Neuropsychological profile in patients with schizophrenia according to the level of adherence to medication

Perfil neuropsicológico en pacientes con esquizofrenia de acuerdo con el nivel de adherencia a la medicación

erfil neuropsicológico de pacientes com esquizofrenia de acordo com o nível de adesão à medicação

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Resumen

La esquizofrenia es un trastorno mental grave, que por su cronicidad y heterogeneidad genera alto impacto sobre la capacidad funcional de las personas que la padecen, por lo cual, este estudio tuvo como objetivo establecer el perfil neuropsicológico de los pacientes con esquizofrenia de acuerdo con el nivel de adherencia a la medicación psiquiátrica, para esto se desarrolló una metodología de tipo analítico retrospectivo de casos y controles, en una muestra de participantes de n= 52 (grupo casos= 26 pacientes con diagnóstico de esquizofrenia y grupo controles= 26 participantes neurotípicos) de la ciudad de Medellín–Colombia, a la vez que el grupo casos se subdividió de acuerdo con el nivel de adherencia a la medicación psiquiátrica. Como resultados se encuentra diferencias estadísticas significativas entre el grupo casos y controles respecto a la prueba U de Mann Whitney en p valor inferior a 0,05 en los aspectos globales evaluados de la batería Neuropsi como total atención y funciones ejecutivas, Total memoria y Atención y memoria /puntuación global, así mismo diferencias en las puntuaciones de la prueba tarjetas de Wisconsin, estas diferencias también se visualizan en las comparaciones por grupos de acuerdo con el nivel de adherencia con la pruebas de Kruskal-Wallis. Como conclusiones, al parecer los pacientes con esquizofrenia presentan alteraciones en el funcionamiento cognitivo global, que a su vez pueden estar afectadas de acuerdo con el nivel de adherencia que estos pacientes presentan frente a la medicación psiquiátrica de primera línea

Resumo

A esquizofrenia é um transtorno mental grave, que por sua cronicidade e heterogeneidade gera alto impacto na capacidade funcional das pessoas que a sofrem, portanto, este estudo teve como objetivo estabelecer o perfil neuropsicológico de pacientes com esquizofrenia de acordo com o nível de adesão aos medicação psiquiátrica, para isso foi desenvolvida uma metodologia analítica retrospectiva de casos e controles, em uma amostra de participantes de n = 52 (grupo caso = 26 pacientes com diagnóstico de esquizofrenia e grupo controle = 26 participantes neurotípicos) da cidade de Medellín. –Colômbia, enquanto o grupo caso foi subdividido de acordo com o nível de adesão à medicação psiquiátrica. Como resultados foram encontradas diferenças estatísticas significativas entre o grupo caso e controle no que diz respeito ao teste U de Mann Whitney com valor de p menor que 005 nos aspectos globais avaliados da bateria Neuropsi como atenção total e funções executivas Memória total e Atenção e memória/escore global, bem como diferenças nos escores do teste de cartas de Wisconsin, essas diferenças também são visualizadas nas comparações dos grupos de acordo com o nível de adesão aos testes de Kruskal-Wallis. Concluindo, verifica-se que os pacientes com esquizofrenia apresentam alterações no funcionamento cognitivo global, que por sua vez podem ser afetados de acordo com o nível de adesão que estes pacientes apresentam à medicação psiquiátrica de primeira linha

Abstract

Schizophrenia is a serious mental disorder, which due to its chronicity and heterogeneity has a high impact on the functional capacity of the people who suffer from it, therefore, this study aimed to establish the neuropsychological profile of patients with schizophrenia according to the level of adherence to psychiatric medication, For this purpose, a retrospective analytical methodology of cases and controls was developed in a sample of 52 participants (case group = 26 patients with a diagnosis of schizophrenia and control group = 26 neurotypical participants) from the city of Medellin-Colombia, while the case group was subdivided according to the level of adherence to psychiatric medication. As results, significant statistical differences were found between the case and control groups with respect to the Mann Whitney U test at a p-value of less than 0.05 in the global aspects of the Neuropsi battery evaluated as total attention and executive functions, Total memory and Attention and memory/global score, as well as differences in the scores of the Wisconsin cards test. These differences are also visualised in the comparisons by groups according to the level of adherence with the Kruskal-Wallis test. As conclusions, it seems that patients with schizophrenia present alterations in global cognitive functioning, which in turn may be affected according to the level of adherence that these patients present to first-line psychiatric medication

