械換気の使用が SBS 症状を下げるという共通の結果が得られていた。子どもを対象に行われた研究は、中国の大気汚染レベルの高い地域に限定されており、一般環境レベルでの研究が必要とされる。換気装置の導入や使用、ダンプネスの改善が SBS 有症率の低下につながると考えられる。一方、換気をしても排出されない SVOC のような新規の化学物質による SBS への影響に関する知見は乏しく、今後はこのような化学物質に着目した検討が必要であると考えられる。

②いわゆる化学物質過敏症に関する世界の動向

化学物質過敏症を訴える患者の身体不調と住宅やシックハウス症候群との関連を逐次検討するうえで、患者の住む住宅や勤務先における化学物質曝露に関する実際の測定データや情報があまりない場合は、近隣の保健所や衛生研究所、労働衛生機関などの相談機関を紹介する必要がある。曝露を推定できるデータがないとき、あるいはすでに環境が改善されているにもかかわらず症状が続くときには、本当に化学物質が問題なのかどうかを検討する必要がある。過去の報告では、実際に自宅などを測定しても厚生労働省のガイドラインを下回るケースが多く、症状が化学物質によるものとは判断できないことがあるとされる。その場合には化学物質ではなくカビやダニアレルゲンなどの生物学的要因、あるいは湿度環境が原因のこともありうる。掃除や換気などの住まい方の改善により症状が良くなることも考えられる。その上で、北欧で行われているマインドフルネス認知療法は（化学物質そのものに対する治療ではないが）、症状を和らげて患者の生活の質を向上させるためには役立つのではないかと勧められる(Hauge et al., 2015; Skovbjerg et al., 2012a)。

F. 研究発表

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G. 知的財産権の出願・登録状況

該当なし

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表 1. オフィスビルにおける研究

著者	年	国	デザイン	対象・年齢	調査票	曝露因子・測定物質	結果
Jaakkola	1995	Finland	cross-sectional	399 workers from 14 mechanically ventilated office buildings	SBS の 9 症状 at least weekly, work related	Ventilaiton rate	ORs for ocular (1.27, 1.11 to 1.46), nasal (1.17, 1.06 to 1.29), skin symptoms (1.18, 1.05 to 1.32), and lethargy (1.09, 1.00 to 1.19) increased significantly by a unit decrease in ventilation from 25 to 0 l/s per person.
Jaakkola	1999	Finland	cross-sectional	2,678 workers in 41 office buildings	SBS の 9 症状 at least weekly, work related	office equipment and supplies	Work with self-copying paper was significantly related to weekly work-related eye, nasopharyngeal, and skin symptoms, headache and lethargy, as well as to the occurrence of wheezing, cough, mucus production, sinusitis, and acute bronchitis.
Jaakkola	1995	Finland	cross-sectional	399 workers from 14 office buildings	SBS の 9 症状 at least weekly, work related:(previous year)	ventilation type (airflow) and other building characteristics	The ORs for ocular, nasal, skin symptoms, and lethargy increased significantly by a unit decrease in ventilation from 25 to 0 l/s per person.
Jaakkola	2007	Finland	cross-sectional	342 office workers	独自の調査票：SBS-related の 6 症状	carbonless copy paper (CCP), paper dust, and fumes from photocopiers and printers (FPP)	・All three exposures were related to a significantly increased risk of general symptoms. ・A dose-response relations was observed between the number of exposures and occurrence of headache. The risk of tonsillitis and sinus infections also increased with increasing number of exposures.
Teculescu	1998	France	cross-sectional	Personnel of air conditioned building (n=425), and of a naturally ventilated building (n=351)	独自の調査票:Burge et al., (1990)	Air-conditioning Air temperature and humidity, bacterial and fungal densities	Air-conditioning was associated with an increased prevalence of symptoms (odds ratios-OR-between 1.54 and 2.84). A significant increase in sickness absence was also found among subjects working in air-conditioned offices.
Mizoue	2001	Japan	cross-sectional	1281 workers	MM040EA	working conditions	Both ETS exposure and extensive amounts of overtime work contribute to the development of SBS symptoms and that the association between overtime and SBS can be explained substantially by the work environment and personal lifestyle correlated with overtime.

