Attention in patients with chronic schizophrenia: Deficit in inhibitory control and positive symptoms

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ABSTRACT – *Background and Objectives:* Attention is a central mechanism controlling information processing, activating and inhibiting processes, and forming a complex system including diferent networks in specific areas of the brain[1]. To correctly assess the role of attention in schizophrenia it is necessary to discriminate its different attentional components, which may by selectively altered. Attention span, focused attention, selective attention, sustained attention and inhibitory response, were assessed in patients with chronic schizophrenia and healthy matched controls.

Methods: The study included 32 patients diagnosed with chronic schizophrenia and 32 healthy subjects. The groups were matched in age, sex, and level of education. Symptom severity (positive symptoms, negative symptoms, and general psychopathology) was assessed with the Scale for the Assessment of Positive and Negative Symptoms (SAPS and SANS). Attentional components were measured by Forward Digit Span, Symbol Search, Digit Symbol Coding, Stroop Test and Picture Completion.

Results: Schizophrenic patients exhibited lower attentional scores in all tests compared to the control group. Inhibitory control and sustained attention were the most affected traits in schizophrenic patients. An inverse correlation was observed between inhibitory control and delusions and disorganized thinking. No significant correlations were observed between negative symptoms and attentional performance.

Conclusions: The pattern of results obtained in this paper evidences the role of an inhibitory control deficit in patients with chronic schizophrenia that could also be involved in other attentional and cognitive failures, and also be connected to positive symptoms.

Introduction

Attention deficits are a main neurocognitive feature of schizophrenia. These disorders have been observed in children with high genetic risk of schizophrenia and in the direct relatives of patients[2-4]. Moreover, attention seems to be the neurocognitive predictor of motor skill ability and social problem solving[5].

Given the conceptual, neuroanatomical and neurofunctional complexity of attention, it cannot be reduced to a simple definition, linked to a single anatomic structure, or assessed by a single test[6]. Attention is a central mechanism for the control of information processing, activating and inhibiting processes, and constituting a complex system that involves different networks in specific areas of the brain[1].

Attention is constituted by several subsystems, each of which is responsible for different operations including selection or focalization, sustained attention and inhibitory attentional control. It is important to discriminate these different components of attention to correctly assess its role in schizophrenia, as they may be altered selectively.

The components most studied in schizophrenia are selective attention and sustained attention. Posner[7] established that selective attention involves performance when there are conflicts between signals. Attention has the role of selecting some signals for higher levels of processing while preventing other signals to access those same high levels of processing. Studies on the function of this component in schizophrenia are still controversial. Some authors have found that selective attention is intact for visual tasks[8,9], while others show that it has a specific role in the inability to correctly perceive reality in schizophrenia[10].

On the contrary, there is consistent evidence regarding alterations in sustained attention. Sustained attention is the ability to maintain attention and remain in a state of vigilance during a determined period of time[11]. Some studies suggest that sustained attention is a valuable endophenotype for schizophrenia[12]. However recently, Carter et al.[13] argued that the attention deficits of patients with schizophrenia probably reflect a deficit in the modulation of the brain activity in response to transitory variations instead of a deficit in sustained attention.

Failures in both these components of attention, selective and sustained attention, are based on the incapacity of eliminating irrelevant stimuli, which in turn is associated with inhibitory control. Different studies showed that inhibitory control is affected in schizophrenic patients[14-17]. This component has been related to the correct function of the executive attention system that participates in tasks involving conflicts within systems, where it is necessary to inhibit usual responses[18].

These deficits in attention have been related to psychotic symptoms and this association is widely discussed. Some authors have found an inverse relation between the severity of negative symptomatology and the performance of schizophrenic patients in attention tasks, with no significant relation to positive symptomatology[19]. On the contrary, other authors, like Krabbendam et al.[20], have observed an inverse relation between positive symptoms, especially disorganization, and failures in inhibitory attentional control.

Based on this contradictory background regarding the importance of the different components of attention in schizophrenic patients, the object of the present study was to assess and compare the role of attention span, selective attention, sustained attention and

inhibitory attentional control processing in chronic schizophrenia. Our main hypothesis was that patients with chronic schizophrenia show general attention alterations, with the inhibitory component being the most affected. Additionally, any connections observed between the function of each attentional component and positive ad negative schizophrenic symptomatology were also studied.

