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The Relationship Between Cavum Septum Pellucidum and Psychopathology and Neuropsychological Functions

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ABSTRACT

Introduction: We aimed to investigate the relationship between cavum septum pellucidum (>6 mm) and cavum septum pellucidum et vergae with psychopathology and neuropsychological functions in individuals with these conditions by comparing them with normal cranial imaging.

Methods: Thirty subjects with cavum septum pellucidum and cavum septum pellucidum et vergae on cranial magnetic resonance imaging and 30 controls without pathology on cranial magnetic resonance imaging were included in our study. A sociodemographic data form, Beck Anxiety Inventory, Beck Depression Inventory, and Barratt Impulsivity Scale-11 were applied to the participants. When it comes to neuropsychological functions, digit span test, Boston Naming Test, Verbal Memory Processes Test, Benton Face Recognition Test, Stroop Test, Verbal Fluency Test, and Wisconsin Card Sorting Test were applied to the patients.

Results: In the anomaly group, 26 had cavum septum pellucidum et vergae, while 4 had enlarged cavum septum pellucidum, presenting no statistically significant difference in the rates of psychiatric disease between the anomaly and the control group. The group with enlarged cavum septum pellucidum and cavum septum pellucidum et vergae had lower performances in working memory, naming, attention, and executive functions than the controls.

Conclusions: Abnormal developmental processes related to the formation and maturation of the septum pellucidum may be responsible for widespread cognitive impairments where these anomalies may act as an indicator for these conditions. In order to better understand the relationship of these anomalies with neuropsychological functions and psychiatric disorders, further studies with larger samples are needed.

Keywords: Cavum septum pellucidum, cavum vergae, psychopathology, cognition, neuropsychology

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INTRODUCTION

Septum pellucidum is a thin, translucent wall consisting of 2 laminae with a width varying from 1.5 to 3 mm. Glial cells include some scattered neurons, fiber bundles, and veins connecting with

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the choroid plexus veins.[1,2] The septal region is an important component of the limbic system bearing widespread connections extending to other regulatory centers in the brain, thus serving as an important center between the hypothalamus, hippocampus, amygdala, and brainstem.[2] Thanks to these connections, the septum pellucidum is involved in such tasks as consciousness, sleep, creation of emotional response, continuity of mental processes, memory functions, attention, and activity necessary for finding food and self-preservation, which is very important in wild animals, and creation of autonomic-vegetative adaptation for homeostasis.[2]

The cavity formed when the 2 leaflets of the septum pellucidum are not completely fused is called the cavum septum pellucidum (CSP). The cavum vergae (CV) occurs when the posterior part of the leaflets of the septum pellucidum is not fused. These 2 cavities may also form a single larger space, which is known as CSP et vergae.[3] The CSP and CV are thought to be neurodevelopmental anomalies. The formation of these structures is closely related to the development of the limbic system. Because of this relationship, enlarged CSP and CV can be considered indicators of neurodevelopmental and psychiatric disorders.[2,4]

Most of the previous studies on CSP and CV were focused on schizophrenia spectrum disorders (SSD). Although the studies have found conflicting results, it has been reported that CSP is one of the strongest cranial magnetic resonance imaging (MRI) findings for SSD and the incidence of enlarged CSP (anteroposterior length > 6 mm) in SSD is higher than in healthy individuals, while small CSP is a normal neuroanatomical variation, and, that the clinical significance of CSP depends on its size rather than presence.[5,6]

The relationship between CSP and neuropsychological dysfunction has still not been fully elucidated as there are few studies on this subject in the literature all conducted on patients with neurodevelopmental syndrome and schizophrenia; thus, they have yielded resembling results. In studies conducted in this area, enlarged CSP has been reported to be associated with neuropsychological impairments and the severity of cognitive impairment increases as the size of CSP increases.[7–13] The lack of sufficient information about the relationship between CSP and non-SSD psychiatric diseases in previous studies as well as the relationship between CSP and neuropsychological functions investigated only in patients with SSD and those with neurodevelopmental syndromes aroused our interest towards the subject. Therefore, we aimed to investigate the relationship between enlarged CSP and CSP et vergae and psychopathology and neuropsychological functions by comparing the individuals who present with enlarged CSP and CSP et vergae with those with normal cranial MRI findings.

MAIN POINTS

- The performance of the group with cavum septum pellucidum (CSP) (>6 mm) in language, complex attention and executive functions was lower than the controls.
- No statistically significant difference was found in the rates of psychiatric disorders between the groups.
- Verbal memory and visuospatial functions of the CSP (>6 mm) group were similar to controls.

MATERIAL AND METHODS

Participants

The study was carried out in the Department of Psychiatry and Radiology at the University of Health Sciences, Sisli Hamidiye Etfal Training and Research Hospital, between October 2017 and December 2017. Reviewing hospital records, we enrolled 30 patients admitted to the hospital between August 2016 and December 2017, who were then aged between 18 and 50 years, at least primary school graduates, presented with enlarged CSP (>6 mm) and CSP et vergae on cranial MRI, and also 30 healthy controls with no pathology on cranial MRI. The control group was matched with the patient group in terms of age, education, and gender. Exclusion criteria of the study included the patients with neurological disease, major or minor additional pathological findings on cranial MRI, history of head trauma, medical diseases likely to affect clinical status and cognitive functions, existing psychiatric disorders likely to affect neuropsychological test performance, history of substance/alcohol abuse, and mental retardation.