表 1. オフィスビルにおける研究（つづき）

著者	年	国	デザイン	対象・年齢	調査票	曝露因子・測定物質	結果
Mizoue	2004	Japan	cross-sectional	116 workers	MM040EA	4 seasons	Symptoms in the mucous membrane and skin increased considerably in the winter and spring.
Kubo	2006	Japan	cross-sectional	1881 office workers	MM040EA	VDT work	・The OR for SBS was significantly2.5 times higher for men engaged in VDT work for 4 or more hours a day compared with less than 1 hour a day, showing a significant trend association.
Azuma	2014	Japan	cross-sectional	3335 employees	United States Environmental Protection Agency (USEPA) Questionnaire	Office indoor quality and Occupational Stress	SBS was associated with multiple factors, including work environment, Indoor Air Quality, and occupational stress. Improving the physical office environment appears to be important for the health of employees, and it may be best achieved by providing appropriate air-condi- tioning and a clean and uncrowded workspace.
Skyberg	2003	Norway	cross-sectional	3562 employees in 32 buildings	16 on specific symptoms The Swedish Indoor Air Questionnaire (Stenberg et al., 1993)	floor surface materials, ventilation, cleaning procedures, heating and cooling. individual factors	Women reported symptoms more frequently than men. Employees with allergy had a 1.8-2.5 times risk of reporting a high score for general, skin, or mucosal symptoms. The risk of a high symptom score increased with VDU work time. Passive smoking and psychosocial load were also relatively strong predictors of symptoms.
Runeson	2006	Sweden	cross-sectional	532 general population aged 20-65yrs.	16 different SBS symptoms, used in earlier investigations (Norbäck and Edling 1991).	demand-control-support (DCS), personal factors	Female gender, low age, asthma, atopy and psychosocial work environment are associated with SBS.
Jung	2014	Taiwan	cross-sectional	143 office workers (≧20 yrs.)in 21 Office spaces	WHO の定義:SBS standard questionnaire	8-OHdG (8-hydroxydeoxyguanosine)	The risks for SBS syndromes were related with euroendocrine and metabolic system of the AL.
Marmot	2006	UK	cross-sectional	4052 participants aged (42-62 years) in 44 buildings	独自の調査票"Have you had any of the following symptoms in the last 14 days?".	physical and psychosocial work environment	・No significant relation was found between most aspects of the physical work environment and symptom prevalence. ・Only psychosocial work characteristics and control over the physical environment were independently associated with symptoms .
Bourbeau	1996	Canada	cross-sectional	1390 workers in 5 buildings	独自の調査票	new building with an improved ventilation system.	The prevalence of most symptoms decreased when workers moved to the new building: skin (54%), respiratory system (53%), nose and throat (46%), fatigue (44%), headach e (37%), eyes (23%).

表 2.　学校における研究

著者	年	国	デザイン	対象・年齢	調査票	曝露因子	バイオマーカー	結果
Bakke	2008	Norway	cross-sectional	173 employees in four university buildings	MM040 NA	Room temperature, humidity, C02, PM10, Air velocity , lightining, Noise	BUT, selfreported-BUT, NAL, ECP, MPO, Total serum IgE, specific IgE	Thermal climate in university buildings may be associated with both perceptions and physiological signs. Reduced night time air temperature, increased difference in air temperature between day and night, and fast changes in air temperature might impair indoor environment.
Zhang	2014	China	prospective	2134 pupils	junior high school	16 symptoms compatible with SBS: (Bjornsson et al., 1998)	-	At baseline, both indoor and outdoor SO2 were found positively associated with prevalence of school-related symptoms. Indoor O3 was shown to be positively associated with prevalence of skin symptoms. At follow-up, indoor PM10 was found to be positively associated with new onset of skin, mucosal and general symptoms.CO2 and RH were positively associated with new onset of mucosal, general and school-related symptoms.
Zhang	2011	China	prospective	1143 school children (11–15 yrs.)	School	16 symptoms compatible with SBS(Bjornsson et al.,, 1998 ; Sahlberg et al.,, 2012).	Airborne pet al.,lergens, fungal DNA 30, Stachybotrys DNA 30, and Asp/Pen DNA in the dust	・Bacterial compounds (LPS and MuA) seem to protect against the development of mucosal and general , but fungal exposure mea- sured as fungal DNA could increase the incidence of school-related .
Zhang	2011	China	prospective	1143 school children (11–15 yrs.)	Classroom	16 symptoms compatible with SBS(Bjornsson et al., 1998 ; Sahlberg et al., 2012).	SO2, NO2, CO2,Temperature, Relative humidity	・The prevalence study indicated that NO2 and SO2 might be related to various of the SBS type. ・Parental asthma and allergy (heredity) and to some extent own atopy were consistent risk factors for both prevalence and incidence of SBS ,

