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Higher inflammation and cerebral white matter injury associated with cognitive deficit in asthmatic patients with depression

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ABSTRACT

Objective: Depression is a common co-morbidity in asthma, worsening asthma control and impairing quality of life. Previous studies have reported a higher risk of cognitive deficit in depression, yet little research has focused on the level of cognition in asthmatic patients with depression. Evidence shows that inflammation may play an important role in both asthma and depression. Cerebral white matter injury, possibly induced by inflammation, has been associated with depression. This study assesses cognitive function in patients with asthma and a depression comorbidity, compared to patients with asthma only or depression only.

Methods: Four groups were studied: Asthma comorbid Depression group (A + D, $n = 26$), Depression group (D, $n = 25$), Asthma group (A, $n = 33$) and Normal controls (N, $n = 28$). Cognitive function was evaluated using Montreal Cognitive Assessment (MoCA). Inflammatory cytokines were measured, including interleukin-1 β (IL-1 β), interleukin-6 (IL-6), tumor necrosis factor- α (TNF- α), high-mobility group box 1 (HMGB1) and Netrin-1. Cerebral white matter injury was assessed by serum myelin basic protein (MBP) and myelin oligodendrocyte glycoprotein (MOG), and their correlations with cognitive performance were calculated.

Results: A + D group showed the highest incidence of cognitive deficit, with the cognitive domain particularly affected. Compared to N group, serum levels of IL-6, HMGB1, Netrin-1, MBP and MOG were significantly elevated in A + D group. MOG level negatively correlated with the MoCA score.

Conclusion: Patients with comorbidities presented with more severe cognitive deficits and higher levels of inflammatory cytokines. Cerebral white matter injury may account for the cognitive deficit in patients and MOG could be a potential biomarker for this process.

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KEYWORDS

Depression; cognitive deficit; asthma; inflammatory cytokine; cerebral white matter

Introduction

Asthma is a common chronic disease characterized by bronchial hypersensitivity and airway inflammation, resulting in reversible airflow obstruction. An estimated 334 million people worldwide suffer from this disorder, causing a huge burden on society and individuals (1). Evidence has shown that patients with asthma have a 1.52 times higher risk of developing depression as compared to those without asthma, and depressive patients have an increased risk of asthma (OR 3.2) as compared to those who do not have depression (2). The comorbidity of asthma and depression is associated with poorer symptom control, impairing a patient's quality of life (3).

Depression, which affects people's thoughts, emotions, interpersonal relationships and work efficiency, is one of the most common mental disorders and is increasingly recognized as a global public health and social problem (4). Recently, more attention has been paid to the relationship between depression and cognition. Few research studies, however, have focused on the cognitive status of asthmatic patients with depression.

The pathogenetic mechanism of asthma is persistent airway inflammation (5), typically characterized by, but not limited to, atopic response with Th2-predominant inflammation (related to secretion of IL-4, IL-5 and IL-13) (6). Meanwhile, systemic inflammation with neutrophilic

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airway inflammation increases in patients with asthma, and is described by increased levels of inflammatory markers such as C-reactive protein (CRP), interleukin-(IL-) 6, IL-1 β , tumor necrosis factor- (TNF-) α , and leptin (7). Inflammation also plays a key role in depression. Accumulative studies have described higher levels of inflammatory cytokines in depressive patients (8–10). Moreover, treatment with anti-inflammatory agents, such as selective COX2 inhibitors and TNF antagonists, has been shown to improve symptoms in depressive patients (11). In recent years, new inflammatory cytokines have been investigated in studies for depression.

Our prior research observed that high-mobility group box 1 (HMGB1), along with traditional inflammatory cytokines, such as IL-1 β , TNF- α , were elevated in depressive mice (12). HMGB1, remaining at a high level 24 h after inflammatory activation and recognized as a late inflammatory mediator (13), has been reported to induce depressive behaviors in mice through neuroinflammation (14). Netrin-1, a new anti-inflammatory factor that plays a critical role in restraining inflammatory respond, was found to promote the proliferation and differentiation of oligodendrocyte precursor cells in favor of myelin recovery, resulting in the repair of cerebral white matter (15).

Given the critical role of inflammation in both asthma and depression, we aimed to seek evidence that inflammation might also be involved in the underlying process of cognitive deficit in the comorbid condition. We also sought to explore the differences in inflammatory cytokines in patients with comorbidity, with asthma alone, and with depression alone.

