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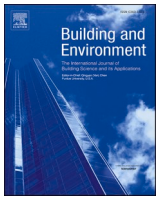

Ventilation causing an average CO_2 concentration of 1,000 ppm negatively affects sleep: A field-lab study on healthy young people

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ABSTRACT

Poor bedroom ventilation, leading to poor indoor air quality (IAQ), has been shown to reduce sleep quality. Ventilation causing a carbon dioxide (CO_2) concentration of 1,000 ppm is assumed to permit optimal sleep quality. The effects of three ventilation levels causing average indoor CO_2 concentrations of 750 ppm, 1,000 ppm and 1,300 ppm, on sleep quality, physiological response and next-day work performance were examined. After a first night for adaptation, thirty-six young and healthy participants slept alone in simulated bedrooms for two nights at each of the three ventilation levels in balanced order. Sleep quality was recorded by a wrist-worn sleep tracker. Physiological parameters were measured before sleep and after waking. The participants' ratings of the bedroom environment, the intensity of the health symptoms they experienced, and cognitive performance were obtained using questionnaires and tests.

Compared with ventilation causing an average CO_2 concentration of 750 ppm, sleep quality was significantly reduced at the ventilation rates causing CO_2 concentrations of 1,000 ppm and 1,300 ppm: Sleep efficiency was reduced by 1.3 % and 1.8 % and time awake increased by 5.0 min and 7.8 min, respectively. Deep sleep duration decreased at the ventilation rate causing CO_2 concentration of 1,300 ppm as compared to 750 ppm along with a significant increase in salivary cortisol after waking, which suggests increased stress and sympathetic activity. Ventilation causing an average CO_2 concentration of 1,000 ppm or above in bedrooms should therefore be avoided. Participants whose sleep quality was poorer performed worse on tests of cognitive performance the next day.

1. Introduction

Sleep is essential for human health and well-being. Good sleep not only helps to restore physical strength [1], improve immunity [2] and reduce the risk of metabolic diseases [3–5] and cardiovascular problems [6], but also ensures improved next-day work performance [7,8], which will have a positive impact on economic development [9].

Recent research has found that bedroom ventilation has an impact on sleep quality. In many field studies, opening windows and doors was used to change the ventilation rate. Mishra et al. [10] reported that when the windows and doors were closed (resulting in a low ventilation rate and an average CO_2 concentration of 1,150 ppm), objectively measured sleep onset latency and wakefulness were higher and sleep efficiency was lower than when the door or a window was open. Fan et al. [11] performed measurements in 40 bedrooms in Denmark and found that both objectively measured sleep duration and subjectively rated sleep quality were worse when the windows were closed. In their recent single-blind experiment in bedrooms in Belgium [12], three different ventilation conditions were studied resulting in average CO_2 concentrations of 1,927 ppm, 1,298 ppm, and 856 ppm. The lowest ventilation rate, resulting in the highest CO_2 concentration, decreased the percentage of deep sleep and increased the number of awakenings compared with the other two conditions. Lan et al. [13] used mechanical ventilation to change bedroom ventilation rates in simulated bedrooms in a laboratory and observed improvements in objectively measured sleep quality at higher ventilation rates.

Some current standards for ventilation set the maximum recommended limits for indoor CO_2 concentration [14]; traditionally the concentration of 1,000 ppm CO_2 has been used since Pettenkofer [15] proposed that it is a marker of unacceptable indoor air quality, CO_2

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being considered as benign. Studies have shown that ventilation rates in bedrooms often result in higher levels of CO_2 that suggest poor air quality and insufficient ventilation rates [16–21].

While Pettenkofer proposed 1,000 ppm, he additionally recommended that the maximum CO_2 concentration in bedrooms for achieving good air quality should be around 700 ppm; in his estimates he assumed an outdoor CO_2 level of 500 ppm [15]. A recent summary of papers published in peer-reviewed journals linked bedroom ventilation with its effects on sleep quality [14]. The conclusion was that sleep quality was not affected when the average CO_2 level resulted by ventilation in bedrooms had been below 750 ppm (e.g., Refs. [10,22]), while average levels above 1,150 ppm were consistently found to cause disruption to sleep (e.g., Refs. [11,13,23]). Average levels above 2,600 ppm were observed to reduce next-day performance [23]. No conclusive results were obtained regarding the effects on sleep quality when average CO_2 levels were between 750 ppm and 1,150 ppm. In a recent field study reported by Fan et al. [12], it was not possible to determine the minimum ventilation rate for sleep quality even though three ventilation rates were examined because insufficient data reduced the sensitivity of the experiment. Building standards in many countries (e.g., Canada [24] and China [25]) stipulate minimum ventilation rates that result in a CO_2 concentration of 1,000 ppm. The main reason is to achieve good perceived air quality. Few standards stipulate minimum bedroom ventilation separately and there are no studies to confirm whether 1,000 ppm is an adequate recommendation for sleeping environments, as discussed above.

In summary, current studies of the effects of ventilation on sleep have some limitations. First, the lowest ventilation rate that negatively affects sleep remains undetermined. Previous studies mainly investigated the effects of high CO_2 concentrations, ranging from 1,500 ppm to 3,000 ppm, and did not narrow the range to a common level that was stipulated in standards. Second, in field surveys, natural ventilation cannot be used to reliably control ventilation rates. Third, existing analytical methods in cross-sectional studies cannot provide a reliable estimate of the minimum ventilation rate for good sleep quality, mainly because of confounding between ventilation rate and other environmental factors in bedrooms such as heat, noise disturbance and light.

The present study was carried out to fill the above gaps in knowledge and focused on effects on sleep quality at ventilation rates leading to average CO_2 concentrations at, below and above 1,000 ppm. This CO_2 concentration has been used as the lower limit of ventilation rate in many standards, although no study has ever confirmed whether the ventilation level resulting in an average CO_2 concentration of 1,000 ppm is sufficient and has no negative effects on sleep. The present study was carried out in a laboratory in simulated bedrooms in which the ventilation rate and other environmental factors were controlled. The main purpose was to examine whether current ventilation standards for sleeping environments, particularly residential buildings, require revision. In addition to the effects of ventilation on sleep, other effects were monitored including physiological responses, and effects on next-day cognitive performance.

2. Methods

2.1. Approach

Thirty-six subjects were recruited to sleep in the bedroom for one week: the first night for adaption and two nights at each of the three ventilation conditions corresponding to average CO_2 levels of 750 ppm, 1,000 ppm and 1,300 ppm. The conditions were created in rooms that simulated a normal bedroom. During each night, sleep quality was monitored with wristband sleep trackers. The participants rated several parameters of the environment where they slept and their own sleep quality. Their physiological reactions were monitored and their next-day cognitive performance was assessed.

2.2. Participants

Participants were recruited only if they stated that they were in good health and if their Pittsburgh Sleep Quality Index (PSQI) scores were less than 5 [26], indicating that they did not have sleep disorders. The other inclusion criteria included taking no medication, no tobacco or e-cigarette smoking, and no alcohol intake. They were asked to maintain a stable and regular lifestyle during the experiment without shift work, travel, or vacation. Female subjects were asked to avoid participating during their period. A total of 36 participants who met the above criteria were recruited from the university campus with an equal number of men and women. In the analyses only the data from 32 participants (Table 1) were used because for four participants it had not been possible to maintain stable indoor temperatures. The exclusion was made even though they remained thermally neutral by adjusting the bed coverings. A post-hoc power analysis was performed based on the repeated within-subject design involving 32 participants in this study [27]. By using G-power software and ANOVA (Repeated measures, within factors), assuming a medium effect size of 0.25, a non-sphericity correction of 0.8 and a correlation coefficient among repeated measures of 0.8, the statistical power was calculated to be 0.99, which was close to the upper limit of 1 [27].

