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Asthma Control and Cognitive Function in a Cohort of Elderly Adults

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Abstract

Background—Asthmatics are at increased risk for cognitive impairment. The association of asthma control with cognitive performance, however, has not been rigorously assessed among older adults.

Objectives—We examined the hypothesis that poor asthma control is associated with cognitive impairment in a cohort of older, inner-city asthmatics.

Design, Setting, and Participants—Adults ages 60+ years with a physician diagnosis of asthma were recruited from outpatient practices in New York City and Chicago. Patients with chronic obstructive pulmonary disease and ≥10 pack-year smoking histories were excluded.

Measurements—Cognitive assessments included processing speed (pattern comparison, Trails A), executive function (Trails B), attention and working memory (letter number sequencing), immediate and delayed recall (Wechsler Memory Scale Story A), word fluency (animal naming), and global cognitive function (Mini-Mental State Exam). Asthma control was measured with the Asthma Control Questionnaire (ACQ) and airway obstruction by spirometry as the predicted forced expiratory volume at 1-second (FEV_1) <70%. Cognitive measures were modeled in linear

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and logistic regression models controlling for age, race, education, English proficiency, and income.

Results—The 452 participants had a mean age of 68; 41% had poor asthma control by the ACQ and 35% had FEV_1<70%. Poor asthma controland FEV_1<70% were significantly associated with all measures of cognitive function in univariate analyses. However, these associations lost their statistical significance after adjusting for age, education, English speaking ability and other covariates. The same pattern was observed when the outcomes were below normal performance on the cognitive measures based on normative data.

Conclusion—Among older adults with asthma, poor asthma control and airway obstruction are not associated with poor performance on various measures of cognitive function.

Keywords

Elderly adults; asthma; asthma control; cognition; executive function

INTRODUCTION

The prevalence of cognitive impairment, including both mild cognitive impairment and frank dementia, increases with age,[1,2] due in part to various chronic illnesses like hypertension, diabetes,[3] and chronic obstructive pulmonary disease (COPD).[4] A small body of research suggests that asthma may also contribute to the development of cognitive impairment in older adults. Affecting up to 9% of adults over age 65,[5–7] asthma poses at least two possible threats to cognitive functioning, chronic inflammation[4,8–14] and exposure to periods of hypoxemia.[4,15–18] As an inflammatory disease, asthma is associated with increased levels of C-reactive protein (CRP)[19–24] and pro-inflammatory cytokines,[21,24] which in turn impact neurocognitive function.[4,9,10,12,13,25,26] Asthmatics may also experience both intermittent and prolonged periods of hypoxemia, especially when the disease is poorly controlled,[17,27] also resulting in cognitive decline.

Despite biologically plausible mechanisms underlying an association between asthma controland cognitive functioning, empirical evidence is in short supply and existing studies have important limitations, like small sample sizes, heterogeneous study samples, and use of non-specific measures of cognitive function.[28,29] In one study, newly diagnosed, older asthmatics had improvements on the Mini-Mental State Exam 1 year after starting asthma therapy, though the study was neither randomized nor blinded.[30] A study of younger adult asthmatics similarly reported improvementsin cognition, specifically on tests of attention and executive function, 6 weeks after initiation of asthma treatment with long-acting beta-agonists and inhaled corticosteroids.[29] Some studies have reported worse performance on measures of general cognition, memory, and executive function among asthmatics compared to non-asthmatics, including one small (n=40) study that involved both asthmatics and COPD patients[17] and another that compared asthmatics with non-asthmatics.[28]

Given the small body of research in this field and their various methodological limitations, we sought to broaden understanding of the role of asthma control on cognitive performance in older adults by examining cognitive performance in a large sample of older asthmatics

using a large battery of neurocognitive assessments. Because the literature has most consistently identified associations between generalized measures of cognition and executive function with treat or untreated asthma, we hypothesized that poor control of asthma would be associated with poor performance on measures of these abilities.