Materials and methods

Subjects

The present study included 64 individuals; 32 hospitalized patients diagnosed with chronic schizophrenia (Schizophrenic Group), and 32 healthy matched individuals (ages 30 to 65 of both sexes) (Control Group). All patients were hospitalized at the Sanatorio Profesor León Morra and the Clínica San Nicolás. The patients had to be psychiatrically stable for at least two weeks on their treatment with antipsychotic drugs before participating in the study. Healthy participants were included considering the following criteria: a) they had no history of any neurological or psychiatry disorders or head injuries; b) they had no history of substance abuse/dependence. All participants were clearly informed regarding the aim of the study and assessment manipulations, and gave their written informed consent prior the beginning of the study.

Measures

Symptom assessment. A Spanish version of the Scale for the Assessment of Positive Symptoms (SAPS)[21] and the Scale for the Assessment of Negative Symptoms (SANS)[22] were used for assessing the severity of the clinical syndrome.

Neuropsychological Tasks. The tests have been chosen to investigate the attentional components involved in schizophrenia are multicomponent, being that each of these involves the coordinated participation of several functions. For example, in most tests used here in addition to assessing attentional function, also assess processing speed (Stroop Tests, Symbol Search, Digit Symbol). However, try to isolate certain components as reported in the literature.

– *Digit Span Forward*[23]. In this task, the participant has to repeat a sequence of numbers exactly as the examiner reads them. If correctly repeated, the examiner reads the next set of numbers, and continues until the participant fails in two series. The amount of digits increases in each subsequent sequence. The test score is the highest number of digits repeated correctly. The forward digit span was used to measure the effectiveness of attention, especially the attention span[24, 25].

– *Symbol Search*[23]. The participant is presented with a series of paired groups, each consisting of a target group and search group. The participant must decide whether either of the target symbols is in the search group, made up of five search symbols. The total score is the number of correct answers minus the number of incorrect answers. This test was used for assessing sustained attention[26].

– *Stroop Color-Word Test*[27]. This task has three parts. First, the participant must read outloud the names of the colors 'red', 'green' and 'blue', printed in black, during 45 seconds. Secondly, the participant is shown rows of 'x' printed in different colors, and he must name the the colors of each row of 'x' for 45 seconds. Thirdly, the words "red", "green" and "blue" are printed in dif-

ferent colors, and the participant must name the colour of the ink the word is printed in, ignoring its meaning, during another 45 seconds. The total score is the number of correct answers in each part. This test was used to evaluate different attentional processes, particularly sustained attention can be evaluated with the first section, and focused attention and inhibitory attentional control with the third[24, 25].

– *Digit Symbol-Coding*[23]. This task consists of rows containing small blank squares, each paired with a randomly assigned number from one to nine. A key is printed above these rows pairing each number with a different nonsense symbol. Following a practice trial on the first seven squares, the participant must fill in the black spaces with the symbol that is paired to the number above the blank space during 120 seconds. In this study, it was especially used to measure sustained attention[28].

– *Picture Completion*[23]. The participant is presented with a series of slides with images that have an important part missing. The participant must read and indicate the missing part of the image. The complexity of the test increases as the participant provides a correct answer. The score of the test is the number of correct answers. This test was used to study selective attention[24].

Statistical Analyses

Differences in performance between patients and controls were examined using an independent *t* test with attention. Results were considered significant with $p < 0.05$. Relations between attentional measures and clinical characteristics were investigated using exploratory Pearson's product moment correlations. Correlations between different attentional tests in a group of patients were analyzed using the Pearson correlation coefficient. Results were considered significant at $p < 0.05$. All statistical tests were carried out using the PAWS statistics 18.

Results

Demographic and clinical results

Participants were matched in terms of age, gender and educational level achieved. The entire sample was composed by 68.75% of women and 31.25% of men, ranging 30 to 65 years old (a mean of 45.44 years old for the control group and 44.87 years old for the patient group). Table 1 shows a detail of the demographic traits.

