

# MULTIPLE CHEMICAL SENSITIVITY

- psychological factors, patient strategies and healthcare practices

PhD thesis

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## The present Ph.D. thesis is based on the following manuscripts:

- 1. Skovbjerg S, Johansen JD, Rasmussen A, Thorsen H, Elberling J: General practitioners' experiences with provision of healthcare to patients with self-reported multiple chemical sensitivity. Scand J Prim Health Care. 2009; 27 (3): 148-52.
- 2. Skovbjerg S, Brorson S, Rasmussen A, Johansen JD, Elberling J: Impact of self-reported multiple chemical sensitivity on everyday life a qualitative study. Scand J Public Health. 2009 Aug; 37(6): 621-6.
- 3. Skovbjerg S, Zachariae R, Rasmussen A, Johansen JD, Elberling J: Attention to bodily sensations and symptom perception in individuals with idiopathic environmental intolerance. Environ Health Prev Med. DOI 10.1007/s12199-009-0120-y.
- 4. Skovbjerg S, Zachariae R, Rasmussen A, Johansen JD, Elberling J: Repressive coping and alexithymia in multiple chemical sensitivity (Submitted manuscript).

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#### **Preface**

The present thesis is based on three studies performed at the Danish Research Centre for Chemical Sensitivities, Department of Dermato-Allergology, Gentofte Hospital, University of Copenhagen, Denmark between 2006 – 2009.

#### Acknowledgements

The studies could not have been performed without the assistance from a number of people to whom I am very grateful.

First and foremost I wish to express my sincere gratitude to my supervisors Jesper Elberling, Jeanne Duus Johansen and Alice Rasmussen for their excellent guidance within the scientific field and fruitful discussions. I especially wish to thank Jesper Elberling for his support throughout the entire process, his always genuine interest and dedication to my studies and to this challenging subject and for creating a warm and inspirational working atmosphere.

I am very grateful to Robert Zachariae for introducing me to the field of psychology and for excellent scientific guidance within this area of research. A great thank to Hanne Thorsen, Lone Schmidt and Rikke Lund for their contributions within the areas of primary healthcare and social medicine. I also wish to thank Søren Vesterhauge for his invaluable assistance in enrolling MCS patients in my study and for his dedication to this subject, Bente Halkier for introducing me to qualitative research, and the many people who undertook the task of completing questionnaires.

A special thank to my colleagues for an always pleasant working atmosphere, academic discussions and invaluable assistance.

Finally the support from my family and friends has been invaluable.

Sine Skovbjerg

#### **Abbreviations**

APQ: Autonomic Perception Questionnaire

**CIDI**: The Composite International Diagnostic Interview

**CHS**: Chemical Hypersensitivity Scale

CNS: Central Nervous System

**CNSS**: CNS Symptom Scale

CSAS: Consequences for Social Activities Scale

**CSS-SHR**: Chemical Sensitivity Scale for Sensory Hyper-reactivity

**DIF**: Difficulties identifying feelings

**DDF**: Difficulties describing feelings

**EOT**: Externally oriented thinking

**GP**: General practitioner

**IEI**: Idiopathic Environmental Intolerance

MCS: Multiple Chemical Sensitivity

MUSS: Mucosal Symptom Scale

MCSD: Marlowe Crowne Social Desirability Scale

**NAS**: Negative Affectivity Scale

SSAS: Somato-Sensory Amplification Scale

**STAI**: State-Trait Anxiety Inventory

SCL-90-R: The Hopkins Symptom Check List 90-Revised

**RLE**: Recent life events

TAS-20: The Toronto Alexithymia Scale

TAS: Tellegen Absorption Scale

TMAS: The Taylor Manifest Anxiety Scale

WHO: World Health Organization

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## 1. Summary in English

Multiple chemical sensitivity (MCS) is a disorder characterized by reports of non-specific symptoms from various organ systems attributed by the individual to exposure to environmental odours at levels below those known to induce adverse health effects. More sets of diagnostic criteria have been proposed but none is currently internationally accepted. Reports of symptoms are common in population-based studies with prevalence estimates ranging from 9-33%. Prevalence estimates of physician-diagnosed MCS or reports of disabling consequences in the form of social and occupational disruptions range from 0.5-6.3%, and it is well established that MCS can be a chronic disorder. The label "MCS" has been criticized for implying unproven assumptions about causation and instead the label *Idiopathic Environmental Intolerance* (IEI) has been recommended to replace it. The scientific literature still uses both terms and without reference to assumptions about causation the term MCS will primarily be used in the present thesis.

MCS is a controversial disorder and the lack of diagnostic possibilities may challenge the health-care system and result in different management strategies. Knowledge is limited of General Practitioners' (GPs) experience with MCS and the strategies they apply in consultations with patients who report these symptoms. Details of how MCS is experienced and coped with by affected individuals are sparse but insight into the individual consequences may provide an understanding of the difficulties faced by affected individuals and aid in the planning of future studies and possible therapeutic interventions. Recent studies suggest that emotional distress and psychological states and traits believed to play a role in the maintenance of symptoms in functional somatic disorders are associated with MCS. However, more studies are needed to explore the role of these psychological factors in MCS, and the possible association with severity of the reported symptoms.

Three studies were performed. The first study was a nationwide cross-sectional postal questionnaire survey including a random sample of 1000 Danish GPs. The objective of this study was to investigate the experience and clinical practice among GPs in relation to patients who seek medical advice due to symptoms attributed to common environmental odours. Our results suggest that many GPs find it difficult to fulfil the healthcare needs expressed by these patients, and there is a great need for evidence-based guidelines and diagnostic tools in relation to this patient group. The second study applied focus-group discussions as data collection method and aimed at describing the impact of self-reported MCS on everyday life including work and social life. The participants experienced that MCS had a severe impact on everyday life by limiting their possibilities of performing normal daily activities. They reported being bothered when shopping, using public transportation, participating in family parties and coping with workplace exposures; avoidance was the primary coping strategy applied.

The third study was a cross-sectional postal questionnaire survey including a sample of 1024 individuals with either self-reported or physician-diagnosed MCS. The objectives of this study were to examine the association between MCS and different measures of emotional distress and psychological states and traits. The following measures were included: the somato-sensory amplification scale (SSAS); the Autonomic Perception Questionnaire (APQ); the Tellegen Absorption Scale (TAS); the Negative Affectivity Scale (NAS); the Marlowe-Crowne Social Desirability Scale (MCSD); the Bendig 20-item version of the Taylor Manifest Anxiety Scale (TMAS); the Toronto Alexithymia Scale (TAS-20) and the Recent Life Events scale (RLE). Results from this study suggest that self-reported severity of MCS is associated with psychological factors involved in symptom perception and maintenance and emotional distress, i.e., negative emotional reactions. The direction of the relationship between MCS and the psychological factors examined in this study cannot be determined from the cross-sectional design, but our results confirm the importance of studying the role of psychological factors and providing knowledge for future studies on risk factors in MCS.

## 2. Summary in Danish

Duft – og kemikalieoverfølsomhed (MCS) er en tilstand, der kan karakteriseres ved selvrapporterede og uspecifikke symptomer fra flere organsystemer udløst ved eksponering for almindeligt forekommende dufte og kemiske stoffer. Der er foreslået flere diagnostiske kriterier til bestemmelse af tilstanden, men på indeværende tidspunkt findes ingen internationalt anerkendte kriterier. Populations-baserede studier peger på, at symptomerne er hyppige i befolkningen med prævalens estimater på mellem 9 og 33 %. Forekomsten af læge-diagnosticeret MCS, eller svær social og erhvervsmæssig påvirkning som følge af MCS, estimeres til mellem 0.5 og 6.3 %. Flere studier peger på, at tilstanden kan være kronisk. Betegnelsen "MCS" er blevet kritiseret for at indeholde udokumenterede associationer omkring kausalitet. I stedet er foreslået den noget bredere betegnelse "idiopathic Environmental Intolerance" (IEI). Den videnskabelige litteratur anvender forsat begge betegnelser og uden antagelser om årsagssammenhænge anvendes her primært betegnelsen "MCS".

