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Assessing mild behavioral impairment with the mild behavioral impairment-checklist in people with subjective cognitive decline

Sabela C. Mallo,1 Zahinoor Ismail,2,3 Arturo X. Pereiro,1 David Facal,1 Cristina Lojo-Seoane,1 María Campos-Magdaleno1 and Onésimo Juncos-Rabadán1

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2Department of Psychiatry and the Mathison Centre for Mental Health Research & Education, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada
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ABSTRACT

Objectives: To estimate the prevalence of Mild Behavioral Impairment (MBI) in people with Subjective Cognitive Decline (SCD), and validate the Mild Behavioral Impairment Checklist (MBI-C) with respect to score distribution, sensitivity, specificity, and utility for MBI diagnosis, as well as correlation with other neuropsychological tests.

Design: Correlational study with a convenience sampling. Descriptive, logistic regression, ROC curve, and bivariate correlations analyses were performed.

Setting: Primary care health centers.

Participants: 127 patients with SCD.

Measurements: An extensive evaluation, including Questionnaire for Subjective Memory Complaints, Mini-Mental State Examination, Cambridge Cognitive Assessment-Revised, Neuropsychiatric Inventory-Questionnaire (NPI-Q), the Geriatric Depression Scale-15 items (GDS-15), the Lawton and Brody Index and the MBI-C, which was administered by phone to participants’ informants.

Results: MBI prevalence was 5.8% in those with SCD. The total MBI-C scoring was low and differentiated people with MBI at a cut-off point of 8.5 (optimizing sensitivity and specificity). MBI-C total scoring correlated positively with NPI-Q, Questionnaire for Subjective Cognitive Complaints (QSCC) from the informant and GDS-15.

Conclusions: The phone administration of the MBI-C is useful for detecting MBI in people with SCD. The prevalence of MBI in SCD was low. The MBI-C detected subtle Neuropsychiatric symptoms (NPS) that were correlated with scores on the NPI-Q, depressive symptomatology (GDS-15), and memory performance perceived by their relatives (QSCC). Next steps are to determine the predictive utility of MBI in SCD, and its relation to incident cognitive decline over time.

Key words: subjective cognitive decline, neuropsychiatric symptoms, mild behavioral impairment, validation, prevalence

Introduction

Subjective Cognitive Decline (SCD) (Jessen et al., 2014) is a diagnostic entity that characterizes people with cognitive complaints but without objective cognitive impairment, and is associated with an increased risk of Mild Cognitive Impairment (MCI) (Masters et al., 2015) and dementia (Gifford et al., 2014). Neuropsychiatric symptoms (NPS), also known as behavioral and psychological symptoms, are non-cognitive, behavioral, or psychiatric symptoms that include disturbances of mood, perception, and behavior related to a neurocognitive disorder (Lyketsos et al., 2011). In cognitively normal adults, NPS can predict progression to MCI (Masters et al., 2015). Relationships between SCD and NPS have been explored in some recent studies. A meta-analysis...
Mild Behavioral Impairment (MBI) (Ismail et al., 2016) is a neurobehavioral syndrome characterized by later life acquired, sustained and meaningful NPS of any severity that cannot be better accounted for by other formal medical and psychiatric nosology. MBI is an at-risk state for incident cognitive decline and dementia, and for some, MBI is the index manifestation of neurodegeneration, observed in advance of cognitive impairment (Taragano et al., 2018). In 2016, the NPS Professional Interest Area of the International Society to Advance Alzheimer Research and Treatment (ISTAART), a subgroup of the Alzheimer’s Association (AA), published research diagnostic criteria for MBI (Ismail et al., 2016), which were intended to standardize research into early non-cognitive markers of dementia. The ISTAART-AA MBI criteria specified later life emergence of symptoms with minimum 6-month duration, thus minimizing false positives from the inclusion of transient and reactive states. Development of MBI is consistent with the inclusion of NPS in the 2011 National Institute on Aging–Alzheimer’s Association (NIA-AA) consensus recommendations for diagnosis of all-cause dementia (McKhann et al., 2011), highlighting the clinical importance of NPS. The relationship between MBI (the neurobehavioral axis) and MCI (the neurocognitive axis) was also made explicit in the ISTAART-AA MBI criteria, in that MBI can precede, co-occur with, or emerge after MCI. Finally, MBI diagnosis requires at least minimal impairment in interpersonal relationships, other aspects of social functioning, or ability to perform at the workplace as a result of the NPS as opposed to cognitive symptoms.