The nature of the experiment was explained to all the participants before it began, although they were not informed about the conditions on any given day during the experiments. They received a modest remuneration. The protocol of the experiment was approved by the Ethics Review Board of Shanghai Jiao Tong University (No E20200018I) and conformed to the guidelines in the Declaration of Helsinki.

2.3. Measurements

2.3.1. Indoor environment

The air temperature (Ta), relative humidity (RH) and CO_2 concentration in the simulated bedroom were recorded on Micron Meters TR-76UI data loggers (Ta, range: 0–55 °C, accuracy: ±0.5 °C; RH: range: 10–95 %, accuracy: ±5 %; CO_2: range: 0–9999 ppm, accuracy: ±50 ppm) at 5-min intervals. Three data loggers were placed 0.5 m above floor height at the head, the middle, and the end of the bed. Their unweighted average was assumed to indicate the indoor Ta, RH and CO_2 concentration. The indoor noise level was recorded at intervals of 1 s by a Cirrus Optimus CR1720 sound level meter (range: 20–140 dB, RMS Single Range) placed at the head of the bed; the indoor noise levels did not exceed 40 dB (A) in any exposure.

2.3.2. Sleep quality

Sleep quality at night was recorded using a Fitbit Inspire 2 wristband sleep tracker which has been shown to record sleep stages that correspond well with polysomnographic analysis (PSG) [28,29]. Movement and heart rate data were analysed by proprietary software to yield total sleep duration, time awake, number of awakenings, sleep efficiency and the percentage of time spent in each sleep stage. An experimenter recorded when participants reported they were going to bed or had woken up, and the total time spent in bed was defined as the time between bedtime and wake-up time.

Table 1
Participant demographics (mean ± SD, (min-max)).

Gender	Number	Age	BMI	PSQI
All	32	23.7 ± 3.6 (18–33)	20.9 ± 2.5 (16.4–29.7)	3.2 ± 1.4 (0–5)
Male	16	23.5 ± 4.4 (18–33)	20.7 ± 2.2 (16.4–23.7)	3.8 ± 1.2 (2–5)
Female	16	23.9 ± 2.6 (20–30)	21.0 ± 2.8 (17.7–29.7)	2.6 ± 1.5 (0–5)

2.3.3. Physiological responses

2.3.3.1. Wrist skin temperature. Wrist skin temperature was measured using a Pyro-button-TH sensor (range: 20 to +85 °C, accuracy: ±0.2 °C) which was attached on the inside of the participants' wrist by a bandage; the measurements were recorded at 1-min intervals throughout sleep. Wrist skin temperature has been shown to be a good proxy of thermal state [30] and this measurement causes less disturbance to sleep than multi-point skin temperature measurements [31].

2.3.3.2. Blood pressure and pulse. Blood pressure and pulse were measured in the evening before going to bed and in the mornings after waking up using an OMRON U12 electronic blood pressure monitor (blood pressure, range: 0–299 mmHg/0~39.9 kPa, accuracy: ±3 mmHg/±0.4 kPa; pulse, range: 40–180 bpm, accuracy: ±5 %). Blood pressure and pulse are indicators related to physiological health.

2.3.3.3. Oxygen saturation of blood. Blood oxygen saturation (SpO2) was measured twice using a Lepu PC-68B Wrist Oximeter (range: 35–99 %, accuracy: 75–99 %, ±2 %; 50–75 %, ±3 %) with a finger-cot sensor on nights before going to bed and in the mornings after waking up. During the measurement, the finger-cot was placed on the tip of the middle finger. Each measurement took about 10 min, and the average value measured over 10 min was taken as the blood oxygen value at that time. Blood oxygen saturation (SpO2) indicates the concentration of oxygen in arterial blood and is closely related to the respiratory cycle [32].

2.3.3.4. Salivary biomarker. Samples of saliva were collected before going to bed and in the morning after waking up. They were analysed to obtain the concentration of lysozyme and cortisol. Lysozyme is a cationic protein with immune function in human mucosal secretions [33]. Cortisol increases during sleep deprivation and is considered to indicate a stress response [34]. Saliva provided by participants was centrifuged at 4000 rpm for 25 min and stored in a refrigerator at −20 °C and then sent to a professional laboratory for analysis using competitive inhibitory enzyme immunoassay technology; the samples were stored and then sent for analysis at the end of the experiment. The lowest detectable doses of lysozyme and cortisol were 7 μg/L and 25 nmol/L, respectively.

2.3.4. Subjective ratings

Participants completed questionnaires at bedtime and after waking. The questionnaire before sleep consisted of two parts. The first part included questions about their activities and the physical conditions they encountered during the day prior to each exposure. Subjective responses were collected using a simple version of the profile of mood states (POMS) questionnaire [35]. The second part collected ratings of the sleeping environment and included thermal sensation, thermal

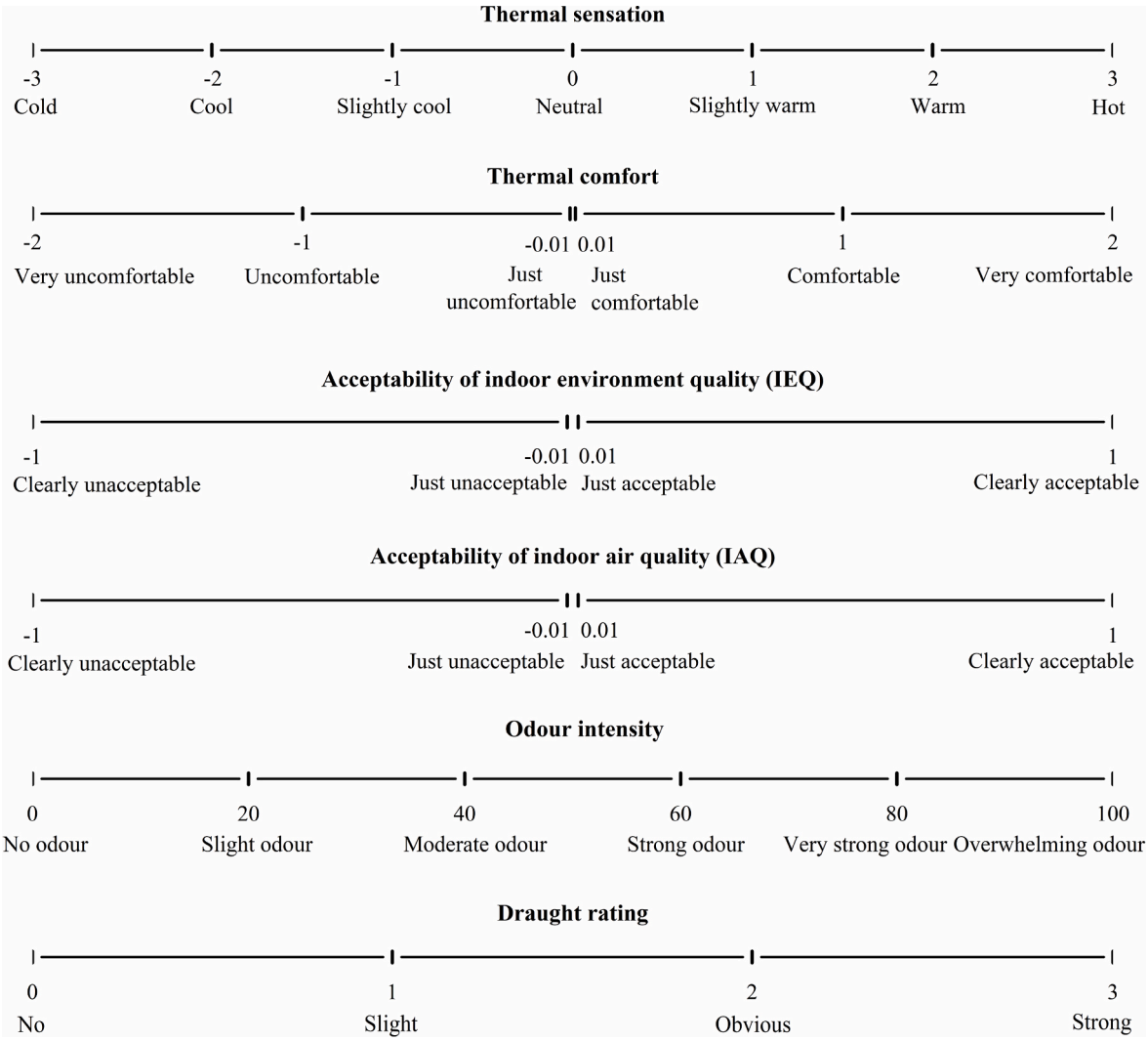

Fig. 1. Scales used for obtaining the subjective responses of the participants.

comfort [36], acceptability of the indoor environment (IEQ) and air quality (IAQ) [36,37], odour intensity [37] and draught (Fig. 1).