表 3. 集合住宅における研究

著者	年	国	デザイン	対象・年齢	調査票	曝露因子	結果
Engvall	2000	Sweden	cross-sectional	609 multi-family buildings with 14,235 dwellings	MM040NA: Weekly symptoms	personal factors and building age	SBS is related to personal factors, building age, and ownership of the building. To identify multi-family buildings with more SBS than expected, it is necessary to adjust for ownership and population characteristics.
Engvall	2001	Sweden	cross-sectional	9808 participants in the dwellings in Stockholm	MM040NA: Weekly symptoms	Dampness	A combination of mouldy odour and signs of high air humidity was related to an increased occurrence of all types of symptoms. A combination of mouldy odour and water leakage.
Engvall	2003	Sweden	cross-sectional	4815 inhabitants in 231 multi-family buildings built before 1961	MM040NA Weekly symptoms	heating, ventilation, energy conservation, and reconstruction	・Subjects in buildings with a mechanical ventilation system had less ocular and nasal symptoms. ・Heating by electric radiators, and wood heating was associated with an increase of most symptoms. ・Major reconstruction of the interior of the building was associated with an increase of most symptoms.

表４．新築一戸建て住居における研究

著者	年	国	デザイン	対象・年齢	調査票	曝露因子	測定物質	結果
Saijo	2004	Japan	cross-sectional	317 residents	MM040EA	VOCs and Dampness	17 VOCs	・VOCs were related to the symptoms, and TVOC was related to throat and respiratory symptoms, although the concentrations of VOCs were relatively low.
Wang	2007	Japan	cross-sectional	24 subjects in 13 houses	MM040EA	VOCs in air and urine	Toluene, ethylbenzene, xylene isomers, styrene and p-dichlorobenzene in the air and urine	Only air VOCs in the bedroom influenced the morning urinary VOC concentrations.
Nakayama	2007	Japan	cross-sectional		MM040EA	Mold, lifestyle	-	presence of Penicillium sp. in females and Alternaria alternata in males increases the risk of SBS, whereas sufficient sleep, moderate alcohol consumption for males, and fewer working hours for females might alleviate SBS symptoms.
Takeda	2009	Japan	cross-sectional	343 residents in 104 houses	MM040EA	Dampness and indoor chemicals	Formaldehyde, acetal., dehyde, VOCs, airborne fungi, and dust mite allergen	Dampness, formaldehyde, and alpha-pinene had significantly higher ORs for SBS symptoms.
Takigawa	2010	Japan	cross-sectional	1,479 residents in 425 houses	MM040EA	Indoor aldehydes and VOCs	-	Formaldehyde dose-dependently showed to be a significant risk factor for SBS.
Kanazawa	2010	Japan	cross-sectional	134 occupants	MM040EA	SVOCs (PFRs and phthalates) in indoor air and dust	-	TBP was strongly and directly associated with mucosal symptoms of SBS. DEP and TBEP were inversely associated with SBS.
Saijo	2011	Japan	cross-sectional	1479 residents in 425 houses	MM040EA	mite allergen and airborne fungi	mite allergen (Der 1), airborne fungi, aldehydes, and VOCs	・Der 1 had a significantly high OR for nose symptoms. ・*Rhodotorula* had a significantly high OR for any symptoms, and Aspergillus had significantly high OR for eye symptoms.

