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Volumetric Magnetic Resonance Imaging Investigation of the Pituitary in Patients with Vaginismus

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WHAT IS ALREADY KNOWN ON THIS TOPIC?

- *Pituitary volume is reduced in several anxiety disorders.*
- *The HPA axis is key in stress and anxiety responses*
- *Vaginismus shows features similar to anxiety disorders.*

WHAT THIS STUDY ADDS ON THIS TOPIC?

- *This study is the first to examine pituitary volume in vaginismus.*
- *It found significantly reduced pituitary volume in affected patients.*
- *The findings suggest a structural link between vaginismus and anxiety-related conditions.*

ABSTRACT

Objective: Many previous studies have reported decreased pituitary volume in various anxiety disorders compared to healthy controls. In this context, this study was conducted with the hypothesis that pituitary volume is reduced in this patient group as in other anxiety disorders.

Methods: Ten women with vaginismus and 10 healthy controls were included in the study. Structural magnetic resonance imaging and volume measurements of the participants were performed in the radiology department.

Results: The mean pituitary volume of women with vaginismus was found to be significantly decreased compared to healthy controls.

Conclusion: The present findings suggest that vaginismus may be closely related to anxiety-related conditions involving at least the pituitary gland.

Keywords: Gland volume, MRI, neuroimaging, pituitary, vaginismus

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INTRODUCTION

A recurrent or persistent involuntary spasm of the outer third of the vaginal muscle that prevents intercourse or vaginal examinations and interferes with sexual activity is known as vaginismus.[1] It seems that the clinical appearance of vaginismus exhibits important similarities with anxiety-related conditions. Moreover, patients with vaginismus behave like those with phobic disorders. Symptoms observed in anxiety and phobic states are accompanied by patients with vaginismus. In this context, neurobiological and endocrine changes determined in anxiety disorders, and particularly phobic states, can be also investigated in vaginismus patients. Concerning this link, it was found that phobias, anxiety, and similar clinical statuses were associated with the hypothalamic–pituitary–adrenal axis

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(HPA). In the HPA, the following alterations occur in stress-related conditions. First of all, the production of the hypothalamic corticotrophin-releasing hormone increases. This increase provokes the release of adrenocorticotropin hormone (ACTH). Consequently, the adrenal cortex secretes more cortisol when ACTH is present. The induction of these hormone shifts may result in feelings of anxiety related to the autonomic nervous system.

Substantially smaller pituitary volumes have been found in patients with obsessive–compulsive disorder (OCD) compared to healthy controls when examining various anxiety disorders.[2] Kartalci et al[3] determined smaller volumes of the pituitary in another anxiety disorder, panic disorder. They discovered that patients with panic disorder had substantially smaller pituitary volumes compared to healthy controls. Agoraphobics had even smaller pituitary volumes than non-agoraphobics. Additionally, they found a strong association between pituitary volume and both symptom severity and illness duration in panic disorder patients, suggesting that reduced pituitary volume may be linked to the functional abnormalities observed in panic disorder. In a recent study conducted by the team, pituitary volume was found to be decreased in patients with social anxiety disorder.[4] As can be seen in these studies performed on a variety of anxiety states, pituitary volumes seem to be affected structurally.

It should be noted the role of the pituitary gland in stress and anxiety-related conditions. The HPA is an important cascade in the occurrence of stress, fear, anxiety, and related situations. Research has shown that stress activates the HPA axis, resulting in elevated cortisol levels, which can influence emotional and behavioral responses associated with anxiety disorders.[5,6] For instance, Hek et al[5] found that anxiety disorders are correlated with increased salivary cortisol levels, indicating a direct relationship between HPA axis activity and anxiety. Similarly, Zhou et al[6] reported that heightened HPA axis activity is linked to impaired glucose regulation in anxiety disorder patients, further emphasizing the physiological implications of HPA dysregulation in anxiety contexts. Moving from this association, investigating pituitary gland volumes in fear and anxiety-related conditions is crucial. Moreover, magnetic resonance imaging (MRI) studies have shown volumetric changes in the pituitary gland that correspond to alterations in its functional state.[7,8] In this context, the current study aimed to evaluate pituitary gland volumes in patients with vaginismus which is associated with anxiety disorders, at least in terms of comorbidity, and is closely related to fear and anxiety, anticipating that gland sizes would show variations in these individuals, similar to findings reported in various anxiety disorders.

