

Magnetic resonance imaging study; does the olfactory bulb volume change in major depression?

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Abstract: *Goal:* The olfactory region function disorders and olfactory bulb volume changes in neurodegenerative and neuropsychiatric disorders are defined. In this study, the olfactory bulb values of patients diagnosed with major depression in accordance with DMS-IV criteria, are measured with MRI, and these values are compared with the values of healthy volunteers to see if there are any statistically significant changes. *Method:* The study was carried out with 20 healthy volunteers and 20 patients who had been diagnosed with acute major depression in accordance with 'diagnostic and statistical manual of mental disorders' (DMS) IV criteria and have been getting treatment for more than 2 years in Istanbul Education and Research Hospital. 1,5 Tesla MRI were used in 40 cases, and the olfactory bulb volume on two hemispheres were measured separately. *Results:* Contrary to the former studies, we found no statistically significant difference between the olfactory bulb volume measurements of the control group and the group diagnosed with major depression.

Key words: Depression, magnetic resonance imaging, olfactory bulb

Introduction

In the recent years, studies about olfactory bulb (OB) function and OB volume in neuropsychiatric disorders have become more and more frequent. It's possible to examine the links between the limbic system, prefrontal cortex and olfactory region thanks to these

studies (1, 6, 10).

The most frequent type of neuropsychiatric disorder is major depression. Its average incidence rate is 2.6%-6.2%. Major depression is the most frequent disorder in psychiatry with its lifelong 15% of prevalence rate in the general society, and 25% of prevalence rate among women (4). Major depression is seen

twice as much among women, independent on culture or country of residence. The average age of onset for major depressive disorder is 40, and 50% of the patients first suffer from it between the ages of 20-50 (4). Many reasons are defined for the development of major depressive disorder. The general opinion is that the cases with organic disorders are triggered by environmental causes. Studies revealed that neurotransmitter changes in brain, and damage in especially affection functioned cortex regions are among the causes for the development of the disorder. In recent years, with the help of studies about OB volume and function, it's thought that the OB volume of patients with depressive affect have differences from the OB volume of a healthy brain (1, 6, 8, 10).

In this study, we examined 20 cases diagnosed with major depression and 20 healthy volunteers in terms of OB volumes using cranial magnetic resonance imaging, and we aimed to determine if there is a statistically significant difference between two groups.

Materials and method

This study was carried out between 2013-2015 with the help of the psychiatry, radiology and neurosurgery clinics of Istanbul Education and Research Hospital. All patients took part in the study had given written consents and the ethics committee of the hospital had approved the study. 20 cases took part in the study; 14 males and 6 females, diagnosed with acute major depression in accordance with the 'diagnostic and statistical manual of mental disorders' (DMS) IV

criteria, and getting treatment for 3 months in average. The neurological examinations of the patients were carried out. Then, with their eyes are closed, we used two pieces of scented cotton which does not damage the nasal mucosa to test their olfactory perceptions. This test was repeated with well-known (mint-coffee etc.) scents and the patients were asked to define what they had smelled. The cases with anosmia and olfactory disorders were left out of the study.

Before the neuroimaging stage, we had consulted the otorhinolaryngology clinic about the patients. The patients suffering from nasal problems such as septal deviation and sinusitis did not take part in the study.

The control group consisting of 20 patients, 10 females and 10 males had been chosen amongst the patients applied to the hospital for various reasons. Detailed neuropsychiatric examinations had been carried out before the study. Patients with former psychiatric complaints, psychiatric disorder history in the family and head trauma history had been removed from the study. All MR imaging work were done using 8 channel head-coil with GE 1,5 Tesla MR (GE, 2011, USA) device which belongs to Istanbul Education and Research Hospital. Each participant was examined with cranial MRI to exclude cranial organic disorders (5 mm thick-standard section 3 dimensional [3D] sequence). 2 mm thick and - T2 weighted fast-spin-echo imaging was run to observe the anterior and central skull base for the OB measurements (Figure 1). Olfactory bulb (OB) volume measurements were calculated separately on lamina cribriform anterior on

each hemisphere. Following the methods used in former studies; the OB's longest part and the length that forms a right angle to that part were multiplied, and the result were multiplied with the number of sections OB's observed on; thus the volume measurements were finalized (5, 6, 13).

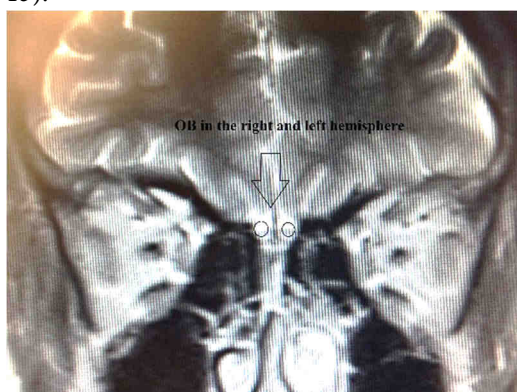


Figure 1 - OB measurements

Statistical Analysis

NCSS (Number Cruncher Statistical System) 2007&PASS (Power Analysis and Sample Size) 2008 Statistical Software (Utah, USA) program was used for statistical analysis. Descriptive statistical methods (centering, standard deviation, median, frequency, ratio, minimum, maximum) were used when analyzing the study data. Student's t-test was used in order to analyze the relationship between variables. Significance level was observed as $p < 0,05$.