Manglen på dokumenteret viden om patologi og kausalitet kan antages at gøre det vanskeligt for sundhedsvæsnet at håndtere denne patient, samt give anledning til forskelligartede udrednings – og behandlingstilbud. Viden om alment praktiserende lægers erfaring med - og håndtering af denne patientgruppe er begrænset. Indsigt i hvordan patienten med MCS oplever og håndterer tilstanden kan give viden om centrale problemstillinger i relation til denne patientgruppe. Viden om hvordan MCS påvirker den enkeltes liv kan være med til at danne grundlag for forskning inden for området, samt indgå i planlægning af eventuelle terapeutiske interventioner. Nyere studier peger på at emotionel sårbarhed og psykologiske karaktertræk, der antages at have betydning for symptomrapportering i funktionelle somatiske tilstande, også er associeret med MCS. Der er dog behov for yderligere studier til undersøgelse af sammenhængen mellem sværere MCS symptomer og reaktioner, emotionelle faktorer og psykologiske karaktertræk.

Afhandlingen er baseret på tre studier: Det første studie var en landsdækkende spørgeskemaundersøgelse henvendt til 1000 tilfældigt udvalgte alment praktiserende læger. Formålet med studiet var at undersøge praktiserende lægers holdning og kliniske praksis i relation til patienter, der søger læge på grund af symptomer over for almindeligt forekommende dufte og kemiske stoffer.

Resultaterne pegede på, at mange alment praktiserende læger oplever, at de har svært ved at imødekomme denne patients forventninger til sundhedsvæsnet, samt at der er et stort behov for evidens-baserede retningslinier og diagnostiske værktøjer.

Det andet studie var et kvalitativt studie baseret på fokusgruppe interviews. Studiet havde til formål at undersøge, hvordan MCS påvirker dagligdagen og herunder sociale relationer og arbejdsliv, samt hvilke strategier patienten anvender for at håndtere tilstanden. Studiets design giver ikke grundlag for at resultaterne kan generaliseres, men diskussionerne pegede på, at MCS kan virke stærkt begrænsende for den enkeltes muligheder for at udføre almindelige dagligdags aktiviteter. Fokusgruppe deltagerne oplevede vanskeligheder ved at gå i butikker, anvende offentlige transportmidler og håndtere eksponeringer på deres arbejdsplads. Undgåelses adfærd var den primære håndteringsstrategi.

Det tredje studie var en spørgeskemaundersøgelse blandt 1024 personer med enten selvrapporteret eller læge-diagnosticeret MCS. Formålet med studiet var at undersøge associationen mellem selvrapporteret sværhedsgrad af MCS og variable til måling af emotionelle og psykologiske faktorer. Følgende variable indgik: Somato-sensorisk forstærkning (SSAS); Autonom perception (APQ); Absorption (TAS); Negativ affekt (NAS); Social ønskværdighed (MCSD); Træk angst (TMAS); Alexithymi (TAS-20) og tidligere, stressfyldte livs begivenheder (RLE). Overordnet pegede studiets resultater på en association mellem selvrapporteret sværhedsgrad og psykologiske variable af betydning for symptom perception, samt negative emotionelle reaktioner. Kausalitet kan ikke bestemmes ud fra et tværsnitsstudie, men resultaterne bekræfter, at det er relevant at inddrage psykologiske variable i studier af MCS. Resultaterne kan derved danne grundlag for fremtidige studier, der vil undersøge risikofaktorer i relation til MCS.

#### 3. Introduction

"My symptoms mean that my home is 100% free of fragrance products, secondly that I avoid things that make me feel ill like, e.g., newly printed magazines, and thirdly that I keep away from people and places whose smell I can't tolerate" (49-year-old woman) [1].

## 3.1 Case-definition

In 1986 Scottenfeld and Cullen reported a case where the patient complained of unexplained medical symptoms that were attributed to exposure to common chemicals and the condition was initially labelled atypical post-traumatic stress disorder [2]. In 1987, based on observations of similar cases at the Institute of Occupational Medicine, Yale University, Cullen proposed the diagnostic label Multiple Chemical Sensitivity (MCS) and defined it as:" an acquired disorder characterized by recurrent symptoms, referable to multiple organ systems, occurring in response to a demonstrable exposure to many chemically unrelated compounds at doses far below those established in the general population to cause harmful effects. No single widely accepted test of physiologic function can be shown to correlate with symptoms" [3]. Although more case definitions have been proposed since Cullen first introduced his diagnostic criteria [4;5], there is currently no widely accepted case definition for MCS [6]. The absence of a clearly defined threshold for what merits an MCS-diagnosis, and thereby what separate cases from individuals who are merely bothered by the presence of specific odours challenges epidemiological and clinical studies in this field. While inadequate as a diagnostic tool, a large number of epidemiological studies on MCS have used eliciting chemical agents, self-reported symptoms and to some extent social and occupational disruptions as criteria for describing and determining the presence and severity of MCS [7-14].

At a WHO workshop in 1996 organized by the International Programme on Chemical Safety the label "*Idiopathic Environmental Intolerance*" (IEI) was recommended to replace MCS because the term "MCS" has been criticised for implying unproven assumptions of causation [15]. IEI is a somewhat broader term that incorporates a number of disorders with overlapping symptoms attributed to environmental factors; nevertheless MCS and IEI are essentially the same. The

scientific literature still uses both terms and without reference to any assumptions about causation the term MCS will primarily be used throughout the present thesis as a purely descriptive label. However, it should be noted that in one of the manuscripts included in this thesis the term "IEI" is used, and when citing studies that refer to the disorder as IEI this label will also be provided in the text.

## 3.2 Prevalence, symptomatology and co-morbidity

Reports of somatic symptoms attributed by the individual to environmental odours are common in population-based studies with prevalence estimates ranging from 9-33% [10;12;13;16-18]. In contrast, prevalence estimates of physician-diagnosed MCS or reports of disabling consequences in the form of social and occupational disruptions range from 0.5-6.3% [10;17;19]. Thus only a subset of individuals who report being sensitive considers themselves to be clinically ill or functionally disabled by their reactions. Although there are only few prospective studies on MCS/IEI, they suggest that the disorder is chronic [9;20].

In general the reported symptoms are attributed to previous chemical exposures and recur on a subsequent exposure to the same or structurally unrelated chemicals at levels normally considered to be non-toxic [21]. It has been described that symptoms may develop either following an initial, high-dose, exposure such as a chemical spill, or repeated lower level exposures from, e.g., office buildings, but data on the initiation of the disorder are limited [21;22]. The reported symptoms typically vary between individuals with women being more sensitive and reporting more symptoms than do men [10;12;16;17]. A typical symptom pattern is thus difficult to establish. Non-specific central nervous system (CNS) complaints are frequently reported including fatigue, headache and difficulty in concentrating [10;12]. Other symptoms include pain and respiratory complaints [10;12;16]. Despite headache being a commonly reported complaint, CNS symptoms other than headache have been found to be a strong predictor of functional disability (OR 3.2) [11]. To some extent the non-specific symptoms in MCS resemble other unexplained disorders, e.g., fibromyalgia and chronic fatigue syndrome [23;24], and it has been suggested that these disorders share common underlying pathophysiological mechanisms [23].

An association between asthma and chemical sensitivity has been reported in several studies [16;25;26]. An asthma prevalence of 12% was reported by respondents in a population-based study (n= 4242/6000, 71% response rate) on chemical sensitivity and the rate increased with severity of chemical sensitivity [10]. Based on a population-based twin study on the heritability of

perfume-related respiratory symptoms (n = 4128/5048, 82% response rate) Elberling and colleagues reported a heritability of 0.35 (95% CI 0.14-0.54) [26]. A mutual genetic correlation of 0.39 (95% CI 0.09 – 0.72) was reported for perfume-related respiratory symptoms and atopic dermatitis, suggesting some genetic pleiotropy for these two factors. No genetic pleiotropy was found between perfume-related respiratory symptoms, hand eczema, contact allergy or asthma [26], suggesting that the association with asthma reported in several studies [16;25;26] might be caused by other mechanisms.

