

Lateralization Pattern in Schizophrenia and Effects of Antipsychotics in This Pattern

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ABSTRACT

Lateralization pattern in schizophrenia and effects of antipsychotics in this pattern

Objective: The aim of the study was to investigate the cerebral lateralization patterns in right-handed medication-free patients with schizophrenia. We were also interested in studying the effect of antipsychotic treatment on the lateralization patterns and whether the lateralization patterns and the clinical symptoms were related.

Method: Nineteen right-handed medication-free patients with schizophrenia were compared with healthy controls on visuospatial and motor tasks with the Corsi's cube placing test, finger tapping test, and the turning preference test. Diagnosis was confirmed by SCID-I interviews based on the DSM-IV criteria. Patients were either antipsychotic-naive or free of oral medication for at least 3 weeks and 6 months for depot medications. All subjects were right-handed. Tests were repeated after 3 weeks of antipsychotic drug treatment. Laterality indices were calculated in favor of right side for all tests [(right-left)/(right+left)].

Results: The left-turning tendency was not significantly different between patients and controls. Antipsychotic treatment had no significant effect on the left-turning tendency in the patient group. There were significant differences on laterality indices of the Corsi's cube placing test, before and after antipsychotic treatment. The laterality indices on the turning and finger-tapping tests were correlated.

Conclusion: It was found that antipsychotic medication decreased right hemispatial inattention in visuospatial tasks.

Key words: Schizophrenia, lateralization pattern, antipsychotic

ÖZET

Şizofrenide lateralizasyon örüntüsü ve antipsikotiklerin bu örüntü üzerindeki etkileri

Amaç: Bu çalışmanın amacı, ilaç kullanmayan sağlak şizofreni hastalarında lateralizasyon örüntüsünü ve bu lateralizasyon örüntüsünün klinik belirtilerle ilişkili olup olmadığını, aynı zamanda antipsikotik tedavinin lateralizasyon örüntüsü üzerine etkisini araştırmaktır.

Yöntem: İlaç kullanmayan sağlak 19 şizofreni hastası, Corsi'nin küp yerleştirme testi, parmak vurma testi ve dönme eğilimi testi olmak üzere, görsel-uzamsal ve motor görevlerde sağlıklı kontrollerle karşılaştırılmıştır. Tanılar DSM-IV'e göre yapılandırılmış klinik görüşme olan SCID-I ile konulmuştur. Hastalar, hiç antipsikotik kullanmamış ya da en az 3 hafta boyunca ağızdan antipsikotik ilaç kullanmamış ve son 6 aydır da depo antipsikotik verilmemiş hastalar arasından seçilmiştir. Hastaların hepsi sağlaktır. Testler 3 haftalık antipsikotik ilaç tedavisinden sonra tekrarlanmıştır. Her üç test için sağ lehine lateralite indeksleri [(sağ-sol)/(sağ+sol)] hesaplanmıştır.

Bulgular: Hastaların ve sağlıklı kontrollerin soldan dönme eğilimleri arasında önemli bir farklılık saptanmamıştır. Antipsikotik tedavi hasta grupta, soldan dönme eğilimi üzerine önemli bir etki oluşturmamıştır. Corsi'nin küp yerleştirme testinde (sağ el), ilaç öncesi ve ilaç sonrası lateralite indeksleri arasında anlamlı bir farklılık saptanmıştır. Dönme testi lateralite indeksi ile parmak vurma testi lateralite indeksleri arasında pozitif korelasyon saptanmıştır.

Sonuç: Antipsikotik ilaç kullanımından sonra görsel-uzamsal görevlerde sağ yarı alan ihmalinin azaldığı görülmüştür.

Anahtar kelimeler: Şizofreni, lateralizasyon örüntüsü, antipsikotik

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INTRODUCTION

Etiological processes of pathophysiology of schizophrenia have not been fully understood yet. However, there are several risk factors known to cause occurrence of schizophrenia (1). Some of the schizophrenia researches were directed towards understanding the role of neurotransmitters in pathophysiology. There is a complex interaction between

different neurotransmitter systems in brain and alteration in a neurotransmitter may lead to functional impairment (2). Cognitive dysfunction seen in schizophrenia was suggested to be related with frontal lobe disorders. At the same time, it is also known that frontal lobe functions are asymmetric and there is an asymmetric dopaminergic projection towards frontal lobes (3).

