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Neuropsychiatric symptoms in community-dwelling Mexican-Americans: results from the Hispanic Established Population for Epidemiological Study of the Elderly (HEPESE) study†

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Abstract

Objective—The Neuropsychiatric Inventory (NPI) is a well-established measure of psychopathology and frequently used in dementia studies. Little is known about its psychometric characteristics at a population level, particularly among Hispanics. We report the frequency of NPI symptoms in a community-dwelling older Mexican-American (MA) population cohort and the degree of symptom-related distress experienced by participant informants.

Methods—Participants were 1079 MA age 80 years and over residing in five southwestern states who were administered the NPI as part of wave-7 of the Hispanic Established Population for Epidemiological Study of the Elderly (HEPESE) conducted from 2010 to 2011.

Results—Nine hundred twenty-five informants rated NPI domains. Prevalence of neuropsychiatric symptoms (NPS) varied by symptom domain and ranged from agitation/aggression (32%) to euphoria/elation (5%). The overall rate of behavioral disturbances was 62.7%. On the other hand, 37.3% of informants reported no NPS. A significant fraction of the informants reported distress from the mood disorder cluster of the scale.

Conclusions—A large percentage (>60%) of community-dwelling older MA have one or more informant-reported NPS. These symptoms have diagnostic, prognostic, and therapeutic implications. Although neuropsychiatric disorders may be the initial clinical manifestation of dementia and often appear before cognitive alterations, the high frequency of these symptoms in

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Conflict of interest

None declared.

Author contributions

Ricardo Salazar: Conception and design; acquisition, analysis, and interpretation of data; drafting of the manuscript; and writing the paper. Donald R. Royall: Conception and design; analysis and interpretation of data; drafting of the manuscript; and supervision. Raymond F. Palmer: Conception and design; acquisition, analysis, and interpretation of data; and supervised integrity of data.

the HEPSE cohort may reflect a high prevalence of these disorders among community-dwelling MA. The pattern we observed also suggests relatively advanced stages of dementia.

Keywords

Neuropsychiatric Inventory (NPI); neuropsychiatric symptoms (NPS); Hispanics; population-based study; Mexican-Americans

Introduction

Hispanic elders represent one of the fastest growing minority populations and are projected to account for 16% of the older US population by year 2050. Most older Hispanics are estimated to be of Mexican origin (2001).

Currently, Hispanics represent 10% of the US population (Census, 1996). Studies show a higher prevalence and incidence of Alzheimer's disease (AD) among Hispanics compared with non-Hispanic Whites (NHW) (Perkins *et al.*, 1997; Tang *et al.*, 2001), with an earlier age of onset (Clark *et al.*, 2005). Among the currently estimated 200,000 Hispanics with AD, a significant number remain undiagnosed and untreated, and Hispanic participation in AD clinical trials has been historically low (Lopez *et al.*, 2008).

Neuropsychiatric disturbances are common manifestations of dementing disorders. The Neuropsychiatric Inventory (NPI) is a well-established measure of psychopathology and frequently used in dementia studies (Cummings, 1997). Little is known about its psychometric characteristics at the population level, particularly in Hispanics. Despite their public health importance, little research has evaluated neuropsychiatric symptoms (NPS) in minority older people and their impact on families (Hinton, 2002).

Clinically significant NPS may have diagnostic implications. NPS are found in approximately one-third of community-dwelling persons with dementia (Lyketsos *et al.*, 2000). The prevalence of NPS increases to nearly 80% among patients with dementia living in skilled nursing facilities (Margallo-Lana *et al.*, 2001).