Importantly, MBI distinguishes between formal psychiatric illness or chronic psychiatric symptomatology, from new-onset psychiatric symptoms in older adults, the latter of which are core to the MBI construct. Historically, older adults with later onset NPS, who did not show obvious cognitive impairment would receive a psychiatric diagnosis, and the possibility of neurodegenerative disease was often overlooked (Cieslak et al., 2018). In MBI, the type, location, and impact of the underlying neuropathology may manifest with changes in personality, behavior, or psychiatric symptomatology instead of overt cognitive impairment. This population has also been traditionally excluded from observational cohorts and disease modifying dementia clinical trials (Morby et al., 2018a). The ISTAART-AA MBI criteria, cluster these later life emergent NPS into domains well described in neuropsychiatric research, such as decreased drive/motivation (Sherman et al., 2018), affective/emotional dysregulation (Ismail et al., 2018), impulse dyscontrol and agitation (Nagata et al., 2014), social inappropriateness (Desmarais et al., 2018), and delusions and hallucinations (Fischer and Agüera-Ortiz, 2018).

Assessment of MBI has been operationalized with the development of the MBI checklist (MBI-C) (Ismail et al., 2017a; available at www.MBItest.org). The MBI-C is a case ascertainment tool, which was tailored specifically to the MBI criteria, and mandates symptoms being later life in onset, and sustained for 6 months. These requirements are not explicit in many NPS rating scales. Further, to ensure relevance to prodromal and preclinical populations, the MBI-C was designed for a community-dwelling, functionally independent, older population.

Recent investigations have estimated the prevalence of MBI symptoms, using only criterion one of the ISTAART-AA MBI criteria with a transformation algorithm of the Neuropsychiatric Inventory (NPI) (Cummings et al., 1994). In a population-based study (Morby et al., 2018b), the prevalence of MBI criterion one symptoms in people with SCD was 43.1% and in a memory clinic study 76.5% (Sheikh et al., 2018). However, in a study of a clinical sample of people with MCI and SCD, using the MBI-C for case ascertainment (Mallo et al., 2017), the prevalence estimated using all the four ISTAART-AA criteria was much lower at 11.6%.

The aims of the present investigation were to study in people with SCD: (1) the prevalence of MBI and the distribution of the scores; (2) the sensitivity and specificity of the MBI-C and its utility for diagnosing MBI; and (3) the relationships between NPS, cognitive status, and activities of daily living. The MBI-C was administrated by phone, since it is a very useful procedure when the patients are not able to travel to the health centers, especially in dispersed populations.

**Methods**

Of the 127 participants aged ≥ 50 years and with cognitive concerns were recruited from Primary...
Assessing MBI with the MBI-C in elders with SCD

Care Health Centers in Santiago de Compostela (Spain) from October 2016 to April 2017. SCD was diagnosed in accordance with Jessen et al., (2014) criteria. The participants underwent clinical, neurological, and neuropsychological examination. A questionnaire on sociodemographic and clinical data was used to obtain information from the patients and/or a family member. A short Spanish version of the Questionnaire for Subjective Memory Complaints (QSMC) (Benedet and Seisdedos, 1996) was administered to participants and to a family member to assess SCD. Cognition was evaluated by the Spanish version (López-Pousa, 2003) of Cambridge Cognitive Assessment-Revised (CAMCOG-R) (Roth et al., 1998) and with the Spanish version (Lobo et al.,1999) of the Mini-Mental State Examination (MMSE) (Folstein et al., 1975), both with norms for age and education. Functional assessment was conducted using the Spanish version of the Lawton and Brody Index, specially designed to evaluate Instrumental Activities of Daily Living (IADL) (Lawton and Brody, 1969).

