Published in final edited form as:
Int Psychogeriatr. 2013 September ; 25(9): 1503–1511. doi:10.1017/S1041610213000811.

The Brazilian version of the Neuropsychiatric Inventory-Clinician rating (NPI-C): Reliability and validity in dementia

Florindo Stella[1,2,3], **Orestes Vicente Forlenza**[2], **Jerson Laks**[4], **Larissa Pires de Andrade**[1], **Michelle A. Ljubetic Avendaño**[2], **Elisandra Villela Gasparetto Sé**[3], **João de Castilho Cação**[5], **Constantine G. Lyketsos**[6], and **Kate de Medeiros**[7]

[1]UNESP – Universidade Estadual Paulista, Biosciences Institute, Rio Claro, Brazil

[2]Laboratory of Neurosciences (LIM-27), Department and Institute of Psychiatry, Faculty of Medicine, University of São Paulo, Brazil

[3]State University of Campinas, Clinic of Geriatric Psychiatry, Faculty of Medicine, Brazil

[4]Centre for Alzheimer's disease and Related Disorders, Institute of Psychiatry, Federal University of Rio de Janeiro, Brazil

[5]FAMERP – Faculty of Medicine, Geriatric Unity, São José do Rio Preto, Brazil

[6]Johns Hopkins University, Department of Psychiatry, and Johns Hopkins Bayview, Baltimore, MD, USA

[7]The Department of Sociology and Gerontology, Miami University, Oxford, Ohio, USA

Abstract

Background—Patients with dementia may be unable to describe their symptoms, and caregivers frequently suffer emotional burden that can interfere with judgment of the patient's behavior. The Neuropsychiatric Inventory-Clinician Rating Scale (NPI-C) is a comprehensive and versatile instrument to assess neuropsychiatric symptoms (NPS) in dementia. In the NPI-C, the clinician incorporates information from caregiver and patient interviews, and any other relevant available data to accurately measure NPS. The present study is a followup to the original, cross-national NPI-C validation evaluating the reliability and concurrent validity of NPI-C in quantifying psychopathological symptoms in dementia in a large Brazilian cohort.

Methods—Two blind raters evaluated 312 participants (156 patient-knowledgeable informant dyads) with the NPI-C totaling 624 observations in 5 Brazilian centers. Inter-rater reliability was determined through calculation of intraclass correlation coefficients for the NPI-C domains and traditional NPI. Convergent validity included correlations of specific domains of the NPI-C with the Brief Psychiatric Rating Scale (BPRS); the Cohen Mansfield Agitation Index (CMAI); the Cornell Scale for Depression in Dementia (CSDD); and the Apathy Inventory (AI).

Results—Inter-rater reliability was strong for all NPI-C domains. There were high correlations between NPI-C/Delusions and BPRS; NPI-C/Apathy-Indifference with the AI; NPI-C/Depression-Dysphoria with the CSDD; NPI-C/Agitation with the CMAI; and NPI-C/Aggression with the CMAI. There was moderate correlation between the NPI-C/Aberrant Vocalizations and CMAI and the NPI-C/Hallucinations with the BPRS.

Conclusion—The NPI-C is a comprehensive tool which provides accurate measurement of NPS in dementia with high concurrent validity and inter-rater reliability in the Brazilian setting. In addition to universal assessment, the NPI-C can be completed by individual domains.

Keywords

neuropsychiatric symptoms; dementia; Alzheimer's disease; scale; neuropsychiatric assessment

INTRODUCTION

In addition to cognitive and functional impairment, neuropsychiatric symptoms (NPS) are a near universal aspect of a dementia diagnosis (Gauthier *et al*., 2010; Dubois *et al*., 2011; Lyketsos *et al*., 2011). NPS contribute to increased patient suffering and caregiver burden, and lead to diminished quality of life for patients and family members. NPS also predict likelihood of earlier institutionalization, interact with other comorbidities, accelerate disease progression, and increase mortality risk (Gauthier *et al*., 2010; Lyketsos *et al*., 2011; Lyketsos *et al*., 2012; Wadsworth *et al*., 2012). In addition, multiple co-occurring NPS (e.g., depression with apathy, irritability with aggression or delusions with agitation) complicate the clinical picture, creating challenges for diagnosis and treatment (Brodaty *et al*., 2001; Lopez *et al*., 2003; de Medeiros *et al*., 2010; Lyketsos *et al*., 2011; Benoit *et al*., 2012). In Brazil, several cohort studies found high prevalences of NPS in dementia, namely apathy, agitation, aggression, depression, sleep disturbances, anxiety, and aberrant motor behavior (Tatsch *et al*., 2006; Camozzato *et al*., 208; Truzzi *et al*., 2013).

