

Environmental perceptions, mental performance, and physiological responses of people with respiratory allergies exposed to reduced Indoor Air Quality

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Abstract

To investigate the need of allergic population for indoor environment quality, exposure effects of poor air quality on subjects with respiratory allergies were compared with those on healthy people, including perceptual responses, health symptoms, mental performance, and physiological responses. The experimental intervention was with and without ventilation at thermally neutral rooms, creating two exposure conditions indicated by CO₂ concentration ranges of 502 to 3297 ppm (2438 ± 1527 ppm) and 517 to 5687 ppm (3615 ± 1527 ppm). 63 subjects (32 allergic subjects and 31 non-allergic subjects) were exposed to both conditions for 3 hours. The main results suggested that, compared with healthy people, people with respiratory allergy seem to be more sensitive or less acceptable to reduced air quality polluted by occupants during instantaneous exposure. Besides, the allergic group performed worse in cognitive tests than non-allergic group. After 3 hours of continuous exposure, people with respiratory allergy reported stronger intensity of respiratory irritations and seemed to suffer more inflammation indicated by a higher level of interleukin 1L-1β.

KEYWORDS

CO₂ concentration, human bioeffluents, mental performance, odor perception, physiological responses, respiratory allergic people

1 | INTRODUCTION

Respiratory allergy, such as allergic rhinitis and asthma, is a type of respiratory tract inflammatory disease caused by IgE, involving a variety of inflammatory cells and inflammatory mediators.¹ In recent years, the prevalence of respiratory allergies has increased significantly around the world. An investigation on the prevalence of self-reported allergic rhinitis in China showed that the prevalence increased from 11.1% in 2005 to 17.6% in 2011.² Another study reported that the prevalence of asthma among Chinese children increased from 1.85% to 5.34% from 1990 to 2010.³ With the increasing in the number of people with allergies, their specific needs

are worthy of attention when establishing indoor environment standards or developing indoor environmental control strategies. However, current Indoor Air Quality standards and ventilation standards are primarily based on the responses of healthy occupants, and provide no terms for allergic population.

Although physiological studies have provided strong evidences on the susceptibility of people with allergies,⁴⁻⁷ only a few studies have compared the environmental assessments and responses of allergic and healthy people exposed to the same indoor environment.

There were some studies comparing Indoor Air Quality perceptions between allergic and non-allergic people, but no consistent conclusions are drawn so far. For example, a telephone survey by

Kreutzer et al. showed that people with asthma reported themselves being more sensitive to chemicals.⁸ In another study, Lundin⁹ investigated 943 students with allergies (asthma, hay fever, eczema) and 772 healthy students at five high schools on perceived indoor environment of school in a small town in southern Sweden. Their results showed that compared with non-allergic students, allergic students sensed environmental factors affecting health earlier, felt that smell, light, and noise inside the classroom were worse ($p < 0.05$), and were more dissatisfied with indoor cleanliness and air quality. On contrary to these two studies, Tham and Fadeyi¹⁰ found that, when exposed to ozone, limonene and its derivatives for 3 hours, asthmatic people were more receptive to Indoor Air Quality and seemed less sensitive to poor air quality than non-asthmatic people, although there was no difference between the two groups in evaluating odors in the room. In the other experiment by Fadeyi et al.,¹¹ they exposed asthmatic and non-asthmatic people to indoor environment with new and old air-conditioning filters for 3 hours, and observed no difference in odor assessment between the two groups. Li et al.¹² compared the perceptual response of 19 pairs of students with and without allergic rhinitis sleeping in the same dormitories on a university campus in China and found no difference in the subjective ratings of odor intensity, air freshness, or air quality acceptability between the two groups before and after sleep. Norbäck et al.¹³ observed also no difference in perceived Indoor Air Quality between 78 allergic students and 277 healthy students when they were exposed in classrooms with different ventilation rates. During 4.25-hour exposure to carbon dioxide and human bioeffluents, Zhang et al.¹⁴ collected the ratings of odor intensity and air quality acceptability by 8 allergic subjects and 17 healthy subjects, and saw no difference between two groups.

Some research compared the thermal and humid sensation of two population groups. In the study by Tham and Fadeyi,¹⁰ compared with non-asthmatics, asthmatic subjects felt cooler at 21°C and warmer at 25°C. Graudenz et al.¹⁵ found that when the room temperature was at 14°C, the group with allergic rhinitis felt the room air was drier than the non-allergic group. The other research reported no difference in temperature and humidity perception between allergic and non-allergic people in the same environment.¹²⁻¹⁴

In addition to environmental perception, some researchers compared differences in health symptoms, work performance, and sleep quality between the allergic subjects and non-allergic subjects. Tham and Fadeyi¹⁰ found that asthmatic people had lower subjective votes for irritants (eyes, nose, and throat) than healthy people, but severe intensity in some of the symptoms (headache and chest tightness); the attention test was completed faster but with lower accuracy. Besides, the variation of saliva α -amylase concentration before and after exposure was significantly higher than that of healthy subjects, indicating that the stress level of asthmatic subjects was more susceptible to adverse environmental effects. Li et al.¹² compared the sleep quality of students with allergic rhinitis and healthy students in the same environment, and found that students with allergic rhinitis had a worse sleep quality indicated by a high proportion of rapid eye movement sleep periods and a low proportion of light sleep periods.

Practical Implications

- Present results supplemented the current evidence on the need of allergic population for indoor air quality, in the case that the primary pollution sources were the building occupants themselves.
- Compared with healthy people, allergic subjects seemed to be more sensitive to reduced air quality and their mental performance was deteriorated more.
- Current findings might suggest that indoor air quality settings should give priority to the needs of allergic people.
- More studies are necessary to verify these findings and to establish exposure-response relationship for allergic people.

As it can be seen, current results on responses of allergic population during indoor exposures were insufficient and controversial. To provide more evidence on this issue, an online survey has been conducted in China inquiring respondents' sensitivity to changes in environmental factors including indoor air temperature, indoor relative humidity, indoor air freshness, and outdoor air pollution. A total of 1293 valid questionnaires were obtained from 30 provinces in China, including 478 allergic subjects and 815 non-allergic subjects. Based on this investigation, over 70% of allergic subjects reported themselves to be more sensitive to four respective environmental factors than general population, which was statistically higher than the ratio of non-allergic subjects. Moreover, allergic population considered air quality as a primary focus among all indoor environment factors.¹⁶

To further investigate the need of allergic population for indoor environment quality, present study was carried out to examine the responses of allergic subjects during typical indoor exposure. According to the online survey mentioned earlier, Indoor Air Quality seems to be the most concerned factor by allergic people. Moreover, an increasing number of studies have shown that indoor air pollution was strongly associated with prevalence of allergic symptoms and risk of allergic diseases.¹⁷⁻¹⁹ Thus, exposure effects of different air qualities were firstly studied on perceptual responses, health symptoms, mental performance, and physiological responses of people with respiratory allergies.

2 | EXPERIMENT DESIGN

2.1 | Subjects

The subjects were recruited from a university in Beijing. A power analysis was conducted to estimate the number of subjects efficient for statistical tests. With the present experimental design, the minimum number of subjects was calculated to be 52

persons. Taking balance of order of exposure into account, totally 64 subjects were recruited for this experiment. In the healthy group, there were 15 males and 16 females, with an average age of 24.4 years and an average body mass index (BMI) of 20.6 kg/m². Among the subjects in the allergic group, there were 25 males and 7 females, with an average age of 24.3 years and an average BMI of 22.5 kg/m². The intension of the present work was to include equal number of male and female subjects in both healthy and allergic groups, but it appeared that allergic subjects were difficult to recruit. As a consequence, allergic subjects participating in the experiment were not even in gender. For healthy group, a male student failed to attend the experiment for personal reason, which resulted in a gender imbalance in the healthy group. The difficulty in recruiting allergic subjects brought another problem. That was not all of the allergic subjects participating in the experiment had been diagnosed by a doctor. Specifically, twenty-eight students (87.5%) in the allergic group were diagnosed with allergic rhinitis and/or asthma by professional physicians, while four subjects (12.5%) reported themselves having allergic rhinitis but had not been medically diagnosed yet. This information was obtained through a questionnaire on general health checkup, which was distributed to respondents during the recruitment process. 53.1% allergic subjects reported that they were suffering allergic symptoms during the experiment. The basic information of the subjects is shown in Table 1. This study was approved by the ethics committee of Beijing University of Technology.

