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ORIGINAL ARTICLE

Decreased olfactory bulb volumes in patients with fibromyalgia syndrome

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Abstract Among the other symptoms, impaired olfactory function such as odor identification, threshold, and discrimination have been reported in patients with fibromyalgia syndrome (FMS). To investigate olfactory bulb (OB) volumes in FMS, by using magnetic resonance imaging (MRI), and to make reasonable suggestions are the goals of the present study. The study included 62 individuals as the FMS group (n = 30) and the control group (n = 32). MRI examinations were performed by a 1.5-T scanner and a standard head coil was used for the images. The coronal T2-weighted images were used for to measure OB volumes. Right, left, and total OB volumes were calculated with the aid of these images. The mean age of the FMS group was 44.2 ± 8.3 years and the control group was 41.7 ± 3.53 years. The mean volume of the right OB was 74.9 ± 12.4 mm^3 in the FMS group and was 92.6 ± 12.9 mm^3 in the control group. The mean value of the left OB volume was 74.3 ± 10.8 mm^3 in the FMS group and 92.8 ± 12.6 mm^3 in the control group. The mean of the total OB volume was 146.6 ± 20.81 mm^3 in the FMS group and 186.5 ± 23.5 mm^3 in the control group. Left, right, and total OB volumes were significantly lower in the FMS group than in the control group (all $p < 0.05$). Female patients with FMS are under the risk of the decreased olfactory bulb volumes. This situation should be kept in mind for proper and reasonable management of this tough syndrome.

Keywords Fibromyalgia syndrome · Magnetic resonance imaging · Olfactory bulb volume

Introduction

Fibromyalgia syndrome (FMS) is characterized by chronic widespread musculoskeletal pain and diverse concomitant symptoms [1, 2]. FMS affects a higher incidence in female gender [3]. The pathogenesis of FMS is still unclear; many factors such as hormones, dysfunction of the nervous/immune systems, as well as deterioration of muscle microcirculation, genetic susceptibility, external stressors, and psychiatric aspects among others have been suggested [4].

The olfactory perception has a significant role in environmental communication of human being. Specific areas of the human brain and nervous system are related to odor detection, identification, and perception. The olfactory bulb (OB) is the first step of the transmittance in the olfactory pathway. Synaptogenesis and neuroplastic changes of the OB throughout adult life have been showed in animal studies [5]. Olfactory dysfunction has been shown in diverse neurological and psychiatric diseases, such as Alzheimer's disease, Parkinson's disease, schizophrenia, and depression [6–8]. Also, it has been mentioned that some neurological autoimmune and some other autoimmune diseases could be associated with decreased OB volumes [9–12]. Decreased OB volumes in patients with olfactory loss have been demonstrated by magnetic resonance imaging (MRI) studies [13, 14]. Among the other symptoms of the FMS, impaired olfactory function such as odor identification, threshold, and discrimination have been reported [15–17]. Although, self-reported olfactory functions have been studied with olfactory tests, olfactory bulb volumes have not been

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studied in patients with FMS. Thus, to investigate OB volumes in patients with FMS, by using MRI examinations, and to make reasonable and correct suggestions are the goals of the present study.

Methods

The study includes 62 female participants who were divided into the two groups as the FMS group ($n = 30$) and the healthy control group ($n = 32$). Patients who were diagnosed by using the 1990 American College of Rheumatology (ACR) classification criteria and the 2010 ACR diagnostic criteria for the FMS between the August 2014 and January 2017 were included into the study. Female patients older than 18 years old with FMS were included into the study. Exclusion criteria were the following: patients with a history of neurodegenerative disorders, neurological diseases, rheumatologic-endocronological diseases, diabetes mellitus, traumatic brain injuries, phsychiatric disorders, chronic rhinitis/sinusitis/rhinosinusitis, malignancies, pregnancy, and chronic drug/alcohol/smoke utilization. Local ethics committee approval was obtained for the study. The control group individuals were selected from the healthy individuals with similar age and gender characteristics. Right, left, and total OB volumes were measured by cranial MRI examinations.