To assess NPS we used, the Spanish version (Boada et al., 2002) of the NPI-Q (Kaufer et al., 2000); the 15-item Spanish version (Martínez et al., 2002) of the Geriatric Depression Scale (GDS-15) (Yesavage and Sheikh, 1986); and the Spanish version of the MBI-C (Agüera-Ortiz and López-Álvarez, 2017). The MBI-C consists of 34 items organized according to the five MBI domains: (1) drive/motivation: six questions including assessments of cognitive, behavioral and emotional apathy; (2) affective/emotional regulation: six items including low mood, anhedonia, hopelessness, and guilt, and one question each for worry and panic; (3) impulse control/agitation: twelve questions assessing agitation, aggression, impulsivity, recklessness, and abnormal reward, and reinforcement; (4) social cognition: five questions describing sensitivity, empathy, and tact; (5) abnormal thoughts/perception: five questions assessing suspiciousness, grandiosity, and auditory and visual hallucinations. For each item, a “yes” or “no” question is followed by a severity rating scale of 1-mild, 2-moderate, or 3-severe. Symptoms should be at least six months persistence and represent a meaningful change from baseline. Due to the population being much dispersed in this region, the questionnaire was administered by phone interview to a relative of the patient, to optimize participant retention.

Diagnosis of MBI was made via a series of semi-structured interviews in addition to medical records, in accordance with all the four ISTAART-AA criteria. To determine criterion one, we asked for the presence of symptoms over the last six months in the initial phone interview and then confirmed it using the NPI-Q (administered to an informant on the patient’s assessment session). For the NPI-Q, both one month (proper measure of the instrument) and six-month symptom duration were necessary (as required in the criteria). For criteria two and three, information was obtained from the phone interview. Criterion four was obtained from the final assessment and diagnosis. Definite MBI diagnosis was made by the research team after incorporating several sources of information that included extensive clinical assessments, cognitive, and neuropsychiatric testing.

Data were analyzed using SPSS v.20. Domain scores for the MBI-C were calculated as well as total scores for each questionnaire. Exploratory analyses were performed to identify any error in the data. The distribution of the scores in MBI-C and the prevalence of MBI diagnosis were determined using frequency and descriptive analyses. Binary logistic regression was used to determine the predictive value of the MBI-C for MBI diagnosis, being MBI diagnosis the outcome variable and the MBI-C total score the predictor variable. A ROC curve was generated to determine the utility of the MBI-C total score for diagnosing MBI and the sensitivity and specificity of the cut-off point. The ROC curve was performed on a non-parametric assumption since the descriptive analyses showed that the distribution of the scores was not normal. The total score on the MBI-C was the contrast variable and the diagnosis of MBI was the static variable. The relations between the total score on the MBI-C and cognitive measures (Questionnaire for Subjective Cognitive Complaints (QSCC), CAMCOG-R, MMSE), NPS scores (NPI-Q, GDS-15), and functional results (IADL) were examined using Spearman bivariate correlations because several measures did not follow a normal distribution. The level of significance was set at p < 0.05.

The study was approved by the Ethics in Clinical Research Committee of the Galician Government and was carried out in accordance with The Declaration of Helsinki, as revised in Fortaleza 2013. Written informed consent was obtained from all participants before the study, and anonymity has been preserved.

Results

Of the 127 participants, six (4.72%) were excluded because, although they were evaluated with the MBI-C, the MBI diagnosis could not be confirmed from all data sources required for the reference standard. Nighty-five participants were female...
Table 1. Descriptive parameters of the sample (n = 121)