Even in prodromal stages of dementia, NPS may also be present; indeed, recent studies have shown that the occurrence of NPS in patients with mild cognitive impairment (MCI) may increase the risk of subsequent progression to dementia (Taragano *et al*., 2009; Di Iulio *et al*., 2010; Lyketsos *et al*., 2011). Sperling and colleagues (2011) postulated that cognitive and behavioral changes could represent an early stage of a progressive dementia in individuals with evidence of a long asymptomatic period characterized by neuropathological Alzheimer's Disease (AD) biomarkers. Accurate measurement of NPS, even at early stages of dementia, is therefore critical for diagnosis and treatment (Sperling *et al*., 2011; Gauthier *et al*., 2010; Lyketsos *et al*., 2011).

Despite approaches to improve accurate measurement of NPS in dementia, there are several major challenges for clinicians and researchers. Many existing measurements are based solely on patient's or caregiver's inputs, leading to significant measurement limitations. The patient may be unable to provide reliable information due to cognitive decline (e.g., forgetfulness) or lack insight; caregivers frequently suffer emotional burden that interferes with appropriate judgment of the patient's behavior (Rosenberg *et al*., 2005; de Medeiros *et al*., 2010; Lyketsos *et al*., 2011). Reports by patients and caregivers alone may therefore not provide a complete or accurate picture of NPS. In contrast, clinicians with training in NPS screening in patients with dementia patients should be able to incorporate caregiver and patient information along with their clinical judgment to achieve a better understanding of the behavioral syndrome. This strategy of using clinical impression ratings can improve accuracy in measuring the clinical relevance of each symptom, as well as in distinguishing neuropsychiatric conditions when symptoms overlap, for instance deciding whether a given symptom is due to apathy or depression, a decision usually difficult for the non-clinician (de Medeiros *et al*., 2010; Benoit *et al*., 2012).

The Neuropsychiatric Inventory-Clinician Rating Scale (NPI-C) is a comprehensive and versatile psychometric scale that has been designed to measure NPS both in clinical and research settings. As compared to similar instruments designed for the same purpose, the NPI-C rating incorporates the expert clinician's impressions (i.e., all relevant information according to his/her clinical judgment and patient records) to the data provided by patients and caregivers. The NPI-C output may be readily compared across distinct investigation sites, which renders it particularly useful for clinical trials (de Medeiros *et al*., 2010; Lyketsos *et al*., 2011). The present study is a followup to the original, cross-national NPI-C validation (de Medeiros *et al*., 2010) evaluating the reliability and concurrent validity of NPI-C in quantifying psychopathological symptoms in dementia in a large Brazilian cohort.

METHODS

Structure of the NPI-C

The development and cross-national validation of NPI-C was led by K. de Medeiros and C.G. Lyketsos with participation of an international group including researchers from Argentina, Australia, Brazil, Canada, France, Greece, Hungary, Italy and the United States. This group worked closely with the original developer of the Neuropsychiatric Inventory (NPI; Cummings, 1994). De Medeiros *et al*. (2010) published the final version of the NPI-C making it available for researchers and clinicians.

NPI-C was translated into Portuguese (Brazil) (Inventário Neuropsiquiátrico – Avaliação do Clínico - NPI-C): An independent expert in English performed the back-translation into English to verify the reliability of the text to be used in Brazil.

In NPI-C, items of the traditional NPI have been expanded. “Agitation/aggression,” one domain in the NPI, was divided into two domains on the NPI-C to capture specific symptoms related to each type of symptom. The domain “aberrant vocalizations” was added to the NPI-C as a new domain to assess symptoms frequently present in advanced dementia (de Medeiros *et al*., 2010).

One limitation of the traditional NPI concerns scoring that is based solely on caregiver reports provided during a clinical interview (Lyketsos *et al*., 2011). Caregivers provide a global rating of frequency, severity and caregiver distress for each of 12 NPS domains. Two relevant changes were incorporated in NPI-C. First, rather than provide a global rating, caregivers are asked to rate individual symptoms within a domain for frequency, severity and caregiver distress. Since it is well known that caregiver informants often suffer emotional burdens that may lead to biased reporting of the patient's symptomatology, the second important change is a clinical judgment rating of NPS. The clinician now provides a rating for each item in each domain based on interview with caregiver (and or other informants) direct observation of and interaction with the patient, and additional information from patient record. The clinician scoring assessment minimizes potential inaccuracies or misinterpretation of symptoms (e.g., confusing apathy with depression) by the caregiver (de Medeiros *et al*., 2010; Lyketsos *et al*., 2011). Thus, changes in NPI-C represent a rating approach that can reduce inappropriate influences from caregivers or family members when they report the nature or severity of neuropsychiatric symptoms.

