Hemispheric Specialization and Psychopathology

Dr. T. Hakan Yöney[1]

SUMMARY:
HEMISPHERIC SPECIALIZATION AND PSYCHOPATHOLOGY

There are differences in the anatomy and functions of right and left cerebral hemispheres. The localization of a function on one side of the brain in preference to the other side is defined as lateralization. In general, it is suggested that the left hemisphere is analytic, the right is holistic, the left is verbal, and the right is perceptual. Linguistic abilities like grammar etc. are concentrated in the left hemisphere, but the right hemisphere also has a role in language and is important for timing and intonation. Right hemisphere is important in processing facial emotional input and it is more important than left in the expression of emotions. Studies on hemispheric determinants of behavior use various methods, among them are behavioral assessments on subjects with various localized brain damage including split-brain surgery, electrophysiological investigations as electroencephalography (EEG) and event-related potentials (ERPs), brain imaging studies as positron emission tomography (PET) and functional magnetic resonance imaging (fMRI), and divided visual field and dichotic listening experiments. Various studies on the relation of hemispheric specialization and psychopathology have been conducted to understand the neural mechanisms of mental disorders. In general, researches suggest that the key anatomical change in schizophrenia is a loss or even a reversal of cerebral asymmetry. The failure to develop normal cerebral asymmetry is suggested to be an important component of the underlying pathology in some forms of schizophrenia. Most of the other psychopathological conditions show varying degrees of lateralization. Emergence of new technological opportunities like transcranial magnetic stimulation (TMS) to effect one side of the brain encourages further studies on the role of lateralization in psychopathology.

Key words: lateralization, mental disorder, neurobiology

Bull Clin Psychopharmacol 2001;11:53-59

ÖZET:
HEMİSFERİK ÖZELLEŞME VE PSİKOPATOLOJİ

Sağ ve sol serebral hemisferlerin anatomi ve işlevlerinde farklılıklar vardır. Bir fonksiyon açısından beynin bir tarafının diğerine göre daha avantajlı olması lateralizasyon olarak tanımlanabilir. Genel olarak sol hemisferin analitik, sağın holistik, solun sözel, sağın ise algısal olduğu düşünülür. Gramer gibi dil ile ilgili yetiler sol hemisferde yoğunlaşmakla beraber sağ hemisferin de bu fonksiyonda rolü vardır ve zamanlama ve vurgulama açısından önemlidir. Sağ hemisfer duygusal yüz ifadelerinin algılanıp anlaşılması ve duyguların ifadesi açılarından sola göre daha önemlidir. Davranışın hemisferik özelliklerini araştıran çalışmalar çeşitli yöntemler kullanırlar, bunların arasında ayrılmış-beyin cerrahisi dahil çeşitli lokalize beyin hasarı olan hastalar üzerinde davranış değerlendirmeleri yapmak, elektrofizyolojik araştırmalar (EEG, ERPs), beyin görüntüleme çalışmaları (PET, fMRI) ve bölünmüş görme alanı ve dikotik dinleme deneyleri sayılabilir. Ruhsal hastalıkların nöral mekanizmalarını anlamak için hemisferik özelleşme ile psikopatolojik durumların ilişkisini araştıran pekçok çalışma yapılmıştır. Yapılan araştırmalara göre şizofrenideki esas anatomik değişiklik serebral asimetrinin kaybı hatta ters çevrilmesidir. Normal serebral asimetri geliştirme eksikliğinin, bazı şizofreni tiplerinde altta yatan patolojinin önemli bir bölümünü oluşturduğu öne sürülmektedir. Diğer psikopatolojik durumlar ise değişen derecelerde lateralizasyon göstermektedirler. Transkranial manyetik stimulasyon gibi beynin bir tarafını etkileyebilen yeni teknolojik olanakların ortaya çıkması, psikopatolojide lateralizasyonun rolü üzerinde daha ileri çalışmaları gerekli kılmaktadır.

Anahtar sözcükler: lateralizasyon, ruhsal hastalık, nörobiyoloji

Klinik Psikofarmokoloji Bülteni 2001;11:53-59

INTRODUCTION

The differences in the anatomy and functions of cerebral hemispheres have been the focus of research activities for the explanation of normal and abnormal behavior on the basis of brain mechanisms. Localization of a function on one side of the brain in preference to the other side can be defined as lateralization.