In a systematic review of provocation studies, Das-Munshi and colleagues concluded that individuals with MCS/IEI were less likely to accurately detect or respond to active provocations in studies incorporating strict blinding procedures and olfactory masks [27]. The authors suggested that behavioural mechanisms, such as conditioning, may be involved in the generation of symptoms [27]. Personality traits such as absorption and negative affectivity may influence conditioning processes since individuals who are high on these traits may be more vulnerable to learning symptoms [28-31]. It can also be speculated whether traits believed to be involved in the maintenance of symptoms in functional somatic disorders, e.g., somato-sensory amplification, may be involved in the maintenance of symptoms in MCS [32;33] due to an increased attention to bodily sensations and a biased symptom perception [8].

#### 3.3 Functional disability and healthcare usage

High levels of functional disability in terms of occupational restraints or job loss and limited public access due to chemical sensitivity has been reported in several studies on MCS/IEI [8;10;16;17;34]. Affective and behavioural consequences as measured by the Chemical Sensitivity Scale for Sensory Hyperreactivity (CSS-SHR) were reported by 19% of the respondents in a population-based study on the prevalence and risk factors of chemical sensitivity (n= 1387/1900, 73% response rate) by Johansson and colleagues [16]. In a previously cited population-based study [10] adjustments in either social life or occupational conditions due to symptoms were reported by 3.3% (95% CI 2.8-3.9), whereas 0.5% (95% CI 0.3-0.7) reported adjustments in both. In an annual behavioural risk factor survey including 4046 respondents (70% response rate) Kreutzer and colleagues reported that of the 15.9 % who reported being unusually sensitive to common chemicals, 51.9% reported taking special precautions at home. Another 20.7% reported being bothered when shopping in stores and eating in restaurants [17].

In general it is well established that medically unexplained symptoms or functional somatic symptoms are frequent sources of encounters with the healthcare system [35], and in relation to MCS a high number of visits to a GP has been reported in several studies [7;36]. Based on a large population-based study (n=13,604/23,437, 58% response rate) Eek and colleagues reported that in terms of healthcare usage environmentally-annoyed respondents do not deviate from hypertensive patients regarding the number of visits to a GP. However, both groups had significantly more visits than healthy controls [37]. The odds ratios of reporting unfulfilled healthcare needs (OR 3.5) or mostly negative experiences of healthcare (OR 3.3) were increased in environmentally-annoyed respondents, when compared with both hypertensive patients and healthy controls [37]. It can be speculated whether the reported negative experiences influence this patient groups' healthcare utilisation and accompanying unfulfilled healthcare needs [37]. There is no generally accepted treatment for MCS, which may offer some explanation as to why these patients report having unfulfilled healthcare needs.

Details are sparse on the areas and extent to which MCS affect everyday life and which strategies affected individuals apply in order to cope with this disorder. The controversy surrounding the aetiology of MCS and lack of diagnostic possibilities may challenge the healthcare system when encountering this group of patients. Furthermore data are limited on GPs´ experience with MCS, the strategies they apply in consultations with patients who report these symptoms and the clinical advice they offer these patients on how to manage the disorder.

## 3.4 Psychology and psychiatric co-morbidity

Increasing evidence points to an association between MCS and personality traits traditionally studied in patients with somatoform disorders, as well as high rates of psychiatric co-morbidity [8;13;14;38-41].

## 3.4.1 Psychological traits and emotional distress

In a clinical study including patients with an IEI diagnosis (n= 23), individuals with self-reported odour sensitivity but no IEI diagnosis (n= 21) and healthy controls (n= 23), Papo and colleagues examined alterations in chemoreception using electrophysiological and psychophysical olfactometric tests [42]. Self-report measures of psychopathology (SCL-90-R) and state and trait anxiety (STAI) were also included. While no significant differences between the groups were found on the parameters of chemoreception, the IEI patients reached significantly higher scores on the SCL-90-R depression, anxiety and somatization sub-scales, and on the STAI for state anxiety.

Significantly higher scores on the STAI for trait anxiety were reported between IEI patients and healthy controls. No significant differences were found on the anxiety measures between the group with self-reported odour sensitivity and the healthy control group, which led the authors to suggest that a moderate degree of anxiety may be characteristic of IEI patients [42]. Other authors also support the hypothesis of trait anxiety and negative affectivity as indicative of a dispositional vulnerability in the acquisition and development of sensitivity reactions to common environmental odours [14;43]. Österberg and colleagues performed a study involving 84 non-patient environmentally-sensitive individuals and 54 healthy controls. Based on findings of elevated scores for neuroticism/trait anxiety in environmentally-sensitive individuals, as measured by the Swedish Universities Scales of Personality, the authors argued that trait anxiety might not reflect only secondary reactions to the disability induced by environmental sensitivity but rather a dispositional vulnerability [14]. In another study including 38 healthy individuals Orbaek and colleagues reported that trait anxiety influenced ratings of mucous membrane irritation, fatigue and symptoms of environmental sensitivity in response to experimental chemical exposures [44].

To assess the stability of IEI and to examine if the disorder could be distinguished from somatoform disorders with respect to symptoms and symptom interpretation or attributions, trait anxiety and body-related cognitions, Bailer and colleagues followed two clinical groups over 32 months. One group consisted of individuals with IEI and the other of individuals with somatoform disorders [8;9;45]. The authors hypothesized that IEI is largely determined by a self-perpetuating cycle of increased attention to environmental factors and bodily sensations that result in biased symptom perception and amplification [7]. Somato-sensory amplification was initially described by Barsky and colleagues as a mechanism in the maintenance of symptoms in functional somatic disorders [32]. At baseline individuals with IEI were divided into a group with overlapping IEI and somatoform disorders and an IEI-only group. A higher prevalence of a DSM-IV diagnosis of current depression was found in the IEI /somatoform disorder group when compared with the remaining groups [7]. Significantly higher scores on measures of trait anxiety, symptom attribution and body-related cognitions were reported for all groups when compared with the control group, and trait anxiety was found to be the strongest predictor of self-reported somatic symptoms in the total sample [7]. Bailer and colleagues concluded that IEI is a variant of somatoform disorders or functional somatic syndromes with the IEI-only group representing a moderate variant without significant accompanying social and occupational disruptions [7]. One year after the baseline assessments the stability of somatic symptoms and features of IEI were evaluated in

96% of the initial study sample [8]. The test-retest κ for the IEI diagnosis was 0.79 and 92% of the initial IEI cases still met the case criteria at follow-up. From multiple, linear regression analyses, trait anxiety and somatic attribution style appeared to be the strongest predictors of somatic symptom severity in the IEI group [8]. Of the initial sample 86% were available for the second follow-up after a median period of 32 months (24 through 40 months) [9]. Of the initial IEI cases 73.9% still met the case criteria, which suggests some fluctuations in scores during follow-up. Trait anxiety and somatic attribution style still emerged as significant predictors of somatic symptoms, but regression analyses suggested that the relationship between trait anxiety and somatic symptoms was partly mediated by a somatic attribution style [9]. When interpreting the results presented by Bailer and colleagues some attention should be given to the present uncertainty regarding the diagnostic criteria for somatoform disorders in both DSM-IV and ICD-10 [46]. Currently, a somatoform diagnosis is not based on positive criteria but on the exclusion of organic disease and is not supported by substantial empirical evidence [46;47]. The substantial overlap between MCS/IEI and somatoform disorders may thus to some extent be explained by the uncertainty of the diagnostic criteria for a somatoform disorder as well as the reliance on self-reported symptoms and disability in establishing the presence of MCS.

Somato-sensory amplification and symptoms of emotional distress as measured by SCL-90-R have also been examined by Bell and colleagues in a study on women with self-reported MCS [48]. When compared with a group of individuals with sensitivity to odours but without functional disability and a healthy control group, significantly higher scores on the somato-sensory amplification scale (SSAS) and on the SCL-90-R subscales of somatization, depression, anxiety, phobic anxiety and obsessive compulsiveness were reported for the MCS group. However, participants were recruited by advertisements which, as noted by the authors, may question whether the groups were representative [48].

