BRAIN ASYMMETRY AND SCHIZOPHRENIA

M. Marinov, R. Radev, I. Marinova*, Z. Stoyanov

Department of Physiology and Pathophysiology, *Department of General Medicine and Clinical Laboratory, Medical University Prof. Dr. Paraskev Stoyanov, Varna

Reviewed by: Assoc. Prof. R. Shishkov, MD, PhD

ABSTRACT

In this review is introduced literature data about fixed structural, neorochemical and functional asymmetry in schizophrenic patients. Anatomical differences in brain left temporal lobe, hippocampus, amygdala and corpus callosum are pointed as well as in thalamus and nuclei thalamic. Differences in dopamine system, glutamate receptors, level of N-acetylaspartat, some brain neuropeptides and their peptidases are present. In functional aspect the accent is on left temporal prefrontal areas in schizophrenics.

Keywords: brain asymmetry, schizophrenia, brain temporal lobe; dopamine; left hemisphere dysfunction

Brain asymmetry is a universal phenomenon which takes effects through motor, perceptive and cognitive functions, through emotions and even through brain control of some somatic functions (Davidson and Hugdahl 1995). Although it is projected not only at normal function realization but also has own places in their disease disorders. In that meaning psychopathologist interests for the problem is obvious.

In 1895 Bruce (cit. by Върбежскътii) describes an interesting case with a patient with manic-depressive psychosis who demonstrated interesting dichotomies at the different disease periods. At the manic period the patient would understand English and would write with the right hand, and at the depressive period he would not understand English and he used to write mostly with the left hand. At the remission period he appeared like ambidexterity one (1).

The real incitement for deeper investigation of the connection between psychopathology and brain lateralization is given in 1969 with Flor-Henry announcement that among the psychotic patients with temporal lobe epilepsy left sight foci are associated with schizophrenia-like psychosis, and right side ones – with bipolar affective disorder. Since then many investigations have been done and many facts in literature have appeared for and against the parallels between brain asymmetry and mental disorders like: depression (3, 4, 16, 28, 43), obsessive-compulsive disorder (17, 32, 45), panic disorders (31, 37, 48), eating disorders (22, 35, 50), violence and aggression (2, 39, 44), attention-deficit / hyperactivity disorder (13, 40), delirium (47) anxiety (38), have appeared. In most of the publications as a rule, the accent is placed on discrepant results and the following inability for synonymous interpretation (1, 51).

Our brief review is directed towards one of the most intensively researched and debated aspects of the problem – the connection between brain asymmetry and schizophrenia.

NEUROANATOMICAL ASYMMETRY AND SCHIZOPHRENIA

There are many facts telling about structural differences between the brain of patients with schizophrenia and the brain of healthy people (Chua and McKenna, 1995). In schizophrenics there have been found: brain size decreases as a whole; frontal, anterior parietal and temporal regions decrease; volume of brain lateral ventricles increases; size of hippocampus, amygdala and thalamus decreases.

In this point it is interesting to mention, that Honea et al. (2005) in their morphometrical investigations determine that the left gyrus temporalis superior and the left gyrus temporalis medialis are very important regions whit structural differences in schizophrenic patients compared to healthy subjects. Structural deficit of left temporal lobe in schizophrenic patients is observed by other authors as well (Chua and McKenna, 1995; Taylor, 2003). These facts correspond to the left temporal dysfunction in schizophrenics found by Muller, Kalus and Strik (2001), which is related to verbal process deficit. Levitan, Nard and Cats (1999) have studied 30 patients with schizophrenia by using functional magnetic resonance imaging (fMRI) and they associate the increased severity of hallucinated experiences with left gyrus temporalis anterior superior smaller volumes (27). Also using a morphological method and applying radiological methods of investigation in schizophrenia, affective illness and dementia Karim and Burns (2003) have found in patients with mental disorders left and right hemi-

Address for correspondence:
Miroslav Dimitrov Marinov, Dept. of Physiology and Pathophysiology, Medical University Prof. Dr. Paraskev Stoyanov, 55 Marin Drinov St., BG-9002, Varna, BULGARIA
sphere differences, regarding size, blood flow and glucose metabolism.

The dates for asymmetry in diminished sizes of hippocampus, amygdala and thalamus in schizophrenic patients are ambiguous. According to Chua and McKenna (1995) summary decreased size of hippocampus and/or amygdala has been found established in 8 of 14 cited investigations—in 5 cases the modifications are bilateral, and in the other 3 are leftward. Other research points a significant decrease of ration between right hippocampus and amygdala correlations (ibidem). Multiplan investigations of other authors, carried out on histological, morphometrical, neurochemical and gene expression level (in vitro and post mortem) determinate that in schizophrenics left hippocampus is damaged more than right one (20). Studying the characteristics of schizophrenic patients Read et al. (2001) indicate changes in hippocampus, brain atrophy and increase in volume of brain ventricles and the authors discuss the functional brain asymmetry in these cases. Comparing post mortem thalamic nuclei of 12 schizophrenic patients and healthy subjects, Danos et al. (2003) have found 19.7% reduction in left and 21.1% in right of medial pulvinar nucleus. Nucleus mediodorsalis in schizophrenia shows reduction in both hemispheres. In general thalamus is reduced in size: leftwards with 16.4% and rightwards—with 15.2% (9). In similar postmortem study of 21 schizophrenic patients compared with 27 mentally healthy individuals, Cullen et al. (2003) do not find any differences in size of nucleus mediodorsalis thalami and hemispheric asymmetry as well.

