Chapter

Trials for Health Promotion by Indoor Environment Modifications

Suni Lee, Naoko Kumagao-Takei, Kei Yoshitome, Nagisa Sada, Yasumitsu Nishimura and Takemi Otsuki

Abstract

Two attempts to address health issues by indoor environment modifications are introduced. One approach involves enhancement of natural killer cell activity by negatively charged particle dominant indoor air conditions (NCPDIAC) resulting from extra-porous charcoal paint and application of an electric voltage on the wall surface to adsorb positively charged small particles (approx. 20 nm in diameter). This apparatus creates relatively continuous NCPDIAC. The other approach involves prevention of pollen allergy symptoms by a cloth containing specific ore powder (CCSNOP). With the former approach, we engaged in short-term (2.5 hour), middle-term (2 W night stay), and long-term (3 M) stays under NCPDIAC and found that IL-2 levels increased under short-term stays and that natural killer cell activity was enhanced in middle- and long-term stay experiments. Implementation of this strategy may partially prevent the occurrence of cancers and viral-mediated diseases. With the latter approach, a 1-hour stay within a CCSNOP room resulted in improvement of symptoms in patients with pollen allergies in addition to a reduction in bad moods caused by any remaining symptoms. In both cases, longer-term experiments should be performed in an effort to confirm and delineate the biological effects of these indoor environment modifications on human health problems.

Keywords: indoor air, negatively charged particle, natural killer cell activity, pollen allergy

1. Introduction

The nature of indoor environments is important in terms of human health. One typical illness related to indoor environments is referred to as sick building syndrome (SBS) and is mainly caused by volatile organic compounds (VOCs) [1–6]. Patients with SBS suffer from a variety of nonspecific symptoms such as irritation of the eyes, nose, or throat. Additionally, certain neurotoxic or general health problems present as skin irritations, with nonspecific hypersensitivity reactions including infectious diseases and odor and taste sensations [1–6]. These patients also suffer from general fatigue. Many efforts have been directed at exploring the etiology of SBS, such as attempts to identify patients by certain genetic or psychological features [1–6]. However, efforts to unambiguously account for the occurrence of this syndrome and strategies to prevent its occurrence by avoiding exposure to specific chemicals remain unclear [1–6].

On the other hand, various attempts have been made to improve human health by modifying indoor air environments. For example, efforts have been devoted to increasing air tightness and thermal insulation properties to avoid marked changes between rooms [7–10]. Additionally, antifungal measures are also important since a variety of fungi can cause health problems such as hypersensitivity pneumonitis and other allergic diseases [11, 12].

In this chapter, two approaches to improve human health by indoor environment modifications are introduced. One approach involves "enhancement of natural killer cell activity caused by negatively charged particle dominant indoor air conditions," while the other involves "improvement of pollen allergy symptoms by cloth containing specific ore powder."

2. Enhancement of natural killer cell activity caused by negatively charged particle dominant indoor air conditions

We previously described the construction of negatively charged particle dominant indoor air conditions (NCPDIAC) [13]. Thereafter, the effects of NCPDIAC on human health have been monitored under short- (2.5 hours), middle- (2-week night stay), and long-term (3-month period of continuous residence) stays [13].

As shown in **Figure 1A**, the NCPDIAC apparatus consists of two components. One comprises the use of extra-porous charcoal paint [13]. This mainly induces dehumidification and deodorization. The important component that enhances natural killer (NK) cell activity comprises an electric voltage on the wall surface (72–100 V) [14, 15]. This electric voltage creates a negative charge on the wall surface [13]. Thus, positively charged particles (approx. 20 nm in diameter) are adsorbed onto the wall surface, and negatively charged particles remain at random in the rooms. As a result, this device creates NCPDIAC.

