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Apathy and cognitive and functional decline in community-dwelling older adults: Results from the Baltimore ECA longitudinal study

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Abstract

Background—Apathy, a complex neuropsychiatric syndrome, commonly affects patients with Alzheimer's disease. Prevalence estimates for apathy range widely and are based on cross-sectional data and / or clinic samples. This study examines the relationships between apathy and cognitive and functional declines in non-depressed community-based older adults.

Methods—Data on 1,136 community-dwelling adults age 50 and older from the Baltimore Epidemiologic Catchment Area (ECA) study, with 1 and 13 years of follow-up, were used. Apathy was assessed with a subscale of items from the General Health Questionnaire. Chi-square, t-tests, logistic regression, and Generalized Estimating Equations were used to accomplish the study's objectives.

Results—The prevalence of apathy at Wave 1 was 23.7%. Compared to those without, individuals with apathy were on average older, more likely to be female, and have lower MMSE scores and impairments in basic and instrumental functioning at baseline. Apathy was significantly associated

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Conflict of Interest
No conflict of interests. However, Drs. Clarke and Eaton received research support from Pfizer Inc. for a non-related study.

Description of authors' roles
Dr. Diana E. Clarke formulated the research questions, analyzed the data and was primarily responsible for writing the article. Jean Y. Ko conducted the literature searches and assisted in data analysis and manuscript preparation. Dr. Constantine Lyketsos provided consultation on the formulation of the research questions, as well as methodological advice and comments on the draft paper. Drs. George W. Rebok and William W. Eaton provided methodological advice and comments on the draft paper.

with cognitive decline (OR = 1.65, 95% CI = 1.06, 2.60) and declines in instrumental (OR = 4.42; 95% CI = 2.65, 7.38) and basic (OR=2.74; 95%CI= 1.35, 5.57) function at 1 year follow-up, even after adjustment for baseline age, level of education, race, and depression at follow-up. At 13 years of follow-up, apathetic individuals were not at greater risk for cognitive decline but were 2-fold more likely to have functional decline. Incidence of apathy at 1- year follow up and 13- year follow-up was respectively, 22.6% and 29.4%.

Conclusions—These results underline the public health importance of apathy and the need for further population-based studies in this area.

Keywords

Basic and Instrumental Activities of Daily Living; MMSE; Apathy correlates

Introduction

Apathy is a neuropsychiatric syndrome that is prevalent in a number of psychiatric diseases, especially dementia, and also commonly seen in individuals who have suffered traumatic brain injury. It is characterized by a lack of motivation that is not attributable to diminished level of consciousness, cognitive impairment, or emotional distress (Marin, 1991). Apathy is associated with many adverse outcomes such as low performance on cognitive tests (Onyike *et al.*, 2007; Turro-Garriga *et al*., 2009), conversion from mild cognitive impairment to Alzheimer's disease (Robert *et al.*, 2006), depression (Lavretsky *et al.*, 1999; Starkstein *et al.*, 2006), and greater impairment in functional activities (Freels *et al.*, 1992; Starkstein *et al.*, 2001; Lechowski *et al.*, 2008). Understanding the public health impact of apathy is limited due to a dearth of research from large and representative population-based samples, particularly with longitudinal designs.

Studies of apathy are often carried out in relation to specific health conditions typically using clinical samples (i.e., hospitalized or community-dwelling individuals presenting at particular clinics) (Robert *et al.*, 2006; Clarke *et al.*, 2007; Clarke *et al.*, 2008). Therefore, the majority of available prevalence estimates and observed correlates of apathy might not reflect the occurrence of apathy in the general population but illustrate apathy in specialized samples. For example, Clarke and colleagues (2007; 2008) reported prevalence rates for apathy ranging from 42.9% – 75% in individuals with Alzheimer's disease, vascular dementia, dementia with lewy-bodies, and frontal temporal dementia, but the study sample was drawn from community-dwelling individuals presenting to the Memory Disorder Clinic at a Geriatric Hospital in Toronto, Canada. In contrast, Onyike and colleagues (2007), used the population-based data from the Cache County study on Memory, Health and Aging and found 1.4%, 3.1%, and 17.3% apathy prevalence among individuals classified, respectively, as cognitively normal, with a mild cognitive syndrome, and with dementia. This study provided valuable population-based results but the Cache County study data may not be generalizable to the entire U.S. population because the county has very low rates of in and out migration (Miech *et al.*, 2002) compared to other U.S. counties. In addition, members of the Church of Jesus Christ of Latter Day Saints, a religious denomination that prohibits the use of alcohol and tobacco, comprise approximately 91% of the population (Miech *et al.*, 2002). The cross-sectional nature of the existing studies (e.g., Lyketsos *et al*., 2002; Clarke *et al.*, 2007; Onyike *et al*., 2007; Clarke *et al.*, 2008) limits the ability to make causal inferences regarding the relationships between apathy and the correlates examined.

