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Original Article

Clinical Characteristics of Disability in Patients with Indoor Air–Related Environmental Intolerance

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ABSTRACT

Background: Chronic nonspecific symptoms attributed to indoor nonindustrial work environments are common and may cause disability, but the medical nature of this disability is unclear. The aim was to medically characterize the disability manifested by chronic, recurrent symptoms and restrictions to work participation attributed to low-level indoor pollutants at workplace and whether the condition shares features with idiopathic environmental intolerance.

Methods: We investigated 12 patients with indoor air–related work disability. The examinations included somatic, psychological, and psychiatric evaluations as well as investigations of the autonomic nervous system, cortisol measurements, lung function, and allergy tests. We evaluated well-being, health, disability, insomnia, pain, anxiety, depression, and burnout via questionnaires.

Results: The mean symptom history was 10.5 years; for disabling symptoms, 2.7 years. Eleven patients reported reactions triggered mainly by indoor molds, one by fragrances only. Ten reported sensitivity to odorous chemicals, and three, electric devices. Nearly all had co-occurrent somatic and psychiatric diagnoses and signs of pain, insomnia, burnout, and/or elevated sympathetic responses. Avoiding certain environments had led to restrictions in several life areas. On self-assessment scales, disability showed higher severity and anxiety showed lower severity than in physician assessments.

Conclusion: No medical cause was found to explain the disability. Findings support that the condition is a form of idiopathic environmental intolerance and belongs to functional somatic syndromes. Instead of endless avoidance, rehabilitation approaches of functional somatic syndromes are applicable.

1. Introduction

Nonspecific symptoms attributed to indoor nonindustrial work environments are common [1]. This kind of ill health varies from annoyance to functional restrictions in daily life, with no objective medical findings to explain the wide symptomatology and disability [2–5]. Symptomatic individuals try to avoid exposure and environments that evoke symptoms [6,7].

Although recognized, disability due to indoor environment is poorly understood from a medical perspective. The term sick building syndrome, launched by the World Health Organization (WHO) in 1983 [8], describes symptoms at the group level [9] but does not explain the chronic disability of individuals. Sick building syndrome includes transient symptoms of a multifactorial origin which may have a possible relation to indoor pollutants [9]. However, despite improvements to indoor air quality, chronic responsiveness to indoor pollutants may still develop and eventually lead to disability [2,5,10]. The dilemma is whether the disability is due to exposure or to increased responsiveness in these individuals [7].

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Increased responsiveness seems to be the mechanism for idiopathic environmental intolerance (IEI) [11,12], which describes reactivity to any environmental factors at levels with no harmful health effects [13]. Multiple chemical sensitivity (MCS) and hypersensitivity to electromagnetic fields (EMFs) are the most studied aspects of IEI, and increasing evidence shows that the condition is not explained by exposures [14,15]. In IEI, the mechanisms involve reactions due to negative expectancy, i.e. nocebo effects [11].

Multiple criteria have been developed to define IEI as an acquired chronic condition of multiple, recurring, nonspecific symptoms that are attributed to environmental factors without medical explanation [13,16]. According to Lacour et al. [17], MCS/IEI criteria should include significant lifestyle or functional impairments, and thus be limited to severe cases. The criteria remain descriptive, and the recognition of IEI is based on subjective symptom reporting without objective findings or diagnostic tests [18].

Epidemiological studies have estimated the prevalence of functional restrictions related to IEI [19,20]. In a Danish general population, 3.3% reported making adjustments to their social lives or occupational conditions due to chemical intolerance [19]. In a sample of fertile-aged pregnant women, 2.2% reported behavioral changes and severe difficulties at work, in household responsibilities, or in their social lives due to intolerance of chemicals, indoor molds, or EMFs [20].

So far, clinical descriptions of disability have mainly been due to MCS. One qualitative study showed the nature of disability causes restraints in lifestyle, social life, and occupational conditions [6]. The clinical evaluation of MCS patients has shown co-occurrence with psychiatric disorders [21,22], somatic diseases such as asthma [22], and functional somatic syndromes (FSSs) [23].

Clinical studies characterizing chronic nonspecific indoor air-related illness and disability are scarce. Follow-up studies show that chronic symptomatologies may reduce the quality of life and social and work functioning [2,3,24]. Applying a qualitative approach has shown that disability affects several aspects of daily life, resulting in alterations, limitations, and emotional consequences for individuals [10]. In our previous clinical study, patients presenting with symptoms due to indoor air and work disability had long-lasting multiple organ system symptoms that were not explained by asthma, allergy, or other somatic diseases [5]. More than half had concerns about a serious disease or loss of health due to indoor air [5]. The aforementioned study [5] and a similar patient series [25] found that asthma or asthma-like persisting symptoms previously attributed to mold were not explained by current exposure.