<table>
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<tr>
<th>CHARACTERISTICS</th>
<th>MEAN</th>
<th>SD</th>
<th>RANGE</th>
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<tr>
<td>Age</td>
<td>64.75</td>
<td>8.75</td>
<td>50–84</td>
</tr>
<tr>
<td>Years of education</td>
<td>11.27</td>
<td>5.73</td>
<td>2–25</td>
</tr>
<tr>
<td>MMSE</td>
<td>28.54</td>
<td>1.62</td>
<td>21–30</td>
</tr>
<tr>
<td>CAMCOG-R</td>
<td>93.26</td>
<td>7.01</td>
<td>67–105</td>
</tr>
<tr>
<td>QSCC (patient)</td>
<td>16.49</td>
<td>3.46</td>
<td>8–26</td>
</tr>
<tr>
<td>QSCC (informant)</td>
<td>14.79</td>
<td>3.97</td>
<td>7–28</td>
</tr>
<tr>
<td>GDS-15</td>
<td>2.77</td>
<td>2.38</td>
<td>0–11</td>
</tr>
<tr>
<td>NPI-Q</td>
<td>2.59</td>
<td>3.23</td>
<td>0–16</td>
</tr>
<tr>
<td>IADL</td>
<td>7.78</td>
<td>0.62</td>
<td>5–8</td>
</tr>
</tbody>
</table>

(78.5% of the sample). Descriptive parameters of the sample (age, years of education, QSCC of the patient, QSCC of the informant, MMSE, CAMCOG-R, GDS-15, NPI-Q, and IADL) are shown in Table 1.

Descriptive parameters of the scoring in each of the five domains and total MBI-C are displayed in Table 2. Percentile 25 and percentile 50 was 0.0 for all domains, except for total scoring in percentile 50, which was 1.0. Percentile 75 was between 0.0 and 4.0, while percentile 90 was between 0.0 and 8.40 (maximum possible for total scoring, 102) (Table 2).

The total MBI-C scoring was low; 88 participants (76.5%) scored 0 and 11 participants (9.6%) scored 1 (Figure 1). The prevalence of MBI according to ISTAART-AA diagnostic criteria was 5.8% (7 participants).

The logistic regression analysis showed that MBI-C is a significant predictor of MBI diagnosis ($\beta = -1.08; \text{ST. E} = 0.50; \text{Wald}=4.63; df=1, p < 0.05$), OR = 0.34 CI (95% CI: 0.12–0.90).

Nagelkerke $R^2$ indicated that the model explains 85% of the variance. The Hosmer–Lemeshow test revealed a good fit for the regression model ($X^2 = 5.29, df = 4, p = 0.09$). ROC analysis indicated that MBI-C total scoring differentiated people with MBI diagnoses. The cut-off point was seated at 8.5 with a good sensitivity= 1.0 (95% CI: 1.0–1.0), specificity = 0.96 (95% CI 0.92–0.99) and AUC = 0.99, p < 0.001 (95% CI: 0.98–1.0).

MBI-C total scoring correlated positively with NPI-Q ($\rho = 0.57; p < 0.01$), QSCC from the informant ($\text{Spearman's r} = 0.30 p < 0.01$) and GDS-15 ($\text{Spearman's r} = 0.22 p < 0.05$). However, not correlation was found between the MBI-C and IADL ($\text{Spearman's r} = -0.18; p = 0.06$), MMSE ($\text{Spearman's r} = 0.09 p = 0.31$), QSCC from the patient ($\text{Spearman's r} = 0.02 p = 0.82$) and CAMCOG-R ($\text{Spearman's r} = -0.02 p = 0.83$) (Table 3).

Discussion

To our knowledge, this is the first study of the MBI-C, administered by phone interview, in a sample of people with SCD. The phone validation is highly beneficial in dispersed populations, where the participants have difficulties traveling to the health centers, or when they are not able to attend due to health reasons or scheduling.

In summary, our results indicated that in people with SCD, the prevalence of the MBI diagnosis estimated with the ISTAART-AA diagnosis criteria and the MBI-C was low (5.8%). The MBI-C detected subtle NPS that were correlated with the NPI-Q, depressive symptomatology (estimated by the GDS-15) and memory performance perceived by the participants’ relatives (measured by the QSCC). Therefore, these results suggest that the phone administration of the MBI-C is useful for detecting MBI in people with SCD. These findings provide a better understanding of the behavioral, cognitive, and functional manifestations of neurocognitive diseases, and have significant implications for prevention and treatment.

