CASE SERIES

Brain morphometric changes in patients with fibromyalgia

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Abstract

The aim of this study was to determine whether there is a decrease or an increase in the volume of different regions of the brain by comparing brain morphometry ofpatients diagnosed with Fibromyalgia Syndrome and healthy control subjects.

The study included 23 female patients who were diagnosed with fibromyalgia, and 18 females, age-matched healthy subjects. Structural Mitral Regurgitation data was processed using Surface-Based Morphometry (SBM) on the Freesurfer 6.0 programme (http://surfer.nmr.mgh.harvard.edu).

As a result of the surface-based analyses, a statistically significant reduction was determined in the Fibromyalgia Syndrome patient group in some brain region. A statistically signficant increase was determined in the FMS patient group with respect to the left anterior occipital sulcus volume, left inferior temporal gyrus thickness and left anterior occipital sulcus area.

The results of this study showed that FMS affected brain morphometry through the brain central pain mechanisms and the normal brain morphology was changed because of atrophy in some areas and hypertrophy in some areas.

Keywords: Brain MRI, Brain morphometry, Fibromyalgia pain.

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Introduction

One of the most frequently seen chronic pain syndromes is fibromyalgia syndrome (FMS). Fibromyalgia syndrome is a chronic musculoskeletal system disease characterised by pain widespread through the body, fatigue, sleep disorders, and sensitive points in certain anatomic regions.[1] The basic mechanism of pain in FMS patients is hyperalgesia, which is an increased response to a normal pain stimulus, and allodynia, which is the perception of pain from a stimulus which is not normally painful.[2]

The aim of this study was to determine whether there is a decrease or an increase in the volume of different regions of the brain by comparing brain morphometry in patients diagnosed with FMS and healthy control subjects.

Case Series

The study included 23 female patients who presented at the Physical Therapy and Rehabilitation Polyclinic, diagnosed with fibromyalgia and 18 age-matched healthy female subjects. Exclusion criteria for both groups were diabetes, cancer, obesity, major psychological disorder, alcohol use, cigarette smoking, and pregnancy. The FMS diagnosis was made according to ACR criteria.[3]

Magnetic resonance imaging (MRI) was performed using a 1.5T system (Magnetom Essenza Siemens, Erlangen, Germany) with an 8-channel head coil. First, 3-dimensional T1-weighted images (TR=2300ms, TE=4,23 ms, slice thickness=0,8 mm, flip angle=12, Bandwidth=130 Hz/Px, SNR=1) were examined considering potential movement artefacts. Then, structural MR data was processed using Surface-Based Morphometry (SBM) on the Freesurfer 6.0 programme.[4] This programme is a free-of-charge software package which automatically differentiates segments according to the intensity values of the subcortical structures and 3-D reconstruction of the cortical surface.

The data pre-processing steps basically comprise motion correction and brain extraction. Grey matter, white matter and cerebrospinal fluid (CSF) were segmented and the brain was divided into two hemispheres with 40,962 vertices in each hemisphere and tessellation of the GM/WM boundary. Inflation and registration of the cortical surface was then performed. Surfaces were parcellated into regions of interest defined by the Desikan atlas. By examining a total of 148 regions, as 74 regions from each cerebral hemisphere, separate comparisons were made of the patients and control group with respect to the volume, area and thickness of the right and left hemispheres.

The study was approved by the local ethics committee (no 80576354-050-99/117) and a written informed consent was obtained from patients. MRI studies were performed before being treated after the diagnosis.

Statistical Analysis: Data obtained in the study were analysed statistically using IBM SPSS (venn). 20 software.

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Table-1: As a result of the surface-based analyses, a statistically significant reduction was determined in different brain regions in the FMS patients.

