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Statistical Shape Analysis of Corpus Callosum in Vaginismus

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Abstract

Aim. Vaginismus is the presence spasm of the muscles in the vagina not allowing sexual intercourse or any interactions in the absence of any disease. Neurological diseases can cause degenerative changes in brain structures such as the corpus callosum (CC), the main white matter structure that connects the hemispheres. Studies have shown that abnormalities in the CC, which acts as a conduit for sensory information transmission. The aim of this study is to evaluate the corpus callosum of patients with vaginismus with statistical shape analysis (SSA) using magnetic resonance imaging (MRI) images and compare it with healthy controls.

Material and Methods. Ten female patients diagnosed with vaginismus in the psychiatry outpatient clinic and healthy individuals who met the study criteria, had no psychiatric diagnosis, were equal in number and age were selected as the control group. Mid-sagittal T1-weighted MRI images of each individual were obtained, and the corpus callosum was marked with software on each selected image using standard anatomical landmarks, and data were collected. The mean of 'Procrustes' landmark points was calculated and shape deformations were evaluated using thin plate spline (TPS) analysis.

Results. A significant slightly difference was found in terms of corpus callosum areas in the mid-sagittal images of patients with vaginismus and controls. Maximum CC deformation was observed in almost all regions markings in those with vaginismus. In the evaluation of allometry, multivariate regression test was used for the relationship between size and shape and a statistically significant model was obtained for CC.

Conclusion. CC analysis with SSA using MRI images revealed significant differences between patients and healthy subjects. The study findings highlighted the abnormal distribution of white matter in the corpus callosum and the variable subregional nature of CC in vaginismus patients. This study may help future studies in terms of vaginismus etiology, diagnosis and treatment options.

vaginismus; phobic disorders; corpus callosum; spatial analysis; image processing, computer-assisted

INTRODUCTION

Vaginismus can be defined as the muscles in the vagina not allowing sexual intercourse or any interactions due to spasm (1, 2). Although vaginismus is considered among sexual dysfunctions, when the clinical picture is examined, the appearance of this disease is similar to anxiety disorder and patients behave like those with phobia (3-6). In general, the somatic components of anxiety accompany other symptoms of vaginismus. In this context, neurobiological changes detected in anxiety disorders and especially in phobic

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conditions can be investigated in patients with vaginismus. Although the findings reported in structural and functional neuroimaging studies in the literature do not adequately explain the pathophysiology of vaginismus, some studies based on neuroimaging and neurophysiological measurements suggest the presence of some accompanying findings (3-9). Anatomical regions, particularly the corpus callosum (CC), have not been investigated by imaging-based statistical shape analysis (SSA) to date in vaginismus.

Neurological diseases can cause degenerative changes in any part of the brain and cause texture, size and shape changes especially in these regions (plasticity). It is inevitable that these changes lead to changes in size and shape by causing changes in the structure of the corpus callosum (CC), which is the major white matter structure that connects the brain hemispheres and contains the most nerve fiber pathways. Essentially, the main function of the CC is to connect regions of the cerebral cortex to achieve interhemispheric integration. It also acts as a conduit to transmit sensory information (10-15). It is known that structural changes in CC are associated with neuropsychiatric symptoms such as epilepsy, Asperger's syndrome, learning disabilities, behavioral problems, depression, adjustment disorder, schizophrenia, alexithymia, delusions, hallucinations and conversion disorder (16, 17).