Dopamine has a non-specific neuromodulator efficacy as well as its specific neurotransmitter action.

Its modulatory action at cortex emerges extensionally through mesocortical projections from ventral tegmental area to whole frontal cortex and scarcely by spreading to some other cortical areas (4).

It was suggested that dopaminergic system augments strong signals and depresses weak signals and in this way increases the ratio of specific signals at cortical neural network and background noise (signal/noise ratio) (5). According to this, dopamine has a regulatory effect particularly at frontal cortex. Dopaminergic projection to frontal lobes is impaired in schizophrenia. Sensory and motor neglect of right side of the space in patients with schizophrenia reflects the hypodopaminergic state of left hemisphere (6). Brugger and colleagues (3) proposed that balance between right and left frontal lobes is impaired, right frontal lobe functions suppress left and become prominent in schizophrenia and this condition explains mental disorders seen in schizophrenia.

Semi-Spatial Neglect: Semi-spatial neglect can be defined as impaired attention towards one side of the space. Patients with semi-spatial neglect do not pay attention to stimuli from one side of the space though not having any primary sensorial or motor loss. For example, these patients may not eat meals at one side of the plate. When requested to copy a picture, they may only copy half of it which is at the same side of the lesion (6). Semi-spatial neglect was seen in patients with brain insult and it was observed that these patients are interested only in right side of their bodies and shave only right side of their faces (7). At the same time, it was found that these patients divide the line showed to them to the right of real mid-point (8).

When visual and tactile division was done by healthy subjects, it was observed that a mid-point that is slightly on left of the real mid-point was determined and ticked by the subject himself. This phenomenon called "pseudo-neglect" is interpreted as right hemi-spatial neglect due to hypo-dopaminergic activity of left hemispheric mesocortical dopamine system. This is consistent with neglect of right side of the space (6). It was suggested that neglect of the right side is not due to over perception of stimuli from the left side but there is a congenital tendency (9). Results of the study done by

Zivotofsky and friends by conducting line-division test (10) in patients with schizophrenia using antipsychotics supported the findings indicating impairment of left hemisphere functions.

Semi-Spatial Neglect and Schizophrenia:

Lateralization of attention dysfunction in pathophysiology of schizophrenia has attracted interest in several studies. Evidence consists of observation of specific impairment in heading towards visual targets at the right visual field among the patients with schizophrenia who have not received any previous antipsychotic medication. Visual hallucinations were generally localized in right semi-field (11).

In the study of Posner et al. (12) which compared visual attention performances of patients with schizophrenia and control group, patients were found to respond a target in right visual field slower than a target in left visual field.

Rotational Asymmetry: Rotational asymmetry is to prefer to turn right or left spontaneously. This asymmetry was shown to be related with asymmetry of dopamine concentration in striatal area in rats. Rats were observed to turn to the hemisphere where dopaminergic activity is low (or contralateral side of the hemisphere with higher dopaminergic activity). Asymmetric turning preferences in these animals were suggested to be related with asymmetric dopaminergic activity between left and right frontal cortices (13-15). In a study, rotational asymmetry was observed as more rotating to left in 10 male schizophrenia patients (16). These findings support dopamine hypothesis in etiology of schizophrenia.

Relationship Between Semi-Spatial Neglect and Psychotic Symptoms:

Left-turning behavior (right motor semi-field neglect) was shown in humans as a result of neurological disorder (right fronto-parietal pathology) which may cause psychotic symptoms (17).

Bracha et al. (18) observed subjects throughout the day with a rotometer attached to their bellies to determine rotation preference and showed that left-rotational preference (i.e., right neglect) is correlated with delusions of patients with schizophrenia. Harvey

et al. (19) found that right hemi-spatial neglect is correlated with severity of psychotic symptoms.

