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The Diencephalon in Schizophrenia: Evidence for Reduced Thickness of the Periventricular Grey Matter

Annette Lesch and Bernhard Bogerts

Psychiatrische Klinik der Universität Düsseldorf, Postfach 120510, D-4000 Düsseldorf[1] and
C. u. O. Vogt-Institut für Hirnforschung, Universität Düsseldorf, Moorenstrasse 5, D-4000 Düsseldorf, Federal Republic of Germany

Summary. To find out whether ventricular enlargement in schizophrenia, as demonstrated by neuroradiological methods, is caused by an atrophy of ventricle surrounding diencephalic structures, volume measurements and linear measurements of the whole thalamus, all large thalamic subnuclei and some extrathalamic brain parts were carried out on serial sections of post mortem brains belonging to the Vogt collection. The only significantly diminished parameter of this study was the thickness of the periventricular grey matter surrounding the third ventricle, while the volume and linear measurements of the whole thalamus and all large thalamic subnuclei were not significantly changed. The findings are discussed with respect to current hypotheses of diencephalic dysfunction in schizophrenia.

Key words: Schizophrenia – Diencephalon – Thalamus – Neuropathology

Introduction

The history of psychiatry is closely linked to the presence or absence of anatomical cerebral substrata for different mental diseases. The fact that morphological alterations in the brain could not be clearly demonstrated in schizophrenia (Winkelman and Book 1949; Weinstein 1954; David 1957; Meyer 1957; Dastur 1959; Meier 1963; Peters 1967; Nieto and Escobar 1972) led to the assumption that this illness is based on psychic factors rather than on structural alterations (Bateson et al. 1956; Lidz et al. 1965).

However, recent studies of cerebral structures quantified from computerized tomography (Johnstone et al. 1976; Weinberger et al. 1979; Tanaka et al. 1981; Gattaz et al. 1981; Gross et al. 1982; Frangos and Athanassenas 1982; Dewan et al. 1983) support older pneumoencephalographic findings (Jacobi and Winkler 1927; Lemke 1936; Huber 1961; Haug 1982) of enlarged ventricles in many schizophrenic patients. These neuroradiological findings indicate either a diffuse moderate brain atrophy or a more or less selective atrophy of ventricle surrounding structures such as thalamic and hypothalamic areas.

Furthermore, the similarities of coenaesthetic symptoms with sensory phenomena associated with organic diseases of the thalamus (Huber 1957; Klages 1954, 1965; Gross and Huber 1972; Czernik 1972) and catatonic-like behaviour of experimental animals with diencephalic lesions (Bailey and Davis 1942; Meyer and Hunter 1952; Schreiner et al. 1953) suggest possible thalamic pathology in schizophrenia.

Since degenerative processes within the brain can be quantified by volume measurements of the affected brain parts (Lange et al. 1976; Bogerts et al. 1984) this study aims to determine the volumes of the whole thalamus, the volume of the large thalamic subnuclei and some extrathalamic areas in the brain of patients diagnosed as schizophrenics in comparison to those of control cases.

Material

Complete frontal serial sections of brains from 15 schizophrenic patients (4 male, 11 female; age 41.66 ± 17.59 years [mean ± SD], Table 1) and 12 age-matched control cases (8 male, 4 female; age 46.83 ± 24.22 years, Table 2) of the C. u. O. Vogt-Institute of Brain Research of the University of Düsseldorf were evaluated. Post-mortem delay (time between death and fixation of brain) was approximately the same in both groups (control cases 2–36 h; schizophrenic patients 4–45 h). Only material from left hemispheres was available except for one right hemisphere in each group.

All brains were collected between 1928 and 1953, fixed by immersion in 4% formalin, embedded in paraffin, cut in 20 μm frontal serial sections, and myelin-stained by the method of Heidenhain-Woelcke. As a control group cases without neurological or psychiatric diseases were used. None of the patients had received convulsive therapy, insulin therapy or neuroleptic drugs.