In general, it is suggested that the left hemisphere is analytic, the right is holistic, the left is verbal, the right perceptual etc. (1). When one of the hemispheres receive attention and increase activity level, the other hemisphere acts in the opposite way and becomes less efficient, it seems that attention can be directed to one side at a time.

In almost all right handed and in a lower percentage of left handed people linguistic abilities are concentrated in the left hemisphere, but the right hemisphere also has a role in language and is important for stress, timing and intonation (2).

Right hemisphere is important in processing facial emotional input and right hemisphere is more important than left in the expression of emotions.

[1]Marmara Üniversitesi Tıp Fakültesi , Psikiyatri AD - İstanbul
Yazışma Adresi / Address reprint requests to: Doç. Dr. Hakan Yöney, Marmara Üniversitesi Tıp Fakültesi Hastanesi, Psikiyatri AD, Tophanelioğlu Cad. 13-15, Altunizade 81190 İstanbul

E -mail: yoney@marun.edu.tr

Left side of the face, controlled by the right side of the brain, is more expressive than the right side of the face (3).

Data on hemispheric determinants of behavior originate from several types of studies, among them are behavioral assessments on subjects with various localized brain damage including split-brain surgery, electrophysiological investigations (EEG, ERPs), and brain imaging studies (PET, fMRI).

The studies on cerebral asymmetry have produced very contradictory results due to various reasons. For example, brain lesion studies have many limitations. The behavioral consequences of a brain damage may be primarily due to dysfunction of that area or to dysfunction of a nondamaged area that is secondarily affected as deprived of normal input from damaged area. Furthermore, the nondamaged parts may compensate to some extent for damaged parts. On the other hand, since a disruption between cortical and subcortical structures results in a reduction in cortical activation, probably more complex processes which require more activation are disturbed more and this may be interpreted as specific dysfunction of related hemisphere. So, in many cases the appearance of specificity may be misleading (1).

Visual or auditory stimulus related to a specific kind of information may be presented to the hemisphere specialized for processing that kind of information or to the other hemisphere which transmits the input to the other hemisphere through the corpus callosum for appropriate processing, however this may cause a degradation of the information and takes about 15 ms which may delay the process. As a result, if the visual or auditory stimulus is presented to the eye or ear projecting primarily to the hemisphere specialized for that function, the performance will be the best. This is the basis for divided visual field and dichotic listening experiments. Attention related factors should also be taken into consideration in these studies.

The laterality in mental disorders has been the subject of various studies and the consistent finding of laterality have been reported in some mental disorders.

MENTAL DISORDERS AND LATERALITY

SCHIZOPHRENIA

In general, researches suggest that the key anatomical change in schizophrenia is a loss or even a reversal of cerebral asymmetry (4,5,6) and the failure to develop normal cerebral asymmetry is suggested to be an important component of the underlying pathology in some forms of schizophrenia (7,8).

Tigges et al. (9) reported soft neurological signs related to right-hemisphere dysfunction in schizophrenic patients. Results of a twin study (10) suggest that the occurrence of neurological soft signs and their lateralization to the left body half are genetically transmitted.

In an in vivo imaging study (5) on neuroleptic-naive patients with first-episode schizophrenia it was found that the patients lack asymmetry in caudate dopamine transporter binding and suggested disrupted brain lateralization in this disorder.

In a study, which investigated the cortical organization of executive control functions in schizophrenic patients and healthy control subjects using event-related potentials, it was reported that patients exhibit deficient processing in a neural network, including left frontal areas (11).

Levitan et al (12) studied 30 patients with schizophrenia and history of auditory hallucinations using MRI along with assessment of functional lateralization, reported that increased severity of hallucinatory experience was significantly associated with smaller left anterior superior temporal gyrus volumes.

Results of a single photon emission computed tomography (SPECT) study on 16 schizophrenic patients suggested reduced right ear (left hemisphere) advantage for dichotic word perception in schizophrenia and overactivity of right temporal lobe regions and positive symptoms are related (13).

Nohara et al (14) measured regional cerebral blood flow (rCBF) in schizophrenia during a verbal learning task and reported results indicating that memory organization deficits in schizophrenia may be related to dysfunction in the prefrontal areas, especially in the left inferior frontal region.

The size and shape of the corpus callosum were assessed on magnetic resonance images in 27 patients with schizophrenia, 13 patients with schizotypal personality disorder (SPD), and 30 healthy volunteers. The decreases in corpus callosal size and differences in shape indicated a decreased connectivity between the left and the right hemispheres in schizophrenia and SPD (15).

