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Incidence of Mild Cognitive Impairment and Alzheimer Disease in Southern Brazil

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The objective of the study was to evaluate incident cases of Alzheimer disease (AD) and mild cognitive impairment (MCI) in an elderly community cohort in a major city of southern Brazil and to determine the variables associated with the development of cognitive dysfunction. Data were drawn from a cohort to investigate healthy aging among community elderly (N = 345) and were derived from the follow-up for a maximum of 8 years. Sociodemographic, psychiatric and medical information, the Mini-Mental State Examination (MMSE), and the Clinical Dementia Rating scale were obtained in each assessment. The *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition; DSM-IV), NINCDS-ADRDA (National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and related Disorders Association), and the Mayo Clinic criteria were applied to ascertain diagnoses of AD and MCI. The incidence rate per 1000 persons-year for MCI was 13.2 (95% confidence interval [CI] 7.79-20.91) and for AD was 14.8 (95% CI 9.04-22.94). Cognitive dysfunction was associated with education (odds ratio [OR] = 0.86; confidence limit [CL] 0.76-0.97 95%) and baseline MMSE (OR = 0.81; CL 0.70-0.94 95%). The AD incidence in this sample was higher than those reported in a previous Brazilian study. The study filled the epidemiological gap in the evaluation of MCI in Brazil.

Keywords: Alzheimer disease; cognitive impairment; dementia; elderly; epidemiology

Introduction

Because the aging of the population is no longer an isolated concern of economically developed areas of the world, many developing countries are also facing the fast demographic aging and its accompanying set of chronic illnesses. Of an estimated 24.3 million people with dementia worldwide in 2005, 14.6 million lived in developing countries and this number will increase in the next decades.[1]

Dementia incidence rates varied from 11.3 per 1000 persons-year in Beijing[2] to 32.4 in Indianapolis, IN.[3] The studies carried out in Nigeria (13.5), Seattle, WA (20.3), and Canada (21.8) presented intermediate values.[3-5] Follow-up varied from 2 years[2] to 5.1 years.[3] Alzheimer disease (AD) incidence rates have showed great variability, as 3.2 per 1000 persons-year in India[6] to 25.2 in Indianapolis, IN.[3] Intermediate rates were 11.5 in Nigeria,[3] and 14.3 and 17.5 in United States.[4,7]

In Brazil, only 2 studies with community-dwelling elderly population have investigated the prevalence and incidence of dementia using contemporary diagnostic criteria.[8,9] Prevalence was 7.1% in a population aged 65 years or older[8] and incidence was 7.7 per 1000 persons-year.[9] Considering the

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prevalence of dementia in Brazil and the elderly population of approximately 15 million, the estimate for dementia is 1.1 million. In terms of public health, in the next decades Brazil will need to develop precise policies in dealing with the aging population and the increasing dementia and comorbid disorders.

Prevalence or incidence of mild cognitive impairment (MCI), and the progression to dementia have demonstrated considerable variability, primarily due to methodological differences in defining this condition. The prevalence rates in epidemiological studies of MCI were found varying between 17% and 85%, depending on the criterion used to define impairment and the population characteristics (eg, age, educational level, sex distribution) under study.[10] When the definition was restricted to the memory impairment, rates have ranged from 2.8% to 5.3%.[11-13] The MCI annual conversion rate to dementia varied from 6% to 25%.[14] The incidence rates ranged from 8.5 per 1000 persons-year[15] to 31.9.[16] The other studies have showed intermediate rates.[17,18] The epidemiology of MCI in Latin America or Brazil is almost inexistent.

The present study aimed at evaluating incident cases of AD and MCI in an elderly community cohort from the catchment area of a university hospital in the largest city of the southernmost state of Brazil. The variables associated with the development of AD and MCI (cognitive dysfunction) were also evaluated.