The purpose of the present study was a more thorough clinical evaluation of the medical cause of disability. The aim was to evaluate patients with chronic responsiveness to workplace indoor air, which had interfered with work participation. We clinically studied the medical cause of the chronic symptoms and activity limitations related to indoor air and whether the condition fulfilled the criteria of IEI. The goal of this thorough clinical characterization of disability was to improve the targeting of aid and support to these patients.

2. Materials and methods

2.1. Study population

The participants were 12 patients referred from their occupational health service (OHS) units to the occupational clinic of the Finnish Institute of Occupational Health (FIOH) for clinical evaluation. All patients had responsiveness to factors in nonindustrial workplace indoor air. This had led to disability, which manifested as functional restrictions to avoid the symptoms, and had interfered with work participation (e.g. inability to work), despite adjustments to occupational facilities. The referring physician had failed to find a solution to manage the patient's ill health and work disability, and had eliminated obvious medical reasons for symptoms. All the recruited patients between June 2015 and November 2015 agreed to participate in the study. At study intake, the condition of all the patients suggested features of IEI.

This study was carried out in collaboration with FIOH and Helsinki University Central Hospital.

Table 1
Assessment and evaluation methods

Occupational and psychosocial functioning	
Self-assessed current work ability[a] [26]	Q
Own prognosis regarding being able to work two years from now[b] [26]	Q
The Social and Occupational Functioning Assessment Scale[c] [27]	I
Sheehan Disability Scale, subdomains work, social life, home[d] [28]	Q
Shirom-Melamed Burnout Measure[e] [29]	Q
Respiratory functioning, inflammation, and allergy	
Peak Expiratory Flow monitoring for two weeks [30]	M
Flow-volume spirometry (Spirostar USB Medikro, Finland)	M
Exhaled lower respiratory nitric oxide and nasal nitric oxide [31]	M
Bronchial hyperresponsiveness [32]	M
Skin prick tests to common environmental allergens and molds (ALK-Abello, Hørsholm, Denmark; Stallergenes SA, Antony, France)	M
Asthma Control Test (ACT)[f] [33]	Q
Autonomic nervous system function and hypothalamic–pituitary–adrenal axis functioning	
Cardiovascular tests [34–36]	M
Hyperventilation provocation test [37]	M
Long-term recording of heart rate variability in beat-to-beat intervals [38,39]	M
Salivary cortisol (LIA, IBL Hamburg, Germany) [40]	M
Psychiatric symptoms and functioning and personality	
Structured Clinical Interview for DSM-IV Disorders (I and II) [41]	I
Yale-Brown Obsessive Compulsive Scale [42]	I
Montgomery–Åsberg Depression Rating Scale [43]	I
Generalized Anxiety Disorder 7-item Scale [44]	Q
Beck Anxiety Inventory [45]	Q
Overall Anxiety Severity and Impairment Scale [46]	Q
The Patient Health Questionnaire-9 [47]	Q
Beck Depression Inventory [48,49]	Q
Insomnia Severity Index [50]	Q
Other characteristics	
Demographics (e.g. age, gender, marital status, education, work, sick leave)	I + Q
Health condition, current symptoms, pain, diseases, medication	I + Q
The Quick Environmental Exposure and Sensitivity Inventory [51] Chemical Intolerance[g], Life impact[h]	Q
Intolerance to indoor air molds[g], intolerance to electromagnetic fields[g]	Q
Environmental-related health concerns[i]	Q
Indoor air quality at workplace and home	I + Q

I, interview; M, medical investigation; Q, questionnaire.
[a] Scale from 0 (total work disability) to 10 (work ability at its best).
[b] Options "fairly sure", "not sure", or "hardly".
[c] Scale 1–100: 51–70 (moderate or some difficulty), 71–80 (slight impairment), 81–100 (good or superior functioning).
[d] Each subdomain on a scale 0–10: 0 (not at all disability), 1–3 (mildly), 4–6 (moderately), 7–9 (markedly), 10 (extremely).
[e] Mean of the 14 items, each item on a scale 1–7: 1 (never or almost never), 2 (very infrequently), 3 (quite infrequently), 4 (sometimes), 5 (quite frequently), 6 (very frequently), 7 (always or almost always).
[f] The Finnish version of the ACT. The ACT is a trademark of Quality Metric Incorporated 2002 GlaxoSmithKline.
[g] Each item on a scale 0–10: 0 (not at all a problem), 5 (moderate symptoms), 10 (disabling symptoms).
[h] Each item on a scale 0–10: 0 (not at all), 5 (moderately), 10 (severely).
[i] Scale from 0 (not at all concern) to 10 (extremely concern).

