# Epidemiology of Apathy in Older Adults: The Cache County Study

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**Objectives:** *The objectives of this study are to describe the distribution of apathy in community-based older adults and to investigate its relationships with cognition and day-to-day functioning.* **Methods:** *Data from the Cache County Study on Memory, Health and Aging were used to estimate the frequency of apathy in groups of elders defined by demographic, cognitive, and functional status and to examine the associations of apathy with impairments of cognition and day-to-day functioning.* **Results:** *Apathy was measured with the Neuropsychiatric Inventory. Clinical apathy (Neuropsychiatric Inventory score ≥4) was found in 1.4% of individuals classified as cognitively normal, 3.1% of those with a mild cognitive syndrome, and 17.3% of those with dementia. Apathy status was associated with cognitive and functional impairments and higher levels of stress experienced by caregivers. Among participants with normal cognition, apathy was associated with worse performance on the Mini-Mental State Examination, the Boston Naming and Animal Fluency tests, and the Trail Making Test—Part B. The association of apathy with cognitive impairment was independent of its association with Neuropsychiatric Inventory depression.* **Conclusions:** *In a cohort of community-based older adults, the frequency and severity of apathy is positively correlated with the severity of cognitive impairment. In addition, apathy is associated with cognitive and functional impairments in elders adjudged to have normal cognition. The results suggest that apathy is an early sign of cognitive decline and that delineating phenotypes in which apathy and a mild cognitive syndrome co-occur may facilitate earlier identification of individuals at risk for dementia.* (Am J Geriatr Psychiatry 2007; 15:365–375)

**Key Words:** Apathy, epidemiology, mild cognitive syndromes, dementia

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Apathy is a disorder of an aspect of executive cognition, the "will": "the human power, potency or faculty to initiate action."[1] When this capacity is diminished, affected individuals manifest diminished desire, goal formulation, and voluntary behavior—characteristics emphasized in an operational definition of apathy proposed by Robert Marin 15 years ago.[2] Apathy presents in the clinic as diminished emotions, low vitality, poor self-motivation, poor initiative, and diminished goal-directed behavior and is a common feature of neuropsychiatric conditions—whether these are primary disorders of mood, ideation, or cognition or the sequels of trauma, stroke, infection, or substance abuse. Apathy has features in common with depression[3–6] and is liable to be misdiagnosed as such, yet it has its own treatments.[7–13]

Dementia is a common context for apathy in older adults[2,3,14–16]; prevalence rates reach 80% in clinic samples of primary dementias[15,17–21] and range from 27%–36% in community samples.[22,23] Apathy frequently complicates the course and management of dementia by contributing to functional disability and self-neglect.[4,15,16,24] Apathy is also prevalent in elders with milder forms of cognitive impairment in clinic-based[25–27] and community-based[23] samples and elders identified as having apathy are more likely than elders who do not have apathy to have impairments in executive domains of cognitive function.[25,28–30]

In addition to their clinical value, relationships between apathy and mild cognitive syndromes have nosologic value since describing early phenotypes of Alzheimer disease (AD) and other primary dementias has high priority in neuropsychiatry. Investigators use several different approaches in their study of predementia phenotypes of AD, including: 1) description of milder cognitive syndromes that are not dementia (i.e., cognitive impairment, no dementia [CIND]), of which "mild cognitive impairment" (MCI)[31,32] is the most widely recognized; 2) evaluation of late-life psychiatric syndromes such as depression and psychosis as predictors of dementia; and 3) characterization of the neuropsychiatric profile of CIND syndromes. This latter approach explores broad phenotypes (cognitive impairment plus a psychiatric profile) as probable predementia states on the premise that several neuropsychiatric phenotypes represent evolving dementia. A few preliminary studies of elders with MCI, based on this approach, and sampling clinic-based cases have correlated apathy with poorer performance on cognitive and functional assessments.[27,30,33,34] One longitudinal study has linked apathy to faster "conversion" from MCI to dementia[25] and another to faster progression of dementia.[35]

Apathy could be a useful "marker" of evolving dementia. In clinical samples of MCI rates of apathy appear to be comparable to rates in mild cases of AD,[27] and the co-occurrence of apathy with impairments in executive domains of cognitive function may be as frequent in patients with MCI as in those with AD.[30] The notion emerges of an MCI plus apathy phenotype that progresses to dementia, and it is also possible that apathy precedes MCI. Because these premises rest on observations derived from clinic-based studies, characterization of the distribution of apathy in a population-based cohort of older adults is necessary. We report here the distribution of apathy in demographic and cognitive strata of a population-based sample of older adults and examine its association with cognitive and functional performance. We also explore whether apathy is associated with cognitive impairments in elders with normal cognition; on the basis of observations in patients with AD,[36,37] we propose that in elders, apathy will be specifically associated with impairments in global cognition, memory, naming, verbal fluency, praxis, and psychomotor speed.

