Characterization of neurological soft signs in a Brazilian sample of stable patients with schizophrenia

Caracterização de sinais neurológicos sutis em uma amostra brasileira de pacientes estáveis com esquizofrenia

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Abstract

Introduction: Neurological soft signs (NSS) have been considered one of the target features and a potential endophenotype for schizophrenia. The present study aimed to characterize NSS in a sample of patients with chronic schizophrenia and to compare them with healthy control individuals.

Methods: In this study, we evaluated the presence of NSS in a sample of stable patients (n = 24) diagnosed with schizophrenia according to DSM-IV criteria, recruited at the Schizophrenia Outpatient Clinic of Instituto Raul Soares, Belo Horizonte, state of Minas Gerais, southeastern Brazil. Assessment was made with the Brief Motor Scale (BMS), and extrapyramidal symptoms (EPS) were evaluated with the Simpson-Angus Scale (SAS) and the Abnormal Involuntary Movement Scale (AIMS). A control group (n = 21) was also submitted to the same battery of tests.

Results: We observed a significant difference in relation to BMS and SAS scores ($p < 0.0001$), revealing that individuals with schizophrenia present more NSS and EPS than healthy ones. BMS total scores correlated positively with SAS scores ($r = 0.495$, $p = 0.014$), but not with AIMS scores, indicating that NSS could be influenced by the intensity of EPS. Nevertheless, we observed that this relationship remained only for motor coordination tasks ($r = 0.550$, $p = 0.005$), while motor sequencing tasks were not influenced by EPS ($r = 0.313$, $p = 0.136$).

Conclusion: The results suggest that NSS are more frequent in patients with schizophrenia and that motor sequencing tasks could be more specific to the syndrome.

Keywords: Neurological soft signs, schizophrenia, extrapyramidal symptoms.

Resumo

Introdução: Sinais neurológicos sutis (SNS) têm sido considerados características básicas e potenciais endofenótipos na esquizofrenia. O presente estudo procurou caracterizar os SNS em uma amostra de pacientes com esquizofrenia crônica e compará-los com indivíduos controles saudáveis.

Métodos: Neste estudo, avaliamos a presença de SNS em uma amostra de pacientes estáveis (n = 24) com o diagnóstico de esquizofrenia de acordo com os critérios do DSM-IV, recrutados no Ambulatório de Esquizofrenia do Instituto Raul Soares, Belo Horizonte, MG, Brasil. A avaliação foi realizada com a Escala Motora Breve (BMS) e sinais extrapiramidais (SEP) foram observados com a Escala de Simpson-Angus (SAS) e a Escala de Movimentos Involuntários Anormais (AIMS). Um grupo controle (n = 21) também foi submetido à mesma bateria de testes.

Resultados: Observamos uma diferença significativa em relação aos escores da BMS e da SAS ($p < 0,0001$), revelando que indivíduos com esquizofrenia apresentam mais SNS e SEP que indivíduos saudáveis. Os escores da BMS se correlacionaram positivamente com os da SAS ($r = 0,495$, $p = 0,014$), mas não com os da AIMS, indicando que os SNS podem ser influenciados pela intensidade de SEP. No entanto, observamos que essa relação permaneceu somente para as tarefas de coordenação motora ($r = 0,550$, $p = 0,005$), enquanto as tarefas de sequenciamento motor não foram influenciadas pelos SEP ($r = 0,313$, $p = 0,136$).

Conclusão: Os resultados sugerem que os SNS são mais frequentes em pacientes com esquizofrenia e que tarefas de sequenciamento motor podem ser mais específicas na síndrome.

Descritores: Sinais neurológicos sutis, esquizofrenia, sinais extrapiramidais.

Introduction

Schizophrenia is usually conceptualized as a disorder characterized by positive, negative and cognitive symptoms. However, ever since the first descriptions were published, most patients with schizophrenia have been reported to also display a wide range of symptoms characterized by aberrant motor functioning. Such symptoms include catatonic features, extrapyramidal signs, psychomotor slowing, reduced motor activity, and motor neurological soft signs (NSS).[1] The latter refer to subtle neurological abnormalities comprising deficits in motor coordination and sequencing of complex motor acts. NSS have been considered one of the target features and a potential endophenotype for schizophrenia. To qualify as an endophenotype, a marker must be reliably associated with the illness, demonstrate state-dependent cosegregation, and reveal heritable familial association.[2] Indeed, evidence has shown that NSS are a stable trait in patients with schizophrenia, are not secondary to the use of medication, and tend to be more frequent in unaffected relatives.[1,3] Besides, studies have yielded significant associations between NSS, negative symptoms and a wide range of neurocognitive dysfunctions, which are often manifested in schizophrenia spectrum disorders and are sensitive to the development of psychosis.[1-4] Nevertheless, NSS literature is still limited, especially in Brazil. The present study aimed to characterize NSS in a sample of patients with chronic schizophrenia and to compare them with healthy control individuals.