The duration of the illness (time between first diagnosis and death) ranged from 19 days to 37 years (mean: 10.48 years). Schneiderian first and second rank symptoms were described in the extensive clinical records of all the schizophrenics studied. Five cases showed predominance of positive symptoms such as hallucinations, delusions, thought disorders (paranoid-hallucinatory subgroup according to ICD-9 295.3, type I according to Crow 1982), in 4 cases more negative symptoms such as affective flattening, loss of drive or catatonic behaviour (more catatonic subtype according to ICD-9 295.2, more type II) prevailed. In 6 cases diagnostic classification under only one of these subtypes was difficult because

1 *Offprint requests to:* B. Bogerts at the address in Düsseldorf

Table 1. Control cases without neurological or psychiatric disease. The control brains were collected between the years 1928 and 1953 and thus date from the same era as the schizophrenic cases

Brain	Age	Sex	Cause of death
A 56	56	m	Laryngeal cancer, death under operation
A 58	24	m	Haemorrhagic shock
A 61	38	m	Uraemic coma
A 64	84	m	Pneumonia
A 76	99	f	Pneumonia
A 77	37	m	Decapitation
A 80	33	f	Carcinoma of the uterus
A 85	30	f	Fat embolism after a street accident
A 88	62	m	Peritonitis
A 97	39	m	Pulmonary embolism
A 100	19	m	Aspiration pneumonia
A 102	41	f	Cardiac arrest

these cases were characterized by alternating phases of catatonic, hebephrenic and paranoid hallucinatory symptomatology.

Methods

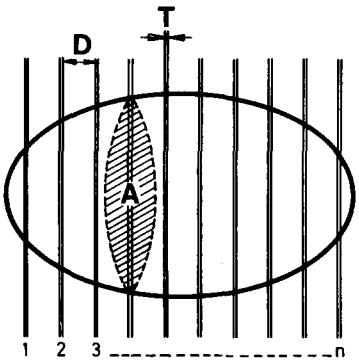
The investigated brain parts were outlined on (× 10) projected enlargements of myelin-stained frontal serial sections evenly distributed from the caudal end to the rostral pole of the thalamus. On the projection of each section planimetric and linear measurements were performed, the distance between the sections being 0.5–1.0 mm.

Volumes were calculated from the sum of the areas multiplied by the distance between sections and by the thickness of sections (determined by focussing upper and lower surfaces at a magnification of 1250).

To allow for shrinkage of paraffin material during histological preparation and to obtain fresh volumes, the volumes calculated from serial sections were corrected by an average

Table 2. Schizophrenic cases. The brains of schizophrenic patients were collected between the years 1930 and 1941, that is before the introduction of neuroleptic drugs

Brain	Age	Sex	Cause of death, year of death	Most prominent psychiatric symptoms	Time between diagnosis and death	Heredity factor
Bu 3	22	f	Cardiac arrest, 1930	Persecution complex, acoustic hallucinations, mutism, negativism	3½ years	+
Bu 7	74	f	Myocardial infarction, 1930	Paranoid ideas, acoustic hallucinations, mutism, manierism	24 years	+
Bu 9	59	f	Bronchopneumonia, 1930	Paranoid ideas, optic hallucinations, coenaesthetic symptoms	4 years	–
Bu 12	51	f	Bronchopneumonia, 1930	Persecution complex, stupor, negativism, mutism	Not known	+
Bu 19	44	f	Pneumonia, 1930	Paranoid ideas, feeling of being watched, acoustic hallucinations	11 months	+
Bu 20	26	f	Bronchopneumonia, 1930	Stupor, catatonia, mutism	7 years	+
Bu 21	42	f	Pneumonia, 1930	Stupor, mutism, flexibilitas cerea, acoustic hallucinations	6½ years	Not known
Bu 24	27	f	Bronchopneumonia, 1930	Optic, acoustic and haptic hallucinations, stereotype movements, manierism, hebephrenic symptoms	4 years	+
Bu 46	19	f	Cardiac illness, 1932	Rigid postures, drawing faces, negativism	Not known	+
Bu 52	24	m	Bronchopneumonia, 1933	Stupor, stereotypy in posture and movement, catatonia, catalepsy	3 years	+
Bu 53	27	m	Cardiac disease, 1933	Optic and acoustic hallucinations, drawing faces, catatonic symptoms, stuporous, hebephrenic symptoms	10 months	+
Bu 62	64	f	Suicide 1933	Delusions, hallucinations, persecution complex	23 years	+
Bu 89	43	f	Pneumonia, 1935	Acoustic hallucinations, paranoid ideas, feelings of electrical stimulation	13 months	+
Md 4	64	m	Tuberculosis of lung, 1938	Paranoid ideas	37 years	+
Cp 81	39	m	Not known, 1941	Hebephrenic symptoms, drawing faces, delusions, manierism, mutism	22 years	+