As shown in **Figure 1B–D** panels, three different types of experiments were performed sequentially. In the first, 2.5 hour short-stay experiments were performed. At that time, three control rooms and three NCPDIAC rooms were built in the wide sub-underground laboratory in the Comprehensive Housing R&D Institute, Sekisui House Ltd., at Kyoto Prefecture, Japan. The control and NCPDIAC rooms were 9.1 m^2 (floor area) and 22.8 m^3 (air volume). As described in **Figure 1B**, 60 volunteers occupied the control or NCPDIAC rooms for a 2.5 hour stay (short-term). There were no differences in temperature, humidity, or concentration of VOCs between control and NCPDIAC rooms during the experimental period. However, the concentration of charged particles differed [13]. As shown in **Figure 1B**, the concentration of positively charged particles in control rooms was slightly but significantly higher than that of negatively charged particles. It was considered that this difference may represent ordinary conditions. However, in NCPDIAC rooms, the concentration of positively charged particles decreased (by adsorption onto the wall surface), whereas that of negatively charged particles remained unchanged. Thus, the difference in concentration between positively and negatively charged particles was significantly greater (approximately 500–800 particles/cm^3 room air) [13].

A second series of experiments was performed comprising 2-week night stays [14]. Fifteen volunteers (all Japanese males) occupied dormitory or Sekisui House rooms for 3 months. At the mid-month period, participants moved into control rooms (no NCPDIAC apparatus), and all participants were now subject to the same conditions at this point in time [14]. However, participants did not know which of the rooms (control or NCPDIAC) they had initially occupied. Participants stayed

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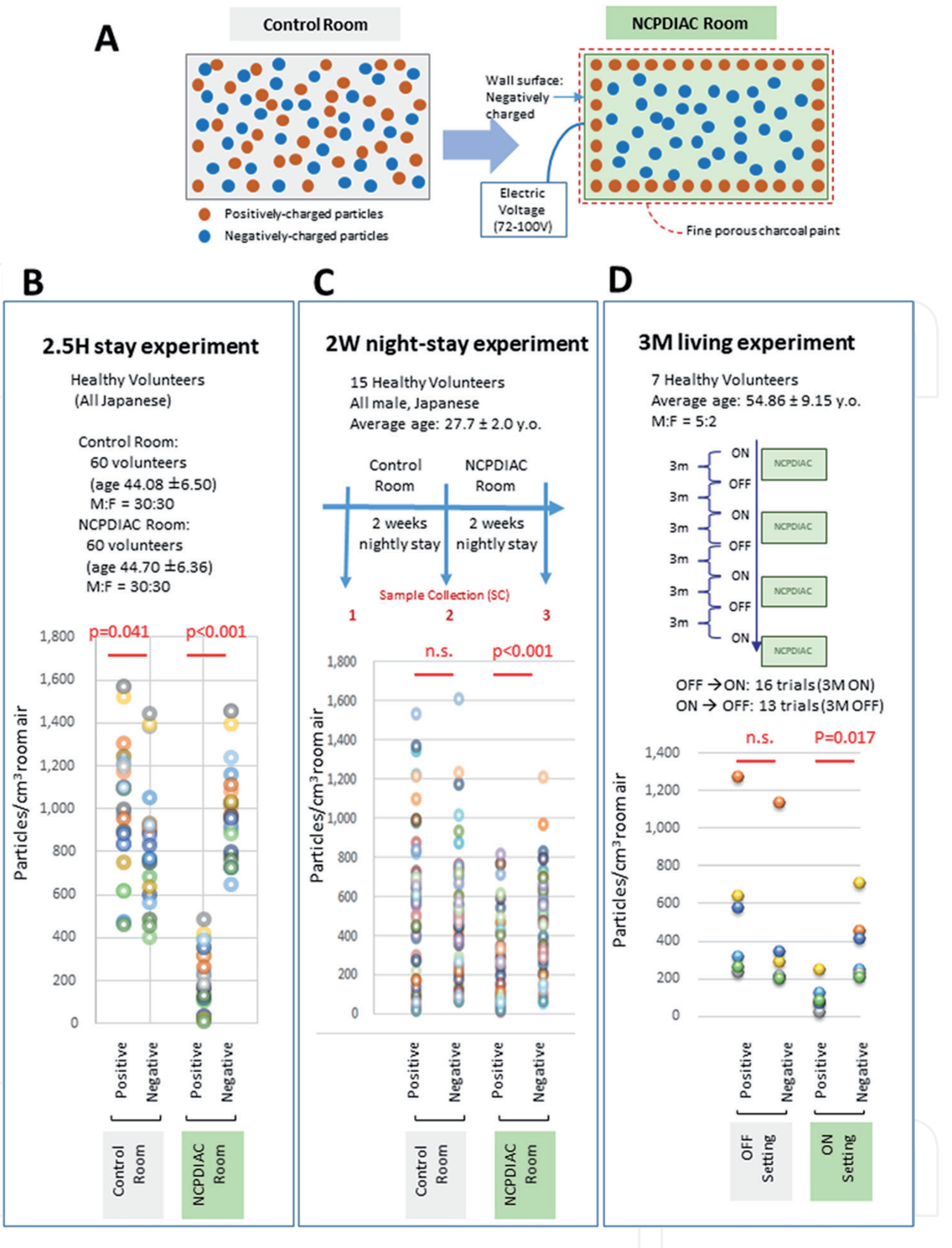

