

BRIEF COMMUNICATION

Relationship between asthma and cognition: the Cooper Center Longitudinal Study

G. Caldera-Alvarado¹, D. A. Khan², L. F. DeFina³, A. Pieper^{1,4} & E. S. Brown¹

¹Department of Psychiatry, The University of Texas Southwestern Medical Center, Dallas; ²Allergy & Immunology Division of the Department of Internal Medicine, The University of Texas Southwestern Medical Center, Dallas; ³The Cooper Institute, Dallas, TX;

⁴Department of Psychiatry, University of Iowa Carver College of Medicine, Iowa City, IA, USA

To cite this article: Caldera-Alvarado G, Khan DA, DeFina LF, Pieper A, Brown ES. Relationship between asthma and cognition: the Cooper Center Longitudinal Study. *Allergy* 2013; DOI: 10.1111/all.12125.

Keywords

asthma; cognition; corticosteroid; elderly; spirometry.

Correspondence

E. Sherwood Brown, Department of Psychiatry, The University of Texas Southwestern Medical Center at Dallas, 5323 Harry Hines Blvd, MC 8849, Dallas, TX 75390-8849, USA.

Tel.: 214-645-6950

Fax: 214-645-6951

E-mail: sherwood.brown@utsouthwestern.edu

Accepted for publication 28 December 2012

DOI:10.1111/all.12125

Edited by: Marek Sanak

Abstract

Background: Minimal data are available on the relationship between asthma and cognitive performance. In this report, we examine the relationship between asthma and cognitive performance in older adults, a subpopulation with elevated risk of cognitive impairment.

Methods: We conducted a cross-sectional, retrospective analysis of 1380 participants age ≥ 55 who completed preventive health examinations at the Cooper Clinic in Dallas, TX. Cognition was assessed using the Montreal Cognitive Assessment (MoCA), a brief test for mild cognitive impairment. Data were analyzed in a multiple logistic regression using MoCA scores suggestive of cognitive impairment as the dependent variable.

Results: When controlling for demographic characteristics, self-rated health status, inhaled corticosteroid use, and FEV₁/FVC, asthma were associated with 78% increased risk of cognitive impairment ($P = 0.02$) as defined by MoCA score.

Conclusions: In the largest sample examined to date, we have identified a significant relationship between asthma and cognitive impairment in older people.

Asthma is a common medical condition with increasing prevalence (1). Clinical characteristics, such as transient hypoxia, could lead to poor cognition in asthma patients as hypoxia is associated with hippocampal neurotoxicity (2). Patients with asthma also have high rates of depression (3) and anxiety disorders (4), which can be associated with poor cognition. The treatment of asthma could compromise cognition, as corticosteroid therapy is associated with cognitive changes (5). Cognition is important in asthma patients because it is a predictor of medication nonadherence in medically ill patients (6, 7).

Minimal data are available on cognition in asthma. In adults, performance on the Bender–Gestalt test suggestive of cognitive impairment was observed in 65% of hospitalized asthma patients (8). Medications were not discussed in this study, but clinical practice suggests patients were likely receiving systemic corticosteroids while hospitalized. However, cognitive performance may also be poor in asthma patients not receiving systemic corticosteroids. We reported

that adults with asthma had mean memory performance in the low-normal to mildly impaired range prior to receiving corticosteroid bursts (9).

In the current study, we hypothesized that individuals age ≥ 55 with asthma seen at a preventive medicine clinic would have greater cognitive impairment than those without an asthma history.

Materials and methods

Participants

From 02/09 to 09/12, 1380 generally healthy patients age ≥ 55 years were seen at the Cooper Clinic in Dallas, Texas for preventive medical examinations that included extensive medical history, Center for Epidemiologic Studies Depression (CES-D) scale, physical examination, laboratory analyses, pulmonary function testing, and the Montreal Cognitive Assessment (MoCA). Participants gave informed consent for

use of their data in the Cooper Center Longitudinal Study database maintained by The Cooper Institute, and approved by the Institute's Institutional Review Board.