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Introduction

Schizophrenia is a severe and chronic mental disorder. Its complexity and heterogeneity make it one of the top ten causes of disability worldwide (Silva and Restrepo, 2019), being one of the 20 causes of disability adjusted to the most relevant years of life, generating a moderate to severe disability in more than 25 percent of patients (Vicente et al., 2016; Ministerio de Salud y Protección Social and Colciencias, 2014). Some risk factors are decisive for the onset and course of this disease. These factors are due to personal variables such as congenital, hereditary and emotional aspects, among others, and environmental variables such as socioeconomic status, substance abuse and educational level (Doering et al, 1998). The presence of cognitive deficit is undeniably as one of the central features of this disorder (Penadés et al., 2015). There is scientific evidence of a 61-78% prevalence of cognitive impairment in patients with schizophrenia (Medina-Garrido, 2012). The most significant areas of cognitive compromise are memory, attention, abstraction, perceptual speed, executive functions, and psychomotor processing (Lozano and Acosta, 2009). It has been scientifically proven that the most effective intervention in schizophrenia is adherence to pharmacological treatment (World Health Organization [WHO], 2019). However, many patients diagnosed with schizophrenia experience difficulties adhering to treatment with psychotropic medication. Consequently, drastically discontinuing antipsychotic medication leads to a substantial increase in symptomatology and alterations in cognitive functioning (Lieberman et al., 2005).

Previous research has shown that low adherence to psychiatric medication treatment affects the performance of domains associated with social cognition. These domains include Theory of Mind (TOM) and other neuropsychological functions such as verbal memory and executive functions (Zhang et al., 2016; Caqueo et al., 2017; El-Missiry et al., 2015). This demonstrates the relevance of the topic under the findings provided by previous research, which indicates the scientific importance that neurocognitive processes in schizophrenia and their relationship with medication adherence are acquiring. However, it is crucial to investigate the issue of adherence because the findings of Inchauspe and Valverde (2018) suggest that there are discrepancies about its impact on cognition and Stucchi-Portocarrero (2019) who claim not to find impairment in cognition in schizophrenic patients associated with the type of antipsychotics.

On the other hand, it becomes relevant to identify cognitive profiles to determine wheter deficits in neurocognition are responsible for the lack of medication adherence, as suggested by the publication by Lam et al. (2013), who propose that specific cognitive deficits are a factor that preventing adherence to the medication. It is relevant to generate knowledge about the topic at the local level at the moment because there is little reflection on the phenomenon, with evidence from studies that only address epidemiological aspects of provision health services to the schizophrenic patient, such as outpatient and emergency care (Alcaldía de Medellín, 2020). Others only emphasize the emotional, social and economic impacts of schizophrenia (Ministerio de Salud y Protección Social and Colciencias, 2014). Finally, they highlight the importance of the neurocognitive profile and adherence to pharmacological treatments. This research aims to establish the neuropsychological profile of patients with schizophrenia according to the level of adherence to psychiatric medication.

Can a neuropsychological profile be identified in patients with schizophrenia according to their adherence to psychiatric medication?

Methodology

The present research is a retrospective analytical type of case-control, in which no variable intervention was performed. Therefore, analytical studies are often valuable for the study of diseases. Data collection occurs over a short period and allows differences between groups to be established (Hernández et al., 2014; Manterola and Otzen, 2014). In this study, a comparison of three groups was carried out: a) case group consisting of people diagnosed with schizophrenia under psychopharmacological treatment, b) control group consisting of neurotypical people, and c) subgroups of patients with schizophrenia according to the level of adherence to psychiatric medication.

Participating subjects

The participants were people diagnosed with schizophrenia in treatment with psychopharmacology and people without any mental or neurological illness. A total sample size of *n= 52* (Male: fi= 42 and 80,8%; Female: fi= 10 and 19,2%; age: X= 35 years SD= 10,5) (Table 1). The sample type was incidental for convenience. Patients with schizophrenia were selected from a population size universe of 115 subjects, and through the inclusion and exclusion criteria a total of 26 patients were established for the case group. These participants belonged to mental health institutions in Medellín and were outpatients with an established psychiatric diagnosis.

