

Temporal Lobe Volume in Disorders with Psychotic Features

Elizabeta Radonić¹, Neven Henigsberg^{1,2}, Marko Radoš^{1,3}, Ninoslav Mimica²
and Vera Folnegović-Šmalc^{1,2}

¹ Croatian Institute for Brain Research, School of Medicine, University of Zagreb, Zagreb, Croatia

² Department of Psychiatry, Psychiatric Hospital »Vrapče«, Zagreb, Croatia

³ Department of Diagnostic and Interventional Radiology, University Hospital Centre »Zagreb«, School of Medicine, University of Zagreb, Zagreb, Croatia

ABSTRACT

Since early neuropathological findings, temporal lobe has been related to the pathophysiology of some disorders with psychotic features. The aim of this study was to compare temporal lobe volumes and asymmetry differences in patients with schizophrenia, schizoaffective and bipolar disorders, disorders that cover the whole psychotic spectrum.

Temporal lobe volumes were estimated using high resolution magnetic resonance imaging in 60 subjects, 15 subjects in each patient and one healthy volunteer (control) group. There are no statistically significant differences in temporal lobe volumes among patient and control groups. Comparison of left and right temporal lobes shows that left temporal lobes are smaller than right temporal lobes, however this difference reaches statistical significance only in groups of patients with schizoaffective and bipolar disorders. Overall temporal lobe volume may be less informative in respect to neuropathology of disorders with psychotic features than volumes of specific temporal lobe structures, in particular medial temporal lobe structures.

Key words: *temporal lobe volume, schizophrenia, schizoaffective disorder, bipolar disorder*

Introduction

In recent psychiatric classifications schizophrenia, schizoaffective and bipolar disorders are classified in different diagnostic categories^{1,2}, albeit sharing psychotic feature as one of the most prominent features of clinical presentation. The position of schizoaffective disorder as an intermediary disorder displaying both psychotic and affective features contributes to the idea of these disorders representing one spectrum of disorders³⁻⁶. Modern neurobiological interpretation of different clinical features as possible dysfunctions in different parts of neuronal network involved in complex aspects of human behavior^{7,8}, provides basis for investigation of possible common neurobiological basis for psychotic features and different neurobiological basis for affective features of these disorders. Since the number of subjects involved in such studies is usually small due to time consuming procedures and limited funding, comparison of results and statistical analysis is often of limited value, and studies

comparing these disorders in the same sample are of particular importance^{9,10}.

Temporal lobe has been implied in the pathophysiology of schizophrenia since the early neuropathological findings in the beginning of the past century^{11,12}. Reduction of temporal lobe volume has been pronounced in left temporal lobe, male patients, and disorders with early onset^{13,14}. These reductions have been associated with delusions and auditory hallucinations¹⁵. Recent possibilities for in vivo imaging of the structure of human brain that have emerged with X-ray and were further developed with computerized tomography and magnetic resonance have supported these early findings. The result of a comprehensive review of magnetic resonance findings in schizophrenia that has taken into account studies in which schizoaffective disorder was not separated, is that the reduction of temporal lobe volume has been de-

scribed in 61% studies¹⁶. Separate studies of schizoaffective disorder are scarce and the findings do not show the reduction of temporal lobe volume¹⁷. Current data for bipolar disorder come from a modest number of studies, often including less than 10 patients, and do not support findings of statistically significant temporal lobe volume reduction¹⁸.

The aim of this study was to compare temporal lobe volumes in separate groups of patients with schizophrenia, schizoaffective and bipolar disorders.

Subjects and Methods

The study included 60 subjects, 15 in each patient and one control group. Age, gender, age at onset, and number of episodes were recorded for all subjects. Psychiatric diagnosis of schizophrenia, schizoaffective and bipolar disorder was made by two independent psychiatrists, and only the subjects fulfilling both Diagnostic and Statistic Manual of Mental Disorders, Fourth Edition (DSM-IV)² and International Classification of Diseases, Tenth Revision (ICD-10)¹ criteria were included. Magnetic resonance imaging was performed in the period of absence of acute episode symptoms. Control group consisted of healthy volunteers. The following exclusion criteria were applied on all study subjects: history of perinatal brain damage, comorbid mental or other disorder of central nervous system, serious general health condition, age below 18 or above 60, left-handedness or ambidexterity. The study was approved by the local ethics committee and informed consent obtained from all participants.