Assessments

Montreal Cognitive Assessment

Cognition was assessed using the MoCA, a validated eight-item test that assesses eight cognitive domains including attention, executive functions, and memory. MoCA scores range from 0 to 30 with a score of <26 defining possible mild cognitive impairment (MCI) (10). As recommended, one additional point was added to scores of participants with ≤ 12 years of education.

Spirometry

Koko PFT System was used to measure lung function with the best of three trials recorded in the database. Hankinson equations were used to calculate forced expiratory volume in the first second (FEV₁) and forced vital capacity (FVC). An FEV₁% score, the ratio of FEV₁ and FVC, of <70 is suggestive of obstructive lung disease (11).

Other assessments

Vitamin D blood levels were measured following standardized procedures as described in Hoang et al. (12). A level <30 ng/ml suggests insufficient vitamin D (12). The 10-item CES-D quantified depressive symptoms during the previous week. A score of ≥ 10 suggests clinically significant depressive symptoms (13). Global health rating of each participant was assessed using a four-point (poor, fair, good, excellent) self-report assessment developed for clinical assessment by the Cooper Clinic. History of depression and anxiety was also assessed by self-report.

Statistical methods

Multiple logistic regression predicted the dependent variable of MoCA score (≥ 26 or <26) based on covariates (e.g., demographic/health information as in other Cooper Clinic data analyses (12), pulmonary function values, variables potentially related to cognition and/or asthma [e.g., vitamin D levels (14), diabetes (15), and asthma medications]) and is presented in Table 2. SPSS® software version 14.0 (SAS Institute, Cary, NC) was used for the analyses, including summary statistics using chi-squared analyses in Table 1.

Results

Participant characteristics are shown in Table 1 for those with and without asthma. Mean MoCA score was 26.9 ± 2.3 (range 10–30, 25%_{oo} = 26, 50th%_{oo} < 27, 75%_{oo} < 29). Groups were similar demographically except for subjective health rating ($P = 0.03$), corticosteroid or combined inhaler use ($P < 0.001$) and FEV₁/FVC ($P < 0.001$). The vast majority of patients had mild asthma, based on FEV₁/FCV, current use of corticosteroid/combined inhaler, and subjective health ratings.

Table 1 Demographic information of participants (N = 1380), Cooper Center Longitudinal Study

Characteristic	Asthma group (n = 102)	Non-Asthma group (n = 1278)	P value
Sex, n (%)			
Female	28 (27.5)	325 (25.4)	0.64
Male	74 (72.5)	953 (74.6)	
Age, n (%)			
<65 years	70 (68.6)	911 (71.3)	0.57
≥ 65 years	32 (31.4)	367 (28.7)	
Body mass index, n (%)			
Underweight or normal	30 (29.4)	433 (33.9)	0.39
Overweight or obese	72 (70.6)	845 (66.1)	
Education, n (%)			
≤ 12 years	16 (15.7)	242 (18.9)	0.51
>12 years	86 (84.3)	1036 (81.1)	
Ethnicity, n (%)			
Non-Hispanic Caucasian	98 (96.1)	1224 (95.8)	1.00
Other	4 (3.92)	54 (4.23)	
Smoking status, n (%)			
Current smoker	10 (9.8)	97 (7.6)	0.44
Nonsmoker or past smoker	92 (90.2)	1181 (92.4)	
Alcohol use status, n (%)			
Current drinker	81 (79.4)	1031 (80.7)	0.80
Nondrinker or past drinker	21 (20.6)	247 (19.3)	
Health rating, n (%)			
Poor or fair	23 (22.5)	177 (13.8)	0.03
Good or excellent	79 (77.5)	1101 (86.2)	
Vitamin D level, n (%)			
<30 ng/ml	28 (27.5)	378 (29.6)	0.74
≥ 30 ng/ml	74 (72.5)	900 (70.4)	
Diabetes, n (%)			
Yes	9 (8.8)	60 (4.7)	0.09
No	93 (91.2)	1218 (95.3)	
CES-D, n (%)			
<10	94 (92.2)	1191 (93.2)	0.68
≥ 10	8 (7.84)	87 (6.81)	
Depression, n (%)			
Yes	13 (12.7)	151 (11.8)	0.75
No	89 (87.3)	1127 (88.2)	
Anxiety, n (%)			
Yes	16 (15.7)	154 (12.1)	0.27
No	86 (84.3)	1124 (87.9)	
FEV ₁ /FVC (FEV ₁ %), n (%)			
<70	25 (24.5)	78 (6.1)	<0.001
≥ 70	77 (75.5)	1200 (93.9)	
Inhaled corticosteroid (ICS) treatment, n (%)			
No ICS use	74 (72.5)	1269 (99.3)	<0.001
Either ICS or combined ICS	28 (27.5)	9 (0.7)	