Neuropsychiatric symptoms may also be indicative of a patient's stage in the dementing process. In a naturalistic study of 100 participants with autopsy-confirmed AD, Jost and Grossberg reported the evolution of NPS in AD. They documented irritability, agitation, and aggression in 81% of subjects an average of 10 months after diagnosis; depression, changes in mood, social withdrawal, and suicidal ideation in 72% of persons 2 years before diagnosis; and hallucinations, paranoia, accusatory behavior, and delusions in 45% of patients close to 0.1 month after diagnosis (Jost and Grossberg, 1996). Finally, Hinton *et al.* described the NPS in Latino elders with dementia or cognitive impairment without dementia (CIND) and factors that modified their association with caregiver depression using the NPI and the Center for Epidemiological Studies Depression scale, respectively. They concluded that prevalence and intensity of NPS was significantly higher in the demented group compared with the CIND group. The overall NPS intensity was significantly associated with caregiver depression and three factors: care-giver's relationship (spouse), caregiver recipient diagnosis (dementia vs. CIND), and care recipient's age influencing the direction and

strength of the association between NPS and caregiver burden (depression) (Hinton *et al.*, 2003).

However, these studies reflect patient samples. We report the prevalence and relative frequencies of the behavioral domains of the scale in an older community-dwelling Mexican-American (MA) population-based sample, and the degree of distress that these symptoms generate in informants.

Methods

Subjects

Subjects included 1079 MA who were administered the NPI as part of wave-7 of the Hispanic Established Population for Epidemiological Study of the Elderly (HEPESE) conducted from 2010 to 2011. HEPESE is a population-based study of a representative sample of community-dwelling MA, aged 80 years. Details of the study design are published elsewhere (Markides *et al.*, 1997). Briefly, individuals were selected from the five southwestern states of Texas, California, Arizona, Colorado, and New Mexico in the USA. Survey was conducted on wave-7 between February of 2010 and September of 2011. The sample was drawn using area probability sampling procedures to represent older MA. As of the 1990 census, over 85% of all older MA resided in these states (Census, 1996). The HEPESE sampling procedure assures a sample that is generalizable to the more than 500,000 older MA living in the southwest. The five states in the HEPESE sampling frame contain 85% of the 65 years and older MA population living in the USA when the study first started with the response rate at baseline interview (1993–1994) of 83% (9). In-home interviews were conducted in Spanish or English, and after complete description of the study to the subjects, written informed consent was obtained. The University of Texas Medical Branch at Galveston Institutional Review Board approved the HEPESE project.

Measures

The subjects' mental and neuropsychiatric disturbances were measured by the NPI (Cummings, 1997). The instrument encompasses neuropsychiatric disturbances that are common in neuropsychiatric disorders, such as dementia and related disorders. The instrument was administered as a structured interview by someone trained in the use of the scale (Research Assistants) to reliable informants, who were asked to rate the presence, frequency, and severity of the 12 domains of the scale during the previous month: agitation/aggression, dysphoria/depression, irritability/lability, apathy/indifference, anxiety, disinhibition, aberrant motor behavior, delusions, hallucinations, euphoria/elation, nighttime behavioral disturbances, and appetite/eating disturbances. Informants were asked to answer "yes" or "no" in response to each screening question regarding the subject's behavior, and either to proceed to the next question if the answer is "no" or to rate the symptoms present in the last 4 weeks if the answer is "yes." The NPI uses a screening strategy to minimize administration time, examining and scoring only those behavioral domains with positive responses to screening questions. Information on the NPI is obtained from an informant who is familiar with the subject's behavior. The total NPI severity score represents the sum of

individual symptom scores and ranges from 0 to 36. Informant distress associated with the symptom was rated on anchored 0-point to 5-point scale.

Analysis

Demographic and descriptive analyses were calculated using Statistical Analysis System (SAS) version 9 (SAS Institute Inc., NC, USA) for windows. Prevalence rates were calculated for each domain of the NPI as well as informant distress from each specific problem behavior.