DEPRESSION

Braun et al (16) reported that patients with mania and/or psychomotor agitation had predominantly right hemisphere lesions, whereas patients with depression and/or psychomotor lethargy had predominantly left hemisphere lesions. There was also a nonsignificant trend for right posterorolandic lesions to predict mania or agitation and for left frontal lesions to predict depression or psychomotor lethargy.

In a study on 84 epileptic patients, male but not female subjects, with left-sided foci were found to be particularly vulnerable to depression (17). In another study on 59 epileptics no significant difference in the level of anxiety was found among the groups, but patients with left-sided temporal lobe epilepsy scored significantly higher than patients with right or bilateral foci on self-ratings for depression. (18)

Cortical regional cerebral blood flow was assessed in minimally medicated, relatively young adults in episodes of either acute mania or major depression and in control subjects, and evidence of abnormal patterns of flow lateralization on a regional basis in both clinical groups compared with normal subjects was reported (19)

In a study on patients with major depression and 18 healthy subjects using Bereitschaftspotential (BP) paradigm, a significant asymmetry of the BP to the left was found in depressives and this asymmetry to the left hemisphere was interpreted as a cortical deactivation of the right cerebral hemisphere. (20)
To assess the relationship between hemispheric differences in information processing and interhemispheric asymmetries in terms of brain bioelectrical activity, Bionti et al (21) correlated scores on the MMPI Depression scale with peak amplitude and latency of the P3 component of somatosensory evoked potentials (SEPs) at the frontocortical region of 14 healthy volunteers. Subjects scoring above the median on the MMPI Depression scale showed a right lateralization at the frontocentral region and a significantly shorter P3 latency at the right hemisphere compared to the left.

In a study using conventional neuropsychological tests before and after therapy in 52 (for the most part therapy-resistant) depressives, no substantial effects in lateralized functioning was found (22).
Volf et al (23) measured hemispheric language lateralization on thirty-seven patients with seasonal affective disorder and 25 control subjects and reported that depressed patients had a shift of laterality from the left to the right which was normalized with light therapy, and this shift of laterality was absent in summer.

Cardiovascular phase, especially diastole, influences attention and the event-related potential of the right hemisphere of the brain. In an interesting study, the ERP was recorded during stimulation triggered by diastole and systole in depressed, schizophrenic, and control subjects. An exaggerated effect of diastole on the ERP in the right hemisphere was observed in depressed patients, however, no cardiovascular effect on the ERP was apparent in schizophrenic patients. These results were interpreted as heart/brain networks being closely related in normal controls, probably exaggerated in depressed patients, and unrelated in schizophrenics. (24)

There is conflicting evidence on the hypothesis that the risk of depression after stroke is influenced by the location of the brain lesion (3,25,26).

Repetitive transcranial magnetic stimulation (rTMS) is a new method that is able to increase cortical activity at high and decrease at low frequency stimulation (27). Application of high frequency rTMS to left dorsolateral prefrontal cortex (DLPFC) (28) and low frequency to right DLPFC (29) was reported to have beneficial effects on symptoms of depression. However, in a study on healthy subjects, application of high frequency rTMS to left DLPFC decreased happiness whereas application to right DLPFC decreased sadness (30).

Other TMS studies (bilateral motor threshold and paired-pulse) on depressed patients showed lower excitability on the left hemisphere which was absent in controls (31).

OBSESSIVE-COMPULSIVE DISORDER

There is a neuroanatomic lateralization in obsessive-compulsive disorder (OCD). In symptom provocation studies of OCD hyperperfusion in the right caudate and right orbitofrontal cortex were reported (32,33). Right medial prefrontal or right orbitofrontal metabolism and perfusion were decreased after successful treatment of OCD patients with pharmacology or behavior therapy (34,35,36).

In a MRI study Szeszko (37) reported lack of normal hemispheric asymmetry of the hippocampus-

amygdala complex in OCD patients.

Greenberg et al (38) reported that application of rTMS to right, but not left, DLPFC decreased the intensity of compulsive urges in OCD patients, providing further support for lateralization in OCD.

PANIC DISORDER

In a PET study on patients with panic disorder, patients who were vulnerable to lactate-induced panic, had several abnormalities in the resting, non-panic state including an abnormal hemispheric asymmetry of parahippocampal blood flow, blood volume, and oxygen metabolism (39). The abnormal right left ratio in panic disorder especially seen in hippocampus and inferior prefrontal regions was also found in imipramin treated panic patients (40).