By reviewing hospital records, 249 patients were detected to be present with enlarged CSP and CSP et vergae were identified based on their cranial MRI in the specified date range. A total of 126 of these patients were excluded as they were not between 18 and 50 years old, 33 were excluded due to their additional pathological imaging findings (partial empty sella: 9, mega cisterna magna: 2, arachnoid cyst: 4, ischemic gliosis or multiple ischemic gliotic focus: 12, intracranial mass: 3, sequelae due to the operation: 3), and 6 were excluded due to neurological disease (epilepsy: 4, Parkinson: 2), though not having any additional findings on cranial MRI. Of the 84 patients who met the inclusion criteria after the screening, 31 could not be reached because their contact information was missing. Of the 53 patients reached, 4 were excluded from the study because they were illiterate, 5 were excluded due to a serious medical condition that could affect their neuropsychological test performance, 1 was excluded due to mental retardation, and 3 were excluded due to major depression. Ten of the patients reached did not want to participate in the study and a total of 30 patients were included in the study. The CSP et vergae was found in 26 of the patients and CSP was found in 4 of them. Of the individuals reached to form the control group, those who did not meet the inclusion criteria were not included in the study. As psychiatric pathology, mental retardation was found in 1 patient and major depression was found in 2 patients, and they were excluded from the study.

Patients and healthy individuals were evaluated with Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-1), a structured interview form for Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV TR) Axis I disorders, and their lifetime psychiatric diagnoses were determined. The participants were administered Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), and Barratt Impulsivity Scale (BIS-11). In order to evaluate the neuropsychological functions, the participants were then applied digit span test (DST), Boston Naming Test (BNT), Verbal Memory Processes Test (VMPT), Benton Face Recognition Test (BFRT), Stroop Test (ST), Verbal Fluency Test (VFT), and Wisconsin Card Sorting Test (WCST). They were informed about the study and the informed consent form was read and their consents were obtained. In this cross-sectional controlled study, the necessary permission was obtained from the Clinical Research Ethics Committee of Health Sciences University, Sisli Hamidiye Etfal Training and Research Hospital (October 17, 2017 Number: 1730).

Assessments

Sociodemographic Data Form: Developed to reveal the sociodemographic characteristics of the participants, the form questions the characteristics of the person such as age, gender, marital status, educational status, occupation, family history of any psychiatric condition, known medical illness, habits, treatments received, psychiatric treatment, as well as suicidal history

Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders -IVAxis I Disorders: The SCID-I is a form structured by First et al.[14] The SCID-I provides a standardized application of diagnostic evaluation, facilitating the screening of DSM-IV diagnostic criteria and thus providing a systematic questioning of symptoms. It also increases the validity and reliability of diagnoses. The validity and reliability study of SCID-I for Turkish was performed by Çorapçıoğlu et al.[15]

Beck Depression Inventory: The BDI consists of 21 items answered in a 4-point Likert type graded between 0 and 3. This is a self-report scale designed by Beck in 1961 which evaluates the presence and severity of emotional, cognitive, somatic, and motivational symptoms of depression.[16] A minimum score of 0 and a maximum score of 63 can be obtained from the test. The validity and reliability study for Turkey was carried out by Hisli.[17]

Beck Anxiety Inventory: The BAI was developed to determine the frequency of anxiety symptoms in adulth.[18] It consists of 21 items answered in a 4-point Likert type graded between 0 and 3. A minimum score of 0 and a maximum score of 63 can be obtained in the test. Higher scores in the assessment indicate a higher level of anxiety. A validity and reliability study for Turkey was conducted by Ulusoy et al[19] in 1998.

Barratt Impulsivity Scale: Developed by Barratt and Patton,[20] the scale is a 30-item self-report test used to assess impulsivity in which an individual is asked to mark the most appropriate statement from the options "rarely/never," "sometimes," "often," and "almost always/always." While evaluating BIS-11, 4 different scores are obtained as total score, inattention, lack of planning, and motor impulsivity. The higher the total BIS-11 score, the higher the impulsivity level of the patient. The Turkish validity and reliability study of BIS-11 was performed by Güleç et al.[21]

Verbal Memory Process Test: The test aids to evaluate different parameters related to memory, which are instant memory, learning, recording, and retrieval. The test contains 15 unrelated words read to the participant per second, and after each reading, the participant is asked to recall as many as they can, 10 attempts are made in this way. After 40 minutes, the participant is asked to recall what she/he can from the words learned, and a delayed recall trial is introduced. Turkish validity and reliability study was conducted by Öktem.[22]

Digit Span Test: Developed by Wechsler in 1945, the test is used as a subtest of Wechsler Memory Scale-Revised, which is a revised version of the Wechsler Memory Scale in 1987.[23] Consisting of 2 parts as the forward and backward, digit span test is used to evaluate simple attention and working memory.