The limited longitudinal studies of apathy (e.g., Starkstein *et al.*, 2006; Lechowski *et al.*, 2008; Turro-Garriga *et al.*, 2009) have indicated high prevalence and one year incidence rates for apathy and found that this neuropsychiatric condition can have significant and negative impact

on cognitive and functional decline. For instance, Starkstein *et al.* (2006) reported an overall prevalence rate of 24% for apathy at baseline in a sample of 354 outpatients attending a dementia clinic in Buenos Aires. This prevalence estimate was similar to that (i.e., 18.7%) reported by Turro-Garriga *et al.* (2009) in outpatients seen at an outpatient dementia clinic in Spain. Starkstein *et al.* (2006) reported that for individuals without depression, the prevalence of apathy was 23% compared to 55% and 41% for individuals with major and minor depression, respectively. The one year incidence of apathy among those without apathy at baseline was 17.5% (Starkstein *et al.*, 2006) and 21.7% (Turro-Garriga *et al.*, 2009). Among those with apathy at baseline, apathy persisted in about 50% of the sample by one year follow-up (Starkstein *et al.*, 2006; Turro-Garriga *et al.*, 2009). Lechowski and colleagues (2008) observed persistent apathy, over three six month follow-up assessment (i.e., 18 months), in 22.1% of 272 female outpatients with AD who were recruited from 16 university hospital centres as in France as part of the REAL longitudinal cohort study. These studies however, utilized specialized outpatient samples, in that participants were attending dementia clinics and therefore the prevalence, incidence, and persistent apathy estimates might be greater than what would be expected in a general population sample. These findings warrant replication in studies that are longitudinal in nature, with larger sample sizes, and with non-clinical samples.

The current study therefore examines the prevalence and incidence of apathy and its correlates in a community-based sample of older adults aged 50 and older using data from the Baltimore Epidemiologic Catchman Area (ECA) follow-up study. More specifically, the study also examines the effects of baseline apathy on cognitive and functional decline at 1 year and 13 years follow-up. Based on available evidence, we surmise our prevalence estimate will fall in the range of 17–37%. Based on current literature, we expect to observe associations between apathy and cognitive impairment, depression, and impairment in functional abilities.

Methods

Data source and Study Population

The study involved secondary data analysis using the Baltimore Epidemiologic Catchment Area (ECA) study. The study sample was comprised of 1,136 participants aged 50 and older at the time the Baltimore ECA study was initiated in 1981 with follow-up in 1982, 1994, and 2004. The ECA was designed to collect data on the prevalence and incidence of mental disorders in an adult community sample, according to DSM criteria, and on the use of and need for services by individuals with mental disorders.

The 1,136 older adults included in this study represented 70.5% of all individuals aged 50 and older who participated in the Baltimore ECA study at its initiation in 1981. Individuals were excluded if they had missing information on the measure that was used to ascertain apathy status (n=95); if they scored below 24 on the Mini-Mental Status Examination (MMSE; Folstein, Folstein, & McHugh, 1975), which was used to indicate significant cognitive impairment (n=211); and if they met DSM-III criteria for major depressive disorder or minor depression (i.e., 3 or more depression symptoms) at the time of the 1981 interview (n= 170) (Eaton *et al.*, 1997). The baseline, 1-year, and 13-year follow-up data for this sample were used to examine changes in apathy status, and its impact on cognition on level of functioning in basic and instrumental activities of daily living.

Measures

Apathy—The items: “full of energy”, “managing to keep yourself busy and occupied”, “getting out of the house as much as usual”, “felt on the whole that you were doing things well”, “felt that you are playing a useful part in things”, and “able to enjoy your normal day-to-day activities as much as usual”, from the 20-item General Health Questionnaire (GHQ;

Goldberg, 1978) were used to ascertain apathy status based on our initial findings that these items loaded onto a single factor (Table 1) with good model fit using Confirmatory Factor Analysis (CFA) within a MPlus Framework (CFI= 0.88; TLI= 0.94; RMSEA= 0.114). Each item was rated on a scale of 0 to 3 giving total scores that ranged from 0 to 18, with higher scores indicating worse apathy. Apathy status was determined by a score of greater than or equal to 6.5 on the GHQ-apathy (i.e. GHQ-apathy score greater than or equal to 6.5 = "having apathy" versus GHQ-apathy score of less than 6.5 = "not having apathy") based on the validation analyses below.

