ASSESSMENT OF MULTIPLE AREAS ON MAGNETIC RESONANCE MIDSAGITTAL BRAIN IMAGES IN MULTIPLE SCLEROSIS PATIENTS*

RENGIN KOSIF, SULE AYDIN TURKOGLU[1], ELIF SULTAN BOLAC[1] and EMINE DAGISTAN[2]

Abant Izzet Baysal University Medical Faculty, Department of Anatomy, [1]Department of Neurology and [2]Department of Radiology, Bolu, Turkey

The aim of the study was to compare the first and last magnetic resonance images (MRIs) in patients diagnosed with multiple sclerosis (MS) with MRIs of normal subjects. We wanted to investigate the region initially involved in MS patients. In this retrospective study, midsagittal plane was explored on brain MRIs taken at the time when MS diagnosis was established and the last MRI was obtained following treatment for MS. Comparison was done between healthy subjects and patients diagnosed with MS. The measures included the area of corpus callosum, cerebrum, cerebellum, pons, bulbus, fourth ventricle and pituitary gland. As a result, while there was growth in the fourth ventricle area, there was shrinkage in the other areas in MS patients. In women, the tissues involved at the beginning of the disease were pituitary gland, cerebrum and bulbus, and in men corpus callosum and cerebrum. Atrophy was not time-dependent. Assessment of the correlation between the Expanded Disability Status Scale (EDDS) and atrophy revealed an increase in EDDS (disease progression) to be associated with a decrease in the area of cerebrum and corpus callosum in men, and an increase in the fourth ventricular area in women. In conclusion, we demonstrated that pituitary gland atrophy develops in the early stage of MS, especially in women. Additional studies are needed to investigate the phenomenon of early pituitary and bulbus atrophy in women versus late atrophy of these tissues in men.

Key words: multiple sclerosis, brain, midsagittal areas, assessment

Adress for correspondence: Rengin Kosif, MD, Associate Professor
Department of Anatomy
Abant Izzet Baysal University
Medical Faculty
Bolu, Turkey
Tel: +903742534656 - 3043
Fax: +903742534559
E-mail: rengink@yahoo.com

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INTRODUCTION

Multiple sclerosis (MS) is a chronic immune mediated, inflammatory, demyelinating disease of the central nervous system (1). New magnetic resonance imaging (MRI) techniques have shown microstructural damage either at white matter or gray matter, proven to be of histopathologic nature (2). Inflammation in MS has been proven, especially in deep white matter, gray matter and interstitial area, so atrophy occurs globally. Atrophy studies performed in MS have revealed the global cerebral volume, white matter and gray matter to be decreased (3). Cortical atrophy has been shown to be more pronounced than atrophy of the gray matter fraction and white matter fraction, also showing slight correlation with the Expanded Disability Status Scale (EDSS) score (4). It has been observed that the most frequent atrophy type is cortical atrophy and corpus callosum atrophy; also, hippocampal atrophy is much notable than global brain atrophy and continues progressively (5).

Pituitary gland is a secreting organ that is formed by adenohypophysis and neurohypophysis. Not many studies have investigated pituitary gland atrophy in

MS. Corticosteroid therapy is the most frequently used mode of MS treatment, mostly administered for 5-10 days. This treatment causes suppression of the at hypothalamus-pituitary-adrenal (HPA) axis (6). This suppression can be reversed spontaneously, as demonstrated by Lević *et al.* (7). HPA axis suppression has been defined as a consequence of long term glucocorticoid utilization. There is evidence for a time-dependent variability in the HPA stress system with an increased cortisol stress response in the first year after diagnosis, along with a more blunted HPA stress response and a diminished Glasgow Coma Scale (GCS) score in subsequent disease stages (8). Dysregulation of the HPA axis has frequently been reported in MS. So far, HPA axis function in MS has predominantly been studied under pharmacological stimulation, which is associated with a series of methodological caveats. The knowledge of circadian cortisol patterns and cortisol awakening response is still limited (9).

During natural course of MS, HPA axis hyperactivation has been observed (10,11). This hyperactivation suggests that HPA activity exerts a protective effect by limiting the potential immune overload in acute lesional inflammation (12,13). However, this activation has been associated with clinical deterioration (8,14). It has been recommended that the activity of HPA axis can be used as a biomarker for the progression of MS (15).