Inclusion criteria

In the present study, the inclusion criteria were the same applied to the original validation of the NPI-C (de Medeiros *et al*., 2010) and were divided into two parts: a) knowledgeable informants and b) patients. For knowledgeable informants (caregiver or family members), inclusion criteria were capacity to identify and to report on NPS in the patient over the past month, and having maintained regular verbal contact with the patient at least three times per week during the past three months. Patients were included is they had a medical diagnosis of probable Alzheimer's disease as well as a knowledgeable informant (caregiver or family member).

Sample

We studied 312 participants from 5 Brazilian centers (156 patient-knowledgeable informant dyads), who completed the NPI-C with two blinded raters, totaling 624 observations. In these centers (São Paulo, Rio de Janeiro, Campinas, São José do Rio Preto, and Rio Claro), the raters determined dementia severity by Mini-Mental State Examination (MMSE; Folstein *et al*. 1975), Clinical Dementia Rating (CDR; Hughes *et al*., 1982), Pfeffer

Functional Activities Questionnaire (Pfeffer, 1982), and Global Deterioration Scale (GDS; Reisberg *et al*., 1982). Table 1 summarizes participant demographic and clinical data including MMSE, CDR, and GDS.

Ethics review boards approved the study, and family members or legal representatives signed written informed consent, as did as patients who were able to understand the purpose of investigation. The research was conducted according to the principals of the Helsinki Declaration.

Procedures

We performed a cross-sectional investigation of patients and respective caregivers to estimate inter-rater reliability and convergent validity of the Brazilian translation of NPI-C. For the validation of the NPI-C, all participants (100%) completed the scale.

a) Inter-rater reliability—At each center, two independent and trained raters interviewed each knowledgeable informant/patient dyad at different times (in general in the same day or at least within the same week) in order to estimate the inter-rater reliability of the NPI-C. Before administering the measure, an investigator (FS) who previously had participated in the original validation of the NPI-C trained the raters on completion of all study scales. Eligible clinician raters for this study were working regularly at specialized centers with patients with dementia observing or making diagnostic procedures, providing appropriate care, counseling caregivers or family members, and establishing or following pharmacological or non-pharmacological treatment.

Each independent rater completed the NPI-C. At first, caregivers were asked to rate the frequency and severity of each item in each domain, as well as estimate their distress level due to the patient's behavior. In addition, raters interviewed the patient. This provided them an opportunity to interact with the patient and, when possible, to obtain the patient's insight into their recent experiences that may be related to NPS. Based on caregiver answers, patient interview, and any additional clinical information (e.g., a specific report from patient record), raters used their experience and judgment to determine the final score in each symptom of the NPI-C. Symptom scores in each of the 14 domains were added up to produce total clinican rating domain scores. Inter-rater reliability was determined through calculation of intraclass correlation coefficients for the NPI-C domain scores, as well as for those of the traditional NPI that was administered as part of the NPI-C (Shrout and Fleiss, 1979).

b) Convergent Validity—The estimates of convergent validity included correlations of specific domains of the NPI-C with other specific measures of NPS the Brief Psychiatric Rating Scale (BPRS; Ventura *et al*., 1993); the Cohen Mansfield Agitation Index (CMAI; Cohen-Mansfield *et al*., 1989); the Cornell Scale for Depression in Dementia (CSDD; Alexopoulos *et al*., 1988); and the Apathy Inventory (AI; Robert *et al*., 2002; 2010). One of two raters completed these four scales. Pearson correlations of these data provided statistical support for convergent validity, as well as for test-retest reliability.

Data analyses

Descriptive analyses including mean, standard deviation, and frequency were estimated for general demographic data such as age, gender, and years of education, as well as clinical performance on scores from performance on MMSE, Pfeffer Functional Activities Questionnaire, CDR, GDS, CMAI, BPRS, CSDD, and AI. Inter-rater reliabilities for each NPI-C and NPI domain were estimated by calculating intraclass correlations (ICC).

Convergent validity was estimated by calculating Pearson correlations coefficient between NPI-C domains and selected scales (NPI-C/Delusions vs. BPRS; NPI-C/Hallucinations vs. BPRS; NPI-C/Agitation vs. CMAI; NPI-C/Aggression vs. CMAI; NPI-C/Aberrant Vocalizations vs. CMAI; NPI-C/Depression vs. CSDD; and NPI-C/Apathy vs. AI). We also examined convergent validity by dementia severity based on CDR scores. All statistical analyses were carried out using SPSS 20.0.

RESULTS

Demographic and clinical features

Table 1 displays demographic and clinical data from patients (n=156) according to severity levels of dementia based on CDR scores: 60 had mild dementia (CDR 1), 53 moderate (CDR 2), and 43 severe (CDR 3).

