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Sex- and diagnosis-related differences in nostril dominance may be associated with hemisphere dysfunction in affective disorders

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Aim: To investigate the differences in nostril dominance in affective disordered patients in comparison with healthy subjects.

Materials and methods: A total of 26 male and 18 female bipolar I disordered inpatients, 11 male and 15 female unipolar depressed inpatients, and 30 male and 34 female healthy control subjects were evaluated. Nostril dominance was assessed by measuring nostril airflow. Nostril airflow was measured 24 times, at 30-min intervals from 08.00 hours to 20.00 hours.

Results: Unipolar depressed patients had significantly more left nostril dominance; bipolar I disordered patients had significantly more right nostril dominance. Both right nostril dominance in bipolar patients and left nostril dominance in unipolar patients were related to female sex.

Conclusion: These results suggest that unipolar depression might be associated with left hemisphere dysfunction or hypofunction in females, in terms of the nasal cycle. However, bipolar I disorder might be associated with right hemisphere dysfunction or hypofunction in females, in terms of the nasal cycle.

Key words: Nasal cycle, nostril dominance, affective disorders, hemisphere dysfunction

Bipolar bozukluklarda burun dominansındaki farklar

Amaç: Affektif bozukluklu hastalardaki burun dominans farklılıklarını sağlıklı bireylerle karşılaştırarak ortaya koymak.

Yöntem ve gereç: Çalışmaya 26 erkek ve 18 kadın bipolar I, 11 erkek ve 15 kadın unipolar depresyonlu, ve 30 erkek ve 34 kadın sağlıklı kontrol denekleri katıldı. Burun dominansı burun hava akımı ölçülerek tayin edildi. Burun hava akımı saat 08.00 ile 20.00 arası 30 dakikalık aralıklarla 24 kez ölçüldü.

Bulgular: Unipolar depresyonlu hastalar anlamlı sol, bipolar I hastalar ise anlamlı sağ burun dominansına sahiptiler. Bipolarlardaki sağ ve unipolarlardaki sol dominanslarının her ikisi de kadınlık cinsiyeti ile ilişkili bulundu.

Sonuç: Bu bulgular unipolar depresyonun kadınlarda nasal siklusda sol hemisfer dis- veya hipo-fonksiyonunu ima etmektedir. Buna karşılık bipolar I kadınlarda sağ hemisfer dis- veya hipo-fonksiyonu ile ilişkili olabilir.

Anahtar sözcükler: Nazal siklus, burun dominansı, affektif bozukluklar, hemisfer disfonksiyonu

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Introduction

Normal lateralization involves relative left hemisphere dominance for language and motor functions and relative right hemisphere dominance for spatial processing (1). The hypothesis that schizophrenia arises from an abnormality in cerebral lateralization has gained support in recent years from studies showing abnormalities in hand, eye, and foot preferences. Anomalous brain asymmetry has been described as characteristic of psychotic disorders, in comparison with healthy subjects (2). This difference has been found in both structural (3-8) and functional (9-13) measures.

Numerous structural and functional studies have suggested that both bipolar (14-18) and unipolar disorders (19-22) may also be associated with hemisphere dysfunction or hypofunction.

The nasal cycle is a phenomenon of the alternating congestion-decongestion response in both nostrils. It manifests as greater or lesser airflow in 1 nostril compared to the other nostril, with a pattern of alternating dominance ranging from 25 min to 8 h and a peak interval between 1.5 and 4 h. The nasal cycle is regulated by the autonomic nervous system, such that unilateral sympathetic activity in the mucosa of one nostril causes vasoconstriction and decongestion, while simultaneous parasympathetic activity in the other nostril causes vasodilatation and congestion. Enhanced sympathetic activity in the mucosa of one nostril would simultaneously correspond to greater sympathetic tone and less hemispheric electrical activity in the ipsilateral hemisphere (23).

Breathing solely out of one nostril or the other is referred to as unilateral forced nostril breathing (UFNB). Werntz et al. (24,25) reported the effects of UFNB on electroencephalographic (EEG) activity in humans and demonstrated how UFNB could produce relatively greater EEG amplitudes in the contralateral hemisphere. It has been reported that UFNB may affect cognitive ability. UFNB through the left nostril is associated with enhanced spatial abilities, whereas breathing through the right nostril is associated with enhanced verbal abilities (26,27).

To date, no study has examined the association of affective disorders with the nasal cycle, and this association may have important implications. In this study, we aimed to investigate the differences in nostril dominance in unipolar depression and bipolar I disorder in comparison with healthy subjects.