Brugger and Graves (20) investigated in order to find out whether there is a similar relationship in healthy people as well. All participants completed the "Magical Ideation" scale which contains items for hallucinatory experiences and delusional beliefs. A correlation between severity of psychotic symptoms and right-sided inattention and between right hemi-spatial neglect and schizophrenia-like perceptual experiences was found. These findings are consistent with mesocortical dopaminergic asymmetry hypothesis of Bracha. It was also proposed that hypodopaminergy of left hemisphere causes shift of attention to left hemi-field and subsequent delusions and magical ideation (21).

Relationship Between Treatment and Semi-Spatial Neglect: In a study done by Bracha in 1987 (16), under-treated patients strongly preferred to turn to left. This preference diminished by antipsychotic treatment.

Role of antipsychotics to correct and/or reverse hemi-spatial neglect was shown in a further study. It was observed with the Mesulam Letter Cancellation Test that severely psychotic patients who were never treated or not treated at least for 26 weeks neglect right hemi-space substantially. This hemi-spatial neglect can be reversed even after a single antipsychotic dose (22).

Aims of our study in which frontal lobe functions (fine motor performance, working memory etc.) were monitored as presenting asymmetric characteristics of frontal lobes and that was done consequently by determining dopaminergic projection asymmetry by tilt test which is a behavioral test are as follows:

1. Investigating similarity of lateralization pattern in visual and motor tests.
2. Understanding whether lateralization pattern of motor and visual tests in patients with schizophrenia are different from healthy controls.
3. Investigating whether antipsychotic treatment change lateralization pattern of patients with schizophrenia.
4. Defining the relationship between lateralization pattern and clinical symptoms.

METHODS

This study was conducted with 19 outpatients and 61 healthy controls. The outpatients were admitted to psychiatry department between 1999 and 2002 and met DSM-IV criteria (23) for schizophrenia or schizophreniform disorder, did not receive any previous antipsychotic treatment or whose medication was discontinued for at least 3 weeks and who were not given any depot antipsychotic for recent 6 months.

Diagnosis of schizophrenia and schizophreniform disorder were done by Structured Clinical Interview for Axis-I Disorders (SCID-I) according to DSM-IV diagnostic criteria. Healthy individuals were taken into control group.

After the aim and impact of the study were told to patients and their relatives, informed consent was taken and those who volunteered were included in the study. Approval was also taken from Ankara University Ethical Committee.

Volunteers from second grade students of medical school were taken as control group. A significant difference was found between control and patient groups for age and duration of education. However, results were affected less from age and education as a result of calculating laterality index.

Three tests administered at Department of Physiology could not be completed by all patients and control group due to reasons such as anxiety from difficulty in adhering to tests. For this reason, number of patients and controls were found to be different for four tests.

Inclusion criteria:

1. Diagnosis of schizophrenia or schizophreniform disorder according to DSM-IV criteria.
2. No history of previous antipsychotic use or at least 3 weeks of non-medicated period for any reason.
3. No any depot antipsychotic use in the previous 6 months.

Exclusion criteria:

1. Important neurological or medical disorder, severe visual loss or orthopedic disability hindering tilt test.

2. History of severe head trauma.
3. Alcohol/substance dependence or abuse.
4. Electro-convulsive therapy in recently initiated treatment.

Scales and Tests Used in the Study

Scale for the Assessment of Positive Symptoms

(SAPS): It consists of 5 sub-scales of hallucinations, delusions, bizarre behavior, positive structural thought disorder and inappropriate mood.

Scale for the Assessment of Negative Symptoms

(SANS): It consists of 5 sub-scales of blunting or flattening of mood, alogia, reduced energy and will, anhedonia and social withdrawal and attention.

These two scales developed by Andreasen et al. (24) in 1983 are used to determine symptom severity of schizophrenia patients in the clinic. Validity and reliability of SAPS and SANS for Turkey were done by Erkoç et al. (25,26).

Magical Ideation Scale (MIS): This scale was developed by Eckblad and Chapman (27) in 1983 to examine schizophrenia-like symptoms. This scale examines hallucinations and hallucinatory experiences (i.e., I sometimes notice sounds which exist or not exist in my cassettes) and pathological beliefs (i.e., I realize people when they think about me) other than traditional ones. Turkish validity and reliability study of Magical Ideation Scale was done by Atbaşoğlu et al. (28). Subjects were asked to fill this 30-item questionnaire according to correct-incorrect chart.