The role of NPS in SCD has not been studied as frequently as in MCI and dementia (Sheikh et al., 2018). In our study, during our recruitment time frame of seven months, the point prevalence of MBI in people with SCD, according to ISTAART-AA diagnosis criteria, was 5.8%. Nevertheless, investigations using traditional rating scales, such as the NPI (Cummins et al., 1994), have indicated that the prevalence of any NPS in controls ranges from 5 up to 27% (Ismail et al., 2017a). This variability can be explained by the differences in demographics, study setting, terminology, and behavioral instruments selected. Previous studies have estimated a much higher MBI prevalence in SCD of 43.1% in a community sample (Morby et al. 2018b) and 76.5% in a clinical sample (Sheikh et al., 2018). Some reasons may explain why these prevalence estimates are higher. The NPI and NPI-Q, used in these studies, require one month of symptoms as the reference frame, whereas the MBI-C involves a more rigorous expectation of six-month symptom duration and explicit later life onset of symptoms. With this more rigorous standard for NPS, the MBI-C minimizes the inclusion of transient and reactive states in case detection. Decreasing the likelihood of infections or other medical conditions, change in living situation or relationships, or medication adjustments and side effects contributing to NPS ascertainment likely results in fewer MBI false positives (Ismail et al., 2017a). These two studies may be prone to lack of specificity due to this short time frame, and a lack of sensitivity due to retrofitting NPI.
Table 2. Descriptive parameters of scores in the five domains and total of the MBI-C (n = 121)

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<th>DOMAINS</th>
<th>MEAN</th>
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<th>%ILE 50</th>
<th>%ILE 75</th>
<th>%ILE 90</th>
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<td>Interest, motivation &amp; drive</td>
<td>0.55</td>
<td>1.26</td>
<td>0–6</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>2.0</td>
</tr>
<tr>
<td>Mood or anxiety</td>
<td>0.83</td>
<td>1.38</td>
<td>0–6</td>
<td>0.0</td>
<td>0.0</td>
<td>1.0</td>
<td>3.0</td>
</tr>
<tr>
<td>Societal norms</td>
<td>1.24</td>
<td>2.26</td>
<td>0–10</td>
<td>0.0</td>
<td>0.0</td>
<td>2.0</td>
<td>4.4</td>
</tr>
<tr>
<td>Delay gratification &amp; control</td>
<td>0.03</td>
<td>0.18</td>
<td>0–1</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Held beliefs &amp; sensory</td>
<td>0.04</td>
<td>0.24</td>
<td>0–2</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>experiences</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total scoring</td>
<td>2.71</td>
<td>4.17</td>
<td>0–19</td>
<td>0.0</td>
<td>1.0</td>
<td>4.0</td>
<td>8.4</td>
</tr>
</tbody>
</table>

Figure 1. Distribution of the total scores in the MBI-C stratified by frequency. MBI-C: Mild Behavioral Impairment-Checklist.

Table 3. Spearman correlations between the MBI-C and the NPI-Q, CAMCOG-R, MMSE, QSCC from the patient, QSCC from the relative, GDS-15 and IADL (n = 121)

<table>
<thead>
<tr>
<th>TESTS</th>
<th>MMSE</th>
<th>CAMCOG-R</th>
<th>QSCC (PATIENT)</th>
<th>QSCC (RELATIVE)</th>
<th>GDS-15</th>
<th>NPI-Q</th>
<th>IADL</th>
<th>mbi-C</th>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAMCOG-R</td>
<td>0.45**</td>
<td>1</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>QSCC (patient)</td>
<td>−0.12</td>
<td>−0.08</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>QSCC (relative)</td>
<td>−0.06</td>
<td>0.01</td>
<td>0.31**</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>GDS-15</td>
<td>−0.15</td>
<td>−0.02**</td>
<td>−0.30**</td>
<td>−0.23**</td>
<td>1</td>
<td></td>
<td></td>
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<tr>
<td>NPI-Q</td>
<td>0.02</td>
<td>−0.08</td>
<td>0.12</td>
<td>0.38**</td>
<td>0.39**</td>
<td>1</td>
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</tr>
<tr>
<td>IADL</td>
<td>0.08</td>
<td>0.12</td>
<td>−0.16</td>
<td>−0.21*</td>
<td>−0.03</td>
<td>−0.17</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>MBI-C</td>
<td>0.09</td>
<td>−0.02</td>
<td>0.02</td>
<td>0.30**</td>
<td>0.22*</td>
<td>0.57**</td>
<td>−0.18</td>
<td>1</td>
</tr>
</tbody>
</table>