MATERIALS and METHODS

Setting and Participants

Data for theseanalyses were obtained from the Asthma Beliefs and Literacy in the Elderly (ABLE)study, a longitudinal cohort study of asthmatic adults ages 60 years and older. Participants spoke English or Spanish and had a physiciandiagnosis ofpersistent asthma as defined by the National Heart, Lung and Blood Institute's Expert Panel on Asthma.[31] We excluded individuals with a smoking history of 10 or more pack-years, a diagnosis of COPD or other chronic respiratory illnesses, a physician's diagnosis of dementia, and uncorrectable visual impairment. Subjects were recruited from inner-city outpatient clinics in New York, NY and Chicago, IL from December 2009 to November 2012. The New York City practices included the general internal medicine, geriatrics primary care, and pulmonary specialtyclinics at the Mount Sinai Medical Center and a federally qualified health center in Brooklyn. The Chicago sites included the Northwestern University Hospital general internal medicine clinic andtwo federally qualified health centers. The study was approved by the Institutional Review Boards of the participating institutions.

Electronic clinic encounter databases were used to identify potentially eligible patients at each site. Trained, bilingual research assistants recruited patients by telephone and conducted screening assessments to determine final eligibility. Eligible patients provided in-person, written informed consent at the time of the baseline interview.

Assessments of Cognitive Function

Research assistants were formally trained and supervised in the administration of neuropsychological assessment by a research psychologist from the Mount Sinai School of Medicine Alzheimer's Disease Research Center. We evaluated cognitive function with a battery that has extensive normative data.[32,33] It uses modifications of eight tests assessing the following domains:processing speed, executive functioning, attention, and working memory, delayed recall, and word fluency. Processing speed was assessed with the Pattern Comparison and Trail Making Atests. For Pattern Comparison, participants determine whether two side-by-side geometric figures are identical.[34] Higher scores are earned by correctly completing more comparisons in a 1-minute trial. Trails A requires subjects to draw lines connecting, in order, numbereddotsscattered across a page; the score represents the time to completion. The Trail Making B Test[35] was used to evaluate executive function. Similar toTrails A, the Trails B score represents the time the subject takes to link an alternating sequence of numbers and letters scattered across a page. Attention and working memory were assessed with the Wechsler Adult Intelligence Scale-III (WAIS) Letter-Number Sequencing[36] test, in whichsubjects repeat strings of letters and numbers spoken by the interviewer. The strings increase in length as the test progresses. The Wechsler Memory Scale-III (WMS), Story A was used to assess immediate recall. It requires the reader to

immediately recall specific details of a brief story that is read to them by the tester.[36] Delayed memory was assessed by having subjects recall as much as possible of the same storyafter a 25-minute delay. Animal Naming is an assessment of word fluency in which the subject names as many animals as possible in one minute.[18,37] Finally, we used the Mini-Mental State Examination (MMSE) to assess global cognitive functioning.[38] The MMSE is a dementia screening tool that evaluates orientation, registration, attention and calculation, recall, and category fluency.

Assessments of Current Asthma Control, Airway Obstruction, and Duration

Current asthma control was assessed at baseline using the validated Asthma Control Questionnaire (ACQ) developed by Juniper et al.[38,39] We used the five-item version that excludes two items about β_2-agonist use and FEV_1. The instrument measures the extent to which an individual has experienced asthma symptoms including disturbance of sleep, asthma immediately after waking, disruption of daily life activities, shortness of breath, and wheezing. Each item is scored on a seven-point scale from 0 (completely controlled) to 6 (very poorly controlled). The average rating on the 5 itemsprovides an overall score, with values greater than or equal to 1.5 indicating poor asthma control.[39]

We used the predicted forced expiratory volume at 1 second (FEV_1) to estimate the degree of bronchial obstruction as another indicator of current asthma control.[40] FEV_1 assessment was performed at baseline in the absence of bronchodilator use, and in accordance with American Thoracic Society criteria[41] using a MidmarkIQspiro Digital Spirometer, model 4-000-0020 (MidMark Diagnostics Group, Gardena, CA). We defined significant airway obstruction as $FEV_1<70\%$.