The questionnaire presented after waking included questions about the bedroom environment at night (by recall) and their willingness to work. The Groningen Sleep Quality Scale (GSQS) [11] was used to rate sleep quality, a higher score indicating worse sleep quality. The participants also rated the intensity of 15 acute subclinical health symptoms [37] by marking horizontal lines labelled 0 at one end, indicating very intense symptoms, and 100 at the other end, indicating no symptoms.

2.3.5. Cognitive performance

A test battery consisting of three different cognitive tests was used. The tests included *Grammatical reasoning* (a test in which three symbols were to be sorted according to their logical description), *Number calculation* (a mental arithmetic test adding two random numbers in the range 10–99) and a *Stroop* test with colour names presented in different colours, requiring attentional focus and flexibility to overcome perceptual/linguistic interference [38]. The test items were generated and presented randomly and had a similar level of difficulty. They were displayed using a mobile telephone application and the accuracy (% of correct responses) and the time to complete each test were recorded. The tests were performed by each participant upon arrival at the laboratory each day, i.e., in the evening. A composite performance index (PI) for each test session was then calculated by dividing the mean accuracy of the responses by the mean reaction time [38].

2.4. Experimental design and protocol

The experimental facility was on the campus of Shanghai Jiao Tong University where the surrounding environment was usually quiet and with low outdoor air pollution. The experiment was conducted in two low-emission rooms that were the same size (3.5 m × 4 m × 2.8 m). The rooms were designed to simulate real bedrooms, to reduce the strangeness and increase the comfort of the participants, with identical decorations and equipment including an air conditioner with an airflow deflector that provided lower air velocities in the bedroom by eliminating the plume, an electric oil-filled radiator, humidifier, dehumidifier and an air exchanger for mechanical ventilation (Fig. 2). The lighting environment was the same in each room. In both bedrooms, before lights off an illuminance of 160 lux was maintained and after lights off it was dark The windows in the rooms were covered with thick curtains to avoid any influence of outdoor light.

Three ventilation conditions were established following a review of the literature [14] resulting in average CO_2 concentrations of 750 ppm (A750), 1,000 ppm (B1000) and 1,300 ppm (C1300). Mechanical ventilation was used to ventilate the bedrooms and the three ventilation rates in each bedroom were estimated to be 33 m^3/h, 15 m^3/h and 8 m^3/h, respectively, by the decay method using CO_2 as a tracer gas [39]. As stated in the Introduction section, when used as a marker of the ventilation level, 750 ppm is the upper limit of CO_2 concentration that has not been found to affect sleep, 1,000 ppm is recommended as an acceptable maximum concentration in many current standards and 1,300 ppm is higher than 1,000 ppm and a level that has been shown to have negative effects on sleep quality.

During the experiment, the bedroom temperature was maintained at 20 °C because this is the recommended bedroom temperature in winter [40]; it is also the design temperature in China [25]. The participants were asked to maintain thermal comfort by adjusting the clothing insulation of their bedding and clothing and it was found they used similar bed coverings. The humidity in the bedrooms was maintained in the range of 40%–60 % by using the dehumidifier and humidifier. In this experiment no mandatory bedtime or wake-up time was imposed so that participants could maintain their normal sleeping routines. The sleep onset time and wake-up time of participants were mostly around 23:00–1:00 and 7:00–9:00, respectively, during the experiment.

The experiment lasted for 18 weeks using a within-subject design with one male and one female participating each week. Each participant slept in the same room for one week, i.e., on seven nights. The first night was for adaptation to the situation in the condition equivalent to B1000. Each ventilation condition was then experienced for two nights in

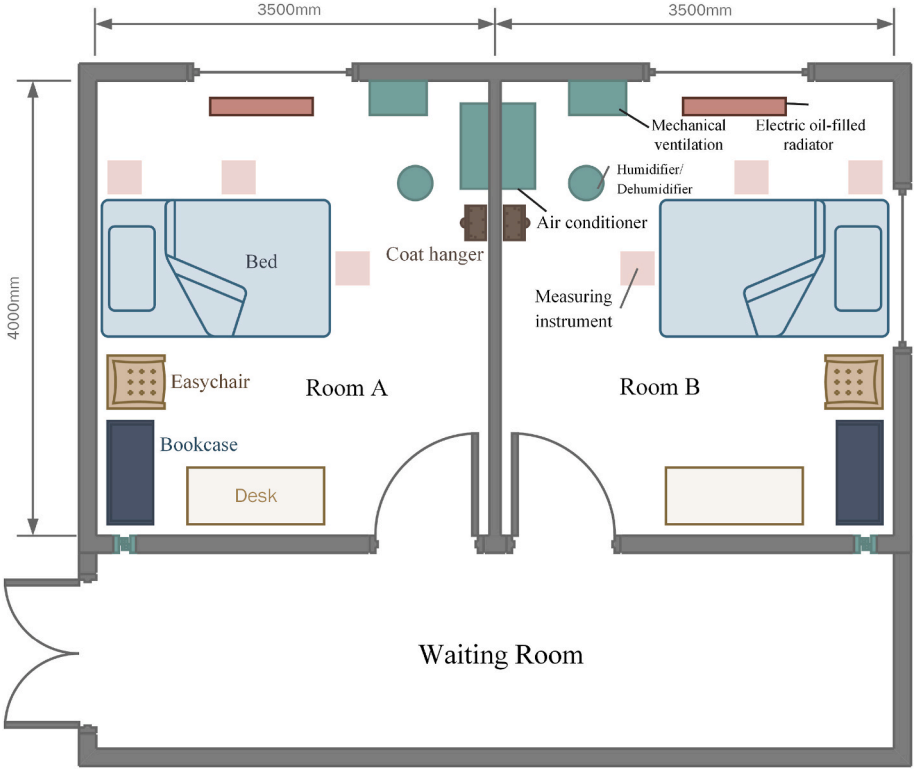

Fig. 2. Layout of the simulated bedrooms.

succession with a completely counterbalanced design for order of presentation to eliminate any bias due to experimental sequence.

Before each exposure, all equipment was turned on to adjust the environment to the required condition. Participants arrived at the waiting room, which was adjacent to the bedroom and had an illuminance of 180 lux, about 1–1.5 h before they went to bed. They took a short rest, then completed the test of work performance and the first part of the questionnaire before sleep. They went into the bedroom and remained there for 15–20 min. Their blood pressure and SpO2 were measured and saliva samples were collected. After that, they could move freely about the bedroom. They completed the second part of the questionnaire just before sleep and then went to bed. The experimenter recorded the time of turning off the light and when they woke up. After waking up in the morning, measurements of blood pressure and SpO2 were obtained and samples of saliva were taken. The participants then completed the morning questionnaire in the bedroom; in the case of perceived air quality, they made their assessment after leaving the bedroom, spending a few minutes in the waiting room and then re-entering the bedroom (Fig. 3).