Immunity diseases targeting white matter, such as multiple sclerosis, have high incidences of depression as well as cognitive deficit (16). Elevated rates of cerebral white matter integrity abnormality on diffusion tensor imaging (DTI) have been reported in depression (17). Our previous research also showed that the serum levels of phospholipids were significantly elevated in patients with post-stroke cognitive deficit, indicating white matter injury (18). We further demonstrated its underlying mechanism, namely that white matter and oligodendrocyte changes driven by inflammatory reaction were associated with depression subsequent to cerebral ischemia (19). Similar results have been observed in other animal models by other researchers (20). These observations developed into a hypothesis that cerebral white matter damage may contribute to cognitive deficit in asthmatic patients with depression.

The present study aimed to assess cognitive function in patients with asthma and depression comorbidity, and to explore the role of inflammation and cerebral white matter injury in cognitive deficit. Furthermore, we attempted to screen for potential biomarkers of cognitive deficit in the comorbid condition and provide effective targets for further treatment.

Methods

Subjects

We recruited four groups of patients from different sources: 26 patients with Asthma comorbid Depression (A + D) (ages 27–70), and 33 Asthma (A) patients (ages 27–70) from the Respiratory Department, Changhai Hospital, Shanghai, China; and 25 Depression (D) patients (ages 24–79 years) from the Psychological Department at the same hospital. Twenty-eight (28) age, sex, and education matched healthy control subjects (N) (ages 40–65 years) were recruited from the general population.

Depression diagnosis was established according to the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-V) criteria (21), as assessed by the Structured Clinical Interview for DSM-V and Hamilton Depression Scale (HAMD). The standard Global Initiative for Asthma (GINA) diagnostic criteria (22) were adopted for including the asthma participants. Asthma related information including phenotype, severity assessment (i.e. respiratory function test, asthma control test (ACT)) and detailed therapy was collected for asthmatic patients. None of the patients were on oral corticosteroids therapy. Exclusion criteria included: (1) severe cardiac, hepatic and renal failure, (2) systemic diseases, such as malignant tumors or other neurological diseases leading to brain structural lesions, (3) history of taking psychotic drugs, (4) unable to complete the neuropsychological tests or unwilling to participate in the research.

The study protocol was approved by the local Institutional Research Ethic Committee and performed in compliance with the Code of Ethics of the World Medical Association (Declaration of Helsinki). All participants completed a written informed consent prior to participation.

Methods

Cognitive assessment

A standard Case Report Form was used to register demographic and medical data. Cognition was

Table 1. Demographic data and cognitive performance in N, D, A and A + D group.

Variables	N (n = 28)	D (n = 25)	A (n = 33)	A + D (n = 26)	F* or χ^2	p value
Demographic data						
Age (years)	50.86 (1.43)	48.36 (2.96)	47.72 (2.31)	55.65 (2.28)	2.419	0.070
Gender (female/all)	15/28	15/25	15/33	18/26	4.240	0.236
Education (years)	12.64 (0.41)	12.12 (0.75)	12.12 (0.54)	10.50 (0.67)	2.338	0.078
BMI (kg/m ²)	24.53 (0.66)	22.18 (0.64)	22.75 (0.50)	23.28 (0.72)	2.502	0.063
Hypertension	3/28	7/25	4/33	5/26	3.582	0.310
Diabetes	0/28	3/25	0/33	1/26	7.119	0.057
Smoking	10/28	5/25	10/33	4/26	7.525	0.058
Drinking	2/28	2/25	1/33	2/26	0.845	0.872
COPD	–	–	8/33	5/26	0.213	0.645
FEV1 (L)	–	–	1.86 (0.83)	2.00 (0.61)	2.583	0.115
FEV1% predicted	–	–	69.21 (15.02)	72.95 (12.42)	0.252	0.618
IgE (IU/ml)	–	–	200.44 (96.06)	244.62 (118.48)	1.469	0.231
FeNO (ppb)	–	–	50.19 (39.77)	74.56 (39.68)	0.000	0.992
Blood eosinophil count ($\times 10^9/L$)	–	–	3.46 (2.95)	3.21 (3.96)	1.888	0.177
Asthma phenotype	–	–				
Allergic asthma	–	–	15/33	12/26	0.003	0.957
Non-allergic asthma	–	–	18/33	14/26	0.003	0.957
Late-onset asthma	–	–	20/33	17/26	0.142	0.706
Asthma control test score	–	–	18.26 (5.14)	15.56 (6.24)	1.326	0.257
Asthma treatment	–	–				
Inhaled corticosteroid	–	–				
High doses	–	–	5/33	6/26	0.602	0.438
Medium doses	–	–	28/33	20/26	0.602	0.438
Long-acting β agonist	–	–	29/33	23/26	0.005	0.945
HAMD score	–	24.60 (2.81)	–	26.62 (4.30)	2.164	0.148
Cognitive performance						
MoCA	27.67 (0.26)	24.32 (0.66)	24.55 (0.68)	23.85 (0.61)	7.495	<0.001*
Naming	3.00 (0.00)	2.40 (0.18)	2.64 (0.12)	2.77 (0.43)	4.018	0.009*
Attention	6.00 (0.00)	5.52 (0.13)	5.64 (0.12)	5.35 (0.56)	5.826	0.001*
Language	2.79 (0.08)	2.88 (0.07)	2.97 (0.03)	2.50 (0.10)	8.503	<0.001*
Abstraction	1.67 (0.10)	0.84 (0.17)	0.64 (0.13)	1.15 (0.09)	12.238	<0.001*
Memory	3.50 (0.20)	2.92 (0.19)	2.70 (0.26)	2.73 (0.22)	2.489	0.064
Orientation	5.92 (0.06)	5.92 (0.06)	5.24 (0.16)	5.35 (0.10)	9.942	<0.001*
Visuoexecutive	4.63 (0.20)	3.48 (0.34)	3.81 (0.18)	3.85 (0.20)	4.036	0.009*