Methods

Briefly, in 1996, 1216 from 5500 individuals aged 60 years and older who were residing in the catchment area of Hospital de Clinicas de Porto Alegre (Rio Grande do Sul state, Brazil) according to data from the 1992 census[19] were enrolled in 2 studies (Figures 1 and 2). Of the 1216 elderly individuals, 848 were diagnosed with cognitive impairment and/or major medical disorders at baseline and composed the sample for a further study. This yielded a sample of 368 eligible participants for the current analyses. Subsequently, 23 eligible participants (6.3%) declined to take part in the thorough assessment, resulting in the 345 participants who fulfilled criteria for the healthy aging study and consented to participate (Table 1). The baseline study was conducted in 2 assessments with a short interval. The first was composed of selection and exclusion instruments and the second, measures of interest. Each participant underwent a standardized neuropsychological and neurological evaluation. A collateral informant was also used to verify the history.

Figure 1. Map of South America and Brazil with a closer aspect of Rio Grande do Sul state, southern Brazil.

Participants were excluded if they had age-related diseases or risk factors for cognitive impairment at baseline. The exclusion criteria include medical conditions such as chronic renal disease, significant head injury, and stroke; psychiatric conditions such as major affective disorder or evidence of current depression; uncorrectable vision or hearing loss; or other conditions such as substance abuse or use of medications that might impair cognitive functioning (Table 1). All participants and their collateral informants should report normal functioning in the community at entry of study. To minimize inclusion of participants with incipient dementia, participants were screened with the Clinical Dementia Rating (CDR) scale.[20-22] Participants with a CDR global score of 0.5 (suggestive of incipient dementia) or greater (suggestive of dementia) were excluded from the sample. The second interview was composed of detailed demographic and medical information, social support, engagement to leisure activities, a scale to rate symptoms of depression (Montgomery-Åsberg Rating Depression Scale,[23,24] a questionnaire for general psychiatric symptoms (WHO Self-Report Questionnaire),[25,26] the *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition; *DSM IV*) criteria for major depression, MD, and the Mini-Mental State Examination (MMSE).[27,28] Independence for daily living activities was assessed with the activities of daily living (ADL) scale.[29]

Participants for this study are participants in an ongoing longitudinal cohort study. Data for the

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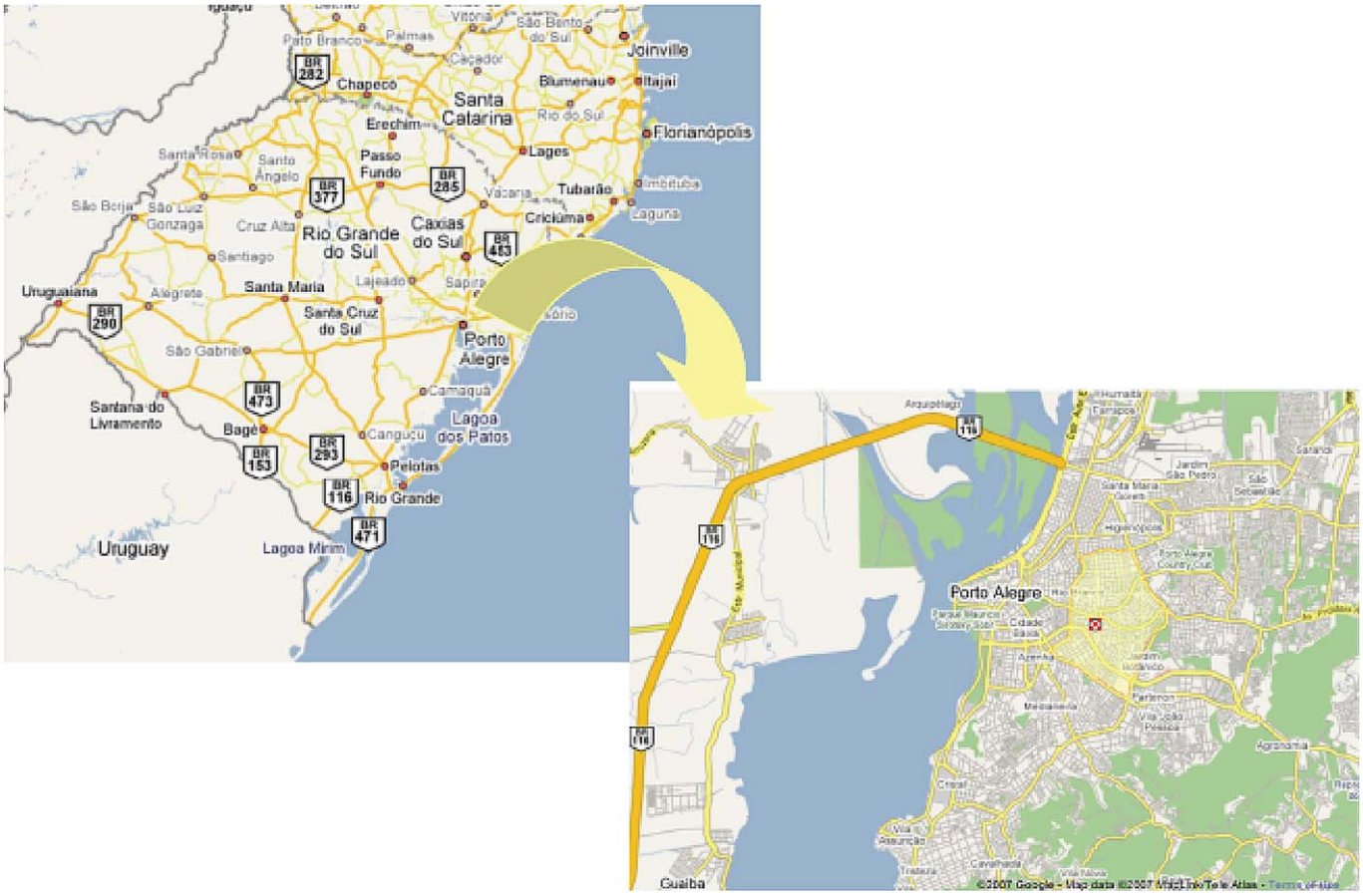

