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ORIGINAL PAPER

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Volumetric analysis of septal region in schizophrenia and affective disorder

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Abstract MRI and post-mortem studies indicate an increased prevalence of cavum septi pellucidi (CSP) in schizophrenia and affective disorder. The aim of this study was to characterize the CSP and the septal tissue among patients with schizophrenia, patients with affective disorder, and control subjects. The volumes of CSP and septal tissue were measured in post-mortem brains in 42 patients with schizophrenia, 14 patients with affective disorder, and 17 normal control cases by planimetry of serial sections. Enlargements of CSP (>100 mm^3) were found in eight of the 42 (19%) patients with schizophrenia. There were no significant differences in CSP volumes between patients with affective disorder and controls. Enlarged CSP in schizophrenia were not associated with reduced septal tissue volumes. By contrast, a significant positive correlation between volumes of CSP and septal tissue volumes in patients with schizophrenia ($P = 0.03$) and in control cases ($P < 0.01$) was found, but not in patients with affective disorder ($P = 0.53$). The finding of enlarged CSP in schizophrenia strongly supports the hypothesis of an early developmental abnormality in this key structure of the limbic system.

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Introduction

The cavum septi pellucidi (CSP) is located in the midline between the two leaflets of the septum pellucidum separating the left and right lateral ventricles. The CSP may reflect a malformation of brain midline structures in schizophrenia. The septal region (or septal tissue) consists of the septum pellucidum and the septal nuclei, which are below the septum pellucidum. Being part of the limbic system the septal region is an important relay structure with connections to the hippocampus, hypothalamus, amygdala, habenula, and reticular formation of the brain stem [1, 2]. Whereas several MRI studies have reported an increased prevalence of CSP in schizophrenia [3–14], and in affective disorder [7, 9, 13, 15], only three CT/MRI studies discuss the possibility of pathological abnormalities in the surrounding septal tissue (i.e. the septum pellucidum; 16–18]. One MRI study measured the lengths of the septum pellucidum in healthy subjects in three different age groups [19]. Vascular and neoplastic lesions of septal tissue result in neuropsychiatric disturbances such as schizophrenia, depressed mood or psychotic symptoms [20–22]. As far as we know, the present study is the first post-mortem investigation to measure the volumes of septal tissue and CSP in psychiatric diseases. This is remarkable, since disturbances of the limbic system (including the septal tissue) are assumed to play an important role in the pathogenesis of schizophrenia and affective disorder [23–29].

It was the aim of this study to investigate the CSP and the septal tissue of patients with schizophrenia

Table 1 Demographic data of control subjects, patients with schizophrenia, and affective disorder (Abbreviation: J-T: Jonckhere–Terpstra test)

	Controls	Affective disorder	Schizophrenia	3-Group comparison values		Affect. versus control values		Schiz. versus control values		Schiz. versus affect. values	
(A) For CSP measurement	$N = 17$	$N = 14$	$N = 42$	J-T (df = 2)		Mann–Whitney test					
				J-T	P	U	P	U	P	U	P
Age (years)	54.6 ± 9.7	48.9 ± 11.8	53.3 ± 9.1	0.48	0.96	83	0.15	320	0.53	216	0.14
Brain volume (ml)	1267 ± 151	1.350 ± 135	1.237 ± 143	−0.96	0.34	77	0.10	243	0.66	124	0.02
Post-mortem delay (h)	36.0 ± 20.8	39.9 ± 23.4	41.1 ± 21.6	0.73	0.46	112	0.78	289	0.35	274	0.90
Duration of illness (years)		11.7 ± 7.6	21.2 ± 11.0							135	0.003
Shrinkage factor	2.12 ± 0.16	2.28 ± 0.38	2.18 ± 0.34	−0.77	0.438	98	0.42	280	0.52	207	0.27
Frequency				Chi-square Test and Fisher's exact probability							
Males/Females	10/7	7/7	19/23	χ^2	P	χ^2	P	χ^2	P	χ^2	P
				0.90	0.64	0.24	0.73	0.89	0.40	0.10	0.77
(B) For septal tissue measurement	$N = 17$	$N = 14$	$N = 20$	J-T (df = 2)		Mann–Whitney test					
				J-T	P	U	P	U	P	U	P
Age (years)	54.6 ± 9.7	48.9 ± 11.8	52.6 ± 8.6	−0.53	0.60	83	0.15	145	0.44	109	0.27
Brain volume (ml)	1267 ± 151	1,350 ± 135	1,257 ± 142	0.02	0.98	77	0.10	130	0.82	78	0.15
Post-mortem delay (h)	36.0 ± 20.8	39.9 ± 23.4	40.5 ± 21.0	0.66	0.51	112	0.78	145	0.46	135	0.88
Duration of illness (years)		11.7 ± 7.6	20.4 ± 11.3							72	0.015
Shrinkage factor	2.12 ± 0.16	2.28 ± 0.38	2.19 ± 0.32	−0.42	0.67	98	0.42	143	0.55	108	0.36
Frequency				Chi-square test and Fisher's exact probability							
Males/Females	10/7	7/7	11/9	χ^2	P	χ^2	P	χ^2	P	χ^2	P
				0.24	0.89	0.24	0.73	0.06	1.00	0.08	1.00

