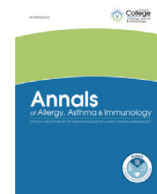




ELSEVIER

Contents lists available at ScienceDirect



Letters

Relationship between olfactory and cognitive function in asthma

Poor asthma control or asthma exacerbation can cause hypoxia, which may be associated with cognitive impairment.^{1,2} Chronic rhinosinusitis (CRS) and allergic rhinitis, typically accompanied by asthma, are the main causes of olfactory dysfunction.³ We investigated the association between olfactory⁴ and cognitive function⁵ in patients with asthma and found that a decrease in olfactory and cognitive functions was typically observed among patients with asthma. In addition, an association between olfactory dysfunction and cognitive impairment has been found in recent studies.^{6,7} However, no study has evaluated the association between olfactory and cognitive functions in patients with asthma thus far. We hypothesized that olfactory and cognitive functions would be related to each other in patients with asthma, and they also might be associated with asthma control. Therefore, we aimed to evaluate this association in patients with asthma.

A total of 146 adults with asthma were included in this cross-sectional study from 2019 to 2020. The clinical variables of the participants were compared according to their olfactory and cognitive functions. The institutional review board approved the study procedure (DAUHIRB-19-175) and written informed consent was obtained from all study participants.

Olfactory function was assessed using the Korean version of the Sniffin' Sticks test II (KVSS II) (Burghart Company, Wedel, Germany) or the YSK olfactory function test (YOF) (Kimex Co, Suwon, South Korea). The degree of olfactory dysfunction was classified, based on our previous study, as follows: (1) anosmia (KVSS II $\leq$ 20, YOF $\leq$ 14.5); (2) hyposmia (20 < KVSS II $\leq$ 27, 14.5 < YOF $\leq$ 21); and (3) normosmia (27 < KVSS II $\leq$ 48, 21 < YOF $\leq$ 36).⁴ The Korean version of the Montreal Cognitive Assessment (MoCA) was used to screen for mild cognitive impairment (MCI) using a cutoff value of 23.⁵

All participants underwent the olfactory function tests (KVSS II, $n = 25$; YOF, $n = 121$) and the MoCA. A total of 68 (46.6%) patients with asthma had olfactory dysfunction (hyposmia, $n = 31$; anosmia, $n = 37$), and 60 (41.1%) patients were classified as having MCI. The demographic and clinical characteristics of the study participants were compared between 4 groups (normal cognition and normosmia, $n = 53$; normal cognition and olfactory dysfunction, $n = 33$; MCI and normosmia, $n = 25$; and MCI and olfactory dysfunction, $n = 35$) (Table 1). There were significant differences in age (51.62 ± 14.58 vs 55.58 ± 14.65 vs 65.84 ± 7.45 vs 69.57 ± 8.2 years, $P < .001$) between the 4 groups. There were also significant differences in the proportion of patients with low education, poor general health status, hypertension, CRS, and nasal polyps between the 4 groups. The duration of asthma (80.67 ± 58.20 vs 89.09 ± 79.58 vs 102.32 ± 78.14 vs 142.2 ± 93.73 months, $P = .003$) and the presence of life-threatening asthma

exacerbation (0% vs 6.1% vs 0% vs 14.3%, $P = .01$) were significantly different between the 4 groups. The YOF scores positively correlated with the MoCA scores after adjusting for age ($r = 0.196$, $P = .03$). However, the duration of asthma and lung function did not significantly correlate with YOF and MoCA scores after adjusting for age. Age (odds ratio, 1.382; 95% confidence interval, 1.084–1.763; $P = .009$) and nasal polyps (odds ratio, 38.578; 95% confidence interval, 1.115–1335.164; $P = .04$) were risk factors for olfactory dysfunction and MCI in patients with asthma compared with patients with asthma who had normal cognition and olfaction by multivariable logistic regression analysis.

