ORIGINAL ARTICLE

Prevalence of Neuropsychiatric Symptoms in Mild Cognitive Impairment and Normal Cognitive Aging

Population-Based Study

Yonas E. Geda, MD, MSc; Rosebud O. Roberts, MB, ChB, MS; David S. Knopman, MD; Ronald C. Petersen, MD, PhD; Teresa J. H. Christianson, BSc; Vernon S. Pankratz, PhD; Glenn E. Smith, PhD; Bradley F. Boeve, MD; Robert J. Ivnik, PhD; Eric G. Tangalos, MD; Walter A. Rocca, MD, MPH

Context: Little is known about the population-based prevalence of neuropsychiatric symptoms in mild cognitive impairment (MCI).

Objective: To estimate the prevalence of neuropsychiatric symptoms in MCI and normal cognitive aging in a defined population.

Design: Cross-sectional study derived from an ongoing population-based prospective cohort study.

Setting: The Mayo Clinic Study of Aging.

Participants: We studied a random sample of 1969 individuals without dementia from the target population of 9965 elderly persons residing in Olmsted County (Minnesota) on the prevalence date (October 1, 2004). Neuropsychiatric data were available for 319 of 329 subjects with MCI (97.0%) and 1590 of 1640 subjects with normal cognition (97.0%). Neurologic, cognitive, and neuropsychiatric data were obtained from the study participants. A classification of MCI, dementia, and normal cognitive aging was adjudicated by an expert consensus panel. Accordingly, 329 subjects were classified as having MCI and the remaining 1640 subjects were classified as having normal cognition.

Main Outcome Measure: Neuropsychiatric Inventory Questionnaire score.

Results: Multivariate logistic regression analyses were conducted after adjusting for age, sex, and educational status. By considering both the odds ratio (OR) and the frequency of a symptom, the most distinguishing features between the 2 groups were apathy (OR, 4.53; 95% confidence interval [CI], 3.11-6.60; $P<.001$), agitation (3.60; 2.18-5.92; $P<.001$), anxiety (3.00; 2.01-4.48; $P<.001$), irritability 2.99; 2.11-4.22; $P<.001$), and depression (2.78; 2.06-3.76; $P<.001$). The OR was highest for delusion (8.12; 95% CI, 2.92-22.60; $P<.001$); however, it was rare in both subjects with MCI (11 of 319 [3.4%]) and those with normal cognition (6 of 1590 [0.4%]). Thus, the population attributable risk for delusion was only 2.62% compared with 14.60% for apathy.

Conclusions: Nonpsychotic symptoms affected approximately 50% of subjects with MCI and 25% of subjects with normal cognition. In contrast, psychotic symptoms were rare.

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Author Affiliations:
Department of Psychiatry and Psychology (Drs Geda, Smith, and Ivnik), Neurology (Drs Knopman, Petersen, Boeve, and Rocca), Health Sciences Research, Divisions of Epidemiology (Drs Geda, Roberts, and Rocca), Biostatistics (Ms Christianson and Dr Pankratz), and Primary Care Internal Medicine (Dr Tangalos), College of Medicine, Mayo Clinic, Rochester, Minnesota.

MILD COGNITIVE IMPAIRMENT (MCI) is the transitional state between normal cognitive aging and dementia,[1-3] although various other terms have been proposed to describe this transitional state.[4-9] Subjects with MCI constitute a high-risk group because they develop dementia at a rate of 10% to 15% per year compared with 1% to 2% per year in the general population.[10]

The original operational definition of MCI focused on amnestic MCI: (1) a memory complaint, preferably corroborated by an informant; (2) impaired memory for age at psychometric testing; (3) normal general cognitive function; (4) intact activities of daily living; and (5) absence of dementia.[1] Although amnestic MCI is the most widely investigated and empirically validated construct, the first international consensus panel on MCI has also endorsed the nonamnestic construct proposed by Petersen.[11] A detailed definition and classification of MCI have been reported.[11,12]