## METHODS

### Sample

The data for this report are from the population sample of the Cache County Study on Memory, Health and Aging (CCSMHA). The design is described in earlier reports.[22,38] In summary, 90% of residents of Cache County, Utah, aged 65 and older in January 1995 (N = 5,092), enrolled in a longitudinal study on memory and aging. All participants gave written consent before enrollment, and the study has been approved by the Institutional Review Boards of the participating institutions. The participants were screened for dementia with the Modified

Mini-Mental State Examination (3MS)[39,40] or the Informant Questionnaire for Cognitive Decline (IQCODE).[41] Individuals scoring below a predetermined cut point on the 3MS, an age/gender/APOE genotype stratified probability sample of those above the cut point, and all individuals aged 90 years and older who had not already been selected were administered the Dementia Questionnaire (DQ),[42] a semistructured telephone interview of an informant. Participants that received DQ ratings of cognitive impairment or dementia (based on criteria in the revised third edition of the *Diagnostic and Statistical Manual for Mental Disorders [DSM*]), and those who had been selected into the probability sample, underwent a detailed clinical assessment and a neuropsychologic battery. A majority of the participants who had dementia had brain magnetic resonance imaging or computed tomography scans. These examination data were used to assign cognitive status (and diagnoses) in adjudication conferences staffed by experienced investigators. This report relies on clinical assessment data from the 1995 wave, the first wave of the study.

### Measures

Apathy and depression were measured with the Neuropsychiatric Inventory (NPI).[43] In this study, apathy scores were categorized as: 0 = none, 1–3 = mild apathy, ≥4 = "clinical" apathy. The use of an NPI domain score of four as the threshold for clinical status in epidemiologic studies has several precedents (for example,[23,44,45]). The NPI depression scores were categorized in the same manner.

Cognitive status was based on consensus clinical diagnoses and the Clinical Dementia Rating (CDR).[46,47] The consensus diagnoses, assigned at adjudication conferences, were "normal," CIND (a broad category for impairments of lesser severity than dementia),[48] and dementia. The CDR measures dementia severity rated in six domains: memory, orientation, judgment and problem-solving, community affairs, home and hobbies, and personal care. Each participant's examiner assigns ratings for each domain, and the final score is derived from an algorithm.[46] Participants with a clinical consensus diagnosis of dementia were assigned severity ranks (mild, moderate, or severe) on the basis of their final CDR score.

The Dementia Severity Rating Scale (DSRS),[49] an informant interview instrument, was used to measure day-to-day functioning. The DSRS rates dementia in 11 clinical domains, six of which refer to activities of daily living (ADL): social activities, housekeeping, personal care, meals/feeding, continence, and mobility. (The other five domains are cognitive.) Mobility is rated from "0" to "6" and the other ADL domains from "0" to "4." Zero indicates the absence of impairment, and the highest rating (four or six) indicates inability or complete dependency with respect to the ADL. In an approach used previously in the CCSMHA,[50] the six ADL ratings (DSRS-ADL) were summed to yield an indicator of overall ADL impairment. The DSRS also includes an item that asks each participant's informant to rate, on a scale of 1 to 10, the burden of providing day-to-day care to the participant.

Cognitive performance was measured with the Mini-Mental State Examination (MMSE)[51] and neuropsychologic tests from a CCSMHA test battery described in an earlier report[52]: Benton Visual Retention Test (BVRT); Boston Naming Test (BNT); word list total recall, constructional praxis, and animal fluency from the battery developed by the Consortium to Establish a Registry for Alzheimer Disease [CERAD]; Controlled Oral Word Association [COWA]; Symbol-Digit Modality Test [SDMT]; and Trail Making Test–Part B. The demographic variables were gender, age at the clinical assessment, apolipoprotein E (APOE) status, years of education, and marital status (a dichotomous variable indicating whether the participant had a living spouse).

### Analysis

The data were analyzed with Stata, version 8.2.[53] NPI apathy and NPI depression were ordinal variables. Gender and marital, APOE, and cognitive status were also categorical variables. Age at clinical assessment, years of education, MMSE and neuropsychologic test scores, and DSRS-ADL, and DSRS caregiver stress scores were intervals. We report descriptive statistics for the entire sample and across apathy strata, and test for significance of associations with $\chi^2$ and Fisher exact tests, 95% confidence intervals, and analyses of variance. The trend test method described by Jack Cuzick, for nonparametric tests

across ordered groups,[54] was used to evaluate the neuropsychologic test scores across apathy strata. The relative odds for apathy within strata of cognitive status (i.e., normal, CIND, and dementia) were estimated in ordinal logistic regression with adjustment for NPI depression and marital status.

## RESULTS

The characteristics of the sample, stratified by apathy status, are shown in Table 1. Gender, age, education, and APOE status were not associated with apathy. Participants with apathy were more likely to not have a spouse (i.e., to be single, divorced, or widowed) than were those who did not have apathy. These participants were also more likely to have CIND and dementia and NPI depression. Although apathy and NPI depression did correlate, 57.9% of individuals with apathy did not have NPI depression, and 62.8% of individuals with NPI depression did not have apathy.