Figure 1.

(A) The mechanism employed to produce negatively charged air dominant indoor air conditions (NCODIAC). Fine porous charcoal paints were painted on the walls, and an electric voltage (72–100 V) was applied to the walls. Hence, wall surfaces became electrically negatively charged. As a result, positively charged particles were adsorbed onto the surface of walls. Therefore NCPDIAC was formed continuously and relatively. (B) 2.5 hour stay experiments were performed with 60 healthy volunteers. In this experiment, control and NCPDIAC rooms were made available. The concentration of positively and negatively charged particles is shown. In control rooms, a slight increase in positively charged particles was found; however, in NCPDIAC rooms the concentration of positively charged particles decreased. Although the concentration of negatively charged particles remained unchanged compared with control rooms, differences resulting from NCPDIAC were significant. (C) Two week night-stay experiments were performed using 15 healthy volunteers. Control and NCPDIAC rooms were made available within a dormitory. Positively and negatively charged particles were measured in control and NCPDIAC rooms on three separate occasions. As a result, NCPDIAC rooms showed a decrease in positively charged particles and a relatively dominant condition of negatively charged particles. (D) Thereafter, 3-month stay experiments were performed with participants in their own home. There were 16 trials comprising OFF (including precondition) to ON periods and 13 trials comprising ON to OFF periods. It was found that during the OFF period, there was no difference between the concentrations of positively and negatively charged particles. However, during the ON period, the concentration of negatively charged particles was significantly higher compared with that of positively charged particles (the concentration of which had decreased).

for 2 weeks during the evenings (night stay) while receiving employee training during the daytime and then moved into NCPDIAC rooms for the following 2 weeks. Thereafter, participants returned to the rooms they had initially occupied. As with the 2.5 hour stay experiments, there were no differences in temperature, humidity, or concentration of VOCs between control and NCPDIAC rooms during the experimental period [14]. However, the concentration of charged particles differed. As shown **Figure 1C**, the concentration of positively charged particles decreased in the NCPDIAC rooms, and there was a significant difference between positively and negatively charged particle concentrations [14].

A third series of experiments was performed comprising 3-month stays [15]. The NCPDIAC apparatus was installed in the bedrooms or living rooms of newly built or renovated homes or condominiums. Seven volunteers participated. Volunteers would switch the NCPDIAC apparatus ON or OFF themselves every 3 months [15]. A total of 16 OFF to ON trials (ON trials) and 13 ON to OFF trials (OFF trials) were performed [15]. When the switch was OFF, there were no differences in concentration between positively and negatively charged particles, whereas when the switch was ON, the concentration of positively charged particles decreased, and there was a significant difference between positively and negatively charged particle concentrations [15], as shown in **Figure 1D**.

3. Biological effects of NCPDIAC

Prior to and following each of the stay periods (2.5 hour, 2-week night, and 3-month ON/OFF trials of NCPDIAC), biological measurements were performed [13–15].