Inter-rater reliability

Based on Pearson correlation coefficient, inter-rater reliability was strong for all NPI-C domains as evident in Table 2. In addition, inter-rater reliability was strong for the NPI traditional score (r=0.923). Table 2 displays these data. Caregiver reliability, which was provided by the clinician rater using a brief questionnaire, was available for 109 individuals and was moderate (r=0.601; 95% CI [0.47, 0.71]).

Convergent validity

Table 3 reports Pearson correlations coefficients with their 95% confidence intervals for convergent validity. There were significant correlations of specific NPI-C domains with selected scales.

Based on dementia severity according to CDR levels, Table 4 includes correlations between specific NPI-C domains and selected scales that measure same psychopathological syndromes, with 95% confidence intervals for concurrent validity.

DISCUSSION

The present study aimed to estimate the convergent validity and inter-rater reliability of the Brazilian version of the NPI-C. In doing so, the study covers an important gap in the measurement of psychopathological symptoms in dementia in Brazilian community.

Validated methodological strategies are critical to assess NPS in patients with dementia. The NPI-C is a special tool for this purpose as it includes simultaneously the point of view reported by caregiver or family member, the observation of the patient achieved by the rater, and the clinician judgment established for each symptom with taking into consideration all information accumulated. NPI-C encompasses all traditional NPI domains, includes more items and one new domain (aberrant vocalizations), and uses clinician judgment to rate the severity of each neuropsychiatric symptom. These improvements rectified important weaknesses of the traditional NPI. In each domain of NPI-C, the clinician ultimately decides on the clinical value of each symptom considering responses from knowledgeable informant, the direct interview with the patient, and additional relevant information from patient's record or from direct observation of patient's behaviors. This clinician judgment provides more accurate assessment of NPS in dementia. NPI-C is available to be used as a broad-spectrum scale or as a single tool driven to selected neuropsychiatric domains.

The results demonstrate strong correlations of NPI-C domains with selected scales, which measure the same psychopathological syndromes in dementia. The high convergent validity

and inter-rater reliabilities provide support for use of NPI-C across clinical and researches settings, as well as in clinical trials.

Given that aging in Brazil is becoming a major challenge, efforts are needed to achieve reliable and valid measures of cognitive, functional, *and* NPS in dementia (Tatsch *et al*., 2006; Memória *et al*., 2013; Truzzi *et al*., 2013). The availability of the Brazilian validated version of the NPI-C could represent a useful contribution for research and clinical trials on neuropsychiatric syndromes in dementia.

Inter-rater reliability

Inter-rater reliability was strong for all NPI-C domains. In general, correlations from this study are consistent with data from the original NPI-C validation by de Medeiros *et al*. (2010). The achieved correlation coefficients of the scores from independent raters can be considered reliable. Likewise, caregiver reliability, available for 109 individuals, was moderate (r=0.601). Concerning total scores from traditional NPI, in our study inter-rater reliability was higher (0.923) than the moderate caregiver reliability. The discrepancy in reliability between raters and caregivers on interpretation of patients' symptoms reinforces the need for the clinician judgment such as the rating method used in the NPI-C regarding NPS in dementia.

Convergent validity

The convergent validity appears to be close to that of the original version of the NPI-C (de Medeiros *et al*., 2010). There was a strong correlation between most NPI-C domains and the selected validation scales. The highest correlation was observed between NPI-C/Apathy domain and Apathy Inventory (0.942), much stronger than data reported in the original validation study. In the original NPI-C validation, the NPI-C/Apathy domain had weaker correlation with the Apathy Evaluation Scale (0.31) (Marin *et al*., 1991). We correlated this domain with the AI (Robert *et al*., 2002; 2010) which is more suitable to the dementia setting. This scale is divided into three core clinical dimensions required for apathy diagnosis: lack of goal-directed behavior, lack goal-directed cognitive activity, and lack emotional reaction (Robert *et al*., 2002; Robert *et al*., 2010; Benoit *et al*., 2012). AI was validated in Brazil with good specificity (97.3%) and sensitivity (99.2%) (Stella *et al*., 2013).

We also examined concurrent validity by dementia severity. We note some differences in strength of correlation by NPS. Specifically, there was exceptionally strong correlation between the NPI-C Apathy and the AI and NPI-C Depression and the CSDD in mild to moderate dementia. The strength of correlation declined in more severe patients. As expected, the strength of correlation was slightly stronger in severe patients for NPI-C Delusions and NPI-C Hallucinations and the BPRS. Perhaps the biggest surprise was the difference in correlation for NPI-C aberrant vocalization and the CMAI for mild and moderate patients (r=0.65 and 0.63, respectively), compared to the severe patients (r=0.09). This is likely due to lack of communicative ability in late stages of dementia.

In general, the concurrent validity was supported by good coefficient correlations of NPI-C domains with selected scales measuring same neuropsychiatric syndromes.

