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Reliability of the Brazilian Portuguese version of the Neuropsychiatric Inventory (NPI) for patients with Alzheimer's disease and their caregivers

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ABSTRACT

Background: Behavioral symptoms and caregivers' responses may differ among various ethnic and cultural groups. Therefore it is important to have a reliable instrument to assess behavioral disturbances of dementia in various cultures. The Neuropsychiatric Inventory (NPI) has been widely used in many countries. To date there has been no reliability study of this instrument in Brazil.

Methods: The psychometric properties of the Brazilian Portuguese version of the NPI were studied in a sample of 36 Alzheimer's disease (AD) outpatients from southern Brazil. Test-retest, inter-rater reliability and internal consistency were estimated. The profile of neuropsychiatric symptoms and caregiver distress were also evaluated. The NPI was translated into Portuguese and then back translated to English.

Results: The Brazilian Portuguese version of the NPI showed good inter-rater and test-retest reliability with the coefficients of all scales > 0.85. Internal consistency was also good (Cronbach's α 0.70 for total severity and distress). Apathy provided higher NPI scores of total severity and distress.

Conclusions: This NPI version was found to be a reliable instrument for the evaluation of neuropsychiatric symptoms and caregiver distress due to dementia in AD. The profile of behavioral disturbances was similar to that observed in other countries. Severity of dementia may have biased some caregivers' answers.

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Introduction

Neuropsychiatric symptoms are very common in Alzheimer's disease (AD) and are associated with significant distress to patients and caregivers, higher costs and poor prognosis (Mega *et al.*, 1996; Lyketsos *et al.*, 2001; 2002; McKeith and Cummings, 2005).

Many scales measure behavioral symptoms in dementia, such as the Cohen-Mansfield Agitation Inventory (Koss *et al.*, 1997), the Behavioral Pathology in Alzheimer's Disease Rating Scale – BEHAVE-AD (Reisberg *et al.*, 1987) and the Neuropsychiatric Inventory (NPI) (Cummings *et al.*, 1994). Even psychiatric rating scales like the Brief Psychiatric Rating Scale (BPRS) (Overall and Gorham, 1988) or the Hamilton Depression Rating Scale were also used for this purpose (Hamilton, 1960).

The Neuropsychiatric Inventory (NPI) is a valid and reliable instrument originally developed to assess 10 neuropsychiatric disturbances commonly observed in dementia (Cummings *et al.*, 1994). Subsequently this instrument was modified to evaluate 12 disturbances (Cummings, 1997). Furthermore, an adjunct scale, the NPI Distress (NPI-D) was developed to provide a quantitative measure of the distress experienced by caregivers in relation to individual symptom domains assessed by the NPI that was also reliable and valid (Kaufer *et al.*, 1998).

The NPI has been translated into many different languages: Japanese, Italian, Spanish, Korean, Taiwanese, Chinese, Dutch, Nigerian and Greek versions have all been shown to have good psychometric properties (Hirono *et al.*, 1997; Binetti *et al.*, 1998; Vilalta-Franch *et al.*, 1999; Choi *et al.*, 2000; Fuh *et al.*, 2001; Leung *et al.*, 2001; Kat *et al.*, 2002; Baiyewu *et al.*, 2003; Politis *et al.*, 2004).

The pattern of behavioral symptoms and caregivers' responses may differ among various ethnic and cultural groups; therefore, it is important to have a reliable instrument to assess behavioral disturbances of dementia in various settings. The NPI has already been used in a previous Brazilian study on the prevalence of neuropsychiatric symptoms in Alzheimer disease and cognitively impaired nondemented elderly (Tatsch *et al.*, 2006). However, no parameters of validation have been published for a Brazilian Portuguese version of NPI.

This study aimed to evaluate the test-retest, inter-rater reliability and internal consistency of the Brazilian Portuguese version of NPI and NPI-D and to determine the NPI profile in a sample of outpatients with Alzheimer's disease in southern Brazil.