	Patient group (Mean ± SD)	Control group (Mean ± SD)	p
Rh_S_front_inf_volume	3026,043±427,7134	3363,833±470,7369	0,021
Rh_S_front_sup_volume	3982,696±678,4564	4482,556±601,1467	0,018
Rh_S_oc_middle_and_lunatus_volume	1222,391±377,7121	1487,444±374,4732	0,031
Lh_G_and_S_cingul-Mid-Ant_volume	2419,087±280,4161	2662,667±348,2146	0,017
Lh_G_cuneus_volume	2309,870±373,5998	2550,778±384,7977	0,050
Lh_S_central_volume	3375,174±404,3304	3770,944±506,8864	0,008
Lh_S_front_inf_volume	3282,652±488,0026	3605,056±514,9443	0,047
Lh_S_oc_middle_and_lunatus_volume	1313,652±315,3328	1548,333±327,4754	0,025
Lh_S_pericallosal_volume	1124,739±147,2667	1280,222±256,0711	0,019
Lh_S_collat_transv_post_thickness	1964,522±1903616	2111,444±165,1592	0,013
Lh_S_pericallosal_thickness	1890,609±186,0886	2052,889±253,5695	0,023
Rh_G_and_S_frontomargin_area	698,435±82,1699	749,722±76,8810	0,048
Rh_S_front_inf_area	1424,304±187,6911	1594,778±150,8679	0,003
Rh_S_front_sup_area	1777,609±272,2004	2011,889±250,0153	0,007
Lh_G_cuneus_area	1299,130±190,1713	1411,278±156,8442	0,050
Lh_S_front_inf_area	1552,435±243,7795	1709,333±237,9169	0,045
Lh_S_oc_middle_and_lunatus_area	758,870±184,9566	888,778±165,7960	0,025
Lh_S_temporal_transverse_area	251,174±39,1380	281,389±46,1534	0,029

Lh_S: Left cerebral hemisphere sulcus.
Lh_G: Left cerebral hemispere gyrus.
Rh_G: Right cerebral hemisphere gyrus.
Rh_S: Right cerebral hemisphere sulcus.

Table-2: A statistically signficant increase was determined in the FMS patients.

	Patient group (Mean ± SD)	Control group (Mean ± SD)	p
Lh_S_occipital_ant_volume	1312,870±370,2798	1060,500±363,0082	0,035
Lh_G_temporal_inf_thickness	2797,609±197,0082	2744,500±229,6599	0,039
Lh_S_occipital_ant_area	650,087±165,1690	523,611±171,5720	0,022

Lh_S: Left cerebral hemisphere sulcus.
Lh_G: Left cerebral hemispere gyrus.

Results were stated as mean±standard deviation, median, minimum and maximum values, or number (n) and percentage (%). Conformity of continuous variables to normal distribution was assessed with the Shapiro Wilk test when the sample size was 50, and with the Kolmogorov-Smirnov test when the sample size was ≥50. In the comparison of two independent groups of data, the Independent Samples t-test was used when normal distribution conditions were met, and the Mann Whitney U-test was applied when the data did not show normal distribution. In the comparison of two dependent groups of data, the Paired Samples t-test was used when normal distribution conditions were met, and the Wilcoxon signed-rank test was applied when the data did not show normal distribution. In the comparison of two groups of quantitative data, the Pearson correlation test was applied when normal distribution conditions were met, otherwise Spearman correlation was used. A value of p<0.05 was accepted as statistically significant.

No significant difference was determined between the 23 patients and the 18 control group subjects with respect to age (p=1.0). The mean age was 37.6 ± 8.1 years (range, 23-55 years) in the FMS patient group and 32.8 ± 6.8 years (range, 21-63 years) in the control group. There was no significant difference between the groups with respect to marital status and the sociocultural characteristics were similar in both groups.

As a result of the surface-based analyses, a statistically significant reduction was determined in the FMS patient group with concerning right inferior frontal sulcus volume (p=0.021), right superior frontal sulcus volume (p=0.018), right middle occipital sulcus and (lunate) sulcus volume (p=0.031), left middle anterior part of the singulate gyrus and sulcus volume (p=0.017), left cuneus volume (p=0.050), left central sulcus volume (0.008), left inferior frontal sulcus volume (p=0.047), left middle occipital and lunatus sulcus volume (p=0.025), left pericallosal sulcus volume (p=0.019), left posterior transverse collateral sulcus thickness (p=0.013), left pericallosal sulcus thickness (p=0.023), right frontomarginal gyrus and sulcus area (p=0.048), right inferior frontal sulcus area (p=0.003), right superior frontal sulcus area (p=0.007), left cuneus area (p=0.050), left inferior frontal sulcus area (p=0.045), left middle occipital sulcus and lunatus sulcus area (p=0.025) and left transverse temporal sulcus area (p=0.029). (Table-1)

A statistically signficant increase was determined in the FMS patient group as seen in the left anterior occipital sulcus volume (p=0.035), left inferior temporal gyrus thickness (p=0.039) and left anterior occipital sulcus area (p=0.022) (Table-2).