We and others[13,14] have reported the frequency of neuropsychiatric symptoms in MCI in clinical settings; however, little is known about these estimates in a population-based setting. The Cardiovascular Health Study (CHS) group reported the first prevalence estimate of neuropsychiatric symptoms in MCI.[15] However, the study did not include control subjects with normal cognition from the same population; therefore, the investigators com-

pared the prevalence of neuropsychiatric symptoms in patients with MCI recruited in one population with the prevalence in control subjects with normal cognition from a study conducted in a different population by other investigators.[16] We measured the prevalence of neuropsychiatric symptoms in subjects with MCI and in subjects with normal cognition from the same population as part of an ongoing population-based study in Olmsted County (Minnesota).[17]

METHODS

STUDY DESIGN

We conducted a cross-sectional case-control study comparing 319 subjects with MCI with 1590 elderly persons with normal cognition. Both groups were identified as part of the Mayo Clinic Study of Aging, a population-based investigation designed to estimate the prevalence and incidence of MCI in Olmsted County (Minnesota). Extensive details of the design and conduct of the study have been reported elsewhere.[17] We describe in brief the study design and methods directly pertinent to the neuropsychiatric study. October 1, 2004, was selected as the prevalence date, and subjects were recruited using a stratified random sampling from the target population of nearly 10 000 elderly individuals in Olmsted County. We used equal allocations of men and women in 2 age strata: 70 to 79 years and 80 to 89 years.[17]

The study was approved by the institutional review boards of the Mayo Clinic and the Olmsted Medical Center. All participants underwent neurologic, psychometric, and neuropsychiatric evaluations. An expert consensus panel of nurses, physicians, and psychologists determined the classification of subjects as having MCI, dementia, or normal cognitive aging on the basis of published criteria.[1,18,19] Subjects with dementia were excluded from the case-control comparison.

NEUROPSYCHIATRIC ASSESSMENT

The Neuropsychiatric Inventory Questionnaire (NPI-Q) was administered to a spouse or other informant for all study participants.[20] The NPI-Q is a shorter version of the Neuropsychiatric Inventory (NPI), which is a structured interview with established reliability and validity.[21] Both the NPI and the NPI-Q measure 12 emotional behavioral domains. We chose to use the NPI-Q because it was selected by the Uniform Data Set initiative of the National Institute on Aging.[22]

Data for observed emotional behavior on the NPI-Q were gathered from a spouse or informant knowledgeable about the study participant. The structured interview addressed 12 neuropsychiatric domains: sleep, apathy, delusion, depression, anxiety, euphoria, agitation, eating/appetite, hallucination, disinhibition, irritability, and aberrant motor behavior. There was a yes or no screening question for each domain. If the respondent answered affirmatively, further questions were asked in order to rate the symptom in terms of severity (1, mild; 2, moderate; or 3, severe). Thus, the maximum score for symptom severity would be 36.

CRITERIA FOR MCI

Subjects who had neither dementia nor normal cognition were classified as having MCI according to published criteria,[11] as follows: (1) cognitive concern expressed by a nurse, physician, informant, or participant; (2) cognitive impairment in 1 domain or more (executive function, memory, language, or visuospatial); (3) normal functional activities; and (4) no dementia. Subjects with MCI could have a clinical dementia rating of 0 or 0.5; however, the final diagnosis of MCI was not based exclusively on the clinical dementia rating but on all available data. Subjects were further classified as having amnestic or nonamnestic MCI, as having single- or multiple-domain MCI, and according to the presumed causes of MCI (eg, vascular, traumatic, psychiatric, or degenerative). The diagnosis of MCI, dementia, Alzheimer disease (AD), or normal cognition was made by consensus, considering all of the data obtained. If the information obtained by 1 of the 3 evaluators (nurse, physician, or psychometrist) was inconsistent with the final diagnosis, this was noted as discordance.[17]