2.2 | Facilities

This experiment was carried out in two adjacent office rooms with same dimensions of 3.3 × 5.7 × 3.3 m (length × width × height). As shown in Figure 1, each office was equipped with 8 worktables consisting of a table, a chair, and a laptop. An individual air conditioner and a humidifier were installed in each room to control the indoor temperature at 22°C and the relative humidity at 50% throughout the experiment. The interventions of two experimental conditions were with or without outdoor fresh air ventilation by running two wall-mounted fresh air units or not. The fresh air supply rate was measured to be about 12.6 L/s in the condition with fresh air units on. Before each session, the doors and windows were opened for thorough ventilation of the experimental rooms in order to get approximative background condition. Then, doors and windows were always kept closed during the experiment sessions.

During the experiment, indoor air temperature, relative humidity, and carbon dioxide (CO₂) concentration were monitored

continuously at three points, which were equidistantly arranged on the central axis of the room at the height of breathing zone of seated subjects (about 1.1 m above the floor). The recording interval was 5 minutes. Besides, noise and illuminance of each room were measured once during each experimental condition. Information of measuring instruments is listed in Table 2.

2.3 | Questionnaires

In order to investigate the comprehensive impacts of indoor environment on people with respiratory allergy, three questionnaires were distributed. Specifically, they concern about: (1) perceptual responses including thermal sensation and acceptability, odor intensity, air quality acceptability, and irritations on nose, throat, and skin; (2) general health symptoms such as headache, chest tightness, difficulty in concentration, fatigue, and depression; and (3) subjective assessments on how they performed on mental tasks. All subjective ratings were collected using visual analog scales. The thermal sensation was obtained using ASHRAE 7-point scale. The acceptability voting scale was consisted of two continuous scales: completely unacceptable to just unacceptable (−1 to −0.01), and just acceptable to completely acceptable (0.01 to 1). Odor intensity was measured with a 6-point scale from none (0) to overwhelming (5). The other outcomes, including irritations, health symptoms, and mental performance assessments, were recorded using two-endpoint continuous scales. The left endpoint indicated no irritation, no symptom, or low performance, while the right indicated very strong irritation, severe symptom, or high performance. The subjects were instructed to mark down at any position according to their feeling by drawing one tick mark on each scale. After the experiment, the ratings were coded by experimenters as continuous values on a scale of 0 to 100, with 0 and 100 assigned to left and right endpoint, respectively.

2.4 | Mental performance

Four cognitive tasks, including a neurobehavioral test battery, d2 attention test, Tsai-Partington test, and numerical calculation, were conducted as measures of mental performance. The neurobehavioral test battery was done on a computer, while the other three were paper version tests.

The neurobehavioral test battery consisting of ten types of tests was used to simulate a variety of office tasks.²⁰ This battery can examine the subjects' attention level (Name of the test: Memory span), the visual perception and semantic interference ability (Stroop

TABLE 1 Basic information of subjects (Mean ± SD)

	Number (male/female)	Age (years)	Height (cm)	Weight (kg)	BMI (kg/ m ²)
Allergic subjects	25/7	24.3 ± 1.8	171.9 ± 8.8	67.5 ± 10.7	22.5 ± 2.3
Non-allergic subjects	15/16	24.4 ± 1.2	167.6 ± 7.4	57.8 ± 7.7	20.6 ± 1.3

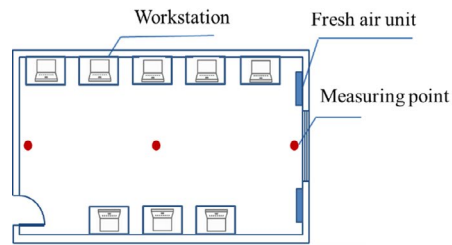


FIGURE 1 Schematic diagram (left) and real scene (right) of experiment room

TABLE 2 Instruments for environmental measurements

Environmental parameters	Model	Range	Accuracy
Air temperature (°C)	TR-76Ui	0–55	±0.5
Relative humidity (RH%)		10–95	±0.5
CO ₂ concentration (ppm)		0–9999	±50
Noise (dB(A))	testo 815	32–130	±1
Illumination (lx)	Z-10	0.01–300 000	4%*

*According to Verification Regulation of Illuminance Meter in China (JJG245-2005).

test), visual signal response ability (Visual choice reaction time), logic reasoning ability (Event sequence), digital memory (Symbol-digital modalities test), spatial reasoning (Overlapping), graphics memory (Picture recognition), quick response ability (Continuous perform test), spatial orientation ability (Re-direction test), and space imagination ability (Graphic abstracting). The indexes of all tests in this battery but memory span test were accuracy and reaction time. For Memory span test, memory span and reaction time were recorded.

The d2 attention test was used to reflect a subject's attention level. In this test, subjects were required to find the “d” with two dots in each line within 20 s. The evaluation indicators were the number of letters checked per minute, the target omission rate, and the number of mislabeling. Tsai-Partington test is a cue-utilization test which can reflect the stress level of the subjects. Participants were required to connect the 32 numbers scattered on A4 paper in ascending order within 40 seconds. The evaluation index was the number of correct connections. For numeric calculation task, the subjects were required to complete the three-digit multiplication within given period. The evaluation index was error rate and speed at which the subjects did the task.

2.5 | Physiological measurements

Previous researches show that exposure to CO₂ and human bioeffluents has significant effects on function of human respiratory system, cardiovascular system, and nervous system.^{14,21,22} Therefore, in this experiment, several physiological parameters that can reflect the function of these three systems were measured. They



FIGURE 2 Measurements of respiratory (left) and cardiovascular (right) parameters

TABLE 3 Balanced exposure order to both conditions of each group

	Tuesday	Wednesday	Thursday	Friday
1st week	C1-A1	C1-B1	C2-A2	C2-B2
	C2-B1	C2-A1	C1-B2	C1-A2
2nd week	C1-A3	C1-B3	C2-A4	C2-B4
	C2-B3	C2-A3	C1-B4	C1-A4

Note:: 1. C represents for condition, C1 and C2 denote the conditions without and with outdoor fresh air supply, respectively;
2. A and B represents allergic group and non-allergic group, respectively; 1, 2, 3, and 4 represent group number.

were fraction of inspiration CO_2 (FiCO_2), end-tidal CO_2 (ETCO_2), airway respiration rate (AwRR), heart rate, blood pressure, saliva α -amylase, and cortisol level. In addition, interleukin 1L-1 β was selected as index of potential inflammatory response of respiratory allergic population.

Parameters of respiratory system : FiCO_2 , ETCO_2 , AwRR. FiCO_2 and ETCO_2 can be used to detect the partial pressure of inhaled and exhaled CO_2 , reflecting the balance between human breathing and metabolism. AwRR represents the number of breaths per minute. These three parameters were measured using PMSH-300 handheld monitor manufactured by Suzhou Beifulai medical Co., LTD. During the measurement, the seated subjects were required to breathe naturally, and to wear a disposable nasal oxygen tube to connect with the monitor (see Figure 2).

Parameters of cardiovascular system : heart rate and blood pressure. These two parameters were measured with ihealth BP5 portable blood pressure monitor, which can record heart rate, systolic blood pressure, and diastolic blood pressure in real time.

Parameters of nervous system : salivary α -amylase and cortisol. The concentrations of salivary α -amylase and cortisol can reflect the level of stress caused by the autonomic nervous system. Saliva contains almost all the biochemical components of blood, and it can be collected by non-invasive means, which is more convenient and effective than blood collection. In this experiment, a special saliva collection tube (SARSTEDT Salivette) was used for collection. The subjects chewed the cotton rolls from the saliva collection tube for 1 minute and then placed them back in the plastic tube. This way of collection is safer, cleaner, and more convenient. After collection, the saliva samples were stored at -20°C and sent to a professional laboratory for analysis by enzyme-linked immunosorbent assay (ELISA).