Magnetic resonance imaging examinations were performed with a 1.5-T scanner (GE 1.5 Signa HDxt MRI scanner, GE Healthcare, Wisconsin) and a standard head coil was used for the images. The coronal T2-weighted images were used for to measure olfactory bulb volumes (Fig. 1). The T2-weighted images were obtained with a 256 × 256 matrix and a 24-cm field of view, TR 5000, TE 130, NEX 2, and a slice thickness of 5 mm. Right, left, and total olfactory bulb volumes were calculated with the aid of these images. All of the measurements were made by a radiologist with 10 years of experience. The contours of the OB were manually delineated by using an electronic cursor (Fig. 1). The surface of the contoured area is computed in mm^2 for each slice. All surfaces are added and multiplied by with front-back length to obtain a volume in mm^3. Minimum of three consecutive measurements were performed for the evaluation of MRI findings by the same observer. Intraobserver variability in the measurements was determined at less than 5%.

Statistical analysis

SPSS 20.0 (SPSS Inc., Chicago, IL, USA) statistical package was used for the statistical assessments. The normality of the variables was evaluated with the Shapiro-Wilks test. Statistical differences between the groups were performed with the independent samples t test. A p value of 0.05 was set as the significance level.

Results

The FMS group included 30 female patients with the mean age 44.2 ± 8.3 years and the control group included 32 female individuals with the mean age 41.7 ± 3.53 years (Table 1). The mean volume of the right OB was 74.9 ± 12.4 mm^3 in the FMS group and 92.6 ± 12.9 mm^3 in the control group. The mean value of the left OB volume was 74.3 ± 10.8 mm^3 in the FMS group and 92.8 ± 12.6 mm^3 in the control group. The mean of the total OB volume (total OB volume = right OB + left OB volumes) was 146.6 ± 20.81 mm^3 in the FMS group and the 186.5 ± 23.5 mm^3 in the control group. Left, right, and total OB volumes were significantly lower in patients with FMS than the control individuals [all $p < 0.05$] (Table 1).

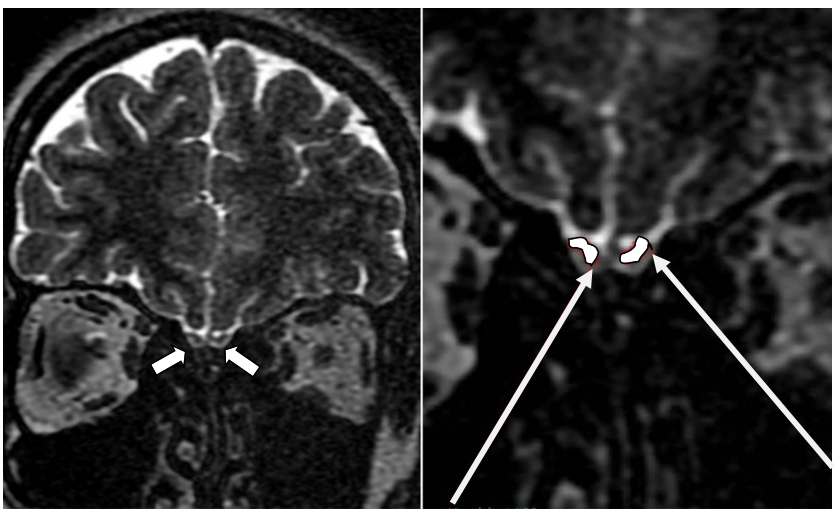

Fig. 1 The coronal T2-weighted sequence of the olfactory bulb from a normosmic patient's MRI. Manual contouring of the olfactory bulb with surface expressed in mm^2

