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Sensitivity and specificity of a neuropsychological instrument in the evaluation of schizophrenia subtypes: a study with a spanish speaking population

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Introduction. Cognitive impairment is a prominent feature of schizophrenia that correlates with functional outcome. In the clinical practice and research, there is a need to count on brief, reliable and standardized instruments to evaluate the cognitive profile in psychiatric, geriatric and neurological patients. There are only a few standardized and validated instruments with the Hispanic population, so the adaptation and validation of instruments become a high relevance issue. The Brief Neuropsychological Test in Spanish (NEUROPSI) is a brief neuropsychological battery evaluating a wide spectrum of cognitive functions and standardized with Spanish speaking population according to age and educational level. The purpose of the present study was to determine the sensitivity and specificity of this instrument for its clinical use in patients with schizophrenia, as well as in distinct subtypes of schizophrenic patients: positive, negative and mixed.

Methods. We studied a total sample of 60 subjects (30 patients with schizophrenia and 30 matched controls). Using the total score we found 87.5% sensitivity and 92.8% specificity. A discriminant analysis using the 25 subtest scores of the NEUROPSI accurately classified 83.3% of the sample. None of the control subjects was classified as patient.

Results. Classification by subtype showed 80% of patients with negative symptoms, 90% of patients with positive symptoms and 70% of patients with mixed symptoms.

Conclusions. The accurate diagnosis of cognitive dysfunction in schizophrenic patients could help in management as well as development of more specific pharmacological treatment for each schizophrenic subtype.

Key words:
Neuropsychology diagnosis. Sensitivity. Specificity. Schizophrenia. Subtypes.

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Sensibilidad y especificidad de un instrumento neuropsicológico en la evaluación de subtipos de esquizofrenia: un estudio con población hispanohablante

Introducción. Las alteraciones cognoscitivas son una característica de la esquizofrenia y se correlacionan con el pronóstico funcional del paciente. Tanto en la práctica clínica como en investigación es importante poder contar con instrumentos breves, objetivos y confiables que permitan evaluar el perfil cognoscitivo de esta población. Existen muy pocos instrumentos estandarizados y validados con población hispanohablante, por lo que la adaptación y validación de instrumentos es de alta relevancia. La Evaluación Neuropsicológica Breve en Español (NEUROPSI) es un instrumento de tamizaje adaptado, validado y estandarizado en población hispanohablante. El objetivo del presente estudio fue evaluar la sensibilidad y especificidad del NEUROPSI para evaluar el perfil cognoscitivo de un grupo de pacientes esquizofrénicos, así como valorar la clasificación de acuerdo a los subtipos: positivos, negativos y mixtos.

Métodos. Se estudió una muestra total de 60 sujetos (30 sujetos control y 30 pacientes esquizofrénicos). Utilizando la puntuación total del NEUROPSI se encontraron valores del 87,5% de sensibilidad y del 92,8% de especificidad. El análisis discriminante en el se incluyó las 25 subpruebas clasificó correctamente al 83,3% de los sujetos. Ningún sujeto del grupo control se clasificó como paciente.

Resultados. La calificación por subtipos fue: 80% de esquizofrenia con síntomas negativos, 90% esquizofrenia con síntomas positivos y 70% esquizofrenia con síntomas mixtos.

Conclusiones. Determinar las alteraciones cognoscitivas que están asociadas con las anormalidades en la esquizofrenia puede ayudar al manejo de los pacientes y en el desarrollo de tratamientos farmacológicos más específicos para rehabilitar los procesos cognitivos alterados en cada subtipo.

Palabras clave:
Diagnóstico neuropsicológico. Sensibilidad. Especificidad. Esquizofrenia. Subtipos.

INTRODUCCIÓN

Schizophrenia is a neuropsychiatric disorder that affects approximately 1 % of the world's population[1]. Neuropsychological studies have reported that the patients have cognitive impairments in multiple cognitive domains that are present from the onset of the disease and that remain stable over time[2]. Based on neuropsychological characterization, the existence of impairments originating in abnormalities of specific brain structures has been hypothesized. Thus, for example, the presence of a cortico-subcortical dysfunction[3-5], a prefrontal lesion[6-8], a dorsolateral prefrontal cortex lesion[9], and abnormalities in both frontal as well as temporal zones and in the connections between these two structures[10] has been suggested while other investigations hypothesize processing deficiencies such as, for example, semantic memory[11,12] or work memory[13,14] disorders. These data suggest that the cognitive manifestations of schizophrenia could be associated with different physiopathological mechanisms that differ in their response to treatment. Green[15] suggests that the cognitive profile may be a better indicator of functional prognosis than psychiatric symptoms. However, there may be a delay in the obtaining of this profile and/or it may be affected because the application of complete neuropsychological batteries required specialized staff and prolonged administration times (i.e., 4 to 6 hours), which makes it possible that populations with dementia, psychiatric pictures or elderly subjects may not be capable of tolerating its application.