Finally, in exploratory analyses, we tested the hypothesis that increased years of asthma would be associated with greater cognitive impairment because late onset asthma is associated with lower FEV_1 and poorer responsiveness to bronchodilators indicating chronic persistent airflow obstruction.[42,43] We used two measures, self-reported total years with an asthma diagnosis, and early (before age 40) vs. late asthma onset as defined in a National Institute on Aging workshop on aging in the elderly.[44]

Other Variables

Our analyses included variables that have a known association with both cognitive performance and, in most cases, asthma control.[45,46] These included age, sex, race/ethnicity, educational level, English-speaking ability, general health status, and comorbidities, which were assessed by self-report. Depression was determined by a score of 10 or greater on the validated patient health questionnaire (PHQ)-9.[47]

Statistical Analysis

Baseline clinical and demographic characteristics were compared between individuals with good and poor asthma control and airway obstruction, as measured by the ACQ and spirometry, and between individuals with good and poor general cognition, as measured by the MMSE, using the chi-square test.[39] In a series of bivariate analyses, we tested the association of poor asthma control and airway obstruction with continuous measures of

cognitive function using the t-test; we used the Wilcoxon rank sum test for the Trail A and B Making Test scores because they were not normally distributed. For each outcome, we then constructed individual linear regression models estimating the association of poor asthma control or bronchial obstruction with a continuous measure of cognitive function, adjusting for age, gender, race, education, English-speaking ability, and comorbid depression. The Trail A and B Making Test Scores were log-transformed to approximate the normal distribution.

We reran these models using dichotomous measures of cognition indicating below normal cognitive functioning based on performance at 1.5 standard deviations below the age or age and education-adjusted norms for each measure.[48–53] These analyses were limited to Trails A and B, letter-number sequencing, animal naming, and the MMSE because age adjusted norms were not publicly available for the other measures. Logistic regression models of the age- and education-normed Trails A and B and MMSE outcomes were adjusted for sex, race, income, English language proficiency and depression, while models of age-normed letter-number sequencing and animal naming were additionally adjusted for education. Finally, we also evaluated these models with using the PHQ-9 depression screening measure as a continuous variable. Use of the continuous measure did not change the statistical significance of the models nor otherwise alter the results in clinically meaningful ways. We therefore report just the results of models that adjusted for dichotomized PHQ-9 scores (≥10 vs. <10). All analyses were performed with SAS statistical software, version 9.2 (SAS Institute, Cary, NC).

RESULTS

Sample Characteristics

Between January 1st, 2010 and November 30th, 2013, 1972 potentially eligible participants were identified from the electronic clinic databases of the study sites. Of these, eight were deceased (<1%), 466 were unreachable (24%), 363 refused participation (27%), and 523 were excluded because they had no history of asthma (14%), they had COPD and other chronic lung diseases (4%), had a ≥10 pack-year smoking history (5%), or for other miscellaneous reasons (4%). Overall, 507 were eligible and 452 completed the interview.

The mean (SD) age of study participants was 67.5±6.8 years; 84% were female, 31% were non-Hispanic black, 40% were Hispanic, 35% had not completed high school and 27% reported fair to poor English-speaking ability (Table 1). Performance on the MMSE was below normal for 36% of patients.

Poor asthma control occurred among 41% of subjects and 35% had an FEV_1<70% predicted (Table 1). The correlation between scores on the ACQ and FEV_1 was −0.12 (p=0.01). Subjects with poor control were more likely to be younger(ages 60–64, 49% vs. ages ≥70, 28%, p=0.0005), black or Hispanicvs. white (43% and 48%, respectively, vs. 28%, p=0.004), and poor or fair English proficiency vs. higher levels of proficiency (50% vs. 37%, p=0.02), among other significant associations. They were not more likely, however, to have late onset asthma or histories of intubation or hospitalizations for asthma. Similar

associations were observed for those with FEV_1<70%, although there was a significant association between this outcome and late onset asthma and a history of intubation.