All 1,033 participants had a cognitive designation. One participant with dementia was missing the CDR score. Completion rates for apathy and NPI depression were 97.6% (N = 1,008) and 97.5% (N = 1,007), respectively. The analyses focused on the 1,008 participants who had an apathy score. Over 90% of these participants completed the MMSE, word list, BNT, animal fluency, COWA, and DSRS caregiver stress rating. Completion was lower for constructional praxis (89.3%), BVRT (83.2%), SDMT (80.1%), Trail Making Test–Part B (64.2%), and the DSRS-ADL (71.1%). Physical impairment, usually visual, accounted for 80% of missing values on constructional praxis and BVRT and 50% of missing values on SDMT. Apathy was not associated with dementia among participants missing values on constructional praxis and BVRT resulting from their physical impairment or refusal to do the tasks ($p > 0.5$, Fisher test). Thirty-six percent refused the SDMT; apathy was not associated with dementia in these subjects ($p = 0.32$, Fisher exact test). Cognitive impairment accounted for 39.9% of missing values on the Trail Making Test (N = 144), physical impairment another 28.8% (N = 104), and 9.7% were refusals (N = 35). Apathy was not associated with dementia among participants missing values on this test because they had cognitive impairment ($p = 0.48$, Fisher test),

**TABLE 1. Description of the Study Population by Apathy Status**

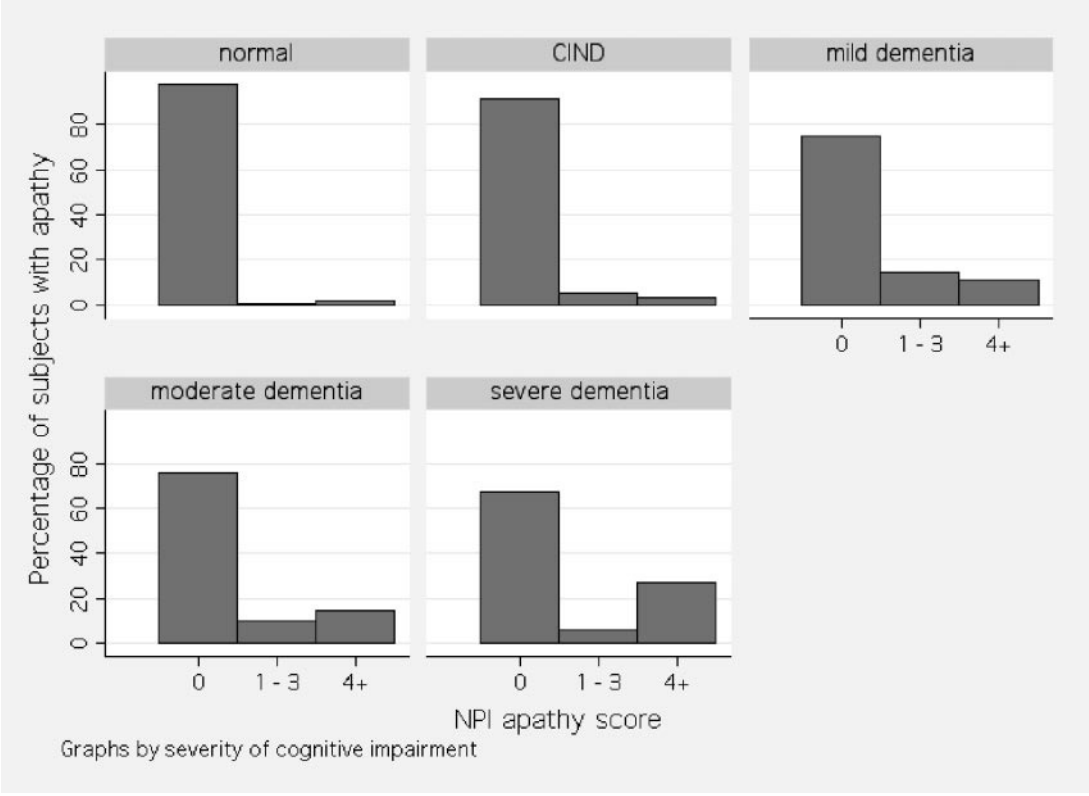
| Characteristics | | Apathy Scores 0 | 1–3 | 4+ | F or $\chi^2$ (df) | p |
|---|---|---|---|---|---|---|
| All subjects | | 893 (88.6) | 46 (4.6) | 69 (6.8) | — | — |
| Gender | Female, N (%) | 511 (57.2) | 31 (67.4) | 37 (53.6) | 2.29 (2) | p = 0.318 |
| | Male, N (%) | 382 (42.9) | 15 (32.6) | 32 (46.4) | | |
| Age (years) | Mean (SD)[a] | 81.3 (7.7) | 83.2 (8.2) | 83.5 (6.4) | 3.72 (2, 1005) | p = 0.246 |
| | Median (IQR) | 81 (76–87) | 83 (77–88) | 83 (79–88) | 5.09 (2)[b] | p = 0.078 |
| Education | Mean (SD) | 12.9 (3.1) | 12.8 (3.2) | 12.5 (2.9) | 0.53 (2, 1002) | p = 0.586 |
| | Median (IQR) | 12 (12–14) | 12 (12–16) | 12 (12–13) | 2.02 (2)[b] | p = 0.364 |
| Marital status | No spouse, N (%) | 409 (46.0) | 31 (67.4) | 42 (60.9) | 12.92 (2) | p = 0.002 |
| | Married, N (%) | 480 (54.0) | 15 (32.6) | 27 (39.1) | | |
| Apo-E4 status | 4/4, N (%) | 85 (9.6) | 3 (6.7) | 7 (10.3) | 1.34 (2) | p = 0.855 |
| | X/4, N (%) | 387 (43.5) | 23 (51.1) | 31 (45.6) | | |
| | X/X, N (%) | 418 (47.0) | 19 (42.2) | 30 (44.1) | | |
| Cognitive status | Normal, N (%) | 483 (54.1) | 3 (6.5) | 7 (10.1) | 121.97 (4) | p <0.001 |
| | CIND, N (%) | 175 (19.6) | 10 (21.7) | 6 (8.7) | | |
| | Dementia, N (%) | 235 (26.3) | 33 (71.7) | 56 (81.2) | | |
| NPI depression score | 0 | 803 (90.9) | 24 (52.2) | 42 (61.8) | 130.66 (4) | p <0.001 |
| | 1–3 | 53 (6.0) | 17 (37.0) | 11 (16.2) | | |
| | 4+ | 28 (3.1) | 5 (10.9) | 15 (22.1) | | |