In the last two decades, statistical shape analysis (SSA) has been widely used in medicine to examine various structures of interest to determine morphometric features of abnormalities of an organ associated with a particular condition or disease. Offering many different methods for measuring anatomical brain structures, SSA has become a growing interest, particularly in neuroimaging. These studies often rely on measurements of volume and area, which are quantitative features that can predict the progression of disease-induced atrophy or dilation. However, structural changes occurring in certain locations may not be adequately reflected in these volume and area measurements, because it is possible for two different individuals to have the same organs in the same volume and area dimensions, but with differences in shape. Today, with technical developments, imaging views and shapes of organs or tissue structures are widely used as photographic input data. With these data, geometric shape changes in any organ or textural structure can be statistically analyzed using certain signs. SSA is a modern geometric-morphometric analysis method that can be used to evaluate the effects of demographic factors, environmental influences or diseases on growth and allometry and compares body shapes with specific anatomical features using static landmarks. This method is a form of analysis that gives more objective results with multivariate and integrated data on morphological shapes compared to analyze using classical linear measurements. SSA is increasingly used in medicine to examine various structures to identify morphometric abnormalities associated with a particular condition or disease that can aid diagnosis and treatment (12, 13, 18-24).

Studies in the literature have shown that abnormalities in the CC, which acts as a conduit for sensory information transmission, are associated with neuropsychiatric symptoms (12, 13, 15, 25, 26). Based on this information, the aim of this study is to evaluate the corpus callosum with SSA using T1-weighted sagittal MR images of patients with vaginismus and compare them with healthy controls.

MATERIAL AND METHODS

Local Ethics Committee approval was obtained and all participants signed an informed consent form.

Study population

Ten female patients who were diagnosed with vaginismus according to the Diagnostic and Statistical Manual of Mental Disorders-5 (2) criteria in the psychiatry outpatient clinic were evaluated. The diagnosis of the patients was confirmed as a result of a psychiatric evaluation by a psychiatrist with 5 years of experience. Inclusion criteria were 18-40 years of age, no other psychiatric diagnosis, no mental retardation, no neurological or physiological disease, and no history of alcohol or substance use in the last 6 months, and no contraindications for MRI examination. These criteria were applied using information

obtained from patient statements. As the control group, 10 age equivalent healthy individuals who met the study criteria and did not have a psychiatric diagnosis were selected.

Imaging process

A 1.5T General Electric Signa Excite scanner (GE, Milwaukee, Wisconsin, USA) with an 8-channel HR brain coil was used for MRI. High resolution structural T1-weighted sagittal 3D fast spin echo MRI images were obtained (TE = 15.6 ms, TR = 2000 ms, resolution = 0.9375×0.9375×1.328 mm). Anteroposterior commissure line and interhemispheric fissure were used to align the brains of all individuals in a standard position in MRI examinations.

Analysis of images

Obtaining Two-Dimensional Landmarks

Mid-sagittal T1-weighted two-dimensional digital MRI images of each individual, most clearly showing the cerebral aqueduct, corpus callosum, and superior colliculus, were selected. Corpus callosum was marked with TpsDig2 version 2.32 software on each selected image using standardized anatomical landmarks (19, 27, 28) and data were collected (29).

Statistical Deformation Analysis

The mean of 'Procrustes' landmark points was calculated and shape deformations were evaluated using thin plate spline (TPS) analysis with Past version 4.07b (30). Areas that show the greatest expansion or contraction as a result of this analysis are marked using different colors to indicate deformations. The homogeneity of the variance-covariance matrices was examined using the Box-M test (30, 31). Because of the non-homogeneous matrices, the James F< test based on a resampling procedure was used to compare the shapes of the corpus callosum between the control and vaginismus groups (31, 32). In addition, the root mean square of Kendall's Riemann distance rho was compared with the mean shape to obtain overall shape variability measures for the controls and vaginismus groups. Allometric evaluation was performed using multivariate regression analysis of centroid sizes and tangent coordinates. Model significance was assessed using the Wilks' lambda test. Assessment of model fit was performed based on the mean square error (MSE) and the coefficient of determination (R^2) (13, 20, 23).

Landmark Reliability

In this study, a single rater manually defined all landmarks. Intra-rater reliability was not calculated, as the high rater reliability of landmark selection was demonstrated by previous studies (13, 23).

