Insula Volume in Patients Diagnosed with Obsessive Compulsive Disorder and its Relation with Clinical Variables

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ABSTRACT

Introduction: Neuroimaging studies performed in recent years on patients with obsessive compulsive disorder have determined anomalies that are possibly associated with the determinant signs and symptoms of the disease. The purpose of this study is to investigate the morphometric changes in insula volume and related parameters in order to understand the etiopathogenesis of obsessive compulsive disorder better.

Method: Throughout the study, 20 patients eligible for the study criteria, who were diagnosed with OCD according to DSM-5 diagnostic criteria and receiving inpatient or outpatient treatment after applying to Firat University Hospital Psychiatry Department, and 13 healthy subjects in the control group have been included in the study. Sociodemographic and Clinical Data Form, Hamilton Depression Rating Scale (HAM-D), Hamilton Anxiety Rating Scale (HAM-A), Yale-Brown Obsession

Compulsive Scale (Y-BOCS) and SCID-I have been applied to the patients. Volumetric measurements were performed on the insula by using magnetic resonance imaging (MRI) in patient and control groups.

Results: No significant difference was observed between patients with Obsessive Compulsive Disorder and healthy controls with regard to insula volume.

Discussion: It may be stated that insula may be associated with both the pathophysiology and clinical course of the disease. It is suggested that studies considering the imaging methods examining the functional characteristics of this area and tests on cognitive functions together may lead to significant and efficient results.

Keywords: Obsessive compulsive disorder; volume; insula; MRI

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INTRODUCTION

Obsessive Compulsive Disorder (OCD) has a chronic course, and it is characterized with obsession and compulsions that significantly affects functionality (1). OCD is an important condition since there is long time between age of onset and time of starting treatment, it affects functionality quite negatively and have a high prevalence in society (2, 3).

Obsessive Compulsive Disorder is the key example of the 'obsessive-compulsive and related disorders', a group of conditions which are now classified together in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (4). To date, a huge number of neurobiological investigations have been performed to account for why OCD occurs, but still little has been known about the occurrence of the disorder.

The etiopathogenesis of OCD has not been completely elucidated although there are recent significant changes on the identification and treatment of OCD. Neuroimaging of OCD revealed important data. It is known that frontal lobe, basal ganglia and limbic system are particularly important in OCD physiopathogenesis (5). In the result of brain imaging studies, it is considered that basal ganglia and thalamus, and mainly orbitofrontal cortex are associated with OCD (6). Furthermore, losses in the asymmetry of caudate nuclei and volume changes in caudate nucleus were determined (7). Increased blood build up in the thalamus and

frontal section and changes in blood build up of basal ganglia have been shown with Single Photon Emission Computed Tomography (SPECT) compared to control group (8).

Insula is below the frontal, temporal and parietal lobe in cerebral cortex. The insula is a cortical structure with extensive connections to many areas of the cortex and limbic system. The insular cortex is involved in the processing of visceral sensory, visceral motor, vestibular, attention, pain, emotion, verbal, motor information, inputs related to music and eating, in addition to gustatory, olfactory, visual, auditory, and tactile data. Changes in insula have been determined to be associated with neuropsychiatric diseases such as mood disorders, panic disorders, PTSD, obsessive-compulsive disorders, eating disorders, and schizophrenia (9-14).

Few studies on insula measurement in OCD patients. In the review article they published on 2007 about insula, Nagai et al. (9) have emphasized that insula may be important in the etiopathogenesis of mood changes, panic disorder, obsessive compulsive disorder, eating disorder and schizophrenia due to its function in psychosomatic conditions.

In the result of brain imaging studies previously performed on obsessive compulsive disorder, differences have been detected in brain structures

that may be related with the etiology of disease. The evaluation of these results is quite significant for diagnosis and treatment. The purpose of this study is to evaluate the insula volumes of patients with obsessive compulsive disorder with magnetic resonance imaging method, and thus contribute in determining the neuroanatomic reasons in the etiology of obsessive compulsive disorder.

MATERIAL AND METHODS

Throughout the study, 20 patients eligible for the study criteria, among the patients who were diagnosed with OCD according to DSM-IV-TR diagnostic criteria and receiving inpatient or outpatient treatment after applying to Firat University Hospital Psychiatry Clinic, have been included in the study. Twenty people consisting of healthy individuals who met the study criteria and have been matched with the patient group with regard to age and gender have been included in the study as the control group. Twenty MRI scans have been performed in the control group consisting of 20 people, however, 7 scans were wasted due to technical failures. For this reason, control group consisted of 13 people. Patients between age 18–65, diagnosed with obsessive compulsive disorder according to DSM-IV-TR, who did not have any concomitant DSM-IV Axis-I disorder (apart from major depressive disorder), a neurological disease or history of any neurological disease or treatment, history of head trauma, any contraindication for MRI scans, significant body pathologies or any somatic disease that will affect the distribution of existing psychiatric symptoms of the patient, alcohol or substance abuse or dependence in the last 6 months, and who have signed the informed consent form, have been included in the study.