$$V = \sum_{i=1}^{n} (A_i \cdot T_i \cdot D_i)$$

Fig. 1. Principle of volume measurements using serial sections. Volumes were determined by planimetry of myelin-stained serial sections (indicated by double lines *1...n*) evenly distributed from the rostral to the caudal poles. Volumes *(V)* were calculated by the sum of all planes *(A)* multiplied by the thickness of the section *(T)* and by the distance between the sections *(D)*

shrinkage factor of 1.89 determined previously in 30 brains of the Vogt collection (Lange et al. 1976); linear parameters were corrected by a linear shrinkage factor of 1.236. Mann-Whitney *U* test was used as a test of significance.

Not all areas could be evaluated in each brain since some sections were excluded because of bad histological condition, or because the distance between two useable sections should not exceed 1.0 mm.

Within the thalamus the volumes of the following subnuclei were determined:

— n. reticularis, n. anterior, n. dorsalis superficialis, n. medialis and n. lateralis.
— the central group containing n. centromedianus. Due to lack of sharp boundaries between this truncothalamic region and the periventricular grey matter in myelin-stained sections, both structures were separated by drawing a line from the centre of the n. medialis to the centre of the red nucleus (Fig. 2a).
— the part of the pulvinar situated caudally to the commissura posterior.
— both the corpus geniculatum laterale and mediale.
— the volume of whole thalamus in order to include structures not measured separately.

All the thalamic nuclei were evaluated up to the level of the commissura posterior. Thalamic structures situated caudally to the commissura posterior were defined as pulvinar. The myelin-stained sections used did not allow more precise delineation of the cytoarchitecture of the pulvinar.

In addition, the volumes of some extrathalamic regions were determined:

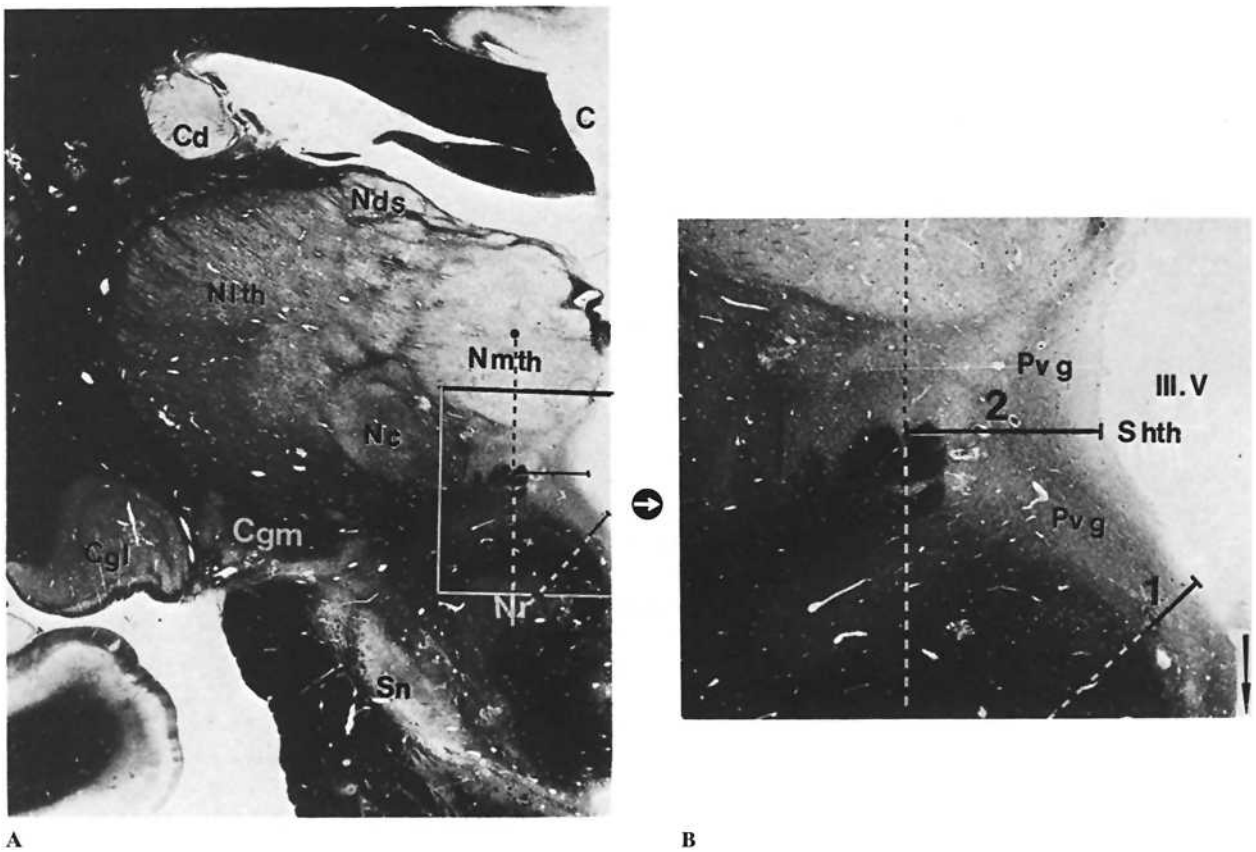


Fig. 2A, B. Topography of the thickness measurements of the periventricular grey matter in the caudal third of the third ventricle (myelin-stained section [× 3]). The *dotted line* between the centre of the red nucleus and the centre of the medial thalamic nucleus was drawn to separate the periventricular grey matter from the central cell group. *1* = thickness measurements above the red nucleus, *2* = thickness measurements at the level of the sulcus hypothalamicus, *C* = corpus callosum, *Cd* = caudatum, *Cgl* = corpus geniculatum laterale, *Cgm* = corpus geniculatum mediale, *Nc* = central cell group, *Nlth* = nucleus lateralis thalami, *Nmth* = nucleus medialis thalami, *Nr* = nucleus ruber, *Pvg* = periventricular grey matter, *Shth* = sulcus hypothalamicus, *Sn* = substantia nigra, *III.V* = third ventricle, *arrow* = midline-cut

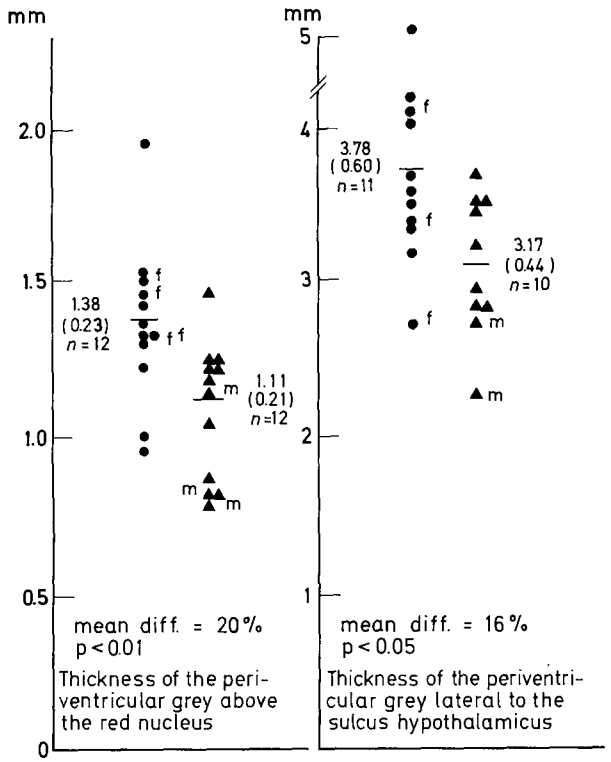


Fig. 3. Single values of the thickness of the periventricular grey matter measured above the n. ruber and at the sulcus hypothalamicus *(mm)*. (○) control brain, (▲) schizophrenic brain (*f* indicates females of the control group, *m* indicates males of the schizophrenic group). Mean, SD, *n* = number of samples, *mean diff.* = mean difference (controls = 100%), *P*-value (using the two tailed Mann-Whitney *U* test)

— n. ruber;
— n. subthalamicus.
— capsula interna between the levels of the rostral poles of the thalamus and the corpus geniculatum laterale.