Results

Descriptive statistics

Table 1 shows the demographic characteristics of 925 subjects and their respective informants. Participants had a mean age in years $\pm$ SD of 86 ± 4 (range 80–102), and 65% were women. Informant's relationship to participant was mostly son/daughter (68%), followed by spouses (7%). Seventy-four percent of the informants were women with a mean age in years of 56 ± 12.5 (range 66–93). On average, the HEPSE sample is characterized by low normal cognitive performance, given their advanced age and low educational attainment. Of the 1079 respondents, 224 (20.8%) scored $<18/30$ on the mini mental state examination (MMSE), that is, below its recommended threshold for cognitive impairment in this demographic (Bohnstedt, *et al.*, 1994). Participants had a mean $\pm$ SD MMSE of 21.2 ± 7.5 .

Figure 1 shows the distribution of NPS by behavioral domain. The most frequent reported symptom was "agitation/aggression" with 32% occurrence rate. The least frequently reported symptom was "euphoria/elation" (5%). The mood disorder cluster [dysphoria/depression (29%); irritability/lability (26%); and apathy/indifference (20%)] was the next most frequently reported behaviors. Nighttime behavioral disturbances and appetite/eating disturbances occurred at an equal rate in this sample (19%). Anxiety (16%), disinhibition (12%), and aberrant motor behaviors (12%) were frequently reported as well. Finally, the psychotic cluster [delusions (10%) and hallucinations (8%)] was less often reported. The overall rate of behavioral disturbances was 62.7%. On the other hand, 37.3% of informants reported no NPS.

Of the 294 informants that reported distress from agitation/aggressive behavior, 49 (17%), 19 (6%), and 2 (0.7%) reported moderate, severe, and extreme/very severe distress, respectively. Furthermore, of the 264 informants that reported distress from dysphoria/depression subdomain, 59 (22%), 15 (6%), and 4 (2%) reported moderate, severe, and extreme/very severe distress, respectively (Figure 2).

Discussion

We found a high frequency of NPS among community-dwelling older MA. Such symptoms are also common in dementia patients and pose unique challenges for caregivers (Cohen-Mansfield *et al.*, 1998; Ory *et al.*, 1999; Lyketsos and Steinberg, 2000). Surprisingly for a population-based cohort, our findings are comparable to past studies of NPS among older

dementia cases. Sixty percent to 80% of such patients have one or more NPS (Lyketsos *et al.*, 2000; Lyketsos *et al.*, 2002). In our study, more than 60% of HEPSE participants exhibited at least one informant-reported NPS. The high level of NPS may reflect dementia because of (i) the sample's advanced age, which is a risk factor for dementia, and (ii) the relative frequencies of individual NPS, which resemble that seen in clinical samples with dementia.

Moreover, the point-prevalence estimates we report from several NPI behavioral domains are similar to those reported by Levy *et al.* (1996) among longitudinally followed elders with AD, that is, symptoms of depression (29% dysphoria/depression vs. 23–29%), aggression (32% agitation/aggression vs. 28–32%), and psychosis (10% delusions and 8% hallucinations vs. 12–25%). We can also confirm the relatively high frequency of mood relative to psychotic symptoms previously observed among NHW demented cases (Yeo and Gallagher-Thompson, 1996).

However, our sample *has not been selected for AD* but is instead representative of community-dwelling older MA. This may suggest that the burden of NPS in MA may be higher than expected in a non-demented population and therefore that MA may be experiencing unexpectedly high rates of dementing illness.

The prevalence of dementia in community-dwelling older MA is unknown but has been estimated to be higher than in NHW (Lopez *et al.*, 2008). The prevalence of dementia in the HEPSE cohort is also unknown but has been estimated to be between 31.1% and 64.4% (Royall *et al.*, 2004). It is likely that other conditions than AD contribute to these high rates. Moreover, the presentation of dementia-related NPS at the time of diagnosis may be somewhat different among Hispanics than the White majority population (Fitten *et al.*, 2001). In addition, cultural and other psychosocial factors are important in shaping the clinical presentation of MA. Additionally, the use of informants or caregivers in assessing NPS in demented Hispanics can be problematic (Hinton *et al.*, 2003). Nevertheless, the frequencies we have observed are typical of both Hispanic and NHW dementia cases.