Benton Face Recognition Test: It was developed by Benton in 1968 to measure face recognition and discrimination functions. Levin, Hamser, and Benton developed a shorter version consisting of 27 items in addition to the longer one containing 54 items.[24] It evaluates the facial recognition disorder that occurs as a result of damage affecting the posterior parts of the right hemisphere. The normative data of the test were collected within the scope of a psychology master's thesis in our country.[25]

Boston Naming Test: Developed by Kaplan et al.[26] the test evaluates naming over lexical retrieval abilities. The test consists of images ranging from easily recognizable objects to increasingly difficult recognizable objects. The participant is asked to retrieve what happens by looking at the image. A validity and reliability study of the BNT was conducted in our country.[27]

Wisconsin Card Sorting Test: Developed in 1948 by Grant and Berg, the test was reviewed and finalized by Heaton.[28] Executive functions evaluated by the test are as follows; planning, information processing speed, abstraction, concept formation, conceptual analysis, reasoning, strategy formation and cancellation ability, mental flexibility, problem solving, category creation, and category changing ability. The normative data of the test were collected within the scope of the BİLNOT battery.[29]

Verbal Fluency Test: It is a test used to evaluate complex attention functions. In the test, the participant is first asked to say the names of the animals for 1 minute and recorded in an attempt to measure semantic fluency. Then, the participant is given the letters "K, A, S" in order and asked to say the object names related to that letter for 1 minute and recorded to measure phonetic fluency. The norms of the Turkish form of the test were collected in a psychology graduate study.[30]

Stroop Test: The test was developed by Stroop in 1935.[31] The ST measures resistance to interference, focused attention, and information processing speed. Karakaş et al[32] carried out an adaptation study for Turkish society.

Magnetic Resonance Imaging

Cranial MRI examination was performed using a standard head coil on a Siemens MRI device with a magnetic field strength of 1.5 Tesla.

Statistical Analysis

Statistical Package for the Social Sciences 15.0 (SPSS Inc., Chicago, IL, USA) for Windows program was used for statistical analysis. Descriptive statistics were given as numbers and percentages for categorical variables, and as mean, SD, minimum, and maximum for numerical variables. Comparisons between 2 independent groups of numerical variables were performed using the Student *t*-test when the normal distribution condition was met, and the Mann–Whitney *U*-test when the normal distribution condition was not met. The ratio of the categorical variable between the groups was compared with the chi-square analysis. The relationships between numerical variables were analyzed through Spearman correlation analysis since the parametric test condition was not met. The statistical alpha significance level was accepted as $P < .05$.

RESULTS

Demographic and Clinical Characteristics

Thirty CSPs and 30 healthy controls were included in the study. Of those with the anomaly, 26 were present with CSP et vergae and 4 with CSP. There was no significant difference between the anomaly and the control group in terms of age, gender, educational status, and other characteristics ($P > .05$). The mean BAI and BDI scores of

Table 1. Demographic and Clinical Data of Participants

	CSP	Control	
	Mean ± SD	Mean ± SD	*P*
Age (years)	36.9 ± 9.9 (18–50)	37.0 ± 9.6 (18–50)	1.000
Sex (female), n (%)	17 (56.7)	16 (53.3)	.795
Education (years)	10.0 ± 4.7 (5–16)	10.0 ± 4.7 (5–16)	1.000
Family history, n (%)	8 (26.7)	12 (40.0)	.273
Comorbidity, n (%)	9 (30.0)	8 (26.7)	.774
Habit, n (%)	12 (40.0)	13 (43.3)	.793
Suicide, n (%)	3 (10.0)	1 (3.3)	.612
Psychiatric treatment history, n (%)	9 (30.0)	7 (23.3)	.559
CSP width	7.88 ± 3.86	(2.3–20.7)	
BAI scale scores	17.7 ± 14.0 (12)	6.3 ± 7.1 (3)	**<.001**
BDI scale scores	10.8 ± 8.2 (9)	4.8 ± 7.2 (2)	**<.001**
BIS-11	54.0 ± 9.5 (53.5)	50.9 ± 9.4 (49.5)	.210

BAI, Beck Anxiety Inventory scale; BDI, Beck Depression Inventory scale; BDI-11, Barratt Impulsivity Scale-11; CSP, cavum septum pellucidum.

the group with anomaly were statistically significantly higher than the control group ($P < .001$ for both). The comparison of sociodemographic data of CSP and control groups is shown in Table 1. No statistically significant dif-ference was found in the lifetime psychiatric disease rates of the groups (Table 2).

Neuropsychological Test Results

In neuropsychological test results, the mean DST—backward score was statistically significantly lower in the anomaly group compared to the control ($P = .029$), while the mean DST—forward score was similar to that of the control group. The BNT self-naming test, which evaluates language functions, was statistically significantly lower in the anomaly group compared to the control group ($P = .002$). The mean naming with clues or not naming at all scores were statistically significantly higher ($P = .008$, $P = .021$, respectively). No statistically significant difference was found between the groups in terms of the mean BFRT, which evaluates visual-spatial functions and VMPT, which evaluates verbal memory.