The following linear measurements were performed on serial sections:
— maximal horizontal breadth of n. medialis thalami;
— maximal horizontal breadth of n. lateralis thalami;
— thickness of the posterior half of the periventricular grey matter rostrally to the n. ruber and at the level of the sulcus hypothalamicus (see Fig. 2a and 2b);
— thickness of periaquaeductal grey matter;
— distance between n. anterior thalami and corpus mamillare.

All measurements were performed blind, i.e. without knowledge of the diagnosis by the individual performing the measurements.

Results

All investigated parameters of the normal and of the schizophrenic group were characterized by extraordinarily high interindividual variance suggesting a considerable inhomogeneity not only of the schizophrenics but also of the controls (Table 3 and Table 5).

I. Volume Measurements

a) Comparison Between Controls and the Schizophrenic Group as a Whole (Table 3). No significant difference between the volumes of the whole thalamus of schizophrenic patients and the controls was found. The volumes of all investigated thalamic subnuclei (n. anterior, central cell group, n. dorsalis superficialis, n. lateralis, n. medialis, n. reticularis, pulvinar thalami, corpus geniculatum laterale, corpus geniculatum mediale) did not differ significantly between patients and controls; however, a trend towards volume shrinkage by approximately 20% ($P < 0.1$) was observed in the central cell group.

The volumes of the additionally evaluated extrathalamic regions, i.e. n. ruber, n. subthalamicus and capsula interna did not differ significantly between both groups.

b) Comparison Between Paranoid and Catatonic Schizophrenics (Table 4). Only five cases with prevailing paranoid-hallucinatory symptoms versus only four cases with predominant catatonic symptoms could be studied; the psychopathological state of the other patients showed catatonic and paranoid symptoms and could be classified under either diagnostic subgroup.

Probably due to this small number of samples and on account of the large variance of data no clear differences both in thalamic and extrathalamic volumes between paranoid and catatonic patients was found except for the volume of the n. anterior thalami being smaller in the catatonic group by approximately 20% ($P < 0.05$).

II. Linear Measurements

a) Normals Versus all Schizophrenics. Thalamic and extrathalamic linear values (Table 5 and Figs. 2a, 2b, 3).

The only significantly diminished value within the diencephalon was the thickness of the periventricular grey matter measured in the caudal third at a level rostral to the n. ruber (Figs. 2a and 2b) and determined as distance between the medial border of the central cell group and sulcus hypothalamicus (Figs. 2a and 2b). The first value was significantly lower in the schizophrenic group by 20% ($P < 0.01$), the second by 16% ($P < 0.05$) (Table 5 and Fig. 3).

The mean maximal horizontal diameters of the n. lateralis and n. medialis thalami, and the thickness of the periaquaeductal grey matter were nearly identical in both groups.

b) Paranoid Versus Catatonic Schizophrenics. Thalamic and extrathalamic linear values:

None of the measurements of linear thalamic and extrathalamic parameters in paranoid and catatonic brains revealed any significant differences.

Beside the diagnostic classification of paranoid and catatonic patients, other subgroups with the following criteria were compared:
— patients with hereditary factors versus patients without hereditary factors;
— patients with short duration of illness versus patients with long duration of illness ($\gtrless 4$ years);
— early-onset patients versus young controls (< 40 years);
— late-onset patients versus old controls (> 40 years);
— early-onset cases versus late-onset cases ($\gtrless 40$ years);
— type I cases versus type II cases.

Possibly because of the small number of samples, neither linear nor volume measurements revealed any significant differences between these subgroups; thus no definite conclusion about the influence of age, duration of illness, heredity factors, and diagnostic classification on the size of the evaluated areas can be drawn.