In the 2.5 hour stay experiments, various general medical checks were performed such as peripheral blood counts, liver and kidney functions, lipids, minerals as well as immunoglobulin, and stress biomarkers (including serum cortisol, salivary immunoglobulin (Ig) A, chromogranin, and amylase), as well as a questionnaire given for mood, various autonomic nerve conditions (heart rate, blood pressure, body sway, and Flicker test), and blood viscosity. Cytokinesrelated to balance between T helper (Th) 1 and Th2 such as interferon (IFN)-γ, tumor necrosis factor (TNF)-α, and interleukin (IL)-2 for Th1, and IL-4, IL-6, and IL-10 for Th2 were also measured.. All variables were recorded as [post-stay]–[pre-stay] values. These values were compared between stays in control and NCPDIAC rooms [13]. As shown in **Figure 2A**, the most significant difference was found in the level of IL-2 [13]. Although the changes were very small, there was a significant difference between stays in control and NCPDIAC rooms. Additionally, statistical significance was observed for changes in IL-4 (higher in NCPDIAC rooms) and fluctuations in heart rate (lower in NCPDIAC rooms). However, the most noticeable difference was in IL-2 [13].

Two-week night-stay experiments were then performed. For this series of experiments, additional items that were checked included NK activity, urine 17-hydroxycorticosteroid (OHCS) as a stress marker, and deoxyguanosine (8-OHdG) as an oxidative stress marker, since it was considered that these factors may change during the 2-week period, even though they remain unchanged in the short term [14]. The only difference observed for the various biomarkers examined prior to and following occupation of the NCPDIAC rooms was in NK cell activity. As shown in **Figure 2B**, relative NK cell activity tended to increase with sample collection (SC) 3 (after a 2-week night stay in NCPDIAC rooms) and SC1 as 1.0, while a significant increase was observed with SC3 and SC2 as 1.0. This was considerable at this point, as the short-term experiments revealed a significant increase in IL-2 [14]. However, IL-2

