

Cognitive function in Brazilian right-handers schizophrenia patients and healthy volunteers

Desempeño cognitivo de pacientes esquizofrénicos diestros y voluntarios saludables

Sônia Beatriz Cócara de Souza^I; Natália Soncini^{II}; Suzana Schönwald^{III}; Márcia Lorena Fagundes Chaves^{IV}

^IMSc, Assistant Professor, School of Nursing and Graduate Program in Physiology, Universidade Federal do Rio Grande do Sul, Brazil

^{II}Graduate Program in Psychiatry, Universidade Federal do Rio Grande do Sul, Brazil

^{III}MD, MSc, Neurology Service, Hospital de Clínicas de Porto Alegre, Brazil

^{IV}MD, PhD, Associate Professor, Behavioral Sciences Program, Graduate Program in Internal Medicine, Universidade Federal do Rio Grande do Sul; and Neurology Service, Hospital de Clínicas de Porto Alegre, Brazil

[Correspondence](#)

ABSTRACT

GOAL: We hypothesized that right-handers schizophrenia patients would be more probable to present the normal brain asymmetry, and therefore their cognitive function could be more similar to that of the normal controls. Thus, the present study aims to compare the cognitive functioning between right-handed schizophrenic patients and normal right-handed comparing group, balanced by sex, educational level, and socioeconomic situation. **METHODS:** Twenty-five (12 men and 13 women) right-handed schizophrenia patients and 35 (19 men and 16 women) right-handed young adults were included in a cross-sectional design. The manual preference was evaluated with the Edinburgh Handedness Inventory, and cognitive performance with a series of neuropsychological tests. Family history of left-handedness and educational attainment were also analyzed. **RESULTS:** The right-handed schizophrenia patients showed poorer performance in 10 of 12 cognitive tests. Cognitive deficit (scores below cutoff in 50% of tests) was present in 60% of the patients with schizophrenia. Among demographic and clinical variables, only diagnostic category and

educational level showed significant association with cognitive deficit in a logistic regression analysis. Family history of left-handedness and educational attainment were similar between groups. **CONCLUSION:** These findings suggested a more diffuse impairment of the cognitive functions, including language, among right-handed schizophrenia patients. Their performance was significantly different from that of the normal group. Our hypothesis of cognitive similarity between right-handed schizophrenics and healthy individuals was refuted.

Keywords: Schizophrenia, manual preference, cognitive function, laterality.

RESUMEN

OBJETIVO: El presente estudio examinó la hipótesis de que pacientes esquizofrénicos diestros puedan presentar asimetría cerebral normal y, por lo tanto, un desempeño cognitivo similar al de los controles normales. De esta forma, el objetivo de este estudio ha sido comparar el funcionamiento cognitivo entre pacientes esquizofrénicos y controles normales diestros, balanceados para sexo, nivel educacional y situación socioeconómica. **MÉTODO:** Se incluyó a 25 pacientes esquizofrénicos diestros (12 hombres y 13 mujeres), y 35 adultos jóvenes diestros (19 hombres y 16 mujeres) en un delineamiento transversal. La preferencia manual ha sido evaluada por el Test de Dominancia Lateral Edimburgo, y el desempeño cognitivo por una batería de pruebas neuropsicológicas. Además, se analizó el histórico familiar de siniestralidad y el nivel educacional. **RESULTADOS:** Los pacientes esquizofrénicos diestros presentaron desempeño inferior en 10 de las 12 pruebas psicológicas. Se observó déficit cognitivo (resultados inferiores a los puntos de corte en el 50% de las pruebas) en el 60% de los pacientes esquizofrénicos. Entre las variables clínicas y demográficas, solo categoría diagnóstica y nivel educacional evidenciaron una asociación significativa con el déficit cognitivo a través del análisis de regresión logística. La historia familiar de siniestralidad fue similar entre los dos grupos, así como el nivel educacional. **CONCLUSIÓN:** Esos hallazgos sugieren que los pacientes esquizofrénicos diestros presenten un perjuicio más difuso de las funciones cognitivas, incluso el lenguaje, significativamente distinto de los controles normales. Nuestra hipótesis, por lo tanto, de que hubiera una semejanza cognitiva entre esquizofrénicos diestros e individuos normales ha sido rechazada.