2.2. Clinical investigations and patient characteristics

Our clinical examinations included systematic evaluations by a specialist in occupational medicine, a pulmonologist, a psychiatrist, and a psychologist. The clinical evaluation was based on structured clinical interviews and questionnaires, as well as on previous medical records and data on indoor quality and pollutants in the work environment from a referring OHS's physician. Investigations

of the autonomic nervous system (ANS), hypothalamic–pituitary–adrenal (HPA) axis functioning, lung function, and allergy tests were included. Patients completed the questionnaires before the clinical sessions, so that the self-assessments could be utilized in the clinical evaluation. Finally, our multidisciplinary team assembled conclusions for an individual treatment and rehabilitation plan, which will be reported in a future paper. Table 1 shows the description of the assessment methods for the results reported in this paper. All the other methods used in the clinical evaluation are shown in supplementary material (Table A.1).

2.2.1. Self-rated assessments

Questionnaires were used to evaluate well-being, health, disability, insomnia, pain, and distress of anxiety, depression, and burnout (Table 1). Multisite musculoskeletal pain was defined using three questions: (i) “Have you recently experienced aches or pains?” (yes/no); (ii) “If yes, where on the body have the pains been?” with options “yes” or “no” for each 16 areas of the body (head, neck, upper back, shoulder, brachium, forearm, arm, wrist, hand, lower back, hip, thigh, knee, leg, ankle, and foot); and (iii) “Have the pains continued over three months?” (yes/no). Only pain over three months and in at least three different areas of the body was taken in consideration.

The self-reported functional measure, the Sheehan Disability Scale (SDS), rated functional impairments in three subdomains (work, social life, home) [28] (Table 1).

From the chemical intolerance screening instrument, the Quick Environmental Exposure and Sensitivity Inventory (QEESI), we used the Chemical Intolerance (CI) and the Life Impact scales [51]. In addition to these, we elicited self-rated intolerance to indoor air molds in moisture-damaged buildings and intolerance to EMFs (Table 1). We also inquired about health concerns regarding environmental exposures and indoor air exposures at the workplace.

2.2.2. Clinical evaluation

The somatic evaluation was conducted using structured interview material (in Finnish, available by request). We elicited the patients’ health condition and diseases, symptom profile and course of illness, occupational and social functioning, as well as prior adjustments at work and in social life. We also determined the onset time of symptoms extending to the disabling level and involving multiple organ systems. The symptoms were divided into the following symptom groups: central nervous system (CNS), respiratory or mucosal, dermal, musculoskeletal, cardiac, and gastrointestinal symptoms. Respiratory evaluation was performed to detect respiratory diseases and assess asthma control among asthma patients (Table 1).

A psychiatrist assessed the presence of psychiatric disorders, functioning in daily life, and well-being using structured interview methods and self-assessed measures (Table 1). The psychiatrist specified the psychiatric International Classification of Diseases, 10th revision (ICD-10) diagnoses after clinical findings in the psychological assessment including the evaluation of cognitive, social, and personality functioning and an additional semi-structured visual expression interview (see supplementary material: Table A.1).

Based on the physician interview, the severity of disability in social and occupational functioning was scored using the DSM-IV Social and Occupational Functioning Assessment Scale (SOFAS) [27].

2.2.3. ANS function and HPA axis functioning

Assessment of the ANS function was included for the evaluation of physiological stress and recovery processes in laboratory and real-life settings. We performed cardiovascular tests and the hyperventilation provocation test to assess the individual reactivity of ANS and to exclude organic disturbances in autonomic regulation (Table 1). The cardiac reactivity tests included controlled and uncontrolled breathing, slow deep breathing, the active orthostatic test, and the sustained hand grip test [34]. Continuous electrocardiogram and peripheral blood pressure were analyzed using special software for ANS metrics (WinCPRS, Absolute Aliens, Turku, Finland). The main indicator of sympathovagal balance in the short-term provocation tests was the ratio of low-frequency power to high-frequency power (LF/HF ration) in heart rate variability (HRV) at rest. A ratio of >2.8 was considered to indicate increased sympathetic dominance [35].