Methods

A cross-sectional study was conducted in a sample of AD patients and their caregivers selected by consecutive referrals from the Alzheimer's Disease Center and Neurogeriatric Clinic from the Hospital de Clinicas de Porto Alegre, Brazil.

Table 1. Demographic data and MMSE scores of 36 outpatients with Alzheimer's disease

	ALZHEIMER'S DISEASE PATIENTS	CAREGIVERS
Age (mean ± SD)	78.78 ± 7.48	51.61 ± 12.30
Education (mean ± SD)	5.06 ± 4.50	12.30 ± 3.30
Sex–female (N,%)	28 (78%)	30 (83%)
MMSE score (mean ± SD)	7.06 ± 6.92	–

The diagnosis of dementia was based on the history of cognitive and functional impairment, and clinical and neurological examination. Impairment of cognitive function was demonstrated using standardized tests. Neuroimaging and routine blood tests (including thyroid hormones, serum vitamin B_{12} level, and screen test for syphilis) were also performed.

All patients fulfilled the DSM-IV criteria for dementia (American Psychiatric Association, 1994) and the NINCDS-ADRDA for probable AD (McKhann *et al.*, 1984). The Mini-mental State Examination (MMSE) (Folstein *et al.*, 1975; Chaves and Izquierdo, 1992) and the Clinical Dementia Rating scale (CDR) were also applied (Hughes *et al.*, 1982; Maia *et al.*, 2006; Chaves *et al.*, 2007).

A sample size of 36 dementia patients was calculated based on a minimum Pearson coefficient correlation test-retest of 0.6 for NPI observed in the study by Choi *et al.* (2000), an alpha error = 5% and beta error = 20%. Demographic data of patients and caregivers, and MMSE scores are shown in Table 1. According to the CDR, nine (25%) subjects were classified as having mild dementia, eight (22.2%) as having moderate dementia and 17 (47.7%) as having severe dementia.

The original English versions of NPI and NPI-D scales were translated into Brazilian Portuguese by two Portuguese native speakers who work in the area of neuropsychiatry and are fluent in English. Subsequently, the Brazilian Portuguese version was back translated into English by an English native-speaking physician who has lived in Brazil for the past 10 years. Final adaptations were carried out to ensure full cultural and educational comprehension.

The interviews followed the same structure and scoring methods described in the original English versions (Cummings *et al.*, 1994; Kaufer *et al.*, 1998) and were performed by trained medical students. A screening question was asked first, followed by subquestions if the answer to the screening question had suggested the presence of abnormalities involving that neuropsychiatric domain. The first interview was rated by two different assessors to allow inter-rater reliability analysis. A second NPI interview was administered within five to seven days by a different interviewer who was kept blind to the results of the previous evaluation. This was carried out for the test-retest reliability analysis.

The NPI and NPI-D scale versions were administered to 36 caregivers who were very familiar with their patient's behavior. Twelve behavioral disturbances (delusions, hallucinations, dysphoria, anxiety, agitation/aggression, euphoria, disinhibition, irritability/lability, apathy, and aberrant motor activity, night-time behavior disturbances, and appetite and eating abnormalities) were evaluated. The NPI consists of three sections for each symptom: frequency, severity, and distress. Frequency and severity of each patient's behaviors were rated as well as the caregiver's distress. The total severity (frequency × severity) score and the total distress score were calculated as the sum of the scores for each symptom. The total NPI score is the sum of the subscales scores.

Descriptive statistics (mean, SD and frequency) were calculated for demographic data, symptoms of NPI, performance on MMSE and CDR. Spearman's rho correlation coefficients were estimated for the test-retest and intra-class correlation coefficients for inter-rater reliability on the total NPI and total distress score. Internal consistency of the scale was analyzed by Cronbach's α.

MMSE correlation with total NPI score was evaluated. The comparison of the total NPI scores between the global CDR scores (≤ 2 and 3) was tested by the non-parametric Mann-Whitney test. The statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS 14).