MATERIAL AND METHODS

Participants

The patient group consisted of individuals who met the DSM-5-TR (Diagnostic and Statistical Manual of Mental Disorders Fifth Text Revision Edition) criteria for genito-pelvic pain/penetration disorder and applied to the Fırat University School of Medicine, Department of Psychiatry, in a sequential sequence. Although it is mentioned as genito-pelvic pain/penetration disorder in DSM-5-TR, the general term vaginismus was preferred throughout the study. All patients with vaginismus were enrolled in a sexual treatment program under the supervision of a senior psychiatrist (S.B.). All patients had lifelong vaginismus. From all the patients, written informed consents were taken to participate in the present investigation. The individuals of the present study were those who had participated in the previous examination in which the hippocampus and amygdala volumes of these patients were assessed.[9] To exclude any organic reason for vaginismus, all the patients had been already examined genitally by the Department of Gynecology. The local Ethics Committee of the Fırat University School of Medicine (Date:11/02/2014, Approval number: 21591) has given its approval to the project. The actions implemented were in line with the Helsinki Declaration of 1975, as amended in 1983. Vaginismus was diagnosed using the Structured Clinical Interview for DSM-5 Disorders-Clinician Version (SCID-CV).[10,11] Of the patients, 1 had a depressive disorder not otherwise specified, and another had social anxiety disorder. Apart from this, no other comorbid condition was detected. The study planned to exclude patients with a history of head trauma, severe medical conditions (current or past), neurological disorders, intellectual disabilities, conditions preventing neuroimaging (such as cardiac stents), and alcohol or substance abuse within the 6 months prior to the study. But none of the patients met the exclusion criteria. Ten healthy control participants were recruited. The healthy control group consisted of female hospital employees who were age-matched and agreed to participate in the study voluntarily. A careful diagnostic interview was conducted on healthy controls to rule out the possibility of a DSM-5 mental illness. The following exclusion criteria were applied: a history of head trauma or seizures, any current or lifetime mental, major medical, or neurological illness, a first-degree relative with a history of mental illness or head trauma, and any condition preventing neuroimaging, such as the presence of a cardiac stent.

Magnetic Resonance Imaging Procedure

Magnetic resonance imaging was performed using a 1.5 T General Electric scanner (General Electric Medical Systems, Milwaukee, WI). A T1-weighted sagittal scout image was captured to confirm head positioning and image quality for both patients and healthy controls. The imaging parameters were as follows: TE = 15.6 ms, TR = 2000 ms, TI = 700 ms, echo spacing = 15.6 ms, Field of View (FOV) = 240 mm, 8 echoes, resolution = 0.9375 × 0.9375 × 1.328 mm, 128 contiguous slices, with a total scan time of 8 minutes and 36 seconds. Tracings for the pituitary gland were performed by 2 radiologists who worked in the neuroradiology department (U.A. and H.Y.). An important point is that the 2 raters were blind to the diagnoses of the patients. All images were processed using a semi-automated software program called GE Volume Viewer Voxtool 4.2. The intra-class correlation coefficient for pituitary was determined to be 0.90.

First of all, neuroradiologists used neuroanatomical atlases when tracing the pituitary gland boundaries.[12,13] Apart from this, as in previous studies,[14,15] the tracking of the pituitary gland was carried out by the team's neuroradiologists, guiding previous volumetric research on the pituitary gland[16,17] and, followed by MacMaster and Kusumakar.[18] During tracings, boundaries were accepted as follows. It was agreed upon that the pituitary gland's inferior border was the sphenoid sinus. The optic chiasm and the third ventricle's infundibular recess establish the pituitary gland's upper limit. Figure 1 displays imaging samples that belong to the pituitary gland. All data on the gland are presented in cubic centimeters in Table 1.