2.5. Statistical analysis

The data obtained during the initial adaptation night were excluded from the analysis. The cognitive test in the evening was assumed to depend on the condition established the previous night so that data obtained following the adaption night were excluded. After excluding data from two person-nights, one person-night for each of two participants during which the experimental conditions had not been maintained as intended, a total of 190 person-nights were analysed. The generalized linear mixed model was used. As the independent variable was the experimental conditions, the dependent variables were the indexes measured during the experiment. The experimental conditions corresponding to each person and the two days in the same condition were set as repeated factors (No significant difference in any parameters was found between the two days in the same condition.). The sequence of three exposures was controlled in the analysis. Two-tail tests were used and the significant level was set to $P \leq 0.05$. Post-hoc analysis for significant effects was also performed to examine the differences between pairs of conditions.

3. Results

3.1. Indoor environment

Table 2 shows the indoor environmental parameters under each condition. The temperature and CO_2 concentration level were maintained at the intended levels and the bedroom CO_2 concentrations were all close to the outdoor concentration before the participants' arrival. The CO_2 concentration rose when they entered the room and changed according to expectations during the night (Fig. 4). Humidity was in the range 40–60 %, as intended, and although average levels were significantly higher in B1000 and C1300 compared with A750, the difference was small. The influence of humidity and its interaction with CO_2 concentration on other parameters was analysed separately (SI Table S1) and did not reach significance. Noise did not exceed 40 dB (A) in any condition.

3.2. Subjective ratings of the indoor environment and acute health symptoms

The subjective ratings obtained before bedtime and after waking up were analysed separately. There were no differences between conditions before going to bed, implying no differences between conditions when falling asleep (Table 3). Thermal sensation before sleep and after waking were close to neutral and the ratings of thermal comfort suggested that a comfortable level was maintained throughout. After waking up, the participants perceived the indoor odour intensity to be significantly higher in C1300 and slightly higher in B1000 than in A750 although the odour intensity was low at all conditions (Fig. 5). It should be noted that after waking in the morning, the participants assessed the odour intensity at the CO_2 concentration of about 1,600 ppm in C1300, 1,110 ppm in B1000, and 780 ppm in A750. A significant difference was observed for draught perception: participants perceived more air movement in A750, in which the air change rate was the highest, but considered the air movement to be low in all three conditions. No significant difference between conditions was observed for any of the acute health symptoms that were rated after waking up (Table 4).

3.3. Sleep quality

The subjectively rated (GSQS) and objectively measured (wristband sleep tracker) sleep quality are shown in Table 5. Sleep efficiency at A750 with high ventilation was significantly higher than in the other two conditions, probably because time awake was significantly shorter (Fig. 6). The duration of deep sleep in the A750 and B1000 conditions was significantly higher than in the C1300 condition. No other significant changes in sleep quality were observed.

3.4. Physiological responses

Physiological responses showed no significant differences except for salivary cortisol measured in the morning (Table 6). Wrist skin temperature measured during sleep did not differ significantly between conditions, which indicates that the micro-thermal environment did not differ. The salivary cortisol level after waking up was significantly higher in C1300 compared with the level measured in B1000 and A750 (Fig. 7).

3.5. Cognitive performance

No significant differences between conditions in cognitive performance were observed (Table 7).

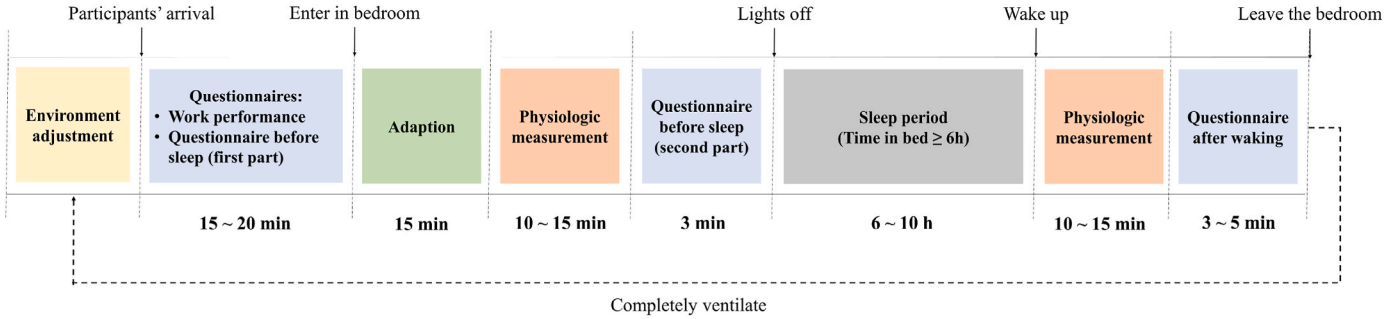

Fig. 3. Experimental procedure during each experimental day.

Table 2
The conditions during experiments (mean ± SD) (*P ≤ 0.05; **P ≤ 0.01; ***P ≤ 0.001).

Conditions		A750	B1000	C1300	F	P
Average levels of measured parameters during sleep	Ta (°C)	19.9 ± 0.6	20.1 ± 0.6	20.0 ± 0.6	2.35	0.10
	RH (%)	52 ± 5	55 ± 4	55 ± 4	10.03	0.00***
	CO_2 concentration (ppm)	771 ± 89	1021 ± 88	1305 ± 228	347.62	0.00***

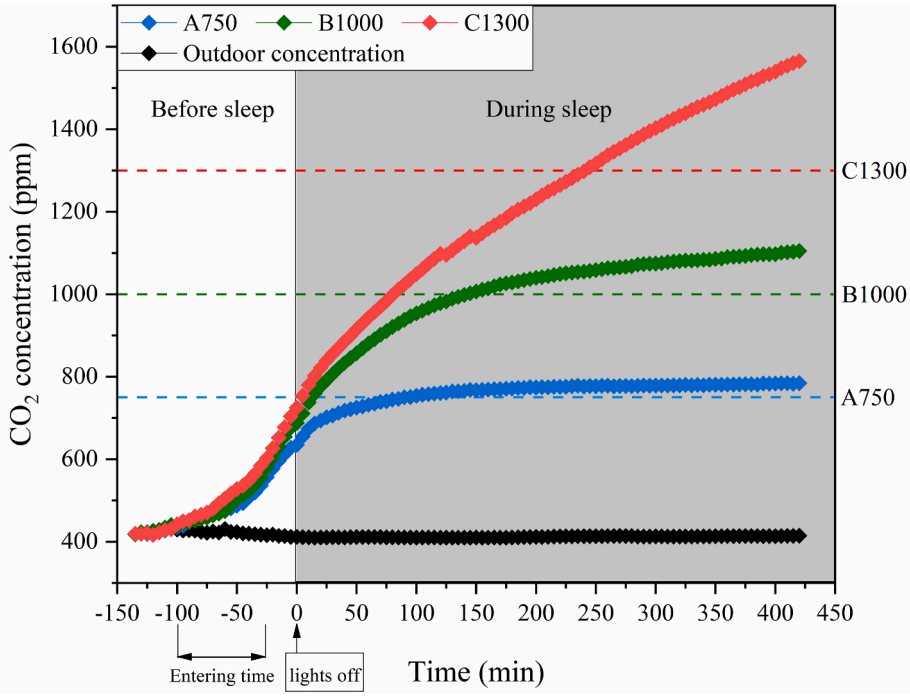

Fig. 4. Changes in the CO_2 concentration with time from about 2.5 h before sleep to about 7 h after sleep (The dashed lines indicated the expected levels in the experimental design).

Table 3
Subjective ratings of environmental conditions (mean ± SD) (*P ≤ 0.05; **P ≤ 0.01; ***P ≤ 0.001).