The study was approved by the Ethics Committee for Medical Research at Hospital de Clinicas de Porto Alegre. Patients and their proxies signed an informed consent before being enrolled into the study.

Results

Test-retest scores of all measures were significantly correlated. Spearman's rho coefficient correlations were 0.82 ($p = 0.01$) for the total severity score, 0.80 for the frequency score ($p = 0.01$), and 0.86 for the severity score ($p = 0.01$). Spearman correlations among the 12 NPI behaviors in the entire group for the total severity subscores for each behavioral domain are shown in Table 2. The test-retest correlation for the caregivers' total distress score was also significant ($r = 0.88$) ($p = 0.01$).

The intra-class correlation coefficients were 0.98 ($p = 0.001$) for the total severity score and 0.96 ($p = 0.001$) for the total distress score. The intra-class correlation coefficient of the total severity score for each NPI domain is shown in Table 3. Cronbach's α for both total severity and total distress reliability (across 12 domains) was 0.7.

Only one out of the 36 patients scored zero on the total severity NPI score. Observing the mean value of the total severity score for all symptoms, apathy showed the highest mean value (5.31 ± 4.91), followed by anxiety (4.11 ± 4.52), aberrant motor behavior (4.03 ± 5.13), dysphoria (3.53 ± 3.98), agitation (3.36 ± 3.96), delusions (2.92 ± 3.85), hallucinations (2.69 ± 3.74), night-time behavior disturbances (2.61 ± 4.46), irritability (2.58 ± 3.97) and appetite/eating abnormalities (2.46 ± 3.88). Euphoria (0.58 ± 2.06) and disinhibition (1.0 ± 2.63) had the lowest mean values. These data are illustrated

Table 2. Test-retest reliability of the total severity NPI items

BEHAVIOR	SPEARMAN'S RHO CORRELATION COEFFICIENT	P-VALUE
Delusions	0.71	0.01
Hallucinations	0.74	0.01
Agitation/aggression	0.62	0.01
Dysphoria	0.71	0.01
Anxiety	0.62	0.01
Euphoria	0.52	0.01
Apathy	0.53	0.01
Disinhibition	0.40	0.05
Irritability/lability	0.62	0.01
Aberrant motor activity	0.60	0.01
Night-time behavior disturbances	0.97	0.01
Appetite and eating abnormalities	0.68	0.01

Table 3. Inter-rater reliability of total severity NPI items

BEHAVIOR	INTRA-CLASS CORRELATION COEFFICIENT	95% CI	P-VALUE
Delusions	0.87	0.75–0.96	0.001
Hallucinations	0.77	0.54–0.88	0.001
Agitation/aggression	0.86	0.73–0.93	0.001
Dysphoria	0.70	0.40–0.85	0.001
Anxiety	0.75	0.50–0.87	0.001
Euphoria	0.12	−0.79–5.61	0.30
Apathy	0.67	0.35–0.84	0.001
Disinhibition	0.39	−0.24–0.63	0.08
Irritability/lability	0.81	0.62–0.90	0.001
Aberrant motor activity	0.67	0.35–0.84	0.001
Night-time behavior disturbances	0.91	0.82–0.95	0.001
Appetite and eating abnormalities	0.80	0.58–0.90	0.001

in Figure 1. Frequency of symptoms (not present, occasional and often, or frequent and very frequent) according to the judgment of caregivers was also evaluated. Table 4 displays the frequency of reported symptoms on the NPI. Apathy was also more frequently reported.