Table 1
Descriptive statistics by groups (cases and controls)

Variables	Indicador	Cases group		Control Group	
		Fi	%	Fi	%
Age	From 18 to 28 years	6	23,1	7	26,9
	From 29 to 39 years	12	46,2	13	50,0
	From 40 to 50 years	5	19,2	2	7,7
	From 51 to 60 years	3	11,5	4	15,4
Gender	Male	21	80,8	21	80,8
	Female	5	19,2	5	19,2
Level of schooling	Primary education	11	42,3	6	23,1
	Secondary education	12	46,2	17	65,4
	Technical Education	1	3,8	1	3,8
	Technology	1	3,8	1	3,8
	Undergraduate	1	3,8	1	3,8

*Note: Fi= Absolute Frequency, %=Percentage

On the other hand, the 26 subjects of the control group were selected based on the equivalence in sociodemographic characteristics with the group participants. The characteristics include gender, level of schooling, age, occupation, and sociodemographic stratum. Finally, group case participants were separated into subgroups based on their adherence to the evaluation scales in Table 2 as inclusion criteria for the case participants the following were used (a) patients with a diagnosis of schizophrenia confirmed by psychiatric and medical history, (b) patients with a diagnosis of schizophrenia between the ages of 18 to 60 years, (c) participants with the minimum of cognitive ability confirmed by interview with clinical psychologist, (d) patients on pharmacological treatment by psychiatry. The exclusion criteria were: a) diagnosis of other comorbid mental disorders or neurological diseases, (b) clinical diagnosis of cognitive impairment or disability confirmed by history and clinical psychiatry, (c) consumption of psychoactive substances in the last two years, (d) being in neuropsychological rehabilitation, and e), a low cognitive ability that is identified in the interview by the clinical psychologist.

Table 2
Distribution of subgroups of participants Cases n=26 according to the level of adherence to psychiatric medication

Test	Indicators	Fi	%
Morisky: Adherence to psychiatric medication. Total score	High	11	42,3
	Medium	8	30,8
	Come on down	7	26,9
DAI Attitude to medication	Negative subjective response	9	34,6
	Positive subjective response	17	65,4

Note: Fi= Absolute Frequency, %=Percentage

Measuring instruments

Adherence to medication

Morisky Medication Adherence Scale (MMAS-8) and Drug Attitude Inventory (DAI) scales were used to assess adherence to antipsychotic medication in elderly adults. The Morisky Scale (Morisky et al., 2008) is an 8-items instrument, of which seven are dichotomous (yes/no) and one of wich is a Likert-type response. This instrument was translated and validated in the Colombian population with a high degree of agreement as evidenced by a Kendall's W coefficient of 0.8. It is widely used to measure measure adherence-oriented behaviours in the intake of pharmacological treatment regimens, validated in patients with physical illness. The patient with a mental illness, the assessment of the level of adhesrence is carried out using a summation of items, in which a high adherence is found with a score of 8, medium adherence between 6 to 7 points, and low scores lower than 6 (De las Cuevas and Peñate, 2015; Valencia-Monsálvez et al., 2017; Chaves et al., 2016).

The purpose of the Medication Attitude Inventory (DAI) is to measure the subjective attitudes of psychiatric patients toward medication and its impact on their treatment. This is achieved through questions with a Cronbach's alpha of .67 in the Spanish version. The answers are recorded as true or false, bridging with + 1 or – 1 depending on the patient's positive or negative response; the higher the final score, the more positive the subjective attitude toward medication (De las Cuevas and Peñate, 2015; Robles et al., 2004).

Neuropsychological profile

Brief Neuropsychological Assessment Battery (NEUROPSI)

According to Ostrosky et al. (2019), the Brief Neuropsychological Evaluation Battery (NEUROPSI) comprises 29 subtests, with the fundamental objective of providing certainty in the early or predictive diagnosis pathologies that alter attention and memory. It has a 0.96% reliability and high neuropsychological validity. Sustained and selective attention and attentional control, executive processes, orienting, working memory, semantic and episodic memory, short – and long-term memory from verbal and visuospatial material, and stages of encoding and evocation of information are some of the domains it assesses.

Wisconsin Card Classification (WCST)

Based on Heaton et al. (2009), the Wisconsin Card Classification Test (WCST) is a neuropsychological battery that consists of a note sheet, four stimulus cards, and 128 response cards organized in two checkbooks

of 64 cards each, which are designed color, shape, and number of figures. This instrument evaluates abstract reasoning and executive function from problem-solving by planning strategy development and maintenance, organized inquiries, achievement orientation, modulation of impulsive responses, and scheme change. "This test has generalizable reliability of 0.60, which indicates good reliability of the results" (Heaton et al., 2009, p.50)

Data analysis

The data were analyzed using the SPSS program trial license offered by IBM. Descriptive statistics were established for the sample and the study variables (Table 1) as measures of central tendency; mean, standard deviation, frequency and percentage. Inferential statistics were used to develop the comparison measures. These measures include non-parametric U tests by Mann Whitney and Kruskal Wallis, association measures like Kendall's Tau b, and data normality tests like Shapiro-Wilk and Levene's homogeneity test.