Associations of Asthma Control and Airway Obstruction with Cognitive Performance—Overall, both poor asthma control and airway obstruction (FEV_1 <70%) were associated at the level of p=0.05 or lower with scores on all measures of processing speed, executive function, attention and working memory, immediate recall, delayed recall, word fluency, and global cognitive function (Table 2). In each case, individuals with poor asthma control or airway obstruction were likely to have poorer performance on the specific cognitive measures. Differences in scores by FEV_1 were more pronounced than differences observed for asthma control, with differences (FEV_1<70% vs. FEV_1 ≥70%,) in scores each achieving, respectively, p<0.0001on measures of processing speed (pattern comparison mean 8.9 [4.1] vs. 10.8 [4.0]; Trail A mean 74.6 [39.4] vs. 59.2 [33.8]) executive function (Trail B mean, 228.1 [89.7] vs. 179.6 [94.9]), attention and working memory (letter-number sequencing mean, 5.2 [3.5] vs. 6.9 [3.5]), and global cognition (MMSE mean, 24.8 [3.9] vs. 26.4 [3.5]).

However, these associations lost their statistical significance when adjusted for age, sex, race and ethnicity, education, income, English language ability, and current depression (Table 3). The association of poor asthma control with worse performance on Trails B approached significance (β = 0.08 [0.04], p=0.08) as did the association of FEV_1<70% with poorer performance on the letter-number sequencing task (β = −0.51 [0.29], p=0.08).

Comparisons to Age and Education Adjusted Norms—Performance on individual assessments relative to age or age and education adjusted norms varied by the assessment. Only 14% of subjects scored 1.5 standard deviations below the age and education adjusted norms for the animal naming test, whereas 69% scored below the norms for the Trails B assessment (Table 4). Poor asthma control and airway obstruction followed a similar pattern of mostly significant associations with below normal performance on the cognitive measures in the unadjusted analyses (Tables 4) but few significant associations in the adjusted analyses (Table 5).

In the adjusted analyses, performance by subjects with poor asthma control was associated with lower odds of a below normal performance on the animal naming test (OR 0.49, 95% CI 0.26–0.94, p=0.03) and FEV_1<70% with greater odds of scoring below age and education norms on the letter number sequencing test (OR 1.76, 95% CI 1.08–2.88, p=0.02).

Duration of Asthma Diagnosis—Neither longer duration of asthma, assessed as a continuous measure, nor the dichotomous measure of late onset asthma, were significantly associated with any of the specific or general measures of cognition in univariate and multivariate analyses (data not shown).

DISCUSSION

Studies of the association between asthma and cognitive impairment are rare, especially in elderly populations, despite findings from laboratory and observational data suggesting that

asthmatics may be at increased risk for cognitive dysfunction. In this study we moved beyond the existing literature to examine the association of cognition with markers of asthma control. In analyses of asthma control and airway obstruction, we neither found few significant associations with continuous measures of cognition in multiple domains nor with performance on these assessments at the threshold of 1.5 standard deviations below age and education adjusted norms. Taken together, these findings indicate that asthma control and airway obstruction have modest and inconsistent associations with cognitive function among older asthmatics.