Figure 2. Map of Rio Grande do Sul state and the capital Porto Alegre: closer view to the catchment area of Hospital de Clinicas de Porto Alegre.

present study were derived from the follow-up for a maximum of 8 years. The statistical analysis was based on the diagnosis established at the last follow-up visit during which the participant underwent a thorough evaluation. At least 1 follow-up was completed for 245 participants. Among the deceased in the follow-up, retrospective data were obtained with structured telephone interview with a knowledgeable collateral source focusing on dementia.[30,31] The AD8 (The AD8, a brief informant interview, intends to distinguish individuals with very mild dementia from those without dementia. It contains eight questions asking the informant to rate change (Yes vs No) in memory, problem-solving abilities, orientation, and daily activities.) was additionally applied during the same telephone interview.[32]

Instruments

At each assessment, participants were interviewed in their home environment by trained medical students and physicians. To identify MCI the Mayo Clinic Alzheimer's Disease Research Center criteria were used,[33] as follows: (*a*) memory complaint by patient, family, or physician, (*b*) normal activities of daily living, (*c*) normal general cognitive function, (*d*) objective impairment in 1 area of cognitive function as evidenced by scores >1.5 SD of age-appropriate norms or abnormal memory function for age, (*e*) CDR Global Score of 0.5, and (*f*) not demented. DSM-IV criteria for dementia and the NINCDS-ADRDA for probable AD,[34] with the additional designation from Kawas and colleagues of consistent AD, were performed to ascertain diagnosis of AD.[35] All participants who were identified as suffering from cognitive dysfunction at follow-up were considered incident cases of either MCI or AD.

The study was approved by the Ethics Committee for Research of the Hospital de Clínicas de Porto Alegre. All participants and/or their proxies signed an informed consent.

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Table 1. Participant Selection Criteria

Requirements for Entry	Major Exclusion Criteria
Functionally independent	Medical conditions
Gives informed consent	Myocardial infarction
Willing to participate in the follow-up	Diabetes mellitus
Score = 0 on Clinical Dementia Rating Scale	Chronic pulmonary disorder
Score > 11 on the Blessed Information-Memory-Concentration Test	Chronic renal disease
	Hypertension (supine blood pressure >160/95)
	Active cancer
	Seizure disorder
	Stroke/transient ischemic attack
	Parkinson disease
	Other neurological disorder (LAS, MS, etc)
	Major surgeries
	Coronary bypass
	Carotid endarterectomy
	Psychiatric conditions (previously diagnosed)
	Schizophrenia
	Major affective disorder
	Phobias
	Chronic anxiety
	Alcohol or drug abuse
	Vision and hearing
	Vision uncorrectable to 20/100 OU
	Hearing loss (interferes with speech perception)
	Other conditions
	Significant head injury
	Unexplained prolonged loss of consciousness
	Use of medications impairing cognitive function