Table 3. Results of the volume determinations in normals and schizophrenics (values in mm^3)

Evaluated areas	Controls			Schizophrenics			Mean difference (controls = 100%)	
	Mean	(SD)	n	Mean	(SD)	n		
Thalamus	7115.54	(1016)	11	6506.53	(783)	15	− 8.6%	NS
N. reticularis th.	359.45	(86)	11	333.66	(89)	15	− 7.3%	NS
N. anterior th.	182.90	(52)	11	181.30	(29)	13	− 0.6%)	NS
N. dors. sup. th.	88.20	(25)	10	82.46	(18)	13	− 7.0%	NS
N. medialis th.	1200.45	(207)	11	1151.00	(168)	14	− 4.1%	NS
N. lateralis th.	2587.72	(432)	11	2444.07	(359)	14	− 5.6%	NS
Central cell group	344.63	(116)	11	276.18	(44)	11	−19.8%	NS ($P < 0.1$)
Corp. genic. med.	124.25	(23)	8	120.42	(10)	7	− 3.3%	NS
Corp. genic. lat.	162.40	(23)	10	160.33	(38)	12	− 1.3%	NS
Pulvinar th.	1903.00	(328)	11	1794.84	(387)	13	− 5.8%	NS
N. subthalamicus	118.66	(26)	9	125.41	(29)	12	+ 5.9%	NS
Capsula interna	2260.36	(479)	11	2049.92	(549)	13	− 9.4%	NS
N. ruber	244.00	(36)	11	269.38	(60)	13	+10.0%	NS

Mean, standard deviation (SD), n = number of samples; mean difference; level of significance: * = $P < 0.05$, ** = $P < 0.01$, NS = not significant (two-tailed Mann-Whitney U test).

Abbreviations: Corp. gen. lat. = corpus geniculatum laterale, Corp. gen. med. = corpus geniculatum mediale, N. dors. sup. th. = nucleus dorsalis superficialis thalami, th. = thalami

Table 4. Mean group volumes (values in mm^3) of cases classified as typical catatonics (ICD-9 295.2) or typical paranoid-hallucinatory schizophrenics (ICD-9 295.3). Cases with symptoms of both subgroups were excluded. Abbreviations and symbols see Table 3

Evaluated areas	Paranoid			Catatonic			Mean difference (catatonics = 100%)	
	Mean	(SD)	n	Mean	(SD)	n		
Thalamus	7193.20	(766)	5	6541.25	(435)	4	+ 9.9%	NS
N. reticularis th.	373.20	(54)	5	322.75	(141)	4	+15.8%	NS
N. anterior th.	206.00	(20)	5	171.00	(21)	4	+20.4%	*
N. dors. sup. th.	92.80	(18)	5	74.50	(20)	2	+24.3%	NS
N. medialis th.	1259.60	(121)	5	1137.66	(167)	3	+10.7%	NS
N. lateralis th.	2557.60	(221)	5	2522.00	(297)	3	+ 1.3%	NS
Central cell group	276.50	(29)	4	315.00	(57)	3	−12.4%	NS
Corp. genic. lat.	169.60	(45)	5	161.00	(70)	2	+ 4.9%	NS
Pulvinar th.	1864.25	(360)	4	1824.25	(647)	4	+ 2.1%	NS
N. subthalamicus	135.80	(30)	5	119.66	(2)	3	+13.4%	NS
N. ruber	295.75	(54)	4	284.75	(31)	4	+ 3.8%	NS

Table 5. Results of the linear measurements and mean brain weight (values in mm or g, respectively). Symbols and abbreviations see Table 3