Statistical analysis

Shapes version 1.2.6 package with the R version 4.1.1, PAST version 4.07b were used for the statistical shape analysis (30, 31). Data were expressed as mean±standard deviation. According to normal distribution analysis (One Sample Kolmogorov-Smirnov test) of variables, Student's t test were used to compare the groups for other data. All statistical analyses were made with IBM® SPSS® Statistics (SPSS for Windows version 25, IBM Corporation, Armonk, New York, USA). p value of <0.05 was considered statistically significant.

RESULTS

All patients and control subjects were female. The mean age was 28.60±6.82 years in the patient group and 29.90±5.28 years in the control group, and there was no significant difference between the groups according to age (t=0.472, p=0.639). A significant difference was found in terms of corpus callosum areas in the mid-sagittal images of patients with vaginismus and controls (6.21±0.46 cm^2, 5.72±0.51 cm^2 respectively) and it was larger in patients (t=-2.259, p=0.037).

As the Box-M test identifies inhomogeneous matrices (F=32.085, p<0.001), the James F< test was applied and corpus callosum shapes of vaginismus patients were found to be significantly different from controls (T^2=238.6229, p<0.001) (Figure 1). The root mean square of Kendall's Riemann distance (rho) to main shape was

0.07368384 for controls, 0.07519119 for vaginismus's, and 0.0696102 for all (Figure 2).

The effect of size-dependent shape changes and deformations in the mean shape on graphs (shrinkage) was demonstrated and compared between controls and vaginismus patients using TPS (Figure 3). The maximum deformation observed at the marked points (landmarks) in the anterior region of the CC was present in almost all of them (especially landmark 9, 4, 5 and 8, 6, 1, 15, 10, 16, 11, 13, 12, 3, 7, 2, and 14 in descending order) (Table 1).

Multivariate regression test was used for the relationship between size and shape in the evaluation of allometry and a statistically significant model (F=569.1, p=6.036E-16, R^2=0.8121, MSE=0.008848 and Wilks' lambda=0.001201) was obtained for CC.

Table 1. Average dissimilarity values and contribution percentages of landmarks.

Landmark	Average dissimilarity	Contribution %	R/p
1	0.001030200	6.49	0.3847/0.0001
2	0.000297500	1.87	
3	0.000651400	4.10	
4	0.001813300	11.43	
5	0.001786100	11.25	
6	0.001279700	8.06	
7	0.000475300	2.99	
8	0.001299900	8.19	
9	0.002047300	12.90	
10	0.000912600	5.75	
11	0.000790000	4.98	
12	0.000653300	4.12	
13	0.000673000	4.24	
14	0.000294400	1.86	
15	0.000964400	6.08	
16	0.000901400	5.68	

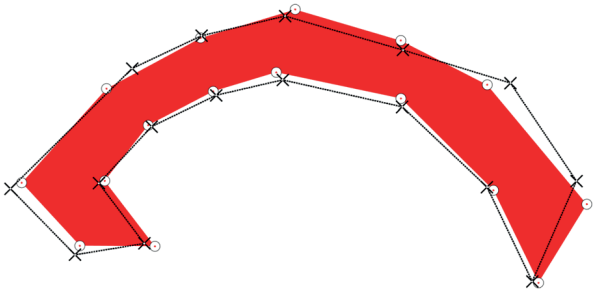
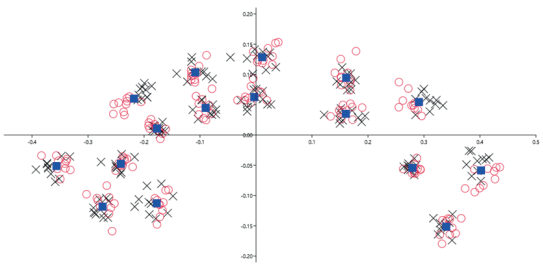
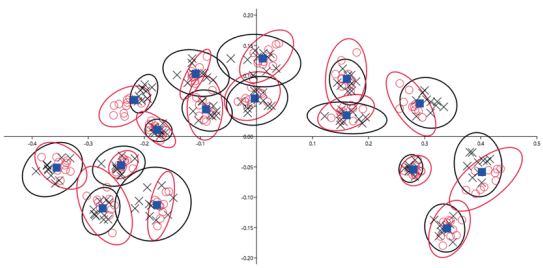