Subjective evaluation[a]	Before sleep					After waking				
	A750	B1000	C1300	F	P	A750	B1000	C1300	F	P
Thermal sensation	0.1 ± 0.9	0.2 ± 0.8	0.3 ± 0.8	0.79	0.46	0.1 ± 0.8	0.3 ± 0.9	0.1 ± 0.7	2.62	0.08
Thermal comfort	1.0 ± 0.8	1.0 ± 0.8	1.0 ± 0.7	0.04	0.96	1.1 ± 0.8	1.1 ± 0.8	1.0 ± 0.8	0.62	0.54
Acceptability of IEQ	0.7 ± 0.3	0.6 ± 0.4	0.6 ± 0.4	1.39	0.25	0.6 ± 0.4	0.6 ± 0.4	0.6 ± 0.4	1.03	0.36
Acceptability of IAQ	0.7 ± 0.3	0.6 ± 0.4	0.6 ± 0.4	1.97	0.14	0.6 ± 0.4	0.6 ± 0.4	0.6 ± 0.4	0.34	0.71
Perceived odour	7.4 ± 16.4	6.8 ± 10.6	7.3 ± 11.0	0.05	0.95	7.4 ± 13.2	8.3 ± 11.6	11.7 ± 15.7	3.00	0.05*,[b]
Draught rating	0.5 ± 0.6	0.3 ± 0.5	0.4 ± 0.5	2.89	0.06	0.5 ± 0.7	0.2 ± 0.4	0.2 ± 0.5	9.06	0.00***

Thermal comfort: very uncomfortable (−2), uncomfortable (−1), just uncomfortable (−0.01), just comfortable (0.01), comfortable (1), very comfortable (2).
Acceptability of IEQ: clearly unacceptable (−1), just unacceptable (−0.01), just acceptable (0.01), clearly acceptable (1).
Acceptability of IAQ: clearly unacceptable (−1), just unacceptable (−0.01), just acceptable (0.01), clearly acceptable (1).
Perceived odour: no (0), slight (20), moderate (40), strong (60), very strong (80), overwhelming (100).
Draught: no (0), slight (1), obvious (2), strong (3).
[a] Thermal sensation: cold (−3), cool (−2), slightly cool (−1), neutral (0), slightly warm (1), warm (2) and hot (3).
[b] Results of post-hoc analysis on the significant difference (bold character) are shown in Fig. 5.

3.6. Associations of physiological responses, work performance and sleep quality

Significant correlations were found between salivary cortisol after waking and the duration and percentage of deep sleep. As shown in Fig. 8, an increase in the duration and percentage of deep sleep was accompanied by a decrease in salivary cortisol level after waking.

The performance of the Stroop test was significantly and positively correlated with the total sleep time and deep sleep duration, while the performance of logical sorting and the average performance on three tests were also significantly and positively correlated with the total sleep time.

4. Discussion

The present results show that ventilation rates in bedrooms should be set at levels resulting in CO_2 concentrations below 1,000 ppm and recommendations regarding CO_2 levels for achieving high indoor air quality in buildings when people are awake should not simply be applied in bedrooms. In the present experiment, ventilation rates resulting in

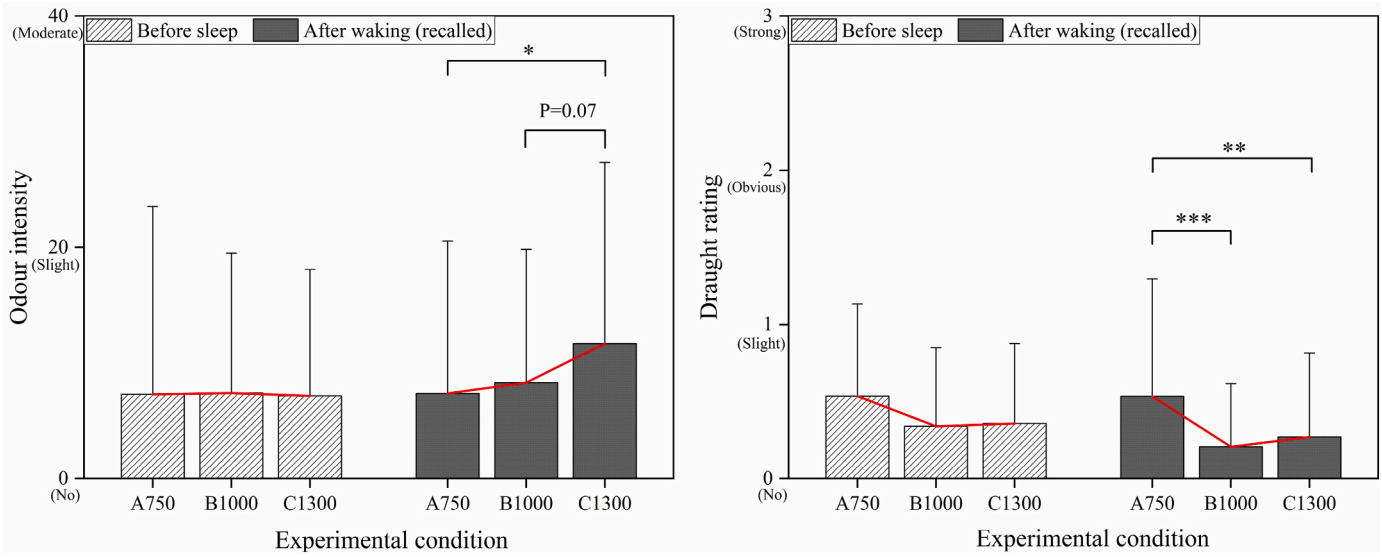

Fig. 5. Perceived odour intensity (left) and draught rating (right) of bedroom environment in the three conditions (mean ± SD) (*P ≤ 0.05; **P ≤ 0.01; ***P ≤ 0.001).

Table 4
Reported intensity of acute health symptoms in the three conditions (mean ± SD).

Acute health symptom	A750	B1000	C1300	F	P
Nose dry (0) – Nose running (100)	56.7 ± 32.6	57.6 ± 31.5	53.3 ± 30.6	0.59	0.56
Throat dry (0) –Throat not dry (100)	53.8 ± 34.5	53.6 ± 33.9	48.8 ± 32.9	0.69	0.50
Mouth dry (0)–Mouth not dry (100)	50.8 ± 32.7	46.3 ± 30.5	50.8 ± 30.9	0.76	0.47
Lips dry (0)– Lips not dry (100)	46.8 ± 31.7	45.0 ± 31.2	46.8 ± 31.2	0.13	0.88
Skin dry (0)– Skin not dry (100)	67.0 ± 29.3	66.4 ± 31.4	65.8 ± 28.6	0.01	0.99
Eyes dry (0)– Eyes not dry (100)	64.0 ± 31.3	63.6 ± 31.6	61.2 ± 32.2	0.18	0.84
Eyes aching (0)– Eyes not aching (100)	78.7 ± 28.4	76.0 ± 31.9	75.8 ± 29.5	0.42	0.66
Severe headache (0)– No headache (100)	81.9 ± 29.6	83.5 ± 28.6	80.7 ± 29.7	0.29	0.75
Difficult to think (0)– Head clear (100)	76.2 ± 25.7	74.9 ± 24.6	76.8 ± 25.0	0.26	0.78
Dizzy (0)– Not dizzy (100)	78.7 ± 31.6	80.1 ± 30.8	79.4 ± 30.3	0.06	0.95
Feeling bad (0)– Feeling good 100)	72.9 ± 26.2	66.1 ± 26.8	69.8 ± 28.6	1.65	0.20
Tired (0)– Rested (100)	72.2 ± 26.7	66.6 ± 29.1	68.8 ± 28.1	0.90	0.41
Difficult to concentrate (0)– Easy to concentrate (100)	73.8 ± 26.8	67.9 ± 27.4	72.4 ± 26.8	1.61	0.20
Depressed (0)– Positive (100)	72.8 ± 27.0	70.1 ± 28.8	70.3 ± 31.1	0.26	0.77
Sleepy (0)– Alert (100)	72.4 ± 25.8	69.1 ± 25.8	69.5 ± 26.1	0.41	0.66