Parameters of inflammation : Interleukin 1L-1 β . Interleukins are a class of cytokines produced by and acting on a variety of cells. They play an important role in a series of processes such as the maturation, activation, proliferation, and immune regulation of immune cells. Interleukin 1L-1 β is a form of interleukin 1L-1 that is also detected in saliva. The majority of interleukin 1L-1 are pro-inflammatory cytokines, whose main role is to stimulate the expression of genes related to inflammation and autoimmune diseases, and play an important role in immune regulation and inflammation.

2.6 | Experiment procedure

The experiment was conducted in the morning from 08:30 to 11:30 in two consecutive weeks in March 2019. Students with and without respiratory allergies were randomly divided into four groups of eight persons, respectively. For group 4 of healthy students, one

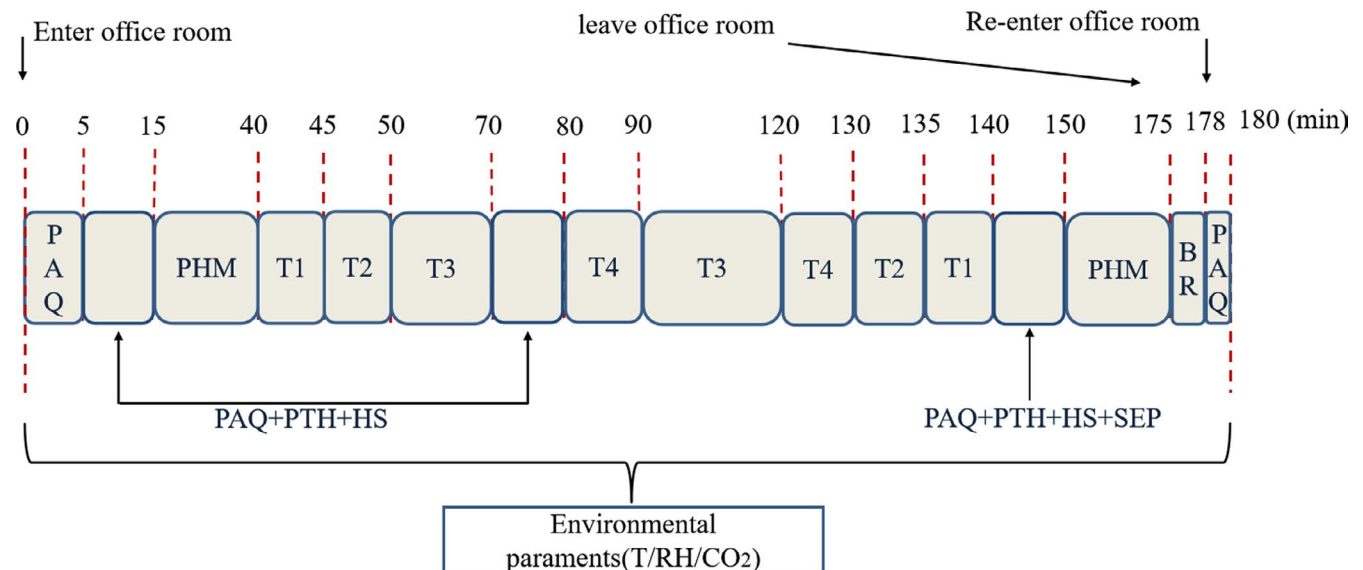


FIGURE 3 Experiment procedure. Note: PAQ stands for perception of Indoor Air Quality. PTH stands for perception of indoor thermal and humid environment. HS stands for health symptom. PHM stands for Physiological measurement. T1, T2, T3, and T4 stand for d2 attention test, Tsai-Partington test, neurobehavioral test battery, and numeric calculation test. SEP stands for self-estimated performance. BR stands for break

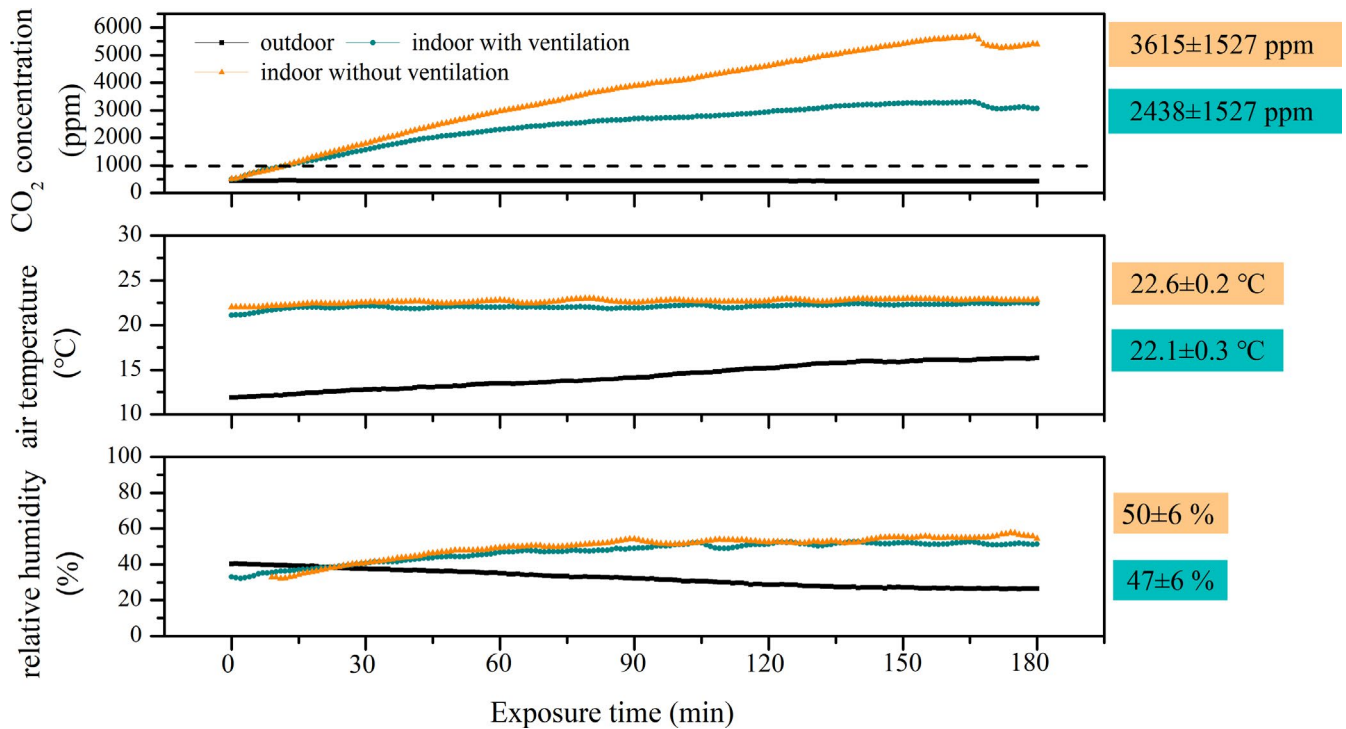


FIGURE 4 Measured indoor and outdoor CO₂ concentration, temperature, and relative humidity during experiments

person was absent. Each subject participated in both conditions. The groups were exposed to two conditions in balanced order, as seen in Table 3. All subjects were required to participate in a training session before the formal experiments. Kind reminder was provided for subjects regarding adequate sleep, a light diet before experiment and adjustable clothes so as to maintain the thermally neutral state. As shown in Figure 2, the clothing of the subjects generally included long-sleeve thick sweater, long-sleeve shirt, thick trousers, ankle-length socks, shoes, and underwear. The thermal resistance of the clothing was estimated to be about 1.12 clo. During the experiment, subjects were prohibited from using personal items with a strong flavor. The experimental procedure on each session is shown in Figure 3. Subjects followed the instruction by experimenter to complete each section.

2.7 | Data analysis method

The data were analyzed using SPSS Statistics 25 software. The data obtained in this experiment do not follow the normal distribution. Therefore, non-parametric test was used to compare whether there is a significant difference in the distribution between different populations. Three tests including Mann-Whitney *U* test, Wilcoxon test, and Friedman test were adopted for different scenarios. Specifically, Mann-Whitney test and Wilcoxon test were used for two independent samples and two paired samples, respectively. Friedman test was applied for comparison among three samples or more. Significance level was set to 0.05.

