

ABSENCE OF DEMENTIA IN LATE-ONSET SCHIZOPHRENIA

A one year follow-up of a Brazilian case series

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ABSTRACT - Background: Cognitive deficits of late-onset schizophrenia (LOS) patients have been reported as stable, although some prospective studies show that a sub-group develop a significant cognitive decline. Data on LOS from developing countries are scarce. **Objective:** To evaluate the cognitive performance of Brazilian patients with LOS over the course of one year. **Method:** Thirteen LOS patients were evaluated at baseline and after one year with the Mini-Mental State Examination (MMSE), the CAMCOG, the Positive and Negative Symptoms Scale, the Pfeiffer's Activities of Daily Living (ADL), and the Neuropsychiatric Inventory (NPI). **Results:** Cognition and activities of daily living remained stable over the course of one year [baseline MMSE= 21.31 (4.87) and CAMCOG=80.31 (16.68); end-point MMSE=20.77 (3.86) and CAMCOG=82.92 (14.42) ($Z=-0.831$; $p=0.40$); baseline ADL=4.31 (5.65); end-point ADL= 5.92 (3.86) ($Z=-0.831$; $p=0.40$); end-point NPI=10.54 (10.69) ($Z=-0.737$; $p=0.46$). **Conclusion:** Like patients from developed countries, Brazilian patients with LOS do not seem develop dementia, at least over the course of one year.

KEY WORDS: psychosis, schizophrenia, late onset, cognition, elderly, evaluation, activities of daily living.

A esquizofrenia de início tardio não evolui para demência: acompanhamento de um ano de uma série brasileira de casos

RESUMO - Introdução: Os déficits cognitivos em pacientes com esquizofrenia tardia têm sido relatados como estáveis, embora alguns estudos prospectivos demonstrem que um sub-grupo evolui com declínio cognitivo significativo. Os dados sobre esquizofrenia de início tardio são escassos nos países em desenvolvimento. **Objetivo:** Avaliar o desempenho cognitivo de pacientes brasileiros com esquizofrenia de início tardio ao longo de um ano. **Método:** Os pacientes com esquizofrenia de início tardio ($n=13$) foram avaliados inicialmente e após um ano com o Mini-Exame do Estado Mental (MMSE), o CAMCOG, a Escala de Sintomas Positivos e Negativos, a Escala de Atividades de Vida Diária de Pfeffer (ADL) e o Inventário Neuropsiquiátrico (NPI). **Resultados:** A cognição e as atividades de vida diária permaneceram estáveis ao longo de um ano [inicial MMSE= 21,31 (4,87) e CAMCOG=80,31 (16,68); final MMSE=20,77 (3,86) e CAMCOG=82,92 (14,42) ($Z=-0,831$; $p=0,40$); inicial ADL=4,31 (5,65); final ADL=5,92 (3,86) ($Z=-0,831$; $p=0,40$); inicial NPI=13,92 (16,87); final NPI=10,54 (10,69) ($Z=-0,737$; $p=0,46$)]. **Conclusão:** Assim como os pacientes de países desenvolvidos, esquizofrênicos de início tardio no Brasil não evoluem para demência, ao menos ao longo de um ano.

PALAVRAS-CHAVE: psicose, esquizofrenia, início tardio, cognição, idosos, avaliação, atividades de vida diária.

Some studies suggest that schizophrenia is in fact a set of related syndromes that, despite phenomenological similarities, can be differentiated according to their age at onset, as well as to cognitive and prognostic factors. For example, patients with late-onset schizophrenia (LOS) are more likely than their

early-onset counterparts to exhibit visual, tactile, and olfactory hallucinations; persecutory and paranoid delusions; and third-person, running commentary, and accusatory or abusive auditory hallucinations¹. Several lines of evidence indicate that cognitive abilities of patients with early-onset schizophrenia tend

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Received 16 March 2006, received in final form 3 July 2006. Accepted 1 August 2006.

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to stabilize after an early stage of cognitive decline². Much less is known, though, about the evolution of cognitive deficits of patients with LOS. Some authors suggest that cognitive impairment in elderly schizophrenic patients is related to a static (neurodevelopmental) rather than to a progressive illness^{3,4}, while other authors argue that a significant percentage of such patients progress to neurodegenerative dementia⁵.