and affective disorder compared with control subjects.

Material and methods

Subjects

All brains used in this study were from the Magdeburg Brain Collection [30]. Brains were obtained from pathologists or medical examiner offices in the years 1987–2002 according to the German law and after approval by the local ethics commission. The mean demographic data of all individual cases (all were Caucasian) including brain volume, post-mortem-delay, and duration of disease are given in Table 1. The three groups showed no significant differences in gender, age, post-mortem-delay, and brain volume. The group of patients diagnosed with schizophrenia included more females (23 of 42; 55%) than the patient group of affective disorder (7 of 14; 50%) or the control group (7 of 17; 41%). Whole brain volumes of female patients with schizophrenia ($P = 0.019$) as well as female control subjects ($P = 0.001$), but not of female patients with affective disorder ($P = 0.128$), were smaller than whole brain volumes of male patients with schizophrenia and male control subjects. However, these differences in gender and whole brain volume did neither affect CSP volume ($P = 0.093$) nor surrounding septal tissue volume ($P = 0.487$). Patients with schizophrenia had a significant larger duration of disease than patients with affective disorder ($P = 0.003$; Table 1). Post-mortem brains of 17 subjects (7 females, 10 males) without any signs of neurological or psychiatric symptoms were used as a control group. Brains of 42 patients (23 females, 19 males) with a clinical diagnosis of schizophrenia according to the Diagnostic and Statistical Manual (DSM-IV, American Psychiatric Association) were included for the measurement of CSP. Additionally, septal tissue volumes of 20 randomly selected cases from the same 42 patients with schizophrenia were also measured.

All patients with schizophrenia received antipsychotic treatment for at least several years. In addition, brains of 14 patients with affective disorder (seven females, seven males) according to DSM-IV were studied; five of these patients were diagnosed as unipolar disorder and nine patients suffered from bipolar disorder. Patients with affective disorder received consistently or periodically psychotropic medication for several years before death. Only patients with detailed clinical records were included. Information for clinical diagnoses was obtained by the careful study of clinical records and/or by structured interviews of physicians involved in treatment and persons, who either lived with or had frequently contact with the subjects before death. The criteria for exclusion for the three groups were (i) organic brain disease, (ii) brain injury, (iii) alcoholism, (iv) chronic somatic diseases affecting the central nervous system (i.e. cachexia, cancer, chronic liver and kidney diseases/corticosteroid treatment).

Tissue processing and delineation criteria

Brains were removed within 4–72 h after death and fixed in toto in 8% phosphate-buffered formaldehyde for at least 2 months (pH = 7.0, $T = 15$–$20°C$).

Frontal and occipital poles were separated by coronal cuts anterior to the genu and posterior to the splenium of the corpus callosum. After embedding of all parts of the brains in paraffin, serial coronal sections of the middle block were cut (20 μm) and mounted. The distance between the sections was 1 mm. The shrinkage factor caused by fixation and embedding of the brains was calculated by a method described previously by Baumann et al. [31]. The mean volume shrinkage factor for patients with schizophrenia, affective disorder and controls was 2.21. No significant differences in the shrinkage factors among the three groups were found. Every 50th section was Nissl and myelin stained (Heidenhain/Woelke).