Palabras clave: Esquizofrenia, preferencia manual, función cognitiva, lateralidad.

INTRODUCTION

Human handedness - the consistent preference for one hand in skilled manipulative tasks - is often said to be a defining trait. While other primates may demonstrate individual preferences for the right or left forelimb in reaching and in manipulating objects, only in human populations is there a consistent tendency for the right hand to be the preferred hand.¹

Around 90% of the population use the right hand to write, and 10% the left hand; 60% choose the right hand for all types of activity, 30% present inconsistent or mixed manual preferences, and just 5% are actually pure left-handed.² Hand preference is perhaps the most evident behavioral asymmetry observed in humans derived from cerebral anatomic and physiological asymmetry.³ Anatomic brain asymmetries that may be associated with hand preference have not been extensively studied, and no clear relationship between asymmetry of the motor system and hand preference has been established. Although no direct measure of motor dexterity and skill was performed, there were data suggesting relation between anatomic asymmetry of the motor hand area and hand preference.

The *planum temporale*, a normally asymmetric area lying on the superior part of the temporal lobe, is intimately involved in the generation and understanding of language⁴ and has been suggested to be a key area affected in schizophrenia.⁵ A striking reversal of the normal asymmetry (left larger than right) in *planum temporale* surface area was observed in almost all schizophrenic patients.⁶ Severity of thought disorder in the patients was related to asymmetry. This was a clear demonstration of a reversal of expected symmetry in the brains of right-handed schizophrenic

patients, which involves a region of key importance in normal human behavior. The nature of the abnormality strongly suggests that schizophrenia is a neurodevelopmental disorder.⁶⁻⁹

The notion that psychotics, particularly schizophrenics, may be less right-handed than the general population and that this deviation is pathophysiologically important still persists. However, relationships between handedness and specific psychopathology are still uninformative, and handedness may not be an important consideration in the study of psychosis.

We hypothesized that right-handers schizophrenia patients would be more probable to present the normal brain asymmetry, and therefore their cognitive function could be more similar to that of the normal controls. Consequently, the objective of the present paper was the analysis of cognitive function among right-handers schizophrenia patients and healthy volunteers balanced in terms of sex, educational attainment, and familial socioeconomic background.

MATERIAL AND METHODS

Of the sixty schizophrenia patients registered at the Schizophrenia Outpatient Program from Hospital de Clínicas de Porto Alegre (RS, Brazil), twenty-five (12 men and 13 women) were included (DSM-IV criteria for schizophrenia - by certificate psychiatrist) in a cross-sectional design. Those who presented medical disorders, fulfilled criteria for psychiatric hospitalization, and abuse of alcohol or drugs were excluded. Patients kept their regular use of anti-psychotics ([table 1](#)). The healthy subjects were 35 individuals (19 men and 16 women) selected at the same location (students, employees, and caregivers) to match patients in terms of sex, educational attainment, and familial socioeconomic background - balanced groups ([table 2](#)). Family history of left-handedness was similar between groups.

Table 1 - Daily range of antipsychotic drugs and number of schizophrenic patients in use of

Drugs	Daily dosage	N
Haloperidol	5-10 mg	9
Clozapine	300-700 mg	2
Chlorpromazine	300-400 mg	5
Risperidone	6-9 mg	3
Thioridazine	100-400 mg	2
Levomepromazine	300-400 mg	4