3 | RESULTS

3.1 | Environmental parameters

Figure 4 shows the trends of indoor and outdoor CO₂ concentration, temperature, and relative humidity during the experiment. It can be seen that the outdoor CO₂ concentration remained at 437 ± 8 ppm; the indoor CO₂ concentration increased continuously due to accumulation of CO₂ generated by the breathing and metabolic processes of subjects. Under the condition of ventilation, due to the continuous supplement of outdoor fresh air, the growth rate of indoor CO₂ was significantly lower than that under the condition of no ventilation. The range of measured indoor CO₂ concentration under the two conditions was 502–3297 ppm (2438 ± 1527 ppm) and 517–5687 ppm (3615 ± 1527 ppm), respectively. At the 165 minutes, the door to experimental room was briefly opened as the subjects left the room, leading to a decrease in CO₂ concentration. During the experiment, the outdoor air temperature increased from 11.9°C to 16.3°C, while the indoor temperature remained stable in both two conditions under the control of air conditioner. The temperature in the condition with ventilation was 22.1 ± 0.3 °C, and that in the condition without ventilation was 22.6 ± 0.2 °C. The outdoor relative humidity fluctuated within 25%–41% and decreased with time. Indoor relative humidity in the two conditions gradually increased due to the application of humidifier and the breathing and skin metabolism of subjects, and eventually maintained at about 55%. Indoor temperature and relative humidity were basically stable with no difference between conditions, while CO₂ concentration was significantly

different. In addition, the noise level was 37 dB(A) and the illumination was 654 lx, which conformed to the limit value of offices by indoor environment standards.

3.2 | Perception of environment

The results of indoor environment perceptions showed that there was no difference between the allergic subjects and non-allergic subjects under the two conditions. Both groups of subjects felt thermally neutral in two conditions and had a high acceptability of thermal and humid environment. Together with the records of environmental parameters, it showed that indoor thermal and humid environment was well controlled and accepted during the experiment.

Figure 5 shows subjects' ratings of odor intensity in the office room. As can be seen from the figure, at the beginning of exposure, when the indoor CO₂ concentration was around 500 ppm, the voting value of the two groups was near 1. That is, subjects sensed only slightly unpleasant odor in the room. Along with exposure, the indoor CO₂ concentration continued to increase under the two conditions (Figure 4), but the subjective evaluation of odor intensity of the two groups remained basically unchanged. By the end of the exposure, subjects were asked to leave the laboratory for three minutes and then re-entered the room to assess odor intensity once again. At this time, the indoor CO₂ concentration was about 3297 ppm with ventilation and 5666 ppm without ventilation. Subjects sensed that the odor intensities were significantly increased compared with the first four ratings. In addition, the odor intensity rated by the two groups in the condition without fresh air supply was significantly stronger than that in the condition with fresh air supply. No significant difference was observed in odor intensity perception between the allergic group and the healthy group.

Figure 6 shows the results of the acceptability of air quality. In the condition with ventilation, the acceptability of Indoor Air Quality assessed by both groups was consistently high throughout the exposure. In the condition without ventilation, the acceptability of the allergy group decreased as a whole. Especially when re-entering the room for an instant vote, the allergy group reported that the Indoor Air Quality was unacceptable, and the average indoor CO₂ concentration was 5666 ppm. At the same time, the air quality acceptability of the healthy group was significantly lower than that of ventilation conditions. The acceptability of two groups was significantly different from the results of the previous four times.

3.3 | Health symptoms and comfort

Figure 7 shows the subjective assessment on health symptom and comfort after 3 hours of exposure. Compared with allergic group, when exposed to the same condition, allergic group reported stronger nose and throat irritations but less headache and chest tightness. In the condition without ventilation, the symptoms of throat irritation, headache, and chest tightness of subjects in both two groups tended to be worse than that in the condition with ventilation.

3.4 | Mental performance

It can be seen from Figure 4, cognitive performance was measured using two identical test blocks which consisted of four tasks. The two test blocks were conducted consecutively, each lasted for 50 minutes representing a common work period. In both conditions, there was no significant difference in results of two test blocks conducted

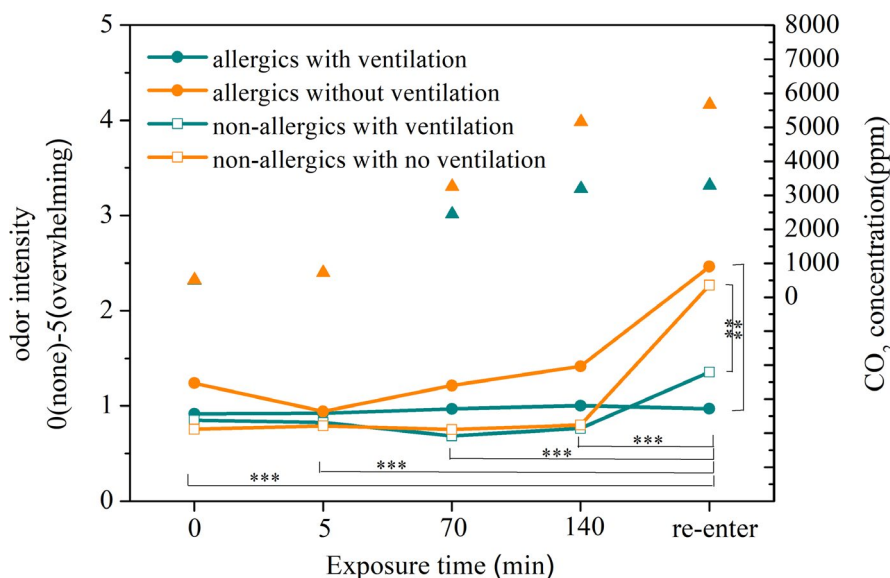


FIGURE 5 Rating of odor intensity (*, **, and *** denotes $p < 0.05$, $p < 0.01$, and $p < 0.001$ respectively)