Procedure

An institutional agreement was established with the psychiatric homes of the city of Medellín-Colombia, which were formalized through meeting minutes signed by the director of each home, attaching the approval format of the ethics committee granted by UNIMINUTO University for this research. Subsequently, each institution pre-selected patients with a diagnosis of schizophrenia without any comorbid disorder. A total of 115 possible candidates were identified and their medical history was reviewed. It was confirmed and diagnosed with the help of a psychiatrist and a checklist based on DSM 5 criteria (American Psychiatric Association [APA], 2013). To confirm the minimum cognitive capacity for the development of neuropsychological tests, each patient underwent an interview with a clinical psychologist. After selecting the patients according to the inclusion and exclusion criteria, the informed consent was signed by the patient's legal representative and the participant's consent. A sample of 28 people was generated for the cases group; however, two were dropped, leaving only 26 in this group.

The application of the instruments was carried out in the spaces designated by each psychiatric home, where aspects such as noise and environmental interference were controlled, and, according to each patient's need, 10-minute rest periods were granted during the application of the neuropsychological tests. Following the collection of data from the cases group, participants for the control group were chosen based on the sociodemographic features of each person diagnosed with schizophrenia. The applications for the tests were carried out in an office destined by the university. Two trained neuropsychologists carried out the application and qualification of the instruments.

Ethical considerations

The ethics committee approved this study with code C120-613. This research was conducted respecting the guidelines set by the Colombian government's resolution 8430 of 1993 (Ministerio de Salud, 1993) for research involving human subjects and inspiring the construction of informed consent. On the other hand, the postulates of the Declaration of Helsinki (World Medical Association, 2017) followed the respect for the bioethical principles regarding autonomy, justice, beneficence and non-maleficence. Finally, this study was constructed on the basis of the elements stipulated by the APA (2010) code of conduct amendments.

Results

Identification of profiles according to the level of adherence to medication

According to the analysis conducted (Table 2), it was possible to establish subgroups according to adherence to psychiatric medication. These subgroups were made in two ways according to the adherence tests a) Subgroups by Morisky Scale: High, Medium, and Low score, and b) subgroups by DAI : Negative subjective response and positive subjective response. For this study, the highest frequency for the Morisky Scale was presented at a high level of adherence. The positive subjective response category obtained the most significant number of people for the DAI, which shows many participants with a diagnosis of schizophrenia adhere to their psychopharmacological treatment schemes.

A Cronbach's alpha reliability analysis of the case group medication adherence tests yields an index of 83 for eight items for Morisky and DAI, and an index of .61 for ten items.

Difference between case and control group in neuropsychological profile

To determine the differences in the neuropsychological profile of patients with schizophrenia compared to the general population, cases and controls were compared. Table 3 shows values at a Mann-Whitney U lower than 0.05 in 32 (85,5%) of the 37 domains evaluated, both for the subtests performed with the battery Neuropsi and for domains of the Wisconsin battery classification Cards. The most relevant result is the sum of total Neuropsi scores in its three domains: Total, attention, and executive functions, in which the case group presented a mean sum rank to the for Mann Whitney U of 15.46 compared to the control group of 37.54. Likewise, for the item Total memory, the case group obtained scores of average rank at the Mann Whitney U test of 16,38 versus the control group 36,62, and for the Total, attention, and memory / Total score, the case group obtained mean ranks of 15,71 and the control group of 37,29. The results of the means by domains or variables in Table 3 show similar disparities. Individuals with schizophrenia had significantly poorer directionality in their scores.

In terms of the Wisconsin card classification subdomains, there are significant differences between the cases and control groups in the following areas Among them is the number of attempts. The average Mann Whitney U rank is 33.90 for the case group and 19.10 for the controls, indicating the directionality of a more significant number of attempts for the case group. For the domain Number of errors, the average U range for the case group was 34.87 and the control 18.13. For the Number of perseverative responses, the case group obtained an average range of 36.54 and the control group 16.46. Indicating that the cases group made more mistakes, persevered and a more significant number of attempts in forming the categories, these scores are also reflected in the averages of Table 3.