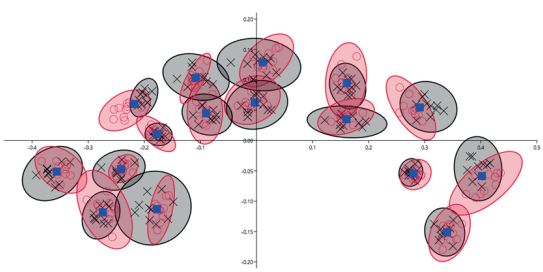
Figure 1. Procrustes mean shape of the CCs of the control (⊙) and vaginismus groups (✕).



a)



b)



c)

Figure 2. Three different landmarks scatter plots with overall mean (■), controls (○) and vaginismus (✕).a)

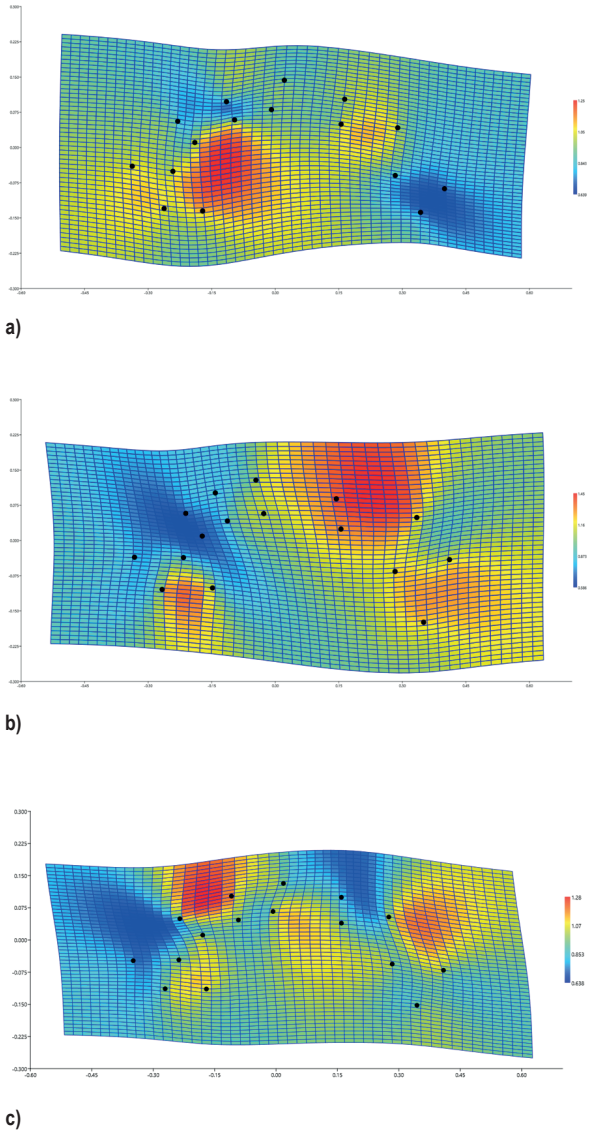


Figure 3. Thin-plate spline transformation grid with expansion factors of the transformation from the overall mean to the control group (a), from the overall mean to the vaginismus group (b) and from the vaginismus group to control group (c).

DISCUSSION

Until recently, it was believed that the sensory, motor and neurovegetative symptoms of vaginismus were not compatible with any neuropathological finding. Therefore, while it is thought that no anatomical or functional pathology will be detected in the brains of these patients with neuroimaging, the latest study findings point to structural and functional changes in the relevant regions of the brain (3, 7, 8, 33, 34).