Thus, the high frequency of neuropsychiatric disturbances in this population-based non-institutionalized, naturalistic, and large sample of MA may have diagnostic, prognostic, and/or treatment implications. NPS are among the initial clinical manifestation of dementing disorders and often precede cognitive alterations (Petry *et al.*, 1988; Lesser *et al.*, 1989; Rubin and Kinscherf, 1989; Gilley *et al.*, 1997). NPI ratings of “depression” (Lyketsos *et al.*, 2000) and “delusions” (Gilley *et al.*, 1997) are predictors of physical aggression among patients with AD.

To help clarify our findings, we offer comparisons with those of dementia cases in three reference studies including the following: $n = 99$ patients with mild AD from Spain (Fernandez-Martinez *et al.*, 2008), $n = 25$ AD and CIND cases with Clinical Dementia Rating scale scores ≥ 1.0 from Brazil (Tatsch *et al.*, 2006), and $n = 362$ NHW and African-American cases with dementias of the Alzheimer type from the USA (Lyketsos *et al.*, 2002). The prevalence of NPS related to dementia and their overall distribution is not that much different from our results in this MA population-based cohort (Figure 3).

Dysphoria/depression

Major and minor depressive symptoms are seen in approximately one-third to one-half of patients with dementia (Olin *et al.*, 2002; Lee and Lyketsos, 2003). We report a prevalence of 29% for this symptom cluster. This is similar to the rates reported in dementia cases from Brazil (28%) and the USA (32.3%), but less than cases from Spain (41.4%) (Figure 3).

Anxiety

Common among patients with mild cognitive impairment at risk of conversion to AD (Peters *et al.*, 2013), anxiety has been reported to occur in between 24% and 65% of persons with dementia and is often associated with dysphoria and agitation in those patients (Mega *et al.*, 1996). We report a prevalence of 16% for this symptom cluster. This is less frequent than among dementia patients in Spain, the USA, or Brazil (i.e., 22.2%, 21.5%, and 36%, respectively) (Figure 3).

Apathy/indifference

Apathy is the most common personality change seen in dementia patients and occurs in 48% to 92% of patients (Mega *et al.*, 1996). In our study, we observed relatively low point prevalence for this symptom (20%). For comparison, see Figure 3; apathy was most frequently reported in Spain, followed by Brazil and the USA (64.6%, 40%, and 35.9%, respectively). Interestingly, Rodriguez-Agudelo *et al.* (2011) described a similar rate to ours (i.e., 20%) among demented cases living in the urban areas of Mexico.

Irritability and mood lability

These behaviors become more frequent as dementia severity progresses. Mega *et al.* described the spectrum of behavioral changes of AD cases and pointed out a prevalence of this behavior of between 35% and 54% (Mega *et al.*, 1996). In our comparison groups, these symptoms are stable across samples with a prevalence of between 20% and 30% (Figure 3). We observed a prevalence of 26%.

Inappropriate behavior cluster (agitation, disinhibition, and euphoria)

Agitation/aggression—This was the most frequently reported symptom in our study with 32% prevalence and compared with similar rates reported for NHW dementia cases in the US (30.3%) and Hispanic cases from Spain (30.3%) (Figure 3).

Disinhibition—Tactlessness impulsivity occurs in 36% of patients with dementia (Mega *et al.*, 1996). We report 12% rate for disinhibition. This rate is similar to that reported in dementia cases from our comparison samples (i.e., 20% in Spain and Brazil, and 12.7% in the USA) (Figure 3).

Euphoria—Studies consistently showed this to be a less common manifestation of dementia with a prevalence rate of approximately 3.5% to 8% (Burns *et al.*, 1990). This is consistent with both our finding (5%) and with those of our three comparison groups (all below 5%) (Figure 3).

Nighttime behavioral disturbances—We observed sleep disturbances in about 19% of our sample. Other studies report slightly higher rates in dementia patients (i.e., 25%) (Rose and Lorenz, 2010). In our comparison groups, this symptom is similarly reported (Spain 27%, Brazil 24%, and the USA 27%) (Figure 3).