The small body of clinical research on asthma and cognitive function has focused on comparing individuals with and without the disease and or has had methodological issues that limited their implications for older asthmatics. For example, older patients with asthma and chronic obstructive pulmonary disease (mean age 74, n=40) had worse performance on measures of attention and executive functioning than controls without lung disease.[17] There is however, a well-demonstrated association of COPD and cognition,[4] so the true association of asthma and cognition in this study is not clear. Caldera-Alvarado and colleagues found that adults ages 55 and older with asthma (n=102) were more likely than similarly aged non-asthmatics (n=1278) to have scores on the Montreal Cognitive Assessment that suggestedmild, or worse, cognitive impairment, though this study provided no insights on the association of asthma control and cognitive function.[28] Bozek and colleagues compared MMSE scores for asthmatics (mean age 69 years, n=359) before and 1 year after starting asthma therapy.[30] MMSE scores improved for patients with and without abnormal MMSE scores at baseline and were significantly correlated with asthma control and FEV_1. However, the study was non-randomized and measurement was not blinded, raising concerns about ascertainment bias. In a small study of younger asthmatics (mean age 28, n=46), Weersink found that greater circadian variation in peak expiratory flow, but not the predicted FEV_1 percent, was associated with poorer performance on measures of attention, processing speed, and executive function. There was also significant improvement in performance on the Trails A and B, Stroop Test, and paced auditory serial addition test (PASAT) tests after 6 weeks of asthma treatment with long-acting beta-agonists and inhaled corticosteroids.[29]

The cumulative data to date, while heterogeneous in populations and study methods, is consistent in demonstrating associations between asthma and cognition. Our findings advance this body of work by exploring the relationship of markers of asthma control with cognition in a large cohort of older adults. Our largely null findings also raise the possibility that greater differences in cognitive performance may exist between older asthmatics and older non-asthmatics than among older asthmatics with different levels of disease control.

We used two measures of asthma activity, the self-reported ACQ and FEV_1measured by spirometry. These tests have fundamental differences. The ACQ documents symptoms of nocturnal wakening, activity limitation, wheezing, and shortness of breath over a 7-day period where as the FEV_1measures bronchial obstruction at one moment in time. Reflecting these differences, the assessments often correlate weakly,[54,55] as they did in our study. Older asthmatics sometimes have diminished perceptions of airway obstruction which may contribute to the weak association.[56] Asthma activity that results in perceptible symptoms

may reflect more persistent symptoms. Alternatively, since the ACQ is self-reported, it could represent a bias resulting from insight impairments in the context of baseline cognitive dysfunction. Additional research is needed to confirm our findings and if confirmed, elucidate the causal pathways.

This study has methodological limitations that should be noted. First, our analyses were limited to measures of asthma control and airway obstruction from a single time point. These single measurements may not reflect asthma control over time. We did examine number of years of asthma diagnosis and found it unassociated with cognition but were unable to assess cumulative control of asthma and thus it remains to be determined whether the cumulative effects of poor asthma control may affect cognitive performance. Relatedly, we were unable to determine whether cognitive impairment observed among those with poor asthma control is a transient result of acute asthma worsening or a result of chronically poor asthma control. Second, because the analyses are cross-sectional, we cannot infer causality. In some instances patients with poor cognitive functioning arising from etiologies unassociated with asthma, may have asthma behaviors that contribute to worse asthma control, such as poor inhaler technique.[57] Third, we used single measures of cognition in the domains of immediate and delayed memory, executive function, and word fluency. A more comprehensive assessment of cognitive function in each domain would have been preferable for this study but we chose to limit the number of assessments to avoid respondent fatigue. Fourth, data were mostly from individuals from socioeconomically disadvantaged communities, which constrains generalizability. Also, the study's participants were primarily recruited from hospital-based settings and such patients often suffer from multiple chronic medical conditions that may contribute to cognitive dysfunction.

In summary, we found few associations between asthma control and airway obstruction with performance on measures of cognitive function. Our findings suggest that the simple condition of having the disease, rather than its level of control, may increase risk of cognitive impairment in older adults. Research on the metabolic and inflammatory pathways underlying asthma in older adults and their link to cognition may further elucidate this issue.