Evaluated areas	Controls			Schizophrenics			Mean difference (controls = 100%)	
	Mean	(SD)	n	Mean	(SD)	n		
Max. horizontal breadth of n. medialis th.	9.43	(0.68)	9	9.73	(0.85)	10	+ 4.0%	NS
Max. horizontal breadth of n. lateralis th.	10.30	(1.47)	10	9.47	(0.94)	11	− 8.0%	NS
Distance between n. anterior th. and corpus mamillare	26.93	(4.23)	10	27.44	(1.91)	11	+ 2.0%	NS
Thickness of periaquaeductal grey matter	4.31	(0.33)	12	4.29	(0.42)	11	− 0.5%	NS
Thickness of periventricular grey matter								
1. above n. ruber	1.38	(0.23)	12	1.11	(0.21)	12	−20.0%	**
2. at sulcus hypothalamicus	3.78	(0.60)	11	3.17	(0.44)	9	−16.0%	*
Mean brain weight	1211.33	(168)	12	1181.07	(101)	14	− 2.5%	NS

III. Brain Weight (Table 5)

Neither the mean brain weight of the schizophrenic group as a whole compared to the controls nor the mean brain weight of any above mentioned subgroup was significantly altered.

IV. Sex Differences

Both groups were age-matched but not sex-matched. Regarding the normal statistical difference between male and female brain weights of approximately 10%, the different sex distri-

Table 6. Thickness of the periventricular grey matter of male and female controls and schizophrenics (values in mm). For explanation see text

Periventricular grey matter above n.ruber

	Males			Females			Difference (males = 100%)
	Mean	(SD)	*n*	Mean	(SD)	*n*	
Controls	1.36	(0.31)	8	1.42	(0.10)	4	+ 4.4%
Schizophrenics	0.95	(0.24)	3	1.15	(0.19)	9	+21.0%

Periventricular grey matter at sulcus hypothalamicus

	Males			Females			Difference (males = 100%)
	Mean	(SD)	*n*	Mean	(SD)	*n*	
Controls	3.89	(0.59)	8	3.48	(0.68)	3	−10.6%
Schizophrenics	2.56	(0.31)	2	3.38	(0.32)	7	+32.0%

bution of the investigated groups could possibly be the cause of the reduced thickness of the periventricular grey matter in the schizophrenic group.

However, this parameter tended to be higher in females than in males both in controls (except for the female controls at the level of the sulcus hypothalamicus having values lower by approximately 10%) and in the schizophrenic group (Table 6, Fig. 3). Thus sex influences on the significantly diminished values of this study seem to be unlikely.

Discussion

The thalamus was thought by many authors to be the principal site of possible neuropathological changes in the brain of schizophrenics (Stoerring 1938; Fünfgeld 1925; Leonhard 1952; Bäumer 1954; Klages 1954, 1965; Huber 1957; Hempel 1958; Treff and Hempel 1959, 1960; Gross and Huber 1972; Czernik 1972).

Cytological alterations (so-called 'dwarf-cells', which were later challenged as post-mortem artefacts (Heyck 1954; Peters 1967)) have been reported to occur especially in the medial and anterior nucleus (Vogt and Vogt 1948; Fünfgeld 1952; Bäumer 1954; Hempel and Treff 1959, 1960; Treff and Hempel 1958, 1959, 1960). Other authors have reported similar alterations throughout the whole thalamus and limbic cortex (Papez and Bateman 1950; Bateman and Papez 1951).

Analogous to well-known degenerative brain diseases such as Parkinson's disease and Huntington's disease, the extent of brain tissue shrinkage in schizophrenia might reflect the degree of functional deficits of the affected brain regions (Lange et al. 1976; Bogerts et al. 1984). If so, the present data do not support the hypothesis that pathology of the thalamus or of any thalamic subnucleus is involved in the aetiology of schizophrenic symptoms. Neither the volume of the whole thalamus nor the volumes of the n. anterior, n. medialis, n. lateralis, n. reticularis, n. dorsalis superficialis, the pulvinar, the corpora geniculata mediale and laterale were found to have changed significantly. Larger samples would need to be evaluated to decide if the volume of the central cell group, which exhibited downward trend, is definitely reduced. In addition, no volume shrinkage of the red nucleus and the subthalamic nucleus was detected.