Magnetic resonance images were acquired using a 2 T Prestige Gyrex scanner (General Electrics/Elscint). A 1.1-mm-thick coronal series (3D gradient echo; repetition time 25 ms; echo time 6 ms; field of view 180×220 mm, matrix 200×256) was processed on O2 (Silicon Graphics) workstation using OmniPro (Elscint/General Electrics) software. Regions of interest were delineated

manually by a single rater blind to the study group, based on well-known neuroanatomical and neuroradiological criteria¹⁹. The rostral, lateral, ventral and dorsal boundaries are defined by the natural limits of the lobe. Medial boundary in posterior parts was defined as the shortest straight line connecting the fundus of the Sylvian fissure and cerebral base. The last caudal slice analyzed was the one where both pairs of mesencephalic colliculi were still visible. Descriptive statistics was used to analyze demographic, clinical and volumetric data. A one-way analysis of variance was used to test for group differences in temporal lobe volumes. All analyses were interpreted at 5% level of significance.

Results

Demographic and clinical features of study subjects are shown in Table 1. There is no statistically significant difference in gender and duration of disorder among study groups. The difference in age of onset is statistically significant among all patient groups. Patients with bipolar disorder are significantly older than healthy control ($p < 0.001$), schizophrenia ($p < 0.00001$), and schizoaffective group ($p = 0.02$). Patients with schizoaffective disorder are significantly older than patients with schizophrenia ($p = 0.02$).

Temporal lobe volumes per study groups are presented in Table 2.

There are no statistically significant differences in temporal lobe volumes among different patients groups. Comparison of left and right temporal lobes shows that left temporal lobes are smaller than right temporal lobes, however this difference reaches statistical significance only in groups of patients with schizoaffective and bipolar disorders (Tables 3 and 4).

TABLE 1
DEMOGRAPHIC AND CLINICAL FEATURES OF STUDY SUBJECTS

| | Healthy control N=15 | | Schizophrenia N=15 | | Schizoaffective disorder N=15 | | Bipolar disorder N=15 | |
|---------------------------------|-------------------------|----|-----------------------|----|----------------------------------|---|--------------------------|---|
| Age (years) | X=38 (SD=11.9) | | X=34 (SD=6.13) | | X=44 (SD=8.85) | | X=54 (SD=4.8) | |
| Gender | 9 | 6 | 10 | 5 | 8 | 7 | 10 | 5 |
| F | | | | | | | | |
| M | | | | | | | | |
| Age at onset (years) | NA | | X=26 (SD=4.10) | | X=32 (SD=5.04) | | X=45 (SD=6.4) | |
| Duration of disorder (years) | NA | | X=8 (SD=5.25) | | X=12 (SD=6.11) | | X=9 (SD=4.9) | |
| Number of episodes | NA | | 4 | | 7 | | 5 | |
| MAN | NA | NA | NA | NA | 4 | 3 | 3 | 2 |
| DEP | | | | | | | | |

F – female, M – male, NA – not applicable, MAN – manic, DEP – depressive

TABLE 2
TEMPORAL LOBE VOLUMES PER STUDY GROUP

| | Healthy control | Schizophrenia | Schizoaffective disorder | Bipolar disorder |
|------------------------|------------------------|-------------------------|--------------------------|------------------------|
| TLL (mm ³) | 69,275 SD=10,415.0 | 65,332 (SD=4,328.20) | 64,898 (SD=6,013.92) | 62,144 (SD=9,357.6) |
| TLR (mm ³) | 73,642 (SD=8,409.0) | 69,017 (SD=7,249.89) | 70,059 (SD=4,903.54) | 68,339 (SD=3,461.2) |

TLL – left temporal lobe, TLR – right temporal lobe

TABLE 3
TEMPORAL LOBE DIFFERENCES PER STUDY GROUPS (p values)

| TLL | | | | |
|--------|----------|----------|----------|----------|
| | HC | SCH | SCHAFF | BIP |
| HC | NA | 0.605181 | 0.519359 | 0.120612 |
| SCH | 0.605181 | NA | 0.999099 | 0.750083 |
| SCHAFF | 0.519359 | 0.999099 | NA | 0.823653 |
| BIP | 0.120612 | 0.750083 | 0.823653 | NA |
| TLR | | | | |
| HC | NA | 0.269779 | 0.495990 | 0.164282 |
| SCH | 0.269779 | NA | 0.976616 | 0.993316 |
| SCHAFF | 0.495990 | 0.976616 | NA | 0.905634 |
| BIP | 0.164282 | 0.993316 | 0.905634 | NA |