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Table 1

Characteristics of Study Patients, by Performance on the Mini-Mental Status Exam and Level of Asthma Control

		Mini-Mental Status Exam Performance			Asthma Control‡			FEV$_1$		
	Total	≥ Normal	< Normal†	P	Good	Poor	P	≥ 70%	< 70%	P
All Subjects, n (%)	**452 (100)**	**287 (63.4)**	**161 (35.6)**		**269 (59.5)**	**183 (40.9)**		**291 (65.1)**	**156 (34.9)**	
Age										
60–64	44.2	69.2	30.8	0.003	51.3	48.7	0.0005	64.8	35.2	0.80
65–69	23.9	50.5	49.5		57.4	42.6		67.6	32.4	
70+	31.9	67.1	32.9		72.0	28.0		63.6	36.4	
Sex										
Female	83.9	63.8	36.2	0.81	57.6	42.4	0.06	68.7	31.3	0.0002
Male	16.1	16.4	15.5		69.4	30.6		45.8	54.2	
Race/Ethnicity										
White	21.2	89.5	10.5	<0.0001	71.9	28.1	0.004	78.1	21.9	0.005
Black	30.6	58.4	41.6		56.9	43.1		67.2	32.9	
Latino	39.7	53.9	46.1		52.2	47.8		56.6	43.3	
Other	8.5	68.4	31.6		73.7	26.3		65.8	34.2	
Education										
Less than high school	34.7	50.3	49.7	<0.0001	51.3	48.7	0.01	51.3	48.7	<0.0001
High school graduate	17.3	74.4	25.6		57.7	42.3		68.0	32.0	
Some college	19.6	58.0	42.1		60.7	39.3		66.3	33.7	
College graduate	28.4	78.7	21.3		70.9	29.1		80.3	19.7	
English proficiency										
Fair-poor	26.6	43.7	56.3	<0.0001	50.4	49.6	0.02	47.9	52.1	<0.0001
Excellent, very good, good	73.4	71.4	28.6		63.0	37.0		71.5	28.5	
Monthly income										
≤$750	24.7	48.2	51.9	<0.0001	47.2	52.8	<0.0001	50.9	49.1	<0.0001
$751-$1350	30.7	63.4	36.6		55.2	44.9		61.0	39.0	
$1351–$3000	24.0	64.8	35.2		60.0	40.0		68.6	31.4	

		Mini-Mental Status Exam Performance			Asthma Control‡			FEV$_1$		
	Total	≥ Normal	< Normal†	P	Good	Poor	P	≥ 70%	< 70%	P
All Subjects, n (%)	**452 (100)**	**287 (63.4)**	**161 (35.6)**		**269 (59.5)**	**183 (40.9)**		**291 (65.1)**	**156 (34.9)**	
≥$3000	20.6	84.4	15.6		81.3	18.7		84.6	15.4	
General health										
Good, fair, poor	77.6	59.1	40.9	<0.0001	53.1	46.9	<0.0001	61.4	38.6	0.003
Excellent, very good	22.4	81.0	19.0		81.2	18.8		77.2	22.8	
Depression										
Yes	21.0	54.4	45.7	0.03	32.6	67.4	<0.0001	60.9	39.1	0.23
No	79.0	66.5	33.5		67.0	33.1		67.5	32.5	
Current use of an inhaled steroid										
Yes	72.5	66.8	33.2	0.05	61.9	38.1	0.09	65.2	34.8	0.88
No	27.5	56.9	43.1		53.2	46.8		64.5	34.5	
Late onset asthma										
Yes	49.6	63.1	36.9	0.66	59.9	40.1	0.87	72.5	27.5	0.001
No	50.5	65.0	35.0		59.1	40.9		57.8	42.2	
History of intubation for asthma										
Yes	9.0	52.5	47.5	0.12	56.1	44.0	0.64	46.3	53.7	0.008
No	91.0	64.9	35.1		59.9	40.2		67.0	33.0	
Hospitalization for asthma, past 12 mos										
Yes	9.4	57.1	42.9	0.34	47.6	52.4	0.10	61.9	38.1	0.65
No	90.6	64.5	35.5		60.7	39.3		65.4	34.6	
ED visit for asthma, past 12 mos										
Yes	23.6	59.1	41.0	0.24	48.6	51.4	0.009	62.9	37.1	0.58
No	76.4	65.3	34.7		62.9	37.1		65.8	34.2	

† 1.5 standard deviations below age and education adjusted norms.