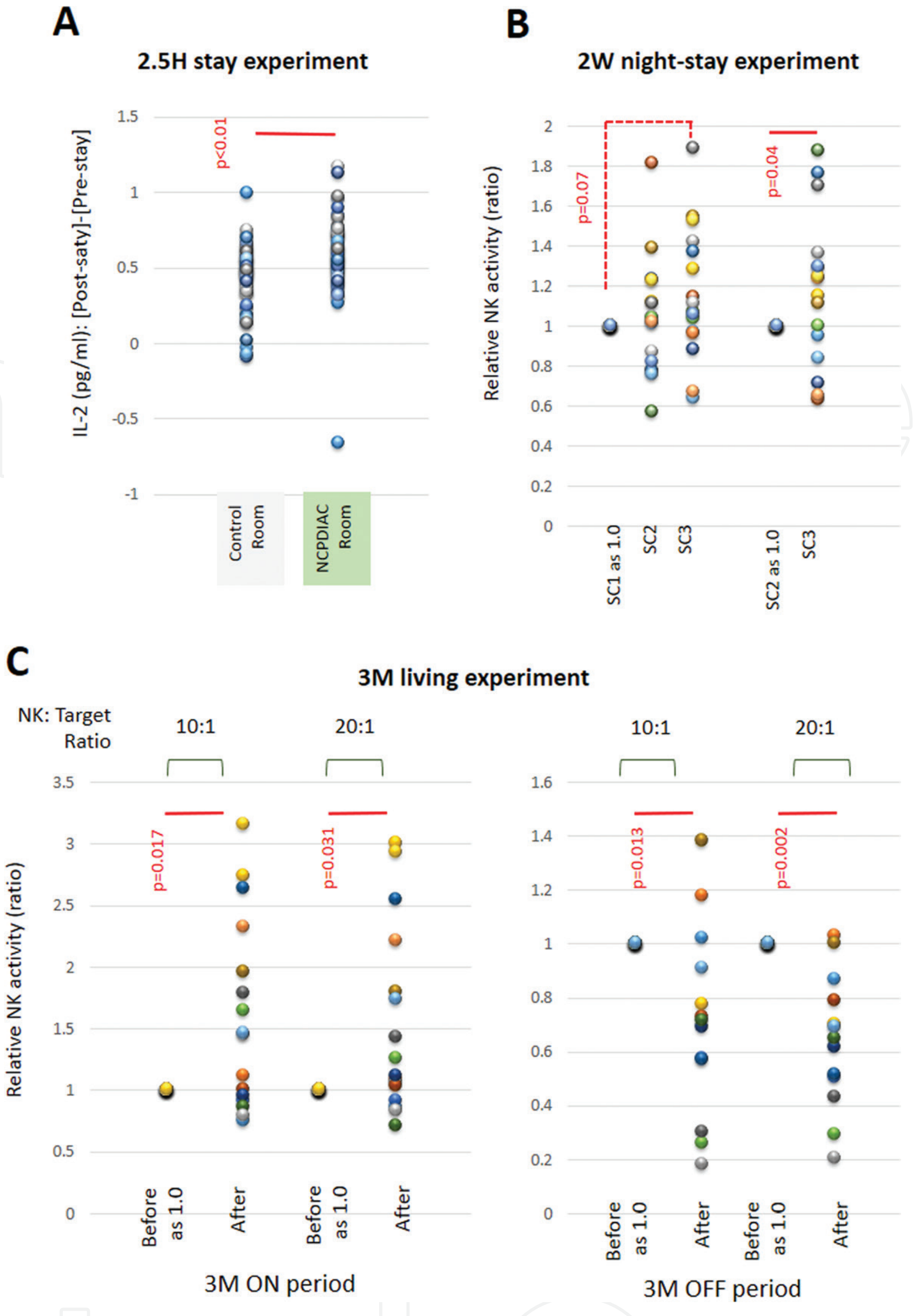

Figure 2.
(A) Of the various biological tests that were employed for the 2.5 hour stay experiments, the greatest change observed in the [post-stay]–[pre-stay] values was in the concentration of serum IL-2. Stays in the NCPDIAC rooms resulted in significant increases in IL-2. (B) During the 2 W night-stay experiments, the relative NK cell activity increased significantly after stays in the NCPDIAC rooms. The relative NK cell activity at SC (sample collection) 3 (after the 2 W night stay in NCPDIAC rooms) compared with SC1 (at the time of leaving control rooms) tended to increase, and when compared with SC2 (just before entering NCPDIAC rooms, after 2 W night stay in control rooms), there was a significant increase in NK cell activity. (C) In the 3 M stay experiments during the 3 M ON period (left panel), the relative NK cell activity increased following stays when activities were measured using 10:1 and 20:1 ratios (NK cells versus target cancer cells in vitro). Additionally, during the OFF period, the relative NK cell activity decreased significantly under 10:1 and 20:1 conditions.

levels were considered to return to basal levels after participants had ceased to occupy NCPDIAC rooms. The slight but significant increase in IL-2 levels during the night-time for the 2-week period may lead to activation of NK cells [14].

The third series of experiments involved participants living in their own homes [15]. Participants had the NCPDIAC apparatus in their bedrooms or living rooms. This apparatus was switched ON or OFF every 3 months by the volunteers themselves. Biological measurements were performed prior to the ON period (including the initial pre-time) and 3 months later (just prior to the OFF period) and then again just prior to the ON period (3 months later). As shown in **Figure 2C**, relative NK cell activity increased during the ON period and decreased during the OFF period [15]. The left panel of **Figure 2C** shows a 3-month ON period, with both NK cell and target cell ratios (10:1 and 20:1, respectively) shown [15]. In both cases, after a 3-month ON period, the relative NK cell activity increased [15]. On the other hand, as shown in the right panel of **Figure 2C**, during the OFF period, even with cell ratios of 10:1 and 20:1, the NK cell activity decreased [15].