MATERIALS

Sociodemographic and Clinical Data Form

In all cases, a sociodemographic and clinical data form has been used, which we have prepared by considering the objectives of the study and in compliance with clinical experiences and information obtained from scanned references. This form is a semi-structured form containing socioeconomic information such as age, marital status, educational status, occupation, gender, residence, economic status and clinical information such as age of onset, disease duration, number of hospitalizations and treatments received throughout the disease.

Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I)

Introduced by Spitzer et al. (15), SCID-I is an interview form structured on 1997 for diagnosing Axis I that was prepared for DSM-IV. SCID-I has been translated into Turkish by Çorapçıoğlu et al., (16) and its safety study has been completed in our country (17).

Hamilton Depression Rating Scale (HAM-D)

It measures the level and severity of depression in the patient. It contains a total of 17 questions. Each item is scored between 0–4 increasingly. The highest score is 51. Turkish validity and safety study was performed by Akdemir et al. (18).

Hamilton Anxiety Rating Scale (HAM-A)

It determines the anxiety level and symptom distribution in the patient, and measures the change of severity. It contains a total of 14 questions that examines both mental and physical symptoms. Each item is scored between 0–4, and total score of the scale varies between 0–56. Validity and reliability study in Turkish was performed by Yazici et al. (19).

Yale-Brown Obsession Compulsive Scale (Y-BOCS)

It measures the type and severity of obsessive compulsive symptoms in

the patient. It is comprised of a total of 19 items. However, only the first ten items (apart from item 1b and item 6b) are used in the determination of the total score. Sub-total of obsession and compulsions are the total of items between 1–5 (apart from 1b) and items between 6–10 (apart from 6b). The validity and safety of Turkish form have been performed by Karamustafaoglu et al. (20).

Magnetic Resonance Imaging and Methods

Process: The imaging was performed using 1.5 Tesla GE SIGNA Scanner (GE Medical System) that provided three-dimensional (3D) T1-weighted MRI images. Following imaging parameters were monitored: 1.5 mm sagittal sections, echo time [TE]: 15.6 ms, repetition time: 14.4 ms, excitation number: 1, angle (field) of view [FOV]: 240 mm, angle of rotation: 20°, band thickness: 20.8, section thickness: 2.4 mm and resolution: 0.9375 x 0.9375 x 2.4 mm. Images obtained with these parameters are treated in work station program.

Volumetric measurements: For each subject from control group and patient group, volumetric examination of the insula sections were performed with MRI (Figure 1).

Insular cortex area has been examined by using “GE Workstation” in coronal, sagittal and axial planes, coronal sections were marked visually, and marked area was measured.

Anatomic limits were determined according to atlas of Johnson and Becker (21) and Talairach's (22) atlas. Evaluation was performed first in the sagittal plane for the determination of limits. Anterior limits were determined as orbitofrontal cortex. Posterior limit was determined as the point gray matter ends, and upper and lower limits were recognized as superior and inferior circular sulci. Limits were re-evaluated and marked in coronal plane. Grey matter-white matter differentiation was used in the determination of medial and lateral limits. Artworks and volumetric measurements were performed by two evaluators who were blind to the gender and diagnosis of cases.

Statistical Assessment

The data obtained from the groups was expressed as mean + standard deviation (mean + SD). Covariance analysis (ANCOVA), Student t test and chi-square test were used as statistical methods. Spearman correlation test was used in the evaluation of the relation between volumetric values with age and disease period. IBM SPSS for Windows, version 22.0 (IBM statistics for Windows version 22, IBM Corporation, Armonk, New York, United States) program was used for statistical evaluation, and significance level was selected as $p < 0.05$.

Figure 1. Anatomic landmarks for the manual tracings of the insula.