Also, there are conflicting reports about prolonged glucocorticoid treatment in MS, some of them stating that this treatment suppresses the HPA axis (16).

In our study, MRI examinations were performed in patients diagnosed with MS before and at the end of treatment period. Comparison was made for corpus callosum, pituitary gland, pons, bulbus, fourth ventricle and cerebellum on midsagittal plane images with normal subjects having the same anatomic structure. To the best of our knowledge, there is no study on comparison using midsagittal plane. There are many studies of corpus callosum in MS patients, however, none examined midsagittal plane involving other anatomic structures. It has not yet been clarified whether or not hypophyseal atrophy is present in MS. In addition, correlation of MS patient EDDS grades with the area was performed. Moreover, the presence of atrophy in the newly diagnosed areas and the ratio were compared with controls.

In the present study, the aim was to compare the first and last MRIs of patients diagnosed with MS, and with MRIs of normal individuals. In patients with MS, we wanted to investigate the region involved first. Thus, we compared the findings in the first affected region and early stage findings in MS patients with the patient final EDSS scores.

SUBJECTS AND METHODS

Study design

The study was conducted in accordance with the Helsinki Declaration principles and approved by the local institutional Review Board (Decision no. 2014/12). Cranial MRIs of patients admitted to the neurology department of our tertiary center and diagnosed with relapsing remitting multiple sclerosis (RRMS) according to McDonald criteria were retrospectively included in the study (patient group). All patients were under first-line or second- line drug treatment for MS and differences between treatment types were not evaluated. MRIs of normal healthy subjects (admitted for any reason and having normal MRI findings, matched by age and gender) were reviewed from the radiology archives (control group).

Magnetic resonance imaging

Images were obtained with a 1.5 Tesla, Magnetom Symphony (Siemens, Germany) MRI device. Images were saved in Dicom format. T1 weighted images were used in calculations. All measurements were done by the same observer. Images were viewed by using the Onis (Ver. 2.5 Ultimate) software. Anatomic images were framed by this program. This program calculates the area automatically at the end of drawing.

Outcome parameters

Reachable first and last MRIs were included in the study. Minimum 6 months and maximum 48 months had elapsed between the first and last MRIs. In patient group, the initial and latest obtained MRIs were also compared. Seven areas were chosen for measurements on brain MRI in midsagittal plane. The initial MRIs in patients obtained at the time of MS diagnosis, the last MRIs in patients by that time and MRIs of healthy subjects were analyzed. The EDSS of patients at the time of the last MRI were collected from patient files.

Measurements were performed using the measurement technique employed by Venkatasubramanian *et al.* in schizophrenia patients (17).

The midsagittal section was selected using the following inclusion criteria:

- getting the midline section in which septum pellucidum can be seen;
- distinct outline of the corpus callosum;
- easily identifiable cerebral aqueduct;
- clearly visible cortical gyral crests both anteriorly and posteriorly to the corpus callosum; and
- absence of visible intrusion into the gray and white matter.

The first and the last images of patients were compared between each other, and also with control ones. We also analyzed whether or not the time period correlated with area reduction.

Patient records of EDSS scores at the time of the last MRI were retrospectively reviewed and calculated. EDSS scores range between 0 (normal neurologic findings) and 10 (MS-related death) points. Correlation between EDSS scores and decrease in sizes was investigated. Also, the existence and rate of atrophies at the new diagnosis were compared with controls.

In our study, patients were diagnosed with definitive clinical MS and all patients were under immunomodulatory therapy such as interferon and glatiramer acetate for first-line drug treatment such as phingolimod and natalizumab for second-line drug treatment. Assessment of immunomodulatory effect of different immunomodulatory therapies on brain atrophy was not aimed in this study. The number of patients was not sufficient to form a subgroup for this analysis. If plaque formation limited measurement at the anatomic regions investigated, it excluded the measurement. Patient attack was not considered since this condition does not affect brain atrophy.