Hand Dominance Questionnaire: Hand dominance questionnaire developed by Chapman and Chapman in 1987 was used to determine hand dominance of subjects. Turkish validity and reliability study was done by Nalçacı et al. (30) in 2002.

Corsi Block Placing Test: Block placing memory test specific to visuo-spatial function is based on Corsi's Block-tapping Test which was first published in 1971 (31). This test in the STIM package software produced

by Neuroscan, was arranged in such a way that it can be presented to the subjects on the computer screen (32). A version of the test was first used by Nalçacı et al. in 1997 (33) to examine accuracy in hemi-spatial fields and right hemi-spatial neglect was demonstrated in a right-handed subject group. This program allows constructing cube series at computer screen at a specific sequence in a required configuration. At each trial, a specific number of white cubes are presented at black screen simultaneously for a certain period of time. Cubes disappear from the screen at the end of the presentation and a new black screen divided into equal compartments by blue lines and each compartment having one cube. Task given to subject is to keep the locations of cubes presented in mind and locate cubes to their previous locations by computer mouse at shortest time possible.

Program automatically calculates the total number of cubes located at same areas for both right and left hands at the end of trial without considering the percentage and accuracy of cubes located correctly at right and left hemi-spaces and at total field. Accuracy scores measuring success of the test, neglect scores demonstrating neglect at fields and lateralization indices indicating the direction of neglect were calculated by using these data. Lateralization index was calculated by this formula: $([\text{accuracy at right hemi-field} - \text{accuracy at left hemi-field}] / [\text{accuracy at right hemi-field} + \text{accuracy at left hemi-field}] \times 100)$. Positive values of this index indicate more correct answers at right hemi-field and failure at left hemi-field, negative values indicate the opposite.

Letter Cancellation Test for detecting hemi-field neglect was not preferred due to possible difficulty in adherence.

Finger Tapping Test: This test has been used to evaluate fine motor performance (34,35). Computer mouse is located in a rectangular wooden platform of 10x42 cm. in this test and subjects are required to push the button of mouse as rapid as possible by their index fingers while their wrists and elbows contacting the platform. Hand used is changed after every trial which is different from other computer tests. Each trial

continues for 10 seconds. Performances of subjects were calculated by the computer which mouse was connected as tap/sec by taking mean of three trials for each hand. Dominance score was obtained by $([\text{right hand speed}-\text{left hand speed}]/ [\text{right hand speed}+\text{left hand speed}] \times 100)$ formula.

Tilt Test: It is known that humans and animals prefer a direction when rotating around their own axis (36). Rotation direction preference in humans was first measured by Bracha (16) in 1987 by a device called rotometer which is sensitive to 360 degrees rotation around axis attached to belts of subjects. Mead and Hampson (37) recorded 180 degree rotation of subjects to sounds from tapes located to four basic directions in a room in 1996. Kalaycıoğlu et al. (38) altered the method of Mead and Hampson and re-constructed it. For this test, four speakers are located at each wall of the isolated room where tests are administered. One-second duration of bell sound is given from speakers every 4 seconds in random sequence. Subjects are required to stand towards one of the speakers in the middle of the room and turn to the speaker which sound comes from.

In this study, out of 88 sounds, 24 were arranged to come from right-side of subject, 24 were arranged to come from left-side of subject and 40 were arranged to come from rear speaker. When test was started, administrator went out of the room and recorded the rotation direction of the subject to sounds by closed video monitoring system. Lateralization index of each subject was calculated by $([\text{rotation from right}-\text{rotation from left}]/ [\text{rotation from right}+\text{rotation from left}] \times 100)$ formula by using these data.