Table 2 - Demographic data of schizophrenia patients and healthy volunteers

Variable	Schizophrenia (N = 25)	Healthy (N = 35)	p value
Age (years \pm SD)*	33.28 \pm 7.11	25.31 \pm 6.19	0.01
Educational attainment (years \pm SD)*	12.00 \pm 2.69	13.49 \pm 2.65	0.04
Sex – M/F**	12/13	19/16	0.83
Parent history of handedness – R/L**	18/07 (72/28%)	28/07 (80/20%)	0.68
Social class**			0.019
A	2 (8%)	12 (34.3%)	
B	7 (28%)	12 (34.3%)	
C+D	16 (64%)	11 (31.4%)	

* Student's t test

** Chi-square test

Sample size was supported by the rate of the general population's cognitive deficit (5%), an estimated relative risk of 5 for schizophrenia, and a ratio unexposed: exposed of 2:1. Size estimation for cross-sectional studies was processed using the Epi-Info 6.4 software, with alpha and beta errors of 5% and 20%, respectively.

The project was approved by the Research Ethics Committee of Hospital de Clínicas de Porto Alegre. All participants and/or their legal informant signed an informed consent form after the nature of all procedures and ethical guarantees were fully explained.

Neuropsychological evaluation

The neuropsychological tests applied were the Mini Mental State Examination¹⁰ (cutoffs 24 and 17 for education \leq 4 and $>$ 4 years, respectively), Digit Span¹¹ (cutoff 5), Word Span¹² (cutoff 4), Spatial Recognition Span¹³ (cutoff 8), Wechsler's Visual Association test and Logic Memory test (short history)¹⁴ (cutoff 4), Token Test¹⁵ (cutoff 30) and Rey-Osterreich Complex Figure¹⁶ (cutoff 20). The study team was composed of a psychiatric nurse, a psychologist, a certified psychiatry, and a neurologist (all previously trained for the applied instruments). Cognitive tests were applied by the psychologist. The handedness instrument was applied by the psychiatric nurse and the neurologist. Cognitive deficit was defined by impaired performance in 50% of the applied tests following an epidemiological strategy.⁹ The three main areas of cognition that are commonly evaluated are intelligence, memory and language.⁵ We have focused memory and language for the evaluation of cognition of groups of same manual preference when classified by an adequate instrument.

Edinburgh inventory

The abbreviated version of the Edinburgh Handedness Inventory¹⁷ was used for the evaluation of manual preference, consisting of 10 behavioral tasks (writing, drawing, throwing a ball with one hand, lighting matches, opening a box, using a knife, a toothbrush, a sweeper, a pair of scissors, and a spoon). The Inventory has already been studied in Brazilian adults.¹⁸ The Inventory scores varied from +100 to -100, and highly left-handers are those who scored from -100 to -40, mixed from -40 to +40, and highly right-handers above +40. The present study selected only right-handers (Edinburgh $>$ 40).

Statistical analysis

Demographic parametric data were analyzed by Student's t test, and categorical variables with chi-square test. Multivariate analysis was carried out by ANOVA, after the normal plotting options tested viability of variables for parametric analysis. The study variables were included in a multivariate logistic regression, following the stepwise backward procedure for the analysis of association with cognitive deficit. A p value of less than 0.20 was required for a factor to be retained in the analysis. Values were considered significant when the type-I error (p) was below or equal to 0.05. Data storage and all procedures were carried out using the Statistical Package for the Social Sciences (SPSS/PC+) and the EPI-INFO 6.4 softwares.

RESULTS

As mentioned on Methods, [table 2](#) shows demographic data of groups. Schizophrenia patients were older ($p = 0.01$) than normal subjects. On the other hand, normal individuals presented higher educational attainment ($p = 0.04$).

[Table 3](#) shows the cognitive performance of patients and healthy controls. Of the twelve neuropsychological tests, 10 presented statistical difference between patients and controls. The Mini Mental State Exam ($p = 0.058$) and the Visual Recognition Span ($p = 0.119$) were those without significant difference between groups. The Token test, and the copy and recall of the complex figure of Rey-Osterreich were the tests with higher variability within schizophrenia group, however healthy controls also showed great variability in the recall of the Rey-Osterreich figure.