Regarding the clinical status of the patient group, 58% of the patients received a diagnosis of paranoid schizophrenia, whereas the remaining 42% exhibited a non paranoid diagnosis including disorganized and residual subtypes. Patients with catatonic and undifferentiated schizophrenia were not included in the study. The first episode of a psychotic break occurred around 25 years old. The average years of illness was 20 years (M = 20.00, SD = 2.69), which correlates with the chronicity of the patient sample. The vast majority of patients, 84.37%, were medicated with atypical antipsychotics at the time of evaluation, whereas the remaining 15.63% were medicated with typical antipsychotics.

Patients had similar values for both positive and negative symptoms in the SAPS and SANS scales. In the analysis of specific symptoms for the positive scale, we found that hallucinations were generally rated as moderate, with a frequency of at least once a week. Most hallucinations were experienced as voices commenting and talking, although there were some cases of patients with visu-

al and kinesthetic hallucinations. Delusions were rated as marked, which are consistently and strongly supported by interfering behavior. Behavioral alterations included mild, occasionally observed unusual behaviors. Formal thought disorder was rated as moderate, with derailment, tangential, incoherent and circumstantial speech and distractibility frequently observed in patients.

Regarding negative symptoms, affective poverty was generally moderate, with reduced facial expressions, spontaneous movements and expressive gestures, poor eye contact and incongruent affective responses. Alogia was rated as mild, with poverty of speech and occasional crashes, and increased response latency. The symptoms of lethargy and apathy were markedly noticeable in the patient group, with a recurring problem in toilet and hygiene, persistence in physical activities and anergy. Anhedonia and antisocial behaviour were both equally valued as high. Attention problems were rated as moderate. A summary of these results is shown in Table 1.

Table 1
Demographic and clinical characteristics of the schizophrenia patients and healthy comparison subjects

Variable	Healthy controls (N 32)	Patients with schizophrenia (N 32)
	Mean (SD) / %	Mean (SD) / %
Age	45.44 (8.55)	44.87 (7.83)
Education (years)	12.53 (3.96)	11.17 (3.93)
Sex (F/M)	68.75% / 31.25%	68.75% / 31.25%
Handedness (R/L)	93.75% / 6.25%	90.63% / 9.37%
Subtype		
Paranoid/ Non paranoid	–	58.10% / 41.90%
Years of illness	–	20.00 (2.69)
Antipsychotic medications		
Typical /Atypical	–	15.63% / 84.37%
SAPS[a]	–	58.83
SANS[b]	–	59.23
Hallucination	–	Moderate
Delusions	–	Marked
Bizarre behavior	–	Mild
Formal thought disorder	–	Moderate
Affective flattening or blunting	–	Moderate
Alogia	–	Mild
Avolition / apathy	–	Marked
Anhedonia / asociality	–	Marked
Attention	–	Moderate

[a] Scale for the Assessment of Positive Symptoms.

[b] Scale for the Assessment of Negative Symptoms.

Attentional performance

Table 2 shows the descriptive statistics of all the attentional tasks. The t test results (Table 2) comparing the patient group and the healthy control group for different attentional tests were significant. The group of patients with chronic schizophrenia performed significantly lower than expected compared to the healthy control group in all tasks. In the test of attentional span (Digits Forward) the control group achieved a length attentional of 7 digits approximately, while the group of patients achieved 5 digits ($t = 6.33$; $p = < 0.001$). In the sustained attention tasks also showed deficits in the performance of the group of patients. For example, in the Symbol Search test the control group averaged 25 correct answers in the two minutes it takes the task, while the group of patients averaged only 10 correct answers ($t = 10.29$; $p = < 0.001$). In the task of Digit Symbol Coding, the patient group only achieved complete 27 symbols correctly, while the control group reached 60 symbols ($t = 12.55$; $p = < 0.001$). Another case is the Word Stroop task, where patients achieved reading in a loud voice for 45 seconds a total of 63 words compared to healthy control group who read a total of 99 words ($t = 8.33$; $p = < 0.001$). In the Picture Completion task of selective attention, the healthy control group was able to establish the missing part of 18 figures, while the schizophrenia group could only do it for 9 figures ($t = 8.66$; $p = < 0.001$). Meanwhile, in the Word Colour Stroop task, patients were able to correctly answer only 15 items, compared to healthy control group who managed to correctly say the colour of the ink in which 42 words were printed ($t = 11.31$; $p = < 0.001$).