It has been reported that patients with schizophrenia from countries outside Europe and the United States have a more favorable short- and medium-term course than those seen in developed ones⁶. However, it is unclear whether this superior outcome is also found among patients with LOS. Although it has been demonstrated that preserved neuropsychological functioning and preserved premorbid functioning are associated with an improved prognosis in cases of schizophrenia in general⁷, it is uncertain if this finding also applies to cases of LOS.

A few prospective studies have shown marked cognitive decline in some Australian and British LOS patients^{5,8}. We are not aware of any previous study investigating cognitive decline among patients with LOS from developing countries. In this pilot study, we aimed at probing the occurrence and evolution of cognitive decline in a series of Brazilian outpatients with LOS.

METHOD

Patients – Individuals with late-onset paranoid syndromes without any apparent cognitive deficit (n=25) were consecutively recruited among the patients attending the outpatient clinic of the Center for Alzheimer's Disease and Related Disorders of the Institute of Psychiatry (Federal University of Rio de Janeiro, Brazil). These volunteers were examined by means of the Structured Clinical Interview for DSM-IV (SCID I)⁹ and 15 patients had their diagnosis of schizophrenia confirmed according to the DSM-IV criteria, whereas the other five patients were diagnosed as bipolar disorder (n=2) and frontal-temporal dementia (n=3). A consensus statement on LOS has proposed 40 years of age as a cutoff for the diagnosis¹. In this study, patients were considered to suffer from LOS if their symptoms of schizophrenia had started after age 50, as was the case in another study regarding the same issue⁵. Exclusion criteria comprised dementia, delirium, current substance abuse, a history of significant traumatic brain injury, and any current unstable medical condition. Individuals were also excluded if they were unable to fill out questionnaires by themselves or to communicate effectively with the research team. The patients were treated with neuroleptics when needed.

The study was approved by the Ethics Committee of the Institute of Psychiatry - Federal University of Rio de Janeiro. All patients and caregivers have given their written informed

consent after all the procedures of the study were fully explained.

Instruments – The individuals with LOS had their cognitive functions, psychopathological profiles, and general activities of daily living evaluated at baseline and after one year. All the patients were assessed by a single research psychiatrist (AC). The cognitive, psychopathological, and functional evaluation of each patient took approximately two hours.

The cognitive assessment comprised the Mini-Mental State Examination (MMSE)¹⁰ and the CAMCOG, which is the section B of the Cambridge Examination for Mental Disorder of the Elderly¹¹ (CAMDEX). The MMSE evaluates orientation, attention, concentration, memory, calculation, language, and praxis. Its score ranges from 0 to 30. The CAMCOG assesses the same domains with more depth and has a cutoff score for dementia of 80 (10). We employed a validated Brazilian version of the CAMCOG¹².

The psychopathological profile of our patients was examined by means of the Positive and Negative Syndrome Scale (PANSS)¹³ and the Neuropsychiatric Inventory (NPI)¹⁴. The PANSS has a positive scale, a negative scale (7 items each), and a scale for general psychopathology (16 items). Scoring varies from 0 (absent) to 7 (severe). The NPI is completed by the caregiver and assesses 10 types of behavioral symptoms. Scoring for each symptom is based on intensity (0-3) multiplied by severity (0-4).

The activities of daily living (ADL) were evaluated with the Pfeffer's Functional Activities Questionnaire (PFAQ). The performance on these activities is assessed by 10 questions, with the scores ranging from 0-3, according to increasing levels of severity. Subjects who score higher than 5 are considered to have functional impairment¹⁵.

Statistics – The socio-demographic and clinical data, as well as the results of the scales were described as mean (M) and standard deviation (SD). The Wilcoxon sum of ranks was employed to compare the results of the cognitive, psychopathological, and functional measurements conducted at baseline and after one-year. The adopted level of significance was 5%.

RESULTS

Fifteen patients were recruited for the study. Two patients were excluded: one because of illiteracy and the other due to a severe hearing deficit. The table shows the socio-demographic and clinical characteristics of the individuals with LOS (five males and 8 females).

At baseline, the MMSE scores of the sample were lower than those of normal Brazilian elderly¹⁶ but the CAMCOG and PFAQ results were within the normal range. The cognitive and functional performance of the sample after a one-year follow up was not significantly different from that of baseline, as shown in the Table.