The mean ST-interference, error, and correction scores were statistically significantly higher in the anomaly group than in the control group ($P = .015$, $P = .043$, $P = .007$, respectively). In the VFT, the mean KAS score was statistically significantly lower in the anomaly group than in the control ($P = .001$). The mean WCST-completed categories

Table 2. Psychiatric Diseases

	CSP		Control		
	n	%	n	%	*P*
Lifetime illness	27	90.0	21	70.0	.053
Multiple diagnosis	19	63.3	13	43.3	.121
Psychotic disorder	1	3.3	0	0.0	1.000
Bipolar disorder	0	0.0	0	0.0	-
Depressive disorder	14	46.7	9	30.0	.184
Anxiety disorder	13	43.3	9	30.0	.284
Obsessive compulsive-related disorders	1	3.3	0	0.0	1.000
Trauma and stress-related disorder	8	26.7	11	36.7	.405
Somatic symptom disorder	10	33.3	4	13.3	.067
Eating disorder	1	3.3	1	3.3	1.000

Table 3. Neuropsychological Tests

	CSP	Control	
Neuropsychological Tests	Mean ± SD	Mean ± SD	*P*
Attention			
DST—forward	5.53 ± 1.28	5.87 ± 1.20	.265
DST—backward	3.77 ± 1.19	4.33 ± 1.03	**.029**
Language			
BNT—total item (31 items)	25.8 ± 2.7	27.8 ± 2.3	**.002**
Verbal memory			
VMPS—immediate memory	5.43 ± 1.50	6.10 ± 2.17	.221
VMPS—total learning score	114.1 ± 13.8	121.7 ± 16.6	.060
VMPS—highest learning	14.4 ± 1.2	14.6 ± 0.9	.360
VMPS—inconsistency score	3.80 ± 2.28	3.43 ± 2.94	.447
VMPS—self recall (delayed recall)	12.4 ± 2.1	12.8 ± 1.7	.666
VMPS—recognition	2.40 ± 1.83	2.20 ± 1.67	.762
Visuospatial functions			
BFRT	46.2 ± 4.3	47.1 ± 3.9	.501
Executive functions			
ST—interference time (s)	52.8 ± 20.3	42 ± 12.1	**.015**
ST—incorrect number	1.23 ± 1.72	0.53 ± 1.11	**.043**
ST—number of fixes	3.87 ± 2.64	2.07 ± 1.72	**.007**
VFT—semantic fluency—animal names	20.4 ± 5.1	22 ± 4.8	.217
VFT—phonetic fluency: K–A–S	30.1 ± 11.9	42.1 ± 14.6	**.001**
WCST—completed category	4.70 ± 2.44	6.40 ± 2.59	**.013**
WCST—perseverative error percentage	19.5 ± 8.7	15.6 ± 7.8	.082
WCST—trials to complete first category	23.5 ± 16.6	18.0 ± 9.1	.244
WCST—failures to maintain set	1.30 ± 1.21	1.13 ± 1.14	.595
WCST—conceptual level response	53.7 ± 17.7	64.4 ± 17.6	**.023**

BFRT, Benton Face Recognition Test; BNT, Boston Naming Test; CSP, cavum septum pellucidum; DST, digit span test; ST, Stroop Test; VFT, Verbal Fluency Test; VMPS, Verbal Memory Processes Scale; WCST, Wisconsin Card Sorting Test.

and the percent conceptual level response scores were statistically significantly lower in the anomaly group than in the control (respectively, $P = .013$, $P = 0.023$). There was no significant difference between the groups in other subscales of WCST. (Table 3)

DISCUSSION

In this study, we aimed to investigate the relationship of enlarged CSP and CSP et vergae with psychopathology and neuropsychological functions by comparing individuals with CSP and CSP et vergae with healthy controls in this study. The presence of lifelong psychiatric disease was investigated over SCID-1 administered to both groups. No previous similar study conducted with individuals with CSP has been encountered in the literature. Since our sample was small and the psychopathology diversity of the participants was high, they were grouped under the current diagnostic titles in line with the ones listed in Diagnostic and Statistical Manual of Mental Disorders-5 (DSM-5) upon the detection of psychiatric diseases with SCID-I. The relationship of enlarged CSP and CSP et vergae with psychopathology was investigated over the diagnostic titles listed in DSM-5.

At least 1 lifetime psychiatric condition was found in 90% (n = 27) of the group with anomaly, which was 70% in the control group

(n=21). No statistically significant difference was found in the rates of psychiatric illness between the groups. The lifetime rate of having more than 1 psychiatric illness was found to be 63.3% (n=19) in the anomaly group and 43.3% (n=13) in the control group, yielding no statistically significant difference between the groups. While most of the studies on CSP and CV were related to SSD, in our study, only 1 patient with CSP et vergae had a diagnosis of atypical psychosis in remission, and no psychotic disorder was found in the group without CSP. However, there are case reports describing psychosis in patients with CSP and CSP et vergae.[33,34] Despite the conflicting results in previous studies conducted on SSD, a meta-analysis of these studies has concluded that CSP (enlarged or normal) prevalence is higher (92%) in the schizophrenia group and that CSP is one of the strongest cranial MRI findings for schizophrenia.[5] In another meta-analysis, while the incidence of enlarged CSP has been found to be significantly higher in the SSD group than in the healthy group, small CSP has been demonstrated to be a normal neuroanatomical variation, adding that the clinical significance of CSP depends on its size rather than its presence.[35] In a study investigating the relationship between CSP and SSD, it was shown that the family history of psychosis was higher in patients with CSP.[36] In our study, a family history of psychiatric disease was found to be 40% (n=12) in the control group and 26.7% (n=8) in the group with anomaly, and no statistically significant difference was found between the groups.