RESULTS

Sociodemographic Characteristics of Patient and Control Group

A total of 20 patients were included in our study, consisting of 11 females and 9 males. The age of patients ranged between 25–50 years, with a mean age of 29.15 ± 8.035 years. Control group was formed by a total of 13 healthy individuals consisting of 4 women and 9 men. Twenty MRI scans have been performed in the control group consisting of 20 people, however, 7 scans were wasted due to technical failures. For this reason, control group consisted of 13 people. The age of controls ranged between 25–45 years, with a mean age of 23.85 ± 2.478 years. There was a significant difference with regard to age between patient and control groups ($p < 0.001$). Considering sociodemographic characteristics; being elementary school or secondary-high school graduate, being married, and having moderate or low socio-economic status were leading characteristics in the patient group.

Insula Volumes of Patient and Control Group

Insula volume was measured as 5.05 ± 0.68 ml at the right and 5.08 ± 0.70 ml at the left in the measurements of patient group with obsessive compulsive disorder. Insula volume of control group was measured as 5.08 ± 0.42 ml at the right and 5.07 ± 0.47 ml at the left. No statistically significant difference was determined between control group and patients with regard to insula volumes in intergroup comparisons. No laterality was observed with regard to insula volumes both in patient and control groups. Data belonging to the insula measurements of patient and control groups are presented in Table 1.

Table 1. Insula volumes of patient and control groups

	Groups		P
	Control (n=13)	Patient (n=20)	
Right insula (ml)	5.08 ± 0.42	5.05 ± 0.68	$p > 0.05$
Left insula (ml)	5.07 ± 0.47	5.08 ± 0.70	$p > 0.05$

Scale Scores and Correlation Analysis

While the scale score determined with Hamilton Anxiety Rating Scale (HAM-A) was 23 ± 9.9 in patients with obsessive compulsive disorder, the score of control group was determined as 5.46 ± 4.72 ($p < 0.001$). Hamilton Depression Rating Scale (HAM-D) score was determined as 30.85 ± 8.25 for the patients; while mean score was 5.54 ± 5.81 in control group ($p < 0.001$). Furthermore, Yale-Brown Obsession Compulsive Scale (Y-BOCS) score was determined as 21.25 ± 6.36 ; and mean score in control group was determined as 0.0 ($p < 0.001$). According to Spearman's correlation analysis, no significant relationships were observed between insula volumes and any sociodemographic and clinical variables including YBOC-S scores ($r = 0.12$, $p > 0.05$).

DISCUSSION

Due to the recent advancements in brain imaging methods, these methods are often used for the elucidation of the etiopathogenesis of psychiatric diseases. In our day, it is known that the neurobiology of OCD has not been elucidated, as in numerous psychiatric diseases. There is a small number of imaging studies on OCD. The purpose of this study is to participate in the elucidation of the etiopathogenesis and biological side of OCD that have not been enlightened yet.

Neuroimaging studies performed on obsessive compulsive disorder up to this date are generally performed by using structural (computed tomography, MRI) or functional (single photon emission computed tomography, positron emission tomography; functional MRI, magnetic resonance spectroscopy) imaging methods. While structural brain imaging studies provide information about the anatomy of the brain;

functional imaging studies give information about the vital efficiency and activity of the brain.

There is a small number of volumetric imaging studies performed on obsessive compulsive disorder until this date. Anomalies of cortico-striatal circuitry including generalized OCD models, orbitofrontal cortex (OFC), anterior cingulate cortex (ACC), thalamus and striatum has been suggested to play an important role in OCD pathophysiology (23–25).

Insula has an important role in intolerance of uncertainty, which is associated with OCD symptomatology (26). Moreover, insula has been shown to be associated with pathways related to aversion (27). There are studies reporting decreased gray matter volume and higher functional activity in subinsular white matter for insula in OCD (28). Increased activity in left insula has been detected in a fMRI study performed on adults with OCD (29).

Yoo et al. studied 71 patients with OCD and 71 healthy controls. In that study, a significant relationship was found between insula volume and OCD (30). However, in our study, no significant relationship was found between insula volume and OCD. This may be related to the small size of our sample group.

Nevertheless, there was no significant difference between patient and control groups upon evaluating the results of our study for insula volume on both right and left, and no correlation was determined between age, educational status, disease duration and disease severity, and insula. Although this suggests there is no volumetric relation between insula and OCD, results from functional and neurochemical imaging studies of the area are needed due to its intense relationship with many sections of the brain.

This study contains a series of disputable limitations. The first one is the small sampling size used in the study, and it limits the significance of the results of the study. Also, the changes caused by the differences in the application of the measurement method used in the study may have affected the results. There is a limited number of brain imaging studies on OCD performed before this study, and this limits the interpretation and generalization of the results obtained from the study.

Consequently, no significant relation was determined between the pathology of obsessive compulsive disorder and insula volume. Nonetheless, further studies are required in larger sampling groups in order for these results to gain importance.

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