Statistical Analysis

Statistical analyses were performed using SPSS for Windows, version 22.0 (SPSS, Armonk, NY: IBM Corp.). A significance threshold of less than 0.05 was applied to the data to assess its importance. First, the volume differences for the pituitary gland between patients with vaginismus and healthy control participants were compared using an independent *t*-test. Additionally, for continuous variables such as age, it was also used. To compare categorical variables like gender,

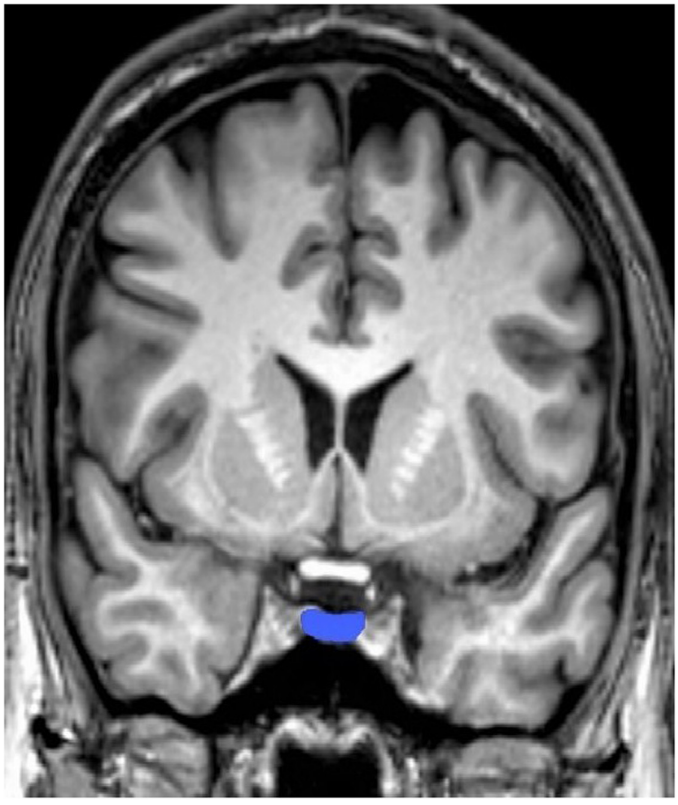

Figure 1. Delimitation of the pituitary according to the proposed tracings.

the chi-square test was applied. Analysis of covariance (ANCOVA) was used for comparisons of pituitary gland volumes while controlling for age. In addition, for correlation analyses, Pearson's correlation test was used.

RESULTS

The mean age of the participants was 27.90 ± 7.25 years in the patient group and 27.40 ± 5.38 years in the control group. After statistical evaluations, no statistical difference was detected between patient and control groups for age, sex distribution, handedness, or duration of education (>0.05). Table 1 lists some demographic and clinical information for each group. Volumetric measurements demonstrated a 38% significant volume reduction in the pituitary gland in patients compared to healthy controls. In terms of absolute pituitary gland volumes, patients with vaginismus had mean pituitary gland volumes that were statistically considerably lower than those of healthy controls (for patients with vaginismus: mean = 0.52 cm^3, SD = 0.09; for healthy control subjects: mean = 0.83 cm^3, SD = 0.14, $t = 5.66$, $P < .001$). In addition, when performing ANCOVA controlled for age, it was found that the statistical significance identified by independent *t*-test continued ($P < .001$). As for the correlational analyses, there was no remarkable association found between the volumes of the pituitary gland and the age or duration of the illness ($P < .05$).

Table 1. Demographic, Clinical and Volumetric Features of Healthy Subjects and Patients with Vaginismus

	Patients with Vaginismus (n = 10)	Controls (n = 10)
Gender (F/M)	10/0	10/0
Handedness (right)	10	10
Age (mean ± SD)	27.90 ± 7.25	27.40 ± 5.38
Pituitary (cm^3)	0.52 ± 0.09	0.83 ± 0.14*

All volumes are in cubic mililiters (cm^3). F, female; M, male; mean ± SD, mean and standard deviation.
*$P < .001$.

DISCUSSION

In the current study, patients with vaginismus and healthy controls were compared in terms of pituitary volume. It was discovered that, when compared to healthy controls, the pituitary gland volumes of individuals with vaginismus were considerably lower. When controlling for age in ANCOVA, this statistical significance remained.