Psychopathological features

In our study, apathy was the syndrome with highest prevalence and with the most clinical severity among NPI-C domain. The highest correlation was observed of NPI-C/Apathy domain with AI (0.942). We also found a high correlation of NPIC/Depression with CSDD (0.736). The question if depression and apathy integrate into the same syndrome or belong

to the distinct psychopathological condition has been in a continuous debatable matter (Aalten *et al*., 2007). The NPI-C includes specific items, which appropriately discriminate one syndrome from another. While the core of apathy regards to reduced goal-directed behavior, reduced goal-directed cognition, and emotional blunting (Robert *et al*., 2010; Benoit *et al*., 2012), depression essentially concerns with emotional suffering by sadness and decreased pleasure in daily activities.

In estimating convergent validity for the NPI-C against the CMAI, the strength of correlation was high concerning agitation (0.772) and aggression (0.769) domains. Whereas agitation may emerge in combination with different neuropsychiatric syndromes, this domain can be targeted as a stand-alone measure as was established in the original version of the NPI-C (de Medeiros *et al*., 2010). Agitation includes uncommon physical or verbal non-threatening behavior, such as wandering, uncooperative attitudes, resistance to care, or unusual non-threatening communication. Conversely, aggression comprises angry behavior, including physical or verbal threatening attitudes, intentionally attempts to hit or hurt people or things, and uncommon threatening screams toward self or other person. Based on specific psychopathological features and different prevalence rates (Brodaty *et al*., 2001; Leketsos *et al*., 1999; Lyketsos *et al*., 2011), the NPI-C considered agitation and aggression as two separate domains with insertion of new items to each (de Medeiros *et al*., 2010).

Aberrant vocalizations was a new domain added to the NPI-C and also was compared with the CMAI since this scale comprises some items concerning verbal behavioral disturbances, with moderate correlation (0.684). Aberrant vocalizations constitute a prominent framework in advanced dementia, and this domain was added to the NPI-C in order to capture symptoms present in this dementia stage (de Medeiros *et al*., 2010).

Delusions domain from the NPI-C highly correlated with the BPRS (0.713). Unlikely, hallucinations domain from the NPI-C presented only a moderate correlation with this mentioned scale (0.432). Psychotic symptoms contribute to patient suffering, caregiver burden, faster functional decline, and earlier institutionalization (Gauthier *et al*., 2006; Gauthier *et al*., 2010; Lyketsos *et al*., 2011), as well as faster functional decline (Gauthier *et al*., 2006; Gauthier *et al*., 2010; Lyketsos *et al*., 2011).

CONCLUSION

The NPI-C is a comprehensive tool, which provides accurate measurement of neuropsychiatric symptoms in dementia with high concurrent validity and inter-rater reliability in the Brazilian setting. In addition to universal assessment, the NPI-C can be completed by individual domains, such as delusions, hallucinations, agitation, depression, apathy, sleep disorders, etc. Additional efforts to use the NPI-C in Brazil targeting a comprehensive approach to psychopathological symptoms in dementia or to apply an individual NPI-C domain to investigate a distinct neuropsychiatric syndrome should be encouraged across clinical trials and research settings, as well as clinical practice.

Acknowledgments

This study was supported by Fundação do Amparo à Pesquisa do Estado de São Paulo (FAPESP, grant n. 2010/18999-6).

References

Aalten P, Verhey FRJ, Boziki M, Bullock R, Byerne EJ, Camus V, et al. Neuropsychiatric Syndromes in dementia. Results from the European Alzheimer Disease Consortium: Part I. Dementia and Geriatric Cognitive Disorders. 2007; 24:457–463. [PubMed: 17986816]

Alexopoulos GS, Abrams RC, Young RC, Shamoian CA. Cornell Scale for Depressionin Dementia. Biological Psychiatry. 1988; 23:271–284. [PubMed: 3337862]

Benoit M, Berrut G, Doussaint J, Bakchine S, Bonin-Guillaume S, Frémont P, et al. Apathy and Depression in Mild Alzheimer's Disease: A Cross-Sectional Study Using Diagnostic Criteria. Journal of Alzheimer's Disease. 2012; 31:325–334.

Camozzato AL, Kochhann R, Simeoni C, Konrath CA, Franz AF, Carvalho A, Chaves ML. Reliability of the Brazilian Portuguese version of the Neuropsychiatric Inventory (NPI) for patients with Alzheimer's disease and their caregivers. International Psychogeriatrics. 2008; 20:383–393. [PubMed: 18257965]

Chilovi BV, Conti M, Zanetti M, Mazzu I, Rozzini L, Padovani A. Differential impact of apathy and depression in the development of dementia in mild cognitive impairment patients. Dementia and Geriatric Cognitive Disorders. 2009; 27:390–398. [PubMed: 19339777]

Cohen-Mansfield J, Marx MS, Rosenthal AS. A description of agitation in a nursing home. Journal of Gerontology: Medical Sciences. 1989; 44:M77–M84.