No correlation was observed between attentional performance and years of illness or medication. A significant negative correlation was observed between the assessment of positive symptoms the Stroop Word-Color test ($r = -0.40$, $p = 0.028$); the presence of delusions was strongly correlated with the performance on this task ($r = -0.42$, $p = 0.01$). Formal thought disorder was also negatively correlated with this test ($r = -0.40$, $p = 0.02$).

The assessment of negative symptoms was not significantly correlated with any of the tests. However, the specific analysis of symptoms showed that alogia is negatively correlated with performance in the Digit Span Forward trial ($r = -0.45$, $p = 0.01$). The assessment of attention in the SANS was only negatively correlated with the Stroop Word – Color test ($r = -0.37$, $p = 0.03$).

Table 2

Mean (SD) scores in performance attentional tasks for schizophrenia patients (N = 32) and healthy comparison subjects (N = 32) and Analysis of Variance results for attentional measure

| Attentional test	Healthy controls (N = 32)	Patients with schizophrenia (N = 32)	t test	
	Mean (SD)	Mean (SD)	t	p
Forward Digit Span	6.59 (1.18)	4.77 (1.09)	6.339	<0.001
Symbol Search	24.97 (5.32)	9.96 (6.90)	10.288	<0.001
Stroop Word	99.24 (14.10)	62.77 (22.56)	8.332	<0.001
Stroop Word – Color	42.26 (11.40)	15.73 (9.75)	11.314	<0.001
Digit Symbol – Coding	60.21 (9.89)	26.65 (10.97)	12.555	<0.001
Picture Completion	18.26 (4.12)	9.19 (5.02)	8.663	<0.001
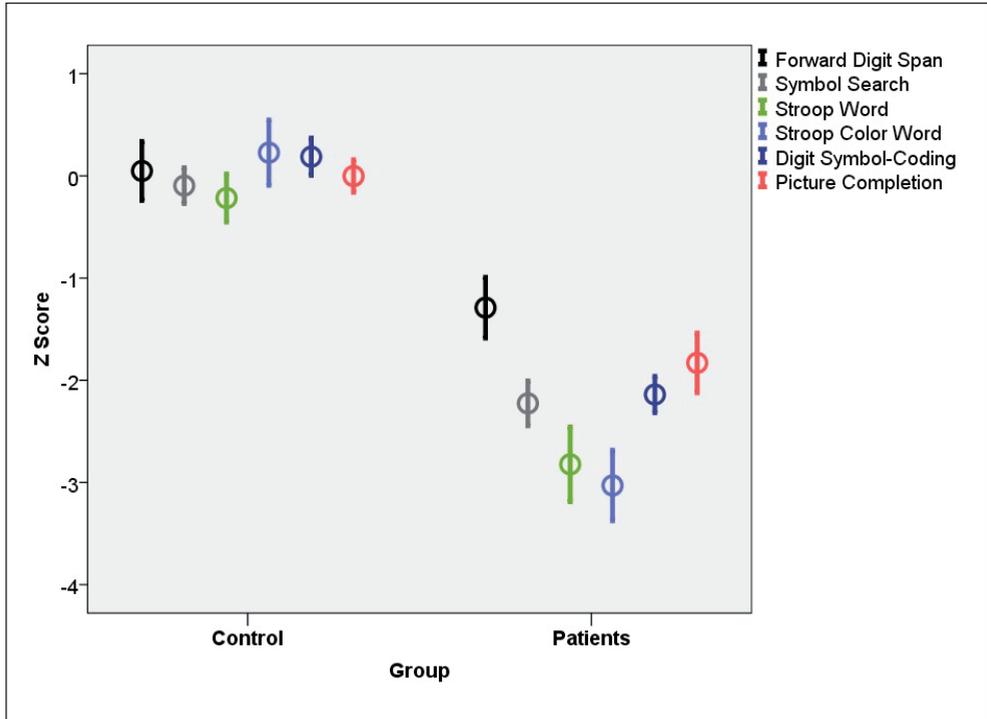
Figure 1. Differences between the control and patient groups in the performance of attentional tasks. Z scores. The dots indicate the mean and the length of the bars indicate the standard deviation.