NOTE: LAS = lateral amyotrophic sclerosis; MS = multiple sclerosis

Data Analysis

The statistical analysis was performed by the *Statistical Package for the Social Sciences* (SPSS for Windows 14.0) software. Person-years incidence rate was calculated by dividing the number of new cases in the specified period of time by the sum of participants who have been observed in this period, with Mid-P exact test for 95% Confidence Interval. Parametric data were analyzed by 1-way ANOVA with Tukey post hoc. The χ^2 test (with Yates correction or Fisher exact) was used for the association analysis. A logistic regression model was used to identify variables with independent association to subsequent cognitive dysfunction, as well as their association level.

Results

Table 2 summarized the baseline characteristics of the sample. The "at least 1 follow-up completed" group did not differ from the whole baseline sample in terms of education, marital status (living with partner), number of confidants, and MMSE. The incident cognitive dysfunction group presented baseline lower educational attainment than the whole sample and the "at least 1 follow-up completed." The group who did not have 1 follow-up assessment (baseline completed) did not differ from the "at least 1 follow-up completed" group, except for age (Table 2).

Variables were compared between the "at least 1 follow-up completed" and the "cognitive dysfunction" groups with univariate χ^2 test or Student *t* test before entering the logistic regression. Education, MMSE, and number of confidants were statistically different, and age showed borderline result (Table 2).

A logistic regression analysis was carried out with the dependent variable "cognitive dysfunction," and education, age, number of confidants, and MMSE as independent variables. Only education and MMSE were kept in the final equation, which explained 79.9% of the variance (Table 3). A logistic regression to test the interaction of education and MMSE with the other variables as well was carried out, and no significant interaction was observed (data not shown).

Sixteen incident cases of MCI and 18 cases of AD were identified during 8 years of follow-up. The

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Table 2. Baseline Population: Variables at Study Entry[a]

Variables	All (N = 345)	Baseline Completed (N = 100)	At Least 1 Follow-up Completed (N = 245)	Cognitive Dysfunction (N = 34)
Age (mean ± SD)	70.37 ± 7.15	69.02 ± 7.74[b]	70.87 ± 6.86[c]	71.94 ± 6.75[d]
Sex, Male (N, %)	103 (30)	27 (27.3)	76 (31)	09 (27)
Marital status (living with partner)	159 (46%)	45 (45.5%)	113 (46%)[c]	11 (32%)[d]
MMSE (mean ± SD)	25.3 ± 3.9[e]	25.2 ± 4.5	25.4 ± 3.6[c]	23.8 ± 3.3[d]
Education (mean ± SD)	9.06 ± 5.50[e]	9.85 ± 6.03	8.76 ± 5.25[c]	5.91 ± 3.17[d]
Family income (mean ± SD)	22.5 ± 30.0	26.0 ± 37.8	21.2 ± 26.6	20.8 ± 29.1
MADRS	6.7 ± 6.2	6.8 ± 6.4	6.6 ± 6.0	7.1 ± 6.4
SRQ	3.4 ± 2.9	3.4 ± 2.8	3.4 ± 2.9	3.9 ± 3.0
Number of children alive	2.6 ± 2.0	2.7 ± 2.2	2.6 ± 1.9	2.3 ± 1.6
Number of confidants	2.3 ± 2.8	2.6 ± 2.9	2.4 ± 2.7[c]	1.6 ± 2.2[d]

NOTE: ANOVA = analysis of variance; MMSE = Mini-Mental State Examination; MADRS = Montgomery-Åsberg Rating Depression Scale; SRQ = self-report questionnaire.

[a] MMSE = ANOVA with Tukey post hoc, e = c = d ($P = .051$); education = ANOVA with Tukey post hoc, d < c, e ($P < .01$); marital status = chi-square, $P = .05$ (c ≠ d); Age = Student *t* test, c < d ($P = .064$), b < c ($P = .040$); education = Student *t* test, c > d ($P = .001$); MMSE = Student *t* test, c > d ($P = .001$); number of confidants = Student *t* test, c > d ($P = .019$).