Validation analyses—In 1994, in-depth clinical psychiatric assessments, using the study's board certified psychiatrists', were carried out on a subsample of individuals in the Baltimore ECA study (i.e., N = 349 of whom 174 were aged 50 and older). Both the GHQ and the Schedules for Clinical Assessment in Neuropsychiatry (SCAN) were completed on this subsample. The psychiatrists' ratings of the SCAN apathy-items, loss of interest, lost energy or vigor, and feeling of being overwhelmed by everyday tasks, was used as the validator in determining a cut-off score for the GHQ apathy subscale. These SCAN items were identified as apathy-related items because their description (WHO, 1994) matches with the definition and description of apathy and apathy-related behaviors in existing literature (Marin, 1991; Marin *et al.*, 1991; Van Reekum *et al.*, 2005). In addition, these items represent three of the six items in the "Thinking, concentration, energy, interest" section of the SCAN (WHO, 1994). Schutzwohl (2007) reported that these 6 items all loaded onto a single factor, giving some strength to their use to determine the cut-off score for apathy in this study. The inherent limitations of this method are discussed in the discussion section below.

More specifically, a cut-off score of 6.5 on the GHQ-apathy (i.e., sensitivity = 0.83 and specificity= 0.69) was determined based on ROC analysis using the psychiatrists' rating of Apathy per the Schedules for Clinical Assessment in Neuropsychiatry (SCAN) as the "gold standard" (see validation study below) and used to categorize the study participants as "having apathy" versus "not having apathy". For the "gold standard" in the ROC analysis, SCAN-Apathy total scores of greater than 3 per the study psychiatrists' were used to classify individuals as "having apathy" and scores less than or equal to three classified individuals as "not having apathy". This cut-off score on the SCAN-apathy was used because it indicated that individuals had at least one item that resulted in moderate or intermittently severe impairment. ROC analysis and the cutoff score of 6.5 on the GHQ-apathy yielded an area under the curve of 0.795 (95%CI: [54.9–1.04]). Furthermore, the GHQ-apathy total score correlated well with SCAN-apathy total score (r= 0.421; p=0.001) but weakly with irritability (r= 0.195, p= 0.012) and anxiety (r=0.060, p=0.433) as measured by the SCAN.

Cognitive Decline—The MMSE was used to assess cognition at each wave of the ECA study. A score of less than or equal to 23 (Folstein *et al.*, 1975) was used to classify individuals as being cognitively impaired versus non-cognitively impaired (i.e., MMSE ≥24) in our initial sample selection. In the follow-up assessment of cognitive status, cognitive decline was defined as greater than or equal to a 3-point reduction in MMSE scores between baseline and 1-year follow-up and between baseline and 13-year follow-up per Mielke *et al.*, 2007 and Silverstein *et al.*, 2006.

Functional Decline—Basic Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (IADL) were two measures of functional abilities assessed at each ECA study visit. In the current study, the variables "any ADL disability" (i.e., Yes vs. No) and "any IADL disability" (i.e., Yes vs. No) were used.

"Any ADL disability" was defined as having difficulty with any of the following tasks: walking, getting in or out of bed, dressing and undressing, taking a bath or shower, using the

toilet, and / or using a knife and fork to cut up food. A decline in ADLs was defined as a worsening of ADL status from baseline to Wave 2 and Wave 3 follow-up interviews respectively (i.e., a change from having no ADL disability at baseline to having any disability in ADL at follow-up).

"Any IADL disability" was defined as having difficulty with any of the following tasks: keeping track of money and bills, cleaning the house, preparing meals, traveling via car / public transport, shopping, medication use, and / or using the telephone. Decline in IADL was therefore defined as a worsening in IADL status from baseline to Wave 2 and Wave 3 follow-up (i.e., a change from having no IADL disability at baseline to having any disability in IADL at follow-up).

Depression—The Diagnostic Interview Schedule (DIS) was administered at each ECA study interview to assess symptoms of depression and ascertain diagnosis of major depressive disorder according to DSM-III or III-R criteria (American Psychiatric Association, 1980; 1987). Individuals having 3 or 4 depressive symptoms of 2 weeks or more duration and with some impairment in function were classified as having minor depression / syndromal depression (Fogel *et al.*, 2006). Baseline depression in this study was based on whether the individual ever (lifetime) met diagnostic criteria for major or minor depression or dysthymia (i.e., Yes vs. No). Only individuals with no lifetime depression were selected for entry into the study sample. Change in depression status over time and its effect on the relationship between apathy and cognitive and functional decline was investigated.

Statistical Analysis

SPSS 15.0 was used for all analyses. Principal axis factor analyses were conducted in SPSS to determine if the apathy-related items of the GHQ loaded onto the same factor. Confirmatory Factor Analysis (CFA) using MPlus software (Muthen and Muthen, 2000) were conducted. A combination of chi-square statistics, t-tests, and logistic regressions were used to examine the relationship between apathy and cognitive decline and apathy and declines in basic and instrumental activities of daily living (i.e., ADL and IADL). The potential effects of age, sex, education, race, and depression were examined. Generalized Estimating Equations (GEE) analyses with exchangeable correlation structure were also conducted. These analyses took into account the repeated assessments of apathy, depression, ADL, IADL and cognitive decline at each follow-up. Of the 1,136 individuals included at baseline, 888 and 488 individuals were available respectively, at 1- and 13-year follow-up for the GEE analyses.