Results are shown as mean ($\pm$ SD); or as frequencies; high-dose was defined as $>640 \mu\text{g/day}$ budesonide or equivalent and medium-dose as ≥ 320 to $\leq 640 \mu\text{g/day}$ budesonide or equivalent.

N, healthy control; D, depression patients; A, asthma patients; A + D, asthma comorbid depression patients; BMI, body mass index; COPD, chronic obstructive pulmonary disease; FEV1, forced expiratory volume 1; IgE, immunoglobulin E; FeNO, fractional exhaled nitric oxide; HAMD, Hamilton Depression Scale; MoCA, Montreal Cognitive Assessment.

*F refers to the ratio of two variances.

evaluated by the Montreal Cognitive Assessment (MoCA) test, a sensitive instrument to measure global cognitive function including naming, attention, language, abstraction, memory and orientation, which is widely accepted for screening mild cognitive impairment. Data were normalized with age and education matched norms, and cognitive deficit was determined by a score of < 26 .

Inflammatory cytokines and white matter related indices

Blood samples were collected, centrifuged at 3000 rpm for 15 min, and stored at -80°C until thaw for further analysis. Serum levels of inflammatory cytokines (i.e. IL-1 β , IL-6, TNF- α , HMGB1, Netrin-1, IgE and eosinophil count), as well as cerebral white matter-related indices [(i.e. Myelin-basic protein (MBP) and myelin oligodendrocyte glycoprotein (MOG)], were assayed using a sandwich enzyme-linked

immunosorbent assay (ELISA, Shanghai Westang Biotechnology Company). All measurements were carried out at the same time in the same laboratory and strictly in accordance with the reagent box standard procedure.

Statistical analysis

Group comparisons were performed with a chi-square test for numeration data (i.e. gender, hypertension, diabetes, smoking, drinking and asthma disease related factors) and with analysis of variance (ANOVA) for measurement data (i.e. cognition score, inflammatory cytokines and white matter-related indices), respectively. The Bonferroni Test was used as a *post hoc* test to examine the differences between groups when a significant difference across four sample means was revealed. In addition, Spearman correlations were assessed between cerebral white matter