Higher caregiver distress was caused by apathy (1.9 ± 2.0), followed by agitation/aggression (1.84 ± 1.61), anxiety (1.80 ± 1.56), night-time behavior disturbances (1.79 ± 1.14), delusions (1.78 ± 1.39), irritability/lability (1.73 ± 1.17). Dysphoria (1.70 ± 1.47), hallucinations (1.35 ± 0.81), disinhibition

Table 4. Frequency of neuropsychiatric symptoms according to the judgment of caregivers

SYMPTOMS	NOT PRESENT	OCCASIONAL/ OFTEN	FREQUENT/VERY FREQUENT
Delusions	17 (47%)	4 (11%)	15 (42%)
Hallucinations	17 (47%)	8 (22%)	11 (31%)
Agitation/aggression	14 (39%)	11 (31%)	11 (31%)
Dysphoria	13 (36%)	10 (28%)	13 (36%)
Anxiety	15 (42%)	4 (11%)	17 (47%)
Euphoria	30 (83%)	6 (17%)	0 (0%)
Apathy	12 (33%)	1 (3%)	23 (64%)
Disinhibition	30 (83%)	4 (11%)	2 (6%)
Irritability/lability	23 (64%)	1 (3%)	13 (36%)
Aberrant motor activity	20 (56%)	1 (3%)	15 (42%)
Night-time behavior disturbances	25 (69%)	3 (8%)	8 (22%)
Appetite and eating abnormalities	23 (64%)	2 (6%)	11 (31%)

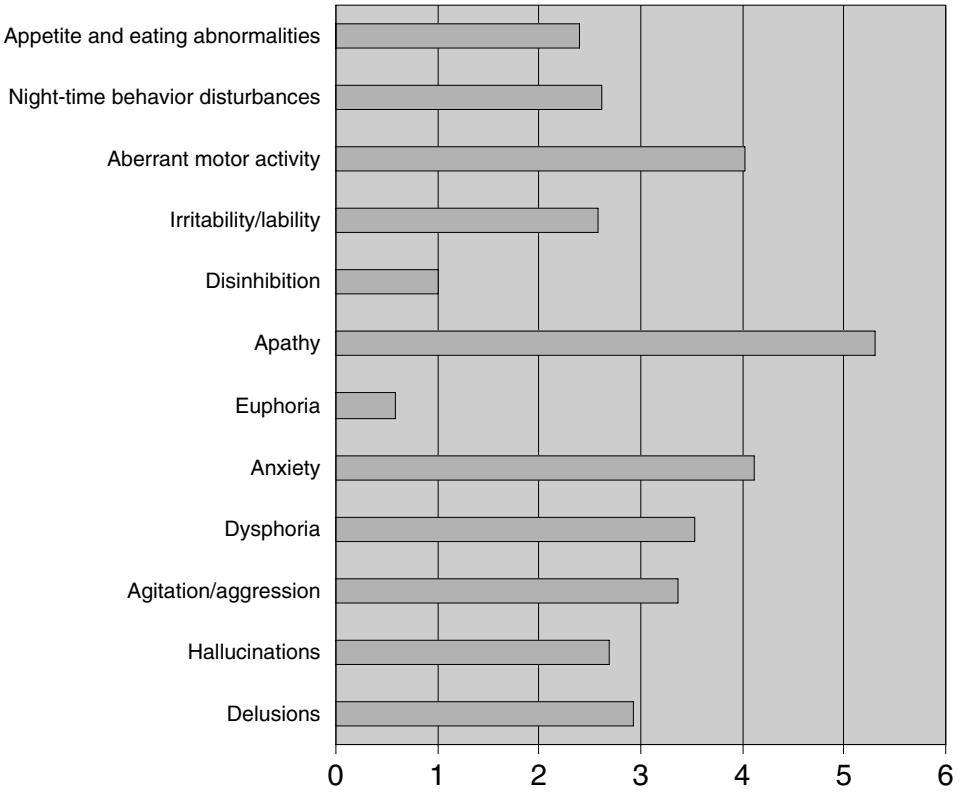

Figure 1. Total severity NPI score for each domain (mean).