The personality trait of absorption [49] is defined as openness to experience and a predisposition to experiencing alterations of cognition and emotion across a broad range of situations [50]. Absorption has been associated with increased sympathetic and parasympathetic reactivity during exposure to an experimental stressor [51], suggesting that individuals who are high on this trait may be more reactive in stressful situations. The reactivity to aversive stimuli points to the possibility that individuals with high absorption are more conditionable [28]. Evidence of a link between absorption and IEI has been reported in a longitudinal study, which led the authors to conclude that absorption may be a specific risk factor in IEI [45].

Alexithymia is another personality construct that has been examined in patients with MCS [41]. The construct was originally developed to specify a set of personality characteristics often observed in patients with somatoform disorders [52-54]. Alexithymic individuals are believed to exhibit difficulties in identifying emotions and distinguishing them from bodily sensations of emotional arousal. They also have difficulties describing feelings, an impoverished fantasy life, and a stimulus-bound, externally oriented cognitive style [53]. The theory of alexithymia suggests that cognitive deficits in distinguishing emotions from their physiological correlates may lead the individual to become preoccupied with physiological sensations and misinterpret them as symptoms of disease [55]. The alexithymia construct has found support in recent evidence suggesting a contribution of genetic factors in the development of this trait [54]. The Toronto Alexithymia Scale (TAS-20) is a commonly used self-report measure of alexithymia, and using only the total TAS-20 score Caccappolo-van Vliet and colleagues reported no evidence of an association between MCS and alexithymia.

#### 3.4.2 Psychiatric co-morbidity

Psychiatric co-morbidity in individuals with MCS is often reported, frequently in terms of major depression, somatoform disorders, anxiety or panic disorder [56]. Bell and colleagues evaluated 28 middle-aged women with MCS, and 68% of the women reported a past diagnosis of depression, anxiety or panic disorder [48]. In contrast 20% of a healthy control group reported having past psychiatric diagnoses. Based on a study of 37 plastic workers who filed compensation claims due to symptoms attributed to workplace exposure to chemicals, Simon and colleagues concluded that their findings of pre-existing anxiety or depression could suggest increased sensitivity to noxious stimuli [57]. The study sample was small, however, and it should be noted that only 13 of the 37 workers were classified as being chemically sensitive based on a four-item symptom score on reactions to common environmental exposures. The higher prevalence of preexisting psychopathology was reported for this group [57]. With the aim of characterising health complaints relevant for MCS, 251 environmental outpatients were examined using a standardized psychiatric interview (CIDI) [58]. Compared with a general population group, environmental outpatients had significantly higher rates of life-time psychiatric disorders, and 76.5% of the environmental patients compared with 36.9% of the general population group fulfilled the diagnostic criteria for at least one psychiatric disorder (12-month prevalence). Women outpatients had higher rates (79.7%) than male outpatients (68.9%). In the majority of the environmental outpatients the psychiatric disorder pre-existed their MCS. However, when comparing the 12-month prevalence of depression and anxiety disorders higher rates were seen in the general population group, whereas the environmental outpatient group showed higher rates of somatoform disorders [58]. Caccappolo-van Vliet and colleagues compared patients with MCS (n= 30), individuals with asthma (n= 19) and healthy controls (n= 31) on measures of lifetime and current psychiatric disorders. They found that current anxiety and depression were significant contributors to physical and cognitive symptoms in MCS [41]. Relative to the control group both MCS patients and asthmatics demonstrated a significantly greater proportion of life-time anxiety disorders, and approximately 50% of the MCS patients met criteria for current depression or somatization disorder. The authors concluded that even when MCS patients do not meet criteria for a psychiatric disorder, dispositions associated with such disorders may nevertheless contribute to symptom reports [41]. However, whether high rates of psychopathology pre-exist the onset of MCS is not consistent in the literature [59]. In a case-control study Simon and colleagues reported a prevalence of current anxiety or depressive disorder in patients with MCS (n= 41) of 44% versus 15% in control subjects (n= 34), while the prevalence of pre-existing anxiety or depressive disorder did not differ between the two groups [60].

Prospective studies on MCS are few and the association with psychological traits and psychopathology has largely been studied in cross-sectional designs using self-report measures. In the evaluation of the prevalence of psychiatric co-morbidity in MCS/IEI, differences in case definitions, study populations and self-report measures should be taken into consideration since it may question the comparability of data across studies. Some authors have even cautioned against administering psychological or psychiatric tests to individuals with a poorly understood condition such as MCS [61]. They argue that symptoms of psychopathology may be secondary to the condition and that both research and treatment strategies may be prematurely directed towards focusing on psychology and psycopathology [61]. The individual reports of social and occupational disruptions which often follow MCS, combined with lack of consistent pathophysiological findings has led to an ongoing debate among researchers and clinicians as to whether MCS is psychogenic in origin and best classified as a functional somatic disorder [7;24]. However, while the diagnostic criteria for somatoform disorders and the self-reported symptoms and consequences of MCS share some similarities, evidence of efficacy of cognitive or psychotherapeutic interventions [62] and psychopharmacological drugs in MCS is still needed. Whether psychopathology and individual susceptibility to sensitivity reactions is part of the aetiology or merely act as amplifying factors can only be speculated at this point. More studies suggest that psychopathology is not present in all cases and the relative importance of psychology in MCS may eventually be difficult to determine. It is likely that the aetiology of MCS is multi-factorial, and as in somatoform disorders [63;64], it can be argued that the complexities of MCS should be studied from a bio-psycho-social perspective. This involves the influence of biological factors such as central sensitization processes [23;65] or changes in reactivity of the hypothalamic-pituitary-adrenal axis [66]; psychopathological processes such as the role of anxiety and depression [56]; processes involved in symptom perception and amplification and in emotional regulation [7-9;67;68]; and socioeconomic factors [10;11].

#### 4. Aims of the thesis

The aims of the thesis were to:

- o investigate the clinical practice of Danish GPs in relation to patients who seek medical advice due to symptoms attributed by the patient to common environmental odours.
- o describe the self-reported impact of MCS on everyday life, including changes in lifestyle, social and occupational consequences, and experiences with health care management.
- examine if somato-sensory amplification, autonomic reactivity and absorption were associated with more severe self-reported reactions attributed to common environmental odours.
- examine if a repressive coping style and the personality construct of alexithymia were associated with more severe self-reported reactions attributed to common environmental odours, and to test whether these associations would be moderated by self-reported stress. Further, to clarify whether negative affectivity was associated with self-reported reactions, and whether it acts as a possible mediator in an association between MCS and the alexithymia construct.

#### 5. Overview of studies

The aims of the thesis described in the previous chapter were investigated in the following three studies:

- 1) A nationwide cross-sectional postal questionnaire survey including a random sample of 1000 Danish General Practitioners (GPs). The study was undertaken in collaboration with the Department of General Practice, Institute of Public Health, University of Copenhagen. (Manuscript 1)
- 2) A qualitative study using focus groups as data collection method. A selective sampling strategy was applied and informants were recruited from a list of people registered at the Danish Research Centre for Chemical Sensitivities because of self-reported MCS. (Manuscript 2)
- 3) A cross-sectional postal questionnaire survey including a sample of 1024 individuals with self-reported or doctor-diagnosed MCS. The study was undertaken in collaboration with the Psychooncology Research Unit, Aarhus University Hospital, Aarhus and the Institute of Public Health, Department of Social Medicine, University of Copenhagen. (Manuscript 3 + 4)

The four manuscripts included in chapters 6-9 are based on these three studies, which were all performed at the Danish Research Centre for Chemical Sensitivities, Department of Dermato-Allergology, Gentofte Hospital, University of Copenhagen, Denmark between 2006 and 2009.