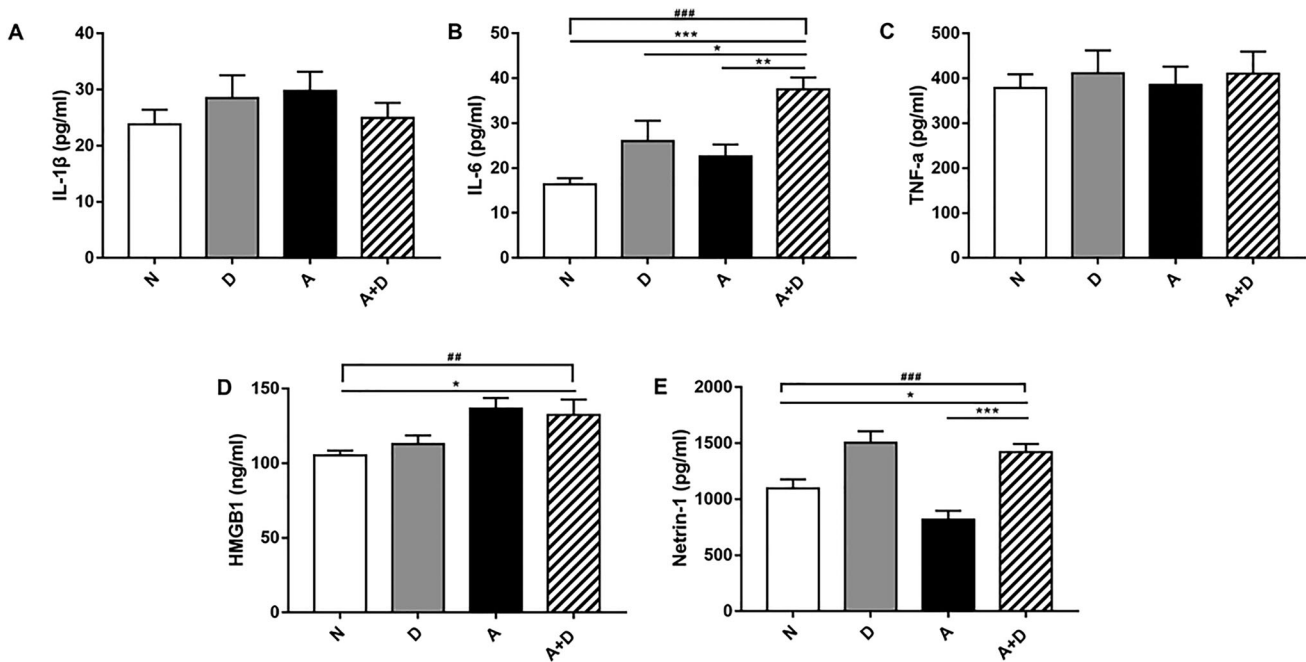


Figure 1. Inflammatory cytokines in four groups. (A) IL-1 β , (B) IL-6, (C) TNF- α , (D) HMGB1 and (E) Netrin-1 in normal control (N), depression (D), asthma (A) and asthma comorbid depression (A + D) group. ## $p < 0.01$, ### $p < 0.001$, for group comparisons; * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, for post hoc analysis.

related indices and inflammatory markers. Associations between MoCA score and cerebral white matter related indices/severity of asthma were also tested by correlation analysis.

Results

Demographic data

Table 1 presents the demographic data for four groups, including age, education, BMI index, gender, hypertension, diabetes, smoking, drinking, COPD history, depression score (HAMD), asthma phenotype, respiratory function test, asthma control condition (ACT), IgE, FeNO, eosinophil counts and therapy. No significant differences were found between groups. Asthmatic patients (i.e., A and A + D groups) were mainly affected by moderate asthma ($60\% \leq \text{FEV1}\% \leq 79\%$) and their symptoms were poorly controlled ($\text{ACT} < 20$). Depressive patients (i.e. D and A + D groups) presented moderate depression ($20 < \text{HAMD} < 35$) at the time of study.

Cognition evaluation

Cognitive deficit was observed in 13, 15 and 19 patients in D, A and A + D groups respectively, with the A + D group having the highest incidence of impaired cognition (73.08%) and the lowest score. The subtests of various cognitive domains in the

MoCA scale revealed significant differences among the four groups, as indicated by the “ F ” value. The degrees of freedom in the numerator and denominator are 3 and 108, respectively, as follows: $F_{\text{Naming}(3,108)} = 4.018$, $p = 0.009$; $F_{\text{Attention}(3,108)} = 5.826$, $p = 0.001$; $F_{\text{Language}(3,108)} = 8.503$, $p \leq 0.001$; $F_{\text{Abstraction}(3,108)} = 12.238$, $p \leq 0.001$; $F_{\text{Memory}(3,108)} = 2.489$, $p = 0.064$; $F_{\text{Orientation}(3,108)} = 9.942$, $p \leq 0.001$; $F_{\text{Visuoexecutive}(3,108)} = 4.036$, $p = 0.009$ (Table 1). The post hoc analyses showed that compared with the N group, the A + D group performed worse in overall MoCA score ($p < 0.001$), attention ($p < 0.001$), language ($p = 0.006$), abstraction ($p = 0.007$), orientation ($p = 0.001$) and visuospatial executive function ($p = 0.023$). In contrast to the D group, performance of the A + D group was better on naming ($p = 0.036$), while poorer on language ($p < 0.001$) and orientation ($p = 0.006$). Compared to the A group, the A + D group showed a significantly lower score for language ($p < 0.001$) and a significantly higher score for abstraction ($p = 0.004$).