On its parts, brief scales such as the Brief Mini-Mental State Cognitive[16] or Blessed[17] Examination are too simple. Even though they are very efficient in relationship to evaluation time, they have many false negatives, are insensitive to mild impairments, their performance is affected by educational levels, they are only sensitive to left cortical damage and they do not supply reliable data on the different cultures[18-20].

Recently, microbateries have been developed, for example the Consortium to Establish a Registry for Alzheimer's Disease (CERAD)[21], Short Neuropsychological Assessment Procedure[22], the Cambridge Mental Disorder of the Elderly Examination[23], or the Brief Neuropsychology Test Battery in Spanish (NEUROPSI)[19] that try to overcome these difficulties.

In Latin American and in Spanish speaking countries, there is an additional problem of being able to count on neuropsychological tests that include performance criteria of the normal Spanish speaking population. Different neuropsychological studies have shown that socio-cultural factors are important variables when neuropsychological tests are carried out[24-27]. However, in Latin American countries, it frequently occurs that only tests developed in other countries are translated and the guidelines of other populations are used, which, undoubtedly invalidates the data. It is not only important for normative data of the Spanish speaking population to exist but also, due to the important influence of the socio-cultural level in the cognitive functions, above all, in Latin American, in which the total and functional illiteracy population is very high, the tests should include this population's performance profiles.

The NEUROPSI[19] is a screening instrument used both in the clinical practice as well as in research in Spanish speaking patients. According to the authors, it was designed to evaluate cognitive functioning in psychiatric and neurologic patients and is made up of simple and short items that make it possible to rapidly assess the cognitive functions. It contains items that are sensitive and relevant for the Spanish speaking population and that may be applied to a null schooling population. It has guidelines obtained in a sample of 1,640 Spanish speaking subjects, considering four educational levels (16-30, 31-50, 51-65 and 66-85 years) and has four levels within each age range: education: 0 years of study, 1-4 years, 5 to 9 years and more than 10 years of study. The grading system supplies quantitative and qualitative data. It is not based on a univariate model of brain damage, but rather an individual profile that indicates the performance of the subject in each one of the areas evaluated is obtained with the independent data of each cognitive skill. The standardization parameters make it possible to obtain an impairment grade or level that is classified in normal, mild, moderate, and severe impairments. Application time is 20 to 25 minutes. Test-retest reliability is 0.89 for the total score. Reliability for the subtests goes from 0.89 to 1.0. Correlation coefficients between judges go from 0.93 to 1.0. Sensitivity and specificity indexes in mild and moderate dementia in subjects with 5 to 9 years of schooling are 93 % sensitivity and 98 % specificity[20,28].

Different investigations have indicated that schizophrenia is not a homogeneous entity and have proposed different classification systems based on clinical symptoms. Andreasen and Olsen[29,30] hypothesize the existence of three schizophrenia subgroups: positive, negative and mixed. Positive schizophrenia is characterized by the predominance of hallucinations, delusions or marked thought disorder, with scarce or null negative symptoms. On the contrary, in negative schizophrenia, symptoms such as poor speech, affect and thought content, psychomotor delay and anhedonia, with minimum or absent positive symptoms predominate. Mixed schizophrenia includes those patients who do not fulfill the criteria for any of the two symptom series or who have a significant number of both.

An attempt has been made to identify the clinical correlates of each one of this group of symptoms and it has been suggested that the three subtypes have different brain correlates that include structural and functional abnormalities in many brain regions[31,32]. However, in spite of these different, structural brain characteristics, the neuropsychological correlates of these three subtypes have hardly been studied. It has been reported that patients with negative and mixed symptoms have more severe cognitive impairments than patients with positive symptoms[33,34] and that the negative

symptoms are inversely related with performance in executive measures[35]. It has also been reported that patients with mixed symptoms have impairments in attentional processes[36].