The stress and recovery balance in real-life settings was assessed using recordings of R–R intervals and analyses of HRV within three days. In the analyses, we used the recovery percentage during a sleep period (from self-reported bedtime to awakening time). Recordings of the Finnish population ($n = 20\,000$, including 51 000 days) report the mean of recovery time during sleep to be 60% using HRV analysis [38]. In this study, we used a recovery time of under 60% during sleep as an indicator of delayed recovery.

As an indicator of the HPA axis, we took salivary cortisol samples three times a day within a two-day period: immediately after awakening, 30 min after awakening, and in the evening. A range of 3.3–6.1 nmol/L in the salivary evening cortisol level has been reported among the nonanxious population using competitive electrochemiluminescence immunoassay analytics [40]. In this paper, we report evening analysis, and levels of >6.1 nmol/L were considered to deviate from the nondistressed population.

2.2.4. IEI definition

We used WHO’s IEI criteria [13], which cover the acquired condition with multiple recurrent symptoms attributed to various environmental factors that are well tolerated by most people and that cannot be explained by any somatic or psychiatric disorder. Further, we used the stricter criteria by Lacour et al. [17], which require a duration of at least six months with significant lifestyle or functional impairments and symptoms to be present in the CNS with at least one symptom of another organ system.

2.3. Data analysis

We calculated descriptive statistics [frequency, mean, median, range, and standard deviations (SDs)]. All the statistical analyses were carried out using SPSS version 25.0 (IBM Corporation, Chicago, Illinois, USA) software.

2.4. Ethical considerations

All procedures performed in the studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The Ethics Committee of the Hospital District of Helsinki and Uusimaa, Finland, approved the study protocol (81/13/03/00/15, dated 5.5.2015). Permission to conduct the study was also granted by the Helsinki University Hospital and the FIOH ethical working group. All participants provided a written informed consent for participation.

3. Results

Of the 12 recruited patients, two withdrew from part of the investigations (one because of suffering symptoms at our clinic facilities and the other due to schedule problems and experiencing no benefit from the study). Therefore, the number of participants in

Table 2
Demographic characteristics and workplace adjustments made

	All ($n = 12$)
Female, *n*	11
Age, years, mean (SD)	49.8 (6.0)
Married or cohabitation, *n*	12
Education	
High level, *n*	6
Mid level, *n*	3
Basic, *n*	3
Nonsmoker, *n*	11
Body mass index, kg/m^2, mean (range)	26.9 (21.3–36.3)
Work absence days during preceding 12 months	
Owing to any reason, days, mean (range)	92.4 (2–365)
Owing to indoor air–related symptoms, days, mean (range)	88.6 (0–365)
Physician visits during preceding 12 months	
For any reason, number, mean (range)	14.8 (2–40)
For indoor air–related symptoms, number, mean (range)	13.0 (0–36)
Duration of indoor air–related symptoms, years (range)	10.5 (2–25)
Workplace adjustments[a] made	
Relocation, *n*	11
Working timetable arrangement, *n*	1
Sabbatical leave, *n*	4
Remote work, *n*	3
Part-time work, *n*	2
Working as a freelancer in several jobs, *n*	1

SD, standard deviation.
[a] An individual may have one or more measures.

Table 3
Self-reported environmental intolerances and concerns, mean (range)

	All ($n = 12$)
QEESI	
Chemical Intolerance score[a]	50.1 (4–91)
Life Impact score[a]	55.5 (1–94)
Intolerance to indoor molds[b]	8.7 (0–10)
Intolerance to EMFs[b]	0.8 (0–6)
Health concerns regarding	
Environmental exposures[b]	8.8 (3–10)
Indoor air exposures at workplace[b]	9.4 (7–10)

EMFs, electromagnetic fields; QEESI, the Quick Environmental Exposure and Sensitivity Inventory.
[a] Sum score 0–100.
[b] Scale 0–10.

the ANS and HPA axis functioning tests was ten, and that in the clinical psychiatric evaluation was eleven.

Table 2 presents the demographic data. The ages of the 12 patients ranged from 39 to 59 years. Most of the patients were female, highly educated, and nonsmokers. Their workplaces were schools and kindergartens (n = 8), office (n = 2), a hospital (n = 1), and a fire station (n = 1). The mean of self-reported absence from work due to indoor air–related symptoms was 88.6 days (median = 15.5 days, SD 134.6) during the preceding year. At the time of evaluation, three patients were not working due to symptoms (sick leave or sabbatical leave).