表 5. 子どもを対象とした研究

著者	年	国	デザイン	対象・年齢	セッティング	調査票	測定物質	結果
Li	2015	China	cross-sectional	children	kindergartens	CCHHstudy Northern Swedish Office Illness study で使用した調査票	-	Univariate analysis showed that living near a main road or highway (OR = 1.40), female gender (OR = 1.44), and ETS (OR = 1.13) were significant risk factors for general symptoms.The adjusted odds ratio (aOR) for the association between living close to a highway and general symptoms remained significant in the multivariablemodel (aOR = 1.39; 95% CI = 1.21: 1.59).
Wang	2012	China	cross-sectional	661 urban preschool children	House and kindergarten	MM075NA	-	Furniture materials, traffic pollution, kindergarten environment quality and allergies were associated with SSWICG and mucosal, dermal and general .
Zhang	2014	China	prospective	2134 pupils	junior high school	16 symptoms compatible with SBS: (Bjornsson et al., 1998)	-	At baseline, both indoor and outdoor SO2 were found positively associated with prevalence of school-related symptoms. Indoor O3 was shown to be positively associated with prevalence of skin symptoms. At follow-up, indoor PM10 was found to be positively associated with new onset of skin, mucosal and general symptoms.CO2 and RH were positively associated with new onset of mucosal, general and school-related symptoms.
Zhang	2011	China	prospective	1143 school children (11–15 yrs.)	School	16 symptoms compatible with SBS(Bjornsson et al., 1998 ; Sahlberg et al., 2012).	Airborne pet al., lergens, fungal DNA 30, Stachybotrys DNA 30, and Asp/Pen DNA in the dust	・Bacterial compounds (LPS and MuA) seem to protect against the development of mucosal and general , but fungal exposure mea- sured as fungal DNA could increase the incidence of school-related .
Zhang	2011	China	prospective	1143 school children (11– 15 yrs.)	Classroom	16 symptoms compatible with SBS(Bjornsson et al., 1998 ; Sahlberg et al., 2012).	SO_2, NO_2, CO_2,Temperature, Relative humidity	・The prevalence study indicated that NO2 and SO2 might be related to various of the SBS type. ・Parental asthma and allergy (heredity) and to some extent own atopy were consistent risk factors for both prevalence and incidence of SBS ,

表 6. 症例対照研究

著者	年	国	デザイン	対象・年齢	調査票	目的	バイオマーカー	結果
Matsuzaka	2014	Japan	case-control	188 Japanese patients with SBS and age- and sex-matched 40 healthy controls	WHO の定義	To determine whether there was a difference in Neuropathy target esterase (NTE) activity in the peripheral blood mononuclear cells (PBMCs) of Japanese patients with SBS and healthy controls and whether PNPLA6 (alias NTE) gene polymorphisms were associated with SBS.	enzymatic activity of NTE, SNPs	We found that the enzymatic activity of NTE was significantly higher in SBS patients compared with controls. Moreover, population with an AA genotype of a single nucleotide polymorphism (SNP), rs480208, in intron 21 of the PNPLA6 gene strongly reduced the activity of NTE.

表 7. 前向きコーホート研究

著者	年	国	デザイン	対象・年齢	セッティング	調査票	曝露因子	測定物質	バイオマーカー	結果
Bourbeau	1997	Canada	prospective	1390 workers in 5 buildings	Office	独自の調査票：SBS の 7 症状: only at work two to three times a week or more often に起こる	new building with an improved ventilation system.	-	-	The decrease of 40% to 50% in the prevalence of most symptoms investigated six months after workers were exposed to a new building with an improved ventilation system was maintained three years later.
Brauer	2006	Denmark	prospective	2164 at baseline, 1402 at follow-up	Office	独自の調査票 (Brauer et al., 2000; Brauer 2005).	Indoor environment	-	-	・Mucous membrane symptoms in the cross-sectional analysis were significantly associated with self-reported high temperature and dry air, the prospective analyses showed that onset of mucous membrane symptoms was associated with the sensation of draught, dry air, and noise.
Takigawa	2009	Japan	prospective	86 men and 84 women residing in Okayama	Newly built detatched House	MM040EA	indoor aldehydes, VOCs, airborne fungi, and dust mite allergens	-	-	Increases in benzene and in Aspergillus contributed to the occurrence of SBS.
Sahlberg	2009	Sweden	prospective	348 adults	House	16 symptoms compatible with SBS(Bjornsson et al., 1998；Sahlberg et al., 2012).	building factors, and personal factors	-	-	・Smokers at baseline reported more onset of SBS symptoms than non-smokers. Furthermore, remission from mucosal symptoms was less likely in subjects that were tobacco smoker. ・Subjects with any indoor painting during follow-up period reported more onset of SBS symptoms, and those with intermediate education level had more onset of skin symptoms.