Identification and management of the psychiatric patient are very important to be able to count on instruments that fulfill the following objectives: identify the presence of cognitive impairments, supply information to the patient, relatives and medical team members in charge of the patient's health care on the specific nature of the abilities and disabilities in the patient's cognitive functioning, contribute with recommendations for the treatment and management of the cognitive and behavioral problems and supply baseline measures in order to quantify the effects of the treatment or of the disease progress[37]. This present study aimed to evaluate NEUROPSI sensitivity and specificity to assess the cognitive profile of a group of patients with clinical diagnosis of schizophrenia as well as to assess NEUROPSI sensitivity and specificity according to the clinical subtypes (positive, negative and mixed).

METHOD

Patients

A total sample of 60 subjects was evaluated (30 control subjects and 30 schizophrenic patients) with a total average age of 38.43 years (range from 20 to 60 and SD: 11.73) and 9.87 years of schooling (range from 4 to 15 and SD: 2.50).

The patient group was made up of 30 right-handed men with schizophrenia diagnosis who were hospitalized in the Mexican Psychiatric Hospital Dr. Samuel Ramírez Moreno of the Secretary of Health. The total average age was 38.97 years (SD: 11.01) and 9.01 years of schooling (SD: 2.35). This sample was divided into three groups with 10 patients each: positive, negative and mixed symptoms. The schizophrenia diagnosis was performed by two independent psychiatrists according to the DSM-IV diagnostic criteria[38] and the Positive and Negative Symptoms Scale (PANSS)[39] was used for classification of the subtypes.

A control group of 30 subjects matched for gender, age, schooling and laterality with the patient groups was formed. These subjects had an average age of 36.81 years (SD: 13.87) and 12.44 years of schooling (SD: 2.94). Inclusion criteria for the control group were: *a)* not presenting a background of psychiatric or neurological diseases; *b)* not having any drug treatment, and *c)* being functionally independent.

Table 1 shows the demographic characteristics of the control sample and patients. No significant differences were found in any of these characteristics among the three patient groups or the control group.

Table 2 describes the clinical characteristics of the patients in terms of their classification (positive, negative and mixed), chronicity or time from the first psychiatric diagnosis and drug treatment. In order to control the effects of the drugs as much as possible, a conversion of the drugs in daily units of chlorpromazine (CPZ) was performed. This conversion was performed with the Ereshefsky proposed formula[40]. Due to the fact that drug treatment in schizophrenia patients must be modified according to the symptoms, the mean and deviation of the time that the patients were maintained under the pharmacological scheme calculated is presented. No statistically significant differences were found among the three patient subtypes in relationship to the average of the equivalent units of daily CPZ or in the chronicity from the appearance of the first symptoms to the present date.

Table 1 Descriptive characteristics of the sample

n = 60

Population type	Age					Schooling			
	N	X	SD	Range Min.	Range Max.	X	SD	Range Min.	Range Max.
Controls	30	36.81	13.87	20	60	12.44	2.94	6	16
Mixed patients	10	39.56	9.86	20	57	9.18	2.25	5	13
Negative patients	10	38.93	12.42	21	60	8.87	2.41	6	14
Positive patients	10	38.44	10.77	23	60	9	2.42	4	14
Total	60	38.43	11.73	20	60	9.87	2.50	4	16

SD: standard desviation.

Material

The NEUROPSI[19], Beck Depression Scale[41] and Positive and Negative Symptoms Scale (PANSS) were used. These tests are described in the following.

Table 2 Clinical characteristics of the patient subgroups

Patients	Chronicity (years)		Pharmacological treatment	
	X (SD)	Range	CPZ units X (SD)	Weeks X (SD)
Positive	15.54 (8.01)	8-32	197.50 (100.31)	15.80 (5.11)
Negative	18.60 (8.19)	10-32	270.40 (114.18)	16.40 (8.26)
Mixed	17.40 (9.11)	6-32	169.00 (120)	11.00 (4.83)

