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Smaller Pituitary Volumes in Patients with Delusional Disorder

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ABSTRACT

Introduction: Delusional disorder shares some clinical characteristics of OCD and hypochondriasis. Delusions compared to obsessions in the OCD and compared to bodily preoccupations in the hypochondriasis are more established beliefs. **Aim:** To measure pituitary volumes in patients with delusional disorder and hypothesized that volumes would be reduced in those patients by a mechanism that we could not account for before for patients with OCD and hypochondriasis. **Methods:** Eighteen patients with delusional disorder and healthy controls were included into the study. Pituitary gland volumes were measured. **Results:** When using independent *t* test, the mean total pituitary volume was 777.22 ± 241.28 mm³ in healthy controls, while it was 532.11 ± 125.65 mm³ in patients with delusional disorder. The differences in regard to pituitary gland volumes between patients with delusional disorder and healthy control subjects were statistically meaningful ($p < 0.01$), as supported by ANCOVA, with the covariates of age, gender and total brain volumes as covariates. **Conclusion:** We determined that patients with delusional disorder had smaller pituitary volumes compared to those of healthy control subjects.

Keywords: Pituitary, delusional disorder, smaller, volumes.

1. INTRODUCTION

Delusional disorder previously known as paranoid disorder, is a kind of serious psychiatric disorders named as a psychosis in which a person cannot discriminate what is real from what is imagined. The main clinical characteristic of the disorder is the existence of the delusions, unshakable beliefs in something untrue or not based on reality. Delusion means an unreal beliefs which are not in accordance with era and public lived and unchangeable by proper rational debates. According to the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), Delusional disorder is a psychiatric disorder characterized by at least one month of delusions but no other psychotic symptoms (1). Patients with delusional disorder generally experience non-bizarre delusions, which involve situations that could occur in real life, such as being followed, poisoned, deceived, conspired against, or loved from a distance. They often can continue to socialize and function normally, apart from the subject of their delusion, and generally do not behave in an obviously odd or bizarre manner. Etiopathogenesis of delusional disorder has not been established

enough. Furthermore, our knowledge on how delusional disorder occur is so limited. However, first of all, genetic factors seems to be important in the occurrence of delusional disorder. In this context, patients are more likely to be diagnosed with delusional disorder if they have family members with schizophrenia or schizotypal personality disorder (2). On the other hand, we did not meet any investigation on the neuroimaging of patients with pure delusional disorder. This is very interesting. Because compared to delusional disorder, almost all of other psychiatric disorders have been extensively evaluated by neuroimaging studies. For example, other psychotic disorder, schizophrenia has been examined in detail regarding neuroimaging (3-6). Our study group measured pituitary volumes in a variety of psychiatric disorders (7-10). Firstly, it was examined pituitary gland volumes in patients with obsessive compulsive disorder (10). In that study, it was found that patients with obsessive compulsive disorder had statistically significantly smaller pituitary gland volumes compared to healthy control subjects. On the other hand, our study group examined pituitary gland volumes in patients with hypochondriasis. Likewise, pi-

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pituitary gland volumes were considerably smaller than those of healthy control comparisons (9).

Delusional disorder shares some clinical characteristics of OCD and hypochondriasis. Delusions compared to obsessions in the OCD and compared to bodily preoccupations in the hypochondriasis are more established beliefs.

2. AIM

To measure pituitary volumes in patients with delusional disorder and hypothesized that volumes would be reduced in those patients by a mechanism that we could not account for before for patients with OCD and hypochondriasis.

3. METHODS

This study was performed at the Firat University School of Medicine Department of Psychiatry and Radiology, Neuroradiology section (Elazig, Turkey). The study was approved by the Local Ethics Committee, and informed consent was obtained from all study participants. We informed all subjects about the study procedure, and we obtained the signed written informed consents following detailed explanation of the study and procedure. Eighteen patients with delusional disorder (eleven females and seven males) and same number of healthy control subjects (ten females and eight males) were included into the study. Patients were suffered from a detailed medical history, physical, and neurological examination, and the Turkish version of Structured Clinical Interview for the DSM-IV (SCID) to ascertain the diagnosis of delusional disorder and to exclude other past or current Axis I diagnoses (11). Some exclusion criteria were administered to patients with delusional disorder. They were existence of any comorbid psychiatric disorder apart from depression, the presence of current medical problems, any past or current history of traumatic brain injury and any neurological disorder or alcohol and/or substance abuse within the 6 months preceding the study, and the use of psychoactive medication within four weeks of the study. On the other hand, patients who had any medical contraindications for an MR examination such as cardiac and joint stent, were excluded from the present study. Meanwhile it was said to patients that it could be given an anti-anxiety drug for their phobic avoidance of entering the MR examination if required. As for the healthy control subjects, they were matched with patients with delusional disorder in terms of age, sex, education and handedness. They had no DSM-IV Axis I disorders in self or in a first-degree relative, as determined by the SCID non-patient version, no current medical problems, neurologic or psychiatric histories. In addition, it was required not to have any past or current history of traumatic brain injury and neurological disorder, or any medical contraindications for an MR examination such as cardiac and joint stent. In addition, Positive and Negative Symptom Scale, Brief Psychiatric Rating Scale and Beck Depression Inventory were administered to patients and healthy control subjects (12,13). We were strictly in accordance with the procedures of the Helsinki Declaration of 1975, as revised in 1983.