Results

General Characteristics of the Sample

The study sample consisted primarily of women (61.6%), individuals who were white (77.1%) and the majority (56.8%) had greater than or equal to high school education. The mean age for the cohort was 65.6 years (±8.8) and the mean MMSE score was 28.0 (±1.6). With respect to functional status, 4.0% reported disability in ADL and 10.9% reported disability in IADL at baseline. In addition, 23.7% of the sample met our criterion for apathy at baseline. Of individuals with apathy at baseline, 46.4% had apathy at one-year follow-up. Among those who did not have apathy at baseline, 22.6% was found to have apathy at the 1-year follow-up and 29.4% was found to have apathy at the 13-year follow-up interview. Apathy was present in 8.2% of the sample at all three study interviews. Among individuals with apathy at baseline, those with apathy at 1-year follow-up were more likely to meet criteria for depression (χ^2 (df = 1) = 12.26; p=0.001), have an IADL disability (χ^2 (df = 1) = 5.18; p=0.033), and score one point lower on the MMSE (t(df = 204) = −2.115; p=0.036) than those without apathy at 1-year follow-up. Among individuals with apathy at 1-year follow-up, those with apathy at 13-year

follow-up were more likely to have IADL (χ^2 (df = 1) = 23.31; p<0.001) and ADL disability (χ^2 (df = 1) = 11.48; p= 0.001) than individuals without apathy at 13-year follow-up. At 1-year follow-up, 2.6% of the sample met criteria for a depressive disorder (i.e., major or minor depressive disorder). Also, among those without any ADL disabilities at baseline, 2.4% reported new ADL disability and among those without baseline IADL disabilities 4.5% reported new disabilities in IADL.

The majority of individuals lost from baseline to 13 year follow-up (n=469) were lost due to death. Among these individuals, 31% had baseline apathy. The remaining individuals (n=113) were loss to follow-up (n= 51) or refusal (n=62). Respectively, 27.5% and 19.4% of individuals lost to follow-up or refusals had baseline apathy. Across apathy groups (i.e., apathy status at baseline), those who died by 13-year follow-up were on average 7 years older than those who did not and were available for the 13-year follow interview (F (1, 1021) = 176.90; p<0.001).

Correlates of Apathy

As indicated in Table 2, individuals with apathy at baseline were older (t (df = 1134) = −2.02; p=.044), more likely to be female (χ^2 (df = 1) = 8.44; p-value=0.004), more likely to be White (t(df= 1)=0.95; p-value= 0.004), and to have had ADL (χ^2 (df = 1) = 72.86; p<0.001) or IADL disabilities (χ^2 (df = 1) = 78.70; p<0.001). Individuals who did have and those who did not have apathy at baseline did not differ in terms of education. Although the entire study sample had MMSE score greater than or equal to 24 at baseline, since it was an inclusion criteria for the study, individuals who met the study's criteria for apathy had significantly lower mean MMSE scores than those who did not (t (df = 1134) = 3.54; p<0.001).

The Association between Apathy and Cognitive Decline at 1-Year Follow-up

Individuals who had apathy had a greater likelihood of exhibiting cognitive decline at 1-year follow-up compared to those who did not have apathy (Odds ratio (OR) = 1.73; 95% confidence interval (CI) = 1.15, 2.60); (Table 3). Using conventional multiple logistic regression analyses, this greater likelihood of cognitive decline in individuals who had apathy, compared to those who did not have apathy, persisted after adjustment for age and sex (Model 2), and age, sex, education, race, follow-up depression, and baseline ADL and IADL disabilities (Model 3: OR= 1.65; 95% CI = 1.05, 2.60).

The GEE analyses, which included repeated assessments of apathy (baseline and one-year follow-up), accounted for the state characteristic of apathy. The significant relationship between apathy and cognitive decline was not observed in these models (Table 3: GEE Models 1–3).