表 7. 前向きコーホート研究（つづき）

著者	年	国	デザイン	対象・年齢	セッティング	調査票	曝露因子	測定物質	バイオマーカー	結果
Zhang	2011	China	prospective	1143 school children (11– 15 yrs.)	School	16 symptoms compatible with SBS(Bjornsson et al., 1998 ; Sahlberg et al., 2012).	-	Airborne pet al.,.lergens, fungal DNA 30, Stachybotrys DNA 30, and Asp/Pen DNA in the dust	-	・Bacterial compounds (LPS and MuA) seem to protect against the development of mucosal and general , but fungal exposure mea- sured as fungal DNA could increase the incidence of school-related .
Zhang	2011	China	prospective	1143 school children (11– 15 yrs.)	Classroom	16 symptoms compatible with SBS(Bjornsson et al., 1998 ; Sahlberg et al., 2012).	School environment	SO_2, NO_2, CO_2,Temperature, Relative humidity	-	・The prevalence study indicated that NO_2 and SO_2 might be related to various of the SBS type. ・Parental asthma and allergy (heredity) and to some extent own atopy were consistent risk factors for both prevalence and incidence of SBS ,
Takigawa	2012	Japan	prospective	871 people living in 260 single-family houses	Newly built detatched House	MM040EA	indoor concentrations of aldehydes and VOCs.	-	-	Increases in aldehydes and aliphatic hydrocarbons contributed to the occurrence of SBS.
Zhang	2012	Sweden	prospective	429 adults	Office	16 symptoms compatible with SBS(Bjornsson et al., 1998 ; Sahlberg et al., 2012).	Dampness	-	EOS, ECP, Slope, IL-6, Slope, HCRP	・Signs of dampness in the floor in any workplace during follow up was associated with incidence of mucosal. ・Cumulative exposure to moldy odor was associated with incidence of work-related. ・Working in a building repaired because of dampness (repaired building) or mould was associated with decreased remission of work-related.

表 7. 前向きコーホート研究 （つづき）

著者	年	国	デザイン	対象･年齢	セッティング	調査票	曝露因子	測定物質	バイオマーカー	結果
Sahlberg	2012	Sweden	prospective	452 adults who were followed from 1992 to 2002 within the Uppsala part of ECRHS.	House	16 symptoms compatible with SBS(Bjornsson et al., 1998 ; Sahlberg et al., 2012).	Medical history, demographic data, and the home environment	-	Slope, Total IgE, CRP (mg/l), IL-6 (ng/l), ECP (lg/l) , EOS (lg/l)	・Dampness or indoor molds at baseline was a predictor of incidence of general ,mucosa, and dermal. ・Bronchial responsiveness, EOS in blood, total IgE and ECP in serum at baseline were predictors of incidence of ・Subjects with doctor-diagnosed asthma at baseline had a higher incidence of general and mucosal.
Zhang	2014	China	prospective	2134 pupils	junior high school	16 symptoms compatible with SBS:The questionnaire was based on previous SBS studies (Bjornsson et al., 1998)	SO_2, NO_2, O_3 and PM_{10}	-	-	At baseline, both indoor and outdoor SO_2 were found positively associated with prevalence of school-related symptoms. Indoor O_3 was shown to be positively associated with prevalence of skin symptoms. At follow-up, indoor PM10 was found to be positively associated with new onset of skin, mucosal and general symptoms.CO_2 and RH were positively associated with new onset of mucosal, general and school-related symptoms.

表 8.　介入研究

著者	年	国	デザイン	対象・年齢	セッティング	調査票	曝露因子	結果
Norback	2008	Sweden	intervention	335 university students	School	独自の調査票	Temperature and CO2	Increased temperature and CO2 may aVect mucosal membrane symptoms, headaches and tiredness. Room temperature was most important. CO2 associations may partly be temperature effects.