Patients with no previous antipsychotic use or stopped medications for any reason at least for 3 weeks were recruited to the study and severity of schizophrenic symptoms were assessed by Scale for the Assessment of Positive Symptoms (SAPS) and Scale for the Assessment of Negative Symptoms (SANS). Magical Ideation Scale was also administered to all subjects in order to detect schizophrenia-like symptoms. Hand-dominance questionnaire was also administered to all subjects to determine dominant hemisphere and

individuals who were found to be right-handed were included in the study. Tilt test, Corsi's cube placing test and finger tapping test were also administered to all subjects. Same tests were re-administered to subjects from patient group after medication use of 3-weeks duration.

Subjects from patient group were not able to complete all tests and scales due to various reasons. From the patient group, 14 subjects completed finger tapping test, 14 subjects completed Corsi's cube placing test and 14 subjects completed tilt test. Different subjects completed different tests. From the control group, 61 subjects completed finger tapping test, 55 subjects completed tilt test and Corsi's cube placing test.

Statistical Analysis

Group matching was done between subjects from the patient group and control group. In order to determine the significance of difference between groups when statistically appropriate, one-way analysis of variance (ANOVA), chi-square test and Mann-Whitney U test were used; to determine significance of difference pre- and post-medication use in patient group Wilcoxon test was used; and to examine the relationship between variables, non-parametric correlation coefficients were calculated.

Gender and familial left-handedness were taken as independent variables. Correlation between Magical Ideation Scale scores and all findings obtained for asymmetry of frontal lobe functions was also examined. Data obtained from patient group when medicated and non-medicated were also compared with each other. Laterality indices $([\text{right}-\text{left}]/[\text{right}+\text{left}])$ in favor of right side were calculated for tilt test, Corsi's cube placing test and finger tapping test separately and laterality indices were compared by Wilcoxon test before and after pharmacological treatment within patient groups. Differences of obtained data from control group data were tested by Mann-Whitney U method. Spearman correlation test was used to determine the relationship of each of the three tests with each other, clinical symptoms and total scores

from Magical Ideation Scale. SPSS for Windows Version 11.0 software package was used for statistical analysis. Statistical significance level was taken as $p < 0.05$.

RESULTS

Ages of 19 patients included in the study were between 14 and 62. Age range was wide due to recruitment of first episode patients and patients with chronic schizophrenia. Because laterality indices were calculated for all three tests, findings were tried not to be affected by education and age as much as possible. Laterality indices of patients were compared with indices calculated at university students with similar characteristics for gender and education (Table 1).

All 19 patients were not able to complete three tests administered at Department of Physiology due to various reasons (anxiety due to difficulty in adhering to tests). For this reason, numbers of patients for each test were different. Five patients were not able to fully

complete all three tests.

Correlations of laterality indices of tests were examined to investigate whether lateralization pattern at visuo-spatial and motor tests measuring laterality characteristics in patients and controls were similar or not.

Laterality indices of tilt test and finger tapping test were found to be correlated in patients ($r=0.62$, $p=0.007$).

No correlation was found between laterality index of tilt test and laterality index of Corsi's cube placing test (Corsi's cube placing test right hand [$r=0.00$, $p=0.99$], Corsi's cube placing test left hand [$r=0.27$, $p=0.35$]). This finding may suggest that mechanisms of asymmetry of motor tasks and visual-spatial tasks are different. A positive correlation between Corsi's cube placing test (left hand) and Corsi's cube placing test (right hand) in healthy controls ($r=0.40$, $p=0.002$) (Table 2).

Statistically significant difference was found in Corsi's cube placing test (right hand) which 10 out of 14 patients completed and correct placing of cubes were

Table 1: Socio-demographic characteristics of patient and control group

	Patients (n=20)	Control group (FTT,CPT) (n=62)	Control group (TT) (n=83)	
Gender (F/M)	11/9	32/30	45/38	$p > 0.05$
Age	27.75 ± 12.39	20.19 ± 1.88	19.88 ± 1.37	$F=15.76$, $p < 0.001^*$
Duration of Education (year)	10.10 ± 2.45	12.00 ± 0.00	12.00 ± 0.00	$F=45.16$, $p < 0.001^{**}$

FTT: Finger Tapping Test, CPT: Cube Placing Test, TT: Tilt Test, F: One way analysis of variance

*Mean age of patients was higher than both control groups, ** Education duration of patients was shorter than both control groups

