Old Worries and New Anxieties: Behavioral Symptoms and Mild Cognitive Impairment in a Population Study

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Objective: *To disentangle the complex associations of depression and anxiety with mild cognitive impairment (MCI) at the population level. We examined subgroups of anxiety symptoms and depression symptom profiles in relation to MCI, which we defined using both cognitive and functional approaches.* **Methods:** *We used an epidemiologic, cross-sectional study with an age-stratified, random, population-based sample of 1,982 individuals aged 65 years and over. Three definitions of MCI were used: 1) a purely cognitive classification into amnestic and nonamnestic MCI, 2) a combined cognitive-functional definition by International Working Group (IWG) criteria, and 3) a purely functional definition by the Clinical Dementia Rating (CDR) of 0.5. Three depression profiles were identified by factor analysis of the modified Center for Epidemiological Studies-Depression Scale: core mood, self-esteem/interpersonal, and apathy/neurovegetative profiles. Three anxiety groups, chronic mild worry, chronic severe anxiety, and recent-onset anxiety, were based on screening questions.* **Results:** *Recent-onset anxiety was associated with MCI by nonamnestic and IWG criteria, chronic severe anxiety was associated with MCI by all definitions, and chronic mild worry was associated with none. Of the depression profiles, the core mood profile was associated with CDR-defined MCI, the apathy/neurovegetative profile was associated with MCI by amnestic, IWG, and CDR definitions, and the self-esteem/interpersonal profile was associated with none.* **Conclusion:** *In this population-based sample, subgroups with different anxiety and depression profiles had different relationships with cognitive and functional definitions of MCI. Anxiety, depression, and MCI are all multidimensional entities, interacting in complex ways that may shed light on underlying neural mechanisms.* (Am J Geriatr Psychiatry 2014; 22:274–284)

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INTRODUCTION

Older adults constitute a growing proportion of those seeking mental health services in specialty and primary care sectors. Clinicians increasingly encounter patients with depression, anxiety, and other behavioral symptoms in the context of cognitive impairment. Mild cognitive impairment (MCI), a cognitive state intermediate between normal aging and dementia, often but not always progresses to dementia.[1] Multiple studies have demonstrated associations of behavioral and psychological symptoms with dementia.[2–4] In contrast, the literature describing associations of MCI with depression and anxiety presents a more patchy landscape, largely focused on the relationship between depression and prognostic risk in MCI.[5,6]

A particular challenge is posed by variations across studies, both in the definition of MCI and in the measurement of behavioral and psychological symptoms. Results also vary because of inherent differences between clinic-based samples of patients seeking services and population-based samples of randomly selected participants. Two large population-based studies used the Neuropsychiatric Inventory[7] to identify behavioral symptoms most often associated with MCI. In the multicenter Cardiovascular Health Study,[8] MCI defined by cognitive assessment was frequently associated with depression, apathy, and irritability. In the Mayo Clinic Study of Aging,[9] apathy, agitation, anxiety, irritability, and depression were associated with MCI defined by the International Working Group (IWG) criteria (also known as the "Winblad criteria").[10] A review described an overall prevalence of 35%–85% of neuropsychiatric symptoms in MCI;[11] depression, anxiety, and irritability were the most common symptoms.

The association between depression and MCI is consistently reported, but the association of MCI with anxiety symptoms remains controversial. Although some studies have reported no differences in anxiety symptoms between cognitively intact individuals and MCI,[12] others showed elevated proportions with anxiety in MCI both in community[8,9] and clinical samples.[13,14]

We sought to deconstruct anxiety and depression and explore their finer-grained relationships with MCI defined in three distinct ways. We used a large, population-based study cohort of older adults.

METHODS

Study Site and Population

The study cohort, named the Monongahela-Youghiogheny Healthy Aging Team, is an age-stratified, random, population sample drawn from the publicly available voter registration list for a small-town region of Pennsylvania.[15] Community outreach, recruitment, and assessment protocols were approved by the University of Pittsburgh Institutional Review Board for protection of human subjects. Recruitment criteria were age 65 years or older, living within the selected towns, and not already in long-term care institutions. Individuals were ineligible if they were too ill to participate, had severe vision or hearing impairments, or were decisionally incapacitated.

We recruited 2,036 individuals over a 2-year period. Because the project was designed to study MCI, we excluded the most severely impaired individuals who scored less than 21 of 30 on the age–education-adjusted Mini-Mental State Examination.[16] The remaining 1,982 individuals underwent the detailed in-home assessment including, but not limited to, the elements below.

Depression and Anxiety Symptoms

Depression symptoms. Participants were screened with the modified Center for Epidemiological Studies-Depression Scale (mCES-D).[17,18] This previously reported modification includes all 20 original CES-D items but asks about their presence "most of the time" over the preceding week in a yes or no format coded as 1 or 0, with a maximum possible score of 20. When treating the score as a categorical variable, we use a threshold reflecting the 90th percentile score on the mCES-D: a score of 5, representing the presence of any five symptoms. Besides the total score, three weighted factors were derived based on exploratory factor analysis (see Results).

Anxiety symptoms. We used three questions to screen for anxiety symptoms: 1) "Would you describe yourself as a worrier?", 2) "Would you say that you easily become nervous or upset?", and 3) "Would you say you had always been this way, or is this a recent change?" We asked Questions 2 and 3 if