The only significantly diminished parameter of this investigation was the thickness of the periventricular grey matter measured in the caudal half of the third ventricle. Therefore, enlargement of the third ventricle in many schizophrenics as demonstrated by pneumoencephalography (Jacobi and Winkler 1927; Lemke 1936; Huber 1961; Haug 1982), echoencephalography (Schüttler et al. 1974) and computed tomography (Johnstone et al. 1976; Weinberger et al. 1979; Tanaka et al. 1981; Gattaz et al. 1981; Gross et al. 1982; Frangos and Athanassenas 1982; Dewan et al. 1983) seems to be caused by atrophy of the diencephalic periventricular grey matter rather than by atrophy of the large thalamic subnuclei.

Quantitative-statistical studies in the thalamus of schizophrenics are scarce. Reports of reduced cell densities in the medio-dorsal nucleus (Hempel and Treff 1959, 1960; Treff and Hempel 1958, 1959, 1960) have not been confirmed by later investigations of the same material (Dom et al. 1981). The latter authors however, found a marked reduction of interneurons in the pulvinar. There is one study of the volumes of the medial thalamic nucleus in schizophrenia (Meyer 1957) in which no significant difference to controls was detected.

If thalamic dysfunction caused schizophrenia-like symptoms, as assumed by some authors (Stoerring 1938; Leonhard 1952; Klages 1954, 1965; Huber 1957; Gross and Huber 1972; Czernik 1972), such a symptomatology might be expected in patients with known organic diseases of the thalamus. In the quite extensive literature on organic lesions of the thalamus and the diencephalon, clinical symptoms such as apathy, drowsiness, tendency towards somnolence, mental lethargy, affective flattening, stuporous conditions, cataleptic-like states, disturbances of memory, and sensory phenomena such as hypaesthesia, hyperpathia, and painful perceptions are described as being most characteristic (Henneberg 1903; Weisenburg 1911; Meyer 1928; Stertz 1931; Cairns et al. 1941; McKissoc and Paine 1958; Poeck and Pilleri 1961; Lapresle and Haguenau 1973). Productive psychotic symptoms (hallucinations, delusions, thought disorders, paranoid symptoms) do not usually occur. Only 10 of 105 patients with organic thalamic and periventricular diencephalic diseases reviewed in the quoted literature exhibited symptoms resembling paranoid schizophrenia (Grünthal 1942; Leutinger 1954; Amler 1956; Malamud 1967; Cramon et al. 1981). Thus, clinical symptoms associated with dysfunctions of the diencephalon apparently resemble the negative symptoms seen in chronic schizophrenia (roughly corresponding to type II of Crow 1982 or the pure defect of Huber 1976) more than acute productive symptoms. This assumption is further supported by the observation that enlargement of the third ventricle, possibly indi-

cating atrophy of surrounding diencephalic structures, mainly occurs in patients with chronic negative symptoms (Johnstone et al. 1976; Gross et al. 1982).

Diencephalic lesions in experimental animals are reported to produce symptoms strikingly resembling catatonia, catalepsy and akinetic mutism (Bailey and Davis 1942; Meyer and Hunter 1952) or catatoniform aggressive behaviour (Schreiner et al. 1953; Pechtel et al. 1955) especially when periventricular regions, the mamillothalamic tract or the medial thalamic nucleus are damaged, while manic symptoms can be elicited by mechanical pressure on anterior hypothalamic areas during neurosurgical operations (Förster and Gagel 1934).

The significant shrinkage of the periventricular grey matter in some schizophrenics, as revealed by this study, is consistent with reports of cell loss in the hypothalamic periventricular grey matter and the tuber cinereum in psychotic patients (Morgan and Gregory 1935) and with the more recent findings of gliosis in brain regions closely surrounding the third ventricle (Nieto and Escobar 1972; Stevens 1982).

The diencephalic periventricular grey matter plays an important role in the integration of central vegetative functions. Atrophy of this brain region might be related to the vegetative symptoms frequently observed in schizophrenic patients (Ewald 1950; Huber 1976). The periventricular grey matter is closely linked to the limbic telencephalic structures, which have also been found to be degenerated in a subgroup of schizophrenics (Bogerts 1984).

It is tempting to speculate that the degeneration of these closely interrelated structures indicates a limbic-vegetative system atrophy in schizophrenia comprising the limbic structures of the temporal lobe (hippocampal formation, amygdala) and the vegetative diencephalic regions.

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