In vaginismus, the reduction in pituitary volume may be linked to several biological mechanisms, including chronic stress and dysregulation of the HPA axis. Individuals with vaginismus may experience chronic psychological stress, often related to anxiety, fear of sexual intercourse, or negative associations with sexual activity. On the other hand, these individuals can experience some conflicts with their or their spouse's families because of child expectancy. This may also be another psychosocial stress factor. This prolonged stress can lead to sustained activation of the HPA axis, which is responsible for regulating the body's stress response. Chronic activation of the HPA axis leads to an overproduction of cortisol, the primary stress hormone. Prolonged exposure to elevated cortisol levels has been linked to structural changes in brain regions, including the hippocampus, prefrontal cortex, and pituitary gland. Research has shown that chronic stress and elevated cortisol may contribute to reductions in pituitary volume, as seen in other stress-related conditions.[2-4] The HPA axis operates on a negative feedback loop where cortisol signals to the brain (including the pituitary gland) to downregulate further cortisol production. In individuals with chronic stress or anxiety disorders, this feedback loop may become dysregulated, leading to prolonged HPA axis activation and sustained cortisol release. Dysregulation of the HPA axis has been associated with structural changes in the pituitary gland, including volume reduction. Finally, the psychological distress experienced in vaginismus could further dysregulate the HPA axis, as sexual activity itself becomes a stressor. This could perpetuate the cycle of HPA axis hyperactivation, further contributing to reduced pituitary volume over time.

Abnormalities in the pituitary gland volumes in patients with vaginismus have not been previously examined. The results revealed that there was a significant volume reduction of the pituitary gland in vaginismus patients compared to healthy control subjects, suggesting that vaginismus might be an anxiety equivalent, at least concerning the pituitary gland structurally. Although it was shown that structural changes occur, there is also a need for functional neuroimaging to examine hormonal changes, as hormonal and other functional changes may be contributing to the structural changes in the pituitary gland in ways that are not yet understood. It has been established that medicines can influence the volume of the pituitary gland. Jung et al[19] found that drug-naïve male patients with OCD had significantly smaller pituitary volumes compared to medicated patients and healthy controls. However, there was no difference between controls and medicated patients. This implies that the impact of medications on the pituitary may be the cause of the elevated pituitary volume in medicated patients. For this reason, a strong aspect of the study is that the sample of the present study

was free of drug use. However, it is clear that there is a need for studies addressing structural and functional imaging as well as simultaneous pituitary gland hormonal changes.

There are certain limitations to the current study that should be discussed. First and foremost, the low sample size is a significant restriction. However, it is very hard to gather patients for an investigation with such a specific diagnosis. Secondly, because of the diagnosis itself, the study consists of only female patients. This may also be considered an advantage in excluding gender effects on pituitary volumes. Another limitation is evaluating a single neuroanatomic region in isolation. Thirdly, while the study highlights the potential role of stress in pituitary gland changes in vaginismus, state and trait anxiety levels in the participants were not directly assessed. Previous studies, such as Tuğrul and Kabakci,[20] have underscored the importance of these anxiety dimensions in vaginismus patients. Including state and trait anxiety assessments using validated tools like the State-Trait Anxiety Inventory would have provided a more comprehensive understanding of the psychological underpinnings of the condition. Furthermore, concurrent hormonal changes associated with the pituitary gland were not examined. Solely evaluating anatomical changes raises questions about whether these changes are a cause or consequence of the condition. Fourth, the cross-sectional design of the current study limits the ability to establish causal relationships. Longitudinal research, involving repeated assessments of patients over time, could provide greater insight into the development and progression of pituitary gland changes in vaginismus.

Future research should aim to address these limitations. Incorporating larger, more diverse samples could improve the generalizability of findings. Assessing both structural and functional changes in the pituitary gland in conjunction with hormonal and psychological evaluations, including state and trait anxiety, would provide a more holistic understanding of the neurobiological underpinnings of vaginismus. Additionally, longitudinal studies could explore how pituitary volume changes correlate with treatment outcomes, further elucidating the condition's pathophysiology.

In conclusion, the present study found that patients with vaginismus had smaller pituitary gland volumes compared to those of healthy control subjects. The present findings suggest that vaginismus may be closely related to anxiety-related conditions involving at least the pituitary gland. However, novel studies with larger sample sizes are required.

Data Availability Statement: The data are not publicly available due to privacy or ethical restrictions. The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics Committee Approval: This study was approved by the Fırat University Faculty of Medicine Local Ethics Committee (Date:11/02/2014, Approval number: 21591).

Informed Consent: Written informed consent was obtained from each participant who participated in this study.

Peer-review: Externally peer-reviewed.