NK cell activity is known to be correlated with the presence of cancer cells in humans and with viral infection of cells. Thus, indoor environments that yield enhancements in NK cell activity may somehow lead to the prevention of cancers in occupants and improvement of symptoms associated with viral-mediated illnesses such as influenza.

4. Other findings regarding NCPDIAC

In addition to the aforementioned results, in vitro studies were performed [16]. Peripheral blood mononuclear cells from healthy volunteers were cultured in a standard CO_2 incubator or with forced influx using an adsorbed negatively charged air incubator. With the latter (experimental) incubator, the concentration of negatively charged particles was higher, at approx. 3000 particles/cm^3 air in the incubator [16].

It was found that NK cell activity was enhanced in the experimental incubator. Moreover, CD25 expression in CD4 T cells and IFN-γ production in supernatants were also enhanced following application of the experimental incubator. These findings also support the notion that NCPDIAC may stimulate the immune status, but not quite pathologically [16]. Then, to demonstrate a representative phenotype, NK cell activity was found to be enhanced as shown in **Figure 2C**.

Furthermore, in the 3-month stay experiments, serum amyloid A (SAA) levels decreased significantly during the ON period [17]. Although the exact meaning of this finding is unclear, SAA is considered to be an acute reactive protein such as C-reactive protein (CRP) [18]. Additionally, the increase in high sensitivity CRP is considered to represent a predictive biomarker of atherosclerosis, and, if SAA levels also fluctuate similar to CRP, NCPDIAC may prevent the progression of atherosclerosis [17].

At present, our efforts are being directed at monitoring participants engaged in living under NCPDIAC for greater than 1 year.

5. Improvement in pollen allergy symptoms by cloth containing specific ore powder

Next, a trial aimed at preventing pollen allergies by indoor environment modifications was introduced [18].

We used specific natural ore powder (SNOP) in the form of a cloth containing this powder (CCSNOP). Details of the experiments have been reported previously. SNOP was obtained near Mount Aso, one of the biggest volcanoes in Japan (Kumamoto Prefecture), and is known to release far-infrared rays [18]. Chemical analyses revealed no specific characteristics of the natural ore found surrounding the Mount Aso area and mainly comprise SiO_2, Al_2O_3, Fe_2O_3, Na_2O, and other small chemical compounds. The Cosmic Garden Co. Ltd., a custom-home building company located in Okayama City, Japan, is the company from which our materials are sourced [18]. Their products and homes contain features of “2 × 4” construction methods for aseismic capacity, the avoidance of chemical substrates and smells by well-sealed and super-insulated areas, and enhanced durability. Additionally, this company has employed SNOP within wall materials. Since clients utilizing these products have provided anecdotal accounts of improvements in symptoms related to pollen allergies, we attempted to investigate these phenomena and provide empirical evidence for any health benefits [18].

As shown in **Figure 3**, 20 pollen allergy patients were recruited in April (the season for pollen allergies in Japan) of 2014. The average age of participants was 36.9 ± 11.2 years and comprised of 11 males and 9 females [18]. Over a 2-week period, participants occupied rooms covered by CCSNOP or by non-woven cloth (NWC), which did not contain the ore powder, for 1 hour. During this 1-hour period, windows were opened for 1–2 minutes every 15 minutes to expose the rooms