The relationship between midline brain structure anomalies and bipolar disorder is not yet fully known. In previous studies investigating the relationship between mood disorders and CSP, no significant differences were found between the study group and controls in terms of CSP incidence. There was no difference in the prevalence of CSP between patients with mood disorders and, schizophrenia spectrum.[37] Also, the CSP incidence in patients with bipolar disorder is seen to vary between 7.2% and 84.6% in these studies.[38,39] In another study, the incidence of CSP in the patient group with bipolar disorder (7.2, n=5) was found to be higher than in the healthy (1.1%, n=1) group, while no difference was observed between the groups in terms of enlarged CSP (2.9%-1.1%).[40] The CSP of any size, including both small and large CSP, has been found to be more common in patients with bipolar disorder than in healthy controls.[41] In our study, no diagnosis of bipolar disorder was encountered in either group.

The rate of lifetime depressive disorders was 46.7% (n=14) in the anomaly group and 30% (n=9) in the control group. The rate of lifetime depressive disorders (major depression, dysthymic disorder, premenstrual dysphoric disorder) was higher in the anomaly group, though not statistically significant. In both groups, there were no individuals with a diagnosis of major depression or under treatment at the time of evaluation. Individuals with existing depression were not included in the study, considering it would affect the neuropsychological test results.

On cranial MRIs in major depression patients, there were predominantly neuroanatomical changes in the amygdala, hippocampus, basal ganglia, orbitofrontal and anterior cingulate cortices, which was also consistent with the limbic-cortical dysregulation model of unipolar depression.[42–44] While corpus callosum enlargement was observed in patients with existing major depression, this was not the case for the patients in remission.[45] Based on this finding, it has been suggested that changes in midline brain structures associated with the depression stage may play a role in the neurobiology of major depression. Takahashi et al[46] investigated CSP in those with current major depression (n=26), in those with depression in remission (n=22) and in healthy subjects (n=28) and found the CSP incidence (1 mm and above) to be 89.7% in the current major depression group, 81.5% in the depression group in remission, and 84.9% in the healthy group. The incidence of enlarged CSP (6 mm and above) was found to be 3.5% in the group with existing MD, 7.4% in the depression group in remission, and 15.2% in the healthy ones.[46] Studies conducted to date have not found a relationship between major depression and CSP.[40,46] In our study, the lifetime major depression rate under the title of depressive disorders was higher in the group with major CSP and CSP et vergae than in the control group (10, n=3). Since our study was conducted with a small group compared to other studies, further studies with larger groups in this area are needed in order to fully comprehend the relationship between enlarged CSP and CSP et vergae and MD.

The septum pellucidum is a part of the septo-hippocampal region that plays a key role in the modulation of anxiety. It has been shown that septal pacemaker cells play a critical role in normal hippocampus function.[47] In a study investigating cranial anomalies on MRI in panic disorder patients, the most common limbic system anomalies were determined and all of these anomalies were observed to be in the septo-hippocampal region. Abnormal right hippocampus volume was found in 5 patients, CSP in 1, and CSP et vergae in 4 patients. The detected CSP in these patients might be suggestive of a functional disorder of the septo-hippocampal system.[48] In another study conducted by Crippa et al[49] with panic disorder patients in which imaging was performed with 1 mm coronal sections on cranial MRI, the incidence of CSP was 76.2% (n=16) in panic disorder patients and 85.7% (n=18) in the healthy group, and there was no statistically significant difference between groups.[49] The reason why no difference was found between the groups in this study could be due to the quite sensitive measurement modality preferred (sections taken at 1 mm intervals). In our study, no significant difference was found between the anomaly group (43.3%, n=13) and the control group (30%, n=9) in terms of lifetime anxiety disorder rate.

In our study, the rate of lifelong somatic symptom disorders was 33.5% (n=10) in the anomaly group and 13.3% (n=4) in the control group. Although somatic symptom disorders was observed at a higher rate in the patient group, this elevation was not statistically significant. Unlike other mental illnesses, neuroanatomy imaging studies on SSD are rare. When the literature was reviewed, no study was found in this area related to CSP. In future neuroanatomy imaging studies with large samples in this group, it will be useful to consider enlarged CSP and CSP et vergae as well.

The relationship between CSP and CV with neuropsychological dysfunction is still not fully elucidated as there are few studies on this subject in the literature all of which were conducted with patients with neurodevelopmental syndrome and schizophrenia. Cognitive dysfunction is associated with enlarged CSP in heterogeneous pediatric groups with neurological anomalies, mental retardation, and developmental delay.[7–10] In a study conducted by Renier et al[11] on patients with Apert syndrome, the team found different brain anomalies in patients and stated that septum pellucidum anomalies were associated with cognitive dysfunction most (low Intellectual quotient). Based on these results, Nopoulos et al[13] investigated the relationship between enlarged CSP and cognitive dysfunction in schizophrenia. Fourteen schizophrenia cases with enlarged CSP (6 mm and above), 14 without CSP, and 14 healthy controls were included in the study. Weschler Adult Intelligence Test-Revised Form was administered to the participants, and yet no significant difference was found in test

scores in the group with and without enlarged CSP. In the group with enlarged CSP, a negative correlation was found between the length of CSP and all test scores, showing that the greater the CSP, the more severe the cognitive impairment. Flashman et al[12] investigated the correlation of CSP with clinical and neuropsychological functions in SSD. They enrolled 57 patients with schizophrenia, 17 with schizoaffective disorder, and 3 atypical psychosis patients and 55 healthy controls. No difference was found between those with SSD and the healthy group in terms of the presence or size of CSP. The study group was divided as minimal CSP (2 mm and below, n = 28-31) and enlarged CSP (6 mm and above, n = 9-10) based on the size of the CSP, and the neuropsychological test performances of the groups were compared. The test performances of the group with enlarged CSP were found to be worse than the group with minimal CSP.