表 9. 化学物質過敏症と遺伝子多型に関する研究

著者	年	国	デザイン	対象	遺伝子多型	結果	考察
Cui	2013	Japan	cross-sectional	男性労働者 324 人	QEESI と遺伝子多型（CYP2E1、 NAT2、 GSTM1、 GSTT1、 GSTP1、 ALDH2、 SOD2）	SOD Val/Val と比較して、Ala/Ala、Val/Ala は化学物質過敏である OR がそれぞれ 4.30(1.23-15.3)、4.53(1.52-13.51)	QEESI カットオフ以上を 3 群にしたとき、最も得点が高い群は SOD2 遺伝子が活性酸素を増やす多型を保持していた。つまり環境化学物質のためではないと思われる。
Fujimori	2012	Japan	cross-sectional	従業員 1084 人	WEESI、MCI 歴、SHS 歴 GSTM1、 GSTT1、 ALDH2、PON1 遺伝子多型	MCS 歴 4 名、SHS 0 人、QEESI 得点で 4 群、あるいは Hojo criteria でカットオフ、遺伝子多型に有意差なし	遺伝子多型の頻度はケースとコントロールに差はみられなかった。
Berg	2010	Denmark	Case-control	MCS 96 人とコントロール 1207 人	CYP2D6、arylamine N-actyltransferase 2、paraoxonase 1、 methylene tetrahydrofolate reductase、chleycstoknin 2 receptor	Arylamin N-actyltransferase 2 は MCS のもっとも深刻なグループで有意 OR3.1	MCS における遺伝子の役割は過去の報告よりも小さいのではないか
De Luca	2010	Italy	Case-control	MCS とコントロール	CYP、UGT1A1、GSTP1、GSTM1、 GSTT1、 SOD、GST、 Gpx 酵素の多型	CYPs、 UGT、 GSTM、 GSTT、 and GST の多型頻度は MCS とコントロールで差なし。MCS では赤血球カタラーゼと GST は低く、Gpx 活性は高い。酸化グルタチオンは低下。MCS では飽和脂肪酸組成、IFNγ、IL-8、IL-10、 MCP-1、 PDGFbb、VEGE は多かった。	MCS では、代謝や抗酸化酵素の発現が抑制されている。脂質酸化、硝酸塩の生成、グルタチオンの枯渇炎症性サイトカインの増加は MCS の診断における生化学的定義として考慮すべき
Wiesmuller	2008	Germany	Case-control	ケースコントロール研究（MCS=59、コントロール=40）	ケースの定義：自己申告 MCS 遺伝子多型：NAT2、 5 HTT、PON1、PON2、SOD2	生体異物代謝酵素に関わる遺伝子多型の頻度は self-reported MCS とコントロールに差はみられなかった。	
Schnakenberg	2007	Hamburg、Germany	Cross-sectional	開業医で、患者から無作為抽出した 800 人のボランティア中同意が得られた 521 人（CRS>20=273 人、≦20=428 人）	ケースの定義：EESI の chemical reactive sensitivity（CRS）得点 20 点以上遺伝子多型：NAT2、GSTM1、GSTT1、GSTP1	CRS 得点 20 点以上の群で、両アレルとも酵素活性を欠損する GSTM1、GSTT1 変異型の保有が多かった（それぞれ、OR:95%CI は 2.08:1.46-2.96、2.80:1.65-4.75）。	

表 9. 化学物質過敏症と遺伝子多型に関する研究 （つづき）

著者	年	国	デザイン	対象	遺伝子多型	結果	考察
McKeown-Eyssen	2004	Canada	Case-control	MCS 203 人、control 162 人	CYP2D6、NAT1、NAT2、PON1、PON2 および MTHFR の遺伝子多型	CYP2D6 と NAT2 の相互作用が、リスク上昇に関与（OR=18.7、P=0.002）ケースでは、CYP2D6 と NAT2 とも、代謝のスピードが速い多型の保有がケースで多かった（それぞれ OR:95%CI は 3.36：1.33-8.50、4.14(1.36-12.64)。	しかし、CYP2D6 は 8 カ所、NAT2 では 9 カ所の変異の組み合わせの分布についての結果で、（多重比較では必須な）P 値の補正はされていない。
Binkley KK.	2001	Canada	Case-control	IEI 症状を呈する患者 11 人と、性・年齢・人種でマッチングした健康者	IEI 患者の血液から cholecystokinin B(CCK-B)受容体と dopamine D4 受容体（DRD4）遺伝子多型を調べた。	化学物質過敏症患者は対照群と比較して、パニック症候群と関与する CCK-B 受容体アレル 7 を有するものが有意に多い（40.9%vs9.1%、p=0.037）	IEI はパニック障害と同じ神経遺伝学的特性があり、遺伝学的特性が IEI 患者が不安を生じる原因を示しているのではないか。