Table 2: Correlations of three tests assessing laterality characteristics of right-handeds

	Laterality index at finger tapping test *		Laterality index at Corsi test* (right hand)		Laterality index at Corsi test* (left hand)	
	Patients	Controls	Patients	Controls	Patients	Controls
Laterality index at Corsi test* (right hand)	$r=-0.19$ $n=13$ $p=0.53$	$r=-0.27$ $n=54$ $p=0.048$				
Laterality index at Corsi test* (left hand)	$r=-0.09$ $n=13$ $p=0.76$	$r=-0.24$ $n=54$ $p=0.079$	$r=0.44$ $n=12$ $p=0.14$	$r=0.40$ $n=55$ $p=0.002$		
Laterality index at tilt test*	$r=0.62$ $n=14$ $p=0.007$	-	$r=0.00$ $n=14$ $p=0.99$	-	$r=0.27$ $n=14$ $p=0.35$	-

*Favors right ([Right-left] / [Right+left]), $p < 0.001$

Table 3: Laterality indices of right-handed patients in three tests before and after medication

	Before medication Mean±SD	After medication Mean±SD	z	P
Laterality index in finger tapping test* (n=14)	8.83±5.96	9.71±5.61	z=-0.03	p=0.97
Laterality index in Corsi test* Right hand* (n=10)	-20.17±25.26	-11.41±14.78	z=-2.66	p<0.01
Laterality index in Corsi test * Left hand* (n=10)	-8.33±10.81	-8.41±11.66	z=-1.75	p=0.08
Laterality index in tilt test*	-4.98±50.21	-17.39±51.35	z=-1.56	p=0.12

*Favors right ([Right-left] / [Right+left]), z: Wilcoxon index test

taken into consideration before and after medication (3 weeks after treatment was initiated) ($z=-2.66$, $p<0.01$). This condition indicates that right hemi-field neglect decreased after medication use. No difference was found between laterality indices of other tests (in favor of right [Right-left]/[Right+left]) which patients completed before and after medication (Table 3).

In rotational preference test, laterality indices were found -4.98 ± 50.21 (mean±SD) in patients and -22.29 ± 37.03 in controls. No significant difference was found between patients and control group for tendency to turn left ($z=-1.26$, $p=0.21$).

No significant difference was found between right-handed patients and control group at finger tapping test ($z=0.66$, $p=0.51$).

In Corsi's cube placing test, no significant difference was found between laterality indices of patients and control group (Corsi's cube placing test [right hand]-controls comparison [$z=-0.97$, $p=0.33$]), (Corsi's cube placing test [left hand]-controls comparison [$z=-0.05$, $p=0.96$]).

In drug-naive right-handed patients, no significant correlation between laterality characteristics and clinical symptoms was found. This finding may be due to low number of subjects. Correlation between laterality index of Corsi's cube placing test (left hand) and SAPS Thought Flow Impairment sub-scale scores ($r=0.46$, $p=0.13$) and correlation between Corsi's cube placing test (right hand) and SANS Attention sub-scale scores were found high ($r=-0.55$, $p=0.06$).

No significant correlation was found between laterality characteristics and clinical symptoms in medicated right-handed patients. However, a positive correlation close to significance was found between Corsi's cube placing test (left hand) and SAPS Thought

Flow Impairment sub-scale scores ($r=0.78$, $p=0.07$).

No significant correlation was found between laterality indices and Magical Ideation Scale scores in right-handed controls.

DISCUSSION

In our study, presence of an asymmetry in visuo-spatial attention and rotational direction preference in right-handed patients with schizophrenia, relationship between asymmetry and clinical symptoms and difference from healthy controls were investigated.

There are some visuo-spatial and tactile-kinesthetic study findings which suggest that hemi-spatial neglect may exist more than controls in patients with schizophrenia (6,39).

In our study, relationship between asymmetry in motor tasks and asymmetry in visuo-spatial functions were investigated. Laterality index of tilt test was found to be correlated with laterality index of finger tapping test but not with laterality index of Corsi's cube placing test. This finding suggests that asymmetry mechanisms of motor tasks and visuo-spatial functions are different. No data supporting this difference was found in the literature.