Materials and methods

We evaluated 44 patients with bipolar I disorder, 26 patients with unipolar depression, and 64 healthy control subjects (Table 1). All subjects were evaluated in our medical faculty and the state hospital psychiatry inpatient clinics between January 2007 and June 2008. Informed consent was obtained from each participant. Psychiatric diagnosis for axis I disorders was made using the Structured Clinical Interview for DSM-IV (SCID-I). Healthy control subjects were selected according to the SCID nonpatient (SCID/NP) edition. Patients with severe or unstable medical illness, organic mental disorders, delusional disorders, schizoaffective disorders, and comorbid axis I disorders such as ethanol and substance addiction or anxiety disorders were not included. Patients and healthy control subjects having infection, marked nasal septum deviation, septum perforation, or other problems that could negatively influence the nasal cycle and nostril air flow were also excluded by otorhinolaryngologic examination. Hand preference was assessed by a modified version of the Edinburgh Handedness Inventory (28). Subjects having handedness scores lower than zero were considered to be left-handed; those with scores higher than zero were considered to be right-handed. Left-handed patients (n = 2) and controls (n = 4) were excluded because they were few in number.

Table 1. Some sociodemographic characteristics of the patients and controls.

Diagnosis	Sex	**n**	Mean age ± SD
Bipolar I disorder (n = 44)	Male	26	35.13 ± 10.79
	Female	18	34.50 ± 11.52
Unipolar depression (n = 26)	Male	11	36.56 ± 13.35
	Female	15	33.13 ± 12.75
Healthy controls (n = 64)	Male	30	34.56 ± 13.35
	Female	34	33.13 ± 12.75

Nostril dominance was assessed by measuring nostril airflow using the method proposed by Gertner et al. (29). A crossed glass with red dye measuring 10 × 12 cm was used. The glass was placed under the nostril horizontally. Nostril dominance was assessed by looking at the size of the bloom formed when the expired air came into contact with the glass. Nostril dominance was assessed 24 times at 30 min intervals from 0800 hours to 2000 hours. Right or left nostril dominance was calculated by a paired sample t-test using the sizes, in centimeters, of the blooms from the right and left nostrils. The lateralization index for nostril dominance was calculated by the following formula: $100 \times (R - L)/(R + L)$, where R is the mean bloom size of the right nostril (cm) and L is the mean bloom size of the left nostril (cm).

For statistical evaluation, the crosstab Pearson, nonparametric chi-square, analysis of variance, and unpaired difference tests were applied in SPSS 11.0.

Results

The difference among patient groups and healthy controls in terms of nostril dominance was statistically significant (chi-square = 25.31, df = 4, P = 0.00). The rate of right nostril dominance in bipolar disordered patients was 2.1-fold higher than that of left (chi-square = 7.14, df = 2, P = 0.03). In unipolar depressed patients, the rate of left nostril dominance was 2.14-fold higher than that of right (chi-square = 7.46, df = 2, P = 0.02). In healthy control subjects (N = 64), the rates of right (n = 14, 21.9%) and left (n = 16, 25.0%) nostril dominance were approximately equal. The majority of healthy control subjects (n = 34, 53.1%) had no lateralization in the nasal cycle (Table 2).

Although the rate of right nostril dominance was 1.71-fold higher than that of left in male bipolar I disordered patients, it was not significant. In male unipolar depressed patients, the rates of right and left nostril dominance were approximately equal (Table 3). In female bipolar I disordered patients, the rate of right nostril dominance was 2.75-fold higher than that of left (chi square = 6.33, df = 2, P = 0.04). In female unipolar depressed patients, the rate of left nostril dominance was 2.5-fold higher than that of right (chi-square = 8.4, df = 2, P = 0.02). Significant right nostril dominance in bipolar patients and significant left nostril dominance in unipolar patients were related to female sex (Table 3).

The mean difference in bipolar I disordered patients (R – L = 0.13) was significantly higher (P = 0.01) than in unipolar depressed patients (R – L = −0.19). The mean lateralization indexes of bipolar I disordered patients (index = 1.19) were significantly higher (P = 0.01) than those of unipolar depressed patients (index = −1.73) (Table 4).

Discussion

In this study, patients with unipolar depression had significantly more left nostril dominance, while patients with bipolar disorder had significantly more right nostril dominance.

Ultradian rhythms of alternating hemisphere dominance have been demonstrated in humans and other mammals during waking hours and sleep (23). Human studies have used psychological testing and EEG results as measures to identify the phases of this natural endogenous rhythm. The periodicity of this rhythm is approximately 1.5-3 h in humans during

Table 2. The number of subjects by nostril dominance in total sample.

Total sample (n = 134)	**Right** n (%)	**Right = Left** n (%)	**Left** n (%)
Bipolar I disorder (n = 44)	***23 (52.3)**	10 (22.7)	11 (25.0)
Unipolar depression (n = 26)	7 (26.9)	4 (15.4)	***15 (57.7)**
Healthy controls (n = 64)	14 (21.9)	34 (53.1)	16 (25.0)

*: significantly higher.

Table 3. The number and rate of subjects by nostril dominance in men and in women.