Table 3
Differences between case and control group in neuropsychological variables

Domain	n= 26 Group Cases		n= 26 Control Groups		Cases Vs Controles	
	X	SD	X	SD	U of Mann	p-Value
Neuropsi: Attention and executive functions						
Guidance	6,5	1,1	7,0	0,2	245,5	0,0*
Digit progression	5,4	0,9	6,0	1,1	219,5	0,0*
Cubes progression	5,1	0,8	6,1	1,0	157,0	0,0*
Visual arrest hits	12,4	5,6	19,8	3,4	97,5	0,0*
Detention digits	8,4	2,3	9,6	1,1	233,5	0,0*
Successive series	1,2	1,4	1,6	1,5	295,0	0,4
Formation of categories	12,7	4,5	20,9	4,6	65,0	0,0*
Semantic verbal fluency	2,3	1,0	3,0	0,9	197,5	0,0*
Phonological verbal fluency	2,0	1,0	3,5	1,0	110,5	0,0*
Nonverbal fluency	2,2	1,1	2,4	0,9	295,0	0,4
Motor functions	17,9	2,4	19,5	0,8	209,5	0,0*

Domain	n= 26 Group Cases		n= 26 Control Groups		Cases Vs Controles	
	X	SD	X	SD	U of Mann	p-Value
Stroop time interference	1,8	1,0	2,6	0,9	177,5	0,0*
Stroop hits interference	2,2	1,3	2,7	1,3	259,0	0,1
Digits regression	3,2	1,0	5,0	1,4	111,5	0,0*
Regression cubes	3,6	1,1	5,4	1,1	93,5	0,0*
Neuropsi: Memory						
Curve memory encoding	4,2	1,3	7,3	1,3	38,0	0,0*
Associated pairs encoding	3,0	2,5	5,8	2,1	131,5	0,0*
Logical memory encoding stories	4,1	2,7	6,9	2,6	152,0	0,0*
Memory logic coding theme	2,5	1,5	3,6	0,9	205,5	0,0*
Semi-complex figure /King-Osterreith coding	25,2	10,3	33,0	6,6	132,5	0,0*
Faces coding	3,3	0,9	3,9	0,3	212,0	0,0*
Spontaneous verbal memory	3,9	2,1	7,1	1,7	81,0	0,0*
Verbal memory by keys	3,6	2,1	7,8	2,1	54,0	0,0*
Verbal memory recognition	5,5	4,2	9,2	2,1	148,0	0,0*
Associated pairs evocation	4,2	3,0	6,9	2,4	167,0	0,0*
Logical memory evocation stories	3,2	2,6	5,0	2,1	202,5	0,0*
Logical memory evocation theme	1,8	1,3	3,1	0,8	157,0	0,0*
Semi-complex figure /King-Osterreith evocation	9,7	6,6	19,1	7,0	115,0	0,0*
Evocation of names	2,1	2,4	5,9	2,3	91,5	0,0*
Face recognition	1,1	1,0	1,5	0,7	272,0	0,2
Neuropsi: Total scores						
Total, attention and executive functions	92,7	20,2	125,5	13,6	51,0	0,0*
Total, memory	84,2	34,6	136,4	24,2	75,0	0,0*
Attention and memory /global score	176,9	53,0	262,0	34,4	57,5	0,0*
Wisconsin ranking cards						
Number of attempts	119,5	14,9	98,2	23,2	145,5	0,0*
Number of correct answers	60,8	18	70,7	10,2	233,5	0,1
Number of errors	58,7	27,9	27,5	17,4	120,5	0,0*
Number of persevering responses	45,3	26,3	14,7	10,3	77,0	0,0*

* Statistically significant difference in a p-value less than alpha 0,05. Note: X= media, Of= standard deviation . P value= significant bilateral asymptotic U test of Mann Whitney

Differences in the neuropsychological profile according to the level of adherence to antipsychotic medication in the cases group

Comparisons were made by subgroups of individuals, according to the degree of adherence to the tests, to demonstrate differences in the neuropsychological profile of patients diagnosed with schizophrenia. According to Morisky, a showed no statistically significant differences in some domains of the batteries tested in subgroups. Fro example, disparity in the ranges and averages of the test Kruskal in verbal Fluency, semantic (high-11,18, average 10,50 and low 20,57), motor Functions (high 12,91, average 8,63 and low 20,00), Temporal Stroop interference (high-11,27, average 11,56 and low 19,21), verbal Memory key (high 11,77, average 10,06 and low 20,14) and Figure semi-complete /Rey-Osterreith evocation (high-13,18, average 8,81, low 19,36). On the other hand, the most relevant result was found in the summation of the total scores of the Neuropsi battery. The Total attention and executive functions presented average ranges in the high 11.14, medium 10.69, and low 20.43 subgroups, and Attention and memory global battery scores in high 11.09, medium 11.38, low 19.71 subgroups. This indicates that apparently, people with low adherence to psychiatric medication performed better on some subtests of cognitive functioning, which can be contrasted according to Table 4.