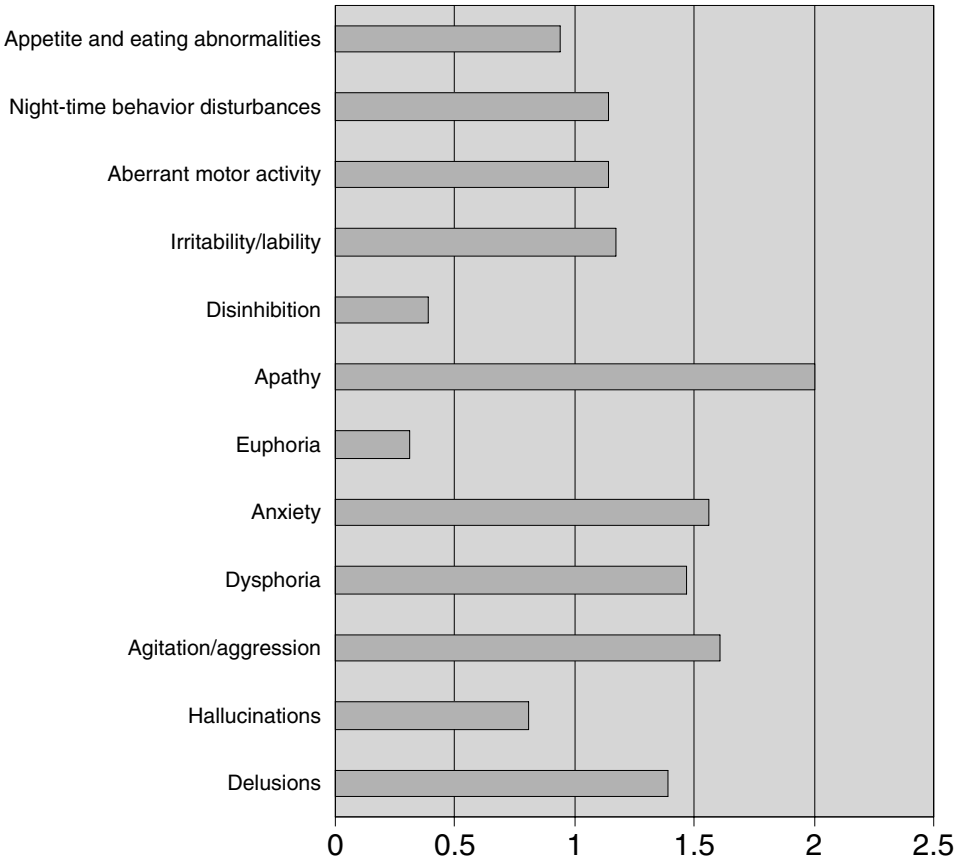

Figure 2. Distress NPI score for each domain (mean).

(1.05 ± 0.39) and euphoria (1.04 ± 0.31) were those that caused the least distress for the caregivers (Figure 2). Caregivers' education showed no correlation with total NPI distress ($r = -0.19$; $p > 0.05$).

No significant correlation among patients' education, age and total NPI score was observed ($r = -0.09$; $p > 0.05$ and $r = 0.04$; $p > 0.05$) respectively. The median (interquartiles) of the total NPI score of CDR ≤ 2 was 38 (17.50–50.50) and of CDR $= 3$ was 25.00 (14.00–35.50) (Mann-Whitney test; $U = 79$; $p = 0.07$). Likewise, no significant difference of total NPI score was observed between male and female patients (Mann-Whitney test; $U = 101.5$; $p = 0.7$).

Discussion

This study of the Brazilian Portuguese version of the NPI has demonstrated that it is a reliable instrument. The good test-retest correlation coefficients for the total NPI score (0.82) and for the total NPI distress score (0.88) were similar to NPI versions in other cultures. American, Italian, Korean and Nigerian versions

of the same instrument also showed good test-retest correlation coefficients ranging from0.64 to 0.86 (Cummings, 1997; Binetti *et al.*, 1998; Choi *et al.*, 2000; Baiyewu *et al.*, 2003). Our very good ($r = -0.96$) inter-rater reliability was measured using intra-class correlation coefficients. Other studies also found similar results (Binetti *et al.*, 1998; Choi *et al.*, 2000; Leung *et al.*, 2001; Baiyewu *et al.*, 2003). The Cronbach's α of 0.7 for the severity scale and for the distress scale also indicated a good internal consistency. These findings guaranteed an important psychometric property of the scale, namely, reliability. We found a low correlation coefficient for some items such as disinhibition and euphoria. The high score dispersion for these symptoms in our sample may have influenced these results. The dispersion could have been caused by the higher caregiver report rate of these symptoms being absent (corresponding to zero on the scale).