CPZ: chlorpromazine

- The NEUROPSI. It includes a brief clinical history in which the relevant medical and pharmacological background and tests for the evaluation of orientation, attention and concentration, verbal and visuospatial memory (immediate and delay recall), language (oral and written) and executive functions. It includes items that are adapted to the Spanish speaking population and that can be used with an illiterate population. Both the linguistic stimuli as well as the drawings that are included were previously standardized according to their high, middle and low occurrence frequency in Spanish[42]. Table 3 describes the areas and description of the processes that are evaluated in NEUROPSI. In all, 25 points are obtained. The total maximum points are 130. Four performance levels are distinguished in each age range and school level: normal (within a standard deviation), mild (between one and two standard deviations), moderate (between two and three standard deviations) and severe (more than three standard deviations in relationship to the means in each age and school group).
- The Beck Depression Scale is an instrument used for the evaluation of the depressive symptoms. It includes 21 items of depression symptoms, which manifest how the patient has felt in the last week.
- The Positive and Negative Symptoms Scale (PANSS) has thirty items divided into three subscales: the positive scale (delusions, conceptual disorganization, hallucinatory behavior, excitement, grandiosity, sus-piciousness/persecution and hostility), the negative scale (blunted or drowsy affect, emotional withdrawal, poor rapport, passive apathetic social with-drawal, difficulty in abstract thinking, lack of spontaneity/flow of conversation and stereotyped thinking and the General Psychopathology Scale (it evaluates varied symptoms such as anxiety, depression, disorientation, concern, etc.). In turn, each scale is classified in severity grades that go from 1 (absent) to 7 (extremely severe).

Procedure

The neuropsychological evaluations of the patients were performed in an out-patient clinic of the Psychiatric Hospital Dr. Samuel Ramírez Moreno. The first step was to corroborate the diagnosis by two independent psychiatrists, using DSM-IV criteria[38]. The PANSS was used for the classification of schizophrenia subtypes. To know the presence of depressive symptoms, the Beck Scale was applied. All the patients were evaluated in clinical stability periods according to the treating physician.

In the case of the patients, written consent was requested for their participation. This authorization was signed by the relatives and when the patient had none, the treating physician signed it.

Statistical analysis

Descriptive statistics, mean and standard deviation were obtained for the sample's demographic and clinical characteristics. To compare the neuropsychological performance in each one of the subtests between the two groups and between the total score of the subgroups, an ANOVA was used as well as a subsequent analysis with the Tukey test, establishing a significance level of $p < 0.05$.

To obtain the cut-off of the total NEUROPSI score, the ROC curve was used[43]. This made it possible to place the lowest number of false positives and negatives within the distribution to obtain a balance between sensitivity and specificity. With the total score, sensitivity, specificity, positive and negative predictive values and concordance values were calculated, both for the total schizophrenic patient population as well as for the patient subgroups classified according to the PANSS in positive, negative and mixed symptoms.

For the diagnosis of schizophrenia, sensitivity was calculated as the number of cases classified as positive cases according to the cut-off (i.e. subjects classified as schizophrenics according to the DSM-IV and psychiatric criteria) and specificity (as the number of cases that obtained scores above or within the cut-off, divided by the number of true negative cases (i.e., normal subjects). Overall accuracy is the percentage of subjects who were classified correctly as controls or as patients according to the total score of the instrument.

In order to consider not only the total points, but also the cognitive profile of the 25 subscales making up the NEUROPSI, a factorial analysis was performed. With the main components obtained, a discriminant analysis was performed.

RESULTS

Significant differences $p > 0.001$ were found in the total scores between the control population and the schizophrenic patient population. When average performance of each group in the NEUROPSI was analyzed, it was observed that the control group obtained the highest scores (X: 113.90; SD: 9.66), followed by the positive symptom group, (93.30) (SD: 17.60), and then by the mixed symptom group (77.35) (SD: 15.86) while the group with negative symptoms obtained the lowest scores (66.95) (SD: 24.78). Differences were compared between the means, using the Tukey test ($p < 0.05$). In the total NEUROPSI score, the four groups were significantly different. The negative patient group and the mixed patient group obtained the lowest scores and no significant differences were found between these two groups, however, both obtained significantly lower points than the patients with positive symptoms and than the control group.