Results

The study was carried out by measuring the OB volumes of 20 patients diagnosed with acute major depression; 14 being male (70%)

and 6 being female (30%), and 20 volunteers; 10 being male (50%) and 10 being female (50%) using cranial magnetic resonance imaging (MRI). The ages of the cases diagnosed with major depression varied between 17 to 65, with an average age of 38,1 years. The ages of cases in the control group varied between 20 to 60, with an average age of 34,5 years. The demographic attributes of the cases participated in the study is summarized (Table 1).

The patients with major depression had three months of past medical history in average. 14 patients had been using selective serotonin reuptake inhibitors (SSRI: citalopram, escitalopram, paroxetine), 6 patients had been using tricyclic antidepressants (mirtazapine, doxepine, trimipramine).

The right and left OBs were measured separately for the patients in the depression group and the control group. Patients with major depression had an OB volume of $39,15 \pm 12,82$ mm³ in average for the right hemisphere, and $40,55 \pm 10,94$ mm³ in average for the left hemisphere. Volumes varied between 14 mm³ and 66 mm³ for the right hemisphere, and between 23 mm³ and 61 mm³ for the left hemisphere. Patients of control group had an OB volume of $35,39 \pm 10,89$ mm³ in average for the right hemisphere, and $36,55 \pm 12,8$ mm³ in average for the left hemisphere. Volumes varied between 22 mm³ and 59 mm³ for the right hemisphere, and between 22 mm³ and 65 mm³ for the left hemisphere (Table 2).

TABLE 1

The demographic attributes of the cases participated in the study

Patients	Number	Female	Male	Age (Average)
Major Depression	20 (50%)	6	14	38,1 (17-65)
Control Group	20 (50%)	10	10	34,5 (20-60)
Total	40 (100%)	16 (40%)	24 (60%)	36,3 (17-65)

TABLE 2

OB volume measurements of patients with major depression and control group

Patients	OB volume (Right)	OB volume (Left)	Range (Right)	Range (Left)
Major Depression	39,15±12,82 mm ³	40,55±10,94 mm ³	14 mm ³ -66 mm ³	23 mm ³ -61 mm ³
Control Group	35,39±10,89 mm ³	36,55±12,8 mm ³	22 mm ³ -59 mm ³	22 mm ³ -65 mm ³
Total	37,27 mm ³ (100%)	38,55 mm ³ (100%)	14 mm ³ -66 mm ³	22 mm ³ -65 mm ³

There was no statistically significant difference found when the OB volume measurements were compared separately for the right and the left hemisphere of the major depression group and the control group $p > 0,05$.

Patients with major depression were split into two groups in terms of the type of medication they used. The two groups using medications with different active ingredients were first compared with each other statistically. There was no statistically significant difference found between patients using medications with different active ingredients.

Discussion

Depression is considered a frequent type of disorder and named as a public health problem in developed and developing communities. Because it's so frequent, most neuroscientists are interested in its causes. In the last two decades, it's revealed that neurotransmitter

pathways pave the way for and speed up the formation of many psychiatric disorders. Having said that, some parts and regions of the brain have very important tasks regarding cognitive function and mood. Prefrontal cortex and the limbic system form close relations with each other, thus, affect the clinical course and medication response (3, 6).

With functional MRI coming into the picture, in neuropsychiatric disorders, we can now examine and reveal the parts of the brain where there is a loss of function. Brain imaging studies in major depression cases have been also carried out for years. We often see imaging studies mainly focusing on the frontal lobe which mostly deals with emotion regulation. Personality changes often seen in cases dealing with frontal lobe trauma or frontal tumors prove the significance of the frontal lobe (2).

Studies in the recent years revealed that OB function losses cause a tendency to depression and may cause changes in medication

response. OB is an area that lies just below cribriform plate, in anterior cranial fossa with a $36,44 \pm 12,8$ mm³ average volume (7). It has fibers reaching out to thalamus.

In 2001, the study by Pause et al. detected reduced olfactory volume and reduced olfactory sensitivity. There are many theories aiming to explain olfactory deficit seen in major depression. Pause et al. thought that the disinhibition in amygdala that affects emotional responses were in fact responsible for olfactory deficit. The abnormal functioning in the paralimbic cortex (especially amygdala and orbitofrontal cortex) were the main reasons for the concurrent early period olfactory area disinhibition in major depression cases (11). In 2010, with their studies, Negoias et al. determined for the first time that depression score is correlated with olfactory function and volume (8).

Olfactory area volume and functions may also change due to psychiatric and neurodegenerative disorders. Major depression and schizophrenia may be the cause of function or volume loss (7, 9, 11, 12, 14, 16). In addition to these, volume deficit and functional disorders may also be determined in multiple sclerosis and Parkinson's disease cases (15). Not all cases of olfactory volume loss indicate a neuropsychiatric disorder. Head trauma, sinonasal diseases, infections and upper respiratory pathologies may also cause changes in measurements. OB may function as a neurotransmitter. Early period changes may also act as precursor symptom (7, 12).

Conclusion

In our study, we measured the olfactory bulb volumes of major depression cases using neuroimaging, compared the findings with those of healthy volunteers and the results are examined to find out whether there is a statistically significant difference between them. Contrary to the findings in former studies, we could not find any statistically significant difference. Further studies with more patients are needed in order to come to a definite conclusion.

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