In our study, no significant difference was found between the groups in the forward DST, which evaluates simple attention, while there was a significant difference in the backward DST scores, which evaluates the working memory capacity. These results demonstrate that working memory is worse in the group with abnormality. In a study investigating the relationship between CSP and cognitive functions in patients with SSD, no significant difference was found in terms of DST between those with and without CSP.[12]

In our study, the performance of the group with enlarged CSP and CSP et vergae in VFT, WCST, and ST, evaluating executive functions, was found to be lower than the controls. No significant difference was found between the group with anomaly and the control group in terms of the task of saying words from a certain category (animals) in an attempt to evaluate semantic fluency. On the other hand, in the KAS test evaluating phonetic fluency, the mean score of the group with anomaly was significantly lower than the control group. Based on these findings, it can be said that the semantic fluency of the group with enlarged CSP and CSP et vergae was maintained, whereas the phonetic fluency was impaired.

The number of categories completed in WCST and the percent conceptual level response were statistically significantly lower in the anomaly group. There was no significant difference between the groups in terms of the percentage of perseverative error, the number of responses used to complete the first category, the failure to maintain the set, and the learning-to-learn scores. In the study by Flashman et al.[12] executive functions in SSDs were evaluated with WCST, and it was found that those with enlarged CSP made more perseverative errors in WCST, which was, however, not statistically significant, and no difference was found between the groups in terms of the number of completed categories. The group with anomaly also performed poorly in the ST. Compared to the control group, the group with anomaly had a longer duration of interference, more false readings, and more corrected readings than the control group, and these findings were statistically significant. The significant differences encountered in the VFT, WCST, and ST, all evaluating different components of attention, can be said to be significant in light of the knowledge that the limbic system is a region that modulates activity and attention by filtering sensory input and that CSP is an anomaly closely related to the abnormal development of the limbic system.

In BNT, evaluating the naming ability which is one of the language skills, the group with anomaly performed lower than the controls. The findings show that the naming ability of the group with enlarged CSP and CSP et vergae was affected by language functions. In the study by Flashman et al[12] on SSDs, it was shown that as the length of the CSP increased, the grasping language skills decreased. In our study, no statistically significant difference was found between the groups in the mean scores of VMPT evaluating verbal memory. Flashman et al.[12] on the other hand, evaluated verbal memory with CVLT-II in SSD and detected the short and long-term free recall performance to be statistically significantly lower in the patient group with enlarged CSP and maintained that this finding could be due to the abnormal development of the hippocampus, which plays a key role in memory functions. In our study, the group with anomaly performed poorly in the sub-dimensions of the verbal memory test. However, this was not statistically significant.

Both Flashman et al[12] and Nopoulos et al[13] reported that cognitive impairment increased as the size (anteroposterior length) of the CSP increased in the schizophrenia group. In both studies, the gold standard measurement method was used. In these studies, coronal sections were imaged over 1.5 mm intervals on cranial MRI, then the brains were resampled as 1 mm sections, and the length was measured based on the number of sections (1 section = 1mm) in which CSP was observed. In our study, those presenting to different clinics with different complaints and those having already undergone cranial MRI were included. In our hospital's standard cranial MRI, the cross-sectional thickness of the coronal images is set to 4.5 mm.

Since only the patients with enlarged anomalies can be determined and reported because of the large section thickness set, the patients with enlarged CSP and CSP et vergae were included in our study. Due to the large section thickness, precise measurements of the anomalies could not be made. For this reason, the relationship between the size of the anomaly and neuropsychological tests and psychopathology could not be examined in the anomaly group. It is not possible to generalize the findings obtained due to the small sample size of our sample group. Although there was no significant difference between the 2 groups in terms of psychopathology, neuropsychological test performances of both the anomaly and the control group may have been adversely affected as psychiatric pathologies were not completely excluded.

CONCLUSION

As a result, while no significant difference was found between the groups in terms of psychopathology in our study, it can be said that the working memory performance of the group with enlarged CSP and CSP et vergae was lower than that of the healthy controls in terms of the language function task of naming and phonetic fluency, attention, and executive functions. There was no difference between the groups in face recognition function, verbal memory, and learning functions. It is unlikely that these anomalies alone are responsible for the cognitive impairment detected in multiple areas. The septum pellucidum is part of the limbic system acting as a linkage point that transmits visceral information between important brain regions. Although the stages of fusion of the 2 leaflets of the septum pellucidum are not well perceived, their fusion is closely related to the development of the surrounding structures (corpus callosum, hippocampus, cerebral hemispheres, and thalamus). More likely, abnormal developmental processes related to the formation and maturation of the septum pellucidum may be responsible for widespread cognitive impairment, and also enlarged CSP and CSP et vergae may be indicators of these impairments. In order to better understand the relationship between these anomalies and neuropsychological functions in addition to psychiatric disorders, further studies to be conducted with large samples are needed in this area.