The Association between Apathy and Functional Decline at 1-Year Follow-up

The risk of developing new IADL disabilities at 1-year follow-up was greater for individuals with apathy compared to those without apathy (Table 4, Logistic Regression Model 1; OR= 4.39; 95% CI= 2.79, 6.90). This increased risk remained after adjustment for age, sex, race, education, and follow-up depression (Table 4, Logistic Regression Model 3). Similarly, the risk of developing new ADL disabilities at the 1-year follow-up was greater for individuals with apathy compared to those without apathy (Table 5, Logistic Regression Model 1; OR= 2.88; 95% CI=1.48, 5.60). This greater risk persisted after adjustment for age, sex, race, education, and depression at follow-up (See Table 5, Logistic Regression Model 3). The GEE analyses, which take into account the repeated measures and associated correlations, provided similar results (GEE models 1–3). More specifically, at one year follow-up, individuals who had apathy at baseline were more likely to have declines in IADL and ADL compared to those who did not have apathy even with adjustments for age, sex, race, education, and depression over time.

The Effects of Apathy on Cognitive and Functional Decline at Thirteen Year Follow-up

Baseline apathy was not predictive of cognitive decline at 13-year follow-up (Table 3, GEE model 4; OR=1.04; 95% CI= 0.76, 1.44). On the other hand, individuals who had apathy at any point over the study, (baseline, 1-year, 13-year follow-up) were more than 2-fold more likely to have functional decline per IADL (Table 4: GEE model 4) and ADL (Table 5: GEE model 4).

Discussion

Apathy is prevalent in this sample of older adults, has a high incidence rate, and is stable in 46.4% of the sample at 1 year follow-up and 8.2% at 13 years follow-up. It does not affect cognitive decline but is significantly associated with functional decline. As well, age, race, and education were independent predictors of the risk of cognitive decline.

It is important to note the limitations of this study. The racial / ethnic composition of the Baltimore ECA study sample was mainly Whites and African-Americans and, as such, the results might not be generalizable to all racial / ethnic groups within the US or globally. The use of GHQ items to assess apathy is a weakness since use of these items in this context has not been validated elsewhere or against existing apathy measures. However, the use of the psychiatrists' ratings of apathy based on the SCAN items to validate the use of the GHQ apathy items lends credibility to the results, since it is validated against a clinical judgment. Furthermore, the use of the GHQ-apathy items allowed us to examine the prevalence, incidence, and correlates of apathy in a community-dwelling sample with a scale that was not designed for and validated in a clinical sample. In addition, the method used to identify functional decline was limited in that it was dichotomous and failed to capture the various levels of functioning. However, since the study involved secondary data analysis, the researchers had to make use of what was available in the data set despite limitations. The results however, provide support for the idea that apathy can negatively impact functional ability, as observed by other apathy researchers (Freels *et al.*, 1992; Starkstein *et al.*, 2001; Lechowski *et al.*, 2008).

Studies on apathy in older adults who were referred to an outpatient memory disorder clinic for neurological and neuropsychiatric assessments due to memory complaints, have reported current prevalence rates ranging from 28.3% (Clarke *et al.*, 2007) to 86.4% (Thomas *et al.*, 2001). The prevalence of apathy observed in the current study (23.7%) is similar to that reported by Starkstein *et al* (2006) and Turro-Garriga *et al* (2009) in the existing longitudinal studies and lower than the range observed in clinic samples, likely reflecting the composition of this less cognitively impaired population-derived sample. However, two studies on community-dwelling older adults using Neuropsychiatric Inventory (NPI) to assess apathy have reported prevalence estimates between 17–37% for the subset of individuals with dementia (Onyike *et al.*, 2007, Lyketsos *et al.*, 2002) and 3.1 (Onyike *et al.*, 2007) to 15% (Lyketsos *et al.*, 2002) for individuals with mild cognitive impairment (MCI). Therefore, the apathy estimate observed in the current study falls within the category of community-dwelling individuals with dementia. It is possible that the measurement used herein to classify individuals as demented was not as sensitive as the measures used in the aforementioned studies. As such, despite our attempts to remove individuals with dementia at baseline (i.e., individuals with MMSE $\leq$ 23 at baseline excluded), it is likely that some individuals with borderline dementia or MCI/cognitive impairment no dementia (CIND) were misclassified as non-demented. This assumption is supported by Kukull and colleagues (1994) finding that the MMSE cut-off score ($\leq$ 23) had a sensitivity of 0.63 and a specificity of 0.96 in a community-dwelling sample with cognitive complaints. In addition, the variations of measures used to ascertain apathy status may account for the observed differences in the prevalence of apathy. Depression diagnosis, and ADL and IADL impairment were associated with apathy; these results are in agreement with the current

literature on apathy (Freels *et al.*, 1992; Lavretsky *et al.*, 1999; Starkstein *et al.*, 2001; Starkstein *et al.*, 2006; Turro-Garriga *et al.*, 2009).