STATISTICAL ANALYSIS

We compared the prevalence of neuropsychiatric symptoms in subjects with MCI and subjects with normal cognitive aging using multivariate logistic regression analysis to adjust for age (continuous variable), sex, and educational status (years of education as a continuous variable). We quantified the magnitude of the association between MCI and a specific neuropsychiatric symptom by computing the odds ratio (OR) and the corresponding 95% confidence interval (CI). We also computed a population-attributable risk (expressed as percentage) using the formula $\{[P(\mathrm{OR}-1)]\div[1+P(\mathrm{OR}-1)]\}\times 100$, where P is the prevalence of the neuropsychiatric symptom in subjects with normal cognition.[23] The population-attributable risk considers both the frequency of a particular neuropsychiatric domain and the magnitude of the corresponding OR. Thus, we used the attributable risk to order the symptoms by overall importance. We also conducted stratified analyses by MCI type (amnestic MCI vs nonamnestic MCI). Statistical testing was done at the conventional 2-tailed α level of .05. All analyses were performed using commercially available software (SAS version 8.2; SAS Institute, Inc, Cary, North Carolina).

In addition, we conducted 2 sets of sensitivity analyses to examine potential sources of bias. In particular, we computed propensity scores to investigate bias in 2 settings. First, we considered missing data as a potential source of bias. Some neuropsychiatric symptoms such as nighttime behavior were prone to have missing data. This resulted either from absence of an informant or from the informant's being unable to recognize the symptom. This happened even though nearly 90% of the informants were spouses. Second, we considered refusal to participate in the study as a potential source of bias. It is possible that refusers might be systematically different from participants. Details of the calculation of propensity scores have been published elsewhere.[24-26] Our propensity scores were based on age (continuous variable), sex, and educational status (continuous variable).

RESULTS

Between October 1, 2004, and September 1, 2007, a total of 1969 participants without dementia were randomly selected and gave consent for the study. There were 329 subjects with MCI and 1940 subjects with normal cognition. Neuropsychiatric data were available for 319 of the 329 participants with MCI (97.0%) and 1590 of the 1640 participants with normal cognition (97.0%). **Table 1** gives their demographic data. There was an almost equal number of men and women in the group with normal cognition; however, there were more men in the MCI group. As expected, subjects with MCI were older than those with normal cognition. Hence, we controlled

for age (continuous variable) by entering it as a covariate in the multivariate analysis. Within the MCI group, more subjects had amnestic MCI (232 of 319 [72.7%]) than nonamnestic MCI (87 of 319 [27.3%]). In the group with amnestic MCI, 61.2% were men, whereas in the group with nonamnestic MCI, 47.1% were men.

The median educational status in the group with normal cognition was 13 years and in the MCI group was 12 years ($P<.01$). The difference between the 2 groups remained significant when educational status was dichotomized at 12 years ($P<.01$). All analyses that compared the OR of neuropsychiatric symptoms between the MCI group and the group with normal cognition were adjusted by age, sex, and educational status.

Table 2 gives the frequency of neuropsychiatric symptoms in elderly participants with MCI and those with normal cognition, along with ORs, associated 95% CIs, and *P* values. Approximately 51% of subjects with MCI and 27% of those with normal cognition had at least 1 neuropsychiatric symptom (**Figure**). The prevalence of neuropsychiatric symptoms in subjects with MCI was significantly higher than in subjects with normal cognition; however, there was no difference between the 2 groups for hallucination and aberrant motor behavior. Symptoms were ordered by descending magnitude of the population-attributable risk, which considers both the frequency of a symptom and the magnitude of the OR. The most distinguishing neuropsychiatric feature between subjects with MCI and those with normal cognition were apathy (OR, 4.53; 95% CI, 3.11-6.60; $P<.001$), followed by agitation (3.60; 2.18-5.92; $P<.001$), anxiety (3.00; 2.01-4.48; $P<.001$), irritability (2.98;2.11-4.22; $P<.001$), and depression (2.78; 2.06-3.76; $P<.001$). Delusion, euphoria, and hallucinations were rare in the group with MCI and virtually absent in the group with normal cognition. For example, delusion was present in 11 of 319 subjects with MCI (3.4%) and 6 of 1590 subjects with normal cognition (0.4%). Thus, the OR of delusion was large and the corresponding CI was wide (OR, 8.12; 95% CI, 2.92-22.6; $P<.001$). However, the population-attributable risk for delusion was only 2.62% compared with 14.60% for apathy. Disinhibition was noted relatively more frequently in the MCI group (15 of 319 subjects [4.7%]) compared with the group with normal cognition (26 of 1590 subjects [1.6%]). There was no difference between the 2 groups regarding hallucinations ($P=.69$).