Based on the clinical interview, the mean duration from onset to the time when symptoms extended to a disabling level was 7.8 (range 0.5–23) years and from this extension point to the current evaluation time was 2.7 (range 1–7) years. All the patients reported indoor air–related symptoms from at least three organ systems (mean 4.5, range 3–6), and all had neurological and respiratory symptoms.

All the patients reported symptoms attributed to workplace indoor environments in nonindustrial workplaces, e.g. offices or schools. Various deficiencies in indoor air quality in previous work environments, mainly moisture and molds, were described by most of the patients (n = 10/12). According to the referring physician's report, the workplace facilities had been repaired or the worker had been relocated. Further, in current work environments, no significant exposure or deficiency in indoor air quality had been detected or suspected. For all the 12 patients, one or more occupational adjustments had been made because of symptoms (Table 2). Despite interventions, the responsiveness to the triggers in the work environment had continued in all patients.

Patients perceived the following environmental factors to be the cause for their current symptoms: indoor molds (n = 10), fragrances (n = 1), or both indoor molds and fragrances (n = 1). Symptoms occurred in various buildings, and/or a wide range of odorous substances provoked them. Seven patients reported symptoms when in the vicinity of people who had been in a moisture-damaged building.

In their clinical interviews, the patients reported restraints on activities imposed by their avoidance behaviors, including work participation (n = 12), attending various places (n = 12), socializing (n = 10), leisure activities (n = 6), and moving or living in conventional homes (n = 3).

3.1. Environmental intolerances and concerns

Chemical intolerance assessed by the QEESI's CI score indicated high probability among eight patients (score $\geq$ 40) and low probability (score $\leq$ 20) among four patients (Table 3). On QEESI's Life Impact scale, ten patients showed a high score (score 24–100). In severity of intolerance to indoor air molds, nine patients scored 10 (scale 0–10), indicating disabling symptoms, and three patients responded with values of 1, 2, or 6 (scale 0–10) to EMFs (Table 3).

All patients reported considerable environment-related concerns about loss of health (Table 3).

3.2. Self-rated scales of somatic and emotional symptoms

Symptoms were characterized using various self-rated measures (Table 4; and supplementary material: Table A.2). Six patients reported insomnia-related symptoms using the Insomnia Severity Index, and two of these scored moderate or severe insomnia. Eight patients reported prolonged multisite pain.

3.3. Disability scales

The self-assessment scales indicated a higher severity of disability than the SOFAS interview tool. The mean of the SOFAS score (higher scores indicating an increasing level of function) was 78.3 (SD 10.5, range 59–92), indicating a slight impairment, and scores by tertiles: moderate or some difficulty (n = 3), slight impairment (n = 3), and good or superior functioning (n = 6). On the inverse SDS (higher scores indicating higher disability), the mean scores were: SDS work 6.1 (SD 2.7, range 1–10), SDS social life 6.7 (1.9, 4–10), SDS home 4.3 (2.3, 0.5–9), and SDS total (mean of the three subscales) 5.7 (1.8, 3.7–9.7). All patients scored $\geq$5 on at least one of the three SDS subdomains, indicating significant functional impairment. The mean of the self-assessed current work ability score [26] was 5.2 (2.4, 0–8). The majority were not sure (n = 8) or hardly sure (n = 2) of their ability to work after two years.

3.4. Clinical evaluation

All 12 patients fulfilled the IEI criteria in terms of responsiveness to indoor molds (n = 11), nine of them also reacted to odorous

Table 4
Self-rated symptoms of anxiety, depression, insomnia, and burnout

		All ($n = 12$)
Anxiety	GAD-7, mean (range)	4.8 (0–13)
	Mild anxiety (score 5–9), *n*	3
	Moderate anxiety (score 10–14), *n*	3
	BAI, mean (range)[a]	7.0 (0–16)
	Mild anxiety (score 8–15), *n*	4
	Moderate anxiety (score 16–25), *n*	1
	OASIS, mean (range)[b]	3.1 (0–10)
	Identification of clinical anxiety (score ≥ 8), *n*	1
Depression	PHQ-9, mean (range)	5.0 (0–12)
	Mild depression (score 5–9), n	4
	Moderate depression (score 10–14), n	2
	BDI, mean (range)[b]	7.2 (1–17)
	Mild depression (score 14–19), n	2
Insomnia	ISI, mean (range)	9.3 (0–27)
	Subthreshold insomnia (score 8–14), n	4
	Moderate severity insomnia (score 15–21), n	1
	Severe insomnia (score 22–28), n	1
Burnout	SMBM total, mean (range)[c]	2.9 (1.4–4.6)
	Mild or moderate burnout (score 2.3–3.7), n	5
	Severe burnout (score ≥ 3.8), n	2

