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Featured Article

Mild cognitive impairment and risk of depression and anxiety: a population-based study

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Abstract

Introduction: Many people with mild cognitive impairment (MCI) suffer from concomitant depression or anxiety. Whether MCI increases the risk of future depression or anxiety is unknown.

Methods: In the Rotterdam Study, cross-sectional (n = 4168) and longitudinal associations (n = 2967) of MCI with *Diagnostic and Statistical Manual of Mental Disorders*—depressive and anxiety disorders—were assessed (2002–2005 to 2009–2011).

Results: At baseline, 413 persons had MCI; 125 (22 MCI and 103 non-MCI) had a depressive disorder and 330 had an anxiety disorder (46 MCI and 284 non-MCI). In longitudinal depression analysis, of the 212 persons with prevalent MCI, 6 (2.8%) developed depression compared with 29 (1%) in the nonexposed group. In longitudinal anxiety analysis, 11 (7.3%) of the 151 with prevalent MCI developed anxiety, compared with 75 (3.4%) in nonexposed group. Persons with MCI had more depressive and anxiety disorders and also a higher risk of developing depressive disorder, odds ratio (OR) 3.13 (95% confidence interval [CI]: 1.26, 7.77), and anxiety disorder, OR 2.59 (95% CI: 1.31, 5.12).

Discussion: MCI is a risk factor for dementia and for depressive and anxiety disorders, suggesting common pathological pathways for cognitive and psychiatric outcomes.

Keywords: Mild cognitive impairment; Depression; Anxiety; Epidemiology; Longitudinal; Population based

1. Introduction

Dementia poses a high burden on society and health care, both in terms of suffering for patients and care givers and financial costs [1]. Because brain pathology is thought to accumulate for years before the onset of dementia, much research has been dedicated to study this preclinical phase of dementia. In this context, mild cognitive impairment (MCI) has been conceptualized as a transitional stage between normal cognition and dementia and serves as a clinical construct in which meaningful interventions are possible [2].

Another important manifestation thought to be a part of dementia prodrome is the occurrence of affective disorders, namely, depression and anxiety [3]. Depression and anxiety were shown to be highly prevalent in MCI [4,5]. However, most available literature built up on this association focused on the prognostic role of affective disorders in MCI. Studies showed that MCI with comorbid affective symptoms has an accelerated progression to dementia [6,7].

There is also ample evidence suggesting that depression in late life is associated with a 2-fold increased risk of dementia [8,9]. Although anxiety has not been associated with a higher risk of dementia [10], it has shown to be

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associated with cognitive decline [11]. Extending these findings, some recent studies have also shown that depression is a risk factor for MCI [12–14]. Studies investigating individual neuropsychiatric symptoms in relation to incident MCI found that anxiety increases the risk of MCI [12]. These studies imply that depression and anxiety precede MCI in the chronological order of events. However, given that both MCI and affective symptoms are considered to manifest during the preclinical stage of dementia, it is also not unlikely that MCI precedes depression and anxiety. However, the association of MCI in relation to risk of depression or anxiety has never been investigated. Therefore, we investigated the cross-sectional and longitudinal associations of MCI with depression and anxiety in a population-based cohort of older adults.

2. Methods

2.1. Setting

This study was part of the Rotterdam Study, a population-based cohort ongoing since 1990 in Ommoord, a district of Rotterdam [15]. In 1990, 7983 participants aged 55 years or older were enrolled. In 2000, the original cohort was expanded by additionally enrolling 3011 participants who had become 55 years of age or moved to the district since the start of the study. Follow-up examinations including home interviews and physical examinations at a research center take place every 3–4 years. The Rotterdam Study is approved by the Medical Ethics Committee of the Erasmus MC and by the Ministry of Health, Welfare, and Sport of The Netherlands, implementing the "Wet Bevolkingsonderzoek: ERGO (Population Studies Act: Rotterdam Study)." A written informed consent was obtained from all the participants.

2.2. Study sample

Between 2002 and 2005, the original cohort and the expanded cohort were reexamined, and an extensive neuropsychological test battery was implemented. Given that extensive neuropsychological testing is required to determine MCI, 2002–2005 was set as baseline for MCI screening in our study. Of the 6061 study participants who underwent examinations between 2002 and 2005, 192 participants were excluded because they were demented, 67 because they were not sufficiently screened for dementia, and another 250 participants because they did not answer the questions regarding subjective cognitive complaints. An additional 1354 participants were excluded because they missed one or more cognitive test scores or had unreliable test scores. Cognitive test results were considered unreliable if there had been any technical problems conducting the tests, if there was refusal or insufficient motivation from the participant to perform the tests, if there were any physical limitations to perform the tests, if there was any deviation from the instructions given to perform the tests, or if the tests were not administered correctly. Consequently, MCI was validly assessed in 4198 participants.

Between 2002 and 2005, depression and anxiety disorders were assessed in the Rotterdam Study. Of the 4198 participants with available MCI data, depression data were available for 4168 participants, whereas anxiety data were available for 4060 participants. At baseline, 125 participants fulfilled the criteria for depressive disorders, whereas 330 participants met the criteria for anxiety disorders (Fig. 1).

Between 2009 and 2012, depressive disorders were reassessed in 3117 participants of the 3370 participants attending the examination round (798 participants died during follow-up, 4168 − 798 = 3370). After excluding 125 depression cases at baseline, and 25 persons who were diagnosed of incident dementia during the study period, depressive disorder data were available for 2967 persons for the analyses of MCI and incident depressive disorders (response rate = 92%) (Fig. 1).

Between 2009 and 2012, anxiety disorders were reassessed in 2714 participants of the 3293 participants attending the examination round (767 participants died during follow-up, 4060 − 767 = 3293). We excluded 330 anxiety cases at baseline, and 9 persons who were diagnosed with incident dementia during the study period. Therefore, 2375 participants were available for the analyses of MCI and incident anxiety disorders (response rate = 82%) (Fig. 1).

2.3. Assessment of MCI

MCI was assessed using the following criteria: (1) presence of subjective memory complaints, (2) presence of objective cognitive impairment, and (3) absence of dementia [16].

Subjective memory complaints were assessed by interview, which included three questions on memory (difficulty remembering, forgetting what one had planned to, and difficulty finding words) and three questions on everyday functioning (difficulty managing financing, problems using a telephone, and difficulty getting dressed). Persons answering "yes" to at least one of these questions were scored positive on subjective memory complaints. Objective cognitive impairment was assessed using a cognitive test battery that comprised letter-digit substitution task, Stroop test (reading, color naming, and interference subtasks) [17], verbal fluency test, and 15-word verbal learning test based on Rey's recall of words [18]. To obtain more robust measures, we calculated different compound scores for various cognitive domains including memory function, information processing speed, and executive function. Briefly, compound score for memory was calculated as the mean Z score for the immediate and delayed recall of the 15-word verbal learning test. For information processing speed, average Z scores for the Stroop reading and Stroop color-naming subtasks and the letter-digit substitution task were used. For calculating compound score of executive function, Z scores of Stroop interference subtask, the letter-digit substitution task, and the verbal