Almost half of the studied sample had severe AD (CDR = 3). Apathy was the most frequently reported symptom, as demonstrated in most other studies (Mega *et al.*, 1996; Hirono *et al.*, 1997; Binetti *et al.*, 1998; Vilalta-Franch *et al.*, 1999; Fuh *et al.*, 2001; Politis *et al.*, 2004). The findings of the Nigerian NPI study showed appetite change, depression and irritability as the most frequently recorded behaviors (Baiyewu *et al.*, 2003). Dysphoria was more infrequent than apathy in our study, and might indicate the hypothesis of domain independence for apathy and dysphoria. There is evidence that apathy in AD either co-exists with depression or is isolated and does not increase depression scores (Starkstein *et al.*, 2001). Anxiety and motor aberrant behavior were also frequent as in other studies (Cummings *et al.*, 1994; Cummings, 1997; Hirono *et al.*, 1997; Binetti *et al.*, 1998; Choi *et al.*, 2000; Fuh *et al.*, 2001). Disinhibition and euphoria were less common, as might be expected in an AD sample but not among frontotemporal dementia patients.

We did not observe significant correlation between the total NPI score with age, sex or education, because neuropsychiatric symptoms might be independent of demographic variables. This lack of correlation has been already shown in other studies (Choi *et al.*, 2000). On the other hand, Mega and co-workers (1996) have demonstrated a significant association between men and agitation. However, in that study the patients had less severe dementia more men than in our sample.

The total distress score test-retest and inter-rater coefficients were also good, and were very similar to the original coefficients (Kaufer *et al.*, 1998). Apathy was the item that caused the highest distress. Depression and irritability have both been shown to promote higher distress scores (Baiyewu *et al.*, 2003). Most caregivers from our sample were middle-aged women with higher levels of education. There was no correlation between the caregiver's education and the total distress score. We had expected higher caregiver distress with other symptoms, such as agitation/aggression, night-time behavior disturbances or motor aberrant behavior, because these symptoms are highly demanding and frequently are the main cause of requiring medical assistance. A misinterpretation of the screening question for apathy could have occurred. Despite the existence of the option "not applied" for this question, caregivers could have figured the severity of cognitive deficit out as apathy and assigned

higher severity and distress scores for this symptom. This may be a difficulty when using the NPI to evaluate severe dementia.

The higher rate of severe dementia patients in the sample could be one of the weaknesses of our study. It might be desirable to increase the proportion of mild and moderate groups to compare the results. The findings regarding frequency of symptoms should be interpreted with caution given the relatively small sample size.

To our knowledge, this is the first validation study of a Brazilian Portuguese version of the NPI. It has shown the reliability and internal consistency of this NPI and NPI-D version in a sample of AD outpatients in southern Brazil and showed a similar behavior profile as studies developed in other countries. Concurrent validity and diagnostic properties were not evaluated and these properties deserve special attention in future studies.

Conflict of interest

None.

Description of authors' roles

Ana Luiza Camozzato supervised the data collection, was responsible for carrying out the statistical analysis and wrote the paper; Renata Kochhann collected the data and was responsible for carrying out the statistical analysis; Camila Simeoni, Cássio Konrath, Adelar Pedro Franz collected the data and assisted with writing the article; André Carvalho designed the study, and collected the data; Márcia L. Chaves designed the study, was responsible for the statistical design of the study, supervised the data collection, and wrote the paper.

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