Table 1 Comparison of the olfactory bulb volumes between the groups

Variable	FMS group (n =30)	Control group (n = 32)	p value
Age (years)	44.2 ± 8.3	41.7 ± 3.53	$p = 0.106$
Right OB (mm^3)	74.9 ± 12.4	92.6 ± 12.9	$p < 0.001$
Left OB (mm^3)	74.3 ± 10.8	92.8 ± 12.6	$p < 0.001$
Total OB (mm^3)	146.6 ± 20.81	186.5 ± 23.5	$p < 0.001$

OB olfactory bulb, *FMS* fibromyalgia syndrome

Discussion

Aggregated sensitivity to nociceptive inputs in patients with FMS can cause a wide range of symptom diversity. These symptoms are studied extensively due to possible concomitant organic pathologies. Although, pathogenesis of the FMS is unclear, it has been associated to be a brain disorder, according to changes in brain activities, neurotransmitters, and anatomical structures [18–20]. Reduced activations and decreased volumes of the some of the specific human brain areas such as hippocampus, amygdala, orbitofrontal cortex, and central gray matter have been reported in patients with FMS [21–23]. On the other hand, these specific brain areas have a close relationship with olfactory pathways which are located in the olfactory cortex, amygdala, hypothalamus, and basal telencephalon [24]. Nevertheless, olfactory functions of the central nervous system can play an important role in the management of the pathophysiology of brain disorders. Although, olfactory functions in patients with FMS have been studied by using subjective odor identification tests, olfactory bulb volumes have never been studied. Thus, the present study aimed to investigate olfactory bulb volumes in patients with FMS and to make reasonable and correct suggestions regarding to the outcomes. In the light of this goal, the present study showed decreased OB volumes in patients with FMS than healthy controls.

Low OB volume is associated with impaired olfactory functions such as odor identification, threshold, and discrimination [13]. Our study showed that both left and right OB volumes were significantly smaller in the FMS group than those in the control group. This significant decrease in the OB volumes can be caused by FMS-related central nervous system changes in neuronal structures and this result can support the etiopathologic hypothesis of FMS which considered it as a brain disorder. Besides, synaptogenesis and neuroplastic changes continue throughout adult life in the olfactory bulbs so, the present results can demonstrate possible impaired neurogenesis in patients with FMS.

Psychiatric disorders such as depression and anxiety are common in FMS [25, 26]. Impaired olfactory functions and reduced gray matter volumes of the specific olfactory areas in the human brain have been shown in patients with depression by neuroimaging studies [27–30]. Therefore, it should be pointed that FMS-associated depression may play a role in the mechanism of the reduced OB volumes in patients with FMS.

Increased level of the serum interleukin-1b and decreased level of interleukin-10 have been reported after olfactory bulbectomy in animal studies [31]. This result can show that OB can play a role in the stability of the inflammatory process of the human brain. Besides, possible increased inflammatory responses have been reported in the FMS [32, 33]. Thus, possible increased inflammatory responses of the brain may impair olfactory functions and decrease OB volumes in patients with FMS.

The relationship between reduced OB volumes and neurodegenerative disorders has been stated [6–8]. Although ethiopathologic picture of the FMS is still unclear, it has been reported that neurodegeneration could be one of the associated processes of the FMS [22, 34, 35]. Therefore, decreased OB volumes in patients with FMS could be related to possible neurodegenerative conditions in FMS.

Our study has some limitations. First, the study was conducted in a single tertiary center and was a small sample. Second, all of the individuals were female. Third, the present study could not perform odor tests (e.g., sniffing sticks, UPSIT) due to financial difficulties. Finally, correlations between the FMS symptom severity/disease duration and OB volumes were not investigated.

In the light of such information, we concluded that patients with FMS are the under risk of the decreased olfactory bulb volumes. Outcomes of the present study should be kept in mind for proper and reasonable management of this tough syndrome and for future studies. **F**uture studies which will include higher study populations and male patients will have beneficial outcomes.

Compliance with ethical standards

Disclosures None.

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