Table 3 gives stratified analyses by MCI subtypes. These analyses were conducted to explore whether the prevalence of neuropsychiatric symptoms varied by MCI subtype. There were 232 subjects with amnestic MCI and 87 subjects with nonamnestic MCI. The comparison between amnestic and nonamnestic MCI was made by computing ORs and the corresponding 95% CIs for each neuropsychiatric domain. The OR was computed by comparing subjects with a specific MCI subtype with all subjects with normal cognition. Hallucinations were not significantly associated in either group. The OR and 95% CI for euphoria approached significance in the group with amnestic MCI (OR, 2.44; 95% CI, 0.49-12.2; $P=.28$), whereas it was significant in the group with nonamnestic MCI (6.64; 1.33-33.1; $P=.02$). However, this finding should be interpreted with caution because euphoria was rare, noted in 2 of 232 subjects with amnestic MCI and 2 of 87 subjects with nonamnestic MCI.

Table 1. Demographic Data in the Study Participants

Variable	Subjects With Normal Cognition (n = 1590)	Subjects With MCI (n = 319)	*P* Value
Men, No. (%)	791 (49.7)	183 (57.4)	.01
Age, median (range), y	79 (70-91)	82 (70-91)	<.001
70-79	816 (51.3)	100 (31.3)	
80-91	774 (48.7)	219 (68.7)	
Educational status, median (range), y	13 (5-25)	12 (2-25)	<.001
>12	869 (54.7)	135 (42.3)	

Abbreviation: MCI, mild cognitive impairment.

The OR and 95% CI for apathy were higher in the group with amnestic MCI (OR, 5.17; 95% CI, 3.44-7.77; $P<.001$) than in the group with nonamnestic MCI (2.82; 1.42-5.58; $P=.003$). Similarly, the ORs for agitation and irritability were slightly higher in subjects with amnestic MCI compared with those with nonamnestic MCI. In contrast, the ORs for depression, delusion, anxiety, and disinhibition were higher in subjects with nonamnestic MCI compared with amnestic MCI. The OR for delusion in the group with nonamnestic MCI (OR, 12.7; 95% CI, 3.70-43.6; $P<.001$) was almost twice that in the group with amnestic MCI (6.65; 2.07-21.4; $P=.001$); however, the symptom was rare in both groups. The OR for appetite was comparable between the 2 groups.

SENSITIVITY ANALYSIS

We used the demographic data obtained (age, sex, and educational status) to compute propensity scores for each subject. We then used these scores in analyses that weighted these data more heavily toward subjects with higher propensity for missing data or for refusal to participate in the study. We performed 2 sets of sensitivity analyses. In the first set of analyses, we adjusted the observed results back to the complete data set of 1969 subjects who participated in the study. In this analysis, the propensity score reflected the propensity of missing data per variable. In the second set of analyses, we adjusted the observed results back to all subjects who were eligible for the study (1969 participants plus 1657 subjects who refused and 669 with partial participation).[17] In neither of these assessments did we observe markedly different results before and after propensity adjustment.

We illustrate our findings using the missing data for nighttime behavior. The primary analyses showed an OR of 1.80 (95% CI, 1.25-2.60). The propensity-weighted analysis adjusted for missing data yielded an almost identical OR of 1.79 (95% CI, 1.24-2.58). The other adjustments for missing data were even smaller because far fewer observations were missing for the other neuropsychiatric symptoms. In the analyses for refusal to participate, the adjustments back to all the individuals who were eligible for the study produced relatively minor differ-

Table 2. Prevalence of Neuropsychiatric Symptoms in Subjects With Normal Cognition and Subjects With MCI