average night-time CO_2 levels of 1,000 ppm significantly reduced sleep efficiency and increased time awake. A further decrease in ventilation that increased night-time average CO_2 levels to 1,300 ppm was observed to reduce the duration of deep sleep. Overall, sleep quality was thus reduced when the ventilation resulted in an average CO_2 concentration at or above 1,000 ppm. Assuming the emission rate of CO_2 is 11 L/h per person [43], the present results show that ventilation rates in bedrooms should be higher than 4–5 L/s of outdoor air per person and if the CO_2 concentration is to be kept around 750 ppm they should be 10 L/s per person [43]. These ventilation rates are higher than have been measured in bedrooms and higher than is recommended by current standards [14], and they incidentally match the recommendations of Pettenkofer [15]. They imply that ventilation standards in bedrooms should be revised. The present results confirm a tentative dose-response relationship that suggested that ventilation rates resulting in CO_2 levels above 1,150 ppm are detrimental for sleep quality and they reduce the upper limit for undisturbed sleep to below 1,000 ppm. Further research is required to confirm these observations but the results obtained by Fan et al. [11,44] support this conclusion.

No effects on cognitive performance were observed at the ventilation rates studied in the present experiment, possibly because even the highest bedroom CO_2 concentration (at the lowest bedroom ventilation rate) was lower than in the field intervention experiment reported by Strøm-Tejsen et al. [23], who found a decrease in next-day performance on awakening after sleeping with a ventilation level that resulted in an average CO_2 concentration of about 2600 ppm. Cognitive performance in Strøm-Tejsen's experiment was obtained from four repeated nights at one condition, while in the present experiment the data was from two repeated nights under each condition, so the accumulated negative effects of low ventilation may have been less due to the different experimental design. Another possible reason for the lack of a significant effect in the present experiment is that the cognitive tests were performed in the evening, not on awakening to avoid the influence of sleep inertia in the morning [45,46], so differences in daily activities causing cognitive fatigue will have contributed to the variance, reducing the significance of any comparison between conditions. In general, sleep studies have shown that poor sleep, however caused, will affect next-day performance [7,47,48], and this conclusion is supported by the finding in the present experiment that correlations at the individual level showed significantly improved performance with improved sleep quality (Fig. 9). It is not known how poor the sleep quality must be to reduce cognitive performance. This should be investigated in future studies, but the precautionary principle means that any negative effect on sleep quality should be avoided as it may lead to negative economic consequences. Recent estimates suggest that sleeping for less than 6–7 h would be expected to have significant negative economic consequences as productivity will be reduced [9].

The average CO_2 concentration during sleep was used in the present study to characterize each ventilation condition. In other studies, the 95th quantile of the measured concentration which is almost the peak value of the continuous measurement was used to estimate ventilation levels. However, it is not known which index is a better indicator of the

Table 5
Sleep quality parameters in the three conditions (mean ± SD) (*P ≤ 0.05; **P ≤ 0.01; ***P ≤ 0.001).

Sleep parameters		All data	A750	B1000	C1300	F	P	Recommend range for appropriate sleep quality[a]
Objectively measured	Time in bed (min)	471.8 ± 46.0	474.6 ± 46.7	470.6 ± 45.9	470.1 ± 40.1	0.37	0.70	N/A
	Total sleep time (min)	406.6 ± 47.8	413.6 ± 45.2	404.7 ± 49.8	401.2 ± 43.5	0.98	0.38	420–540min
	Sleep efficiency (%)	86.2 ± 4.9	87.2 ± 4.4	85.9 ± 5.2	85.4 ± 5.1	8.97	0.00***	≥85 %
	Time awake (min)	65.0 ± 23.0	60.9 ± 21.8	65.9 ± 23.6	68.7 ± 24.4	7.10	0.00***	N/A
	Sleep onset latency (min)	16.1 ± 18.5	12.9 ± 16.5	17.3 ± 18.1	17.8 ± 20.5	2.21	0.11	≤30min
	REM sleep (min)	95.4 ± 23.8	94.2 ± 20.8	94.5 ± 25.8	97.8 ± 24.7	0.64	0.53	N/A
	Light sleep (min)	229.6 ± 36.6	235.9 ± 39.7	226.1 ± 35.2	226.7 ± 34.6	1.62	0.20	N/A
	Deep sleep (min)	81.6 ± 22.9	83.4 ± 18.2	84.2 ± 26.1	76.7 ± 21.8	4.50	0.01**	N/A
	REM sleep (%)	23.4 ± 5.0	22.8 ± 4.5	23.3 ± 5.5	24.3 ± 5.2	1.71	0.18	21–30 % [b]
	LST sleep (%)	56.5 ± 6.6	56.9 ± 6.0	56.1 ± 7.2	56.6 ± 6.6	0.34	0.71	N/A
	Deep sleep (%)	20.0 ± 5.0	20.3 ± 4.6	20.6 ± 5.3	19.2 ± 5.3	1.62	0.20	16–20 % [c]
Subjectively assessed	GSQS	1.7 ± 2.0	1.3 ± 1.7	2.1 ± 2.2	1.6 ± 1.9	2.22	0.11	N/A

[a] Referred by the National Sleep Foundation (NSF) [41,42].
[b] The recommended range of REM sleep and deep sleep for adults (26–64 years old) was given by NSF but not for young adults (18–25 years old).
[c] The recommended range of REM sleep and deep sleep for adults (26–64 years old) was given by NSF but not for young adults (18–25 years old).

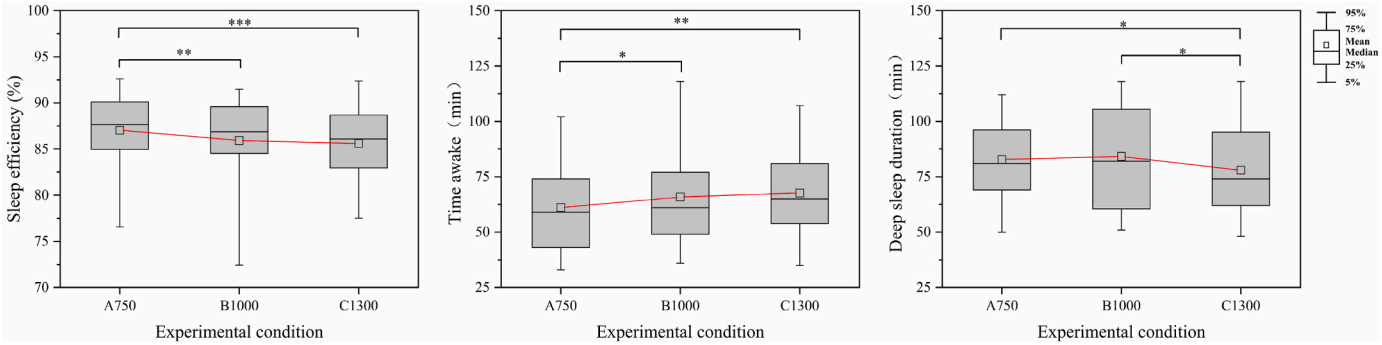

Fig. 6. Sleep efficiency (left), time awake (middle) and deep sleep duration (right) in the three conditions (*P ≤ 0.05; **P ≤ 0.01; ***P ≤ 0.001).

Table 6
Physiological responses in different experimental conditions before sleep and after waking up (mean ± SD) (*P ≤ 0.05; **P ≤ 0.01; ***P ≤ 0.001).