Table 3 - Mean and standard deviation of scores of cognitive tests (confounders - age and education - controlled by ANOVA with covariance)

Test	Schizophrenia	Healthy	p value
	(N = 25)	(N = 35)	
MM	25.73 ± 3.56	28.43 ± 1.56	0.058
DS	4.62 ± 1.81	6.33 ± 2.82	0.009
WS	4.89 ± 1.53	7.03 ± 1.59	0.002
C-F 1	2.15 ± 1.80	4.30 ± 1.98	0.006
C-F 2	2.42 ± 1.60	5.49 ± 1.73	0.000
C-F 3	2.12 ± 1.84	4.87 ± 1.89	0.001
VRS	7.68 ± 2.87	9.24 ± 3.75	0.119
LM 1	4.08 ± 2.33	6.96 ± 1.50	0.000
LM 2	3.42 ± 2.23	6.89 ± 1.38	0.000
TOKE N	29.76 ± 6.29	33.77 ± 1.90	0.029
REY C	27.39 ± 8.92	34.76 ± 1.91	0.000
REY R	8.69 ± 6.70	26.72 ± 6.81	0.000

MM = Mini Mental; DS = digit span; WS = word span;
 C-F 1 = color-form association – immediate recall;
 C-F 2 = color-form association – second recall;
 C-F 3 = color-form association – third recall;
 VRS = visual recognition span;
 LM 1 = logic memory – immediate recall;
 LM 2 = logic memory – recent recall; TOKEN = Token Test;
 REY C = Rey-Osterreich figure – copy;
 REY R = Rey-Osterreich figure – recall.

Of the 25 schizophrenic patients, 15 (60%) presented cognitive deficit by the applied strategy and none of the healthy subjects did.

The scores of all, but the ball, tasks were not different between schizophrenic patients and controls ([table 4](#)). The behavioral tasks ball (B = 6.017, beta = 0.24, p = 0.000) and knife (B = 5.55, beta = 0.23, p = 0.311) presented correlation to educational attainment. More years of education contributed to increase the use of the right hand for these activities.

Table 4 - Mean and standard deviation of the Edinburgh Handedness Inventory and its items (Student's *t* test for independent samples)

Test	Schizophrenia (N = 25)	Healthy (N = 35)	p value
EDINBURG	82.09 ± 14.19	86.49 ± 15.32	0.252
WRI	100.00 ± 0.00	94.60 ± 32.88	0.406
DRAW	92.31 ± 39.22	94.60 ± 32.88	0.803
BALL	68.97 ± 39.30	100.00 ± 0.00	0.000
SCIS	100.00 ± 0.00	95.94 ± 24.66	0.406
TOOTH	97.44 ± 13.08	100.00 ± 0.00	0.236
KNIF	100.00 ± 0.00	93.24 ± 33.67	0.311
SPOO	100.00 ± 0.00	98.65 ± 8.22	0.406
BROOM	30.77 ± 97.03	33.78 ± 92.09	0.901
MAT	92.31 ± 39.22	89.19 ± 45.84	0.779
BOX	64.74 ± 61.78	62.16 ± 73.98	0.885

EDINBURG = Edinburgh Handedness Inventory total score;

WRI = writing; DRAW = drawing;

BALL = throwing ball with one hand; SCI = using scissor;

TEETH = brushing teeth; KNIF = using knife;

SPOO = using spoon; BRO = using a broom;

MAT = lighting a match; BOX = opening a box.

The association between cognitive deficit and the variables social class, educational attainment, sex, age, family history of left-handedness, diagnostic group (schizophrenia and control), and the Edinburgh Handedness Inventory was analyzed by logistic regression analysis ([table 5](#)). It revealed that diagnostic group (schizophrenia and control) (OR = 9.97) and educational attainment (OR = 1.3) were the only variables presenting a coefficient and standard error significant for the association with cognitive deficit, although the 95% confidence limits of the odds ratio for education included 1. The model rejected all other variables because they did not present significance for the outcome.