All measurements were done blindly, as both investigators (R.B. and R.S.) were unaware of diagnosis, age, and gender. An independent investigator (R.S.) randomly revaluated four different brains in order to establish interrater reliability. The interrater reliability for the volumes of the septal tissue was 0.98 and for the volumes of the CSP 0.97 (intraclass correlation coefficient). The coronal sections of the brains were delineated according to the borders proposed by Horvath and Palkovits [32] and Mai et al. [33]. The delineation criteria of the borders are shown in Fig. 1a–f. The anterior border of the septal tissue is the genu of the corpus callosum, the upper border the body of the corpus callosum, the posterior the anterior limb and pillars of the fornix, the inferior the rostrum of the corpus callosum and the anterior commissure, and the lateral borders are the lateral ventricles. Basally the septal tissue is surrounded by the nucleus accumbens and the stria terminalis.

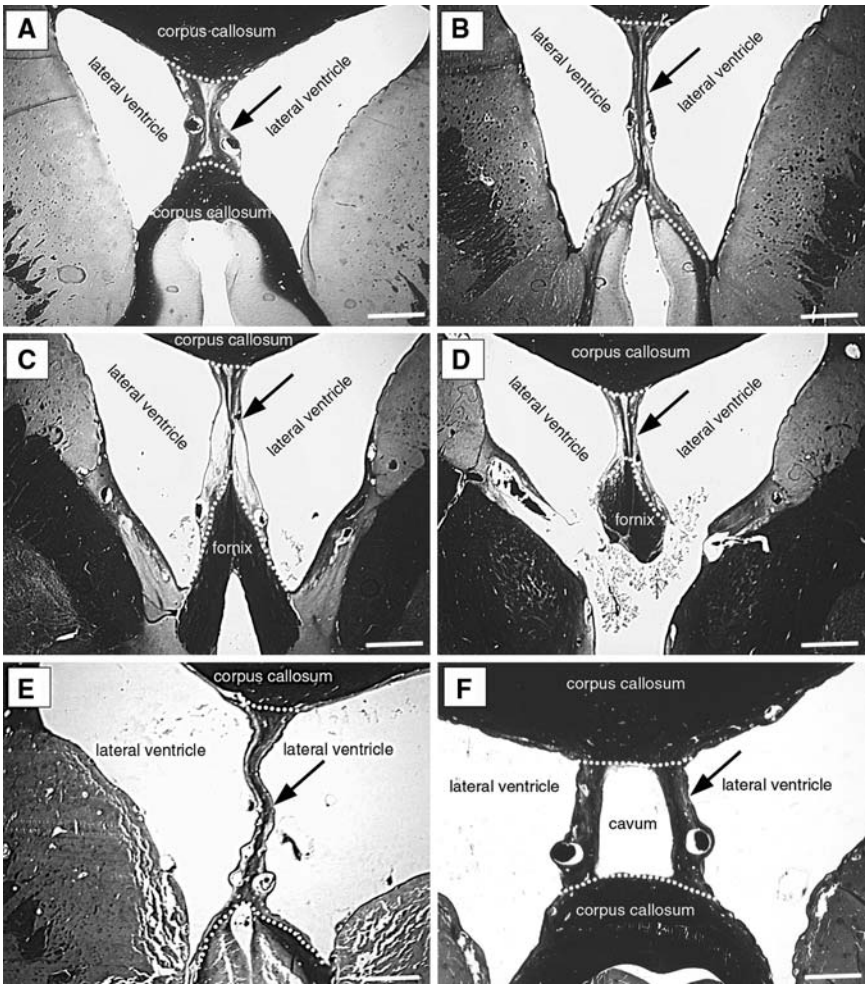

Fig. 1 (**A**–**D**) Delineation of Septal Tissue: (Legend) Photomicrographs of Nissl-myelin stained coronal sections from the anterior to the posterior portion of the human septal tissue (dotted area). A sequence of photomicrographs of coronal sections taken at a mean interval of 5.8 mm showing the delineation of the human septal tissue in anterior–posterior direction. Scale bars correspond to 3 mm. (**E**, **F**) Delineation of Septal Tissue: (Legend) Photomicrographs of Nissl-myelin stained coronal sections of two patients with schizophrenia showing septal tissue with no CSP (**E**) and septal tissue with enlarged CSP (**F**) (dotted area). Scale bars correspond to 3 mm

The CSP extends from the genu of the corpus callosum to the columns of the fornix and the anterior commissure. The borders of the septal tissue and the CSP were delineated under a stereomicroscope (Olympus SZX12, Olympus Optical, Japan).