All measurements were done by one observer. Images at MS diagnosis compared with second images at the last follow up visit, relation according to the time period elapsed between the two images and atrophy were investigated. The respective structures area was calculated in normal subjects and statistically compared. The cranial areas measured are shown in Figures 1 and 2. The measures included the area of corpus callosum, cerebrum, cerebellum, pons, bulbus, fourth ventricle and pituitary gland (Figs. 1 and 2).

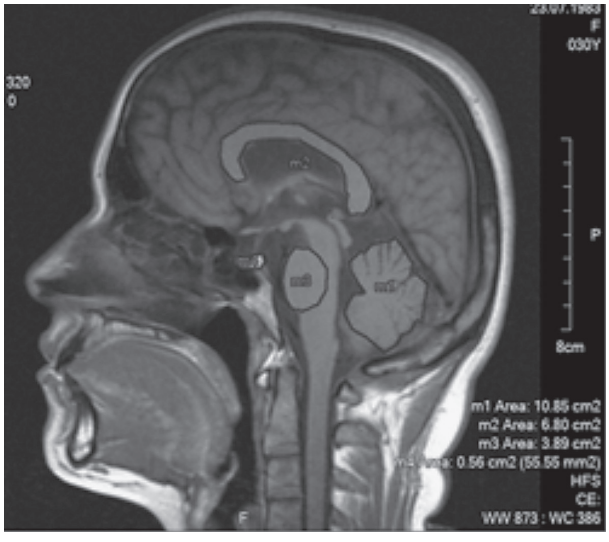

Fig. 1. *Areas: m^1 = cerebellum, m^2 = corpus callosum, m^3 = pons, m4 = pituitary gland*

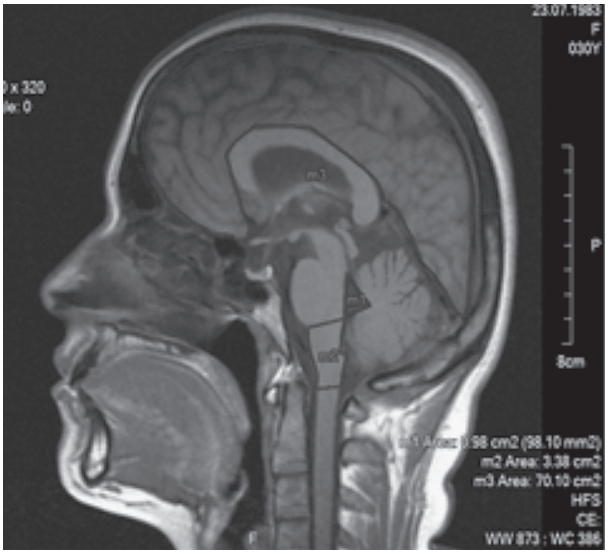

Fig. 2. *Areas: m^1 = fourth ventricle, m^2 = bulbus, m^3 = cerebrum.*

Statistical analysis

Data were analyzed using the IBM Statistical Package for Social Sciences v. 17 (SPSS Inc., Chicago, IL, USA). Parametric tests were applied to data of normal distribution and nonparametric tests were applied to data of non-normal distribution. Student's t-test was used for normal distribution and Man Whitney U test for non-normal distribution. Data were expressed as mean ± standard deviation (SD) or median (interquartile range), as appropriate. All differences associated with a chance probability of 0.05 or less were considered statistically significant.

RESULTS

Brain MRI images in midsaggital plane of 48 patients with RRMS (21 male and 27 female) and 47 healthy control subjects (23 male and 24 female) were analyzed. The mean age of MS patients was 36.33±11.65 and 37.29±11.22 years in female and male patients, respectively. The results obtained were compared with those in 24 female and 23 male healthy subjects, where the mean age was 37.96±9.68 and 40.48±11.93 years, respectively. Data were analyzed according to whether or not fitting normal distribution. The variables showing non-homogeneous distribution in the cerebellum, bulbus, pituitary gland and fourth ventricle were evaluated by Mann-Whitney U test, whereas other variables with homogeneous distribution were expressed as mean ±SD and evaluated by independent sample t-test.