Skovbjerg S, Johansen JD, Rasmussen A, Thorsen H, Elberling J: General practitioners' experiences with provision of healthcare to patients with self-reported multiple chemical sensitivity. Scand J Prim Health Care. 2009; 27 (3): 148-52.

Skovbjerg S, Brorson S, Rasmussen A, Johansen JD, Elberling J: Impact of self-reported multiple chemical sensitivity on everyday life - a qualitative study. Scand J Public Health. 2009 Aug; 37(6): 621-6.

Skovbjerg S, Zachariae R, Rasmussen A, Johansen JD, Elberling J: Attention to bodily sensations and symptom perception in individuals with idiopathic environmental intolerance. Environ Health Prev Med. DOI 10.1007/s12199-009-0120-y.

Skovbjerg S, Zachariae R, Rasmussen A, Johansen JD, Elberling J: Repressive coping and alexithymia in multiple chemical sensitivity (Submitted manuscript).

## Title:

Repressive coping and alexithymia in multiple chemical sensitivity

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**Keywords:** Alexithymia; chemical sensitivity; functional somatic syndromes; negative affectivity; repressive coping; stress

#### **Abstract**

Objective: To examine if non-expression of negative emotions, i.e., repressive coping and differences in ability to process and regulate emotions, i.e., alexithymia, were associated with more severe self-reported multiple chemical sensitivity (MCS), and if such associations were moderated by stress.

*Methods*: The study included participants from a general population-based study with self-reported MCS (n=787) and patients with MCS (n=237). Participants completed questionnaires assessing MCS, a measure of repressive coping combining scores on the Marlowe-Crowne Social Desirability Scale (MCSD) and the Taylor Manifest Anxiety Scale (TMAS), the Toronto Alexithymia Scale (TAS-20), a Negative Affectivity Scale (NAS) and a measure of stressful life events. Multiple, hierarchical linear regression analyses were conducted with four MCS severity features as the dependent variables.

*Results*: Both the TMAS and MCSD were independently associated with MCS, but there was no evidence of a role of the repressive construct. While total alexithymia scores were unrelated to the dependent variables, the TAS-20 subscale of difficulties identifying feelings (DIF) was independently associated with more severe symptoms. Although the associations with MCS were not moderated by stress, negative affectivity was a strong independent predictor of all MCS-related variables.

Conclusion: Our results provide no evidence for a role of repressive coping in MCS, and the hypothesis of an association with alexithymia was only partly supported. Strong associations between severity of MCS and negative emotional reactions, defensiveness and difficulties identifying feelings were found, suggesting a need for exploring the influence of these emotional reactions.

## **Abbreviation list**

CHS: Chemical Hypersensitivity Scale; CNSS: CNS Symptom Scale; CSAS: Consequences for Social Activities Scale; CSS-SHR: The Chemical Sensitivity Scale for Sensory Hyper-reactivity; DIF: Difficulties Identifying Feelings; DDF: Difficulties Describing Feelings, EOT: Externally Oriented Thinking; MCS: Multiple Chemical Sensitivity; MUSS: Mucosal Symptom Scale; MCSD: Marlowe Crowne Social Desirability Scale; Stress: RLE: Recent life events; NAS: Negative Affectivity Scale; TAS-20: the Toronto Alexithymia Scale; TMAS: the Taylor Manifest Anxiety Scale.

#### Introduction

Multiple chemical sensitivity (MCS) is an unclarified disorder characterized by non-specific symptoms from various organ systems attributed by the individual to exposure to common environmental odours [1]. The symptoms overlap with other unexplained disorders, such as fibromyalgia and chronic fatigue syndrome [2], and several studies have reported associations between chemical sensitivity and emotional distress, e.g., increased levels of anxiety, somatization and depressive symptoms [3-12]. Evidence also points to a role of psychological traits thought to be involved in the maintenance of symptoms in functional somatic disorders [3;4;10;13;14]. The association between MCS and symptoms of emotional distress and psychological traits related to emotional inhibition suggest that affect regulation may play a role.

Affect regulation is a term involving various types of both conscious and unconscious styles of

experiencing, processing, and modulating emotions [15]. Intensely experienced emotions that are avoided, inhibited, or not expressed may lead to physiological hyper-reactivity and physical symptoms [16]. Patients with chronic illness have been described as having difficulties identifying and describing emotions, being unaware of or repressing emotions, or avoiding and being ambivalent about expressing emotions [15]. Likewise, affect regulation characterized by avoidance and non-expression has been related to maladjustment to chronic illness [16]. Such strategies may, if sufficiently dominant, serve as a moderator of the association between negative emotional reactions and health outcomes and could thus be considered both as a process of relevance to the pathology of certain disorders and as a potential focus of intervention [17;18]. Research has focused on different types of emotional regulation. One theoretical construct, emotional repression, focuses on unconscious emotional inhibition [19]. The theory suggests that individuals characterized by repressive coping will have a tendency to disattend to important negative emotional feedback, thereby exhibiting a discrepancy between psychological reactions (e.g., no perception or recall of negative emotions) and physiological responses (e.g., high skin conductance levels) to stressful stimuli. If the repressive/defensive response pattern constitutes a relatively stable trait, it may prevent the individual from coping effectively [20;21] and lead to misinterpretation of emotions as physiological reactions or symptoms [22;23]. One approach to assess repressive coping, suggested by Weinberger [19], combines a trait measure of anxiety, e.g., the Taylor Manifest Anxiety Scale (TMAS), with the Marlowe Crowne Social Desirability Scale (MCSDS), believed to measure defensiveness [24]. This two-dimensional approach combines high and low scores on each scale into four prototypical coping styles.

The alexithymia construct was originally developed to specify a set of personality characteristics often observed in patients with somatoform disorders [25-27]. Alexithymic individuals are believed to exhibit difficulties identifying emotions and distinguishing them from bodily sensations of emotional arousal. They also have difficulties describing feelings; an impoverished fantasy life; and a stimulus-bound, externally oriented cognitive style [26]. The theory of alexithymia suggests that cognitive deficits in distinguishing emotions from their physiological correlates may lead the individual to become preoccupied with physiological sensations and misinterpret them as symptoms of disease [28]. The alexithymia construct has found support in recent evidence suggesting a contribution of genetic factors in the development of this trait [27]. As alexithymia is also associated with negative affectivity [29], an association between alexithymia and MCS could be mediated by negative affectivity.

Taken together, emotional regulation may hypothetically contribute to the aggravation of chemical sensitivity by increasing focus on physiological sensations and interpreting these as symptoms of disease [24]. Five hypotheses were tested in the present study. We expected: 1) that a repressive coping style and 2) alexithymia would be independently associated with more severe self-reported reactions attributed to environmental odours; 3) that the associations would be moderated by self-reported stress, i.e., the association would be stronger in individuals with high levels of stress; 4) that the severity of MCS would be independently associated with negative affectivity; and 5) that the association between MCS and alexithymia would be either completely or partly mediated by negative affectivity.

#### Methods

#### **Participants**

Three groups were invited to participate in the study 1) Individuals from the general population, 2) Patients with physician diagnosed MCS, and 3) Individuals who had contacted the Danish Research Centre because of symptoms attributed to environmental, odorous chemicals. Group 1 included respondents to a population-based cross-sectional survey (n=4260) consisting of 18-69-year-old individuals randomly drawn from the Danish Civil Registration System (8). Respondents (n=1134) were invited to participate in the present study providing they had: 1) reported being bothered by exposure to at least one common chemical (e.g., fragranced products, newly printed magazines), 2) confirmed that exposure to odourous chemicals was associated with symptoms and not perceived as merely unpleasant, and 3) given consent to be contacted again (n=787). Group 2 included individuals who had contacted the Danish Research Centre for Chemical Sensitivities because of MCS between 1 January 2006 - 1 August 2007 and who had agreed to participate in the present study (n=101). Group 3 included individuals who had received a diagnosis of MCS either at the Copenhagen University Hospital, Rigshospitalet, or at Hamlet, Private Hospital, Denmark 1 January 1990 - 1 January 2007. This group received a letter inviting them to participate (n=136).