Table 5 - Results of stepwise backward logistic regression analysis of the association between

	B	S.E	p value	R	Odds ratio	95%CI
Variable in the equation						
Educational attainment	0.308	0.152	0.043	0.162	1.36	0.11-4.81
Diagnostic group	9.301	1.705	0.000	0.394	9.97	5.96-12.64
Constant	-1.795	1.795	0.304	-	-	-
Variable not in the equation						
Age	0.203		0.652	0.000		
Social class	0.766		0.381	0.000		
Sex	0.762		0.383	0.000		
Handedness family history	0.025		0.873	0.000		
Edinburgh Inventory	0.203		0.652	0.000		

The partial correlation is expressed by the R statistic, ranging from -1 to +1.

DISCUSSION

Our study evaluated patterns of cognitive performance of right-handed schizophrenia patients and normal controls. The hypothesis under investigation was that right-handers schizophrenia patients would present cognitive function similar to normal controls. However, patients performed significantly worse than the comparison subjects on every neuropsychological variable, except the digit span and the first recall of the color-form association test. Cognitive deficit, defined by impairment in 50% of the cognitive tests,⁸ was observed in 60% (N = 15) of the schizophrenic patients and in none of the healthy subjects. These findings suggested a more diffuse impairment of the cognitive function, including language. Other authors have agreed upon the existence of a global cognitive deficit in schizophrenia.¹⁹ The greatest relative impairments on the Wechsler Adult Intelligence Scale-Revised digit symbol and comprehension subscales, are congruent with others demonstrating that significant cognitive and motor impairment across multiple ability domains is a core characteristic of schizophrenia, and is not caused by chronic illness, treatment, or institutionalization.²⁰

Patients with schizophrenia have a generalized deficit that is not easily explained by a single anatomical region or ability area. However, many researches strongly suggested specific memory dysfunction in schizophrenia that may be neither drug induced or secondary consequences of attentional disorders, indicating that those deficits deviate from normal function in a relatively stable way.^{21,22} But there are a number of uncertainties in interpreting such deficits. Schizophrenics showed a significant decrease in memory test performance, compared with both normal controls and other psychiatric patients.²³ Chronic schizophrenics seem to be characterized by qualitatively different memory functioning compared with non-chronic subjects. In a free recall task, chronic subjects showed significantly decreased performance for the initial (primacy) and final (recency) items.²⁴ Memory functioning was not correlated with performance on the Wisconsin Card Sorting Test indicating a selective cognitive dysfunction of an amnesic nature in chronic schizophrenics.¹³ Some deficits found in schizophrenics seem to be symptom-related and other dysfunctions might be vulnerability indicators.²⁵ On the other hand, information-processing deficits do not seem to be specifically related to schizophrenia.

Schizophrenia is among the most severe and debilitating of the psychiatric disorders. Diagnosis is currently done by criterion-based classifications, including positive (e.g., hallucinations and delusions) and negative (e.g., avolition and alogia) symptoms. The importance of negative

symptoms in the course and outcome of the illness has been increasingly studied. Current research seeks to detect causal mechanisms in schizophrenia through studies of neural connectivity and function, as well as models of genetic transmission, such as polygenic models of inheritance in genetic research.^{2,26} Potential genes have been identified that may confer vulnerability to the illness, perhaps in conjunction with environmental factors. Since its earliest conception as a 'dementia praecox' (i.e. early-onset dementia), impaired cognitive function has also been considered a core feature. Clear evidence to suggest that cognitive dysfunction is intrinsic to schizophrenia, however - rather than the result of chronic illness, institutionalization or medication - is only now emerging: cognitive deficits are already present in adolescents at risk for schizophrenia and in untreated first-episode schizophrenic patients.²⁷ Moreover, cognitive performance does not deteriorate over the first few years of illness when patients are treated.