Form and size of corpus callosum are compared as well. Performed (fMRI) study of 27 schizophrenic patients, 13 with schizotypal personality disorder and 30 healthy volunteers determine reduction of size and differences in the form of corpus callosum which authors associate with decreased connection between left and right hemisphere in schizophrenia and schizotypal personality disorder (11).

**NEUROCHEMICAL ASYMMETRY AND SCHIZOPHRENIA**

According to recent concepts 3 key neurotransmitters—dopamine, glutamate and serotonin, are related with schizophrenia pathophysiology (Ereshefsky and Miller, 1999). Hyperactivity of dopaminergic system in schizophrenia is the most popular theory. Also there are investigations showing increased dopamine activity according to relative hyperactivity of the left hemisphere (Cutting, 1992).

In principle the concentrations of dopamine are higher in left hemisphere and that is obvious in basal nuclei system (Wittling, 1995). That is why it is interesting to mention that some studies with schizophrenia do not find asymmetry in dopamine transporter binding of nucleus caudatus and that is a prerequisite for discussion of disordered brain lateralization in this disease (26).

In post mortem study of glutamate receptors in schizophrenics Harrison, Law and Eastwood (2003) have found that comparing to healthy people the number of these receptors is decreased, and it is greater in the left than in the right hippocampus (21). There are some interesting investigations concerning some brain metabolites which contain N-acetylaspartat. The latter is taken as a marker for neuronal/axonal density and viability. Its physiological role is still not clear in details, but in some diseases characterized with neuronal and axonal loss, N-acetylaspartat decreases (Hammen, Stefan and Tomandl, 2002). Data of Molina et al. (2005) suggest that the levels of N-acetylaspartat in the left prefrontal dorsolateral areas are decreased in schizophrenics who have suffered for a long time (9.7 +6.1 years after the finding of disorder) however on earlier stages (1.8 ±0.6 years from disorder beginning) there are no differences in comparison with healthy controls.

Very interesting is report of Ramirez et al. (2004) which has stated that in schizophrenia, depression, autistic children, Alzheimer’s disease there are asymmetric patterns in the release of brain neupeptides (corticotropin-releasing hormone, cholecystokinin, luteinizing hormone-releasing hormone, thyrotrpin-releasing hormone and angiotensin II), as well as their neupeptidases.

**FUNCTIONAL ASYMMETRY AND SCHIZOPHRENIA**

It is accepted that impaired development of normal brain asymmetry is not incidental to schizophrenia as a whole, but it can be attributed to some of its forms (25, 29). The early theories about the abnormal brain lateralization in schizophrenia are concentrated on the left hemisphere. Based on above observation, Flor-Henry (1969; 1976) presumed the availability of left hemisphere dysfunction. Other findings come to the hypothesis for left hemisphere overactivation, and as a result evidences are piled up regarding left hemisphere dysfunction, as well as left hemisphere overactivation in schizophrenia (Burder, 1995). Information for right hemisphere dysfunction appears too (8). Also it is supposed that paranoid form of schizophrenia is connected with hyper activity of left hemisphere processes, and the opposite is probably responsible for the nonparanoic schizophrenia. Later it has been proposed a model, known as hemisphere imbalance syndrome. According to it delusions, excitement, cognitive acceleration are connected with domination of left hemisphere activation, and negative symptoms are related to contrary directed hemisphere imbalance (4).

More recent theories begin to connect anatomical asymmetry in schizophrenia and lateralized cognitive functions. For example in (fMRI) studies were found evidences for the relation among the deficit of the left temporal region in schizophrenia and auditory hallucinations (Burder, 1995). Generally it is pointed out that the degree of expression of positive symptoms (hallucinated behavior is also included in the group of positive symptoms according to Positive and Negative Syndrome Scales (PANSS) is in opposite relation with the volume of left gyrus temporalis superior. As far as this region (planum temporale is also located
there) is connected to speech dominance, it could be supposed that in forms of schizophrenia with positive symptoms there is disturbance of hemispheric dominance in securing linguistic functions (bidem). In this direction are the results of Malaspina, Bruder (2000) from single photon emission computed tomography (SPECT) by 16 schizophrenic patients – it is found decreased dominance of the right ear (left hemisphere) in dichotic perceiving of words. Authors also make connection between some areas of hyperactivity from the right temporal part and the positive symptoms of schizophrenia. Dysfunction of left hemisphere is also supported by the tests with lateralized stimuli presentation in left and right halves of visual fields (4). It must also be said that in functional plan it is paid attention not only to the temporal region, but to the prefrontal areas as well. It is raised a question about hypofrontality in schizophrenia. There are data that schizophrenics are not doing well with tasks demanding high activation of the left prefrontal cortex and it is objectively shown, that activation of the left prefrontal cortex in such conditions is reduced. In other experiment Nohara et al. (2000) registered the regional brain blood flow during verbal memory task and they have come to the conclusion that the organization of the memory in schizophrenics is affected by disturbances in the functions of the prefrontal areas and especially the left frontal inferior region (36). The clinical researches show that by means of high frequency repetitive transcranial magnetic stimulation (rTMS) of the left prefrontal cortex in schizophrenics could be achieved reduction in auditory hallucinations and improvement of psychotic symptoms (Haraldson et al., 2004).

**CONCLUSION**

The cited in our review data suggest that most authors relate schizophrenia mostly with left hemisphere dysfunction. The science however is still far away from detail clearing up the reasons and mechanisms which determine mental disorders. In this context the survey data confirm the opinion that examination of each problem related to brain function is useful to be done in the light of the brain asymmetry.

**REFERENCES**

1. Введенский, Г. Е. Функциональные асимметрии у больных эндогенными психозами. Ж. невропат. и психиат. им. С. С. Корсакова. 1990, 90, 5: 129-140.