Inflammatory cytokines

Variance analyses showed significant differences in IL-6, HMGB1 and Netrin-1 among the four groups ($F_{\text{IL-1}\beta(3,108)} = 0.791$, $p = 0.502$; $F_{\text{IL-6}(3,108)} = 9.630$, $p < 0.001$; $F_{\text{TNF-}\alpha(3,108)} = 0.161$, $p = 0.922$; $F_{\text{HMGB1}(3,108)} = 4.495$, $p = 0.005$; $F_{\text{Netrin1}(3,108)} = 13.258$, $p < 0.001$). The post

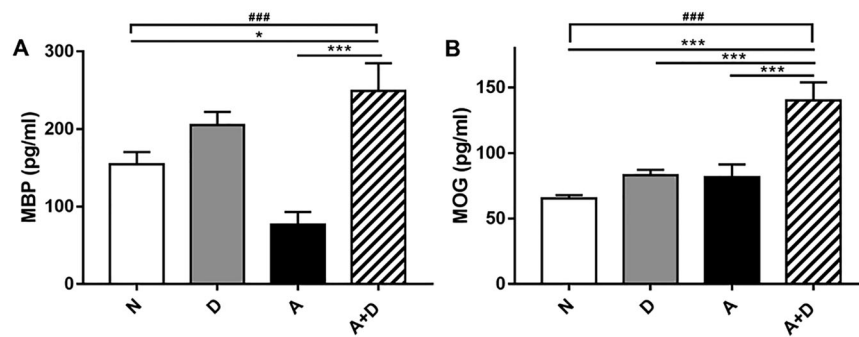


Figure 2. Cerebral white matter related indexes in four groups. (A) MBP and (B) MOG in normal control (N), depression (D), asthma (A) and asthma comorbid depression (A + D) group. $^{##}p < 0.01$, $^{###}p < 0.001$, for group comparisons; $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$, for post hoc analysis.

hoc analyses showed that IL-6 increased significantly in the A + D group compared to the N group ($p < 0.001$), D group ($p = 0.044$), and A group ($p = 0.0027$). Similar results were observed for HMGB1, which was significantly elevated in the A + D group versus the N group ($p = 0.041$). In contrast to the N and A groups, the A + D group showed a significantly increased Netrin-1 level ($p = 0.04$, $p < 0.001$) (Figure 1).

Cerebral white matter related indices

As shown in Figure 2, ANOVA results showed a significant difference between groups in MBP and MOG ($F_{\text{MBP}(3,108)} = 9.743$, $p < 0.001$; $F_{\text{MOG}(3,108)} = 13.714$, $p < 0.001$). Post hoc analyses revealed that MBP was significantly higher in the A + D group than in N ($p = 0.0214$) and A groups ($p < 0.001$). MOG was significantly enhanced in the A + D group compared with the other three groups ($p < 0.001$).

Association between cerebral white matter related indices and inflammatory markers

Table 2 shows the correlation coefficients between cerebral white matter related indices (i.e. MBP and MOG) and the peripheral inflammatory markers (i.e. IL-1 β , IL-6, TNF- α , HMGB1, Netrin-1, eosinophil and IgE) in the A + D group. Significant correlation was found between TNF- α and MBP ($r = 0.525$, $P = 0.008$). However, there was no significant correlation between other white matter related indices and inflammatory markers.

Correlation related to MoCA score

In order to screen a sensitive biomarker for cognitive deficit in depression, we conducted the Spearman correlation analysis within the A + D group between the

MoCA score and the peripheral serum indices, which showed significant between-group variance (i.e. IL-6, HMGB1, Netrin-1, MBP and MOG). We observed a negative correlation between the MoCA score and MOG ($r = -0.476$, $P = 0.014$, Figure 3) in the A + D group, indicating that white matter injury revealed by elevated MOG could imply a cognitive deficit in patients with comorbidity. However, no significant correlation was found between MoCA and MOG in the N, D, and A group. In addition, inflammatory indices were not correlated with MoCA score in all groups.