Table 2 shows the association between asthma and cognition. When controlling for the noted covariates, asthma was significantly associated with MCI (OR 1.78, [95% CI, 1.09–2.91]) as defined by the MoCA. Variables potentially related to asthma severity (e.g., corticosteroid inhaler use, FEV₁/FVC, health rating) were not associated with MoCA performance.

Table 2 Multiple logistic regression models of the Montreal Cognitive Assessment score, Cooper Center Longitudinal Study

Characteristic	Odds ratio (95% confidence interval)	P value
Sex		
Female vs male	0.87 (0.63–1.20)	0.40
Age		
<65 vs ≥ 65 years	2.20 (1.68–2.89)	<0.001
Body mass index		
Underweight or normal vs overweight or obese	1.11 (0.84–1.49)	0.46
Ethnicity		
Other race/ethnicity vs non-Hispanic Caucasian	0.43 (0.24–0.75)	0.003
Smoking status		
Current smoker vs nonsmoker or past smoker	1.53 (0.98–2.39)	0.06
Alcohol use status		
Current drinker vs nondrinker or past drinker	1.06 (0.77–1.46)	0.74
Health rating		
Poor or fair vs good or excellent	1.06 (0.73–1.54)	0.77
Vitamin D level		
<30 vs ≥ 30 ng/ml	0.68 (0.51–0.89)	0.006
Diabetes		
Yes or no	1.29 (0.74–2.25)	0.36
CES-D		
<10 vs ≥ 10	1.07 (0.62–1.84)	0.81
Depression		
Yes or no	0.84 (0.53–1.35)	0.47
Anxiety		
Yes or no	1.08 (0.69–1.70)	0.74
FEV ₁ /FVC (FEV ₁ %)		
<70 vs ≥ 70	1.14 (0.70–1.85)	0.59
Inhaled corticosteroid (ICS) treatment		
No ICS vs ICS or combined ICS	1.10 (0.49–2.46)	0.83
Asthma		
Yes vs no	1.78 (1.09–2.91)	0.02

Discussion

Prior cognition research in adults with asthma is limited to reports in inpatients who were likely receiving systemic corticosteroids (8), and patients with asthma exacerbations scheduled to initiate oral corticosteroid therapy (9). The current report adds to these findings by examining older, generally healthy patients with relatively mild asthma. The 78% increased risk of MCI in the asthma patients is concerning and suggests that older asthma patients may be a target population for cognitive impairment screening.

References

1. Yawn BP, Wollan P, Kurland M, Scanlon P. A longitudinal study of the prevalence of asthma in a community population of school-age children. *J Pediatr* 2002;**140**:576–581.
2. Leblond J, Krnjevic K. Hypoxic changes in hippocampal neurons. *Journal of neurophysiology* 1989;**62**:1–14.
3. Goodwin RD, Fergusson DM, Horwood LJ. Asthma and depressive and anxiety disorders among young persons in the community. *Psychol Med* 2004;**34**:1465–1474.
4. Goodwin RD, Fischer ME, Goldberg J. A twin study of post-traumatic stress disorder

The etiology of increased risk of MCI with asthma is not clear. Groups were similar related to demographic and co-morbid factors other than those related to asthma. Given the generally mild asthma in the sample, hypoxia and recent corticosteroid exposure are also not likely causes of the cognitive changes.