#### Measurements

The following self-report measures were included:

Repressive coping was assessed by combining the Danish translations of 33-item Marlowe-Crowne Social Desirability Scale (MCSD) [31] and the Bendig 20-item version of the Taylor Manifest Anxiety Scale (TMAS) [32]. Responses are rated as true or false. The Danish version of both scales has previously been shown to have acceptable internal consistencies and test-retest reliabilities [24]. As suggested by Weinberger [19], emotional repressors were defined as individuals scoring below the median of TMAS and above the median of the MCSD, with the remaining individuals characterized as true low anxious (low TMAS/low MCSD), true high anxious (high TMAS/low MCSD), and defensive high-anxious (high TMAS/high MCSD). Sexdependent cut-off values were used, if statistically significant sex differences were found for either of the scales.

Alexithymia was assessed using the Danish translation of the Toronto Alexithymia Scale (TAS-20) [33-35]. TAS-20 is a 20-item questionnaire with responses rated on a 5-point Likert scale

and scores ranging 20-100. The presence of alexithymia can be investigated using a continuous approach including both the total score and the scores of the three subscales: difficulties identifying feelings (DIF), difficulties describing feelings (DDF) and externally oriented thinking (EOT) corresponding to the original factor structure [27;34]. Moderate to good internal consistency has been reported for the Danish translation of TAS-20, both for the total scale ( $\alpha = 0.81$ ) and the three subscales (DIF;  $\alpha = 0.82$ , DDF;  $\alpha = 0.77$ , EOT;  $\alpha = 0.66$ ) [27].

Recent life events (RLE) is a list of potentially stressful events judged by the respondent as having had a negative impact on his or her quality of life [36]. The score expresses the number of stressful life events within the past year experienced as having had a negative impact [36].

The negative affectivity scale (NAS) includes 15 items measuring the tendency to experience and report negative emotions, including anxiety, guilt, hostility and depression, with low negative affect reflecting a state of calmness [37;38]. Responses are rated on a 5-point Likert scale. Satisfactory internal consistency (0.87) and moderate test-retest reliability (0.48) has been reported [38].

Chemical sensitivity was assessed by: 1) number and severity of CNS symptoms including: headache, exhaustion, dizziness, difficulties concentrating, grogginess, sleep difficulties, panic attacks, 2) number and severity mucosal symptoms: eyes, nose, sinuses, mouth, throat, and lungs, 3) number of symptom-inducing environmental odours: fragranced products, cleaning agents, nail polish remover, newly printed papers or magazines, new furniture, soft plastic or rubber, cooking fumes, motor vehicle exhaust, tar or wet asphalt, smoke from a wood burner, and new electric equipment, and 4) social consequences that were phrased: "Do reactions caused by environmental odours lead you to avoid": a) social activities (e.g., family- or other private parties), b) inviting guests, c) going on holiday, d) sports activities, e) using public transportation, f) going to the cinema or theatre, g) going to restaurants?

#### Statistical analysis

Initially 63 items covering symptoms, symptom eliciting chemical agents, consequences in terms of the degree to which reactions had influenced social relations and work were analysed using principal components analysis with Varimax rotation. Factors were selected on the basis of an eigenvalue greater than 1 and items to show loadings of 0.5 or higher for the central factor. Seven factors were identified of which four grouped into clusters of five or more items with cross loading no higher than 0.25 {Costello, 2005 709 /id}.

Factor 1 can be described as the responses to symptom-eliciting environmental odours, i.e., fragranced products, cleaning agents, nail polish remover, newly printed papers or magazines, new furniture, soft plastic or rubber, cooking fumes, motor vehicle exhaust, tar or wet asphalt, smoke from a wood burner, and new electric equipment. These 11 items were summarized in the Chemical Hypersensitivity Scale (CHS), which based on the response format to the questions yields a total score ranging 0-33. Cronbach's Alpha for the CHS was 0.95. Factor 2 includes social or public events that are avoided because of symptoms attributed to common environmental odours, i.e., social activities (e.g., family or other private parties), inviting guests, going on holiday, sports activities, using public transportation, going to the cinema or the theatre, or going to restaurants. These items were summarized in the Consequences for Social Activities Scale (CSAS) that yields a total score ranging 0-14. Cronbach's Alpha for the CSAS was 0.92. Factor 3 consists of 8 items that describe symptoms from the central nervous system, i.e., headache, exhaustion, dizziness, difficulties concentrating, grogginess, sleep difficulties, panic attacks and breathlessness. These items were summarized in the CNS Symptoms Scale (CNSS), with total scores ranging 0-8. Cronbach's Alpha for the CNSS was 0.68. Factor 4 consists of 6 items describing mucosal symptoms, i.e., eyes, nose, sinuses, mouth, throat, and lungs, summarized in the Mucosal Symptoms Scale (MUSS) with total scores ranging 0-6. Cronbach's Alpha for the MUSS was 0.59.

All continuous variables were inspected for normality. Non-normally distributed variables were log-transformed. If the transformation was considered successful, the log-transformed variables were used in subsequent analyses.

## Repressive coping

The possible influence of repressive coping was analyzed using three approaches [19;24]: 1) the hypothesis of an association between repressive coping and higher scores on any of the independent variables (CHS, MUSS, CNSS, CSAS) was considered supported if emotional repressors scored significantly higher than the remaining three coping groups. This was tested with one-way analysis of variance ANOVA with the four coping styles as grouping factor and Scheffe post-hoc tests controlling for multiple comparisons; 2) the hypothesis of an effect of repressive coping was also tested with a two-factor ANOVA, with high vs. low anxiety (TMAS) and high vs. low defensiveness (MCSD) as grouping variables - a confirmation of the hypothesis required the finding of a significant TMAS x MCSD interaction; and 3) to minimize risk of type-2 error due to dichotomization, the continuous scores of TMAS and MCSD were entered at the first step in a multiple, linear regression analysis, and the continuous interaction variable (MCSD x (max TMAS-score - actual TMAS score) at the second step - this interaction algorithm yields a continuous variable with high scores representing high repressive coping and low scores representing a high degree of true high anxiety. Confirmation of our hypothesis required a significant effect of the interaction variable when entering this at the second step of the regression. Finally, to test the hypothesis that effects of repressive coping would be more prominent in individuals exposed to stress, the analyses were repeated for individuals scoring above and below the median on the RLE.

## Alexithymia

Alexithymia was analyzed as a continuous variable using both the total TAS-20 score and scores on the three subscales (DIF, DDF, EOT). Multiple, hierarchical linear regression analyses were performed with the four dependent variables and the total TAS-20 score as the independent variable, entered at step 1. NAS was entered at step 2, age and sex at step 3, and patient vs. population group at step 4. Corresponding analyses were also performed using the three TAS-20 subscales as independent variables at step 1. Analyses were repeated for individuals scoring above and below the median on the RLE.

# Mediation analyses

Finally, if associations were found between alexithymia and the dependent variables, the possible mediating effects of NAS were explored using the method described by Baron and Kenny [39]. The Sobel test was used as a direct test of mediation [40].

## Level of significance

The level of significance was set at p < 0.05.

## **Approval**

The study was approved by the Danish Data Protection Agency.

#### **Results**

#### Group characteristics

A total of 1024 individuals were invited to participate. The overall response rate was 71.5% (n=732). The characteristics of the two groups are summarized in Table 1. Significant differences were found between the groups with respect to sex, age, and mean scores on the CHS, MUSS, CNSS, CSAS and for the variables MCSD, TMAS, TAS-20, TAS20-DIF, TAS20-DDF and TAS20-EOT. No significant differences were found for NAS and RLE.

#### **Correlations**

Relatively high intercorrelations were found between CHS, MUSS, CNSS and CSAS, while relatively small correlations were found between these variables, the independent variables (MCSD, TMAS, TAS-20, TAS20-DIF, TAS20-DDF and TAS20-EOT), and the control variables (NAS, RLE, age and sex). Moderate to high correlations were found between TMAS, TAS-20, and the three subscales, NAS, and RLE (Table 2).