‡ Based on subject responses to the Asthma Control Questionnaire.

FEV$_1$ denotes forced expiratory volume at 1 second; ED, emergency department.

Table 2

Cognitive Measure Scores by Levels of Asthma Control and Forced Expiratory Volume at 1 Second

Measure	Test Scores	Asthma Control†			FEV_1		
	All Subjects	Good	Poor		≥70%	<70%	
	Mean (SD)	Mean (SD)	Mean (SD)	P	Mean (SD)	Mean (SD)	P
Processing Speed							
Pattern Comparison	10.1 (4.2)	10.6 (4.2)	9.4 (3.9)	0.003	10.8 (4.0)	8.9 (4.1)	<0.0001
Trail Making A‡	64.6 (36.5)	60.8 (34.9)	70.2 (38.3)	0.007	59.2 (33.8)	74.6 (39.4)	<0.0001
Executive Function							
Trail Making B‡	196.7 (95.9)	184.4 (97.6)	214.5 (90.7)	0.001	179.6 (94.9)	228.1 (89.7)	<0.0001
Attention, Working Memory							
Letter-number sequencing	6.3 (3.6)	6.7 (3.6)	5.7 (3.5)	0.008	6.9 (3.5)	5.2 (3.5)	<0.0001
Immediate Recall							
WMS Story A	9.7 (4.3)	10.0 (4.5)	9.2 (4.1)	0.05	10.2 (4.4)	8.9 (4.1)	0.002
Delayed Recall							
WMS Story A	8.1 (4.5)	8.5 (4.7)	7.5 (4.2)	0.02	8.7 (4.5)	7.0 (4.3)	0.0001
Word Fluency							
Animal naming test	15.5 (5.6)	16.0 (5.9)	14.8 (5.1)	0.02	16.0 (5.5)	14.6 (5.7)	0.01
Global Cognitive Function							
Mini-Mental State Exam	25.8 (3.7)	26.2 (3.7)	25.3 (3.7)	0.01	26.4 (3.5)	24.8 (3.9)	<0.0001

†Based on subject responses to the Asthma Control Questionnaire.

‡Higher scores on Trail Making A and B indicate worse performance.

FEV_1 denotes forced expiratory volume at 1 second; WMS, Wechsler Memory Scale.

Table 3

Association of Cognition with Poor Asthma Control and Forced Expiratory Volume at 1 Second<70%

Measure	Poor Asthma Control†				FEV_1 <70%			
	Unadjusted β (SE)	P	Adjusted* β (SE)	P	Unadjusted β (SE)	P	Adjusted* β (SE)	P
Processing Speed								
Pattern Comparison	−1.20 (0.40)	0.003	−0.30 (0.31)	0.35	−1.87 (0.40)	<0.0001	−0.33 (0.32)	0.30
Trail Making A‡	0.15 (0.05)	0.003	0.01 (0.04)	0.84	0.23 (0.05)	<0.0001	0.03 (0.04)	0.51
Executive Function								
Trail Making B‡	0.20 (0.06)	0.0003	0.08 (0.04)	0.08	0.29 (0.06)	<0.0001	0.06 (0.04)	0.15
Attention, Working Memory								
Letter-number sequencing	−0.92 (0.35)	0.008	−0.07 (0.29)	0.80	−1.73 (0.35)	<0.0001	−0.51 (0.29)	0.08
Immediate Recall								
WMS Story A	−0.81 (0.41)	0.05	0.03 (0.38)	0.94	−1.31 (0.42)	0.002	0.14 (0.39)	0.73
Delayed Recall								
WMS Story A	−1.00 (0.43)	0.02	−0.10 (0.38)	0.79	−1.72 (0.44)	0.0001	−0.11 (0.39)	0.78
Word Fluency								
Animal naming test	−1.22 (0.53)	0.02	0.27 (0.50)	0.60	−1.41 (0.55)	0.01	0.05 (0.51)	0.92
Global Cognitive Function								
Mini-Mental State Exam	−0.89 (0.36)	0.01	0.06 (0.30)	0.83	−1.56 (0.36)	<0.0001	−0.16 (0.30)	0.61

†Based on subject responses to the Asthma Control Questionnaire.