We additionally conducted the correlation analysis between MoCA score and severity of asthma in A group, A + D group and both asthmatic group (i.e. A and A + D group) respectively. Results showed that MoCA score did not correlate with FEV1% ($r_A = -0.165$, $p_A = 0.475$; $r_{A+D} = 0.086$, $p_{A+D} = 0.691$; $r_{\text{both}} = -0.069$, $p_{\text{both}} = 0.655$), nor with ACT score ($r_A = -0.280$, $p_A = 0.195$; $r_{A+D} = -0.036$, $p_{A+D} = 0.895$; $r_{\text{both}} = -0.183$, $p_{\text{both}} = 0.265$) in all three groups, indicating that cognitive deficit was not directly affected by the severity of asthma.

Discussion

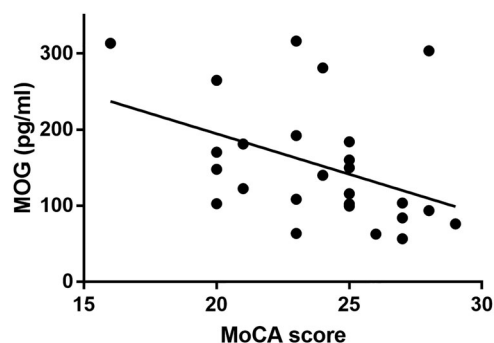
The present study demonstrated impaired cognitive performance, as well as elevated inflammatory cytokines (IL-6, HMGB1, Netrin-1) in patients with asthma and depression comorbidity. Moreover, we found a significant elevation in white matter lesion-related indices (MBP, MOG), one of which negatively correlated with cognitive performance. These findings provide important evidence on the potential mechanism of cognitive deficit in asthmatic patients with depression.

Existing studies have recognized cognitive burden in patients with asthma (23). Specifically, asthma has a strong effect, not only on broader capacities

Table 2. Association between white matter related indices and inflammatory markers in the A + D group.

		IL-1 β	IL-6	TNF- α	HMGB1	Netrin-1	Eosinophil	IgE
MBP	<i>R</i>	-0.059	-0.173	0.525	0.15	0.349	0.229	0.012
	<i>P</i>	0.785	0.42	0.008	0.466	0.087	0.332	0.954
MOG	<i>R</i>	0.283	-0.129	0.31	0.184	0.096	-0.137	-0.144
	<i>P</i>	0.181	0.549	0.141	0.389	0.654	0.588	0.503

A + D, asthma comorbid depression patients; IL-1 β , interleukin-1 β ; IL-6, interleukin-6; TNF- α , tumor necrosis factor- α ; HMGB1, high-mobility group box 1; IgE, immunoglobulin E; MBP, myelin basic protein; MOG, myelin oligodendrocyte glycoprotein.

**Figure 3.** Correlation between MoCA score and MOG in the A + D group by Spearman's analysis.

involving academic achievement and global intellect, but also on particular cognitive domains, such as processing speed, executive function, attention, visuospatial functioning, language, learning, and memory (24). However, there is little research on cognition in patients with asthma and depression comorbidity. Our preliminary investigation showed that the A + D patients presented higher incidence of cognition deficit compared to patients with single asthma or depression and healthy controls. The particularly vulnerable cognition domains included attention, language, abstraction, orientation, visuospatial and executive function. The vulnerability of specific cognitive domains remains to be verified with more delicate neuropsychological assessments, and its underlying mechanism needs to be further explored.

Alterations in the immune systems are very likely to contribute to the increased risk of co-occurrence of asthma and depression (25). One study reported an elevated CRP level in children and adolescents with both diseases (26). Another study on gene expression of blood CD4⁺ T cells from comorbid patients showed that the main active pathways in depressive asthma are IL-6 and CRP signaling (27). In our study, the acute inflammatory mediator IL-6 was elevated significantly in the A + D group. This finding partly aligns with a previous meta-analysis illustrating that concentrations of cytokines, such as IL-1, IL-4, IL-6, TNF- α , were higher in depressive patients than in non-depressive controls (2). Furthermore, we discovered a significant increase in HMGB1 and Netrin-1 in A + D patients. HMGB1 has been shown to be

involved in the diseases characterized by chronic inflammation, especially in pulmonary pathology (28), and is elevated in the depressive animal models established for chronic stress (29). Considering that asthma comorbid with depression could be a chronic inflammatory reaction, it would be reasonable to find increased HMGB1 in patients with both diseases.