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REFERENCES

1. Bystritsky A, Craske M, Maidenberg E, Vapnik T, Shapiro D. Autonomic reactivity of panic patients during a CO2 inhalation procedure. *Depress Anxiety*. 2000;11(1):15-26. (doi:10.1002/(sici)1520-6394(2000)11:1<15::aid-da3>3.0.co;2-w)
2. Atmaca M, Yildirim H, Ozler S, Koc M, Kara B, Sec S. Smaller pituitary volume in adult patients with obsessive–compulsive disorder. *Psychiatry Clin Neurosci*. 2009;63(4):516-520. [CrossRef]
3. Kartalci S, Dogan M, Unal S, Ozcan AC, Ozdemir S, Atmaca M. Pituitary volume in patients with panic disorder. *Prog Neuropsychopharmacol Biol Psychiatry*. 2011;35(1):203-207. [CrossRef]
4. Koç M, Mermi O, Aslan S, Atmaca M. Pituitary volume in individuals with social anxiety disorder. *Psychiatry Clin Psychopharmacol*. 2022;32(1):28-32. [CrossRef]
5. Hek K, Direk N, Newson RS, et al. Anxiety disorders and salivary cortisol levels in older adults: a population-based study. *Psychoneuroendocrinology*. 2013;38(2):300-305. [CrossRef]
6. Zhou Y, Dong Z, A R, et al. The prevalence of impaired glucose regulation in anxiety disorder patients and the relationship with hypothalamic–pituitary–adrenal axis and hypothalamic–pituitary–thyroid axis activity. *J Evid Based Med*. 2019;12(1):51-55. [CrossRef]
7. Herbert J, Goodyer IM, Grossman AB, et al. Do corticosteroids damage the brain? *J Neuroendocrinol*. 2006;18(6):393-411. [CrossRef]
8. Lurie SN, Doraiswamy PM, Husain MM, et al. In vivo assessment of pituitary gland volume with magnetic resonance imaging: the effect of age. *J Clin Endocrinol Metab*. 1990;71(2):505-508. [CrossRef]
9. Atmaca M, Baykara S, Ozer O, Korkmaz S, Akaslan U, Yildirim H. Hippocampus and amygdala volumes in patients with vaginismus. *World J Psychiatry*. 2016;6(2):221-225. [CrossRef]
10. First MB, Williams JBW, Karg RS, Spitzer RL. *User's Guide for the SCID-5-CV Structured Clinical Interview for DSM-5® Disorders: Clinical Version*. Washington, DC: American Psychiatric Publishing, Incorporated; 2016.
11. Elbir M, Alp Topbaş Ö, Bayad S, et al. Adaptation and reliability of the structured clinical interview for DSM-5-disorders - clinician version (SCID-5/CV) to the Turkish language. *Turk Psikiyatri Derg*. 2019;30(1):51-56. [CrossRef]
12. Duvernoy HM. *The Human Brain: Surface, Three-Dimensional Sectional Anatomy with MRI, and Blood Supply*. Springer Science & Business Media; 1999.
13. Bertolino A, Nawroz S, Mattay VS, et al. Regionally specific pattern of neurochemical pathology in schizophrenia as assessed by multislice proton magnetic resonance spectroscopic imaging. *Am J Psychiatry*. 1996;153(12):1554-1563. [CrossRef]
14. Atmaca M, Yildirim H, Sec S, Kayali A. Pituitary volumes in hypochondriac patients. *Prog Neuropsychopharmacol Biol Psychiatry*. 2010;34(2):344-347. [CrossRef]
15. Yildirim H, Atmaca M, Sirlier B, Kayali A. Pituitary volumes are reduced in patients with somatization disorder. *Psychiatry Investig*. 2012;9(3):278-282. [CrossRef]
16. Sassi RB, Nicoletti M, Brambilla P, et al. Decreased pituitary volume in patients with bipolar disorder. *Biol Psychiatry*. 2001;50(4):271-280. [CrossRef]
17. Thomas LA, De Bellis MD. Pituitary volumes in pediatric maltreatment-related posttraumatic stress disorder. *Biol Psychiatry*. 2004;55(7):752-758. [CrossRef]
18. MacMaster FP, Kusumakar V. MRI study of the pituitary gland in adolescent depression. *J Psychiatr Res*. 2004;38(3):231-236. [CrossRef]
19. Jung MH, Huh MJ, Kang DH, et al. Volumetric differences in the pituitary between drug-naïve and medicated male patients with obsessive–compulsive disorder. *Prog Neuropsychopharmacol Biol Psychiatry*. 2009;33(4):605-609. [CrossRef]
20. Tuğrul C, Kabakci E. Vaginismus and its correlates. *Sex Marital Ther*. 1997;12(1):23-34. [CrossRef]