Table 3 **Description of the areas, processes and description of NEUROPSI**

Processes	Areas	Score
Orientation	*Time* (day, month and year), *place* (city and specific site) and *person* (how old she/he is?)	6
Attention and concentratrion	*Digits backwards.*	27
	Visual detection. The subject is asked to mark all the figures on a sheet that are equal to that which he/she is shown. The number of correct answers and number of errors are recorded	24
	Twenty minus three, five times consecutively	
Verbal memory	*Verbal memory.* A list of six words (animals, fruits and body parts) is presented in three trials. After each trial, the subject is asked to say all the words he/she can remember. Intrusions, perservations and primacy and recency effects are recorded	
	Recall of verbal information.	
	Spontaneous recall. The subject is asked to say all the words that he/she remembers from the list that he/she is given. The number of correct answers, perseverations and intrusions is recorded	
	Recall by codes. The subject is asked to say what words of the list were animals, fruits or body parts. The number of correct answers, perseverations and intrusions is recorded	
	Recall by recognition. The subject is asked to say if the words that he/she has been given belong to or do not belong to those that were previously given to him/her. The number of correct answers, perseverations and intrusions is recorded	
Visuospatial memory	*Copy of the semi-complex figure.* The subject is asked to copy the figure presented	24
	Recall of the semi-complex figure.	
Language	*Naming.* Eigth figures corresponding to animals, musical instrument, body parts and objects are shown and the subject is asked to name them	31
	Repetition. The subject is asked to repeat the words and phrases presented to him/her	
	Comprehension. The subject is shown a sheet on which two squares (large and small) and two circles (large and small) are drawn. After, he/she is asked to respond to the instructions giver	
	Semantic verbal fluency. The subject is asked to mentioned all the animals he/she knows in one minute. The number of correct words is recorded and coded on a scale from 0 to 4. Intrusions and perservations are also recorded	
	Phonological verbal fluency. The subject is asked to mention all the words that he/she knows that begin with the letter F in one minute. The number of correct words is recorded and coded on a scale from 0 to 4. Intrusions and perservations are also recorded	
	Reading. The subject is asked to read a paragraph aloud loud and he/she is asked three questions	
	Writing. The subject is asked to write the sentence that he/she is going to be dictated and to copy another sentence	
Executive functions	*Conceptual functions*	18
	Similarities. Three pairs of words are presented and the subject is asked to say how they are similar	
	Calculation. Three simple arithmetic problems are presented	
	Sequences. The subject is asked to continue with the sequences of figures that he/she is shown	
	Motor functions	
	Changing the position of the hand. The subject is asked to perform movements presented with the hand (first to the right and then to the left)	
	Alternating movements. The subject is asked to perform the movements that he/she is shown	
	Opposite reactions. The subject is asked to follow the instructions: if the examiner shows subject a finger, he/she should show the fist and vice versa	
Total		130

To obtain the cut-off of the total NEUROPSI score, the ROC curve was used and it was found that the optimum cut-off that discriminated between normality and disease was 109 points. With this cut-off, values of 87.5 % for sensitivity and 92.8 % for specificity were obtained. When making the analysis for each one of the clinical subgroups, adequate specificity and sensitivity values were found for the negative group and for the mixed group, however, the sensitivity for the positive schizophrenia group was 92.8 %, while specificity was 66.6 %. These data reflect that in the patient group

Table 4 Sensitivity, specificity, false positives, false negatives, positive predictive value (PPV), negative predictive value (NPV) and NEUROPSI concordance. Comparison of schizophrenic patients and clinical sugroups with the control population (n = 30)

NEUROPSI	Schizophrenic patients (n = 30)	Positive schizophrenia (n = 10)	Negative schizophrenia (n = 10)	Mixed schizophrenia (n = 10)
Sensitivity	87.5%	92.8%	100%	100%
Specificity	92.8%	66.6%	100%	100%
False positives	12.5%	17.2%	0%	0%
False negatives	7.2%	43.4%	0%	0%
VPP	93.3%	86.6%	100%	100%
VPN	86.6%	80%	100%	100%
Concordance	90%	85%	100%	100%

classified as positive, 20 % of the subjects (two patients) obtained a total score within the normal range. Table 4 shows the sensitivity and specificity of the total NEUROPSI score as well as the positive predictive value, the negative value and the concordance index of sensitivity and specificity for the total patient group and for each one of the clinical subgroups (positive, negative and mixed).