Morphometry

The difference between the most anterior and most posterior septal poles was used for the calculation of the anterior–posterior extension of CSP and septal tissue. On all serial sections the areas of septal tissue and CSP were measured using software based morphometrical methods as described by Bogerts et al. [34]. The volume shrinkage factor (due to paraffin embedding) and the thickness of slices were controlled by methods described previously in detail by Baumann et al. [31] and Danos et al. [29]. There were no significant differences in the shrinkage factor for each of the diagnostic groups (Table 2). The tissue volume was multiplied with the shrinkage factor for each individual brain to obtain a shrinkage correction.

Statistical analysis

As normal distribution was not given in all parameters (tested by Kolmogoroff–Smirnoff test), non-parametric statistical procedures were used. First all three groups were compared with the Jonckhere–Terpstra test for an ordinal classification of CSP size. Then unadjusted pairwise comparisons with the Mann–Whitney test were carried out. The closure testing principle guarantees the maintenance of the family wise type I error, when both the global and the pairwise tests are considered in combination. Chi-square Test and Fisher's exact probability test were used for evaluating the frequency of events (such as incidence of enlarged CSP). Correlations were calculated with Spearman's correlation coefficient. Gender differences in the three groups were tested with a two-way analysis of variance (ANOVA).

Results

Parameters of CSP

The volumes of CSP in patients with schizophrenia (Table 2) were not distributed normally ($P < 0.001$). As shown in Fig. 2, a logarithmic transformation was used to transfer these data to a normal distribution ($P = 0.82$). There were significant differences among the three groups for the volumes of CSP ($P = 0.045$), patients with schizophrenia having the largest mean volumes (Table 2). Volumes of CSP larger than 100 mm^3 were found only in patients with schizophrenia (8 of 42 cases or 19%, $P < 0.001$) (Figs. 2, 3). The patients with schizophrenia showing volumes of CSP >100 mm^3 included six males and two females.

The anterior–posterior extensions of CSP ($P = 0.18$) showed no significant differences among

Table 2 Parameters of CSP and septal tissue. The values are given as mean ± standard deviation. Volumes of CSP and mean cross-sectional areas of CSP are given as median (lower quartile, upper quartile) because of their non-gaussian distribution. The values are given after shrinkage correction. Asterisk equals *p*-value <0.05

	Controls	Affective disorder	Schizophrenia	3-Group comparison *P*-value	Affect. versus control *P*-value	Schiz. versus Control *P*-value	Schiz. versus affect. *P*-value
(A) For CSP measurement	$N = 17$	$N = 14$	$N = 42$				
Anterior–posterior extension of CSP (mm)	28.7 ± 9.5	25.4 ± 8.5	25.2 ± 7.9	0.179	0.164	0.086	0.813
Volume of CSP (mm^3)	26.9 (12.3, 51.1)	32.4 (17.5, 52.9)	46.6 (18.1, 82.6)	0.045*	0.451	0.076	0.241
Mean cross-sectional area of CSP (mm^2)	0.88 (0.56, 1.66)	1.45 (0.75, 2.11)	1.61 (0.79, 3.98)	0.016*	0.112	0.021*	0.374
(B) For septal tissue measurement	$N = 17$	$N = 14$	$N = 20$				
Anterior–posterior extension of septal tissue (mm)	34.3 ± 7.0	33.4 ± 7.4	29.2 ± 7.3	0.027*	0.427	0.046*	0.139
Volume of septal tissue (mm^3)	904 ± 315	843 ± 227	901 ± 230	0.986	0.451	0.976	0.506
Mean cross-sectional area of septal tissue (mm^2)	26.0 ± 6.4	25.4 ± 5.3	31.7 ± 7.0	0.008*	0.905	0.016*	0.007*

patients with schizophrenia, patients with affective disorder, and control subjects (Table 2). However, the mean cross-sectional areas of CSP were significantly changed ($P = 0.016$) among patients with schizophrenia, patients with affective disorder, and control subjects. This was due to larger mean cross-sectional areas of CSP in patients with schizophrenia compared with control subjects ($P = 0.021$) (Table 2).

A separate analysis of gender by the Jonckhere–Terpstra test did not confirm the significant differences of the whole group (females and males) for the CSP parameters ($p_{\text{male/extension}} = 0.880$; $p_{\text{male/volume}} = 0.083$; $p_{\text{male/cross-sectional area}} = 0.073$; $p_{\text{female/extension}} = 0.066$; $p_{\text{female/volume}} = 0.294$; $p_{\text{female/cross-sectional area}} = 0.117$). The *U*-test presented no significant differences in the CSP parameters ($p_{\text{extension}} = 0.699$; $p_{\text{volume}} = 0.518$; $p_{\text{cross-sectional area}} = 0.518$) between patients with unipolar disorder and bipolar disorder.