Comparison of initial patient MRIs with control group MRIs revealed the area of bulbus (p=0.04), pituitary

gland (p=0.02), corpus callosum (p=0.0) and cerebrum (p=0.0) to be decreased significantly in the patient group. Comparison of final patient MRIs with control group MRIs showed a significant decrease in the area of corpus callosum (p=0.00), pituitary gland (p=0.00) and cerebrum (p=0.00). These results are shown in Table 1.

Table 1
First and last magnetic resonance imaging (MRI) results in multiple sclerosis and control groups (cm^2) - all subjects

First MRI	Cerebellum	Bulbus	Fourth ventricle	Pituitary gland	Corpus callosum	Pons	Cerebrum
Control group (n=47)	12.03±2.02	4.07±0.48	0.93±0.32	1±0.36	6.35±1.05	3.35±0.43	79.3±7.47
Patient group (n=48)	11.97±2.16	4.2±0.71	0.86±0.24	0.97±0.36	5.39±1.35	3.5±0.37	73.07±7.38
p value	p=0.81	p=0.04	p=0.5	p=0.02	p=0.00	p=0.99	p=0.00
Last MRI	Cerebellum	Bulbus	Fourth ventricle	Pituitary gland	Corpus callosum	Pons	Cerebrum
Control group (n=47)	12.03±2.02	4.07±0.48	1.0±0.36	0.66±0.14	6.35±1.05	3.50±0.43	79.3±7.47
Patient group (n=48)	11.44±2.03	4.07±0.5	1.26±0.75	0.58±0.11	5.00±1.37	3.37±0.4	71.43±7.79
p value	p=0.16	p=1.0	p=0.61	p=0.00	p=0.00	p=0.11	p=0.00

On comparison between the initially obtained MRI images in healthy men and men with MS, a significant decrease was detected in the size of corpus callosum (p=0.00) and cerebrum (p=0.01). Although not statistically significant, the pons, bulbus, cerebellum and pituitary gland were smaller, and the fourth ventricle was larger than their normal sizes. On comparison between the last MRI images in healthy men and men with MS, the areas occupied by corpus callosum (p=0.00), cerebrum (p=0.00) and pituitary gland (p=0.03) were significantly decreased. Although not statistically significant, there was a decrease in the size of the cerebellum and pons, but increase in the area occupied by the fourth ventricle. These results are shown in Table 2.

Table 2
First and last magnetic resonance imaging measurements in multiple sclerosis and control groups – male (cm^2)

Male (first)	Cerebellum	Bulbus	Fourth ventricle	Pituitary gland	Corpus callosum	Pons	Cerebrum
Control group (n=23)	11.85±1.9	4.3±0.49	1.07±0.38	0.63±0.17	6.44±1.18	3.63±0.39	81.63±7.63
Patient group (n=21)	11.75±1.8	4.5±0.52	1.1±0.44	0.57±0.11	5.07±1.25	3.58±0.44	76.07±6.33
p value	p=0.86	p=0.16	p=0.81	p=0.32	p=0.00	p=0.67	p=0.01
Male (last)	Cerebellum	Bulbus	Fourth ventricle	Pituitary gland	Corpus callosum	Pons	Cerebrum
Control group (n=23)	11.85±1.9	4.31±0.49	1.08±0.38	0.63±0.17	6.44±1.18	3.64±0.4	81.63±7.64
Patient group (n=21)	11.25±1.6	4.36±0.52	1.28±0.5	0.54±0.08	4.77±1.4	3.46±0.41	74.55±7.12
p value	p=0.26	p=0.76	p=0.1	p=0.03	p=0.00	p=0.15	p=0.00

When the initially MRI images in healthy women and women with MS were compared, a significant decrease in the areas occupied by the bulbus (p=0.05), cerebrum (0.002) and pituitary gland (p=0.022) was recorded. When the first and last MRI images in healthy women, and in women with MS were compared, a significant decrease was found in the areas occupied by the bulbus (p=0.05), cerebrum (p=0.00) and pituitary gland (p=0.02). Although not statistically significantly, corpus callosum (p=0.06), and fourth ventricle were enlarged, while cerebellum and pons were smaller than normal**.** When the last MRI images of healthy women and women with MS were compared, a significant decrease was recorded in the areas occupied by corpus callosum (p=0.0), cerebrum (p=0.0) and pituitary gland (p=0.02). Despite the lack of any statistical significance, a decrease was found in the size of the cerebellum and pons, and enlargement of the fourth ventricle. Data on MS patient group and control group are shown in Table 3.