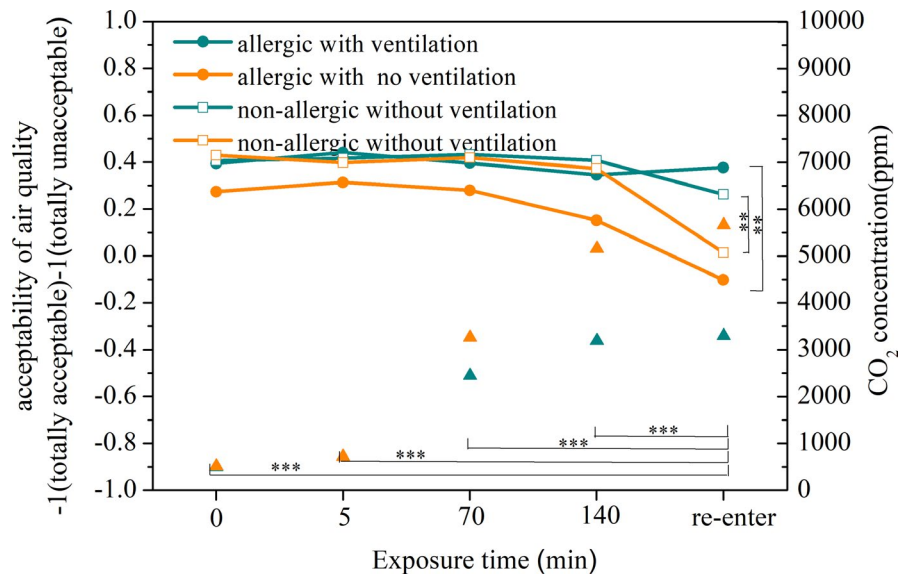


FIGURE 6 Rating of acceptability of air quality

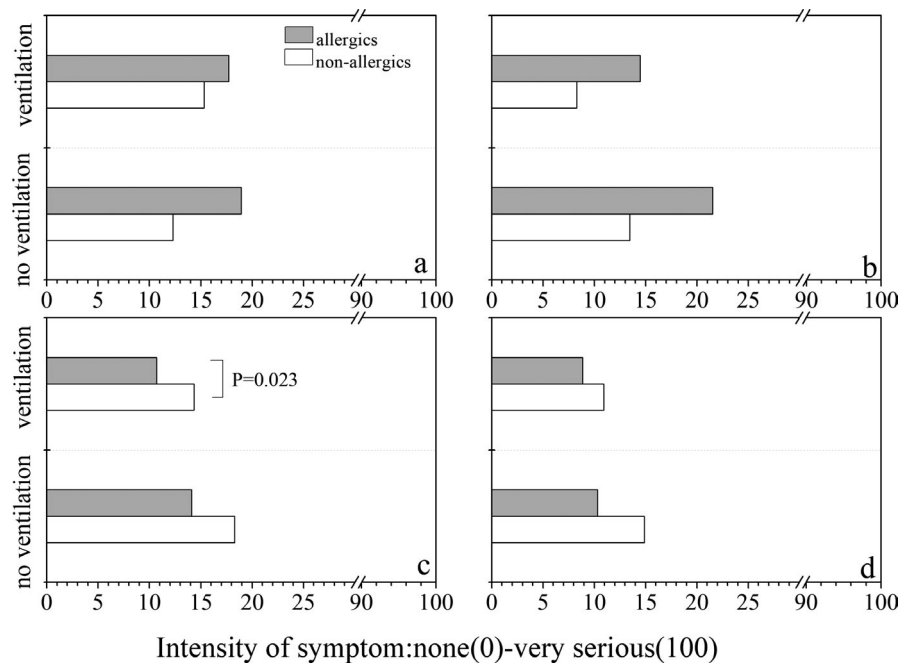


FIGURE 7 Ratings of health symptoms (A: nose irritation; B: throat irritation; C: headache; D: chest tightness).

at different exposure times. Therefore, average measures of two blocks were presented in this subsection.

As shown in Figure 8, compared with healthy group, allergic group generally took longer to complete neurobehavioral tests. In the ventilation condition, allergic subjects needed significantly longer response time on Event sequence test than healthy subjects. In the condition without ventilation, significant difference between two groups in response time for more tests was observed including Visual choice response time, Picture recognition, Re-direction test, Symbol-digit modalities test, Event sequence, and Graphic abstracting. Furthermore, for Event sequence test and Graphic abstracting which were more mentally demanding, the

difference in response time between the two groups was more obvious than that of the other simple tests. There was no difference between the two groups in Memory span, and response time of Stroop test, Overlapping and Continuous perform. No difference between subject groups in accuracy of all tests was observed either. Comparison between conditions showed that the allergic group took significantly longer to complete the Visual choice response time and the Re-direction test in condition without ventilation than that in ventilation condition.

Figure 9 shows the error rate and speed at which subjects performed multiplication task. In the condition with ventilation, allergic subjects spent more time on each unit on average and made

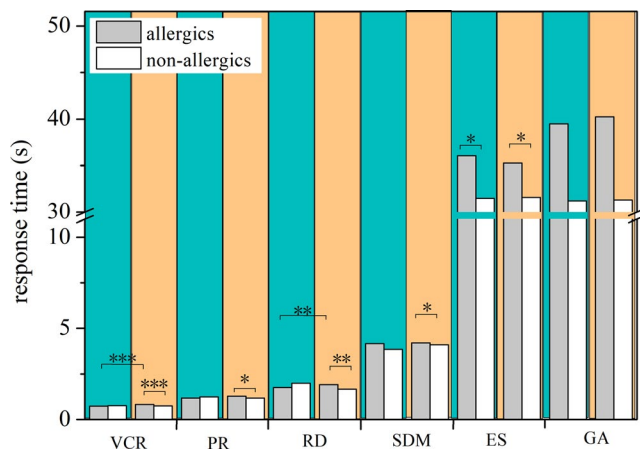


FIGURE 8 Results of neurobehavioral test (Green/orange fillings represent ventilation/no ventilation condition respectively, VCR stands for Visual choice response time, PR stands for Picture recognition, RD stands for Re-direction test, SDM stands for Symbol-digit modalities test, ES stands for Event sequence, GA stands for Graphic abstracting)

more errors than healthy subjects. The differences in both indexes between two groups were statistically significant. In the condition without ventilation, no such difference was observed. For healthy group, subjects completed multiplication task with a significantly lower speed in the condition without ventilation than that in ventilation condition. For allergic group, no difference between conditions was observed.

Figure 10 shows the results of d2 attention test. It can be seen that, in the condition with ventilation, the number of letters examined per minute by the allergy group was significantly less than that by the health group. In the condition without ventilation, opposite trend was observed between groups. This was because the speed of the health group significantly decreased while the

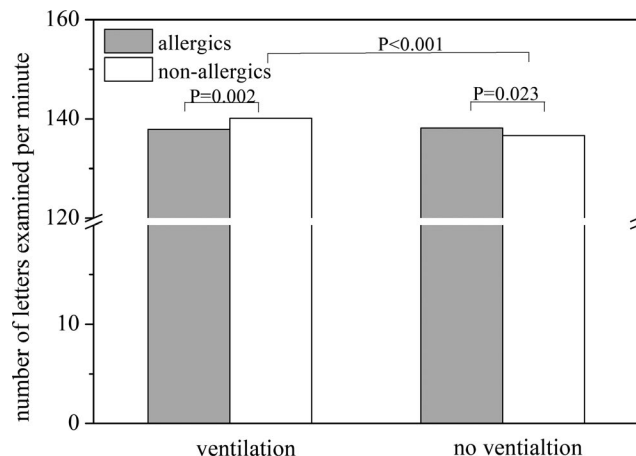


FIGURE 10 Results of d2 test

speed of the allergy group remained unchanged when the condition altered.

Figure 11 shows that in Tsai-Partington test, the number of letters connected per minute by the allergy group was consistently higher in both conditions than that by the healthy group, but it was not statistically significant.

3.5 | Physiological parameters

Physiological measurements were conducted twice during each exposure at the 15th and 150th minute. Table 4 shows the measured values and difference between two measurements. The results showed that the changes in measured physiological parameters of both groups in both conditions were in accordance with the rhythm of human body. That is, along with exposure, blood pressure, heart rate, and salivary cortisol concentration decreased, while the