[a]Data for each characteristic are means with standard deviations (SD), medians, with interquartile ranges (IQR), or proportions with percentages (%). We use analysis of variance to compare means across apathy categories (using the F-statistic) and $\chi^2$ to compare proportions.
[b]The median test is used to compare age and education medians across apathy categories. The test statistic is the $\chi^2$.
NPI: Neuropsychiatric Inventory.

**FIGURE 1. Distribution of Apathy States Across Strata of Cognitive Impairment**

| Cognitive status* | Apathy scores† | | |
|---|---|---|---|
| | 0<br>N *(%)* | 1-3<br>N *(%)* | 4+<br>N *(%)* |
| **Normal** | 483 *(98.0)* | 3 *(0.6)* | 7 *(1.4)* |
| **CIND** | 175 *(91.6)* | 10 *(5.2)* | 6 *(3.1)* |
| **Mild dementia** | 95 *(74.8)* | 18 *(14.2)* | 14 *(11.0)* |
| **Moderate dementia** | 69 *(75.8)* | 9 *(9.9)* | 13 *(14.3)* |
| **Severe dementia** | 71 *(67.0)* | 6 *(5.7)* | 29 *(27.4)* |

*Cognitive classification is based on the clinical consensus diagnoses: normal cognition, "Cognitive impairment not dementia" (CIND) and dementia. Subclassification of dementia into "mild," "moderate," or "severe" status is based on scores on the Clinical Dementia Rating (CDR).[8]




†$\chi^2 = 164.6$, $p < 0.001$. Graphs are plotted from data the shown. The frequency and severity of apathy increases with the severity of cognitive impairment.

CIND: Cognitive impairment, not dementia.

**TABLE 2. Mean Neuropsychological Test Scores Across Apathy Strata**

| Neuropsychological Tests | Apathy = 0 | | Apathy = 1-3 | | Apathy = 4+ | | Cuzick's Trend Test | |
|---|---|---|---|---|---|---|---|---|
| | N | Mean (SD) | N | Mean (SD) | N | Mean (SD) | z | p |
| MMSE | 884 | 23.7 (7.6) | 45 | 20.1 (7.0) | 67 | 13.7 (10.3) | −9.04 | <0.0001 |
| Word list recall | 868 | 14.5 (6.5) | 43 | 10.3 (4.5) | 59 | 7.2 (6.7) | −8.33 | <0.0001 |
| BNT | 863 | 12.1 (3.6) | 44 | 10.9 (3.3) | 65 | 8.5 (5.1) | −7.02 | <0.0001 |
| BVRT | 753 | 3.9 (2.4) | 35 | 2.4 (1.7) | 51 | 1.6 (2.0) | −7.03 | <0.0001 |
| Constructional praxis | 803 | 9.0 (2.5) | 42 | 8.2 (2.4) | 56 | 5.7 (4.1) | −7.04 | <0.0001 |
| Animal fluency | 883 | 13.4 (6.6) | 45 | 9.8 (5.6) | 66 | 6.1 (5.3) | −9.05 | <0.0001 |
| Controlled oral word association | 843 | 26.4 (13.4) | 38 | 21.5 (15.1) | 57 | 13.4 (12.6) | −6.78 | <0.0001 |
| Symbol–digit modality | 725 | 25.1 (13.2) | 31 | 18.8 (11.7) | 51 | 8.7 (11.4) | −7.95 | <0.0001 |
| Trail Making Test–Part B | 608 | 166.2 (88.9) | 19 | 211.6 (81.2) | 20 | 211.0 (84.5) | −3.23 | 0.001 |