Table 3
First and last magnetic resonance imaging measurements in multiple sclerosis and control groups – female (cm^2)

Female (first)	Cerebellum	Bulbus	Fourth ventricle	Pituitary gland	Corpus callosum	Pons	Cerebrum
Control group (n=24)	12.2±2.15	3.85±0.35	0.93±0.32	0.68±0.12	6.27±0.92	3.38±0.42	77.07±6.71
Patient group (n=27)	12.14±2.4	3.97±0.75	0.86±0.24	0.6±0.14	5.63±1.39	3.44±0.31	70.73±7.4
p value	p=0.93	p=0.05	p=0.5	p=0.02	p=0.06	p=0.51	p=0.00
Female (last)	Cerebellum	Bulbus	Fourth ventricle	Pituitary gland	Corpus callosum	Pons	Cerebrum
Control group (n=24)	12.2±2.15	3.85±0.35	0.93±0.32	0.68±0.12	6.27±0.92	3.38±0.42	77.07±6.7
Patient group (n=27)	11.59±2.33	3.85±0.36	1.23±0.9	0.6±0.12	5.19±1.34	3.29±0.38	69±7.53
p value	p=0.33	p=0.95	p=0.27	p=0.02	p=0.00	p=0.46	p=0.00

The following differences were recorded between the first and last MRI images in male MS patients: significant decrease in the areas occupied by the cerebellum (p=0.0), corpus callosum (p=0.0), pons (p=0.05), bulbus (p=0.01), and cerebrum (p=0.00), and enlargement of the fourth ventricle (p=0.00). With the exception of pituitary gland, all measured areas were different between the two groups**.** The following differences were found in the areas occupied by the respective cerebral structures between the first and last MRI images in female MS patients: enlarged fourth ventricle (p=0.04) and significantly decreased areas occupied by the cerebellum (p=0.00), cerebrum (p=0.00), corpus callosum (p=0.00) and pons (p=0.00). No significant changes were recorded in the bulbus and pituitary gland measurements**.** These results are shown in Table 4.

Table 4
Comparison between first and last magnetic resonance imaging (MRI) measurements in male and female MS patients (cm^2)

Male (n=21)	Cerebellum	Bulbus	Fourth ventricle	Pituitary gland	Corpus callosum	Pons	Cerebrum
First MRI	11.75±1.8	4.5±0.52	1.1±0.44	0.57±0.11	5.07±1.25	3.59±0.44	76.07±6.34
Last MRI	11.24±1.6	4.36±0.52	1.28±0.5	0.54±0.08	4.77±1.4	3.46±0.41	74.55±7.12
p value	p=0.00	p=0.01	p=0.00	p=0.61	p=0.00	p=0.05	p=0.00
Female (n=27)	Cerebellum	Bulbus	Fourth ventricle	Pituitary gland	Corpus callosum	Pons	Cerebrum
First MRI	11.59±2.42	3.97±0.75	0.86±0.24	0.6±0.14	5.62±1.39	3.44±0.31	76.73±7.4
Last MRI	11.14±2.33	3.85±0.36	1.24±0.91	0.6±0.12	4.19±1.34	3.29±0.38	69.01±7.54
p value	p=0.00	p=0.33	p=0.04	p=0.55	p=0.00	p=0.00	p=0.00

When the pooled first and last MRIs obtained in MS patients were compared, significant difference was recorded in all the parameters measured except for the bulbus and pituitary gland. These results are shown in Table 5

Table 5
First and last magnetic resonance imaging (MRI) measurements in all MS patient group (cm^2)

Study group (n=48)	Cerebellum	Bulbus	Fourth ventricle	Pituitary gland	Corpus callosum	Pons	Cerebrum
First MRI	11.97±2.16	4.2±0.71	0.96±0.36	0.59±0.13	5.39±1.35	3.5±0.37	73.07±7.39
Last MRI	11.43±2.03	4.07±0.5	1.25±0.75	0.57±0.11	5.01±1.37	3.37±0.4	71.43±7.8
p value	p=0.00	p=0.06	p=0.00	p=0.1	p=0.00	p=0.00	p=0.00

In MS patients, MRI images were obtained at minimum 6 and maximum 48 months apart. There was no significant difference in the time interval between the first and last measurement, or in the atrophy progression in either male or female patients. There was no correlation of the percent differences between the first and last measurements of particular areas in MS patients.