‡Higher scores on Trail Making A and B indicate worse performance; scores log transformed to approximate the normal distribution.

*Adjusted for age, sex, race and ethnicity, education, English-speaking ability, income, and depression.

FEV_1 denotes forced expiratory volume at 1 second; WMS, Wechsler Memory Scale.

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Table 4

Rates of Below Normal Performance on Cognitive Measures, by Levels of Asthma Control and Forced Expiratory Volume at 1 Second

Measure	Subjects with below normal performance on the measure (%)	Asthma Control§			% Predicted FEV_1		
		Good (n=269, 60%)	Poor (n=183, 40%)	P	(≥70%) (n=269, 60%)	(<70%) (n=183, 40%)	P
Trail Making Test A|‡	51.1	45.0	60.2	0.002	44.4	63.9	<0.0001
Trail Making Test B|‡	69.2	63.3	77.9	0.001	63.5	80.0	0.0003
Letter-Number Sequencing†	29.7	25.7	35.5	0.02	21.4	44.9	<0.0001
Animal naming test|	13.6	13.5	13.8	0.92	10.6	19.4	0.01
Mini-Mental State Exam|	35.9	32.6	40.9	0.07	31.1	45.2	0.003

† 1.5 standard deviations below adult population averages.

| 1.5 standard deviations below age and education adjusted averages.

‡ Higher scores indicate worse performance

§ Based on subject responses to the Asthma Control Questionnaire.

FEV_1 denotes forced expiratory volume at 1 second; WMS, Wechsler Memory Scale.

Table 5

Unadjusted and Adjusted Associations of Below Normal Performance on Cognitive Measures with Asthma Control and Forced Expiratory Volume at 1 Second

	Poor Asthma Control[§]				FEV_1 <70%			
Outcome Measure	**Unadjusted OR (95%) CI**	**P**	**Adjusted[*] OR (95%) CI**	**P**	**Unadjusted OR (95%) CI**	**P**	**Adjusted[*] OR (95%) CI**	**P**
Below Normal Processing Speed								
Trail Making A[|‡]	1.86 (1.26–2.72)	0.002	1.12 (0.69–1.81)	0.65	2.22 (1.49–3.31)	<0.0001	1.20 (0.73–1.98)	0.48
Below Normal Executive Function								
Trail Making B[|‡]	2.04 (1.33–3.14)	0.001	1.28 (0.75–2.18)	0.37	2.30 (1.45–3.64)	0.0004	1.10 (0.62–1.93)	0.75
Below Normal Attention and Working Memory								
Letter-number sequencing[†]	1.60 (1.06–2.40)	0.02	1.04 (0.64–1.70)	0.87	2.99 (1.97–4.55)	<0.0001	1.76 (1.08–2.88)	0.02
Below Normal Word Fluency								
Animal naming test[|]	1.03 (0.59–1.78)	0.92	0.49 (0.26–0.94)	0.03	2.03 (1.18–3.50)	0.01	1.30 (0.70–2.42)	0.40
Below Normal Global Cognitive Function								
Mini-Mental State Exam[|]	1.43 (0.97–2.12)	0.07	0.99 (0.63–1.55)	0.97	1.83 (1.22–2.73)	0.003	1.41 (0.89–2.23)	0.14

[†] 1.5 standard deviations below adult population averages.

[|] 1.5 standard deviations below age and education adjusted averages.

[‡] Higher scores indicate worse performance.

[§] Based on subject responses to the Asthma Control Questionnaire.

[*] Adjusted for sex, race and ethnicity, English-speaking ability, income, and depression.

FEV_1 denotes forced expiratory volume at 1 second.