TLL – left temporal lobe, TLR – right temporal lobe, HC – healthy control, SCH – schizophrenia, SCHAFF – schizoaffective disorder, BIP – bipolar disorder, NA – not applicable

TABLE 4
VOLUME DIFFERENCES BETWEEN LEFT AND RIGHT TEMPORAL LOBES (p values)

| Healthy control | Schizophrenia | Schizoaffective disorder | Bipolar disorder |
|-----------------|---------------|----------------------------|----------------------------|
| 0.216845 | 0.102046 | 0.015563 (L < R) | 0.023047 (L < R) |

L – left, R – right

Discussion

All patients included in the study had multiple disorder episodes. The differences in age of onset are characteristic of the particular disorder⁴, and therefore significantly different among study groups. Since there is no significant difference in the duration of disorder, the difference in age among all patient groups is statistically significant.

In this study, the reduction of temporal lobe volume was not found in patients with schizophrenia. According to the review of literature, 39% studies failed to prove this reduction¹⁶. One of the possible explanations is the limited sample size that is the shared difficulty in most magnetic resonance studies in psychiatry. Another possible explanation is that morphological changes affect smaller structures, in particular hippocampal formation and superior temporal gyrus. These changes were associated with impairment of working and verbal memory, verbal fluency and auditory hallucinations^{15,20}.

Thus symptom specific morphological changes may not to be expected on the level of temporal lobes.

The reduction of temporal lobe volume was not detected in patients with bipolar disorder which is more consistent with literature data¹⁸. If detected, changes in temporal lobe are also reported for smaller structures, such as amygdala^{21,22}. These changes are associated with emotional aspects of behavior, learning and memory^{21,23}. This study failed to find significant volumetric changes in patients with schizoaffective disorder as well. The result is consistent with the results of the few studies in which this diagnosis was separated from schizophrenia¹⁷.

When asymmetry differences were analyzed, left temporal lobes were smaller than right temporal lobes which is consistent with literature data^{14,18}. These differences reach statistical significance only in patients with bipolar and schizoaffective disorder,

further supporting the idea that schizophrenia symptom specific morphological changes may not be expected on the level of whole temporal lobe volumes.

These results support the conclusion that overall temporal lobe volume may be less informative in respect to

neuropathology of disorders with psychotic features than volumes of specific temporal lobe structures, in particular volumes of medial temporal lobe structures.