Ethics Committee Approval: The participants were instructed on the purpose and design of the study and informed consent was obtained from each. The trial was approved by the ethics committee of Health Sciences University, Sisli Hamidiye Etfal Training and Research Hospital (October 17, 2017, Number: 1730).

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

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REFERENCES

1. Gray H, Warwick R, Williams PL. *Gray's Anatomy*. 36th ed. Philadelphia: Saunders; 1980.
2. Sarwar M. The septum pellucidum: normal and abnormal. *AJNR Am J Neuroradiol*. 1989;10(5):989-1005.
3. Oteruelo FT. On te cavum septi pellucidi and the cavum vergae. *Anotomischer Anz*. 1986;162(4):271-278.
4. Kim KJ, Peterson BS. Cavum septi pellucidi in Tourette syndrome. *Biol Psychiatry*. 2003;54(1):76-85. [CrossRef]
5. Shenton ME, Dickey CC, Frumin M, McCarley RW. A review of MRI findings in schizophrenia. *Schizophr Res*. 2001;49(1-2):1-52. [CrossRef]
6. Trzesniak C, Oliveira IR, Kempton MJ, et al. Are cavum septum pellucidum abnormalities more common in schizophrenia spectrum disorders? A systematic review and meta-analysis. *Schizophr Res*. 2011;125(1):1-12. [CrossRef]
7. Schaefer GB, Bodensteiner JB, Thompson JN. Subtle anomalies of the septum pellucidum and neurodevelopmental deficits. *Dev Med Child Neurol*. 1994;36(6):554-559. [CrossRef]
8. Breeding LM, Bodensteiner JB, Cowan L, Higgins WL. The cavum septi pellucidi; a magnetic resonance imaging study of prevalence and clinical associations in a pediatric population. *J Neuroimaging*. 1991;1(3):115-118. [CrossRef]
9. Bodensteiner JB, Schaefer GB. Wide cavum septum pellucidum: a marker of disturbed brain development. *Pediatr Neurol*. 1990;6(6):391-394. [CrossRef]
10. Bodensteiner JB, Schaefer GB, Craft JM. Cavum septi pellucidi and cavum vergae in normal and developmentally delayed populations. *J Child Neurol*. 1998;13(3):120-121. [CrossRef]
11. Renier D, Arnaud E, Cinalli G, Sebag G, Zerah M, Marchac D. Prognosis for mental function in Apert's syndrome. *J Neurosurg*. 1996;85(1):66-72. [CrossRef]
12. Flashman LA, Roth RM, Pixley HS, et al. Cavum septum pellucidum in schizophrenia: clinical and neuropsychological correlates. *Psychiatry Res*. 2007;154(2):147-155. [CrossRef]
13. Nopoulos P, Krie A, Andreasen NC. Enlarged cavum septi pellucidi in patients with schizophrenia: clinical and cognitive correlates. *J Neuropsychiatry Clin Neurosci*. 2000;12(3):344-349. [CrossRef]
14. First MB, Gibbon M, Spitzer RL, Williams JBW, Benjamin LS. *Structured Clinical Interview for DSM-IV Axis II Personality Disorders, (SCID-II)*. Washington, DC: American Psychiatric Press; 1997.
15. Çorapçıoğlu A, Aydemir Ö, Yıldız M, Esen A, Köroğlu E. *DSM-IV Eksen I Bozuklukları (SCID-I) İçin Yapılandırılmış Klinik Görüşme, Klinik Versiyon*. Ankara: Hekimler Yayın Birliği; 1999.
16. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. *Arch Gen Psychiatry*. 1961;4(6):561-571. [CrossRef]
17. Hisli N. Validity and reliability of Beck Depression Inventory for university students. Turkish. *J Psychol*. 1989;23:3-13.
18. Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: psychometric properties. *J Consult Clin Psychol*. 1988;56(6):893-897. [CrossRef]
19. Ulusoy M, Sahin N, Erkmen H. Turkish version of the Beck Anxiety Inventory: psychometric properties. *J Cogn Psychother*. 1998;12(2):163-172.
20. Patton JH, Stanford MS, Barratt ES. Factor structure of the Barratt impulsiveness scale. *J Clin Psychol*. 1995;51(6):768-774. [CrossRef]
21. Güleç H, Tamam L, Güleç MY, et al. Psychometric properties of the Turkish version of the Barratt impulsiveness scale-11. *Klin Psikofarmakol Bul*. 2008;18(4):251-258.
22. Öktem Ö, Süreçleri ÖSB. *Testi (ÖKTEM SBST) el Kitabı*. Birinci Baskı, Ankara: Türk Psikolog Derneği Yayınları; 2011.
23. Wechsler D. *Wechsler Memory Scale Revised*. New York: The Psychological Corporation; 1987.
24. Benton AL, Sivan AB, Hamsher KD, Varney NR. *Contributions to Neuropsychological Assessment: A Clinical Manual*. USA: Oxford University Press; 1994.
25. Keskinkılıç C, Testi'nin BYT. Türkiye Toplumu normal yetişkin Denekler üzerindeki Standardizasyonu. *Türk Nöroloji Derg*. 2008;14(3):179-190.