In a preliminary PET study on 7 medication free panic patients, Malizia et al (41) reported a global reduction in benzodiazepine site binding throughout the brain in patients with panic disorder compared with controls; and the largest regional decrease in binding were found in the right orbitofrontal cortex and right insula.

In an EEG study, Wiedemann et al (42) reported that patients with panic disorder showed greater activation of a right frontal avoidance-withdrawal system than controls in the presence of negative stimuli.

EATING DISORDERS

In a study on anorexia nervosa patients with and without habitual binge/purge behavior, SPECT examination was performed before and after the subjects were asked to imagine food. The anorexia nervosa patients with habitual binge/purge behavior had a significantly higher percent change in the inferior, superior, prefrontal, and parietal regions of the right brain than the patients with purely restrictive anorexia and the healthy volunteers. These findings suggest a relation between right brain activation and habitual binge/purge behavior. (43)

In a patient with bulimia nervosa it was found that in the anorexic state, the cerebral blood flow in the temporal, parietal, and occipital lobes on the right side was lower than that on the left side and in the binge-eating state there was no laterality. (44)

In a controlled study on eight women with bulimia using PET, during the performance of a visual vigilance task the metabolic rate was higher in the right hemisphere than in the left in control subjects but patients with bulimia did not have this normal asymmetry. (45)

VIOLENCE and AGGRESSION

In a study on the relationship of EEG abnormalities and violent criminal behavior in 222 defendants referred to psychiatric evaluation, it was reported that while there was no relation between the number of violent offenses and EEG abnormalities in general, focal abnormalities especially on the left hemisphere were related to a significantly higher number of violent offenses, which suggests a left hemisphere dysfunction in violent behavior (46).

A SPECT study on 40 adolescents and adults who exhibited aggressive behavior within the six months prior to evaluation by physically attacking another person or destroying property, found decreased activity in the prefrontal cortex, increased activity in the anteromedial portions of the frontal lobes, left sided increased activity in the basal ganglia, and/or limbic system in comparison to the whole brain, and focal abnormalities in the left temporal lobe (47).

In a study (48) on adult patients with left, right, or bilateral temporal lobe epilepsy or absence epilepsy and normal controls, it was reported that patients with left temporal lobe epilepsy scored higher than other groups on hostile feelings, normal controls scored higher on covert aggression and bitemporal patients scored higher on overt aggression.

Stein et al (49) found increased left-sided neurological soft signs in impulsive and aggressive patients.

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER

In an electroencephalography study in unmedicated preschool and school boys and girls with attention-deficit/hyperactivity it was reported that boys with ADHD exhibited a less, but girls more, right-lateralized frontal activation pattern than normal controls (50).

Pliszka et al (51) measured event-related potentials in 10 children with ADHD and 10 healthy children during a response inhibition task and reported right frontal abnormalities in ADHD.

In a study to examine the integrity of presynaptic dopaminergic function in children with ADHD

through use of PET, accumulation of [18F]DOPA in synaptic terminals, a measure of dopa decarboxylase activity in the right midbrain was found to be higher in ADHD than normals and correlated with symptom severity (52).

OTHER MENTAL CONDITIONS

Trzepacz (53) proposes that delirium involves particular neural pathways and lateralization to the right. Prefrontal cortices, anterior and right thalamus, and right basilar mesial temporoparietal cortex may play a significant role in delirium symptoms as disorientation, cognitive deficits, sleep-wake cycle disturbance, disorganized thinking, and language abnormalities.

Petruzzello et al (54) reported postexercise increase in activation of the left frontal area with respect to the homologous right frontal site together with decrease in anxiety level, bringing an explanation to why anxiety is reduced with exercise.

Conversion symptoms tend to appear more commonly on the left side of the body, particularly the sensory symptoms, and some EEG studies support the role of the nondominant hemisphere in conversion (55).

The results of a PET study on PTSD patients during symptom provocation suggest that PTSD symptoms are mediated by the limbic and paralimbic systems within the right hemisphere (56).

CONCLUSION

The laterality in mental disorders seems to be an important and interesting subject for research. According to the available data most of the psychopathological conditions show varying degrees of right or left hemisphere dysfunctions.
Emergence of new technological opportunities like TMS to effect one side of the brain encourages further studies on the role of hemispheric specialization in psychopathology.