The observed incidence of apathy at 1-year follow up in individuals without apathy at baseline (i.e., 22.6%) is similar to the 21.7% reported by Turro-Zarriga and colleagues (2009) in which the NPI was used to ascertain apathy status. This finding lends support to the use of the GHQ-apathy related items to ascertain apathy status in the current study. The observation of persistent apathy in 46.4% of the sample at 1-year follow-up was slightly lower than the 51.7% ascertained with the NPI in the longitudinal study on apathy conducted by Turro-Zarriga and colleagues (2009) or the 50% reported by Starkstein *et al* (2006) in which the 10-item Apathy Scale was used to ascertain severity of apathy. The fact that the study by Turro-Zarriga and colleagues consisted of individuals with mild to severe AD might account for the slight difference in the percentage of the two study samples with persistent apathy at 1 year follow-up. On the other hand, Lechowski and colleagues (2009), using the NPI to ascertain apathy status, found that only 22.1% of their sample of women with AD had persistent apathy at 18-months follow-up. The current study is the first to report the persistence of apathy at 13 years follow-up and using a non-specialized clinical sample. Unfortunately, the number of individuals with persistent apathy at 13 years follow-up was small (n=22), and hence lacked the study power to conduct in-depth inferential analyses. Given that apathy is highly prevalent across a number of disorders and related to significant cognitive and functional decline, it is important to identify and further characterize this high risk group (i.e., individuals with persistent apathy) in terms of socio-demographic, clinical, and genetic factors. An initial attempt at this line of research was carried out by Lechowski and colleagues (2009) in their study involving females with AD in outpatient care that found persistent apathy was associated with “rapid loss of autonomy in activities of daily living”. It would be important to know if these results extend to other dementia groups, males and general community samples.

Individuals who had apathy at baseline were more likely to experience functional decline in instrumental (IADL) and basic (ADL) activities of daily living at one and 13 years follow-up compared to those who did not have apathy. This greater risk of functional decline in individuals who had apathy, which persisted despite adjustment for age, sex, race, education, and the changing state of apathy and depression, is consistent with results observed by Starkstein *et al.*, (2006), Turro-Zarriga *et al.*, (2009), and Lechowski *et al.*, (2009) in their respective longitudinal studies. These more recent results advance our knowledge of the effects of apathy that mainly had been based on the observation of statistically significant associations in cross-sectional studies (e.g., Landes *et al.*, 2005; Onyike *et al.*, 2007; Clarke *et al.*, 2008). These cross-sectional studies have also indicated significant associations between apathy and poor cognitive functioning (Landes *et al.*, 2005; Onyike *et al.*, 2007; Clarke *et al.*, 2008). The existing longitudinal studies, albeit limited in that they utilized dementia patients in outpatient care at various dementia clinics, have provided supporting results that indicated a causal relationship between apathy and cognitive functioning (Robert *et al.*, 2006; Starkstein *et al.*, 2006; Lechowski *et al.*, 2009; Turro-Zarriga *et al.*, 2009). More specifically, such studies have shown that apathy at baseline was associated with significant decline in cognitive functioning at one year follow-up. Although the current study also found a statistically significant relationship between apathy and cognitive decline at one year follow-up this was not observed at 13-year follow-up. Furthermore, the significant relationship between apathy and cognitive decline at one year follow-up did not hold true when the changing state of apathy, depression, and functional status were taken into account using GEE analyses. The observations from this study might suggest the potential benefits of the reversal of apathy on cognitive functioning. Further investigations into the longitudinal relationship between apathy and cognitive functioning are needed.

The discrepancy between the results from this study and the existing longitudinal studies that have also taken into account the repeated measure of apathy could be related to the differences in how cognitive decline and apathy were measured. It is possible that the GHQ apathy-related items were not sensitive enough to capture all individuals with apathy (i.e., misclassification of individuals with apathy as non-apathetic), thereby diluting the measure of effect. Furthermore, survival bias and the observation of a transient apathy group (i.e. individuals with apathy at baseline but not at follow-up) might account for the lack of significant association between baseline apathy and cognitive decline at 13-year follow-up. In other words, it is possible that individuals with transient apathy sought treatment and the remaining individuals with apathy who survived through the 13-year follow-up interview were the healthiest of the stable apathetic group. This line of reasoning is supported by the observation that across apathy groups, those who died by the 13-year follow-up interview were on average 7 years older and possibly had more health problems.

In summary, the current study supports the notion that apathy is an important predictor of functional decline and possibly cognitive decline in older adults. Given the high prevalence of apathy across a number of disorders, it is important to gain better understanding of apathy and its long-term impact on cognitive and functional status. This enhanced knowledge can improve treatment and prevention of cognitive and functional declines.