Table 4
Differences in the level of adherence and attitude towards medication in the group cases

	n= 7 Low adhesion		n= 8 Medium Adhesion		n= 11 High Adhesion		Kruskal Wallis	n= 17 positive subjetive response		n= 9 Negative subjective response		U Mann-Whitney
	X	SD	X	SD	X	SD	p valor	X	SD	X	SD	p valor
Neurpsi: Atención y funciones ejecutivas												
Guidance	6	0,8	6	1,7	7	0,6	0,53	7	0,7	6	1,7	0,60
Digit progression	6	1,0	5	1,1	5	0,5	0,18	6	0,7	5	1,2	0,37
Cubes progression	5	1,0	5	1,0	5	0,6	0,56	5	0,8	6	0,7	0,01*
Visual arrest hits	16	6,0	12	5,8	10	4,1	0,16	11	5,2	15	5,6	0,12
Detention digits	10	0,4	8	2,3	8	2,7	0,08	8	2,4	9	2,1	0,28
Successive series	1	1,4	1	1,4	1	1,4	0,63	1	1,4	1	1,3	0,50
Formation of categories	16	2,9	11	5,4	12	4,0	0,12	12	4,4	13	4,8	0,77
Semantic verbal fluency	3	0,8	2	1,1	2	0,7	0,01*	2	1,0	2	1,2	0,89
Phonological verbal fluency	3	1,2	2	0,8	2	0,7	0,08	2	0,9	2	1,2	0,65
Nonverbal fluency	3	1,0	2	1,0	2	1,0	0,07	2	1,0	2	1,2	0,43
Motor functions	20	0,8	16	3,0	18	2,0	0,01*	18	2,7	18	2,1	0,74
Stroop time interference	3	1,3	2	0,8	1	0,7	0,04*	2	1,0	2	1,0	0,32
Stroop hits interference	3	1,2	2	1,4	2	1,3	0,14	2	1,4	2	1,3	0,62
Digits regression	4	0,5	3	1,4	3	0,8	0,58	3	0,8	3	1,3	0,54
Regression cubes	4	1,3	3	1,2	4	0,9	0,26	4	0,9	4	1,5	0,82
Curve memory encoding	5	1,3	4	1,5	4	1,0	0,17	4	1,1	4	1,7	0,68
Guidance	4	3,1	3	2,6	2	1,7	0,22	3	2,6	3	2,3	0,40
Digit progression	6	2,5	4	2,8	3	2,2	0,09	4	2,6	5	2,6	0,14
Cubes progression	4	1,4	2	1,7	2	1,3	0,10	2	1,3	3	1,9	0,11
Semi-complex figure /King-Osterreith coding	32	6,6	25	10,6	21	10,8	0,07	25	10,0	25	11,5	0,94
Neuropsi: Memory												
Faces coding	4	0,8	3	1,2	3	0,8	0,54	3	1,0	3	0,9	0,86
Spontaneous verbal memory	5	2,9	4	1,6	3	1,6	0,39	3	1,9	5	1,9	0,04*

	n=7 Low adhesion		n=8 Medium Adhesion		n=11 High Adhesion		Kruskal Wallis	n=17 positive subjetive response		n=9 Negative subjective response		U Mann-Whitney
	X	SD	X	SD	X	SD	p valor	X	SD	X	SD	p valor
Verbal memory by keys	5	1,8	3	2,1	3	1,6	0,02*	3	1,8	5	2,3	0,05
Verbal memory recognition	8	4,7	6	3,1	4	4,0	0,07	5	4,5	7	2,8	0,14
Associated pairs evocation	6	3,5	4	3,2	4	2,6	0,45	3	3,1	6	2,5	0,07
Logical memory evocation stories	4	2,4	3	2,9	2	2,3	0,33	3	2,6	4	2,4	0,37
Logical memory evocation theme	3	1,3	2	1,5	1	1,1	0,16	2	1,2	2	1,5	0,18
Semi-complex figure /King-Osterreith evocation	16	8,5	6	4,4	9	3,8	0,03*	9	6,1	11	7,7	0,87
Evocation of names	3	3,2	2	2,7	2	1,8	0,98	2	2,1	3	3,0	0,59
Face recognition	1	1,1	1	0,9	1	1,0	0,48	1	1,0	1	0,9	0,07
Neuropsi: Total scores												
Total, atención y funciones ejecutivas	111	12,7	84	23,0	87	15,4	0,02*	91	19,0	97	22,9	0,31
Total, memoria	111	37,3	76	35,1	73	24,4	0,07	79	32,1	94	38,9	0,17
Atención y memoria puntuación global	222	46,7	160	56,7	160	39,0	0,04*	170	48,6	191	60,9	0,19
Wisconsin ranking cards												
Number of attempts	106,4	20,9	123,0	8,2	125,3	9,0	0,02*	120,4	14,1	117,9	17,1	0,57
Number of correct answers	69,0	16,3	54,1	22,1	60,4	14,9	0,29	59,1	18,8	63,9	17,0	0,63
Number of errors	37,4	28,6	68,9	28,9	64,9	20,8	0,08	61,2	29,1	54,0	26,5	0,57
Number of persevering responses	29,0	22,6	51,3	29,8	51,3	23,6	0,12	48,8	28,3	38,7	22,1	0,42