References:

1. Kosslyn Sm, Gazzaniga MS, Galaburda AM, Rabin C. Hemispheric specialization. In: Zigmund MJ, Bloom FE, Landis SC, Ronerts JL, Squire LR, editors. Fundamental Neuroscience. San Diego: Academic Press, 1999: 1521-1542

2. Dronkers NF, Pinker S, Damasio A. Language, thought, mood, and learning, and memory. In Kandel ER, Schwartz JH, Jessel TM, editors. Principles of Neural Science. New York: McGraw-Hill, 2000: 1169-1187

3. Heilmann KM, Bowers D. Emotional disorders associated with hemispheric dysfunction. In: Fogel BS, Schiffer RB, Rao SM, editors. Neuropsychiatry. Baltimore: Williams & Wilkins, 1996: 401-406

4. Crow TJ. Twin studies of psychosis and the genetics of cerebral asymmetry. Br J Psychiatry 1999;175:399-401

5. Laakso A, Vilkman H, Alakare B, Haaparanta M, Bergman J, Solin O, Peurasaari J, Rakkolainen V, Syvalahti E, Hietala J. Striatal dopamine transporter binding in neuroleptic-naive patients with schizophrenia studied with positron emission tomography. Am J Psychiatry 2000;157:269-71

6. Galderisi S, Mucci A, Mignone ML, Bucci P, Maj M. Hemispheric asymmetry and psychopathological dimensions in drug-free patients with schizophrenia. Int J Psychophysiol 1999;34:293-301

7. Maher BA, Manschreck TC, Yurgelun-Todd DA, Tsuang MT. Hemispheric asymmetry of frontal and temporal gray matter and age of onset in schizophrenia. Biol Psychiatry 1998; 44:413-7

8. Klar AJ. Genetic models for handedness, brain lateralization, schizophrenia, and manic-depression. Schizophr Res 1999;39:207-218

9. Tigges P, Mergl R, Frodl T, Meisenzahl EM, Gallinat J, Schroter A, Riedel M, Muller N, Moller HJ, Hegerl U. Digitized analysis of abnormal hand-motor performance in schizophrenic patients. Schizophr Res 2000;45:133-143

10. Niethammer R, Weisbrod M, Schiesser S, Grothe J, Maier S, Peter U, Kaufmann C, Schroder J, Sauer H. Genetic influence on laterality in schizophrenia? A twin study of neurological soft signs. Am J Psychiatry 2000;157:272-274

11. Weisbrod M, Kiefer M, Marzinzik F, Spitzer M. Executive control is disturbed in schizophrenia: evidence from event-related potentials in a Go/NoGo task. Biol Psychiatry 2000;47:51-60

12. Levitan C, Ward PB, Catts SV. Superior temporal gyral volumes and laterality correlates of auditory hallucinations in schizophrenia. Biol Psychiatry 1999;46:955-62

13. Malaspina D, Bruder G, Furman V, Gorman JM, Berman A, Van Heertum R. Schizophrenia subgroups differing in dichotic listening laterality also differ in neurometabolism and symptomatology. J Neuropsychiatry Clin Neurosci 2000;12:485-92

14. Nohara S, Suzuki M, Kurachi M, Yamashita I, Matsui M, Seto H, Saitoh O. Neural correlates of memory organization deficits in schizophrenia. A single photon emission computed tomography study with 99mTc-ethyl-cysteinate dimer during a verbal learning task. Schizophr Res 2000;42:209-22

15. Downhill JE Jr, Buchsbaum MS, Wei T, Spiegel-Cohen J, Hazlett EA, Haznedar MM, Silverman J, Siever LJ. Shape and size of the corpus callosum in schizophrenia and schizotypal personality disorder. Schizophr Res 2000;42:193-208

16. Braun CM, Larocque C, Daigneault S, Montour-Proulx I. Mania, pseudomania, depression, and pseudodepression resulting from focal unilateral cortical lesions. Neuropsychiatry Neuropsychol Behav Neurol 1999;12:35-51

17. Strauss E, Wada J, Moll A. Depression in male and female subjects with complex partial seizures. Arch Neurol 1992;49:391-2

18. Altshuler LL, Devinsky O, Post RM, Theodore W. Depression, anxiety, and temporal lobe epilepsy. Laterality of focus and symptoms. Arch Neurol 1990;47:284-8