Appetite/eating disturbances—Patients with dementia have clinically significant weight loss, and weight loss tends to occur more frequently in patients with more severe stages of the illness (White *et al.*, 1998). Rapid cognitive decline is associated with more pronounced weight loss (White, 1998). We report a 19% prevalence for this symptom versus 22% in demented cases (White *et al.*, 1998). In our comparison groups, appetite and eating disturbances predominated in the Brazilian and US NHW ethnic groups (28% and 19.6%, respectively) and were less predominant in mild AD cases seen in Spain (15.2%) (Figure 3).

Aberrant motor behaviors cluster

Aberrant motor behaviors—These behaviors are present in 12% of our cohort. They are more common in moderate-to-severe stages of disease and vary widely among patients with dementia (12% to 84%) (Mega *et al.*, 1996). This symptom varies widely among our comparison groups (i.e., 21.2%, 4%, and 16% in Spain, Brazil, and the USA, respectively) (Figure 3).

Psychotic cluster

Psychosis usually develops early in dementia (e.g., 0.1 month after diagnosis) and affects 45% of cases in an autopsy-confirmed longitudinal study by Jost and Grossberg (1996). Bassiony and Lyketsos (2003) found that a median of 36.5% of patients with AD presented with delusions and a median of 23% of subjects with AD presented with hallucinations at some time during the course of their illness. We report a relative low rate of these symptoms, with delusions and hallucinations being present in 10% and 8%, respectively. Among our comparison ethnic groups (Figure 3), delusions were particularly prominent in Spain and the USA (20.2% and 18%) respectively. Hallucinations were unusually higher in the US study (10.5%).

Caregiver burden/distress

Paranoia, aggression, and sleep–wake cycle disturbances appear to be particularly important factors in increasing caregiver burden and institutionalization of patients (O'Donnell *et al.*, 1992). In our study, 32% of informants reported distress from the agitation/aggressive behavior domain of the scale. Furthermore, 28.5% of informants reported distress from the dysphoria/depression behavioral domain. The development of NPS of dementia is a major risk factor for caregiver burden and depression (Kaufer *et al.*, 1998).

In a recent population-based study of dementia in Mexico with 2003 participants, Rodriguez-Agudelo *et al.* (2011) reported the frequency of NPS in older adults with and without dementia in urban and rural regions as results of the 10/66 Dementia Research Group in Mexico. They concluded firstly that in both regions, all symptoms were more severe in subjects with dementia; secondly, a high frequency of affective symptoms (depression and apathy specially) was observed, and irritability and anxiety in second term;

and finally, the caregiver stress levels were associated with the frequency and severity of NPS. Furthermore, Rodriguez-Agudelo and colleagues reported on their study that 60% and 65% of the older population in the urban and rural areas, respectively, and without dementia had at least one NPS (29).

In summary, our findings, in a population-based cohort of community-dwelling older MA, are comparable to the high rates of NPS expected among dementia patients in Hispanic and NHW samples from several countries. Our study is limited by its lack of longitudinal NPI data and by the absence of formal psychometrics and clinical diagnoses. Caregiver burden is only addressed in two predominant NPI domains in this study. On the other hand, NPI severity and frequency may more accurately predict distress than the presence or absence of a symptom alone. NPS that are mild in severity or infrequent often do not warrant intervention and are thus not clinically significant.

Even so, these data provide potential insights into the NPS burdens of older Hispanics and their caregivers. Moreover, this population is rapidly growing. Census projections suggest that one in three older Americans will be from populations other than NHW by mid-century and that the largest of these will be Hispanic (Census, 1996).