BAI, Beck Anxiety Inventory (sum score 0–63); BDI, Beck Depression Inventory (sum score 0–63); GAD-7, Generalized Anxiety Disorder (sum score 0–21); ISI, Insomnia Severity Index (sum score 0–28); OASIS, Overall Anxiety Severity and Impairment Scale (sum score 0–20); PHQ-9, Patient Health Questionnaire-9 (sum score 0–27); SMBM, Shirom-Melamed Burnout Measure (score 1–7).

[a] $n = 10$.

[b] $n = 11$.

[c] $n = 9$, three patients who were on sick leave were excluded.

chemicals, three to electric devices, and one individual was responsive to only odorous chemicals.

Ten patients (of 12) had one or more somatic diseases based on clinical evaluation and medical history (Table 5). Six patients had asthma, and according to the Asthma Control Test (ACT), asthma was more often controlled (n = 4, ACT ≥ 20) than "not well controlled" or "uncontrolled" (n = 2, ACT ≤ 19). Low lung function in spirometry was detected in none of the asthma patients according to forced vital capacity (FVC) or forced expiratory volume in one second (FEV1) (<80% of the predicted values) or a positive FEV1% bronchodilator response (≥12%). There was no excessive variability in the daily diurnal peak expiratory flow (>10% average daily variability) or in positive bronchodilator response (≥15% and 60 L). Some degree of hyperresponsiveness (mild or moderate) was present in two patients with asthma (of 5, data missing n = 1). Exhaled nitric oxide was mildly raised (≥25 ppb) in two patients, one of whom had asthma. None had positive skin prick test reactions to molds. The results of the investigations of allergy and respiratory tract are shown in supplementary material (Table A.2). Our evaluation did not reveal any need for additional somatic investigations.

Table 5
Current somatic diseases and psychiatric disorders based on clinical evaluation and medical history.

Somatic diseases[a]	$N = 12$
Asthma	6
Benign arrhythmia	1
Fibromyalgia	1
Hypothyreosis (controlled by medication)	2
Irritable colon syndrome	2
Anal fissure	1
Migraine	2
Musculoskeletal disorder	4
Psychiatric disorders[a]	**$N = 11$**
Anxiety disorders	
Social phobia	1
Specified phobic anxiety disorder	1
Other specified anxiety disorder	4
Reaction to severe stress and adjustment disorder	1
Depressive disorders	
Moderate depressive disorder	1
Recurrent depressive disorder, current episode mild	1
Somatoform disorders	
Undifferentiated somatoform disorder	1
Somatoform autonomic dysfunction	1
Personality disorders	
Obsessive-compulsive personality disorder	1

[a] An individual may have one or more somatic diseases or psychiatric disorders.

Table 6
Results of investigations of autonomic nervous system function and hypothalamic–pituitary–adrenal axis functioning, mean (range)

	$N = 10$
Laboratory testing	
Rest	
Heart rate, bpm	66 (59–69)
Root mean square of successive differences of adjacent RR-intervals, ms	34 (16–88)
Baroreceptor sensitivity, ms/mmHg	10 (6–17)
Systolic brachial blood pressure, mmHg	129 (100–154)
Diastolic brachial blood pressure, mmHg	80 (70–90)
Active orthostatic test, power of low frequency band to high frequency band in the spectral analysis of heart rate variability (LF/HF ratio)	
Supine	4.3 (0.7–21.0)
Standing	8.7 (1.0–23.0)
Home monitoring	
Heart rate variability in beat-to-beat R–R interval recording	
Percentage of recovery during sleep (recovery index)[a]	56.1 (22.0–89.7)
Salivary cortisol	
Evening sample, nmol/L[b]	6.2 (1.8–15.9)

[a] Average of the mean of three values within three days.

[b] Average of the mean of two different evening samples.