19. Rubin E, Sackeim HA, Prohovnik I, Moeller JR, Schnur DB, Mukherjee S. Regional cerebral blood flow in mood disorders: IV. Comparison of mania and depression. Psychiatry Res 1995;61:1-10

20. Haag C, Kathmann N, Hock C, Gunther W, Voderholzer U, Laakmann G. Lateralization of the Bereitschaftspotential to the left hemisphere in patients with major depression. Biol Psychiatry 1994;36:453-7

21. Biondi M, Parise P, Venturi P, Riccio L, Brunetti G, Pancheri P. Frontal hemisphere lateralization and depressive personality traits. Percept Mot Skills 1993;77:1035-42

22. de Groot MH, Nolen WA, Huijsman AM, Bouvy PF. Lateralized neuropsychological functioning in depressive patients before and after drug therapy. Biol Psychiatry 1996;40:1282-7

23. Volf NV, Senkova NI, Danilenko KV, Putilov AA. Hemispheric language lateralization in seasonal affective disorder and light treatment. Psychiatry Res 1993;47:99-108

24. Sandman CA, Vigor-Zierk CS, Isenhart R, Wu J, Zetin M. Cardiovascular phase relationships to the cortical event-related potential of schizophrenic, depressed, and normal subjects. Biol Psychiatry 1992;32:778-89

25. Carson AJ, MacHale S, Allen K, Lawrie SM, Dennis M, House A, Sharpe M. Depression after stroke and lesion location: a systematic review. Lancet 2000;356:122-6

26. Singh A, Herrmann N, Black SE. The importance of lesion location in poststroke depression: a critical review. Can J Psychiatry 1998;43:921-7

27. Post RM, Kimbrell TA, McCann UD et al. Repetitive transcranial magnetic stimulation as a neuropsychiatric tool: Present status and future potential. J ECT 1999; 15:39-59

28. George MS, Wassermann EM, Kimbrell T et al. Mood improvement following daily left prefrontal repetitive transcranial magnetic stimulation in patients with depression: a placebo-controlled crossover trial. Am J Psychiatry 1997; 154:1752-1756

29. Klein E, Krenin I, Christyakov A et al. Therapeutic efficacy of right prefrontal slow repetitive transcranial magnetic stimulation in major depression double-blind controlled study. Arch Gen Psychiatry 1999; 56:315-320

30. George MS, Wassermann EM, Williams WA et al. Changes in mood and hormone levels after rapid-rate transcranial magnetic stimulation (rTMS) of the prefrontal cortex. J Neuropsychiatry Clin Neurosci 1996; 8:172-180

31. Maeda F, Keenan JP, Pascual-Leone A. Interhemispheric asymmetry of motor cortical excitability in major depression as measured by transcranial magnetic stimulation. Br J Psychiatry 2000;177:169-73

32. Rauch SL, Jenike MA, Alpert NM, Baer L, Breitner HC, Savage CR, Fischman AJ: Regional cerebral blood flow measured during symptom provocation in obsessive-compulsive disorder using oxygen 15-labeled carbon dioxide and positron emission tomography. Arch Gen Psychiatry 1994;51:62-70

33. McGuire PK, Bench CJ, Frith CD et al. Functional anatomy of obsessive-compulsive phenomena. Br J Psychiatry 1994; 164:459-468

34. Benkelfalt C, Nordahl TE, Semple WE. Local cerebral glucose metabolic rates in obsessive-compulsive disorder. Patients treated with clomipramin. Arch Gen Psychiatry 1990;47:840-848

35. Hoehn-Saric R, Pearlson GD, Harris GJ, Machlin SR, Camargo EE. Effects of fluoxetine on regional blood in obsessive-compulsive paients. Am J Psychiatry 1991; 148:1243-5

36. Baxter LR Jr, Schwartz JM, Bergman KS, Szuba MP, Guze BH, Maziotta JC, Alazraki A, Selin CE, Ferng HK, Munford P et al. Caudate glucose metabolic rate changes with drug and behavior therapy for obsessive-compulsive disorder. Arch Gen Psychiatry 1992; 49:681-689

37. Szeszko PR, Robinson D, Alvir JM, Bilder RM, Lencz T, Ashtari M, Wu H, Bogerts B. Orbital frontal and amygdala volume reductions in obsessive-compulsive disorder. Arch Gen Psychiatry 1999;56:913-9

38. Greenberg BD, George MS, Martin JD et al. Effect of prefrontal repetitive transcranial magnetic stimulation in obsessive-compulsive disorder: a preliminary study. Am J Psychiatry 1999;154:867-869

