus were significantly lower than those of the control group (p = 0.047, p = 0.000, p = 0.023, respectively).

DISCUSSION

Demyelination is accepted to be the primary pathological course in MS, although the exact mechanisms causing it are not well understood.7,8

In MS investigations, nonconventional MR imaging techniques, such as DWI, play a significant role in highlighting brain microstructural injury not visible when conventional sequences are used. DWI principles are attributed to the measurement of the motion of water molecules within tissues and can be used to search the structural characteristics of tissue.9-11 Diffusion of water molecules are influenced by microstructures and microdynamic processes, and ADC can be measured quantitatively. The diffusion is constricted in MS plaques, and normal-appearing white matter is actually affected in these patients.12

The latest studies have defined abnormalities, including both fractional anisotropy and mean diffusivity changes, in the cortical or subcortical normal appearing grey matter of RRMS patients when compared to controls. While mean diffusivity usually rises, fractional anisotropy has been found to either increase or decline.13-15

Table 2: The mean ADC values (ADC×10–3 mm2/s) of the left and right amygdala and hippocampus

<table>
<thead>
<tr>
<th></th>
<th>MS group</th>
<th>Control group</th>
<th>MS vs Control</th>
<th>MS R vs L</th>
<th>Control R vs L</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>P value</td>
<td>P value</td>
<td>P value</td>
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<tr>
<td>Right amygdala</td>
<td>821.3 ± 68.6</td>
<td>854.5 ± 123.9</td>
<td>0.149</td>
<td>0.345</td>
<td>0.648</td>
</tr>
<tr>
<td>Left amygdala</td>
<td>807.1 ± 64.0</td>
<td>849.9 ± 117.5</td>
<td>0.047</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right hippocampus</td>
<td>823.0 ± 56.1</td>
<td>905.6 ± 103.0</td>
<td>0.000</td>
<td>0.151</td>
<td>0.233</td>
</tr>
<tr>
<td>Left hippocampus</td>
<td>838.0 ± 64.6</td>
<td>891.4 ± 127.0</td>
<td>0.023</td>
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</table>
Larsson et al. found that acute lesions less than 3-months old (by review of serial examinations) had higher diffusion coefficient ratios than did chronic lesions. A relationship exists between trace ADC and the pattern of enhancement in MS lesions. There are significant increases in trace ADC in non-enhancing lesions and ring-enhancing lesions, which show histopathological evidence of increased myelin loss relative to homogeneously enhancing lesions, which are predominantly inflammatory with more myelin preservation.

Diffusion in enhancing portions of enhancing lesions was decreased when compared with non-enhancing portions. This finding concurs with diffusion-tensor measurements reported in acute MS lesions as defined by contrast enhancement. This relatively decreased diffusion may be the result of cellular infiltration. Alternatively, restriction of diffusion may reflect remyelination or relative preservation of structural integrity (e.g., preservation of axons). Although the precise histopathological correlates of these various areas seen on MR imaging are uncertain, the data are consistent with the hypothesis that the presence of a macromolecular structure (e.g., remyelination, proteins) is the common substrate in enhancing lesions.

In contrast to most studies, which revealed increased diffusion in different parts of the central nervous system, except in some acute plaques, we observed restricted diffusion in the hippocampus and amygdala. This is a new finding. All of these may be the result of neuronal degeneration observed in the hippocampus and amygdala as in the study of Wall et al. This decreased diffusion may be the result of a shift in intracellular water protons, ischaemia, cellular infiltration, demyelination processes, or demyelination. As the diffusion restriction in acute plaques is related to acute inflammation, we can conclude that the hippocampus and amygdala are involved through inflammatory reaction, even though they appear normal.

There is contradictory information about normal-appearing white matter. Normal-appearing white matter changes are more likely to be found in patients with MS than in other conditions that can mimic MS clinically and radiologically. One study found that ADC values were abnormal in all white matter regions assessed in a population study found that ADC values were abnormal in normal-appearing white matter. However, in another study, although ADC values were significantly altered in plaque and periplaque regions, a significance difference was not found in normal-appearing white matter.

Since there is no published information on ADC values of normal appearing hippocampus and amygdala, our study needs to be supported by multicenter DWI and diffusion tensor imaging studies.

DISCLOSURE
Conflicts of interest: None

REFERENCES
13. Filippi M. Magnetic resonance imaging findings...