3.5. Assessment of ANS and HPA axis functioning

Table 6 illustrates the results of ANS and HPA axis functioning among ten patients. The analysis of the time domain parameters of HRV showed no changes indicating significant clinical cardiovascular disorders. Resting blood pressure was above normal in one patient. The LF/HF ratio at rest in a supine position was elevated (>2.8) in three patients, and two of them also showed highest values while standing. None of the patients showed pathognomonic responses in the hyperventilation provocation test.

In a real-life setting, six (of 10) patients showed insufficient recovery during sleep (recovery index < 60%) in the long-term monitoring of HRV. Three patients had elevated cortisol levels in their evening salivary cortisol samples (>6.1 nmol/L). Three patients had both insufficient recovery in HRV during sleep and an elevated cortisol level. In total, six patients had either an elevated LF/HF ratio, insufficient recovery during sleep, or elevated evening cortisol levels.

In eight (of 11) patients, one or more psychiatric disorders were diagnosed (Table 5). Five patients had one diagnosis and three patients had two or more. Two patients had previous psychiatric diagnoses (major depressive disorder, anxiety/phobic anxiety disorder, social phobia). Six patients met the diagnostic criteria for an anxiety disorder according to ICD-10, two of whom also had a depressive disorder. One patient with anxiety and depressive disorders also had a personality disorder. Another two patients met the diagnostic criteria for a somatoform disorder.

4. Discussion

Our study consisted of patients with work disability attributed to indoor air in nonindustrial work environments. The referring OHS physician had found no ways in which to intervene in the worker's ill health and support work participation. The aim was to characterize disability in order to better target aid and support these patients.

The disability manifested in all the 12 patients, as an acquired long-term state of responsiveness to the indoor work environment, which patients attributed to indoor pollutants, mainly molds. In their current work environments evoking symptoms, there was no evidence of or suspicion of harmful indoor exposures. Self-assessment and a physician interview tool assessing disability showed that the patients had functional impairments not only at work but also at home and in their social lives. The questionnaire revealed that insomnia-related symptoms (in 6 of 12) and multisite pain (in 8 of 12) were prevalent. ANS or cortisol measurements were elevated in some (in 6 of 10). No medical cause was found to explain the disability, although the patients had somatic diseases such as asthma and psychiatric disorders. Based on our results, the features of disability were consistent with those described in IEI and FSSs.

All our patients fulfilled the WHO consensus criteria for IEI [13]. They also met the MCS criteria [16], in which exposures are expanded from chemicals to indoor exposures. All had significant functional and lifestyle impairments which are required by the extended MCS criteria [17]. Our patients were similar to those described in several reviews on IEI [7,18,52]. Almost all the patients were women and had multiorgan symptoms, including CNS, and respiratory symptoms triggered by ordinary indoor environments with no known health risks, restrictions in everyday life, and comorbidity of diseases. Negative beliefs and high concerns regarding the impact of exposure on health were also prevalent among our patients, as described earlier [11,53]. As inherent to IEI [14], we did not find toxicological causes to explain disability. Symptoms had continued despite actions taken in workplaces and the absence of abnormal exposure in the patients' current work environments.

Features of prolonged multiple symptoms, (work) disability, and the co-occurrence of variable health conditions with no explanatory medical condition appear as manifestations of FSSs [54]. Lacour et al. [17] summarize the overlap between IEI and FSSs, and shared mechanisms have been suggested for the maintenance of IEI and FSSs, i.e., sustained stress and arousal due to central sensitization [55]. The increasing evidence of central mechanisms of chronic responsiveness [11] enables targeting treatment strategies to reduce disability.

Our patients had long-lasting symptoms in multiple organ systems, which have shown to associate with poor prognosis in previous clinical samples [2,3]. A study by Baliatsas et al. [56] has also shown that in IEI to electric devices, an increasing number and duration of nonspecific symptoms associate with increased functional impairments and illness behaviors. Our study showed a gradual exacerbation and increase of symptom spectrum and functional impairments. We also saw a spreading of responsiveness to other triggers in our patients, which is a typical feature of IEI [11,18]. In addition to indoor molds, symptom triggers also included odorous chemicals and electric devices. This kind of overlap with building-related ill health and other IEIs has previously been seen in very few clinical materials [2,10] and in questionnaire-based studies [20,57]. In our study, we used the QEESI to identify chemical intolerance and avoidance behavior. To identify indoor air and EMF-related intolerance, we formed additional questions analogous to the QEESI. The instruments supported the information gained by clinical history.