39. Reiman EM, Raichle ME, Robins E, Butler FK, Herscovitch P, Fox P, Perlmutter J. The application of positron emission tomography to the study of panic disorder. Am J Psychiatry 1986 ;143:469-77

40. Nordahl TE, Stein MB, Benkelfat C, Semple WE, Andreason P, Zametkin A, Uhde TW, Cohen RM. Regional cerebral metabolic asymmetries replicated in an independent group of patients with panic disorders. Biol Psychiatry 1998;44:998-1006

41. Malizia AL, Cunningham VJ, Bell CJ, Liddle PF, Jones T, Nutt DJ. Decreased brain GABA(A)-benzodiazepine receptor binding in panic disorder: preliminary results from a quantitative PET study. Arch Gen Psychiatry 1998;55:715-20

42. Wiedemann G, Pauli P, Dengler W, Lutzenberger W, Birbaumer N, Buchkremer G Frontal brain asymmetry as a biological substrate of emotions in patients with panic disorders. Arch Gen Psychiatry 1999;56:78-84

43. Naruo T, Nakabeppu Y, Sagiyama K, Munemoto T, Homan N, Deguchi D, Nakajo M, Nozoe S. Characteristic regional cerebral blood flow patterns in anorexia nervosa patients with binge/purge behavior. Am J Psychiatry 2000;157:1520-2

44. Hirano H, Tomura N, Okane K, Watarai J, Tashiro T. Changes in cerebral blood flow in bulimia nervosa. J Comput Assist Tomogr 1999;23:280-2

45. Wu JC, Hagman J, Buchsbaum MS, Blinder B, Derrfler M, Tai WY, Hazlett E, Sicotte N. Greater left cerebral hemispheric metabolism in bulimia assessed by positron emission tomography. Am J Psychiatry 1990;147:309-12

46. Pillmann F, Rohde A, Ullrich S, Draba S, Sannemuller U, Marneros A. Violence, criminal behavior, and the EEG: significance of left hemispheric focal abnormalities. J Neuropsychiatry Clin Neurosci 1999;11:454-457

47. Amen DG, Stubblefield M, Carmicheal B, Thisted R. Brain SPECT findings and aggressiveness. Ann Clin Psychiatry 1999;8:129-137

48. Devinsky O, Ronsaville D, Cox C, Witt E, Fedio P, Theodore WH. Interictal aggression in epilepsy: the Buss-Durkee Hostility Inventory. Epilepsia 1994;35:585-590

49. Stein DJ, Hollander E, Cohen L, Frenkel M, Saoud JB, DeCaria C, Aronowitz B, Levin A, Liebowitz MR, Cohen L. Neuropsychiatric impairment in impulsive personality disorders. Psychiatry Res 1993;48:257-266

50. Baving L, Laucht M, Schmidt MH. Atypical frontal brain activation in ADHD: preschool and elementary school boys and girls. J Am Acad Child Adolesc Psychiatry 1999;38:1363-71

51. Pliszka SR, Liotti M, Woldorff MG. Inhibitory control in children with attention-deficit/hyperactivity disorder: event-related potentials identify the processing component and timing of an impaired right-frontal response-inhibition mechanism. Biol Psychiatry 2000;48:238-46

52. Ernst M, Zametkin AJ, Matochik JA, Pascualvaca D, Jons PH, Cohen RM. High midbrain [18F]DOPA accumulation in children with attention deficit hyperactivity disorder. Am J Psychiatry 1999;156:1209-15

53. Trzepacz PT. Update on the neuropathogenesis of delirium. Dement Geriatr Cogn Disord 1999;10:330-4

54. Petruzzello SJ, Landers DM. State anxiety reduction and exercise: does hemispheric activation reflect such changes? Med Sci Sports Exerc 1994 ;26:1028-35

55. Ron MA. Somatization and conversion disorders, in Neuropsychiatry. Edited by Fogel BS, Schiffer RB, Rao SM. Baltimore, Williams & Wilkins, 1996, pp 625-634

56. Rauch SL, van der Kolk BA, Fisler RE, Alpert NM, Orr SP, Savage CR, Fischman AJ, Jenike MA, Pitman RK.A symptom provocation study of posttraumatic stress disorder using positron emission tomography and script-driven imagery. Arch Gen Psychiatry 1996;53:380-387