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Table 1

Factor Structure of 20-item General Health Questionnaire (GHQ) using Principal Axis Analysis with Varimax Rotation Method

General Health Questionnaire Items‡	Factor Loadings*		
	Factor 1	**Factor 2**	**Factor 3**
Able to concentrate		0.341	
Feeling reasonably happy	0.414		
Full of energy		0.542	
Managing to keep yourself busy and occupied		0.629	
Getting out of the house as much as usual		0.496	
Felt on the whole that you were doing things well		0.671	
Felt that you are playing a useful part in things		0.654	
Felt capable of making decisions about things		0.491	
Felt constantly under strain	0.680		
Felt you couldn't overcome your difficulties	0.539		
Able to enjoy your normal day-to-day activities as much as usual		0.509	
Been taking things hard	0.623		
Able to face up to your problems		0.261	
Found everything getting too much for you	0.607		
Feeling unhappy and depressed	0.654		
Been losing confidence in yourself			0.622
Been thinking of yourself as a worthless person			0.616
Felt that life was entirely hopeless			0.723
Losing sleep because of worry	0.469		
Feeling nervous and strung-up all the time	0.600		
Eigenvalue (% of variance)	6.285 (31.42)	2.407 (12.04)	1.196 (5.98)

‡adapted from the 60-item General Health Questionnaire by Goldberg (1978)

*Factor analysis on the 28-item GHQ from ECA Wave 3 data found that all six apathy items loaded onto a single factor as found with Wave 1 data based on 20 items from the GHQ. The items and their factor loadings are: full of energy: 0.557; managing to keep yourself busy and occupied: 0.597; getting out of the house as much as usual: 0.426; felt on the whole that you were doing well: 0.407; felt that you are playing a useful part in things: 0.618; able to enjoy your normal day-to day activities as much as usual: 0.546. When a confirmatory factor analysis using MPlus software was conducted, the same factors were identified with good model fit (CFI= 0.88; TLI= 0.94; RMSEA=0.114).

Table 2

Baseline Sociodemographic and clinical characteristics of study sample (N= 1136).

Variables	Overall N(%)	Have Apathy N (%)	Not have Apathy N (%)	X^2 (df)	p-value
Sex				8.44 (1)	.004
Male	436 (38.4)	353 (40.7)	83 (30.9)		
Female	700 (61.6)	514 (59.3)	186 (69.1)		
Race				0.95 (1)	.004
White	880 (77.5)	672 (77.5)	208 (77.3)		
Non-Whites	256 (22.5)	195 (22.5)	61 (22.7)		
Education				0.71 (2)	.699
<High School	491 (43.2)	374 (43.1)	117 (43.5)		
High School	533 (46.9)	404 (46.6)	129 (48.0)		
>High School	112 (9.9)	89 (10.3)	23 (8.6)		
LADL disability				72.86 (1)	<.001
No	1090 (96.0)	856 (98.7)	234 (87.0)		
Yes	46 (4.0)	11 (1.3)	35 (13.0)		
LADL disability				78.70(1)	<.001
No	1012 (89.1)	812 (93.7)	200 (74.3)		
Yes	124 (10.9)	55 (6.3)	69 (25.7)		
	Mean (SD)	**Mean (SD)**	**Mean (SD)**	**t-test (df)**	**P-value**
Age (year)	65.56 (8.79)	65.27 (8.80)	66.50 (8.69)	−2.02 (1134)	.044
MMSE score	28.04 (1.64)	28.13 (1.61)	27.73 (1.73)	3.54 (1134)	<.001

X^2 = Chi-Square statistic; df= degree of freedom; SD = Standard Deviation; p = level of significance

Table 3

Estimated Odds Ratios and 95% Confidence Intervals for the Effect of Apathy on Cognitive Decline at 1-Year and 13- Year Follow-up in the ECA Data (N=1136).

	I. Logistic Regression			II. General Estimating Equations §			
Variables	**Model 1 OR(95% CI)**	**Model 2 OR(95% CI)**	**Model 3 OR(95% CI)**	**Model 1 OR(95% CI)**	**Model 2 OR(95% CI)**	**Model 3 OR(95% CI)**	**Model 4 OR(95% CI)†**
Apathy	1.73 (1.15–2.60)*	1.61 (1.05–2.46)*	1.65 (1.06–2.60)*	1.21 (0.94–1.55)	1.12 (0.86–1.45)	1.01 (0.77–1.33)	1.04(0.76–1.44)
Age (years)	---	1.06 (1.04–1.09)*	1.06 (1.03–1.08)*	---	1.04 (1.02–1.06)*	1.04 (1.01–1.06)*	1.09(1.05–1.12)*
Female	---	1.06 (0.70–1.61)	1.06 (0.70–1.61)	---	1.10 (0.79–1.53)	1.06 (0.76–1.50)	0.75(0.49–1.14)
Non-Whites	---	2.29 (1.50–3.51)	2.29 (1.50–3.51)*	---	1.80 (1.27–2.57)*	1.76 (1.23–2.52)*	2.62 (1.63–4.21)*
<High School	---	---	2.22 (1.01–4.87)*	---	---	1.64 (0.93–2.90)	1.75(0.88–3.50)
High School	---	---	1.28 (0.57–2.87)	---	---	1.27 (0.72–2.25)	1.32(0.68–2.57)
Depression	---	---	0.71 (0.20–2.50)	---	---	1.63 (0.66–4.03)	0.98(0.72–1.33)
IADL disability	---	---	0.85 (0.32–2.24)	---	---	1.11 (0.76–1.62)	1.37(0.86–2.20)
ADL disability	---	---	0.94 (0.50–1.77)	---	---	1.38 (0.83–2.28)	0.83(0.46–1.51)