The total NEUROPSI score is obtained from the sum of the 25 subtests that evaluate different neuropsychological conditions. Thus, to determine if there are specific dimensions that underlie the neuropsychological battery and to examine the correlation between the symptoms and these dimensions, a factorial analysis was performed, using the points of the 25 subtests and the total NEUROPSI score. A variamax rotation was applied to the solution of main components. Five factors were identified with an eigen value greater than one, which, as a whole, accounted for 72.5 % of the variance. Table 5 lists the tests that significantly contributed to each factor ($p < 0,05$). Factor 1 accounted for 21.37 % of the variance and included tests that evaluated verbal memory and functions related with the integrity of the left temporo-parietal area, factor 2 accounted for 20.22 % of the variance and included tests related with pre-motor functions and that were associated with the integrity of the frontal lobules, factor 3 accounted for 14.08 % of the variance and included tests related with visuospatial functions associated to the integrity of the parietal zones, factor 4 accounted for 8.99 % of the variance and included the repetition subtest, and factor 5 accounted for 7.84 % of the variance and included person orientation.

Using the 5 factors, a discriminant analysis was performed by stages to assure that only the factors that substantially contributed to the discrimination would enter the analysis. The analysis by stages used Wilks λ (lambda) in each stage. To assure that only relevant predictors would enter, the likelihood of F to enter was 0.2 and to remove was 0.3[28]. Classification coefficients as well as the validation of the «leaving one out», in which the data of one case is not included, were calculated and the coefficient to classify the case was calculated and this was repeated for each case of the combination.

Table 5 Factorial analysis of NEUROPSI. Subtests that made up the five factors

Factor	NEUROPSI subtests	
1	Coding verbal memory	21.37 %
	Verbal memory by recognition	
	Spontaneous verbal memory	
	Semantic verbal fluency	
	Visual detection	
	NEUROPSI total	
	Curve of spontaneous verbal memory	
	Reading	
	Visouspatial memory	
2	Changing position	20.22 %
	Alternating movements	
	Opposite reactions	
	Digits backward	
	Comprehension	
	NEUROPSI total	
	Writing	
	Copy of the semi-complex figure	
3	Naming	14.08 %
	Copy of the semi-complex figure	
	Orientation-space	
	Calculation	
4	Repetition	8.99 %
5	Orientation-person	7.84 %
	Total	72.5 %

Four factors entered the discriminant analysis in the order shown in table 6. The centroids of each group (the mean of the group in the discriminant function) were significantly different (control: 1.607; mixed: –1.778; negative: –2.493, and positive: –0.550). The Wilks λ is a statistical separation, that goes from zero to one, and smaller statistical values represent greater separation. These values can be transformed to a chi squared statistics to verify their significance. Table 7 includes the values of the discriminant functions, that include the Wilks λ, chi squared values and significance level.

When all the cases were used to derive the classification coefficients (table 8), 83.3 % of the subjects were correctly

Table 6 Factors that entered in the discriminant analysis. The factors were listed in the order in wich they with their associated value and function classification coefficient

Coefficients of the function classification				
Variables	Controls	Mixed	Negative	Positive
Factor 1	2.600	−2.622	−3.487	−1.691
Factor 2	1.408	−1.830	−2.233	−0.160
Factor 3	0.907	−0.605	−2.578	0.461
Factor 5	0.755	−1.620	−1.198	−2.386
(Constant)	−2.698	−3.346	−4.882	−2.386

classified. With the validation technique of «leaving one out», the accuracy was slightly reduced to 71.7 %. In this analysis, three discriminant functions that explained 100 % of the variance were formed. Function 1 only included the repetition score, function 2 included factor 3 (visuospatial processing) and factor 1 (verbal memory and total NEUROPSI score) and function 3 included factor 2 (pre-motor functions and total NEUROPSI score) and factor 5 (person orientation). No control group subject was classified as patient, the patients with negative schizophrenia (80 %) were correctly classified, one patient was classified as mixed and one as positive (90 %) of the patients with positive Schizophrenia were correctly classified, one patient was classified as control. The mixed schizophrenia patients were the most difficult to classify (70 % accuracy) since two patients were classified as negative and one as positive).