Parameters of septal tissue

No significant differences in the volumes of septal tissue among patients with schizophrenia, affective disorder, and control subjects were found ($P = 0.99$; Table 2).

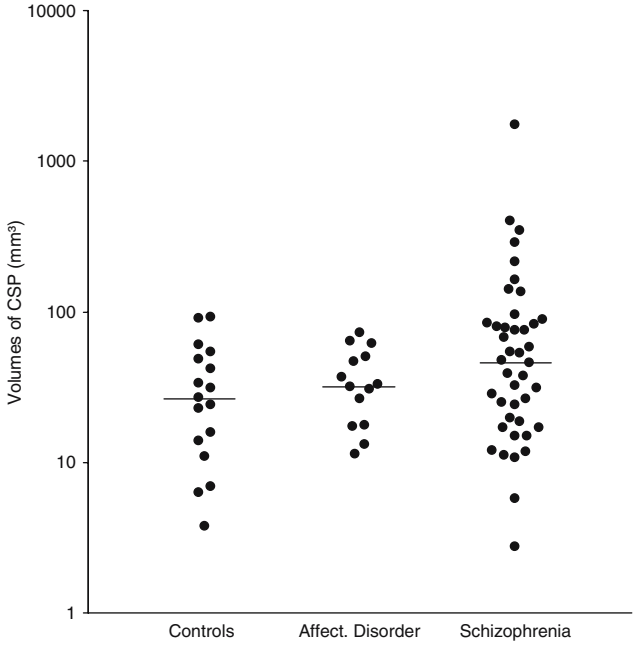

Fig. 2 Volumes of CSP in control subjects ($N = 17$), patients with affective disorder ($N = 14$), and patients with schizophrenia ($N = 42$). (Legend) The medians are marked by horizontal bars. Note the logarithmic scale of volumes. The values are given after shrinkage correction

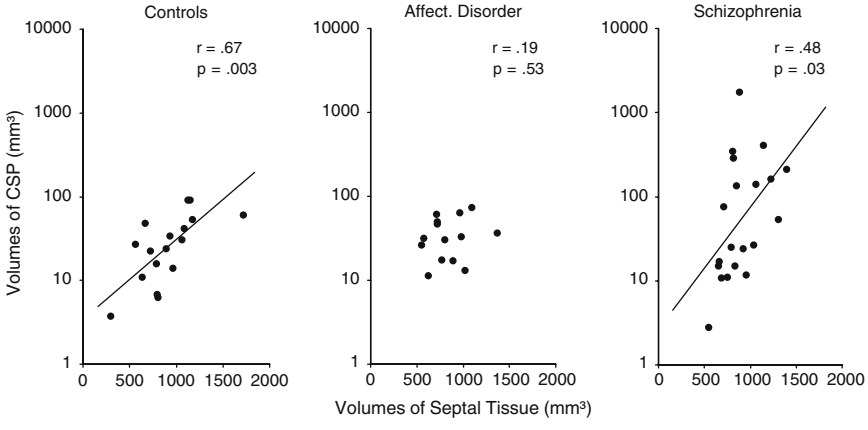

Fig. 3 Correlations between volumes of CSP and volumes of septal tissue in control subjects ($N = 17$), patients with affective disorder ($N = 14$), and patients with schizophrenia ($N = 20$). (Legend) Note the logarithmic scale of volumes. The values are given after shrinkage correction