REFERENCES

1. WORLD HEALTH ORGANIZATION, The ICD-10 Classification of Mental and Behavioral Disorders. Tenth Revision (WHO, Geneva, 1992).
2. AMERICAN PSYCHIATRIC ASSOCIATION, Diagnostic and Statistic Manual of Mental Disorders, Fourth Edition (American Psychiatric Press, Inc., Washington, DC, 1995).
3. CROW TJ, Two syndromes of schizophrenia as one pole of the continuum of psychosis: a concept of the nature of the pathogen and its genomic locus. In: HENN FA, DELISI LE (Eds), Handbook of Schizophrenia, vol 2. Neurochemistry and Neuropharmacology of Schizophrenia. (Elsevier, New York, 1987).
4. FOLNEGOVIĆ-ŠMALC V, FOLNEGOVIĆ Z, KULČAR Ž, Br J Psychiatry, 156 (1990) 368.
5. MAZIADÉ M, ROY MA, MARTINEZ M, CLICHE D, FOURNIER JP, GARNEAU Y, NICOLE L, MONTGRAIN N, DION C, PONTON AM, POTVIN A, LAVALLEE JC, PIRES A, BOUCHARD S, BOUTIN P, BRISEBOIS F, MERETTE C, Am J Psychiatry, 152 (1995) 1458.
6. SCHWARTZ JE, FENNING S, TANENBERG-KARANT M, CARLSON G, CRAIG T, GALAMBOS N, LAVELLE J, BROMET EJ, Arch Gen Psychiatry, 57 (2000) 593.
7. GOLDMAN-RAKIC PS, Annu Rev Neurosci, 11 (1988) 137.
8. ANDREASEN NC, Science, 275 (1997) 1586.
9. MARNEROS A, DEISTER A, ROHDE A, Eur Arch Psychiatry Clin Neurosci, 241 (1991) 187.
10. RADONIĆ E, HENIGSBERG N, UZUN S, FOLNEGOVIĆ-ŠMALC V, Period Biol, 100 (1998) 201.
11. BOGERTS B, FALKAI B, GREVE T, SCHNEIDER T, PFEIFFER U, J Hirnforsch, 34 (1993) 193.
12. BROWN R, COLTER N, CORSELLIS JAN, CROW TJ, FRITH CD, JAGOE R, JOHNSTONE EC, MARSH L, Arch Gen Psychiatry, 43 (1986) 36.
13. COLLINSON SL, MACKAY CE, JAMES AC, QUESTED DJ, PHILLIPS T, ROBERTS N, CROW TJ, Br J Psychiatry, 183 (2003) 114.
14. WRIGHT IC, RABE-HESKETH S, WOODRUFF PWR, DAVID AS, MURRAY RM, BULLMORE ET, Am J Psychiatry, 157 (2000) 16.
15. GOLD JM, WEINBERGER DR, Curr Opin Neurobiol, 5 (1995) 225.
16. SHENTON ME, DICKEY CC, FRUMIN M, MCCARLEY RW, Schizophr Res, 49 (2001) 49.
17. GETZ GE, DELBELLO MP, FLECK DE, ZIMMERMAN ME, SCHWIERS ML, STRAKOWSKI SM, Schizophr Res, 55 (2002) 55.
18. MCDONALD C, ZANELLI J, RABE-HESKETH S, ELLISON-WRIGHT I, SHAM P, KALIDINDI S, MURRAY RM, KENNEDY N, Biol Psychiatry, 56 (2004) 411.
19. DUVERNOY HM, The human brain: surface, three-dimensional sectional anatomy and MRI. (Springer Verlag, Wien, New York, 1995).
20. GUR RE, COWELL PE, TURETSKY BI, GALLACHER F, CANNON T, BILKER W, GUR RC, Arch Gen Psychiatry, 55 (1998) 145.
21. ALTSHULER LL, BARTZOKIS G, GRIEDER T, CURRAN J, JIMENEZ T, LEIGHT K, WILKINS J, GERNER R, MINTZ J, Biol Psychiatry, 48 (2000) 147.
22. BRAMBILLA P, HARENSKI K, NICOLETTI M, SASSI RB, MALLINGER AG, FRANK E, J Psychiatr Res, 37 (2003) 287.
23. LEDOUX JE, Behav Brain Res, 58 (1993) 69.

E. Radonić

Croatian Institute for Brain Research, School of Medicine, University of Zagreb, Šalata 12, 10000 Zagreb, Croatia
e-mail: eradonic@hiim.hr

VOLUMEN TEMPORALNOG REŽNJA U POREMEĆAJIMA S PSIHOTIČNIM OBILJEŽJIMA

SAŽETAK

Već temeljem ranih neuropatoloških analiza, temporalni režanj povezan je s patofiziološkom podlogom nekih duševnih poremećaja s psihotičnim obilježjima. Cilj ovog istraživanja bio je usporediti volumen temporalnog režnja u pacijenata sa shizofrenijom, shizoafektivnim i bipolarnim poremećajem – poremećajima koji tvore spektar psihotičnih poremećaja. Za mjerenje volumena temporalnog režnja rabljena je metoda oslikavanja mozga magnetskom rezonancijom visoke rezolucije na 60 ispitanika, po 15 u svakoj skupini oboljelih kao i u skupini duševno zdravih dobrovoljaca. Nema statistički značajnih razlika u volumenu temporalnog režnja između skupina oboljelih ispitanika i zdravih dobrovoljaca. Usporedba volumena lijevog i desnog temporalnog režnja pokazuje kako je volumen lijevog manji od volumena desnog temporalnog režnja, no ova je razlika statistički značajna samo u skupinama ispitanika sa shizoafektivnim i bipolarnim poremećajem. Ukupni volumen temporalnog režnja vjerojatno je manje značajan za neuropatološku podlogu poremećaja s psihotičnim obilježjima od volumena specifičnih struktura, posebice struktura medijalnog dijela temporalnog režnja.