Methods

For the purpose of this study, a sample of stable patients (n = 24) diagnosed with schizophrenia according to criteria from the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) was recruited at the Schizophrenia Outpatient Clinic of Instituto Raul Soares, Belo Horizonte, state of Minas Gerais, southeastern Brazil. Stability was defined as a score < 19 on the Positive and Negative Syndrome Scale (PANSS) – positive scale, scores ≤ 3 on each one of the positive subscale items, and no intercurrence recorded in the 3 months prior to the evaluation.[5] Exclusion criteria for controls were the same general criteria used for patients, i.e., presence of neurological disease, history of drug abuse, diagnosis of other axis I disorder, and age under 18 or over 65 years. Both patients and controls underwent a structured interview with the Mini-International Neuropsychiatric Interview-Plus (MINI-Plus).[6]

In order to evaluate the presence of NSS, patients were assessed with the Brief Motor Scale (BMS), composed of 10 tasks divided into two subscales of motor coordination (MOCO) and motor sequencing (MOSE) tests.[7] The occurrence of extrapyramidal symptoms (EPS) was evaluated with the Simpson-Angus Scale (SAS) and the Abnormal Involuntary Movement Scale (AIMS).[8,9] The control group (n = 21) was also submitted to the same battery of tests. Analysis was made with the Mann-Whitney test, chi-square test, and the Spearman correlation test.

The study was approved by the local research ethics committee. All individuals included in the study provided written consent.

Results

As can be seen in Table 1, groups did not differ with respect to age, gender, or AIMS scores. However, we

Table 1 - Characterization of the study sample

	Patients with schizophrenia (n = 24)	Healthy controls (n = 21)	p-value
Age (years)	43.25 (12.22)	37.86 (11.83)	0.139
Gender	12 male	13 male	0.550
Brief Motor Scale (BMS)			
Total	9.83 (3.75)	2.14 (1.74)	< 0.001
Motor sequencing (MOSE)	5.50 (2.12)	1.19 (1.29)	< 0.001
Motor coordination (MOCO)	4.33 (2.16)	0.95 (1.12)	< 0.001
Simpson-Angus Scale (SAS)	2.92 (3.13)	0.29 (0.64)	< 0.001
Abnormal Involuntary Movement Scale (AIMS)	1.46 (3.13)	0.43 (1.96)	0.087

Results expressed as mean (standard deviation).

observed a significant difference in relation to BMS and SAS scores (p < 0.0001), revealing that individuals with schizophrenia present more NSS and EPS than healthy ones. BMS total scores correlated positively with SAS scores (r = 0.581, p = 0.002), but not with AIMS scores, indicating that NSS could be influenced by the intensity of EPS. Nevertheless, when we considered the MOCO and MOSE subscales of the BMS separately, we observed that MOCO still correlated positively with SAS (r = 0.582, p = 0.002), while MOSE did not (r = 0.375, p = 0.065). Finally, we evaluated correlations between the presence of NSS and the intensity of symptoms measured by PANSS. We did not observe any significant association, except for a specific correlation between MOSE and the negative symptoms subscale (r = 0.423, p = 0.039).

Discussion

The intensity of NSS in patients with schizophrenia is higher in comparison to unaffected individuals. Most studies have demonstrated a prevalence of 50 to 65% in these patients, in contrast to approximately 5% in control populations.[10]

According to the literature, patients with schizophrenia present NSS related to sensory integrative function, motor coordination and sequencing of complex motor tasks, as well as primitive reflexes.[11] Evaluations focused on motor signs only are widely used. This strategy was emphasized by Manschreck & Ames[12] and Woods et al.,[13] because it is believed that specific motor signals, such as dysdiadochokinesia, can be valid indicators of neurointegrative deficits in schizophrenia and because of the greater reliability in the reproduction of motor tests.

Taken together, our results suggest that motor NSS are more frequent in patients with schizophrenia than in unaffected individuals and that motor sequencing tasks, as evaluated by MOSE, could be more specific to the syndrome, in the sense of revealing traits that are independent from the use of medication – since MOSE did not correlate with SAS. In this sense, it is interesting to note that MOSE also correlated with the intensity of negative symptoms measured by the PANSS negative scale.

A meta-analysis conducted by Bachmann et al. concluded that NSS scores decrease in the clinical course of schizophrenia, with remission of psychopathological symptoms, but not to the levels observed in healthy individuals. The authors provided an indication that this effect is more pronounced in patients with a remitting course than in those with non-remitting schizophrenia.[3] NSS in schizophrenia are more closely related to morphological changes and abnormal neural activity in pre- and postcentral, inferior frontal, parietal, thalamic,

striatal, and cerebellar structures.[14] Unfortunately, we could not find studies in the Brazilian literature that have evaluated to date the presence of NSS in patients with schizophrenia.

Since researchers have proposed that NSS and conventional neurocognitive tests capture the same underlying brain functions in schizophrenia spectrum disorders, the brevity of NSS assessment (less than 10 minutes) could make it feasible for clinicians to screen for neurocognitive dysfunction in patients with schizophrenia.[14,15]

The major limitations of this study are the size of the sample and its cross-sectional design. Studies including a larger number of patients and that can longitudinally assess the manifestation of NSS may assist in understanding the significance of these markers in schizophrenia.

Disclosure

No conflicts of interest declared concerning the publication of this article.

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