Examination of the correlations between EDSS scores of all male and female MS patients yielded negative (p=0.000) correlation between the first MRI measurements of corpus callosum area and EDSS scores, but positive correlation between EDSS scores and the first measurement of the ventricular area (p=0.001).

In men, there was negative correlation between EDSS scores and the first (p=0.000) and last (p=0.001) measurements of the areas occupied by corpus callosum and cerebrum (p=0.024). In women, the first measurement of the ventricular area correlated positively (p=0.005) with EDSS scores.

As the EDSS scores increased, i.e. as the patient condition worsened, the area of corpus callosum decreased, while that of the fourth ventricle increased.

DISCUSSION

According to recent literature, brain atrophy is present in MS, even in the initial stages of the disease (18). There are many reports stating that brain atrophy occurs due to lesions located both in the gray and white matter (19,20). In our study, we also found that all brain tissues decreased in size, resulting in an increase in the fourth ventricle area. The initial size reduction was observed in the bulbus, pituitary gland, corpus callosum and cerebrum, when we compared first MRIs of MS patients and control subjects. In contrast, there was no significant reduction in the areas of cerebellum and pons on initial scans. The areas of cerebellum and pons were found to be decreased when the last scans were compared with the initial ones. This finding suggested that the cerebellum and pons areas were affected later than the other areas. Atrophy detected in all measured parameters did not correlate with the time elapsed.

In male MS patients, the initial size reduction was observed in corpus callosum and cerebrum, which is consistent with literature data. In female patients, the initial size reduction was observed in pituitary gland and cerebrum.

Hyperactivation of the HPA axis is observed in many patients with MS. This activation is associated with the course of the disease and comorbid mood disorders. Especially in women with secondary progressive disease, correlation was demonstrated between increased cortisol levels and slowly progressing disease. Comparison of patients with higher and lower cortisol levels revealed a relatively greater number of active lesions and smaller number of remyelinated plaques. In patients with MS, hyperactivity of the HPA axis was found to be correlated with lower degrees of inflammation or more severe neurodegeneration. This phenomenon is important in suppression of disease activation (21). MS patients with short illness duration were found to have high cortisol stress response. At long term, however, a significantly decreased HPA activity was recorded. This means that at long term post, the stress glucocorticoid sensitivity decreased. In other words, in the first year, the HPA stress response is high and declines with time. HPA axis activation is regulated by corticotropin-releasing hormone (CRH) and arginine vasopressin (AVP). These two types of neurons are located in the paraventricular nucleus of the hypothalamus. HPA activation is provided by neuroendocrine regulation. The recovery in MS was shown to be associated with the activation of the neuroendocrine HPA axis (14).

When evaluated by EDSS, MS patients with gradually higher EDSS scores responded more markedly to cortisol stimulation tests (15). EDSS scores increased more rapidly in patients with stronger HPA reactivity, which was found to be correlated with cognitive affect (16). In another study, indicators of HPA were found to be correlated with neurological disability; however, no correlation between them and duration of the disease, number of previous relapses, corticosteroid therapies or depressive mood was detected (22). In our study, correlation was observed between EDSS scores and decreased areas of cerebrum and corpus callosum in men, and enlargement of the fourth ventricle in women.

All these studies demonstrated that HPA activity, which is increased in the early stage of MS, decreased with time. As a response to preclinical inflammation, hyperactivation of the HPA axis develops. Besides fatigue and mood disorders seen during this stage of the disease, the grade of patient disability worsens. Especially in women, fatigue is most frequently seen during preclinical stage.