NPI Domain	No. (%) Subjects With Normal Cognition (n = 1590)	No. (%) Subjects With MCI (n = 319)	OR (95% CI)[a]	*P* Value	Population-Attributable Risk,[b] %
Depression/dysphoria	182 (11.4)	86 (27.0)	2.78 (2.06-3.76)	<.001	16.96
Apathy/indifference	77 (4.8)	59 (18.5)	4.53 (3.11-6.60)	<.001	14.60
Irritability/lability	121 (7.6)	62 (19.4)	2.99 (2.11-4.22)	<.001	13.13
Anxiety	80 (5.0)	45 (14.1)	3.00 (2.01-4.48)	<.001	9.13
Nighttime behavior[c]	141 (10.9)	49 (18.3)	1.80 (1.25-2.60)	.002	8.07
Agitation	45 (2.8)	29 (9.1)	3.60 (2.18-5.92)	<.001	6.84
Appetite/eating change	84 (5.3)	34 (10.7)	2.02 (1.31-3.10)	.001	5.11
Disinhibition	26 (1.6)	15 (4.7)	2.74 (1.42-5.32)	.003	2.77
Delusion	6 (0.4)	11 (3.4)	8.12 (2.92-22.6)	<.001	2.62
Euphoria/elation	7 (0.4)	4 (1.3)	3.58 (1.02-12.6)	.047	1.12
Aberrant motor behavior	9 (0.6)	4 (1.3)	2.30 (0.70-7.61)	.17	0.73
Hallucinations	6 (0.4)	2 (0.6)	1.39 (0.27-7.05)	.69	0.15

Abbreviations: CI, confidence interval; MCI, mild cognitive impairment; NPI, Neuropsychiatric Inventory; OR, odds ratio.

[a] The ORs and 95% CIs were adjusted for age (continuous variable), sex, and educational status (continuous variable).

[b] Population-attributable risk was calculated using the formula $[P(OR - 1)] \div [1 + P(OR - 1)] \times 100$, where P is the prevalence of the neuropsychiatric symptom in subjects with normal cognition.[23]

[c] Nighttime behavior data were missing for 353 subjects because their informant was unable to assess. The percentage without data was similar in both groups: 19.0% of subjects with normal cognition and 16.0% of subjects with MCI ($P = .21$). Sensitivity analyses adjusted for missing data using propensity scores yielded similar results (OR, 1.79; 95% CI, 1.24-2.58).

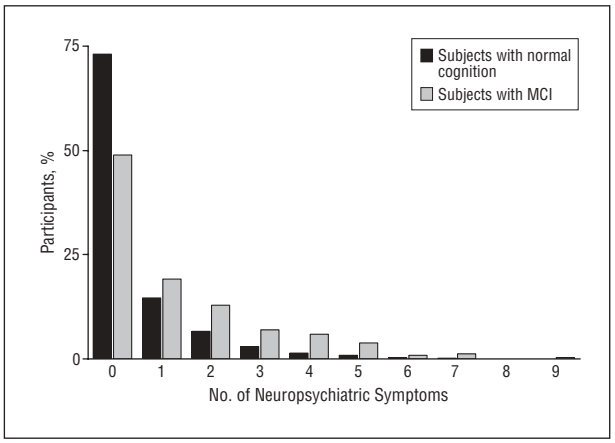

Figure. Number of neuropsychiatric symptoms in subjects with normal cognition and subjects with mild cognitive impairment (MCI).

ences in ORs. For only 1 symptom, aberrant motor behavior, the adjustment resulted in a qualitatively different conclusion because the OR increased from 2.30 (95% CI, 0.70-7.61; $P = .17$) to 3.17 (95% CI, 1.04-9.66; $P = .04$). However, even this difference was relatively small and statistically not significant.