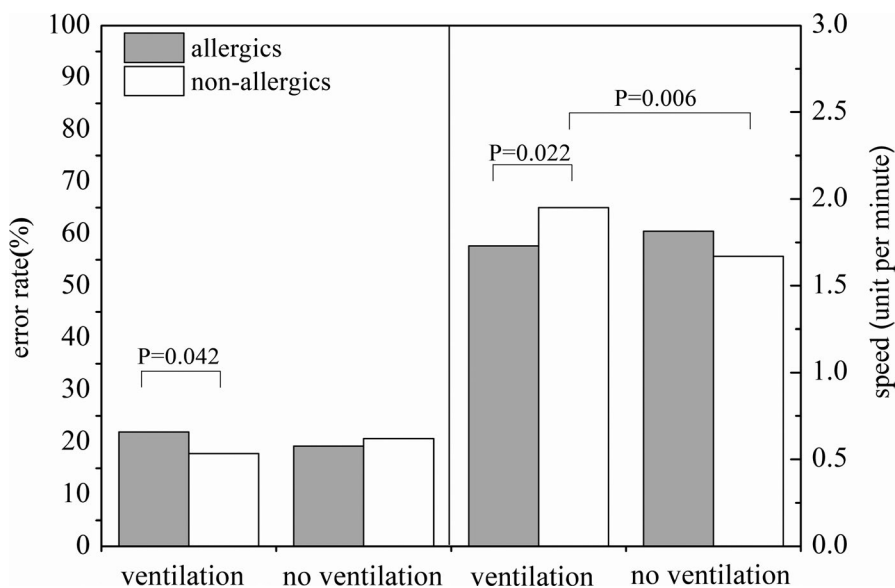


FIGURE 9 Results of multiplication test

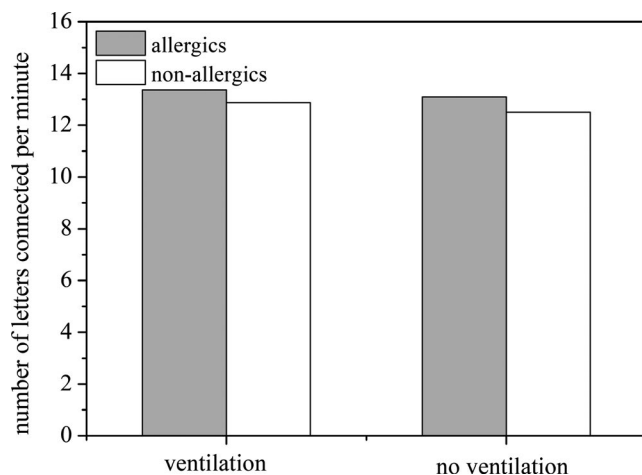


FIGURE 11 Results of Tsai-Partington test

concentration of salivary α -amylase and interleukin 1L-1 β increased. Besides, there were more changes in systolic blood pressure, heart rate, and cortisol level of both subject groups in the condition without ventilation than that with ventilation condition, while the change in concentrations of salivary α -amylase and interleukin 1L-1 β showed the opposite trend. In addition, FiCO₂ increased more in the condition without ventilation, while changes in ETCO₂ and airway respiration rate were similar in two conditions. Comparing the data of the allergic group and the healthy group, it was found that the decrease in heart rate of the former group during exposure was significantly greater than that of the latter group in the condition without ventilation. There was no difference in other physiological parameters between the two groups.

4 | DISCUSSION

It is known that the evaluation of the indoor odor by occupants and visitors is different.²³ As Figure 5 shows, during continuous exposure, the evaluation of unpleasant odor at 5th, 70th, and 140th minute by all subjects remained nearly unchanged, although the indoor CO₂ concentration increased and Indoor Air Quality decreased with the increase in the exposure time. This was due to the olfactory adaptation. By the end of each exposure, upon re-entering into the room with high CO₂ concentration and poor Indoor Air Quality, the subjects as visitors reported significantly stronger odor than the previous four evaluations. There was no difference in odor intensity assessment between allergic subjects and non-allergic subjects. However, the acceptability of Indoor Air Quality exhibited difference between subject groups. For allergic group, overall Indoor Air Quality acceptability reduced significantly in the condition without ventilation compared with ventilation condition. For healthy group, significant reduce in air quality acceptability was observed only upon re-entering the experiment room when indoor CO₂ concentration was as high as 5666 ppm.

Present result shows that allergic subjects seem to be less acceptable to reduced air quality polluted by occupants than healthy

people. This agrees with the finding by Lundin⁹ who reported that allergic students seem to be more sensitive to the environmental factors affecting health. There were other three similar studies performed at student dormitories, classrooms, and climate chambers.¹²⁻¹⁴ Like present study, in these three studies, the dominate pollutant sources were humans and the intervention was ventilation rate. However, none of them observed differences in air quality perception by allergic people and non-allergic people. One thing worthy of mention is that the number of two subjects groups in two of the three studies was uneven, which may interfere their results.^{13,14} One study by Tham and Fadeyi¹⁰ observed opposite results. They found that asthmatic people were less sensitive to unpleasant Indoor Air Quality polluted by ozone, limonene, and their derived chemical products. In their other study, they observed no difference in the air quality perception by subjects with and without asthma in the room ventilated with new or used air-conditioning filters.¹¹ According to the above findings, air quality perception by allergic people may be related with pollutants. More studies are needed for firm conclusion.

Allergic group reported more severe irritation in nose and throat than healthy group. This was consistent with the results we obtained in a field investigation on sleep environment.¹² After a whole night sleep in same dormitory, allergic students tended to feel more dryness in nose and throat. The reason people with allergic rhinitis are more vulnerable to poor air quality may be that the nasal mucosa of the allergic is more fragile. Oxidative stress reactions will occur when the harmful substances in the environment come into contact with the nasal mucosa. In a stress state, a large number of reactive oxygen radicals are suddenly produced due to metabolic abnormalities, which damage biomolecules, and further cause cell death and tissue damage, resulting in irritation and dryness symptoms.²⁴ In addition, oxidative stress response also leads to an increase in neutral inflammatory cells and aggravation of inflammatory response.²⁵ The relationship between CO₂ concentration and interleukin 1L-1 β concentration was depicted in Figure 12. It was estimated that interleukin 1L-1 β concentration achieves a peak level when CO₂ concentration was around 4000 ppm. When CO₂ concentration was less than 4000 ppm, interleukin 1L-1 β concentration was positively correlated with CO₂ concentration, while above 4000 ppm, the two were negatively correlated. This finding was consistent with the literature. Thom et al.²⁶ incubated human and murine neutrophils ex vivo in buffer equilibrated with 0.1%–0.4% additional CO₂, and observed increased production rate of microparticles with elevated amounts of interleukin 1L-1 β content. Their result showed that the interleukin 1L-1 β concentration first increased then decreased with increasing CO₂ concentration, and the peak was at 4000 ppm. In the other paper by Thom et al.,²⁷ they confirmed this result using a murine model. They exposed mice to 2000 or 4000 ppm CO₂ for 2 hours and found elevations in circulating microparticles and interleukin 1L-1 β content. Moreover, the increase was much greater after 4000 ppm exposure than that after 2000 ppm. According to Thom et al., elevations of CO₂ commonly occurring in modern buildings will stimulate neutrophils to produce microparticles containing high levels of 1L-1 β , and activate inflammasome due to mitochondrial

TABLE 4 Physiological parameter measurement results (Mean $\pm$ SD)

	Time (min)	Ventilation		No ventilation	
		Allergic subjects	Non-allergic subjects	Allergic subjects	Non-allergic subjects
Systolic blood pressure	15	117 $\pm$ 12	109 $\pm$ 9	116 $\pm$ 12	114 $\pm$ 11
(mmHg)	150	116 $\pm$ 15	110 $\pm$ 10	113 $\pm$ 8	111 $\pm$ 10
Δ		-1 $\pm$ 10	1 $\pm$ 7	-3 $\pm$ 9	-3 $\pm$ 8
Diastolic blood pressure	15	73 $\pm$ 8	71 $\pm$ 8	73 $\pm$ 9	73 $\pm$ 9
(mm Hg)	150	75 $\pm$ 10	72 $\pm$ 9	73 $\pm$ 8	73 $\pm$ 7
Δ		1 $\pm$ 9	2 $\pm$ 8	1 $\pm$ 9	0 $\pm$ 8
Heart rate	15	77 $\pm$ 14	74 $\pm$ 10	78 $\pm$ 12	76 $\pm$ 11
(times/min)	150	70 $\pm$ 13	66 $\pm$ 7	67 $\pm$ 10	69 $\pm$ 10
Δ		-8 $\pm$ 7	-8 $\pm$ 6	-11 $\pm$ 7*	-7 $\pm$ 6*
Cortisol	15	14.8 $\pm$ 0.8	14.9 $\pm$ 0.8	17.6 $\pm$ 1.9	17.8 $\pm$ 1.4
(nmol/L)	150	13.2 $\pm$ 1.2	13.2 $\pm$ 1	14.5 $\pm$ 0.8	14.7 $\pm$ 0.8
Δ		-1.7 $\pm$ 1.5	-1.7 $\pm$ 1.4	-3.2 $\pm$ 2.1	-3.2 $\pm$ 1.4
Salivary α -amylase	15	82 $\pm$ 9.9	84.1 $\pm$ 9.3	78.3 $\pm$ 13.8	75.8 $\pm$ 9.4
(U/L)	150	106.4 $\pm$ 15.3	109.1 $\pm$ 13.6	88.3 $\pm$ 12.4	88.6 $\pm$ 11.3
Δ		24.4 $\pm$ 19	25 $\pm$ 14.2	10 $\pm$ 16.6	12.9 $\pm$ 15.4
Interleukin 1L-1 β	15	41 $\pm$ 4	40.2 $\pm$ 2.4	40.8 $\pm$ 4.3	40.7 $\pm$ 3.9
(pg/mL)	150	53.6 $\pm$ 4.9	52.2 $\pm$ 3.9	48.6 $\pm$ 5.3	48.8 $\pm$ 5.4
Δ		12.7 $\pm$ 6.5	12 $\pm$ 4.3	7.8 $\pm$ 6.2	8.2 $\pm$ 7.6
ETCO ₂	15	4.9 $\pm$ 0.6	5 $\pm$ 0.5	5.2 $\pm$ 0.5	5.1 $\pm$ 0.5
(%)	150	5.2 $\pm$ 0.7	5.2 $\pm$ 0.6	5.3 $\pm$ 0.5	5.3 $\pm$ 0.6
Δ		0.3 $\pm$ 0.7	0.2 $\pm$ 0.5	0.2 $\pm$ 0.4	0.3 $\pm$ 0.5
FiCO ₂	15	0.4 $\pm$ 0.2	0.4 $\pm$ 0.2	0.4 $\pm$ 0.2	0.4 $\pm$ 0.1
(%)	150	0.9 $\pm$ 0.1	0.9 $\pm$ 0.1	1.2 $\pm$ 0.1	1.2 $\pm$ 0.1
Δ		0.6 $\pm$ 0.2	0.6 $\pm$ 0.3	0.8 $\pm$ 0.2	0.8 $\pm$ 0.2
AwRR	15	15 $\pm$ 6	16 $\pm$ 5	13 $\pm$ 4	15 $\pm$ 4
(times/min)	150	16 $\pm$ 5	15 $\pm$ 4	14 $\pm$ 4	16 $\pm$ 4
Δ		0 $\pm$ 6	-1 $\pm$ 4	1 $\pm$ 3	1 $\pm$ 4