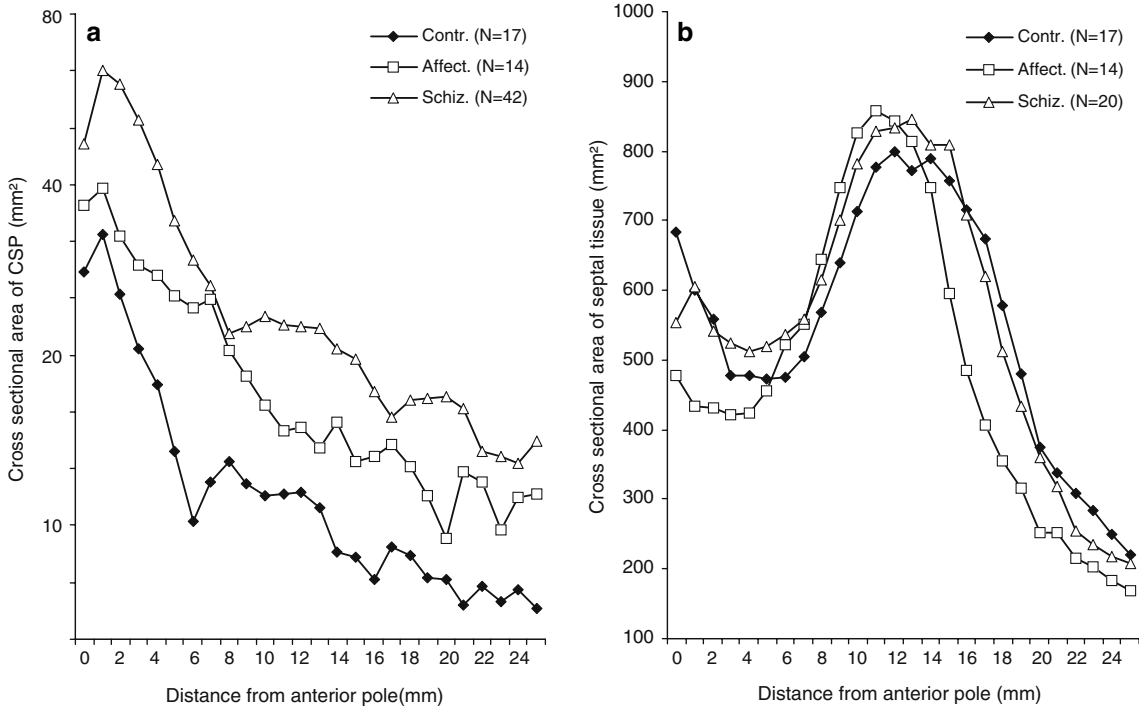

Fig. 4 Anterior–posterior profiles of mean cross-sectional areas of CSP and septal tissue in patients with schizophrenia, patients with affective disorder, and control subjects. (Legend) The anterior poles of structures were chosen as reference points. Single values show area measurements of consecutive serial sections. Note the logarithmic scale of areas in figure **a**. The values are given after shrinkage correction

However, there were significant differences in anterior–posterior extensions ($P = 0.027$; Table 2) and mean cross-sectional areas ($P = 0.008$; Table 2) of septal tissue among patients with schizophrenia, affective disorder, and control subjects; patients with schizophrenia having significant shorter anterior–posterior diameters compared with control subjects ($P = 0.046$; Table 2) and significant increased mean cross-sectional areas compared with control subjects ($P = 0.016$; Table 2) and patients with affective disorder ($P = 0.007$; Table 2). Furthermore, there were no significant differences in mean cross-sectional areas between patients with affective disorder and control subjects ($P = 0.91$, Table 2).

A separate analysis of gender by the Jonkhere–Terpstra test did not confirm the significant differences of the whole group (females and males) for most of the septal tissue parameters ($p_{\text{male/extension}} = 0.065$; $p_{\text{male/volume}} = 0.458$; $p_{\text{male/cross-sectional area}} = 0.156$; $p_{\text{female/extension}} = 0.308$; $p_{\text{female/volume}} = 0.184$) except the female mean cross-sectional area ($p_{\text{female/cross-sectional area}} = 0.030$).

The *U*-test displayed no significant differences in the septal tissue parameters ($p_{\text{extension}} = 0.699$; $p_{\text{volume}} = .898$; $p_{\text{cross-sectional area}} = 0.898$) between patients with bipolar disorder and unipolar disorder.

Correlations of CSP and septal tissue

In patients with schizophrenia ($P = 0.03$) and in control subjects ($P < 0.01$) a significant positive correlation between volumes of CSP and volumes of septal tissue was found (Fig. 3), indicating that larger CSP volumes were associated with larger septal tissue volumes. No such correlation was found in patients with affective disorder ($P = 0.53$; Fig. 3).

Comparisons of cross-sectional areas in the anterior–posterior extensions for CSP and septal tissue

Cross-sectional areas of all measured sections in the anterior–posterior extensions for CSP and septal tissue are illustrated in Fig. 4a and b. Patients with schizophrenia have the highest values of CSP areas at all measured levels in comparison with CSP areas of patients with affective disorder and control subjects (Fig. 4a). The difference of CSP areas between patients with schizophrenia and control subjects is significant ($P < 0.05$) at several distances (1–7, 13–15, 19–21 mm) (Fig. 4a). The cross-sectional areas for septal tissue did not show significant differences among the groups (Fig. 4b).