Notes: MMSE: Mini-Mental State Examination; CAMCOG-R: Cambridge Cognitive Examination-Revised; QSCC: Questionnaire for Subjective Cognitive Complaints; NPI-Q: Neuropsychiatric Inventory- Questionnaire; GDS-15: Geriatric Depression Scale-15 items; IADL: Activities of Daily Living; MBI-C: Mild Behavioral Impairment Checklist.

*The correlation is significant at p < 0.01. **The correlation is significant at p < 0.05.
criteria into MBI domains. Hence, our diagnosis was made in a stricter way, incorporating all the four ISTAART-AA MBI criteria, resulting in a more accurate estimate of prevalence. In a pilot study with a pooled clinical sample of people with MCI and SCD, the prevalence estimated using all the four ISTAART-AA criteria was 11.6% (Mallo et al., 2017). We consider that the 5.8% prevalence in SCD represents an accurate estimate of MBI, reflecting an enriched sample at-risk for incident cognitive decline and dementia, in the absence of objective cognitive findings.

In our investigation, the MBI-C total scoring was a significant predictor of MBI diagnosis. The cut-off point of 8.5 correctly classified 99% of the SCD sample, differentiating people with and without an MBI diagnoses with a sensitivity of 100% and a specificity of 96.3%. Since the MBI-C was developed specifically as a case ascertainment instrument for the ISTAART-AA MBI criteria, and structured to be consistent with the MBI domains, high sensitivity and specificity was expected. MBI-C total scoring correlated significantly and positively with NPI-Q and GDS-15, showing the validity of MBI-C to assess NPS. In agreement with a previous study, broad measures of NPS are related to SCD (Mewton et al., 2014). In the population-based Mayo Clinic Study of Ageing (Geda et al., 2014), symptoms of agitation, anxiety, apathy, irritability, and depression increased the risk of developing MCI in healthy adults. The positive and significant correlation with the GDS-15 (Yesavage and Sheikh, 1986) is also in concordance with recent studies that showed that depression is a strong indicator of SCD (Chin et al., 2014; Burmester et al., 2016). All the same, this relationship may be limited to clinical samples, because the patients are already concerned about their performance.

There was no correlation between MBI-C and Lawton IADL. Importantly, criterion two of the MBI diagnosis assesses if the NPS produce minimal impairment in interpersonal relationships, other aspects of social functioning or ability to perform at the workplace (Ismail et al., 2016). Commonly, people with MCI have problems to perform complex functional tasks which they used to perform in the past (Albert et al., 2011), in contrast to people with SCD (Jessen et al., 2014). However, in MBI diagnosis, these impairments in social, occupational, or interpersonal function must be related to changes in personality and behavior, not to cognitive decline (Ismail et al., 2016). It is important to note that many patients from our study did not meet criterion two because NPS were not of sufficient severity to affect function. This requirement speaks to the clinical relevance of the MBI criteria, and increase specificity by excluding symptoms without functional impact, which may not be risk factors for MCI and dementia. Further research needs to be done in order to clarify this issue.