Disability in IEI is based on self-reporting of symptoms and limitations in everyday functioning [7,17]. The subjective SDS assessment tool showed functional impairments in activities and participation in the varying domains of work, social life, and home functioning. The restraints in functional areas of everyday life were due to individual situation-bounded avoidance behavior due to symptom triggers in certain surroundings. The self-assessed (SDS and work ability score) function related to the psychosocial (activity and participation) environments indicated higher severity of disability than the physician assessment using the SOFAS interview tool. A recent study of psychiatric patients at a tertiary outpatient clinic [58] did not find this disparity between subjective (SDS) and physician (SOFAS) measures of function. This may reflect the nature of perceived suffering in IEI. Patients with IEI often report not being taken seriously by others and that their suffering is not recognized by healthcare professionals [10].

Most of our patients met the ICD-10 criteria for at least one psychiatric disorder, mainly an anxiety disorder. Psychiatric comorbidity has previously received little attention in indoor air–related disability, although high psychiatric comorbidity has been seen in patients with MCS/IEI (e.g. [21]). The self-reported psychiatric symptoms were quite modest, which may reflect patients' resistance to psychological and psychiatric labels [7,59].

Somatic comorbidity, such as asthma, has also been shown in previous studies of IEI (e.g. [22]). A half of our patients had asthma, and in all of them, it was well controlled by objective measurements. It should, however, be noted that, as ACT is based on self-assessed symptoms, it may exaggerate the noncontrol of asthma due to overlapping IEI symptoms [5]. After a thorough examination, neither somatic nor psychiatric disorder could be identified as the major cause of the disabling symptoms. However, psychiatric causes may have contributed to disability. Comorbidity must be recognized because treating other conditions may reduce disability.

The patients reported insomnia-related symptoms and multisite pain, which have also been reported in some previous studies among MCS patients [23,59] and are a typical feature of FSSs [60,61]. In addition, our patients reported work-related burnout on facets of physical, cognitive, and emotional functioning. Burnout typically co-occurs with distress disorders such as impaired sleep, pain, and anxiety [62,63]. Various underlying health conditions and psychosocial load affecting function and well-being may not necessarily be recognized if they are not systematically elicited. Recognition enables various stress-reducing interventions in disability.

The physiological stress and arousal indicators of ANS and HPA axis functioning showed varying results. We did detect a tendency of insufficient recovery in HRV recording and raised evening cortisol levels but found no specific profile in the ANS or HPA axis function. Physiological measurements do not always necessarily correspond with symptoms and their severity [64].

The preponderance of indoor molds as a trigger of IEI may be explained by the general concern that indoor molds are an environmental health hazard in Finland. In a recent study, 11.4% of a sample of working-aged people perceived their workplaces' indoor environments as harmful due to molds [65]. Another Finnish study among pregnant women attributed the most severe cases of environmental intolerance to indoor molds [20]. Cultural and societal factors may also contribute to IEI. The differences between the environmental factors to which IEI is attributed in different countries reflect the risk perceptions of the population [66].

The strengths of this study were its thorough multiprofessional clinical evaluation and the use of validated and widely used instruments. Its limitation was the small number of patients, which restricts generalization of the results. In addition, participants who were more able to consider their condition from a biopsychosocial

point of view may have been selected. As this study was a case series of 12 patients, we did not include control groups, such as healthy controls or other disease groups, which can also be seen as a limitation. Previously, indoor air–related disability has not been sufficiently characterized; thus, the current clinical series is valuable.

5. Conclusions

The studied indoor air–related disabling condition seems to be a form of IEI. We found co-occurring somatic and psychiatric diagnoses and signs of distress but no medical disease to explain disability. The findings in our patients and in IEI, in general, are typical to FSSs. Recognition of IEI enables FSS interventions to support recovery and reduces the need to continuously search for medical and environmental explanations.

Conflicts of interest

A.V. worked as a part-time medical consultant at the Social Insurance Institute of Finland (KELA) until 31.11.2018; A.V. works as a part-time medical consultant at OP Insurance Ltd; K.K. works as a part-time medical consultant at Varma Mutual Pension Insurance Company; H.L. works for Nokia Bell Labs; and M.S. works as a part-time medical advisor for the Finnish Patient Insurance Centre (in accordance with the Patient Injuries Act). These affiliations (A.V., K.K., H.L., and M.S.) cause no conflicts of interest regarding this article. None of the authors declared conflicts of interest regarding this article. Neither the authors' institutions nor the funders have any authority over the study or over the preparation of the manuscript.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.shaw.2019.06.003.

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