Correlations between disease duration and sepal tissue or CSP in schizophrenia

A positive correlation ($P = 0.004$) was found between disease duration and anterior and posterior extension for sepal tissue, but also a negative correlation ($P = 0.022$) existed between disease duration and

Table 3 Demograhic profile of patients with schizophrenia presenting enlarged CSP (>100 mm^3), (m = male, f = female, * = in years)

	Gender/Age*	Duration of illness*	Syndrome of schizophrenia	Suicide	Co-morbid conditions
Patient 1	f, 49	2	Paranoid schizophrenia	Yes	–
Patient 2	f, 61	3	Catatonic schizophrenia	No	Cardiosclerosis, hypertension
Patient 3	m, 49	18	Paranoid schizophrenia	No	Healed tubercolosis, acute epydymitis
Patient 4	m, 57	23	Residual schizophrenia	No	Mental retardation, diabetes mellitus
Patient 5	m, 34	2	Paranoid schizophrenia	Yes	–
Patient 6	m, 58	25	Paranoid schizophrenia	No	Pulmonary emphysema, pneumonia
Patient 7	m, 54	34	Residual schizophrenia	No	Bronchopneumonia
Patient 8	m, 45	20	Paranoid schizophrenia	No	Malignant non-Hodgkin-lymphoma

mean cross-sectional area for sepal tissue in schizophrenia. There were no correlations between disease duration and CSP parameters in patients with schizophrenia.

Gender differences in three diagnostic groups

Analysis of variance showed no significant gender differences among the three groups ($F = 2.03$, $P = 0.174$ for controls; $F = 0.096$; $P = 0.762$ for patients with affective disorder; $F = 0.57$, $P = 0.046$ for patients with schizophrenia).

Discussion

The main finding of enlarged CSP suggests an abnormal brain development. Enlarged CSP (>100 mm^3) were found only in patients with schizophrenia, but not in patients with affective disorder or control subjects. The eight patients with schizophrenia showing enlarged CSP (>100 mm^3) were mainly patients with paranoid schizophrenia in absence of suicidal behaviour ($P = 0.32$; Table 3). There were no differences in the volumes of the septal tissue among patients with schizophrenia, affective disorder, and control subjects. Enlarged CSP volume was found to be associated with no septal tissue volume loss in patients with schizophrenia and control subjects, but not in patients with affective disorder.

A separate analysis of gender did not confirm the significant differences of the whole group (females and males) for the CSP and most septal tissue parameters. Although the subgroup of patients with schizophrenia presenting enlarged CSP included more frequently male patients than female patients, the chi-square test presented no significant differences from the expected uniform distribution in the subgroup (chi-square = 2; $P = 0.157$; df = 1). Although no differences in the CSP and the septal tissue were found between patients with unipolar disorder and patients with bipolar disorder, future analysis should extend the sample sizes of patients with bipolar disorder and unipolar disorder in order to determine, if alterations are present in one of these affective disorders (unipolar versus bipolar). For example, in a recent volume study by Bielau et al. [35] subcortical structures differences between patients with affective disorder and control subjects with the predominant affection of patients with bipolar disorder were reported. The hypothesis that septal pathology might be linked to mental illnesses was first expressed by Meyer [36]. Meyer [36] described five patients with psychiatric-neurological symptoms, who displayed non-communicating cysts of the septum pellucidum (as evaluated by pneumoencephalography). Lewis and Mezey [1] mentioned a potential association between CSP and schizophrenia. George et al. [37] reported a case of a patient with schizophrenia having a completely absent septum pellucidum. There are reports of clinical cases of professional boxers with paranoid psychosis, schizophrenia and dementia, who had septal damage or an enlarged CSP [38–40]. Enlarged CSP were shown in one patient with post-traumatic stress disorder [41] and in children with intellectual dysfunction [42]. A recent study by Kim and Peterson [43] reported smaller CSP in children with Tourette syndrome compared with controls. While the size and prevalence of CSP are normal in subjects with panic disorder [44], there are reports that even patients with post-traumatic stress disorders [45, 46] and HIV-infected individuals [47] have an increased prevalence of CSP.