*Stand for a statistical difference between the allergy group and the healthy group ($p = 0.026$).

oxidative stress. These reactions could cause further negative impacts on human body. Abolhassani et al.²⁸ analyzed in vitro the inflammatory responses induced by exposure to CO₂ for 48 hours (0, 5, 10, 15, and 20% with a constant O₂ concentration of 21%), and observed in vivo the responses of mice exposed to elevated levels of CO₂ for 1 hours (0, 5, 10, and 15% with a constant O₂ concentration of 21%). They demonstrated pulmonary inflammatory effects of CO₂ exposure by increased secretion of pro-inflammatory cytokines such as interleukin, but at levels higher than the environmentally relevant concentrations. Figure 12 also shows that the level of interleukin 1L-1 β in the allergic group was higher when CO₂ concentration was above 4000 ppm which may indicate that in the case of poor air quality, the inflammatory response in the allergic group was stronger. This provided new evidence on the hypothesis, proposed by previous researchers, that allergic subjects were more vulnerable to

indoor air pollutants due to various inflammatory responses. When inhaling increased concentration of CO₂, allergic subjects' C-fiber sensory nerves will be stimulated due to damaged epithelial barrier and release neuropeptides.²⁹ These contents had been demonstrated to be responsible for various inflammatory diseases,³⁰ and thus, they could aggravate the inflammatory effects of CO₂ exposure on allergic subjects.

Present results also show that compared with the CO₂ concentration of 2438 ppm, when the indoor average CO₂ concentration was 3615 ppm, the respiratory irritation symptoms, headache, and chest tightness of healthy subjects were worsened. This was consistent with the results of previous studies on exposure effects of ventilation rates and elevated CO₂ concentrations on healthy subjects. Seppänen et al.³¹ reviewed the relationship between SBS symptoms and ventilation rate and indoor CO₂ concentration, and found that

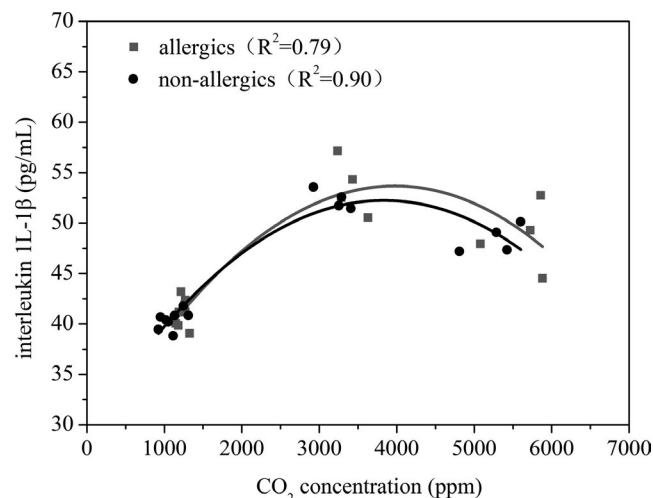


FIGURE 12 The relationship between carbon dioxide concentration and interleukin 1L-1 β level

when ventilation rate was lower than 10 L/s/p, ventilation rate was significantly negatively correlated with SBS symptoms. Zhang et al.¹⁴ compared the acute healthy symptoms of people at different levels of human metabolic pollutants, which were characterized by CO₂ concentrations of 500, 1000 and 3000 ppm, respectively. Their results showed that when CO₂ concentration was 3000 ppm, the symptoms of headache and fatigue were significantly worse compared with that when CO₂ concentration was 500 ppm.

In this experiment, allergic subjects performed less well in mental tests than healthy subjects. They took longer to complete the neurobehavioral ability test, had higher error rate and lower speed in multiplication task, and examined fewer letters in the d2 attention test. The influence of Indoor Air Quality on mental performance is complex and multifaceted. In terms of neural mechanism, work performance is mainly affected by the central nervous system. Poor Indoor Air Quality with unpleasant odor could affect cognitive performance in two possible pathways.³² On the one hand, odorous substances in the environment can make subjects to have olfactory judgment through the olfactory system. On the other hand, they can have an impact on the limbic system and trigger behavioral responses. Hippocampus and the amygdala in limbic system are the basic structures responsible for learning, memory, motivation, and emotion.^{33–36} Indoor exposure to pollutants can lower the activity of astrocytes in nerve cells and affect neuronal regulation, transmission of neurotransmitters, and the function of the hippocampus and the amygdaloid nucleus.^{37,38} Consequently, learning and memory ability, work motivation, and enthusiasm might be reduced. Physiological researches show that the epithelial layer which protects the C-fibers is either denudated or damaged in asthmatics.³⁹ C-fibers carry message toward the central nervous system. Stimulation of C-fibers by unfavorable exposure will cause various physiological problems. This may explain why asthmatic people are more vulnerable to adverse exposure to environmental pollution.

A number of studies on the relationship between ventilation rate, CO₂ concentrations, and work performance have shown that

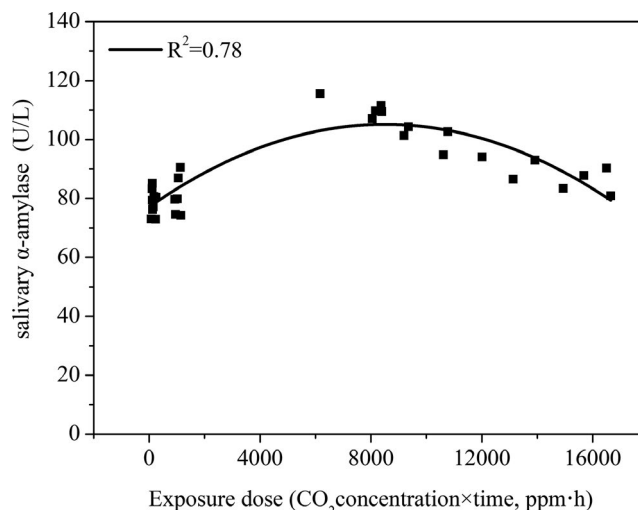


FIGURE 13 The relationship between salivary α -amylase levels and CO₂ exposure dose

reduced ventilation rate or increased CO₂ levels deteriorating Indoor Air Quality could worsen mental performance. In the study by Zhang et al.,¹⁴ subjects were exposed for 4 hours to three indoor CO₂ concentrations at 500, 1000, and 3000 ppm by changing ventilation rates. They observed significant reduce in performance of addition task and Tsai-Partington test under the condition of 1000 and 3000 ppm. Maula et al.⁴⁰ exposed subjects to two different indoor CO₂ concentrations at 2260 ppm (2.3 L/s/p) and 540 ppm (28.2 L/s/p) for 4 hours and found that the speed at which subjects completed the information retrieval test decreased at 2260 ppm. Shaughnessy et al.⁴¹ asked the subjects to complete strategic management simulation tests under CO₂ concentrations of 900 ppm (8.5 L/s/p) and 1800 ppm (2.6 L/s/p). Under the CO₂ level at 900 ppm, subjects scored higher on completing the test. In this experiment, response of allergic subjects was slower in Visual choice response time and Re-direction test (Figure 8) in the condition without ventilation. For non-allergic subjects, the performance of multiplication was reduced indicated with an increased error rate and a reduced speed (Figure 9). So was decreased the speed of d2 attention test (Figure 10). Present results exhibit same trend with the previous findings.