Physiological responses	Before sleep					After waking				
	A750	B1000	C1300	F	P	A750	B1000	C1300	F	P
Systolic blood pressure (mmHg)	106.6 ± 9.4	106.1 ± 9.2	107.8 ± 9.8	0.80	0.45	105.9 ± 9.2	105.6 ± 8.6	106.1 ± 8.8	0.89	0.41
Diastolic blood pressure (mmHg)	70.3 ± 7.4	69.5 ± 8.0	69.3 ± 7.8	0.94	0.39	68.2 ± 8.9	69.5 ± 8.3	68.8 ± 7.9	0.78	0.46
Pulse (bpm)	70.3 ± 9.3	70.8 ± 9.5	72.5 ± 10.7	2.13	0.12	71.7 ± 10.2	72.4 ± 10.6	71.3 ± 9.8	0.85	0.43
Blood oxygen saturation (%)	97.5 ± 0.6	97.6 ± 0.5	97.5 ± 0.7	0.48	0.62	97.7 ± 0.5	97.7 ± 0.6	97.7 ± 0.6	1.13	0.33
Salivary lysozyme (μg/L)	852.5 ± 68.2	869.8 ± 78.4	840.1 ± 78.8	1.54	0.22	854.0 ± 73.5	860.6 ± 74.3	847.9 ± 74.4	0.12	0.89
Salivary cortisol (nmol/L)	35.7 ± 2.6	35.8 ± 2.6	35.1 ± 2.6	1.34	0.27	35.2 ± 2.5	35.7 ± 2.7	36.4 ± 2.7	4.36	0.01**

effects of ventilation on sleep. We chose to use average CO_2 to permit comparison with previous studies that generally reported average CO_2 levels during sleep [10,13,23] and also to support a proposed dose-response relationship that used average CO_2 levels [14]. It is good practice to report more indicators such as average, maximum value and quantile etc. to better and more comprehensively describe the dynamic characteristics of the ventilation.

No measurements of airborne pollutants other than CO_2 were made in the simulated bedrooms so the effects observed might be due to any of the pollutants whose concentration increased with reduced ventilation. These will have been other bioeffluents as well as the gases and vapours emitted from the materials and equipment in the bedrooms, and also airborne particulates. It is also be noted that the bioeffluent concentrations were initially low in the present experiment and they would be higher in real bedrooms if they had been occupied for any length of time before bedtime, as is often the case. That no measurements of these pollutants were made is a limitation of the present research and such measurements should be made in future studies. The ratings that the participants performed in the morning confirm that the perceived air quality was reduced with reduced ventilation, as odour intensity increased (Table 3) although the reduced air quality did not cause a significant increase in the intensity of any health symptoms. Other parameters did not change much with changes in the ventilation and the analysis did not find that the small but significant increase in relative humidity had any effect on the overall findings (Table S1), so the effects observed can be attributed to poor ventilation.

Another limitation of the present study is that the participants were young and healthy and did not usually experience any sleep problems, according to NSF recommendations. The results observed in this study should not be assumed to be valid for other demographic groups,

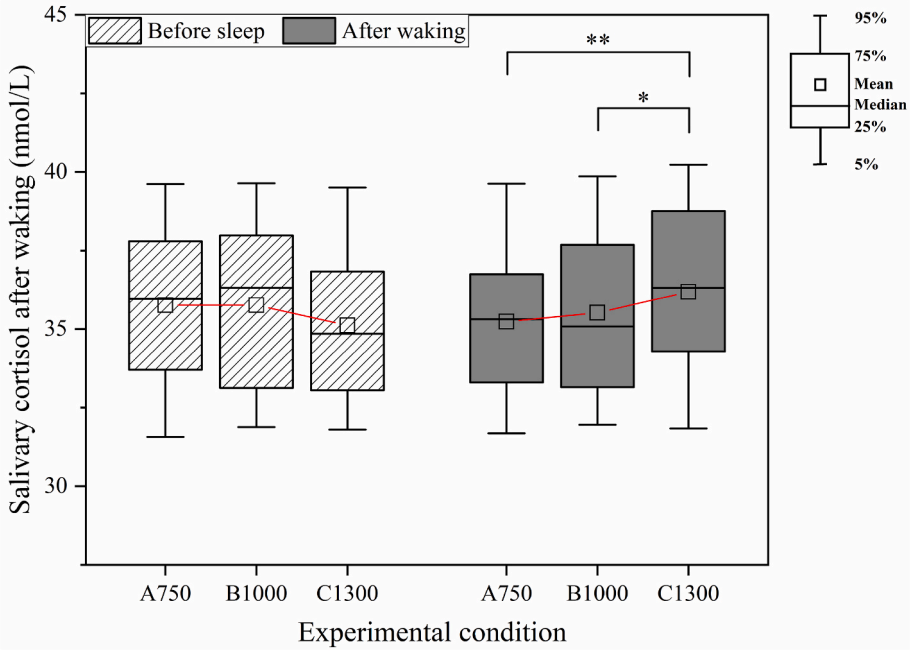

Fig. 7. Salivary cortisol before and after waking in the three conditions (*P ≤ 0.05; **P ≤ 0.01; ***P ≤ 0.001).

Table 7
Cognitive performance after each of the different experimental conditions (mean ± SD).

Performance test	A750	B1000	C1300	F	P
Grammatical reasoning	0.95 ± 0.37	0.87 ± 0.35	0.93 ± 0.37	1.58	0.21
Number calculation	2.19 ± 0.59	2.00 ± 0.70	2.16 ± 0.66	1.71	0.19
Stroop	3.23 ± 1.11	3.00 ± 1.07	3.19 ± 1.01	1.48	0.23
Average score (on three tests)	0.53 ± 0.17	0.48 ± 0.16	0.52 ± 0.16	1.73	0.18

although it is reasonable to expect that the observed effects on sleep would be still worse for people who are already experiencing sleep problems, e.g., older people [49,50]. The present results thus provide a strong argument that ventilation rates that maintain CO_2 concentrations in bedrooms below 1,000 ppm are necessary.

In other studies [10,23,44], poor ventilation increased sleep onset latency, meaning that sleep quality was reduced, while in the present study no effects on sleep onset latency were found. It is possible that most of the negative effects of the reduced outdoor air supply rates on sleep occurred in the latter part of the night as the CO_2 concentration resulting from a constant outdoor air supply rate takes a considerable time to reach its peak, but this was not investigated in the present analysis. Future studies should look closely into this possibility.

The salivary cortisol level after waking was found to be significantly higher in the low ventilation condition C1300 than that in the other two