26. Kaplan EF, Goodglass H, Weintraub S. *The Boston Naming Test: Experimental edition*. Philadelphia, PA: Lea, Febiger; 1978.
27. Kurt M, Can H, Karakas S. Research and development study for Boston naming test Turkish form. *Yeni Symp*. 2016;54(1):6-14. [CrossRef]
28. Heaton RK. *Wisconsin Card Sorting Test Manual*. Psychological Assessment Resources; 1981.
29. Karakaş S. *BİLNOT Bataryası El Kitabı: Nöropsikolojik Testler için Araştırma ve Geliştirme Çalışmaları*. Ankara: Dizayn Ofset; 2004.
30. Tumaç A. *Normal Deneklerde Frontal Hasarlara Duyarlı Bazı Testlerde Performansa Yaş ve Eğitimin Etkisi*. İstanbul Üniversitesi; 1997.
31. Stroop JR. Studies of interference in serial verbal reactions. *J Exp Psychol*. 1935;18(6):643-662. [CrossRef]
32. Karakaş S, Erdoğan E, Sak L, et al. Stroop testi TBAG formu: türk Kültürüne standardizasyon çalışmaları, Güvenirlik ve Geçerlilik. *Klin Psikiyatr Derg*. 1992;2(2):75-88.
33. Lewis SW, Mezey GC. Clinical correlates of septum pellucidum cavities: an unusual association with psychosis. *Psychol Med*. 1985;15(1):43-54. [CrossRef]
34. Rajasekharan C, Karthik V, Harikrishnan M, Lekshmi S. Cavum vergae and psychiatric illness: substantive or serendipity? *BMJ Case Rep*. 2018;2018:bcr-2018. [CrossRef]
35. Trzesniak C, Schaufelberger MS, Duran FLS, et al. Longitudinal follow-up of cavum septum pellucidum and adhesio interthalamica alterations in first-episode psychosis: a population-based MRI study. *Psychol Med*. 2012;42(12):2523-2534. [CrossRef]
36. Uematsu M, Kaiya H. Midsagittal cortical pathomorphology of schizophrenia: a magnetic resonance imaging study. *Psychiatry Res*. 1989;30(1):11-20. [CrossRef]
37. Wang LX, Li P, He H, et al. The prevalence of cavum septum pellucidum in mental disorders revealed by MRI: a meta-analysis. *J Neuropsychiatry Clin Neurosci*. 2020;32(2):175-184. [CrossRef]
38. Takahashi T, Malhi GS, Wood SJ, et al. Midline brain abnormalities in established bipolar affective disorder. *J Affect Disord*. 2010;122(3):301-305. [CrossRef]
39. Brisch R, Bernstein HG, Krell D, et al. Volumetric analysis of septal region in schizophrenia and affective disorder. *Eur Arch Psychiatry Clin Neurosci*. 2007;257(3):140-148. [CrossRef]
40. Shioiri T, Oshitani Y, Kato T, et al. Prevalence of cavum septum pellucidum detected by MRI in patients with bipolar disorder, major depression and schizophrenia. *Psychol Med*. 1996;26(2):431-434. [CrossRef]
41. Beraldi GH, Prado KS, Amann BL, Radua J, Friedman L, Elkis H. Meta-analyses of cavum septum pellucidum in mood disorders in comparison with healthy controls or schizophrenia. *Eur Neuropsychopharmacol*. 2018;28(12):1325-1338. [CrossRef]
42. Mayberg HS. Modulating dysfunctional limbic-cortical circuits in depression: towards development of brain-based algorithms for diagnosis and optimised treatment. *Br Med Bull*. 2003;65(1):193-207. [CrossRef]
43. Lorenzetti V, Allen NB, Fornito A, Yücel M. Structural brain abnormalities in major depressive disorder: a selective review of recent MRI studies. *J Affect Disord*. 2009;117(1-2):1-17. [CrossRef]
44. Konarski JZ, McIntyre RS, Kennedy SH, Rafi-Tari S, Soczynska JK, Ketter TA. Volumetric neuroimaging investigations in mood disorders:

bipolar disorder versus major depressive disorder. *Bipolar Disord*. 2008;10(1):1-37. [CrossRef]
45. Walterfang M, Yücel M, Barton S, et al. Corpus callosum size and shape in individuals with current and past depression. *J Affect Disord*. 2009;115(3):411-420. [CrossRef]
46. Takahashi T, Yücel M, Lorenzetti V, et al. Midline brain structures in patients with current and remitted major depression. *Prog Neuropsychopharmacol Biol Psychiatry*. 2009;33(6):1058-1063. [CrossRef]
47. Gray J, McNaughton N. *The Neuropsychology of Anxiety: an Enquiry into the Function of the Septo-Hippocampal System*. 2nd ed; 2003.
48. Dantendorfer K, Prayer D, Kramer J, et al. High frequency of EEG and MRI brain abnormalities in panic disorder. *Psychiatry Res*. 1996;68(1):41-53. [CrossRef]
49. Crippa JAS, Uchida R, Busatto GF, et al. The size and prevalence of the cavum septum pellucidum are normal in subjects with panic disorder. *Braz J Med Biol Res*. 2004;37(3):371-374. [CrossRef]