Featured Article

Neuropsychiatric symptoms as risk factors of dementia in a Mexican population: A 10/66 Dementia Research Group study

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Abstract

Introduction: Cognitive and/or memory impairment are the main clinical markers currently used to identify subjects at risk of developing dementia. This study aimed to explore the relationship between the presence of neuropsychiatric symptoms and dementia incidence.

Methods: We analyzed the association between neuropsychiatric symptoms and incident dementia in a cohort of 1355 Mexican older adults from the general population over 3 years of follow-up, modeling cumulative incidence ratios using Poisson models.

Results: Five neuropsychiatric symptoms were associated with incident dementia: delusions, hallucinations, anxiety, aberrant motor behavior, and depression. The simultaneous presence of two symptoms had a relative risk, adjusted for mild cognitive impairment, diabetes, indicators of cognitive function, and sociodemographic factors, of 1.9 (95% confidence interval, 1.2–2.9), whereas the presence of three to five, similarly adjusted, had a relative risk of 3.0 (95% confidence interval, 1.9–4.8).

Discussion: Neuropsychiatric symptoms are common in predementia states and may independently contribute as risk factors for developing dementia.

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Keywords: Neuropsychiatric symptoms; risk factors; dementia

1. Background

In 2015, it was estimated that there were 46.8 million people with dementia worldwide, of whom 58.0% were living in low- and middle-income countries [1], and that there were annually 9 million new global cases (2014–2015) of dementia. In response to the high prevalence of dementia, the aging global population (8%–9% of the population aged 60 years or older), and its important socioeconomic impact, the World Health Organization made dementia a "public health priority" that requires immediate action [2]. While it has been estimated that if dementia care were a country, it would be the world's 18th largest economy [1], it has become clear that there is a significant imbalance in the global distribution of the quantity and quality of the resources available to treat this illness.

Because a curative treatment is not available so far, several recent lines of research have focused on looking for markers (clinical or biological) that may allow subjects at risk of developing dementia to be identified [3–6] to undertake timely interventions to modify the course of the disease or delay its progress [7]. Neuropsychiatric symptoms (NPSs) have been proposed as potential clinical markers [8–10] for dementia, and it has been considered that some of them, such as depressive and anxiety

symptoms, may increase the risk of developing dementia [11–15]. This has been documented even after controlling for known sociodemographic, genetic, cognitive, and metabolic (diabetes) risk factors [16,17]. However, evidence for the capacity of NPSs to predict the onset of dementia is still inconclusive [18]. The diversity in the results in this field can be partly explained by differences among the studies in terms of the populations, follow-up time, control of risk factors, assessment and diversity of the NPSs, and a range of other factors. In addition, this evidence has been generated in high-income countries, and their study in low- and middle-income countries is limited.

Given the speed of population aging in our country, and the urgent need of markers for preclinical identification of dementia, this report aimed to analyze the relationship between the presence of NPSs and dementia incidence, testing their capability to identify subjects at risk of dementia, through a 3-year follow-up study of Mexican older adults from the general population.

2. Methods

2.1. Sample and procedure

Our report comprised information about 1823 adults aged 65 years and older, living in urban and rural zones, without dementia diagnosis at baseline evaluation (2003–2006), followed in accordance with the 10/66 Dementia Research Group (DRG 10/66) protocols. All the participants were contacted for a 3-year follow-up interview and evaluation (2007–2010). The details of the selection, recruitment, and follow-up method of the cohort have been described in detail elsewhere [19–21].

The urban zones selected for the recruitment were located in the south of Mexico City, and rural recruitment was done in the municipalities of Huitzilac and Tepoztlan, in the state of Morelos. Participants were identified through a door-to-door census, with a response rate at baseline of 85.1%. In both phases (baseline and follow-up), the following assessments were applied: (1) household questionnaire, (2) cognitive evaluation, (3) semistructured geriatric mental state interview, (4) sociodemographic and risk factors questionnaire, (5) an informant or principal caregiver interview (who was close to the older adult), and (6) general physical assessment and blood extraction for clinical analysis (mainly blood cell count and chemistry). Evaluations were performed by Psychology and Social Work undergraduates, and physicians trained at the National Institute of Neurology and Neurosurgery. All the evaluations were based on the DRG 10/66 manuals and training sessions. Participants signed an informed consent; illiterate participants provided verbal consent in the presence of a witness. The study was approved by the scientific and ethical committees of the National Institute of Neurology, Mexico and for the King's College London, United Kingdom [21].

2.2. Measurements

2.2.1. Dementia

We established a dementia diagnosis according to 10/66 and the Diagnostic and Statistical Manual of Mental Disorders IV criteria. The algorithms to operationalize these criteria were developed by the 10/66 DRG and have been reported and described elsewhere [22,23]. Briefly, 10/66 dementia cases score above a cutoff point of predicted probability for dementia based on cognitive test, informant report scores, and diagnostic output from clinical interviews [22]. Diagnostic and Statistical Manual of Mental Disorders IV dementia cases must meet all four qualifying criteria: (1) characteristic cognitive impairment, (2) decline in social or occupational functioning, (3) not accounted for by another mental disorder, and (4) not occurring only during delirium [23]. These algorithms were validated in population samples, having as gold standard the diagnosis made by specialist doctors [23].

2.2.2. Neuropsychiatric symptoms

The questionnaire version of the Neuropsychiatric Inventory (NPI-Q) [24] was used to assess NPSs. The NPI-Q is a structured interview that is applied to the caregiver or an informant close to the older adult and collects information on the presence of the 12 most common symptoms in patients with dementia, during the previous month: delusions, hallucinations, agitation/aggression, depression, anxiety, euphoria, apathy, disinhibition, irritability, aberrant motor behavior, and eating and sleep disorders. In this study, we considered the presence/absence of each one of the 12 NPSs evaluated, analyzing their prevalence and their association with incident dementia.

2.2.3. Other variables

2.2.3.1. Mild cognitive impairment

This was diagnosed in compliance with the Mayo Clinic criteria, again using an algorithm developed by DRG 10/66, which considers (1) subjective complaints regarding memory, (2) slight impairment in cognitive tasks, (3) preservation of functionality for daily activities, and (4) absence of dementia; those who met the criteria were classified as mild cognitive impairment (MCI) cases [25].

2.2.3.2. Diabetes mellitus type 2

Diabetes mellitus type 2 was diagnosed if (1) fasting glycemia at baseline was ≥126 mg/dL or (2) the older adult reported having been diagnosed as diabetic by a health professional [26].

2.2.3.3. Disability

We classified participants as disabled based on a score equal to or above the 90th percentile of the World Health Organization disability scale whose psychometric properties have been described elsewhere [27].