Discussion

Stimuli which are painless in healthy subjects are perceived as painful by FMS patients and a series of substances related to pain are activated from the relevant brain regions.[5] The currrent study aimed to show morphometric changes in the brain through comparisons of FMS patients with healthy control subjects. Although the total grey matter volume of FMS patients was shown to be lower than that of a control group in a pioneering

study by Kuchinad et al. and later by Jensen et al, many similar studies have not found a significant difference between FMS patients and a control group.[6,7] In the current study, a statistically significant decrease was determined in the cuneus volume and area, the cingulate gyrus volume and the frontomarginal gyrus volume of the FMS patients compared to the control group, and a statistically significant increase was determined in the left inferior temporal gyrus thickness.

Most importantly, there is still uncertainty about whether or not morphological restructuring only affects pain processing, and whether areas of local restructuring reflect specific models of brain functional conditions seen for different types of chronic pain. Recent studies have shown that the changes formed in the grey matter of pain patients have reduced with termination of the pain.[5] It has also been shown that the morphological changes observed in chronic pain conditions are correlated with the severity and duration of the pain.[6]

According to Diaz-Piedra et al, events such as anxiety, stress, sleeplessness and overuse of analgesics could lead to structural differences in total grey matter volume and total white matter volume between FMS patients and healthy control subjects. At the local level, a decrease in grey matter in the medial orbitofrontal cortex is associated with more severe psychological problems for both groups. Furthermore, local increases in grey matter in the superior frontal gyrus, cerebellum, medial orbitofrontal cortex and frontal superior medial cortex have been found to be related at a positive rate to pain sensitivity, depression, anxiety and insomnia.[8]

T. Schmidt-Wilce et al determined varying patterns in brain morphology, such as reduced grey matter in the right superior temporal gyrus and left posterior thalamus, and increased grey matter in the left orbitofrontal cortex, left cerebellum and in bilateral basal ganglions.[9] In a study by Zheng et al investigating age-related changes in brain structures, there was determined to be a reduction together with advancing age in cortical thickness and local gyrification index in all brain regions. With the exception of the fourth ventricle and total white matter volume, there was seen to be a non-linear correlation with age of all the total grey matter volume, white matter hyperintensity, and the third ventricle and lateral ventricle volume. Thalamus volume was seen to decrease with age, while hippocampus volume first increased then decreased.[10] Using MRI DTI, Lutz et al showed that microstructural changes in the brain correlated with the intensity of FMS symptoms.[11] Kuchinad et al first showed grey matter atrophy in fibromyalgia patients. In a surprising manner, it was seen that compared to their healthy age groups, FMS patients lost more grey matter each year than normal.[6]

Chronic pain and stress-related disorders are characterised by a reduction in grey matter in the brain and regional differences between the reductions in grey matter can be explained by different symptoms. The loss of grey matter in FMS patients is usually in stress-related areas such as the parahippocampal gyrus, and pain processing areas such as the singulate, insular and prefrontal cortex showing that the symptoms are long-term. The prefrontal cortex and the singulate gyrus are effective in pain modulation. Grey matter atrophy in the parahippocampal and frontal cortex occurs together with cognitive defects in FMS.

In the current study, although a reduction was determined in grey matter areas such as the cuneus, singulate gyrus and frontomarginal gyrus, the reduction was statistically significant compared to the control group in the inferior and superior frontal sulcus and transverse temporal sulcus areas, suggesting that this could be associated with hypertrophy in the adjacent gyrus.

Conclusion

FMS affected brain morphometry through the brain central pain mechanisms and the normal brain morphology was changed because of atrophy in some areas and hypertrophy in some areas.

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