Subjects	Sex	Right n (%)	Right = Left n (%)	Left n (%)
Bipolar I disorder (n = 44)	Men (n = 26)	12 (46.2)	7 (26.9)	7 (26.9)
	Women (n = 18)	***11 (61.1)**	3 (16.7)	4 (22.2)
Unipolar depression (n = 26)	Men (n = 11)	3 (27.3)	3 (27.3)	5 (45.4)
	Women (n = 15)	4 (26.6)	1 (6.7)	***10 (66.7)**
Healthy controls (n = 64)	Men (n = 30)	7 (23.3)	18 (60.0)	5 (16.7)
	Women (n = 34)	7 (20.6)	16 (47.1)	11 (32.3)

*: significantly higher.

Table 4. Means of mean difference (R – L) and mean lateralization index [100 × (R – L)/(R + L)] values of bipolar and unipolar patients.

	Bipolar I disorder mean ± SD	Unipolar depression mean ± SD
Difference	0.13 ± 0.41	−0.19 ± 0.56
Index	1.19 ± 4.02	−1.73 ± 5.26

waking hours. This cerebral rhythm is tightly coupled to another ultradian rhythm known as the nasal cycle (23). Shannahoff-Khalsa et al. (23) reported that greater cognitive ability in one hemisphere corresponds to UFNB in the contralateral nostril, and cognitive performance ratios can be influenced by forcibly altering the breathing. Metaphorically, this rhythm of alternating hemisphere dominance, which is tightly and mutually coupled with the nasal cycle, can be conceptualized as cerebral breathing.

Dane et al. (30) reported that right UFNB increased and left UFNB slightly decreased systolic and diastolic blood pressures. In addition, Chen et al. (31) reported that there was a tendency for left UFNB to produce a greater decrease in arterial blood pressure in subjects with higher baseline blood pressure levels. Backon et al. (32) reported that right hemispheric activation via left UFNB led to no significant increase in intraocular pressure (IOP), whereas left hemispheric stimulation via right UFNB led to a significant decrease in IOP. They claimed that right UFNB caused functional vagotomy and that left UFNB caused functional sympathectomy. Some authors (33) also reported an average decrease in IOP of 4 mmHg by functional vagotomy via right UFNB. In addition, Backon et al. (34) reported that a functional vagotomy induced by right UFNB decreased IOP in open- and closed-angle glaucoma. Chen et al. (31) reported that right UFNB produced a statistically significant decrease in IOP, while the effect of left UFNB on IOP was not significant. Finally, Dane and Balci (35) reported that the majority of children with autism had almost continuous left nostril dominance, in comparison with healthy controls.

Both bipolar and unipolar disorders may also be associated with a hemisphere dysfunction and cerebral lateralization abnormality. Okada et al. (22) examined 36 patients with major depression to find and qualify disturbances in brain oxygenation and hemodynamics during a psychological task. They reported that the nondominant hemisphere may become dominant during the course of depression. Additionally, some studies in unipolar depression have shown structural and functional abnormalities in left hemisphere structures. Gonul et al. (20) suggested that there might be a possible defect in neuronal integrity in the left medial frontal (mainly the left anterior cingulate) cortex of patients with major depression. Lefaucheur et al. (21) suggested the existence of interhemispheric asymmetries in the frontal cortex activities of patients with unipolar

depression, in favor of a left-sided reduced excitability. Chistyakov et al. (19) found that the antidepressant effect of electroconvulsive therapy was associated with an enhancement of left hemispheric excitability. The literature suggests that unipolar depression may also be associated with a cerebral lateralization abnormality and left hemisphere dysfunction or hypofunction. Our results suggest the female-sex-related left nostril dominance in unipolar depression, which would correspond to greater sympathetic tone and less electrical activity in the left hemisphere (23), may be a factor worsening left hemisphere dysfunction or hypofunction.

Individuals with bipolar disorder exhibit motor, perceptual, and cognitive disturbances involving predominantly right hemisphere dysfunction, suggesting that the right hemisphere might be dominant in mood regulation (15). Relative functional deficits in the nondominant (generally right) hemisphere can be found in both phases of manic-depressive illness (16). The presence of both left and right hemisphere disturbances in mania may explain the coexisting psychotic and affective symptoms observed in this condition (15). Savitz et al. (18) suggested that left-hemisphere dominance in bipolar disorder is associated with right-hemisphere dysfunction, which leads to deficits in emotional regulation. Relative right hemisphere dysfunction is implicated in bipolar disordered patients. This is supported by reports of relatively greater impairment in visuospatial functioning, lateralization abnormalities, and mania secondary to right hemisphere lesions (14). A strong association between mania and direct or indirect dysfunction of the basotemporal cortex in the right hemisphere has been shown (17). The literature suggests that bipolar disorder may also be associated with a cerebral lateralization abnormality and right hemisphere dysfunction or hypofunction. Our results suggest that the female-sex-related right nostril dominance in bipolar I disorder, which would correspond to greater sympathetic tone and less electrical activity in the right hemisphere (23), may be a factor that worsens right hemisphere dysfunction or hypofunction.

As a general conclusion, it can be stated that nostril dominance may be a good index for cerebral lateralization abnormality studies in psychiatric disorders.

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