COMMENT

We report the prevalence of neuropsychiatric symptoms in 319 subjects with MCI and 1590 subjects with normal cognition randomly sampled from the elderly population residing in Olmsted County (Minnesota) on the prevalence date (October 1, 2004). Approximately 50% of subjects with MCI and approximately 25% of those with normal cognition had at least 1 neuropsychiatric symptom. After adjusting for age, sex, and educational status and considering both the frequency of a symptom and its corresponding OR, the most distinguishing features between subjects with MCI and those with normal cognition were apathy, depression, agitation, anxiety, and irritability. The OR was highest for delusion, but with a wide 95% CI because it was rare in both the subjects with MCI (3.4%) and those with normal cognition (0.4%). The population-attributable risk, which considers both the OR and the frequency of a symptom, was only 2.62% for delusion compared with 14.60% for apathy.[23]

We also observed that the prevalence of apathy, agitation, and irritability were slightly higher in subjects with amnestic MCI than in those with nonamnestic MCI. In comparison, depression and anxiety were slightly higher in subjects with nonamnestic compared with amnestic MCI. Although delusion was relatively rare, the OR in subjects with nonamnestic MCI was almost twice that in those with amnestic MCI. Similarly, the OR for disinhibition was higher in subjects with nonamnestic MCI compared with amnestic MCI. We hypothesize that apathy, agitation, and irritability may be neuropsychiatric markers of amnestic MCI that is likely to progress to AD, whereas symptoms such as delusion and disinhibition may be neuropsychiatric markers for progression of nonamnestic MCI to non-AD dementia. This hypothesis must be tested in studies involving longitudinal follow-up of subjects over many years.

There have been a few studies of the frequency of neuropsychiatric symptoms in MCI conducted in clinical settings.[13,14] Our study can be directly compared with the population-based study of Lyketsos et al[15] of the CHS group. Between 1989 and 1994, the CHS group collected data on cognition and neuropsychiatric symptoms from 3 counties on the East Coast (Washington County [Maryland]; Allegheny County [Pennsylvania]; and Forsyth County [North Carolina]) and 1 county on the West Coast (Sacramento County [California]). The

Table 3. Prevalence of Neuropsychiatric Symptoms in Subjects With Amnestic or Nonamnestic MCI

	Subjects With Amnestic MCI (n = 232)			Subjects With Nonamnestic MCI (n = 87)		
NPI Domain	No. (%)	OR (95% CI)[a]	*P* Value	No. (%)	OR (95% CI)[a]	*P* Value
Apathy/indifference	48 (20.7)	5.17 (3.44-7.77)	<.001	11 (12.6)	2.82 (1.42-5.58)	.003
Irritability/lability	46 (19.8)	2.96 (2.01-4.36)	<.001	16 (18.4)	2.89 (1.61-5.20)	<.001
Agitation	22 (9.5)	3.79 (2.20-6.54)	<.001	7 (8.0)	3.30 (1.42-7.69)	.006
Depression/dysphoria	60 (25.9)	2.66 (1.88-3.74)	<.001	26 (29.9)	3.14 (1.92-5.12)	<.001
Anxiety	32 (13.8)	2.97 (1.89-4.66)	<.001	13 (14.9)	3.05 (1.61-5.79)	<.001
Nighttime behavior	34 (17.3)	1.65 (1.08-2.51)	.02	15 (20.8)	2.13 (1.16-3.89)	.01
Disinhibition	10 (4.3)	2.42 (1.13-5.16)	.02	5 (5.7)	3.53 (1.30-9.57)	.01
Delusion	6 (2.6)	6.65 (2.07-21.4)	.001	5 (5.7)	12.7 (3.70-43.6)	<.001
Euphoria/elation	2 (0.9)	2.44 (0.49-12.2)	.28	2 (2.3)	6.64 (1.33-33.1)	.02
Appetite/eating change	25 (10.8)	1.98 (1.23-3.21)	.005	9 (10.3)	1.97 (0.95-4.11)	.07
Aberrant motor behavior	2 (0.9)	1.66 (0.35-7.80)	.52	2 (2.3)	4.43 (0.92-21.2)	.06
Hallucinations	1 (0.4)	0.85 (0.10-7.23)	.88	1 (1.1)	2.72 (0.32-23.3)	.36

Abbreviations: CI, confidence interval; MCI, mild cognitive impairment; NPI, Neuropsychiatric Inventory; OR, odds ratio.
[a]The ORs and 95% CIs were adjusted for age (continuous variable), sex, and educational status (continuous variable). The entire group of subjects with normal cognition (n = 1590) was used for comparison (see Table 2 for frequency data).