## Repressive coping

MCSD scores appeared normally distributed, whereas TMAS was negatively skewed, and TMAS was therefore log-transformed prior to further analyses. Women had significantly higher TMAS-scores than did men (p < 0.001) (Table 1), and sex-dependent scores were therefore used in the classification of coping styles. As seen in Table 2, a significant inverse correlation was found between TMAS and MCSD and a significant positive correlation was seen between age and MCSD-scores. TMAS showed moderate positive correlations with all four dependent variables, while MCSD was correlated with CHS and CSAS.

#### Categorical data

Approach 1: When comparing the four coping styles with one-way ANOVA, significant effects were found for CHS, CNSS, and CSAS. Emotional repressors had significantly higher CSAS scores than true low-anxious. No other differences were found (data not shown). When comparing high vs. low stress individuals, no significant differences were found (data not shown).

Approach 2: Both TMAS and MCSD were independently significantly associated with scores on CHS, CNSS, and CSAS (F=16.0-2.3; p=0.04-0.001) (data not shown). No significant interactions between TMAS and MCSD were found for any of the four dependent variables (F=0.00)

-0.44; p= 0.51 - 0.91) in the two-way ANOVA analysis using high-low TMAS and high-low MCSD as group factor. This pattern of results was unchanged when analyzing the data for high and low stress individuals (data not shown).

#### Continuous data

Approach 3: The results of a series of multiple, hierarchical linear regression analysis are shown in Table 3. At the first step, TMAS and MCSD were significantly independently associated with all four dependent variables. Entering the TMAS-MCSD interaction term did not significantly explain any additional variation. At the final step, age and sex explained a significant proportion of the variance of CHS, and group a significant proportion of the variance for all four dependent variables. MCSD and TMAS only explained a minor proportion of the variance (R<sup>2</sup>= 0.03 – 0.05), while the demographic variables, primarily group, explained an additional 16% to 54%. Analyzing high and low stress individuals separately did not change the results.

## Alexithymia

TAS-20 total and EOT subscale scores appeared normally distributed, whereas DIF and DDF were negatively skewed and therefore log-transformed prior to analyses. Mean scores are shown in Table 1. Significant differences were found both between the population and patient group, and between men and women (p < 0.05) with patients and women exhibiting lower scores than did individuals from the population group and men. These differences were also generally found for the TAS-20 subscales of DDF and EOT, but not DIF, where patients and women showed slightly higher scores.

## Associations between TAS-20 and the dependent variables

Multiple, hierarchical linear regression analyses were performed using CHS, MUSS, CNSS and CSAS as the dependent variables, and the total TAS-20 score as the independent variable. Results are shown in Table 4. While no associations with alexithymia were found for CHS and CSAS, alexithymia was associated with significantly *lower* severity scores for MUSS.

Alexithymia showed a statistically significant inverse association with CNSS when controlling for NAS, age, and sex, and a near-significant association when entering group in the model. Conversely, NAS was associated with higher scores on all four dependent variables. Alexithymia, NAS, age, and sex accounted for only small-to-moderate proportions of the variance, with

R<sup>2</sup> ranging 0.02-0.12. Belonging to the patient group was the strongest predictor, accounting for an additional 14-51% of the variation in symptoms (data not shown).

# Associations between TAS-20 subscales and the dependent variables

The results for TAS-20 subscales are shown in Table 5. When entered independently, DIF was associated with more severe scores on all dependent variables. DIF continued to be associated with greater severity for CHS and CNSS while a borderline association was seen for CSAS when controlling for NAS, age, and sex. In contrast, DDF was associated with less severe scores, except MUSS, both at step 1 and 2. When entering group at the final step, only DIF remained significantly associated with more severe scores on the CNSS. NAS was associated with higher scores for all four dependent variables, and again group appeared to be the most significant predictor of severity, explaining from 17-57% of the variance (data not shown).

# Comparing high and low stress individuals

The RLE was dichotomized and the regression analyses were repeated separately for individuals with high and low number of stressors. No differences were found between high and low stress individuals for CHS, CNSS, and CSAS (data not shown). The inverse association between MUSS and alexithymia appeared somewhat stronger in high stress individuals (data not shown).

#### Mediation analyses

As NAS was positively associated with TAS-20, DIF and DDF, and the four dependent variables, a series of mediation analyses were conducted.

TAS-20: MUSS was the only dependent variable significantly associated with TAS-20. However, entering the mediator (NAS) did not reduce the independent variable - dependent variable association (from B = -0.012; p = 0.016 to B = -0.017; p = 0.002). DIF: For CHS, MUSS, and CNSS, the independent variable - dependent variable associations were reduced to non-significance (p = 0.14 - 0.84) when entering the mediator into the equation. Direct tests of mediation (Sobel test) confirmed that NAS acted as a mediator of the association between DIF and CHS, MUSS, and CNSS (Z = 2.99 to 3.29; p = 0.001 to 0.002). DDF: NAS could only be considered a mediator for the association between DDF and CHS. Entering the mediator did not reduce the independent variable - dependent variable association, as the associations grew stronger, not weaker (data not shown).

**Table 1**. Means and standard deviations of the dependent and independent variables

**Population sample** 

#### **Total** <sup>1</sup>P-value Men Women Men Women **Total** N 194 571 140 161 **≤ 0.001** 377 21 (34 %) (66 %) (100%)(87 %) (100%)(13%)50.1 (11.8) 47.1 (12.6) 48.1 (12.4) 50.9 (11.2) 53.3 (10.6) 53 (10.6) Age ≤ 0.001CHS 12.3 (6.9) 13.7 (6.8) 13.2 (6.9) 26.3 (5.6) 25.2 (6.3) 25.3 (6.2) **≤ 0.001 MUSS** 2.2 (1.3) 2.3 (1.4) 2.3(1.3)3.5 (1.8) 3.9 (1.7) 3.8 (1.7) $\leq$ 0.001 **CNSS** 1.9 (1.3) 2.1 (1.3) 2.0(1.3)5.2 (1.4) 4.8 (1.9) 4.9 (1.9) $\leq 0.001$ **CSAS** 0.3 (0.82) 0.4 (1.5) 6.5 (4.0) 6.2 (4.1) $\leq$ 0.001 0.4(1.3)6.2(4.1)MCSD 18.8 (5.0) 19.2 (5.6) 21.9 (3.7) < 0.001 19.1 (5,4) 20.6 (4.5) 20.8(4.4) $TMAS^2$ 5.3 (4.3) 6.7 (4.6) 6.2(4.5)5.6 (3.7) 7.1 (4.4) 6.8(4.4)< 0.05 TAS20 43.0 (11.5) 47.5 (11.6) 44.5 (11.7) 44.3 (12.3) 42.1 (11.2) 42.3 (11.3) < 0.05 Total **TAS20** 13.1 (5.0) 13.5 (5.2) 13.4 (5.1) 14.4 (6.2) 14.4 (5.1) 14.4 (5.2) < 0.05 DIF **TAS20** 13.0 (4.5) 10.9 (4.4) 11.6 (4.5) 10.0 (4.3) 10.2 (4.4) 10.2 (4.4) < 0.001 **DDF** 17.6 (5.3) 21.5 (5.5) 18.5 (5.3) 19.6 (5.6) 19.6 (5.2) 17.9 (5.3) < 0.001 **TAS20 EOT** 14.0 (9.9) NAS 12.4 (9.0) 13.6 (9.0) 13.2 (9.0) 11.8 (9.5) 14.4 (10.0) 0.35 RLE 2.8 (3.2) 3.8 (3.7) 3.4 (3.6) 1.9 (2.5) 3.3 (3.4) 3.2(3.4)0.38

Patient sample

CHS: Chemical Hypersensitivity Scale; MUSS: Mucosal Symptom Scale; CNSS: CNS Symptom Scale; CSAS: Consequences for Social Activities Scale; MCSD: Marlowe-Crowne Social Desirability Scale; TMAS: Taylor Manifest Anxiety Scale; TAS-20: The Toronto Alexithymia Scale; TAS20-DIF: Difficulties identifying feelings; TAS20-DF: Difficulties describing feelings; TAS20-EOT: Externally oriented thinking; NAS: Negative Affectivity Scale; RLE: Recent Life Events.