Benoit M, Berrut G, Doussaint J, et al. Apathy and depression in mild Alzheimer's disease: a cross-sectional study using diagnostic criteria. Journal of Alzheimer's Disease. 2012; 31:325–334.

Brodaty H, Draper B, Saab D, Low LF, Richards V, Paton H, Lie D. Psychosis, depression and behavioral disturbances in Sydney nursing home residents: Prevalence and predictors. International Journal of Geriatric Psychiatry. 2001; 16:504–512. [PubMed: 11376467]

Cummings JL, Mega M, Gray K, Rosenberg-Thomson S, Carusi DA, Gornbein J. The Neuropsychiatric Inventory: Comprehensive assessment of psychopathology in dementia. Neurology. 1994; 44:2308–2314. [PubMed: 7991117]

De Medeiros K, Robert P, Gauthier S, Stella F, Politis A, Leoutsakos J, et al. NPI-C Research Group. The Neuropsychiatric Inventory-Clinician rating scale (NPI-C): reliability and validity of a revised assessment of neuropsychiatric symptoms in dementia. International Psychogeriatrics. 2010; 22:984–994. [PubMed: 20594384]

Di Iulio F, Palmer K, Blundo C, Casini AR, Gianni W, Caltagirone C, Spalletta G. Occurrence of neuropsychiatric symptoms and psychiatric disorders in mild Alzheimer's disease and mild cognitive impairment subtypes. International Psychogeriatrics. 2010; 22(4):629–640. 2010. [PubMed: 20367890]

Dwyer M, Byrne GJ. Disruptive vocalization and depression in older nursing home residents. International Psychogeriatrics. 12(4):463–471. [PubMed: 11263713]

Dubois B, Feldman HH, Jacova C, Cummings JL, DeKosky ST, Barberger-Gateau P, et al. Revising the definition of Alzheimer's disease: a new lexicon. Lancet Neurology. 2010; 9:1118–1127. 2010. [PubMed: 20934914]

Folstein MF, Folstein SE, McHugh P. Mini-Mental State: a practical method for grading the cognitive state of patients for the clinician. Journal of Psychiatric Research. 1975; 12:189–198. [PubMed: 1202204]

Gauthier S, Vellas B, Farlow M, Burn D. Aggressive course of disease in dementia. Alzheimer's Dementia. 2006; (3):210–217.

Gauthier S, Loft H, Cummings J. Improvement in behavioral symptoms in patients with moderate to severe Alzheimer's disease by memantine: a pooled data analysis. International Journal of Geriatric Psychiatry. 2008; 23:537–545. [PubMed: 18058838]

Gauthier S, Cummings J, Ballard C, Brodaty H, Grossberg G, Robert P, Lyketsos C. Management of behavioral problems in Alzheimer's disease. International Psychogeriatrics. 2010; 22(3):346–372. [PubMed: 20096151]

Hughes CP, Berg L, Danziger WL, Coben LA, Martin RL. A new clinical scale for the staging of dementia. British Journal of Psychiatry. 1982; 140:566–572. [PubMed: 7104545]

Lechowski L, Benoit M, Chassagne P, Vedel I, Tortrat D, Teillet L, Vellas B. Persistent apathy in Alzheimer's disease as an independent factor of rapid functional decline: the REAL longitudinal cohort study. International Journal of Geriatric Psychiatry. 2009; 24:341–346. [PubMed: 18814198]

Lopez OL, Becker JT, Sweet RA, Klunk W, Kaufer DI, Saxton J, Habeych M, DeKosky ST. Psychiatric symptoms vary with the severity of dementia in probable Alzheimer's disease. The Journal of Neuropsychiatry and Clinical Neurosciences. 2003; 15:346–353. [PubMed: 12928511]

Lyketsos CG, Steele C, Galik E, Rosenblatt A, Steinberg M, Warren A, Sheppard JM. Physical aggression in dementia patients and its relationship to depression. American Journal of Psychiatry. 1999; 156:66–71. [PubMed: 9892299]

Lyketsos GC, Carrillo MC, Ryan JM, Khachaturian AS, Trzepacz P, Amatniek J, et al. Neuropsychiatric symptoms in Alzheimer's disease. Alzheimer's & Dementia. 2011; 7:532–539.

Lyketsos CG, Miller SS. Addressing the Alzheimer's disease crisis through better understanding, treatment, and eventual prevention of associated neuropsychiatric syndromes. Alzheimer's & Dementia. 2012; 8:60–64.