MRI Procedure

All MRI imaginations were obtained from the 1.5-Tesla GE signs Excite high speed scanner (Milwaukee, WI, USA). In addition, when scanning, following parameters were used: Echo time (TE)=15.6 ms, flip angle=20°, bandwidth=20.8, (TR)=2000 ms, field of view (FOV)=240 mm, slice thickness=2.4 mm, echo spacing=15.6 ms, resolution=0.9375×0.9375×2.4 mm.

As much tracings of the pituitary gland were manually done by one senior neuroradiologist (HY) blind to subject diagnosis, to obtain anatomic measurements, a computer advanced workstation with the GE Volume Viewer voxtool 4.6 program was used. We obtained pituitary gland volumes. When measuring, we benefited from the standard neuroanatomical atlases with methods (14,15) and definitions adapted from neuroimaging studies on the pituitary (16-18) and followed by MacMaster et al. (19) According to guide mentioned above, we determined optic chiasm and infundibular recess of the third ventricle as the superior boundary of pituitary gland and sphenoid sinus as the inferior one. We present example imagination of pituitary gland in Fig 1. All volumes were reported in cubic millimeters.

Statistical Analysis

First of all, results were expressed as mean±standard deviation. The Statistical Package for Social Sciences (SPSS for Windows, version 22.0, SPSS, Chicago, IL, USA) was used for statistical analysis. Student's t-test was used to compare the mean age of the patients. Chi-square analyses were used to assess the categorical variables such as the gender distribution. Analysis of covariance (ANCOVA) in General Linear Model in the SPSS was used to compare pineal gland volumes, with age, total brain volume and gender as covariates. Correlation analyses was done by using Spearman's rank test. Statistical significance was defined as $P<0.05$ by a two-tailed test.

4. RESULTS

Demographic data for the patients and healthy control subjects such as age, gender distribution were not different ($p>0.05$). On the other hand, the groups did not differ in regard to total brain volumes ($p>0.05$) Table 1.

We did not find group differences in the brain measurements, i.e., whole brain volume, white, and gray matter volumes ($P>0.05$). When using independent *t* test, the mean total pituitary volume was 777.22±241.28 mm³

	Patients (n=18)	Healthy controls (n=18)	p
Age (years)	44.28±10.24	44.44±6.07	>0.05
Gender (Female/Male)	11/7	10/8	>0.05
Handedness (right)	18	18	>0.05
Hamilton Depression Rating Score	12.02±3.85	5.89±2.20	<0.001
Brief Psychiatric rating Scale	19.12±5.34	5.09±2.07	<0.001
Pituitary Volume	532.11±125.65	777.22±241.28	<0.001

Table 1. Demographic, volumetric and clinical data for the subjects
*Volumes presented are in mm³.