* Indicates significant statistical difference. Kruskal Wallis Test and SD Mann Whitney . Note: X= mean, Sd = standard deviation.

For the results of card sorting test, Wisconsin is the only statistically significant difference in the domain Number of attempts in which directionality was found (Morisky groups: low 16,73, average 13,94, high 7,93) in favor of the group of patients with high adherence since that was the group that minor attempts made in the performance of the test, and the group with the most significant efforts in the task was the group with low adherence, indicating that there is a factor favoring adherence on some aspect of executive function.

The data were studied by subgroups distributed according to the Drug Attitude Inventory results (DAI) to contrast the Morisky subgroups' results. The following differences are found in the domains; the one in which the average ranges of the Man Whitney U test show that the subgroup with a positive subjective response has a score of 10.88 and the negative subjective response subgroup an 18.44. For the spontaneous verbal memory domain, the subgroup with positive subjective response had an average score of 11.26, and the negative subjective response subgroup was 17.72. This indicates that the results for subgroups of the DAI test match with the subgroups distributed by the Morisky scale. People with diagnoses of schizophrenia with the subjective and harmful response to the medication showed better performance on cognitive tests. However, it is essential to note that both scales (DAI and Morisky) assess medication adherence.

Association between neuropsychological variables and psychiatric medication adherence variables

Finally, the test was conducted by Tau-b Kendall for the categorical and numerical variables to confirm the relationship between the neuropsychological variables studied for the batteries with the medication adherence variables. An association was found to exist in all three domains of the total scores of the Morisky battery and a single aspect of the Wisconsin Card Sorting Test. This indicates that the relationship between cognitive variables and adherence variables is better explained by the results of the Morisky scale, as shown in Table 5.

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Table 5
Association of cognitive variables with adherence variables

Adherence Variables		Total attention and executive functions	Total, memory	Total, attention, and memory / global score	Number of attempts	Number of correct answers	Number of errors	Number of persevering responses
Morisky	Tau	,34*	,33*	,34*	-,49**	0,15	-0,25	-0,28
	p	0,03	0,04	0,03	0,01	0,36	0,11	0,08
DAI	Tau	0,17	0,23	0,22	-0,11	0,08	-0,09	-0,13
	p	0,31	0,17	0,19	0,57	0,63	0,57	0,42

Kendall´s Tau b test
*. The correlation is significant at the 0.05 level (bilateral)
**. The correlation is significant at the 0.01 level (bilateral)

Discussion

This study conducted a comparative analysis by groups in both cases and controls as sub-groups by the level of adherence to the psychiatric medication of the participants in the group case to achieve the aim of the study to establishing the neuropsychological profile of patients with schizophrenia according to the level of adherence to psychiatric medication. From which the following is found; patients with schizophrenia have worse performance in all areas that evaluated neuropsychological functioning, such as selective, sustained, and alternating attention functions and short-term memory understood from encoding functions. Long-term memory from both graphic and verbal auditory content and poor performance in executive processes such as semantic fluency, non-verbal fluency, apparent difficulties in cognitive flexibility amid more significant errors, and perseverative reactions. As for participants control group, it indicates a greater degree of cognitive inflexibility, as well as problems with modulation of inhibitory responses, planning, and maintenance of cognitive responses and abstract thinking. This, supports the definition of the DSM 5, which states that cognitive dysfunction is a common aspect of this diagnosis, as it is present at the onset of the disease, as well as in the course, which lingers with cognitive deficits established even in adult age, and can persist even when the positive and negative symptoms disappear, contributing noticeably to the disability that causes difficulties in academic and labor processes (APA, 2013) Thus, it can be identified that alterations in cognitive functioning manifest globally, resulting in cognitive impairment rather than deficits in a single area of mental processing. These findings are consistent with the results found by different studies, which determine the importance of the involvement of cognition in this type of disorder since cognitive dysfunction is part of the common alterations of the disease (Penadés et al. 2015), which is consistent with the results of Lozano and Acosta (2009), who complement that these alterations are present in the global cognition of patients affecting multiple domains, such as attention, memory, executive functions, motor skills and social and affective cognition, which can be synthesized in three fundamental structures "(1) cognitive flexibility, (2) interference and memory control and (3) processing speed and attention" (Gaviria et al. 2017, p. 124; Peña et al., 2018; Sahbaz & Kurtulmus, 2019; Karabanowicz et al., 2020; Alkan et al., 2021; Ochoa-Jimenez., Sánchez y Herrera, 2023)