There are studies aimed to show the role of antipsychotics in correcting or reversing hemi-spatial neglect. Hemi-spatial neglect was shown to reverse even after a single antipsychotic dose (22). A statistically significant difference was found in Corsi's cube placing test (right hand) before and after (3 weeks after) medication was started in our study. This finding indicates that right hemi-spatial neglect decreases after medication use. However, no difference was found in left-rotation tendency of patients before and after

medication use.

Drug-naive patients with schizophrenia were shown to neglect right hemi-space compared to controls by cancellation test (10,22). It was proposed that brain cortical activity is asymmetric between hemispheres and right or left rotation preference of the individual is affected by dopamine asymmetry (16).

In our study, tests to detect asymmetry were administered to same patient group in order to detect relationship between asymmetry of rotation preference and asymmetry of visuo-spatial attention which has not been studied in the same patient group. No significant difference was found for left-rotation preference between control group and patients. Indifference of left rotation preference between patient and control groups is inconsistent with previous study findings. This may be due to different assessment method of left-rotation preference. Bracha et al. (18) monitored subjects throughout the day by a rotometer attached to their belts to determine their rotation preference and showed a correlation between left-rotation preference (i.e., right-neglect) and hallucinations of patients with schizophrenia.

Several studies investigating asymmetry of visuo-spatial attention in patients with schizophrenia were done. In a study, visual attention performances of patients with schizophrenia and control group were compared and patients with schizophrenia were found to respond slower to targets in right visual field than left (12).

In our study, we used Corsi's cube placing test which we thought to be an appropriate test to study visuo-spatial attention asymmetry. Although no difference was found in laterality indices between patients and control group at Corsi's cube placing test, this insignificant difference was thought to be due to low number of subjects. This indicates that a significant difference may be found if these studies continue.

In our study, no significant difference was found between asymmetry in rotational preference and visuo-spatial functions and clinical symptoms. This finding may be due to low number of subjects. However, a positive correlation close to significance between laterality index of Corsi's cube placing test (right hand)

and SAPS thought flow sub-scale scores was found. This positive correlation suggested that similar pathophysiological changes may have different symptoms. Correlation between visuo-spatial functions and impairment in thought flow support impairment in both lateralizations of linguistic functions and dominance pattern in general in schizophrenia. This correlation indirectly supports the theory which connects speech disorder with weakness of dominance pattern of brain (40).

Studies showed that left-rotation preference and severity of psychotic symptoms are correlated (18,19). In our study, no significant correlation was found between right hemi-spatial neglect and clinical symptoms; this may be due to low number of subjects.

Eckblad and Chapman (27) reported the relationship between scores from Magical Ideation Scale and right hemi-spatial neglect in rod division test. Other studies also reported a relationship between right hemi-spatial neglect and schizophrenia-like perceptual experiences (19,41). Results of this study are not consistent with the literature. Scores of Magical Ideation Scale which is administered in healthy individuals and provides detection of schizophrenia-like symptoms and laterality indices of finger tapping test and cube placing test were compared and no significant difference was found between them. This may be due to low number of subjects.

CONCLUSION

Important difficulties were encountered when implementing the study. Many practical difficulties were observed while administering these tests to patients due to low treatment adherence and incooperation with physicians which are the nature of psychopathological symptoms present in patients with schizophrenia. Difficulty in finding drug-naive schizophrenia patients and in adherence of them to tests due to various reasons are difficulties limiting number of subjects in the study. Increasing anxiety due to difficulties of tests caused many patients not completing the tests.

Several controlled studies are needed in order to

conclude to clear results after evaluating these findings. Sample size should be expanded to obtain significant statistical findings. Corsi's cube placing test is an appropriate test to study visuo-spatial attention asymmetry so studies on this test should be maintained.

It is clear that by studies to enlighten pathophysiology

of schizophrenia, more accurate and beneficial findings can be obtained and its etiology can be clarified. Despite having three tests, increased anxiety due to difficulties in tests and not being able to complete all tests, results of this study are promising to require expanding the sample.

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