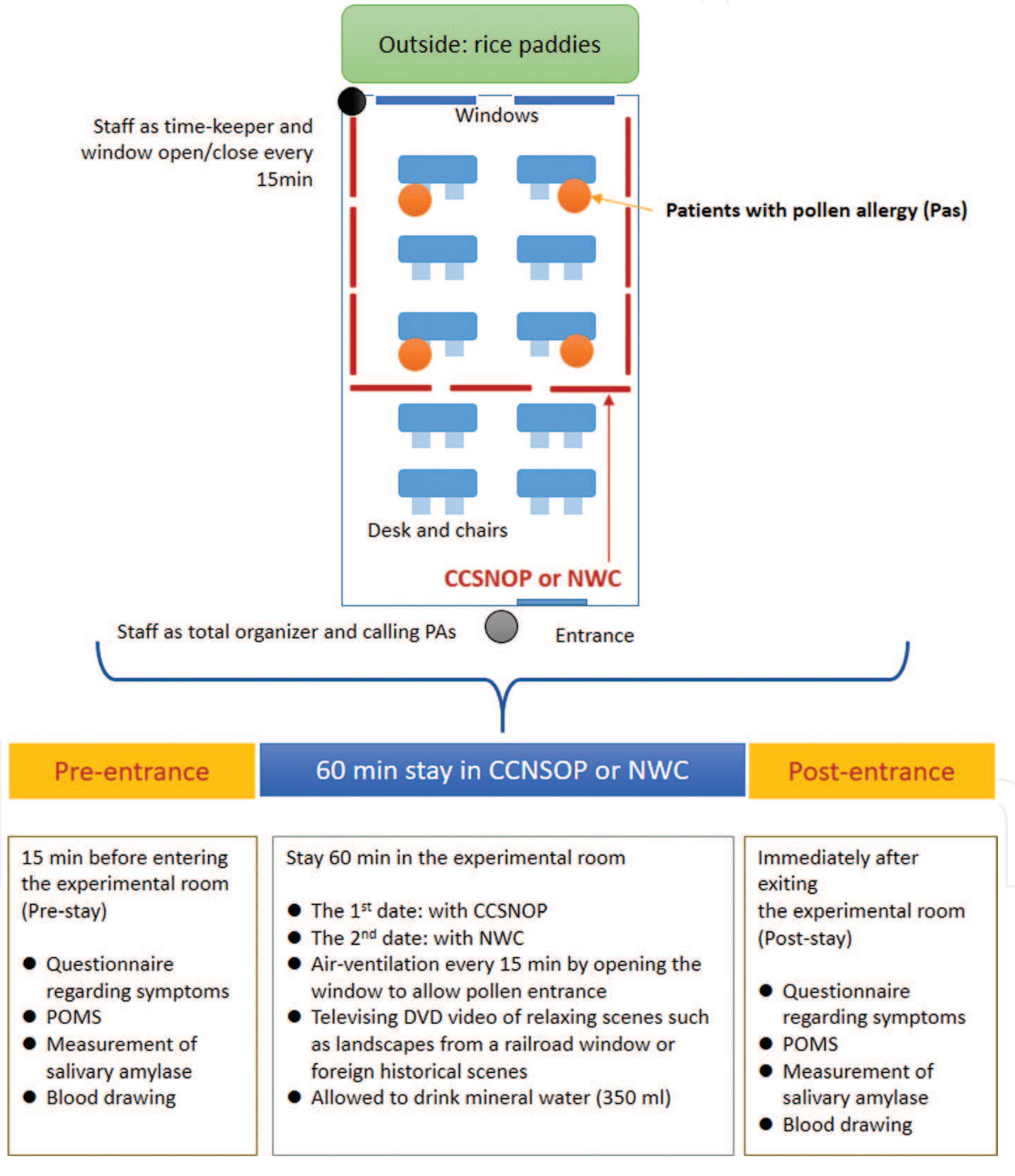

Figure 3.
Twenty patients with pollen allergies occupied rooms covered by CCSNOP or NWC in the spring (season for pollen allergies in Japan) of 2014. During the 1-hour stay in the CCSNOP or NWC rooms, windows were opened for 1–2 minutes every 15 minutes to expose the rooms to pollen. Participants were subjected to various tests as shown in the lower panel. Prior to and following entry into the rooms, participants completed a questionnaire related to symptoms and mood [profile of mood status (POMS)], as well as tests for salivary amylase as a stress biomarker, and blood drawing. The questionnaire was evaluated by the chi-square test, and CCSNOP and NWC stays were compared. Other biological markers were also compared and represented as [post-entrance]–[pre-entrance] values.

to pollen [18]. Prior to and following occupation of the rooms, participants completed a questionnaire regarding symptoms and mood (a POMS (profiles of mood status) questionnaire was employed), and a variety of blood tests were performed including peripheral blood counts, liver and kidney functions, minerals, specific Ig E for various allergens, and cytokines. The measured items were represented as [post-admission] – [pre-admission] [18].