As a new anti-inflammatory factor, Netrin-1 is expressed in both acute and chronic inflammatory response. Considerable numbers of studies have demonstrated that Netrin-1 plays a role in acute inflammation, such as acute lung injury or pancreatitis by restraining inflammatory damage (30,31). Interestingly, we also found elevated Netrin-1 in asthma patients with depression. A possible explanation is that the chronic inflammatory response in the A + D group may induce a simultaneous process of compensatory protective reaction. Therefore, IL-6, HMGB1 and Netrin-1 may be sensitive indices that reflect the activation of multiple inflammatory pathways in comorbid asthma and depression.

As cerebral white matter-related indices maintain the structure and function of myelin in the central nervous system (CNS), MBP and MOG have been reported to increase significantly in the peripheral blood of depressive individuals (32,33). To our knowledge, there is still a lack of data on the alterations in white matter-related markers in asthma patients. Our study showed that both MBP and MOG increased significantly only in patients with asthma and depression comorbidity, similar to the findings in patients with depression. This may indicated that MBP and MOG were more affected by asthma-induced depression, but not by pathophysiological reaction of asthma itself. We assumed that asthma may induce depression by certain triggers (i.e. stress, systematic inflammation, etc), and the increase of MBP and MOG could be a manifestation of depression related pathophysiological process. The relationship between inflammation and white matter has been largely explored. In the present research, we found that TNF- α was associated with MBP in the A + D group, indicating that the type-1 inflammation, rather than the type-2 inflammation, could be more related to white matter injury. Our previous work (34), as well as other research (35), has

demonstrated that systemic inflammation could alter the development of white matter by blocking the maturation process of oligodendrocytes through changing the coordinated expression of several transcription factors. Given the above empirical evidence, our results of elevated MBP and MOG may suggest an important pathophysiological alteration in asthma and depression comorbidity, that is, white matter damage.

Furthermore, our study showed that cognitive deficit was negatively correlated with MOG, indicating that white matter lesions may result in cognitive alteration in asthmatic patients with depression. This result was consistent with a previous imaging study, showing a negative correlation between cognition, depressive syndrome and white matter hyperintensities (36). A recent DTI study further illustrated that MOG correlated positively with white matter damage in depression (33). Despite a minor component of myelin sheath (0.01–0.05% of the membrane protein) compared to MBP (30% of the membrane protein) (37). MOG has been exclusively expressed in oligodendrocytes in the CNS (38). MBP, however, was found to additionally express in the peripheral nervous system and cells of the immune system (39). We hypothesize that MOG may be a more specific index than MBP to reflect CNS myelin injury in brain, and therefore, could be a more sensitive biomarker of cognitive deficit in asthma patients with comorbid depression.

The present study has some limitations. First, this is a cross-sectional study, and therefore is unable to determine a causal relationship between cognitive deficits and inflammation or white matter injury. Indeed we included a relatively small sample size which limited the statistical power of the present study. It would be of greater value to investigate the emotion and cognition alterations in a larger number of patients with different severity of asthma and in a follow-up observation cohort. Nevertheless, we observed a phenomenon, which could provide a clue on this relationship. Further research is needed to elucidate its potential mechanism. Second, we performed only the MoCA test as an assessment tool of cognition, which is used routinely as a screen test for mild cognitive deficit. Complete and detailed neuropsychological assessments are encouraged, such as the Wechsler Intelligence Scale and other cognition battery tests, which evaluate multiple cognitive domains. Third, we provided evidence of white matter injuries by means of serum markers, but there is a lack of structural or functional image findings. More research using advanced neuroimaging technic is needed to explore the unique

characteristics of white matter injury in the asthma and depression comorbid condition.

Conclusion

The present study identified a high incidence of cognitive deficit and inflammatory cytokine levels in patients with asthma and depression comorbidity. Cognitive deficit was not directly affected by the severity of asthma. Cerebral white matter injuries characterized by increased levels of MOG could be a potential biomarker of this process.

Disclosure statement

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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