Whether Hispanics are at exceptional risk for dementia and NPS cannot be determined from these data. The literature on this topic is conflicting (Yeo and Gallagher-Thompson, 1996; Harwood *et al.*, 1998; Cohen and Magai, 1999; Chen *et al.*, 2000; Hargrave *et al.*, 2000). In a recent study, Sink *et al.* (2004) examined 5776 Medicare patients with moderate to severe dementia (5090 White, 469 African-American, and 217 Latino; mean age = 78.9 years) to determine the prevalence of dementia-related behaviors, adjusting for patient and caregiver characteristics to explain any differences in prevalence in NPS. They concluded that African-American and Latino community-dwelling patients with moderate to severe dementia have a higher prevalence of dementia-related behaviors than NHW. Others (Ortiz *et al.*, 2006) compared the NPS of 367 community-dwelling subjects (70 Hispanic and 230 NHW patients with AD, and 22 healthy, age-matched Hispanic and 45 NHW controls). They found that NPS were common in AD regardless of ethnicity but that Hispanic AD cases presented to the initial assessment with more NPS than NHW. However, our sample exhibits exceptionally low rates of apathy and psychosis, both early symptoms of dementia, and a relatively high rate of weight loss and agitation/aggression compared with our comparison groups. These observations suggest a relatively late stage of dementia's evolution. This suggests that a high fraction of demented MA patients are being cared for at home into the later stages of their illness. That conclusion is also consistent with the high rates of caregiver burden reported by our informants.

In conclusion, NPS occur frequently in community-dwelling older MA. This may be indicative of a high prevalence of dementing illness in that population. The causes of this cannot be determined from these data, but the pattern of NPS endorsed by informants may suggest a more advanced dementia status. This may point out that a high fraction of demented MA patients are being cared for at home into the later stages of their illness. That conclusion is also consistent with the high rates of caregiver burden reported by our informants. The quality of this caregiving and its effects on both patient and caregiver

outcomes alike may be of interest, as chronic care is shifting away from institutionalization and Hispanics represent a rapidly growing fraction of the total long-term care population. The experiences of today's Hispanic caregivers may offer a window onto tomorrow's healthcare delivery.

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Key points

- Neuropsychiatric symptoms occur frequently in community-dwelling older Mexican Americans. This may be indicative of a high prevalence of dementing illness in that population.
- The pattern of NPS endorsed by informants may suggest a more advanced dementia status. This may point out that a high fraction of demented MA patients are being cared for at home into the later stages of their illness. That conclusion is also consistent with the high rates of caregiver burden reported by our informants.

Figure 1.
Frequency of Neuropsychiatric Inventory symptoms among community-dwelling older Mexican-Americans ($n = 925$).

Figure 2.

Frequency of distress reported by informants from mood disorder cluster (Agitation/Aggression, $n = 294$; Dysphoria/Depression, $n = 264$).

Figure 3.

Comparison of frequency of Neuropsychiatric Inventory (NPI) symptoms in community-dwelling Mexican-Americans (US MA, $n = 925$ from HEPESSE cohort) non-selected for dementia with prevalence rates of NPI symptoms in other population-based studies selected for dementia [Spain ($n = 99$ with mild Alzheimer's disease), Brazil ($n = 25$ with dementia of the Alzheimer's type), and US non-Hispanic Whites (NHW) and African Americans ($n = 362$ with Alzheimer's disease and related dementias)]. HEPESSE, Hispanic Established Population for Epidemiological Study of the Elderly.

Table 1Demographic characteristics of the HEPese sample ($n = 1079$)

Variable	N or mean $\pm$ SD	Range or %	Total N
Subjects			
Male		35%	
Female		65%	
Age (years)	85.6 $\pm$ 4.0	80–102	
MMSE	21.2 $\pm$ 7.5		
Informants			
Male		26%	242
Female		74%	683
Age (years)	56 $\pm$ 12.5	66–93	925
Relationship of informant to subject			
Spouse			66
Son/daughter			629
Son/daughter-in-law			30
Other relative/non-relative			119/76

HEPESE, Hispanic Established Population for Epidemiological Study of the Elderly; MMSE, mini mental state examination.