The results of the questionnaire of symptoms and mood are shown in **Figure 4**. In the upper panel, it can be seen that nasal obstruction, lacrimation, and difficulty of daily life improved in participants occupying the CCSNOP rooms compared with those occupying the NWC rooms. However, eye redness became worse in participants occupying the CCSNOP rooms. In the lower panel, moods for "tension and anxiety," "depression," and "fatigue" improved in participants occupying the CCSNOP rooms compared with those occupying the NWC rooms. Additionally, total mood disturbance also improved. All of these statistical analyses employed the chi-square test [19].

Total Ig E was found to increase slightly but significantly in participants occupying the CCSNOP rooms compared with those occupying the NWC rooms. Moreover, the percentage of eosinophils also increased in participants occupying the CCSNOP rooms. The reason for the changes in IgE and eosinophils remains unclear. Our experiment comprised just a 1-hour stay. Thus, although symptoms and moods may change rapidly, IgE and eosinophils changes may require more time [19].

	CCSNOP		NWC		
Symptom	Improved	No change or getting worse	Improved	No change or getting worse	P value (X^2 test)
Sneezing	14	2	13	5	0.271
Nasal juice	12	6	10	6	0.464
Nasal obstruction	12	6	9	8	* 0.003
Eye redness	4	7	7	7	* 0.010
Lacrimation	7	4	4	11	* <0.001
Difficulty of daily life	11	5	5	7	* 0.021

Statistically significant differences were found for items "Sneezing", LAcrimation" and "Difficulty of daily life". These items indicated that associated symptoms improved in CCSNOP compared to NWC. However, item "Eye redness" showed an improvement that was significantly higher in NWC than in CCSNOP.

	CCSNOP		NWC		
Score Change [Post-Pre] x number of HVs	Down	Up	Down	Up	P value (X^2 test)
Tension & Anxiety	-53	0	-19	4	* <0.001
Depression	-23	2	-8	4	* 0.002
Anger & Hostility	-11	3	-8	1	0.440
Vigor	-29	6	-30	10	0.274
Fatigue	-40	9	-19	10	* 0.010
Confusion	-21	8	-23	3	0.050
Total Mood Disturbance (TMD)	-109	21	-75	39	* <0.001

Moods for "Tension & Anxiety", "Depression" and "Fatigue" decreased significantly when Health Volunteers (HVs) stayed in CCSNOP when compared to NWC. In addition, TMD decreased significantly when HVs stayed in CCSNOP compared to NWC.

Figure 4.
Results of the symptom questionnaire and POMS. Statistical data were analyzed by the chi-square test.

In future experiments we intend to make available bedrooms that can be utilized by participants with pollen allergy during spring (season of pollen allergies) for at least 2 weeks in an effort to further investigate changes in symptoms, moods, and biological factors.

6. Conclusion

We have presented the outcome of two different strategies aimed at improving human health by modification of indoor environments. A consideration of several factors is required to maintain human health and minimize physical and mental disturbances while indoors, including the avoidance of chemical substances such as VOCs and other chemicals. Future investigations will involve participants occupying variously modified rooms (including NCPDIAC and SNCBOP) for longer periods of time. These studies should contribute toward the creation of healthy indoor environments for human habitation.

Acknowledgements

All experiments presented in this chapter were approved by the Ethic Committee of the Kawasaki Medical School, Kurashiki, Japan, and written informed consent was obtained from all participants.

Conflicts of interest

For the NCPDIAC experiments, the Department of Hygiene, Kawasaki Medical School, obtained research funding from Sekisui House Ltd., Osaka, Japan, and from Yamada SXL Home (now known as Yamada Home) Co. Ltd., Takasaki, Japan. Additionally, the extra-porous charcoal paints were provided by Artech Kohboyu, Co. Ltd., Omura, Nagasaki, Japan. For the CCSNOP experiments, the Cosmic Garden Co. Ltd. provided the CCSNOP apparatus.

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