Table. General description of our patients with late-onset schizophrenia.

Socio-demographic and clinical characteristics			
	Mean (SD)		
Current age (in years)	66.08 (11.02)		
Schooling (in years)	7.23 (5.09)		
Age at onset (years)	59.38 (11.91)		
Duration of illness (in years)	6.69 (6.13)		
Global PANSS	63.69 (17.99)		
Positive scale	14.77 (1.16)		
Negative scale	19.38 (5.04)		
General psychopathology	29.54 (7.92)		
Cognitive features at baseline and one-year follow-up			
Scales	Mean scores at baseline (SD)	Mean scores at follow-up (SD)	Wilcoxon Z; p value
MMSE	21.31 (4.87)	20.77 (3.86)	-0.561; 0.57
CAMCOG	80.31 (16.68)	82.92 (14.42)	-0.831; 0.40
PFAQ	4.31 (5.65)	5.92 (3.86)	-0.06; 0.90
NPI	13.92 (16.87)	10.54 (10.69)	-0.737; 0.46

SD, standard deviation; PANSS, Positive and Negative Schizophrenia Scale; MMSE, Mini Mental State Examination; CAMCOG, Section B of the CAMDEX (cognitive evaluation); PFAQ, Pfeffer Functional Assessment Questionnaire; NPI, Neuropsychiatric Inventory.

DISCUSSION

We found in our study with a cohort of Brazilian patients with LOS that the baseline and endpoint results on the CAMCOG and on the ADL were both in the normal range and not significantly different from each other, thus suggesting that our patients maintained normal levels of neuropsychological functioning and of activities of daily living after a one-year follow-up. Nonetheless, both MMSE baseline [(±SD)=21.31 (±4.87)] and endpoint scores [(±SD)=20.77 (±3.86)] were both somewhat below the standards for the Brazilian elderly population adjusted to years of formal education [MMSE (±SD)=26.57 (±1.51)]¹⁵. These lower scores may be already a symptom of the disease, since there is usually a cognitive decline at the early stages of schizophrenia with a maintained stability afterwards. It should be mentioned, however, that there was no significant decline between the two assessments.

Given the mean duration of the disease (±SD) [6.69 (±6.13) years], our findings suggest that, although our patients may have suffered some modest early cognitive decline, they clearly do not have a marked neurodegenerative condition. Despite the fact that only long-term prospective studies would

be able to confirm this suggestion, it would be reasonable to expect that a chronic neurodegenerative disease with an average duration of 6 years would be associated with a marked impairment in most cognitive and functional domains either at baseline or after a follow up period.

Previous studies have found that a sizeable subgroup of patients with LOS showed significant cognitive decline after several years of follow-up. Although some authors have stated that schizophrenic patients have a lower risk of developing Alzheimer's disease¹⁷, longer prospective studies with LOS did observe a strong trend toward progression to dementia. Brodaty et al.⁵ showed that 47.4% of the subjects with LOS became demented within five years (an incidence rate of 9.5% per year) and that these patients were characterized by lower cognitive and functional scores at baseline. Another study showed that 35% of the patients with very late onset schizophrenia (aged 60 and above) became demented after 3 years (an incidence rate of 11.7% per year)⁸. These rates were higher than those found in the general population for the conversion to Alzheimer's disease and led some authors to suggest that, while early-onset schizophrenia may be a neurodevelopmental condi-

tion, some cases of LOS may represent a neurodegenerative one⁵.

This study presents some limitations that need to be acknowledged. In view of the small number of patients, the short term follow-up, and the lack of an early-onset schizophrenia group of patients for comparison, our results should be considered as a preliminary report.

To the best of our knowledge, this is the first report on the course of cognitive and functional symptomatology of LOS in a Brazilian sample. The present data of cognitive and functional stability over a one-year observation period of LOS patients from a developing country may be useful for further studies with longer follow up periods in order to ascertain whether our preliminary findings are valid for other populations.

Acknowledgements – The authors thank the Instituto Virtual de Doenças Neurodegenerativas da Fundação de Apoio à Pesquisa do Estado do Rio de Janeiro (IVDN-FAPEJ) for the support and Luzinete N.O. Alvarenga for the editorial assistance.

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