CHS group reported the first population-based estimate of the prevalence of neuropsychiatric symptoms in MCI.[15] There are 3 grounds that permit comparison of our findings with those of the CHS group. First, both studies were population-based. Second, both studies used essentially identical instruments to measure the 12 behavioral domains. The CHS used the NPI[21] to measure 12 emotional behaviors and we used the NPI-Q to measure exactly the same 12 behavioral domains.[20] The NPI-Q is a shorter version of the NPI and has been selected by the Uniform Data Set initiative of the National Institute on Aging.[22] Third, both studies used similar criteria to measure MCI and also had comparable numbers of subjects with MCI: 320 in the CHS study and 319 in our study. One major difference pertains to the group with normal cognition. In our study, we were able to compare the MCI group with 1590 subjects with normal cognition from the same Olmsted County population, whereas the CHS study did not have subjects with normal cognition from the same population. Thus, the CHS investigators compared the prevalence of neuropsychiatric symptoms in patients with MCI from the CHS study with the published data on the prevalence of neuropsychiatric symptoms in control subjects with normal cognition from Cache County (Utah).[16]

The CHS reported that the 3 most common neuropsychiatric symptoms in MCI were depression (20%), apathy (15%), and irritability (15%). Similarly, we found that the 3 most frequent neuropsychiatric symptoms in MCI were depression (27.0%), apathy (18.5%), and irritability (19.4%). Furthermore, the CHS group suggested that selection bias might have led to underestimation of their prevalence estimates. This bias may account for the differences in crude frequency rates across the 2 studies. We could not make similar comparisons for neuropsychiatric prevalence estimates in persons with normal cognition because the CHS study did not include any participants with normal cognition. The Cache County study reported prevalence figures for depression (7.2%), apathy (3.2%), and irritability (4.6%) in persons with normal cognition.[16] We observed slightly higher figures for depression (11.5%), apathy (4.8%), and irritability (7.6%). Some of these differences may be the result of differences in age and sex distributions in the 2 samples.

There are several strengths to our study. First, we used a population-based sample involving a large number of study participants. Second, we measured MCI using a face-to-face evaluation adjudicated by an expert consensus panel at a clinical center that has a well-established reputation for measuring MCI. Third, the neuropsychiatric symptoms were measured using an instrument similar to that used in the CHS study, thus enabling us to make comparisons. Fourth, we measured the prevalence of neuropsychiatric symptoms in both amnestic and nonamnestic MCI.

The study has limitations. The NPI-Q gathered information from an informant who was knowledgeable about the participant. In our sample, 90% of the informants were spouses; nevertheless, it is possible that an informant may overreport or underreport neuropsychiatric symptoms. However, it is reassuring that despite its smaller sample size (47 subjects with MCI), a Swedish population-based study that used a structured face-to-face interview to measure neuropsychiatric symptoms reported comparable frequency of symptoms.[27] In addition, our sensitivity analyses did not reveal bias emanating from either missing data (nonresponse) or nonparticipation in the study.

Our findings may have implications for future studies. A prospective follow-up of our patients will clarify whether subjects with MCI with neuropsychiatric symptoms are at greater risk of developing AD or other dementias compared with subjects with MCI without neuropsychiatric symptoms.[27] Recent publications indicate that MCI is a heterogeneous entity that can evolve into different types of dementia.[12] The most empirically validated type, amnestic MCI, evolves to AD at a higher rate than in the general population. However, nonamnestic MCI could also evolve into AD or other types of dementia. We hypothesize that subjects with MCI with disinhibition or delusion may be at increased risk of devel-

oping dementia including frontotemporal dementia or dementia with Lewy bodies. In addition, a prospective follow-up of the 1590 subjects with normal cognition will enable us to investigate whether baseline neuropsychiatric symptoms are predictive of increased risk of incident MCI.[28]

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Correspondence: Yonas E. Geda, MD, MSc, Department of Psychiatry and Psychology, College of Medicine, Mayo Clinic, 200 First St SW, Rochester, MN 55905 (geda.yonas@mayo.edu).
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