In our study, a significant decrease in the areas occupied by the pituitary gland and cerebrum was detected when the first patient MRI images were compared with control group MRIs. When the first and last MRI patient findings were compared and evaluated as a whole or separately for male and female patients, significant differences persisted in all parameters except for the pituitary gland and bulbus, while pituitary gland did not shrink furthermore. This phenomenon demonstrated that pituitary gland was affected in the early stage; however, this effect did not persist at the same level and rate.

The most important and the frequently seen disabling symptom encountered in patients with MS is chronic fatigue (23). Fatigue is seen as the first symptom, along with sensory manifestations in 81% of MS patients du-

ring the first year of the disease (24). In particular, fatigue is found more frequently in women as compared with men (25). The studies performed demonstrated the lack of any correlation between fatigue and MRI findings. Many authors have suggested the presence of probable correlation between basal ganglions and deeply situated structures such as subcortical and frontal circuits, cerebral cortex, thalamus and caudate nucleus, but no satisfactory explanation has been reached (26,27). However, some studies indicated the presence of a relationship between fatigue and HPA axis dysfunction (28,29). In addition, Gottschalk *et al*. performed a study which demonstrated correlation between fatigue felt in MS and hyperactivity of HPA axis (30). Especially in our female patients, atrophy of the pituitary gland was the first manifestation of the disease. Fatigue is seen more frequently in female MS patients and during the first years of the disease. Since our study had a retrospective design, we could not question our patients about their complaints of fatigue. Consequently, we could not evaluate the relationship between atrophy of the pituitary gland and fatigue. Larger scale studies that will investigate the relationship between pituitary atrophy and fatigue in patients with MS are needed.

CONCLUSION

In the literature, numerous studies have reported correlations between MS and MRI findings, especially related to atrophy of the cortex and corpus callosum. However, in our study, differently from other studies, we demonstrated that atrophy of the pituitary gland developed in the early stage of MS, especially in women, but it did not persist at the same level and rate. Therefore, attention should be paid to early atrophy of pituitary gland in women and late atrophy of this tissue in men. Based on our findings, we found that early manifestation of pituitary gland atrophy occurred in female MS patients.

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SAŽETAK

OCJENA MNOGOSTRUKIH PODRUČJA NA SREDNJESAGITALNIM SLIKAMA MAGNETSKE REZONANCIJE MOZGA U BOLESNIKA S MULTIPLOM SKLEROZOM

R. KOSIF, S. AYDIN TURKOGLU[1], E. SULTAN BOLAC[1] i E. DAGISTAN[2]

Sveučilište Abant Izzet Baysal, Medicinski fakultet,[1] Klinika za neurologiju, i [2]Zavod za radiologiju, Bolu, Turska

Cilj rada bio je usporediti prve i posljednje slike magnetske rezonancije (MR) u bolesnika s multiplom sklerozom (MS) sa slikama zdravih osoba. Kod bolesnika s MS htjeli smo ispitati najranije zahvaćeno područje. U ovoj studiji se srednjesagitalno područje kod bolesnika s postavljenom dijagnozom MS pregledalo na slikama MR mozga u vrijeme postavljanja dijagnoze i nakon liječenja. Uspoređivalo se zdrave osobe s bolesnicima kojima je dijagnosticirana MS. Mjerenje je uključilo područje korpusa kalozuma, mozga, malog mozga, ponsa, bulbusa, četvrtog ventrikula i hipofize. Kod bolesnika s MS došlo je do porasta na području četvrtog ventrikula, a do smanjenja u drugim područjima. Utvrđeno je da su zahvaćena tkiva u žena na početku bolesti bila hipofiza, mozak i bulbus, a kod muškaraca korpus kalozum i mozak. Otkriveno je da atrofija ne ovisi o vremenu. Kada se promatralo korelaciju između zbira na *Expanded Disability Status Scale* (EDDS) i atrofije, vidjelo se da s povećanjem EDDS (kada bolest napreduje) dolazi do smanjenja područja malog mozga i korpusa kalozuma u muškaraca, a povećanja područja četvrtog ventrikula u žena. Pokazali smo da se atrofija hipofize razvija u ranoj fazi MS, osobito u žena. Pozornost privlači rana atrofija hipofize i bulbusa u žena te kasna atrofija ovih tkiva u muškaraca.

Ključne riječi: multipla skleroza, mozak, srednjesagitalna područja, procjena