DISCUSSION

Cognitive impairments form a part of the clinical picture that characterizes schizophrenia and are correlated with

Table 7 Values of the discriminant functions. The Wilks' λ, chi-squared values and significance level are included

Wilks λ			
Discriminant function	Wilks λ	Chi squared	p
1	0.134	109.502	0.000
2	0.610	26.965	0.001
3	0.836	9.784	0.020

Table 8 Frequency and percentage of classification reached by the discriminant analysis, in wich the belonging to the four groups studied is reported. Reaching 83.3 % correctly classified and 71.7% in the crossed validity

Classification of belonging to group					
Population	Controls	Mixed	Negative	Positive	Total
Controls	30	0	0	0	30
Mixed	0	7	2	1	10
Negative	0	1	8	1	10
Positive	1	0	0	9	10
%					
Controls	**100** %	0	0	0	100
Mixed	0	**70** %	20	10	100
Negative	0	10	**80** %	10	100
Positive	10	0	0	**90** %	100

the patient's functional prognosis. Both in the clinical practice as well as in investigation, it is important to be able to use brief, objective and reliable instruments that make it possible to evaluate the cognitive profile that is present in this population. There are very few standardized and validated instruments with a Spanish-speaking population, so that the adaptation and validation of instrument are very important.

NEUROPSI is a screening instrument for the rapid evaluation of cognitive functioning that all the patients adequately tolerated. The results of our investigation revealed that NEUROPSI is a sensitive and specific instrument for the detection of cognitive impairments in schizophrenia patients. Using the total score, NEUROPSI found sensitivity values of 87.5 % (it correctly identified the presence of cognitive impairments in 87.5 % of those affected) and 92.8 % specificity (i.e., it correctly identified the absence of cognitive disorders in 92.8 % of the healthy subjects). It was estimated that the false positive index was 12.5 % and the false negative one 7.2 %. The analysis according to the clinical subgroup showed high sensitivity and specificity for the classification of negative and mixed patients, in which, in relationship with a control population, the positive false and negative false index was 0 %. However, in patients with positive schizophrenia, sensitivity and specificity indexes decreased, finding 92.8 % sensitivity and 66.66 % specificity. These data agree with other investigations that reported that schizophrenia is a heterogeneous entity in which there are different cognitive patterns. While in the positive

subtype, mild cognitive impairments and/or performances were reported within the normal range[33,34], in the negative and mixed subtypes, there were severe clinical and cognitive impairments.

The results of the discriminant analysis in which the total score and all the subtests forming a part of NEUROPSI were included, through which the control group and three subgroups were compared, revealed that the control group can be distinguished from the patient group with an 83.3 % classification accuracy. The patient group with mixed schizophrenia was the one that showed the lowest indexes (70 %), since it shared symptoms with the positive and negative subtypes.

As in the previous studies[33] in the present investigation, it was found that the group with negative symptoms showed a generalized deficit. Its performance was significantly lower than all the areas of the group with positive symptoms and than the control group. It has been reported that these patients have a poor response to medications and poor prognosis for treatment[44]. The negative symptoms have also been related with frontal hypofunctioning in cognitive and neuroradiological tests[45]. Positron emission tomography studies report disorders that involve the dorsolateral and orbitofrontral prefrontal cortex and its connections with subcortical structures[12]. However, the neuropsychological profile detected suggests generalized cerebral dysfunction[45].

On the contrary to other studies[33], that report that the mixed group is the one presenting the most severe cognitive impairments, this present investigation found that this group had a more intact cognitive profile than the negative group. As the patients with negative symptoms, the neuropsychological profile of this group indicates generalized cerebral dysfunction, although less severe than that of the negative group.

Compared to the patient group with negative and mixed symptoms, the group with positive symptoms was characterized by having performances similar to the controls. These data indicate that this group is not associated with a generalized global dysfunction, but, as Elliot[14] mentions, they present a deficit in the dorsolateral prefrontal cortex, which has been associated with attentional processes and with the information recall[46]. It has also been reported that this population shows a good response to neuroleptics and that the impairments are due to dopaminergic transmission deficiencies[47]. The presence of dysfunctions in the fronto-mesencephalic-thalamic circuit has been hypothesized as the neuronal substrate of the cognitive impairments in this subgroup[3,5], thus their positive response to pharmacological treatment.

Being able to determine the neuronal networks that are associated with the abnormalities in schizophrenia may help to develop more drug treatments that are more specific to rehabilitate impaired cognitive processes, present in each subtype.

Among the limitations of this present investigation is the reduced number of patients in each one of the subgroups. Thus, it is necessary to increase the sample and thus be able to determine if there is a quantitative differentiation between the patient group with negative symptoms and the mixed patient group. It would also be important to be able to study a sample without drug treatment to thus avoid the effects of the neuroleptic response on the symptoms.

In conclusion, the NEUROPSI in the Mexican population was shown to be a screening instrument with high specificity and sensitivity to detect cognitive impairments in subjects with schizophrenia diagnosis.

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