The negative effects of reduced ventilation rate on mental performance have been hypothesized to be associated with increased arousal/stress level under poor air quality condition.^{11,42,43} It has also been demonstrated that the elevated arousal/stress level will increase the salivary α -amylase secretion, which reflects the activity of the sympathetic part of the autonomic nervous system.^{44,45} In this study, by fitting the relationship between salivary α -amylase level and exposure dose, it was found that the concentration of salivary α -amylase increased first and then decreased with the increase in cumulative exposure level (Figure 13). Present data agreed with previous findings. In two series of experiments, Zhang et al.^{14,42} analyzed the levels of salivary amylase at four different CO₂ exposure doses (2125, 4250, 12 750, and 20 000 ppm·h) and found that the

concentration of salivary amylase increased with the level of exposure up to 12 750 ppm·h, then reduced at the exposure level of 20 000 ppm·h. Vehviläinen et al.⁴⁶ also found lower salivary amylase levels at high exposure dose of 10 304 ppm·h compared with a low exposure level at 3624 ppm·h. Summarizing current evidences, it can be speculated that exposure to moderate concentrations of CO₂ and other human bioeffluents commonly experienced in civil buildings could cause increase in the subjects' stress level, as indicated by elevated salivary α -amylase levels. As a consequence, the mental performance may be affected. The results also showed that relatively high exposure dose will inhibit the secretion of salivary α -amylase levels. However, the reason for the contrary effect observed at relatively high exposure dose was unclear based on current evidence, and more investigations on this observation are needed.

In this experiment, the conditions were created to simulate typical indoor condition where building occupants were the major pollutant sources. Previous research has shown that other indoor environmental factors could also be associated with allergic diseases/symptoms. Deng et al.¹⁷ investigated 2598 Chinese children and found that indoor renovation and mold/dampness were risk factors. Redecoration activities and new furniture materials could emit many VOCs and SVOCs, while dampness could stimulate growth of various biological agents. As a result, they suggested that initiatives to avoid exposure to new furniture and house redecoration and measures to prevent indoor mold/dampness are beneficial to reduce the prevalence of allergic diseases/symptoms. In order to avoid emissions from other indoor surface or materials, present experiment was carried out at an office room without any furniture or decorations. There was no mold or dampness occurring inside the experimental room, either. Nevertheless, the negligible emission from other indoor sources than human bodies cannot be assured due to a lack of comprehensive measure of indoor air pollutants. On the other hand, since the components of human bioeffluents are extremely complicated and vary with time, CO₂ concentration was selected as indicator of exposure level. Therefore, it needs to be clarified that the observed effects in this experiment should be attributed to all pollutants generated by occupants not only CO₂ itself. Unfortunately, exact characteristic of bioeffluents was not provided in the present experiment, although such work is necessary. Especially the components of bioeffluents should be determined resulting in sensory discomfort and related symptoms. It is essential that future studies address this issue.

Another characteristic of exposure conditions in present study is that steadily increasing CO₂ concentration was adopted, which differed from those studies using constantly elevated CO₂ levels throughout the exposure. Although we retained the original statement of exposure conditions in the referred researches, which were average concentrations generally, it should be kept in mind when understanding current findings since different exposure patterns could produce different effects. For instance, in terms of physiological reactions to CO₂, the body adaptation and compensation process is dependent on the concentration administrated as well as the exposure duration.^{47,48} There have been extensive evidences from special work

environment such as spacecrafts and submarines, but these concentrations were very higher than exist in normal buildings. As for cognitive performance of increased CO₂ exposure in humans, the findings of existing research were conflicting.^{49,50} The inconsistency may be attributable in part to the wide variability in CO₂ concentration, exposure duration, and the techniques achieving experimental conditions. To draw firm conclusions, it is worth study whether the same cumulative exposure quantity occurring indoors but different exposure pattern will lead to different effects.

One limitation of this study was that no condition with CO₂ level lower than 1000 ppm was examined. Conditions with more CO₂ levels should be set and compared with conditions below 1000 ppm, so as to provide more suggestions for the indoor environmental demand of respiratory allergic people. Another limitation of the present work could be that the subjects were not balanced in gender. To examine whether males and females responded differently in the present experiment, supplementary analyses were performed on assessments of Indoor Air Quality and healthy symptoms and the results of mental performance. No significant differences were observed between responses of male subjects and female subjects in either healthy group or allergic group. Thus, there is no indication that the results of the present experiments were biased by gender of subjects. However, it should be noticed that the number of male subjects was much higher than the number of female subjects in allergic group and that the order of presentation of exposures to these subjects was not balanced either. This could disturb the results of analyses.

Furthermore, it should be noted that only 17 out of 32 allergic subjects were in allergic state during the experiment, while the other 15 subjects were not. Allergic subjects' reactions might be related to whether or not they were in allergic state. According to a previous field investigation on allergic students concerning about dormitory environment and their sleep quality, students suffering allergic symptoms during investigation reported stronger intensities of nose dryness and throat dryness and seemed to sleep less well than those allergic students who were not in allergic state.¹² So supplementary comparison of responses between these two groups was also conducted in the present study, but no difference was observed between the allergic subjects with and without symptoms during the experimental exposures. This result seemed to be inconsistent with expectation, but it could be possible. Since the allergic state of the subjects cannot be deliberately controlled, it was not possible to assign equal number of subjects in two different states to each exposure day in advance. Consequently, with the current experimental design, the number of subjects who were in allergic state or not was not even, and the exposure order of both groups was imbalanced. Moreover, the number of subjects in both groups was halved, reducing the power of statistical analysis, which could also affect the comparison results. In summary, based on present data, it cannot be determined whether there was difference in exposure responses between subjects who were suffering allergic symptoms or not. Nevertheless, present outcomes can still provide practical implications. Since in actual indoor environment there are in fact

both allergic populations with and without symptoms. Considering there was no significant difference between the responses of two groups, their data were pooled together for analysis in current study. However, adequate comparison between different allergic states of subjects is worth to do.

In addition, although present study intended to provide comprehensive understanding on whether allergic subjects responded differently with healthy subjects, it should be acknowledged that the findings of the present study were not firmly conclusive due to the limitations mentioned above. In order to establish the accurate exposure-response relationship of allergic population in typical indoor environment, each exposure aspect examined in the present experiment was worthy of further studies with more rigorous subject recruitment and more robust experimental design.

5 | CONCLUSION

1. This study examined the responses of people with respiratory allergies during 3-hour exposure to reduced air quality polluted by occupants, as indicated by an average CO₂ concentration of 2500 and 3600 ppm, respectively. Subjective ratings of Indoor Air Quality indicate that people with respiratory allergy seem to be more sensitive or less acceptable to reduced air quality polluted by occupants during instantaneous exposure.
2. Compared with non-allergic subjects, the allergic group performed worse in cognitive tests, manifested by lower rates and more errors.
3. After 3 hours of continuous exposure, people with respiratory allergy reported stronger intensity of respiratory irritations. Meanwhile, the level of interleukin 1L-1 β was higher in allergic group than that in healthy group, which may indicate more inflammatory responses in allergic subjects during exposures. According to present results, priority should be given to the needs of allergic group when the major pollution sources were the occupants.

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