Discussion

The results of the present study confirm the hypothesis that patients with chronic schizophrenia have a general attention deficiency. These results are in accordance with consistent evidence of attention disorders in this clinical population[29-32]. The importance of these results is based on the fact that attention is a central cognitive function enabling precision, rapidity and continuity to information processing[33], and interacts with other cognitive functions such as sensory perception, memory, language, executive functions, among others. This could explain the existence of generalized failures in different cognitive functions.

The present study specifically focused on the function of different components of attention and found that inhibitory attentional control and sustained attention were the most affected in patients with chronic schizophrenia. These observations are partly supported by other studies that found significant alterations in both these components of attention[14,29,34-36]. Breton *et al.*[14], recently found that patients had a specific attention deficient and a significantly worse performance in tests involving the executive attention network, while the alertness and orientating attentional networks remained intact.

Failures in both these components, sustained attention and inhibitory control, could be considered closely related because

sustained attention works by two mechanisms: one involving excitatory processes, associated with the stimulating object, and the other involving inhibitory mechanisms, associated to unknown stimuli[37].

In this study we found no significant relations between the global severity of the negative symptoms and the different attentional components. These results are inconsistent with studies that suggest a relationship between severity of negative symptoms and inhibitory control failures. In our study only found that the severity of alogia was associated with short attention span, and problems of attention during the interviews were significantly associated with a deficiency in inhibitory control.

The most significant results were found in relation to the global severity of positive symptoms. Significant inverse correlations were observed between positive symptoms and performance in the Stroop Colour-Word test. Additionally, these results are supported by recent findings that evidence a connection between failures in inhibitory control and the presence of positive symptoms, especially symptoms of disorganization[14,20].

It has been shown that the deficiency in the executive attention network of schizophrenia patients is related to an abnormal function in tasks involving executive processes and some of the characteristic symptoms of the disorder such as formal thought disorder and weak associations[14]. The problems patients have in the Stroop Colour-Word test could be associated with an attenuated activation in the cingulate cortex and left inferior frontal gyrus, as changes in the positive symptoms appear to be correlated with the activation of these areas[20].

Failures in inhibitory attentional control were found to be related to the presence of delirium and disorganized thinking, and this has not been previously established in other studies. This relation could be explained by regarding attentional control as the ability to guide thought and actions according to changes in the physical context and internal intentions and goals; this ability is the basis for the correct function of other more complex cognitive processes[35].

In favour of these results, there are references of studies in patients with methamphetamine abuse that establish a possible relation between the frequency of paranoid delirium and the magnitude of Stroop interference[39]. Thus, it is possible to hypothesize that alterations in the dopaminergic function (well-established in schizophrenia and in methamphetamine abuse) could be associated to attention abnormalities, especially inhibitory control and the appearance of delirium symptoms[39].

The pattern of results of this study suggests the presence of a deficient inhibitory control in patients with chronic schizophrenia, which could also have an important role in other attention and cognitive failures, as well as in positive symptomatology. Future investigations should further analyze the relations between sustained attention, inhibitory control, and the schizophrenic symptoms that are closely linked with thought and language. Moreover, and considering the fact that inhibitory control has been included in the executive attention system[18], it would also be interesting to study the relation between attention and executive functions, such as working memory and cognitive flexibility, which have been associated with attentional control[40].

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Contributors

FSG participated in the literature review, data extraction and first draft of the manuscript draft. AMB and CAM participated in the conception of the study and provided scientific supervision. IRO and MJK provided statistical advice and scientific supervision. MCFF, ASF and DAP helped draft the manuscript. FG contributed data extraction, literature review and contribuited with the written manuscript. FSG, AMB and CAM contributed content knowledge and made suggestions on the written manuscript. All authors read and approved the final manuscript.

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