*p-value < 0.05

OR: Odds Ratio; CI: Confidence Interval

†Used 13 year follow-up data

§used repeated measures for apathy, IADL, ADL, and depression (except for Model 3, where depression was only measured at Wave 2)

Table 4

Estimated Odds Ratios and 95% Confidence Intervals for the Effect of Apathy on Impairment in Instrumental Activities of Daily Living (N=1136), ECA.

	I. Logistic Regression			II. General Estimating Equations §			
Variables	**Model 1 OR (95% CI)**	**Model 2 OR (95% CI)**	**Model 3 OR (95% CI)**	**Model 1 OR (95% CI)**	**Model 2 OR (95% CI)**	**Model 3 OR (95% CI)**	**Model 4† OR (95% CI)**
Apathy	4.39(2.79–6.90)*	4.30(2.62–7.04)*	4.42(2.65–7.38)*	3.98(2.80–5.67)*	3.70(2.56–5.34)*	4.04(2.80–5.84)*	2.33(1.65–3.29)*
Age (years)	---	1.10(1.07–1.13)*	1.09(1.06–1.12)*	---	1.10(1.07–1.14)*	1.09(1.05–1.13)*	1.10(1.05–1.14)*
Female	---	0.90(0.54–1.53)	0.91(0.53–1.55)	---	1.02(0.611.70)	1.00(0.59–1.71)*	2.53(1.41– 4.54)*
Non-Whites	---	1.72(0.99–2.97)	0.89(0.72–1.09)	---	1.62(0.93–2.82)	1.54(0.87–2.73)	0.92(0.50–1.68)
<High School	---	---	2.03(0.75–5.47)	---	---	1.91(0.72–5.07)	0.78(0.35–1.75)
High School	---	---	1.01(0.36–2.83)	---	---	1.01(0.36–2.81)	0.76(0.35–1.64)
Depression	---	---	0.86(0.23–3.18)	---	---	0.74(0.20–2.80)	2.30(0.74–7.16)

*p-value < 0.05

OR: Odds Ratio; CI: Confidence Interval

†Used 13 year follow-up data

§used repeated measures for apathy, IADL, ADL, and depression (except for Model 3, where depression was only measured at Wave 2

Table 5

Estimated Odds Ratios and 95% Confidence Intervals for the Effect of Apathy on Impairment in Basic Activities of Daily Living (N=1136), ECA.

	I. Logistic Regression			II. General Estimating Equations §			
Variables	**Model 1 OR (95% CI)**	**Model 2 OR (95% CI)**	**Model 3 OR (95% CI)**	**Model 1 OR (95% CI)**	**Model 2 OR (95% CI)**	**Model 3 OR (95% CI)**	**Model 4† OR (95% CI)**
Apathy	2.88(1.48–5.60)*	2.76(1.39–5.47)*	2.74(1.35–5.57)*	3.16(1.89–5.29)*	2.91(1.73–4.89)*	3.03(1.77–5.17)*	2.37(1.57–3.57)*
Age (years)	---	1.07(1.03–1.11)*	1.06(1.02–1.10)*	---	1.08(1.03–1.12)*	1.06(1.01–1.11)*	1.06(1.01–1.11)*
Female	---	0.86(0.41–1.67)	0.91(0.43–1.91)	---	0.83(0.41–1.71)	0.88(0.41–1.89)	1.35(0.71–2.57)
Non-Whites	---	2.06(1.01–4.22)*	1.82(0.86–3.85)	---	1.91(0.94–3.91)	1.70(0.82–3.52)	1.03(0.51–2.08)
<High School	---	---	2.06(0.47–9.11)	---	---	2.10(0.47–9.43)	2.08(0.68–6.39)
High School	---	---	1.35(0.29–6.26)	---	---	1.50(0.32–7.05)	1.73(0.58–5.20)
Depression	---	---	0.74(0.92–5.88)	---	---	0.35(0.01–2.73)	1.56(0.94–2.59)

*p-value < 0.05

OR: Odds Ratio; CI: Confidence Interval

†Used 13 year follow-up data

§used repeated measures for apathy, IADL, ADL, and depression (except for Model 3, where depression was only measured at Wave 2.