Marin RS, Biedrzycki RC, Firinciogullari S. Reliability and validity of the Apathy Evaluation Scale. Psychiatry Research. 1991; 38:143–162. [PubMed: 1754629]

Memória CM, Yassuda MS, Nakano EY, Forlenza OV. Brief screening for mild cognitive impairment: validation of the Brazilian version of the Montreal cognitive assessment. International Journal of Geriatric Psychiatry. Jan; 2013 28(1):34–40. 2013. [PubMed: 22368034]

Pfeffer RI. Measurement of functional activities in older adults in the community. Journal of Gerontology. 1982; 37(1):323–329. [PubMed: 7069156]

Reisberg B, Ferris SH, De Leon MJ. The Global Deterioration Scale for assessment of primary degenerate dementia. American Journal of Psychiatry. 1982; 139:1136–1139. [PubMed: 7114305]

Robert PH, Clairet S, Benoit M, Koutaich J, Bertogliati C, Tible O, et al. The Apathy Inventory: assessment of apathy and awareness in Alzheimer's disease, Parkinson's disease and mild cognitive impairment. Internationsl Journal of Geriatric Psychiatry. 2002; 17:1099–1105.

Robert PH, Mulin E, Malléa P, David R. Apathy diagnosis, assessment, and treatment in Alzheimer's disease. CNS Neuroscience & Therapeutics. 2010; 16:263–271. [PubMed: 20345973]

Rosenberg PB, Mielke MM, Appleby B, Oh E, Leoutsakos JM, Lyketsos CG. Neuropsychiatric symptoms in MCI subtypes: the importance of executive dysfunction. International Journal of Geriatric Psychiatry. 2011; 26(4):364–372. [PubMed: 20845402]

Rosenberg PB, Mielke M, Lyketsos CG. Caregiver assessment of patients' depression in Alzheimer disease: longitudinal analysis in a drug treatment study. American Journal of Geriatric Psychiatry. 2005; 13:822–826. [PubMed: 16166413]

Shrout PE, Fleiss JL. Intraclass correlations: uses in assessing rater reliability. Psychological Bulletin. 1979; 86:420–428. [PubMed: 18839484]

Sperling RA, Aisen PS, Beckett LA, Bennett DA, Craft S, Fagan AM, et al. Toward defining the preclinical stages of Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimer's Dementia. 2011; 7(3):280–292.

Stella F, Andrade LP, Garuffi M, Vital TM, Hernández SSS, Ruocco M, et al. Validation of the Brazilian version of the Apathy Inventory. International Journal of Geriatric Psychiatry. 2013 in press.

Taragano FE, Allegri RF, Krupitzki H, Sarasola D, Serrano CM, Loñ L, Lyketsos CG. Mild behavioral impairment and risk of dementia. Journal of Clinical Psychiatry. 2009; 70(4):584–592. [PubMed: 19323967]

Tatsch MF, Bottino CM, Azevedo D, Hototian SR, Moscoso MA, Folquitto JC, et al. Neuropsychiatric symptoms in Alzheimer disease and cognitively impaired, nondemented elderly from a community-based sample in Brazil: prevalence and relationship with dementia severity. American Journal of Geriatric Psychiatry. 2006; 14(5):438–445. [PubMed: 16670248]

Truzzi A, Ulstein I, Valente L, Engelhardt E, Coutinho ES, Laks J, Engedal K. Patterns of neuropsychiatric sub-syndromes in Brazilian and Norwegian patients with dementia. International Psychogeriatrics. 2013; 25(2):228–235. [PubMed: 23113901]

Ventura J, Green MF, Shaner A, Liberman RP. Training and quality assurance with the brief psychiatric rating scale: “the drift buster.”. International Journal of Methods in Psychiatric Research. 1993; 3:221–224.

Wadsworth LP, Lorius N, Donovan NJ, Locascio JJ, Rentz DM, Johnson KA, et al. Neuropsychiatric Symptoms and Global Functional Impairment along the Alzheimer's Continuum. Dementia and Geriatric Cognitive Disorders. 2012; 34:96–111. [PubMed: 22922821]

Key points

- Neuropsychiatric symptoms in dementia increase patient suffering and caregiver burden, and lead to diminished quality of life for patients and family members.
- The patient may be unable to provide reliable information due to cognitive decline or lack insight, and caregivers frequently suffer emotional burden that interferes with appropriate judgment of the patient's behavior.
- The Neuropsychiatric Inventory-Clinician Rating Scale (NPI-C) is a comprehensive and versatile rating that incorporates the expert clinician's impressions to the data provided by patients and caregivers.
- The NPI-C provides accurate measurement of neuropsychiatric symptoms in dementia with high concurrent validity and inter-rater reliability in the Brazilian setting.
- In addition to universal assessment in Brazil, the NPI-C can be completed by individual domains, such as delusions, hallucinations, agitation, depression, apathy, sleep disorders, or other psychopathological domains.

Table 1

Mean for selected demographic features and scales according to Clinical Dementia Rating (CDR).