In this study, patients with MCI were older, had lower educational status, and were more likely to have hypertension than those with normal cognition, which is consistent with the findings of a previous study.⁸ Patients with olfactory dysfunction had CRS and nasal polyps more frequently than those with normosmia. Patients with olfactory disorders have impaired quality of life and daily life function.⁹ Cognitive dysfunction was significantly associated with worse health-related quality of life in a cross-sectional study of community-dwelling adults aged 60 years and older.¹⁰ Our results revealed that poor general health status was more common in the MCI and olfactory dysfunction group than in the other groups. Concurrent olfactory dysfunction and cognitive impairment seemed to have a more negative impact on general health status than either entity alone.

The duration of asthma was significantly longer in the MCI and olfactory dysfunction group than in the 2 other groups with normal cognition. In addition, the groups with olfactory dysfunction had a longer duration of asthma than the groups with normosmia with a similar cognitive status (either normal cognition or MCI). The duration of asthma could be associated with olfactory dysfunction and cognitive impairment.

Interestingly, life-threatening asthma exacerbation was not found in patients with normosmia, and it was more common in patients with MCI than in patients with normal cognition among patients with olfactory dysfunction. Olfactory dysfunction may be related to life-threatening asthma exacerbation. In addition, impaired cognitive and olfactory functions could have synergistic negative effects on asthma control.

A marked correlation between olfactory and cognitive function was confirmed, as observed in previous studies.^{6,7} Potential mechanisms underlying the association between olfactory and cognitive dysfunction have been proposed, such as decreased volume of the brain cortex⁶ or damage to neurotransmitter systems.⁷ However, the precise pathologies are unknown. To the best of our knowledge, this is the first study to report an association between olfactory and cognitive function in patients with asthma. Furthermore, olfactory and cognitive functions may also be associated with asthma control. The presence of life-threatening asthma exacerbation differed according

Disclosures: The authors have no conflicts of interest to report.

Funding: This work was supported by the Dong-A University research fund.

<https://doi.org/10.1016/j.anai.2021.06.020>

1081-1206/© 2021 American College of Allergy, Asthma & Immunology. Published by Elsevier Inc. All rights reserved.

Table 1
Clinical Characteristics of the Study Participants According to Olfactory and Cognitive Function

Characteristics	Normal cognition and normosmia (n = 53)	Normal cognition and olfactory dysfunction (n = 33)	MCI and normosmia (n = 25)	MCI and olfactory dysfunction (n = 35)	P value
Age, ^a y	51.62 ± 14.58 ^{b,c}	55.58 ± 14.65 ^{d,e}	65.84 ± 7.45	69.57 ± 8.2	<.001
Female sex	29 (54.7)	13 (39.4)	17 (68.0)	21 (60.0)	.15
Low income	5 (9.4)	2 (6.1)	4 (16.0)	8 (22.9)	.16
Low education	11 (20.8)	7 (21.2)	8 (68.0)	26 (74.3)	<.001
Poor general health	39 (73.6)	25 (75.8)	16 (64.0)	33 (94.3)	.03
Diabetes mellitus	8 (15.1)	3 (9.1)	2 (8.0)	9 (25.7)	.17
Hypertension	9 (17.0)	2 (6.1)	9 (36.0)	17 (48.6)	<.001
Depression	3 (5.7)	3 (9.4)	2 (8.0)	5 (14.3)	.58
Allergic rhinitis	22 (41.5)	18 (54.5)	15 (60.0)	18 (51.4)	.42
Chronic rhinosinusitis	24 (45.3)	26 (78.8)	9 (36.0)	19 (54.3)	.005
Nasal polyps	8 (15.1)	13 (39.4)	2 (8.0)	5 (14.3)	.008
Asthma duration, ^a mo	80.67 ± 58.20 ^c	89.09 ± 79.58 ^e	102.32 ± 78.14	142.2 ± 93.73	.003
Severe asthma	14 (26.4)	9 (27.3)	5 (20.0)	4 (11.4)	.32
Life-threatening asthma exacerbation	0 (0)	2 (6.1)	0 (0)	5 (14.3)	.01
ICS treatment	43 (82.7)	28 (84.8)	19 (76.0)	32 (91.4)	.44
INS treatment	19 (35.8)	11 (33.3)	7 (28.0)	8 (22.9)	.60
FEV ₁ , ^a %	76.01 ± 20.05	80.12 ± 14.83	75.68 ± 21.03	68.17 ± 21.35	.09

Abbreviations: FEV₁, forced expiratory volume in 1 second; ICS, inhaled corticosteroids; INS, inhaled nasal steroids; MCI, mild cognitive impairment; MoCA, Montreal cognitive assessment.