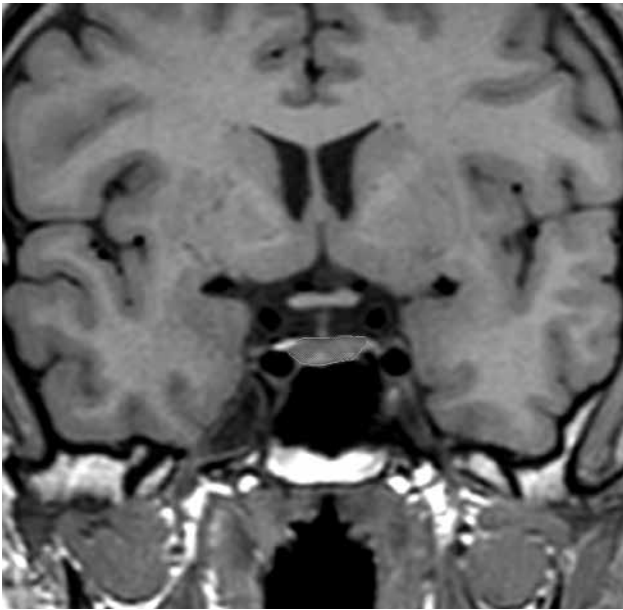


Figure 1. A sample image of landmarks for pituitary gland

in healthy controls, while it was $532.11 \pm 125.65 \text{ mm}^3$ in patients with delusional disorder. The differences in regard to pituitary gland volumes between patients with delusional disorder and healthy control subjects were statistically significant ($p < 0.01$). When performing an ANCOVA, with the covariates of age, gender and total brain volumes as covariates, we found that statistical significance implicating that pituitary volumes were smaller in patients with delusional disorder compared to those of healthy control subjects lasted ($p < 0.01$, for age as covariate, $p < 0.01$, for gender as covariate, $p < 0.01$, for total brain volume as covariate). We did not find any correlation between scale scores and any clinical and demographic characteristics and pituitary gland volumes ($p > 0.05$).

5. DISCUSSION

In this study, we obtained some important findings. When using independent t test, the mean total pituitary volume was $777.22 \pm 241.28 \text{ mm}^3$ in healthy controls, while it was $532.11 \pm 125.65 \text{ mm}^3$ in patients with delusional disorder. The differences in regard to pituitary gland volumes between patients with delusional disorder and healthy control subjects were statistically significant ($p < 0.01$). When performing an ANCOVA, with the covariates of age, gender and total brain volumes as covariates, we found that statistical significance implicating that pituitary volumes were smaller in patients with delusional disorder compared to those of healthy control subjects lasted ($p < 0.01$, for age as covariate, $p < 0.01$, for gender as covariate, $p < 0.01$, for total brain volume as covariate). In literature search, we could not find any study on the neuroimaging of patients with pure delusional disorder. This seems very interesting. Because compared to delusional disorder, almost all of other psychiatric disorders have been extensively evaluated by neuroimaging studies. For example, other psychotic disorder, schizophrenia has been examined in detail regarding neuro-

imaging (3-6, 20). Our study group measured pituitary volumes in a variety of psychiatric disorders (7-10). Firstly, it was examined pituitary gland volumes in patients with obsessive compulsive disorder (10). In that study, it was found that patients with obsessive compulsive disorder had statistically significantly smaller pituitary gland volumes compared to healthy control subjects. On the other hand, our study group examined pituitary gland volumes in patients with hypochondriasis. Likewise, pituitary gland volumes were considerably smaller than those of healthy control comparisons (9). Delusional disorder shares some clinical characteristics of OCD and hypochondriasis. Delusions compared to obsessions in the OCD and compared to bodily preoccupations in the hypochondriasis are more consolidated beliefs. With regard to this, it was so important to examine pituitary volumes in patients with delusional disorder. In literature, it has been emphasized that factors leading to increase in the reactivity of the hypothalamic-pituitary-adrenal (HPA) axis could cause enlarged pituitary gland. In this context, Pariante et al. found that patients with first episode psychosis had larger pituitary volumes compared to patients with established schizophrenia and healthy controls (4). Gruner et al. reported that patients with first episode schizophrenia had similar pituitary gland volumes compared to those of healthy control subjects (3). In addition, Klomp et al. determined that there was no significant difference in volumes of the hypothalamus and pituitary gland between patients with schizophrenia and healthy controls (5). Interestingly, patients with delusional disorder, another psychotic disorder, had smaller pituitary gland volumes in the present study which is the first one in the literature. For the reasons why delusional disorder patients had reduced volumes of the pituitary gland, some speculations could be done. First, in practice also, delusional disorder behaves differently from schizophrenia and other psychotic disorders. These clinical differences might be reflecting to neurobiological and neuroanatomic variables. Second, it has been emphasized that endocrinological function disturbances in peripheral endocrinologic functions could affect the pituitary morphology so, underlying endocrinological abnormalities might be interacting with the structure of pituitary gland (21). Because of the fact that we did not measure peripheral hormone values, we did not know if there was such type of interaction.

We should mention about the limitation of our present study of small number of subjects. Second, method of manual tracing has a limitation itself because of the subjectivity of measurement. Third, we permitted the existence of depression, this might have affected our results. Final limitation was cross-sectional design of the present study.

6. CONCLUSION

Patients with delusional disorder had smaller pituitary volumes compared to those of healthy control subjects.

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- **Authors contribution:** M.G.G., M.A , H.Y., S.K. and D.D.K gave substantial contribution to the conception or design of the work and in the acquisition, analysis and interpretation of data for the work, M.A, H.Y., M.Ç.K. and M.G.G. had role in drafting the work and revising it critically for important intellectual content. Each author gave final approval of the version to be published and they are agree to be accountable for all aspects of the work.
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