*Notes*: Data are mean scores (with the standard deviations [SD]) for each neuropsychologic test. Maximum scores for each test are: Mini-Mental State Examination (MMSE): 30 points; Benton Visual Retention Test (BVRT): 10 points; word list recall: 29 points; Boston Naming Test (BNT): 15 points; constructional praxis: 11 points; animal fluency: 35 points; controlled oral word association: 67 points; Symbol–digit modality: 53 points; Trail Making Test–Part B: time (in seconds) taken to complete the task. We use Cuzick's trend test (the test statistic is the z score) to evaluate trends in the scores across apathy categories for each neuropsychologic test.

**TABLE 3. Mean Neuropsychological Tests Scores Across Apathy Strata Stratified by Cognitive Status**

| Neuropsychological Tests | Apathy = 0 | | Apathy = 1–3 | | Apathy = 4+ | | ANOVA | | Cuzick's Trend Test | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | Mean (SD) | N | Mean (SD) | N | Mean (SD) | F (df) | p | z | p |
| Normal cognition | | | | | | | | | | |
| MMSE | 481 | 27.7 (2.4) | 3 | 21.0 (6.1) | 7 | 21.4 (10.6) | 26.83 (2,488) | <0.0001 | −2.81 | 0.005 |
| Word list recall | 480 | 18.1 (4.3) | 3 | 15.3 (3.2) | 6 | 14.3 (7.6) | 2.77 (2,486) | 0.064 | −1.54 | 0.125 |
| BNT | 474 | 13.6 (1.8) | 3 | 11.0 (2.0) | 7 | 12.9 (3.6) | 3.51 (2,481) | 0.031 | −0.61 | 0.541 |
| BVRT | 443 | 5.1 (1.9) | 2 | 3.0 (0) | 6 | 4.0 (2.1) | 2.18 (2,448) | 0.114 | −1.65 | 0.100 |
| Constructional praxis | 460 | 9.9 (1.2) | 3 | 9.7 (1.2) | 6 | 7.7 (4.1) | 8.90 (2,466) | 0.001 | −1.60 | 0.110 |
| Animal fluency | 481 | 17.0 (4.7) | 3 | 9.3 (5.9) | 7 | 10.0 (6.7) | 11.29 (2,488) | <0.001 | −3.17 | 0.002 |
| Controlled oral word association | 474 | 32.2 (10.6) | 3 | 29.7 (2.5) | 6 | 23.8 (15.1) | 1.90 (2,480) | 0.151 | −1.27 | 0.204 |
| Symbol–digit modality | 433 | 31.9 (9.2) | 3 | 26.7 (7.5) | 5 | 24.4 (14.1) | 2.06 (2,438) | 0.128 | −1.32 | 0.186 |
| Trail Making Test–Part B | 427 | 140.3 (70.7) | 2 | 247.5 (47.4) | 4 | 175.0 (41.8) | 2.76 (2,430) | 0.064 | 2.22 | 0.026 |
| Cognitive impairment not dementia (CIND) | | | | | | | | | | |
| MMSE | 173 | 24.9 (4.0) | 10 | 25.4 (3.3) | 6 | 20.2 (7.7) | 4.01 (2,186) | 0.020 | −1.04 | 0.297 |
| Word list recall | 171 | 14.1 (4.2) | 10 | 14.0 (3.6) | 5 | 10.6 (6.3) | 1.64 (2,183) | 0.196 | −1.27 | 0.205 |
| BNT | 172 | 12.4 (2.4) | 10 | 13.1 (1.2) | 6 | 11.5 (3.0) | 0.84 (2,185) | 0.433 | −0.25 | 0.804 |
| BVRT | 145 | 3.3 (1.7) | 9 | 3.4 (1.24) | 2 | 4.5 (3.5) | 0.52 (2,153) | 0.596 | 0.51 | 0.608 |
| Constructional praxis | 158 | 9.2 (1.6) | 10 | 9.1 (1.4) | 2 | 10.0 (1.4) | 0.25 (2,167) | 0.776 | 0.18 | 0.860 |
| Animal fluency | 172 | 13.0 (4.6) | 10 | 16.0 (4.4) | 6 | 11.5 (8.1) | 2.23 (2,185) | 0.110 | −0.03 | 0.978 |
| Controlled oral word association | 165 | 26.4 (10.9) | 9 | 25.2 (14.6) | 5 | 23.8 (9.5) | 0.70 (2,176) | 0.498 | −1.35 | 0.177 |
| Symbol–digit modality | 433 | 22.9 (9.6) | 3 | 27.1 (7.9) | 5 | 21.5 (12.0) | 0.78 (2,149) | 0.462 | 0.95 | 0.343 |
| Trail Making Test–Part B | 123 | 209.9 (89.1) | 6 | 147.8 (50.1) | 3 | 193.0 (134.7) | 1.43 (2,129) | 0.243 | −1.22 | 0.222 |
| Dementia | | | | | | | | | | |
| MMSE | 230 | 14.3 (8.6) | 32 | 18.4 (7.2) | 54 | 12.0 (9.9) | 5.43 (2,313) | 0.0005 | −0.82 | 0.413 |
| Word list recall | 217 | 6.8 (5.4) | 30 | 8.7 (4.3) | 48 | 5.9 (6.0) | 2.28 (2,292) | 0.104 | −0.82 | 0.411 |
| BNT | 217 | 8.6 (4.6) | 31 | 10.2 (3.5) | 52 | 7.6 (5.0) | 3.14 (2,297) | 0.045 | −0.60 | 0.551 |
| BVRT | 165 | 1.0 (1.3) | 24 | 2.0 (1.8) | 43 | 1.2 (1.6) | 4.61 (2,229) | 0.012 | 0.97 | 0.332 |
| Constructional praxis | 185 | 6.6 (2.7) | 29 | 7.8 (3.7) | 48 | 5.3 (4.0) | 4.23 (2,259) | 0.016 | −1.27 | 0.205 |
| Animal fluency | 230 | 6.2 (4.8) | 32 | 7.9 (4.6) | 53 | 5.0 (4.2) | 3.91 (2,312) | 0.021 | −0.90 | 0.366 |
| Controlled oral word association | 204 | 12.9 (11.0) | 26 | 19.3 (15.8) | 46 | 11.2 (11.8) | 4.28 (2,273) | 0.015 | −0.50 | 0.616 |
| Symbol–digit modality | 150 | 7.9 (9.0) | 20 | 14.3 (11.3) | 44 | 6.4 (9.3) | 5.27 (2,211) | 0.006 | −0.69 | 0.492 |
| Trail Making Test–Part B | 58 | 264.7 (104.0) | 11 | 239.9 (81.2) | 13 | 211.0 (84.5) | 0.97 (2,79) | 0.385 | −1.21 | 0.227 |