Edinburgh Handedness Inventory

In the present study, the items ball, scissors and box of the Edinburgh Handedness Inventory, correlated with years of schooling. Higher education conferred 30 to 40% the use of the right-hand in these behavioral tasks. The formal training in school and related activities (i.e., sport, art) during childhood and adolescence may induce individuals to use the right hand, because most of their kins did (as throwing a ball), or the object available was the type made for right-handers (as scissors).

The analysis of the tasks of the Handedness Inventory showed that the ball was the only item from the Edinburgh Inventory significantly different between controls and schizophrenia patients. All controls used the right hand, while 15 (60%) schizophrenics used the right hand and 11 (44%) used the right and the left hands (mixed). This difference may be explained by the difficulties schizophrenia patients may have experienced as early as during childhood for the practice of sports and other recreations, resulting in less training.

Different methods of dividing subjects into handedness groups include preference (a 12-item questionnaire), performance (speed, strength, dexterity), and preference plus performance, and they are significantly intercorrelated.^{13,14} These handedness measures have evidenced significant correlation with a dichotic test (for lateral specialization), and ambidextrous subjects performed as well as right- or left-handers on unimanual tasks despite a lack of hand preference. An investigation with 14 patients and 14 normal controls demonstrated association between mixed handedness and schizophrenia.¹⁵ The hand used for writing has shown to be too limited to be used as the sole index of handedness in studies related to cognition.

We observed similar parent handedness in both groups. This aspect was already observed in a previous study.²⁸ Furthermore, the study of Grosh et al.²⁹ suggested that schizophrenics and their parents have similar abnormalities in hemispheric activation at baseline, but when exposed to stimuli with negative emotional valence, only schizophrenics demonstrated a further decrease in left hemispheric activation. Hecaen & Sauguet³⁰ reported that, according to a handedness inventory measure, familial sinistrality among left-handers (brain-damaged patients) was associated with weak left-handedness. Degree of left-handedness has not showed general relationship to familial sinistrality, suggesting weak influence of family sinistrality upon performance of manual preference of primary or secondary left-handers.³¹

The analysis of association of all variables with cognitive deficit showed diagnosis and education as the variables significantly related to deficit. The chance of a schizophrenia patient to present cognitive deficit was 10 times higher than a comparing subject of same educational level. Schizophrenia is often associated with cognitive deficits, particularly within the domains of memory and language. Specific cognitive deficits have recently been linked to psychotic phenomena, including verbal hallucinations and disorganized speech. Impairments of working and semantic memory are primarily due to dysfunction of the frontal cortex, temporal cortex, and hippocampus. Cognitive skills in schizophrenia predict social functioning and may serve as outcome measures in the development of effective treatment strategies.¹⁶

Study limitations

The main limitation of our study is the relative small number of participants (N = 60) for the logistic regression, which requires at least 100 participants for more accurate results. However, our main hypothesis was tested with the comparison of performance between groups ([Table 3](#)), and the

identification of cognitive deficit with the application of the 12 tests (requiring deficit in 50% of them).

Further investigation with a sample of mixed and left-hander patients with schizophrenia are necessary for a more clear comprehension about the patterns of cognitive abilities related to hand preference, i.e., the cerebral anatomic and physiological asymmetry and the anomalous lateralization in schizophrenia.

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Correspondence to

Márcia Lorena Fagundes Chaves
Serviço de Neurologia - Hospital de Clínicas de Porto Alegre
Rua Ramiro Barcelos, 2350, sala 2040
CEP 90035-903 - Porto Alegre - RS - Brazil
Phone: (+55-51) 2101-8520
E-mail: mchaves@plugin.com.br, sbcs@terra.com.br

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Sociedade de Psiquiatria do Rio Grande do Sul

Av. Ipiranga, 5311/202
90610-001 Porto Alegre RS Brasil
Tel./Fax: +55 51 [3024-4846](tel:+555130244846)

 e-Mail

revista@aprs.org.br