It was observed that subjects with a better attitude of acceptance and a positive attitude towards medication performed worse on neuropsychological tests in the domains of verbal fluency, semantic and motor functions. Stroop-time interference is part of executive functions. Likewise, in the final summations of the Neuropsi test, patients with better adherence also scored worse on Total attention and Executive functions and attention and Memory global score, indicating more significant difficulties in cognitive processing. Finally, in tests that measure cognitive flexibility, this subset of participants showed worse performance only in the number of attempts to develop the classification categories. This shows difficulties in planning maintenance strategies and abstract thinking, which is consistent with the Neuropsi test, in which cognitive impairment is manifests in more than one area of executive functions. These findings are inconsistent with the results of several studies, in which patients with a diagnosis of schizophrenia with low adherence and poor clinical knowledge of the illnes were found to have poorer cognitive performance on global and affective cognition tasks (Zhang et al., 2016; MacKenzie et al., 2018; Ochoa-Jimenez et al., 2023). Thus, functions involving neurocognitive components such as verbal memory and global executive functions, are usually related to the lack of adherence in these patients, as these deficits apparently play an essential role in patients' adherence to their psychiatric treatment regimens (El-Missiry et al., 2015; Rangel et al., 2015). In this regard, Sabina-Roméu et al. (2016) show that there is an impairment in cognitive psychological functions in patients with low adherence, predominantly alterations in sensorimotor thinking, affective functions, synthesis functions and relational functions. Other authors, on the contrary, argue that the level of adherence is intimately linked to the dose of antipsychotics, for example, evidencing significant improvements after reducing the dose of antipsychotics in processing speed, attention and vigilance, working memory, and general cognitive function (Husa et al., 2017; Zhou et al., 2018; Meltzer et al., 2020). Case contrary to the results is shown by Hou et al. (2020). They found that general cognitive performance improved after treatment with atypical antipsychotics, showing significant progress in cognitive domains such as processing speed, working memory, attention, executive function, and fine motor skills.

Finally, the level of adherence to psychiatric medication is associated with some domains of the cognitive functions evaluated, which is better explained by the results of the Morisky test. This finding is consistent with the results of the studies of MacKenzie et al. (2018), who determined that there may be a bidirectional association between the level of medication adherence and cognitive functioning. Subjects with present better adherence are those who, in turn, in the different studies, present better functioning in neuropsychological tests. However, this relationship between adherence and cognition is not clear, as the term adherence has different definitions that make it difficult to objectify. In addition, there is no scientific consensus in the literature on the role of adherence to psychiatric medication and cognitive performance in these patients (Gratacós and Pousa, 2018).

Conclusion

In light of the results and the discussions, the global cognition in people with schizophrenia is affected, indicating a clear risk for cognitive impairment. This increases the degree of disability and psychological helplessness in this population. It clarifies the importance of interventions in rehabilitation or stimulation of neuropsychology for the maintenance of mental functions. On the other hand, this shows that the level of adherence to the psychiatric measure indicated that patients with better adherence were the ones who performed worse on the tests. However, this may be due to the type and dose of medication, phase, time suffering from the disease and evolution, among other sociodemographic factors, which clarifies that these patients' level of adherence and cognitive performance presents a clear relationship.

As a limitation, the results of this study may not be generalizable because the sample is not representative of the population diagnosed with schizophrenia in Medellin. The lack of access to a larger sample is a severe constraint. This is partly due to the population's difficulty in obtaining mental health care, preventing diagnosis, intervention and increased information about the illness. On the other hand, these findings should be interpreted with caution, as changes in cognition in schizophrenia patients are influenced by several factors in the causal chain. They include dose and type of medication, time spent suffering from mental illness, type of diet, mental stimulation activities, level of education, stage of mental illness, physical activity, psychosocial interventions and instrument. Finally, the associations between the level of adherence and some cognitive domains do not indicate causality, but only express relationships.

As a prospective study, it is recommended that the findings be considered as a basis for future studies to further explore the importance of cognitive impairment in schizophrenia and how adherence to different treatments operates as protective or aggravating factor.

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