*Notes*: Data are mean scores (with the standard deviations [SD]) for each neuropsychologic test. Maximum scores for each test are: Mini-Mental State Examination (MMSE): 30 points; Benton Visual Retention Test (BVRT): 10 points; word list recall: 29 points; Boston Naming Test (BNT): 15 points; constructional praxis: 11 points; animal fluency: 35 points; controlled oral word association: 67 points; Symbol–digit modality test: 53 points; Trail Making Test–Part B: time (in seconds) taken to complete the task. We use analysis of variance (ANOVA) to compare means across apathy categories (with the F-statistic) and Cuzick's trend test (with the z score) to evaluate trends in the scores across apathy categories for each neuropsychologic test.

physical impairment ($p > 0.597$), or refusal ($p = 0.936$). Forty-two percent of participants with missing values on the DSRS-ADL had dementia, and 24% of these had apathy (7% had mild apathy and 17% clinical apathy). Apathy was associated with cognitive status in these participants ($p < 0.001$, Fisher test).

Figure 1 shows the frequency and severity of apathy across cognitive strata. Apathy was uncommon and relatively mild in individuals with normal cognition, and its frequency and severity correlated positively with the severity of cognitive impairment. In an ordinal logistic regression, in which NPI depression and marital status were covariates, the association of apathy with cognitive status (i.e., with CIND and dementia) was independent of NPI depression and marital status. Apathy was associated with cognitive status (odds ratio [OR]: 5.7, $z = 5.1$, 95% confidence interval [95% CI]: 2.9–11.2 for mild apathy; and OR: 9.2, $z = 6.9$, 95% CI: 4.9–17.4 for clinical apathy). NPI depression was associated with cognitive status in the same regression (OR: 2.0, $z = 2.8$, 95% CI: 1.2–3.1 for mild depression; OR: 3.6, $z = 3.9$, 95% CI: 1.9–6.8 for clinical depression). The relative odds for association of apathy with cognitive status were over twofold higher than the relative odds for association of NPI depression with cognitive status.

Apathy was associated with worse scores on several neuropsychologic tasks and longer completion times on the Trail Making Test (Table 2). These associations were not evident when analyses adjusted for cognitive status. We asked whether apathy is predominantly associated with impairments in executive domains of cognitive function by examining neuropsychologic test scores within each stratum of cognitive status (data shown in Table 3). Among the cognitively normal, apathy was associated with lower scores on the MMSE, the Boston Naming, constructional praxis, and animal fluency tests and longer completion times on the Trail Making Test. In those with CIND, clinical apathy was associated with a lower MMSE score but not with scores on the other tests. Apathy was not associated with worse neuropsychologic test scores in participants with dementia. Apathy was associated with the DSRS-ADL and caregiver scores of participants with normal cognition and those with dementia (Table 4) and was still associated with the scores after adjustment for cognitive status.