The corpus callosum provides integration between the hemispheres by connecting the relevant cerebral cortex regions in the brain (10, 11, 13-15, 26, 35). Disruption of this connection causes decreased transfer of information from one hemisphere to the other, impaired harmony between right and left visual fields, alexithymia, delusions and hallucinations. In addition, the presence of schizophrenia, Asperger's syndrome, personality disorder, depressive symptoms and conversion symptoms in CC agenesis has also been shown (12, 13, 15, 17, 25, 26, 36). Furthermore, the association of white matter, including CC, with psychogenic conditions has been investigated in many studies, and empirical evidence from neuroimaging studies suggests that the corpus callosum plays an important role in mood states, but structural neuroimaging fails to extract information about its functionality (13-15, 37-40).

Statistical shape analysis has received more attention recently for its potential to demonstrate morphological changes, but relatively few medical studies have analyzed the shape of CC to investigate the etiology of psychiatric disorders (13, 23, 24).

As the assessment of general form differentiation using neuroanatomical landmarks was considered most appropriate, analyzes were performed using the traditional landmark-based TPS method to examine the shape abnormalities of CC in vaginismus in this study. To our knowledge, this study was the first to use landmark-based SSA methods to analyze CC abnormalities in vaginismus, and local shape comparison had not been performed before.

Interestingly, in this study, a significant difference was found between vaginismus and controls in favor of vaginismus patients in terms of CC areas in cross-sectional images, and it was observed that the corpus callosum shape of the patients was also different when examined by SSA. The fact that this CC is larger in vaginismus, which we have not encountered in the literature, may be due to the small number of samples.

Some studies using shape analysis have reported significant findings about various CC subdivisions, such as in Alzheimer's disease, where the CC is globally atrophic and this is more prominent in the posterior segment, and

the lower border is longer than the upper margin; in autism, there are differences in the body segment of CC; and in multiple sclerosis, there are differences in body and anterior segments of CC. Regional distribution differences of CC injury should result from variable regional fiber amounts associated with different neuroanatomical regions (12, 13, 20, 28, 36).

In this study, it was determined that the maximum deformation was located in the anterior region (genu and rostrum), posterior region (isthmus), inferior of mid-body and anterior region of body of the CC. The first two regions predominantly connect the prefrontal and cingulate cortex regions (landmarks = 9, 1, 8 and 15) and are associated with gustatory stimuli. The first two regions are also connecting the regions of predominantly prefrontal and cingulate cortex (landmarks = 9, 1, 8 and 15) which they associate with stimuli. The next region (landmarks = 6, 10 and 13) are the connecting regions of the motor activation cortical areas, which they associate with tactile stimuli. The last region (landmarks = 5, 4 and 11) are the connecting regions of the temporal (especially superior), occipital and cingulate cortex, where they combine with auditory, peripheral and central visual stimuli (14, 41-43).

In this study, CCs of patients with vaginismus differed in size and shape in some CC regions by SSA analysis. This shows that neuropsychiatric, possible basic mechanisms can also be applied in patients with vaginismus. However, the reason for this cannot be explained because there is not enough research in patients with vaginismus and the effect of feature differences cannot be evaluated clearly.

Limitations

The present study had certain limitations. Since there were no previous studies that analyzed CC with SSA in patients with vaginismus, we were not able to compare the study findings. Small sample size of patients and controls was another major limitation of the study. Although morphological evaluation with 3D data may seem difficult now, it is certain that it will give results that are more accurate in the morphological analysis of organs in spatial dimensions.

Conclusion

In this study, SSA and CC analysis using MRI images revealed significant differences between patients with vaginismus and healthy controls. The study findings highlighted the abnormal distribution of white matter in the corpus callosum and the variable subregional nature of CC in vaginismus patients. Future studies with larger samples may contribute to further elucidation of these findings. This study may help future studies in terms of vaginismus etiology, diagnosis and treatment options.

In this study, CC analysis by SSA using MRI images revealed significant differences between vaginismus patients and healthy controls. Study findings highlighted the abnormal distribution of white matter in the corpus callosum and the variable subregional nature of CC in vaginismus patients. Future studies with larger samples may contribute to further clarification of these findings. This study may help future studies in terms of vaginismus etiology, diagnosis and treatment options.

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