The CSP first appears in week 12 of gestation as an opening of the solid lamina terminalis. The lamina terminalis becomes the septum pellucidum because of the growth of the corpus callosum. Due to the stretching of the septum pellucidum a midline cleavage develops. At the 20th week of gestation, the leaves of the septum pellucidum close in the posterior to anterior direction [2, 43, 48]. In normal fetuses CSP can always be visualized between 18 and 37 weeks [49]. Mott et al. [50] found a CSP in 36% of normal fetuses, who had 40 weeks estimated gestational age. Whereas Falco et al. [49] reported a prevalence of 79% in normal fetuses at 38–41 gestational weeks with CSP. The two sheets of the septum pellucidum usually fuse completely around birth. Thus, a later appearance of a CSP obviously reflects a developmental arrest in the latest stages of pregnancy. Previous post-mortem studies have reported an increased prevalence of CSP in schizophrenia [4, 51–55]. In most MRI and post-mortem studies the CSP was graded on a

semi quantitative scale of 0–4, based on the size of the visible cavity or a large CSP was defined as 6 mm or longer [8, 9, 13]. As far as we know, this is the first study to simultaneously measure the volumes of septal tissue and CSP by applying well defined neurohistological criteria in a post-mortem study of patients with schizophrenia, affective disorder, and control subjects. Six other post-mortem studies estimated the prevalence, surface area, and the linear parameters of CSP in patients with schizophrenia without analysing septal tissue [4, 51–55]. Previous MRI studies stated a wide range from 0.8% to 74% in the prevalence of CSP in patients with schizophrenia [56, 57] and suggested that enlarged CSP is associated with schizophrenia [3–14, 58]. Only six MRI studies did not find differences in the prevalence of CSP between patients with schizophrenia and control subjects [15, 56, 57, 59–61]. The differences in the prevalence of CSP are caused by the difficulty to define clinically significant CSP and by the different resolutions obtained from different MRIs [62].

Large CSP have been correlated not only with a left temporal lobe volume reduction in male patients with schizophrenia [63, 64], but also with a volume reduction of the hippocampus in chronic male patients with schizophrenia [64]. On the other hand, previous studies found no association between the size of the CSP and brain morphology such as the size of the hippocampus–amygdala complex, the caudate nucleus, and the superior temporal gyrus volumes [5, 11]. Also in our brain collection, no such correlations between hippocampal volumes and CSP volumes were found by comparing patients with schizophrenia having enlarged CSP volumes (>100 mm^3) and normal CSP volumes (data unpublished). Male patients with schizophrenia presented more frequently a large CSP than females [8, 11, 15, 58], which is consistent with our finding. A correlation between enlarged CSP and cognitive dysfunction was shown in schizophrenia by Nopoulos et al. [58]. Cognitive dysfunction [65] and frontal lobe alterations [66, 67] were presented in schizophrenia. Other studies found a correlation between CSP and poor prognosis [60] and formal thought disorder [68] in schizophrenia. In patients with affective disorder, previous MRI studies reported frequencies in the prevalence of CSP, ranging from 7% to 82% in affective disorder and from 1% to 92% in control subjects [7, 9, 13, 15]. Jurius et al. [15] reported no different prevalence of enlarged CSP among patients with schizophrenia, patients with affective disorder, and control subjects. Shiori et al. [7] found no higher prevalence of enlarged CSP (Grade 3–4) in patients with bipolar disorder compared with control subjects. Whereas two MRI studies stated a prevalence of enlarged CSP with a range from 18% to 20% in affective disorder and from 8% to 10% in control subjects [9, 13], our sample of patients with affective disorder did not show large CSP. A limitation of our study is that the group of patients with schizophrenia for the CSP study included 42 cases, but due to time constraints the analysis of septal tissue was studied in a randomly chosen subgroup of male and female patients with schizophrenia. When the subgroup of patients with schizophrenia was chosen from the whole sample of patients with schizophrenia, no systematic bias did occur as shown by the results in Table 1. The number of cases was regarded as being representative for septal tissue measurements. Another major limitation of the post-mortem analysis of CSP and septal tissue, especially in comparison with methods of in-vivo-analysis, is the risk of deformation, since these are vulnerable regions close to the ventricles. However, if these regions undergo distortions, a systematic error occurs randomly in all three groups, since the brains of all three groups are randomly affected.

In summary, enlarged CSP were found in patients with schizophrenia suggesting a neurodevelopmental abnormality. An increase in septal tissue volume was found in those cases, where enlarged CSP were observed. Hence, the septal tissue does not show a volume reduction as other limbic or cortical structures do in schizophrenia (for example the hippocampus and the frontal and temporal association cortex [69–72]).

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