^aData are presented as mean ± SD.

^bNormal cognition and normosmia vs normal cognition and olfactory dysfunction ($P < .05$).

^cNormal cognition and normosmia vs MCI and olfactory dysfunction ($P < .05$).

^dNormal cognition and olfactory dysfunction vs MCI and normosmia ($P < .05$).

^eNormal cognition and olfactory dysfunction vs MCI and olfactory dysfunction ($P < .05$).

to olfactory and cognitive function in this study. In addition, age and nasal polyps were risk factors of impaired cognitive and olfactory function in patients with asthma in this study, and they might be the link among olfaction, cognition, and asthma.

This study has some limitations. First, this was a cross-sectional study, and it was not possible to confirm the causal relationship between the 3 factors—olfaction, cognition, and asthma. Second, study participants were heterogeneous, and in particular, age had a significant influence on cognition and olfactory function.^{3,8}

In conclusion, olfactory and cognitive function may be associated with each other in patients with asthma. Furthermore, olfactory and cognitive function may be associated with general health and asthma control status. Further studies with a large population are needed to clarify the relationships.

Hyo-In Rhyou, MD, PhD*

Woo Yong Bae, MD, PhD†

Young-Hee Nam, MD, PhD‡

* Department of Internal Medicine

Samsung Changwon Hospital

Sungkyunkwan University School of Medicine

Changwon, Korea

† Department of Otorhinolaryngology—Head and Neck Surgery

College of Medicine

Dong-A University

Busan, Korea

‡ Department of Internal Medicine

College of Medicine

Dong-A University

Busan, Korea

yhnam@dau.ac.kr

References

- Caldera-Alvarado G, Khan DA, Defina LF, Pieper A, Brown ES. Relationship between asthma and cognition: the Cooper Center Longitudinal Study. *Allergy*. 2013;68(4):545–548.
- Irani F, Barbone JM, Beausoleil J, Gerald L. Is asthma associated with cognitive impairments? A meta-analytic review. *J Clin Exp Neuropsychol*. 2017;39(10):965–978.
- Mullol J, Mariño-Sánchez F, Valls M, Alobid I, Marin C. The sense of smell in chronic rhinosinusitis. *J Allergy Clin Immunol*. 2020;145(3):773–776.
- Rhyo HI, Bae WY, Nam YH. Association between olfactory function and asthma in adults. *J Asthma Allergy*. 2021;14:309–316.
- Rhyo HI, Nam YH. Association between cognitive function and asthma in adults. *Ann Allergy Asthma Immunol*. 2021;126(1):69–74.
- Dintica CS, Marzegli A, Rizzuto D, et al. Impaired olfaction is associated with cognitive decline and neurodegeneration in the brain. *Neurology*. 2019;92(7):e700–e709.
- Roberts RO, Christianson TJH, Kremers WK, et al. Association between olfactory dysfunction and amnesic mild cognitive impairment and Alzheimer disease dementia. *JAMA Neurol*. 2016;73(1):93–101.
- Reitz C, Tang MX, Manly J, Mayeux R, Luchsinger JA. Hypertension and the risk of mild cognitive impairment. *Arch Neurol*. 2007;64(12):1734–1740.
- Croy I, Nordin S, Hummel T. Olfactory disorders and quality of life—an updated review. *Chem Senses*. 2014;39(3):185–194.
- Pan CW, Wang X, Ma Q, Sun HP, Xu Y, Wang P. Cognitive dysfunction and health-related quality of life among older Chinese. *Sci Rep*. 2015;5:17301.