## DISCUSSION

This is the first detailed epidemiologic study of apathy in later life, and the context is a community-based sample that underwent detailed neuropsychiatric examinations and had cognitive designations assigned in a formal process. In this cohort, apathy

**TABLE 4. Mean Dementia Severity Rating Scale Activities of Daily Living (DSRS-ADL) and Caregiver Stress Scores by Apathy and Cognitive Status**

| | Apathy = 0 | | Apathy = 1–3 | | Apathy = 4+ | | ANOVA | | Cuzick's Trend Test | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Neuropsychological Tests** | **N** | **Mean (SD)[a]** | **N** | **Mean (SD)** | **N** | **Mean (SD)** | **F (df)** | **p** | **z** | **p** |
| DSRS-ADL[b] | | | | | | | | | | |
| Normal | 394 | 6.5 (1.4) | 3 | 9.3 (0.5) | 4 | 11.8 (4.5) | 30.66 (2,398) | <0.001 | 5.24 | <0.001 |
| Cognitive impairment not dementia (CIND) | 108 | 8.6 (3.2) | 7 | 9.0 (2.8) | 3 | 7.7 (1.0) | 0.19 (2,115) | 0.828 | 0.28 | 0.779 |
| Dementia | 145 | 17.3 (4.3) | 25 | 16.2 (6.5) | 36 | 20.3 (7.2) | 3.15 (2,203) | 0.045 | 1.83 | 0.068 |
| Total | 647 | 9.3 (5.8) | 35 | 14.1 (6.4) | 43 | 18.6 (7.7) | 57.38 (2,722) | <0.0001 | 10.02 | <0.001 |
| DSRS caregiver stress scale[c] | | | | | | | | | | |
| Normal | 450 | 1.5 (1.0) | 3 | 4.3 (2.5) | 7 | 3.1 (1.3) | 19.02 (2,457) | <0.0001 | 4.86 | <0.001 |
| CIND | 166 | 2.3 (1.5) | 10 | 2.9 (1.1) | 6 | 4.0 (1.9) | 4.70 (2,179) | 0.01 | 2.88 | 0.021 |
| Dementia | 220 | 3.8 (1.8) | 31 | 3.8 (1.9) | 50 | 4.9 (1.7) | 6.79 (2,298) | 0.001 | 3.48 | 0.025 |
| Total | 836 | 2.3 (1.7) | 44 | 3.6 (1.8) | 63 | 4.6 (1.7) | 65.62 (2,940) | <0.0001 | 10.48 | <0.001 |

[a]Data are mean scores (with the standard deviations [SD]) for each scale.

[b]DSRS-ADL: Dementia Severity Rating Scale–Activities of Daily Living subscale. Range of scores 0–26; "0" indicates that participant has no ADL impairment, and higher scores indicate worse ADL impairment.

[c]The DSRS caregiver stress scale is a 10-point scale; higher indicate higher levels of caregiver stress.

was uncommon among elders with normal cognition and most frequent and severe in elders with dementia. As predicted, apathetic elders with normal cognition performed worse on neuropsychologic tests than elders who were not apathetic. These elders had impairments in global cognition (indicated by lower MMSE scores) and in object naming, constructional praxis, category fluency, and Trail Making Tests. Those with CIND and clinical apathy (NPI apathy scores $\geq$4) performed poorly on the MMSE. The observation that apathy did not influence cognitive performance in elders with dementia was unexpected. Apparently, in CIND and dementia, apathy has little impact on neuropsychologic test performance. This observation, that apathy is associated with impaired cognitive performance in normal elders, and not in CIND and dementia, can be explained; it is likely that when cognitive impairment is sufficiently severe, the influence of apathy on test performance is obscured or confounded by other gross cognitive disability.

This report contributes to a growing literature on the status of apathy in CIND and dementia. It has become established that, on average, apathetic elders with CIND show poorer performance on cognitive tasks than do their counterparts who do not have apathy[25–27,29,30,33,34]; ours is the first study to report a similar observation in elders with normal cognition. The observation is intriguing, because it implies that apathy is a very early sign of cognitive decline, especially when the correlation between the severity of apathy and the severity of cognitive impairment, and results from recent longitudinal studies are taken into consideration. Maura Copeland and her colleagues reported that CIND patients with "passivity" (their term for apathy) had cumulatively higher rates of "conversion" to dementia in 3 years of follow up, and they suggested that in CIND apathy is an indicator that cognitive decline may be occurring.[25] Recently, Sergio Starkstein and his colleagues observed that in mild and moderate dementia apathy was associated with faster cognitive and functional decline[35] and offered the interpretation that apathy may be a "behavioral marker" of "faster progression of cognitive, functional and emotional deficits." Philippe Robert and his colleagues observed that in elders with MCI, apathy was associated with impaired free recall (and correlated with impairment in episodic memory).[34] Apathy was associated with worse decline in memory after 1 year, and this group concluded that apathy should be considered "a marker of the severity and evolution of MCI." In our study, the co-occurrence of CIND and apathy was not associated with worst performance on cognitive tasks, but CIND is a more heterogeneous construct than MCI, our CIND sample was small, and Robert and colleagues used a different instrument to measure apathy (the apathy inventory [IA][55]) and a less conservation definition of apathy (IA score $>$0). Because other reports have found an association between apathy and impairments in the executive domain in MCI or CIND,[25,29,30] we can agree with Robert and colleagues that there may exist several mechanisms for the development of apathy in CIND states.