Demographic and clinical features	CDR 1 N=60 (F:42/M:18)	CDR 2 N=53 (F:44/M:9)	CDR 3 N=43 (F:29/M:14)	Total N=156 (F:115/M:41)	*p*-value
Age (years)	77.4	76.8	75.6	76.7	0.45
Education (years)	5.9	5.8	4.4	5.5	0.15
Mini Mental State Examination	22.8	17.4	9.2	17.2	0.00*
Pfeffer Functional Activities Questionnaire	8.3	18.3	26.2	16.6	0.00*
Global Deterioration Scale	2.7	4.3	6.0	4.2	0.00*
Apathy Inventory	2.9	5.9	10.1	5.9	0.00*
Brief Psychiatric Rating Scale	10.6	26.0	55.3	28.1	0.00*
Cohen-Mansfield Agitation Index	7.7	25.4	56.4	27.1	0.00*
Cornell Scale for Depression in Dementia	5.6	6.5	7.9	6.6	0.09

F: female; M: male; CDR: Clinical Dementia Rating.

* $p<0.05$ (one-way ANOVA).

Table 2

Inter-rater reliability (ICCs) with 95% confidence limits for NPI-C domains (156 patients).

NPI-C, traditional NPI, and inter-rater reliability	ICC (CI)
NPI – Traditional total score	0.923 (0.897–0.944)
NPI-C Domains:	
- Delusions	0.937 (0.914–0.954)
- Hallucinations	0.777 (0.707–0.832)
- Agitation	0.903 (0.869–0.928)
- Aggression	0.879 (0.838–0.910)
- Depression / Dysphoria	0.812 (0.751–0.860)
- Anxiety	0.826 (0.769–0.870)
- Elation / Euphoria	0.916 (0.887–0.938)
- Apathy / Indifference	0.865 (0.819–0.900)
- Disinhibition	0.947 (0.928–0.961)
- Irritability / Lability	0.904 (0.870–0.929)
- Aberrant Motor Behavior	0.899 (0.864–0.925)
- Sleep Disorders	0.844 (0.792–0.884)
- Appetite and Eating Disorders	0.877 (0.835–0.909)
- Aberrant Vocalizations	0.915 (0.885–0.937)

ICC: Intraclass correlations; NPI-C: Neuropsychiatric Inventory-Clinician Rating Scale; NPI: Neuropsychiatric Inventory. CI: confidence interval.

Table 3

Pearson correlations for concurrent (convergent) validity involving NPI-C and. selected scales (patients = 156) by strength of correlation.

Rater 1 plus Rater 2	Pearson correlation r (CI)
NPI-C/Apathy-Indifference × Apathy Inventory	0.942 (0.921–0.958)
NPI-C/Agitation × Cohen-Mansfield Agitation Index	0.772 (0.700–0.829)
NPI-C/Aggression × Cohen-Mansfield Agitation Index	0.769 (0.696–0.826)
NPI-C/Depression-Dysphoria × Cornell Scale for Depression in Dementia	0.736 (0.655–0.801)
PI-C/Delusions × Brief Psychiatric Rating Scale-delusions	0.713 (0.626–0.783)
NPI-C/Aberrant Vocalizations × Cohen-Mansfield Agitation Index	0.684 (0.591–0.760)
NPI-C/Hallucinations × Brief Psychiatric Rating Scale-hallucinations	0.432 (0.295–0.552)

NPI-C: Neuropsychiatric Inventory–Clinician Rating Scale; CI-confidence interval.

Table 4

Pearson correlations (95% confidence intervals) for concurrent (convergent) validity involving NPI-C and selected scales by CDR (patient severity) rating.

	CDR 1(mild) N=60	CDR 2 (moderate) N=54	CDR 3 (severe) N=43
NPI-C Apathy × AI	0.89 (0.82–0.93)	0.910 (0.85–0.95)	0.796 (0.65–0.89)
NPI-C Agitation × CMAI	0.691 (0.53–0.80)	0.619 (0.42–0.76)	0.745 (0.57–0.85)
NPI-C Aggression × CMAI	0.615 (0.43–0.75)	0.717 (0.56–0.83)	0.710 (0.52–0.83)
NPI-C Depression × CSDD	0.701 (0.54–0.81)	0.648 (0.46–0.78)	0.579 (0.34–0.75)
NPI-C Delusion × BPRS	0.514 (0.300–0.68	0.53 (0.30–0.69)	0.645 (0.43–0.79)
NPI-C Aberrant Vocalization X CMAI	0.650 (0.47–0.77)	0.631 (0.44–0.77)	0.09 (−0.22–0.38)
NPI-C Hallucinations × BPRS	0.146 (−0.11–0.39)	0.080 (−0.19–0.34)	0.258 (−0.05–0.52)