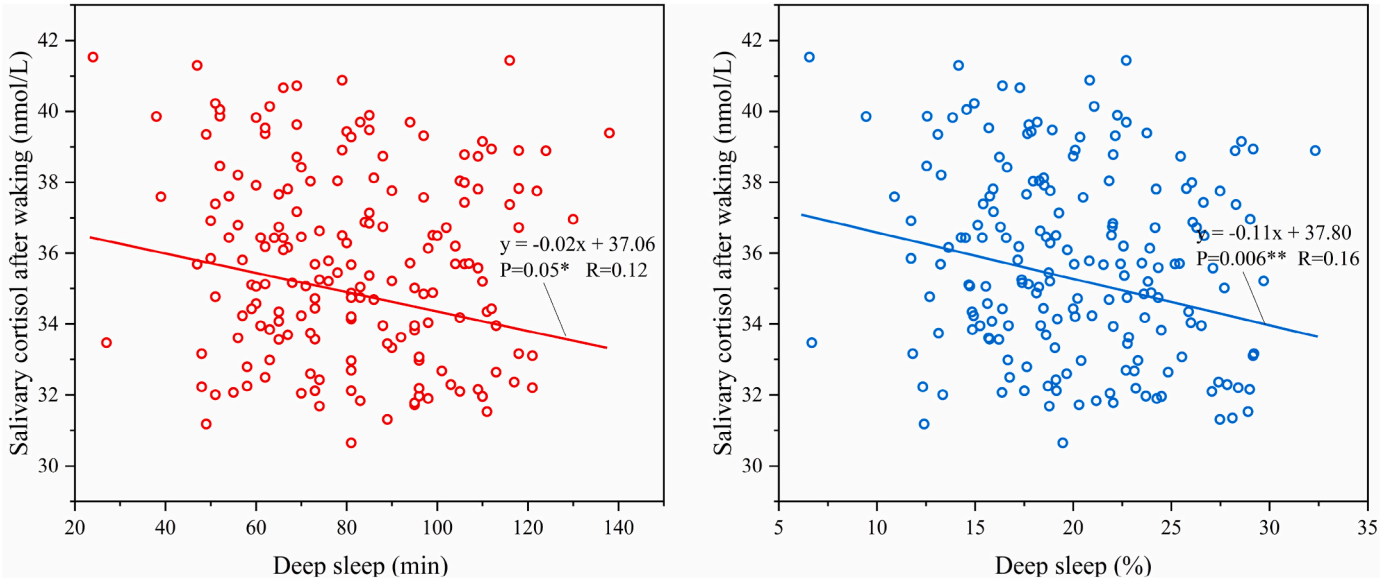

Fig. 8. Correlations of salivary cortisol after waking with duration (left) and percentage (right) of deep sleep.

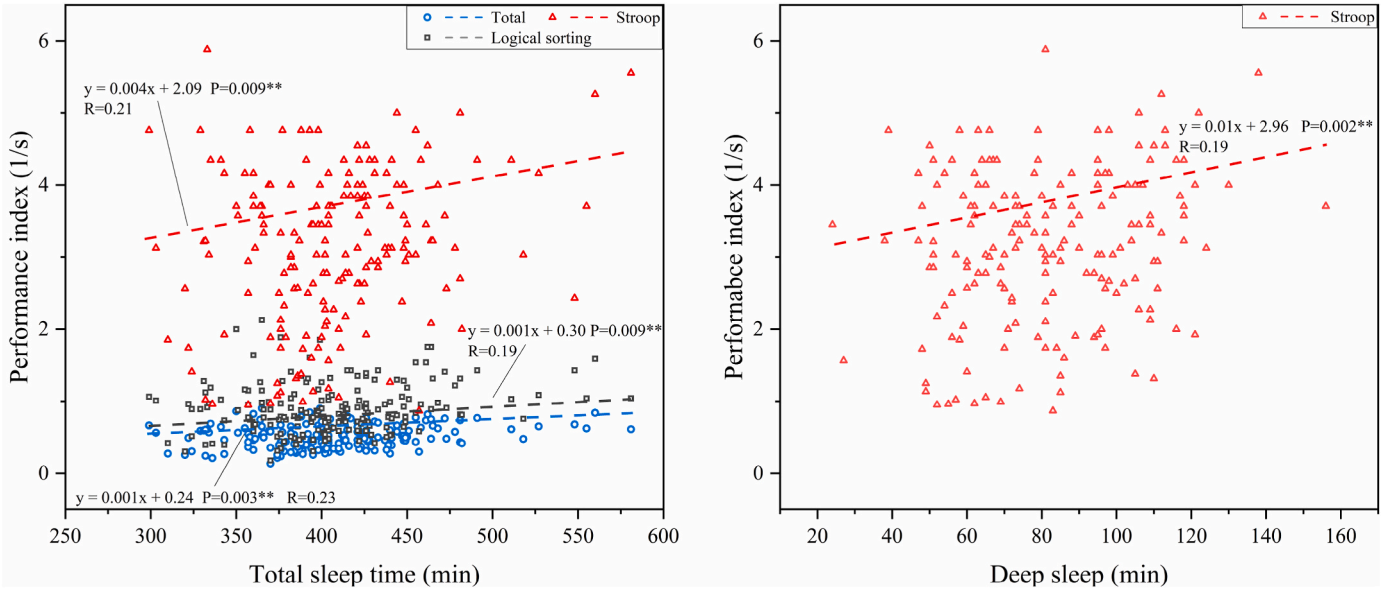

Fig. 9. Correlations between performance and total sleep time (left) and deep sleep time (right).

conditions. In this condition, the hormone regulation of the HPA axis could be activated and this would increase sympathetic nervous system activity, causing negative effects on sleep; this is consistent with the conclusions of previous studies [13,36,51] and probably the reason why deep sleep was also affected. Yan et al. [36] measured physiological parameters such as heart rate and breathing rate throughout the night under conditions with reduced and improved ventilation as indicated by the measured CO_2 concentrations: sleep efficiency decreased and wakefulness increased as heart rate increased, and deep sleep decreased as the apnea hypopnea index (AHI) increased and increased with increased inter-beat heart intervals longer than 50 ms (pNN50) [36]. AHI indicates the frequency of apnea or hypoventilation during sleep [52] while heart rate and pNN50 reflect the activity of the autonomic nervous system [53]. pNN50 is reduced when the sympathetic nervous system plays a dominant role and at the same time the heart rate increases indicating increased stress [53,54]. These findings suggest plausible physiological mechanisms by which sleep quality might be affected. In the present study, a negative correlation was found between salivary cortisol after waking and the duration and percentage of deep sleep (Fig. 8). Salivary cortisol is an acute stress biomarker [55,56] indicating the activity of the hypothalamic-pituitary-adrenal (HPA) axis [57,58]. An increase is related to an active sympathetic nervous system [57], which may be related to hypoxia [59], inflammation [60], and changes in blood pressure [61]. It is associated with poor sleep continuity and an increase in waking events [51,62–64]; such events were more frequent with reduced ventilation in the present experiment (Table 5). During the whole sleep process, NREM sleep is mainly dominated by the parasympathetic nervous system [62]. A higher level of salivary cortisol after waking may indicate poor sleep resulting in inadequate rest and the high levels of stress known to be detrimental to health [58,63].

In summary, sleep quality improved when increased bedroom ventilation reduced the average CO_2 concentration to 750 ppm and although the condition in which the average CO_2 concentration was 1000 ppm could not be shown to have significant effects on deep sleep or on the intensity of acute health symptoms, negative effects on sleep quality were observed in the form of increased time awake and decreased sleep efficiency. When the ventilation rate was reduced to a level that caused an average CO_2 concentration of 1300 ppm, adverse changes in sleep structure and health indicators were observed, and these may lead to sleep disorders and chronic fatigue in the long term.

5. Conclusions

Ventilation with outdoor air resulting in an average CO_2 concentration of 1,000 ppm reduced sleep efficiency by 1.3 % and increased time awake by 5.0 min compared with a ventilation rate resulting in an average CO_2 concentration of 750 ppm.

Ventilation with outdoor air resulting in an average CO_2 concentration of 1,300 ppm reduced sleep efficiency by 1.8 % and time awake by 7.8 min compared with a ventilation rate resulting in an average CO_2 concentration of 750 ppm. Additionally, under this reduced ventilation condition the duration of deep sleep was 6–7 min shorter.

Significantly higher salivary cortisol levels after waking suggest that acute stress and increased sympathetic nervous system activity caused the negative effects on sleep that were observed.

Group average cognitive performance did not differ significantly between conditions but at the individual level reduced sleep quality was significantly correlated with reduced cognitive performance.

The present results indicate that current ventilation rate requirements for bedrooms should be revised and should stipulate outdoor air supply rates resulting in CO_2 levels below 1,000 ppm. These recommendations should be validated for other population groups such as the elderly and those already experiencing sleep problems.

CRediT authorship contribution statement

Mengyuan Kang: Writing – review & editing, Writing – original draft, Visualization, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Yan Yan:** Methodology, Investigation, Formal analysis. **Chao Guo:** Writing – review & editing. **Yige Liu:** Writing – review & editing. **Xiaojun Fan:** Methodology. **Pawel Wargocki:** Writing – review & editing. **Li Lan:** Writing – review & editing, Project administration, Methodology, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.buildenv.2023.111118.

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