From the foregoing, it is reasonable to conceive of apathy in late life as a predementia phenotype; it represents a decline in the capacity for volition, it is uncommon in elders that do not have dementia, and it is associated with cognitive impairments in "normal" individuals and in CIND. Its tendency to persist[45,56] and the correlation of its severity with that of dementia[35,57] suggest that it should also be construed as an embedded feature of dementia. Our results suggest that apathy may appear before a mild cognitive syndrome is evident; the accumulating evidence, from this study and others, suggests that in many cases, dementia begins with apathy (i.e., with a decline in the individual's capacity for volition) and subtle cognitive impairments.

Apathy was accompanied by measurable decrements in day-to-day functioning in our normal elders and with worse day-to-day functioning and caregiver stress in dementia. (The associations with worse functioning and caregiver stress in elders with normal cognition may reflect the impact of apathy in other nondementia conditions, and the absence of association with functional impairment in the CIND group could be the result of the limited sample size.) These observations are consistent with earlier reports of association between apathy and functional status in patients with dementia (reviewed by Landes and colleagues[15]). A positive relationship between apathy and caregiver stress is consistent with clinical experience—apathetic patients usually require more directive hands-on care than nonapathetic patients,

which adds to the physical and emotional strain caregivers experience. These observations are also important from a phenomenologic perspective, because the associations of apathy with functional impairments suggest that it can influence when cognitive impairments reach classification thresholds for a dementia diagnosis. In other words, wider recognition of apathy and its association with mild cognitive syndromes should facilitate earlier diagnosis of dementia.

In this study, apathy was frequent in individuals with NPI depression consistent with observations that it can overlap with major depression (for example, 4,58). Yet, apathy is distinct from major depression.[3,6,59] In this study, the majority of patients with apathy did not have NPI depression, and the reverse was true. During late-life depression, apathy may be accompanied by worse impairments in executive domains of cognitive function,[60] and patients with dementia frequently have depression and apathy.[59,61] When Gabriela Kuzis and her colleagues compared groups of patients with AD defined by apathy and DSM depression status, AD cases with apathy performed worse on tests of verbal memory, naming, set shifting, and verbal fluency than cases without apathy, irrespective of depression status.[36] Susan McPherson and her colleagues observed that AD cases with apathy performed worse on the digit symbol, Trail Making, and Stroop color interference tests than those that did not have apathy; depressed mood had no influence on cognitive performance.[37] We report that the association between apathy and cognitive status is independent of NPI depression status and is observed in analyses restricted to participants who had apathy and did not have the depression. As a practical matter, recognition of the relationship between apathy and impaired cognition serves as a counterpoint to today's emphasis on depression and is important because depression treatment can result in a delay of several months or years in the diagnosis of a progressive dementia.

This study has some limitations. We had a relatively small number of subjects with apathy, which probably resulted in underestimation of associations of apathy with cognitive and functional performance and failure of potential associations to achieve statistical significance among individuals with normal cognition or CIND. Also, for a few neuropsychologic tasks, and for the DSRS-ADL and DSRS caregiver stress scales, response rates were not optimal. The Trail Making Test results, in particular, were vulnerable to selection bias because the 36% of participants who did not complete the task had disproportionately severe impairment of cognition (median MMSE score: 17 versus 26 for the entire sample). However, any bias should not affect the scores of elders with normal cognition or CIND, nor should it have effect on the other neuropsychologic tests. Nonresponses on the DSRS-ADL scale (28.9% of participants) are unlikely to have resulted in any bias, because the direction and strength of associations between apathy and cognitive impairment among participants missing these data are similar to the results for the entire sample. The depression data presented in this report are based on the NPI; nevertheless, our results are consistent with earlier studies that used DSM criteria for major depression. The cross-sectional design limits the range of inferences and precludes our ascertaining rates of cognitive decline in apathetic elders; in this study, our objectives were primarily descriptive and exploited the strengths of the CCSMHA, which are population sampling, detailed neuropsychologic and behavioral assessments, and reliance on physician diagnoses of cognitive status.

The nature of the relationships between apathy and mild cognitive syndromes, and cognitive decline are not settled in this report. (After all, many individuals who have dementia are not apathetic at an early stage in their cognitive decline.) Nevertheless, our findings point to an important question: whether apathy, in normal and CIND elders, is an indicator of future dementia. It also is of practical value to ascertain the degree of functional impairment and caregiver stress that can be attributed to apathy. Ultimately, elaboration of the relationships between apathy, cognitive decline, and functional competence will depend on larger studies that have longitudinal designs and generate the data for statistical modeling of these complex processes.

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