The study has limitations. While asthma diagnosis was confirmed by a clinic physician, the patients were not assessed by an allergist or pulmonologist and thus lacked extensive asthma history (e.g., years) and evaluation. While the MoCA is a widely used and sensitive instrument for assessing cognition (10), formal neurocognitive assessment was not performed. As the sample was almost exclusively non-Hispanic Caucasian and men were overrepresented (74.4%), the findings may not be generalizable to other populations. Medication use, spirometry, and subjective health rating did not raise suspicion for chronic obstructive lung disease (COPD), and smoking was comparable in both groups. However, in a sample of older asthma patients, the diagnosis may actually represent COPD.

Conclusion

In a large sample of older participants, asthma was associated with a significantly increased risk of cognitive impairment. Additional research is needed to confirm this finding and determine the etiology and impact of cognitive changes in asthma.

Acknowledgments

We thank the Cooper Clinic for data collection and The Cooper Institute for data management.

Conflicts of interest

There are no conflicts of interest for any of the authors to report.

Author contributions

G Caldera-Alvarado assisted with data analysis and wrote portions of the manuscript. D Khan assisted with design of the study and edited the manuscript. L DeFina was involved in data collection, study design, and wrote portions of the manuscript. A Pieper wrote portions of the manuscript and extensively edited the manuscript. ES Brown designed the study, performed the data analysis, and wrote portions of the manuscript.

- symptoms and asthma. *Am J Respir Crit Care Med* 2007;**176**:983–987.
5. Brown ES. Effects of glucocorticoids on mood, memory, and the hippocampus. Treatment and preventive therapy. *Ann N Y Acad Sci* 2009;**1179**:41–55.
 6. Osterberg L, Blaschke T. Adherence to medication. *N Engl J Med* 2005;**353**:487–497.
 7. Mackin RS, Areal PA. Cognitive and psychiatric predictors of medical treatment adherence among older adults in primary care clinics. *Int J Geriatr Psychiatry* 2007;**22**:55–60.
 8. Schraa JC, Dirks JF, Jones NF, Kinsman RA, Bender-Gestalt performance and recall in an asthmatic sample. *J Asthma* 1981;**18**:7–9.
 9. Brown ES, Frol AB, Khan DA, Larkin GL, Bret ME. Impact of levetiracetam on mood and cognition during prednisone therapy. *Eur Psychiatry* 2007;**22**:448–452.
 10. Nasreddine ZS, Phillips NA, Bedirian V, Charbonneau S, Whitehead V, Collin I, et al. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. *J Am Geriatr Soc* 2005;**53**:695–699.
 11. Chronic obstructive pulmonary disease. National clinical guideline on management of chronic obstructive pulmonary disease in adults in primary and secondary care. *Thorax* 2004;**59**(Suppl 1):1–232.
 12. Hoang MT, Defina LF, Willis BL, Leonard DS, Weiner MF, Brown ES. Association between low serum 25-hydroxyvitamin D and depression in a large sample of healthy adults: the Cooper Center longitudinal study. *Mayo Clin Proc* 2011;**86**:1050–1055.
 13. Lue BH, Chen LJ, Wu SC. Health, financial stresses, and life satisfaction affecting late-life depression among older adults: a nationwide, longitudinal survey in Taiwan. *Archives of gerontology and geriatrics* 2010;**50**(Suppl 1):S34–S38.
 14. Ehlayel MS, Bener A, Sabbah A. Is high prevalence of vitamin D deficiency evidence for asthma and allergy risks? *Eur Ann Allergy Clin Immunol* 2011;**43**:81–88.
 15. Thomsen SF, Duffy DL, Kyvik KO, Skytthe A, Backer V. Risk of asthma in adult twins with type 2 diabetes and increased body mass index. *Allergy* 2011;**66**:562–568.