Table 3. Logistic Regression Analysis With MMSE Scores, Number of Confidants, Education, and Marital Status (Living With Partner) in the First Evaluation for the Outcome "Cognitive Dysfunction" During the Follow-up

Variables	B	Wald	*P* Value	OR (95% CI)
Number of confidants	–0.191	2.816	.09	0.83 (0.66-1.03)
MMSE	–0.186	5.440	.020	0.83 (0.71-0.97)
Education (years)	–0.139	5.982	.014	0.87 (0.78-0.97)
Age	0.058	2.491	.114	1.06 (0.99-1.14)

NOTE: MMSE = Mini-Mental State Examination; OR = odds ratio.

incidence rate for MCI was 13.2 (95% CI 7.79-20.91) per 1000 persons-year and for AD was 14.8 (95% CI 9.04-22.94) per 1000 persons-year.

Discussion

This study was developed to evaluate incident rates of AD and MCI, and to identify baseline variables associated with incident cases of AD and MCI (cognitive dysfunction). The incidence rate for MCI was 13.2 per 1000 persons-year and for AD was 14.8 per 1000 persons-year. The previous evaluation of AD incidence in Brazil showed the rate of 7.7 per 1000 persons-year.[9] The difference between these 2 studies may be explained by methodological aspects as sample selection, cohort duration, and also the small sample size. The criteria selection used in the current study focused on very healthy participants, which could have increased the occurrence of AD in place of causes such as vascular dementia. In relation to rates reported worldwide, the present AD incidence is intermediate.[3,4,6,7]

The epidemiological evaluation of MCI was a gap to be filled in Brazil. This healthy aging elderly cohort was selected with proper baseline characteristics to study the development of MCI. The MCI assessment with Mayo Clinic criteria incorporated the CDR scale, which was, in the present investigation, highly supportive. In a study using Mayo Clinic criteria, CDR appeared to be the most important part of the criteria and was considered more applicable to community residents.[36] The present study reported a rate of 13.2 per 1000 persons-year for MCI, which can be considered closer to the lower reported rates.[12,15] The variability of rates may not be solely explained by sample characteristic or diagnostic criteria diversity, partially because of the relatively recent description of the MCI.

The logistic regression analysis showed lower education and the lower scores on the MMSE as risk factors for subsequent cognitive dysfunction. The selection criteria for this cohort emphasized healthier and independent participants, which may have led to the inclusion of a more homogeneous group, with higher average education in comparison to the Brazilian ($P < .001$) and to the state ($P < .001$) elderly population. The mean estimate of education in the general elderly population of Brazil is 3.4 years of schooling (±0.02) and is 4.1 (±0.06) for participants living in Rio Grande do Sul state.[19] Therefore,

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the small proportion of participants with lower education might have had a role in this finding. An odds ratio of 0.86 is protective against cognitive dysfunction: each additional year of education adds 1.4% protection against dysfunction. However, a reduction of 1 year of education adds 1.4% risk for dysfunction. Education is associated to level of cognitive function among older persons with and without AD,[37,38] senile plaques and level of cognitive function differs by level of education,[39] and it is accepted that lower education is associated with a higher risk of AD.[40-42] Those who started the study with lower MMSE score showed higher risk for cognitive dysfunction, independent on educational level. Lower scores on modified MMSE, a global cognitive screening instrument, has already been observed to be associated to MCI.[43]

Limitations of the Study

The stringent exclusion criteria, focused on a very healthy elderly cohort, could have influenced the current results leading to lower incidence rates in the study. The small sample size could also have influenced these rates. The strength of the study is the length of the follow-up of this elderly sample in a Latin American country. To succeed in following a sample of elderly in Brazil, a country which until recently was known as the "country of the youth," is a great challenge. Obtaining data from collateral informants for the deceased during the cohort was also important in the study. There is evidence demonstrating moderate agreement between the informant CDR and the clinician CDR, suggesting the valid role for CDR as a substitute in situations in which the participant could not be examined.[30]

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