MBI-C scoring was correlated with QSCC scores from the informant but not with QSCC from the patient. Juncos-Rabadán et al. (2012) concluded that memory difficulties reported by the informant, not the participants themselves, have a greater prognostic value predicting objective performance. Further work is required to establish this. It is important to note that SCD (from the informant and/or the patients themselves) constitute a criterion for diagnosing MCI (Albert et al., 2011). Our findings highlight the importance of assessing NPS in people with SCD since they could be early markers of decline. No correlation was found between the MBI-C and cognitive performance measured by the MMSE or the CAMCOG-R. Despite the fact that MCI and MBI can co-occur, some authors have suggested that they are different syndromes (cognitive and behavioral) and that both increase the likelihood of dementia (Ismail et al., 2016). The absence of correlation found in this investigation may suggest that MBI and MCI are indeed two different entities, one reflecting the neurobehavioral axis, and the other reflecting the neuropsychological axis of predementia syndromes. Future research should be done to establish this.

Our study is characterized by several strengths. An extensive neurocognitive assessment, including tests with norms for age and education, was performed. Hence, participants were classified in accordance with diagnostic criteria, instead of cut-off points in instruments like the MMSE, which are prone to bias from language, education, and culture (Ismail and Mortby, 2017). Additionally, to increase retention, the MBI-C was administered by phone interview, since the population is very spread out in this area. Furthermore, we used all the four ISTAART-AA diagnosis criteria instead of only criterion one, to diagnosis MBI, thus reflecting the most accurate assessment of MBI.

Nevertheless, several limitations should be acknowledged. Of the 127 participants, six were eliminated (4.72%) because we could not confirm an MBI diagnosis from all data sources required for the reference standard. We provided the MBI prevalence in people with SCD, but not in those without cognitive complaints nor in people with neurocognitive disorders. While the cross-sectional design has provided validation of the MBI-C, for measuring MBI in people with SCD, it is not possible to make any conclusions in relation to changes in prevalence over time, nor risk factors...
for evolution to objective cognitive impairment. Longitudinal data are required to determine the predictive utility of the MBI-C for developing cognitive impairment.

This research has raised many questions in need of further investigation. In our study, a clinician administered the MBI-C by phone, but further study is required with face-to-face assessments to generate other validations of the MBI-C. While our study is focused on the MBI-C total score, differences in prediction of cognitive impairment based on the various aggregate domain scores need to be determined. Different MBI domains may predict different MCI and dementia subtypes, which may have implications for treatment. Furthermore, in future studies, psychometric properties of the MBI-C need to be determined with large and transcultural samples. As this study was performed with a primary care clinical sample, more research is required to determine if the results vary in community samples, since prior literature has concluded that NPS are more frequent in clinical versus community samples (Ismail et al., 2017b).

Moreover, more research is needed in order to determine if the new MBI criteria can be used to assist the diagnostic process and if the MBI-C is a helpful instrument for the early identification of individuals at risk of cognitive impairment. Taken together, these findings suggest that the Spanish version of the MBI-C could be a useful tool for detecting MBI in primary care patients with SCD. Recent literature has suggested that disease modifying agents have been unsuccessful in improving dementia outcomes due to poor signal detection and poor recruitment and retention in early phase or prodromal illness (Mortby et al., 2018a). Since NPS are linked to a higher risk of dementia (Pocnet et al., 2015), the MBI-C could be useful as an inexpensive and scalable instrument to capture an enriched sample for further workup, biomarker screening, and potential clinical trial enrolment.

Conflict of interest

None.

Description of author's roles

Sabela C. Mallo, study concept and design, acquisition of data, analysis and interpretation of data and manuscript writing. Zahinoor Ismail, study concept and design and critical revision of manuscript. Arturo X. Pereiro, interpretation of the data and critical revision of the manuscript. David Facal, interpretation of the data and critical revision of the manuscript. Cristina Lojo-Seoane, study supervision and preliminary analyses. Maria Campos-Magdaleno, acquisition of data and preliminary analyses. Onésimo Juncos-Rabadán, study concept and design, study supervision and preliminary analyses. Cristina Lojo-Seoane, study supervision and preliminary analyses. María De las Quejas de Memoria en La vida Cotidiana (2018). The diagnosis of mild cognitive impairment due to Alzheimer’s disease: Recommendations from the national institute on aging-alzheimer’s association workgroups on diagnostic guidelines for alzheimer’s disease. Alzheimer’s & Dementia, 7, 270–279. doi:10.1016/j.jalz.2011.03.008.


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