<sup>&</sup>lt;sup>1</sup> Independent samples t-test for equality of means (total) between population and patient sample. <sup>2</sup> TMAS was log-transformet prior to comparison.

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Table 2: C	Correlation	ns between t	the CHS, M	IUSS, CN	SS, CSAS,	TAS-20, T	TAS-DIF, T	CAS-DDF,	TAS-EO	Γ, MCSD,	TMASlo	g, NAS, ag	e, and sex.	
	CHS	MUSS	CNSS	CSAS	MCSD	TMAS	TAS20	DIF	DDF	EOT	NAS	RLE	Age	Sex
CHS	-	0.47**	0.60**	0.58**	0.09*	0.16**	-0.01	0.13**	-0.10**	-0.05	0.16**	0.08*	0.26**	0.18**
MUSS	-	-	0.60**	0.44**	0.06	0.14**	-0.09*	0.08*	-0.11**	-0.18**	0.14**	0.15**	0.09*	0.14**
CNSS	-	-	-	0.62**	0.04	0.18**	-0.07	0.14**	-0.12**	-0.18**	0.18**	0.09*	0.06	0.15**
CSAS	-	-	-	-	0.16**	0.09*	-0.06	0.05	-0.13**	-0.07	0.09*	-0.004	0.15**	0.15**
MCSD	-	-	-	-	-	-0.27**	-0.13**	-0.23**	-0.15**	0.05	-0.29**	-0.16**	0.17**	0.05
<b>TMAS</b>	-	-	-	-	-	-	0.31**	0.50**	0.26**	-0.01	0.57**	0.33**	-0.05	0.15**
<b>TAS-20</b>	-	-	-	-	-	-	-	0.73**	0.86**	0.73**	0.25**	0.03	0.07	-0.17**
DIF	-	-	-	-	-	-	-	-	0.55**	0.16**	0.43**	0.19**	0.03	0.05
DDF	-	-	-	-	-	-	-	-	-	0.47**	0.18**	0.002	0.00	-0.20**
EOT	-	-	-	-	-	-	-	-	-	-	-0.01	-0.14**	0.12**	-0.25**
NAS	-	-	-	-	-	-	-	-	-	-	-	0.39**	-0.16**	0.08
RLE	-	-	-	-	-	-	-	-	-	-	-	-	-0.14**	0.12**
Age	-	-	-	-	-	-	-	-	-	-	-	-	-	-0.05
Sex	-	-	-	-	-	-	-	-	-	-	-	-	-	-

CHS: Chemical Hypersensitivity Scale; MUSS: Mucosal Symptom Scale; CNSS: CNS Symptom Scale; CSAS: Consequences for Social Activities Scale; MCSD: Marlowe-Crowne Social Desirability Scale; TMAS: Taylor Manifest Anxiety Scale; TAS-20: The Toronto Alexithymia Scale; TAS20-DIF: Difficulties identifying feelings; TAS20-DDF: Difficulties describing feelings; TAS20-EOT: Externally oriented thinking; NAS: Negative Affectivity Scale; RLE: Recent Life Events.

Note: \* Correlation is significant at the 0.05 level (2-tailed), \*\* Correlation is significant at the 0.01 level (2-tailed).

**Table 3.** Results of multiple, hierarchical linear regression analysis' with the Chemical Hypersensitivity Scale (CHS), the Mucosal Symptom Scale (MUSS), the CNS Symptom Scale (CNSS) and the Consequences for Social Activities Scale (CSAS) as the dependent variables and defensiveness (MCSD), anxiety (TMAS), and repressive coping (MCSD-TMAS-interaction) as independent variables.

	Dependent variables	CHS		MU	USS	CN	ISS	CS	AS
Step	Independent variables	Beta	P -value	Beta	P-value	Beta	P -value	Beta	P -value
1	MCSD	0.15	0.001	0.10	0.006	0.10	0.009	0.20	0.001
	$TMAS^1$	0.21	0.001	0.17	0.001	0.21	0.001	0.16	0.001
2	MCSD	0.16	0.09	0.03	0.78	0.17	0.07	0.28	0.003
	$TMAS^1$	0.20	<0.05	0.24	0.007	0.14	0.14	0.09	0.34
	MCSD-TMAS- interaction term	-0.01	0.97	0.13	0.37	-0.11	0.44	-0.12	0.37
3	MCSD	0.02	0.82	-0.06	0.47	0.09	0.24	0.15	<0.05
	$TMAS^1$	0.13	0.09	0.20	0.02	0.05	0.52	0.00	1.0
	MCSD-TMAS- interaction term	0.00	0.97	0.14	0.26	-0.14	0.21	-0.11	0.23
	Age	0.18	0.001	0.04	0.26	-0.05	0.12	0.02	0.44
	Sex (Men=1, Women=2)	0.06	0.05	0.05	0.13	0.00	0.99	0.00	0.99
	Population (1) vs patient sample (2)	0.54	0.001	0.39	0.001	0.63	0.001	0.72	0.001
	Total adjusted R <sup>2</sup>	0.40		0.19		0.41		0.55	

MCSD: Marlowe-Crowne Social desirability Scale (defensiveness); TMAS: Taylor Manifest Anxiery Scale. 1) log-transformed

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**Table 4.** Results of multiple, hierarchical linear regression analysis' with the Chemical Hypersensitivity Scale (CHS), the Mucosal Symptom Scale (MUSS), the CNS Symptom Scale (CNSS) and the Consequences for Social Activities Scale (CSAS) as the dependent variables and alexithymia (TAS20) as independent variable, controlling for age, sex, and group.

	Dependent variables	C	HS	MU	MUSS CNSS		ISS	CSAS		
Step:	Independent variables Model 1:	Beta	P -value	Beta	P-value	Beta	P -value	Beta	P -value	
1	TAS-20	-0.01	0.84	-0.09	0.03	-0.07	0.10	-0.04	0.31	
2	TAS-20	-0.05	0.22	-0.13	0.001	-0.12	0.01	-0.07	0.11	
	NAS	0.17	0.001	0.17	0.001	0.21	0.001	0.10	0.01	
3	TAS-20	-0.05	0.21	-0.13	0.01	-0.11	0.01	-0.06	0.17	
	NAS	0.21	0.001	0.18	0.001	0.21	0.001	0.12	0.01	
	Age	0.31	0.001	0.13	0.001	0.11	0.01	0.18	0.001	
	Sex (Men=1, Women=2)	0.17	0.001	0.11	0.01	0.12	0.01	0.14	0.001	
4	TAS-20	-0.01	0.80	-0.10	0.02	-0.06	0.07	0.00	0.99	
	NAS	0.17	0.001	0.16	0.001	0.17	0.001	0.07	0.02	
	Age	0.20	0.001	0.06	0.13	-0.01	0.80	0.04	0.19	
	Sex (Men=1, Women=2)	0.07	0.03	0.04	0.33	0.00	0.91	0.01	0.77	
	Population (1) vs patient sample (2)	0.54	0.001	0.38	0.001	0.62	0.001	0.74	0.001	
Final model	Total adjusted R <sup>2</sup>	0.41	F=85.3 P<0.001	0.19	F=29.4 P<0.001	0.42	F=87.0 P<0.001	0.57	F=159.5 P<0.001	

TAS-20: The Toronto Alexithymia Scale; NAS: Negative Affectivity Scale.

**Table 5.** Results of multiple, hierarchical linear regression analysis' with the Chemical Hypersensitivity Scale (CHS), the Mucosal Symptom Scale (MUSS), the CNS Symptom Scale (CNSS) and the Consequences for Social Activities Scale (CSAS) as the dependent variables and the TAS20 subscales of Difficulties Identifying Feelings (DIF), Difficulties Describing Feelings (DDF), and Externally Oriented Thinking (EOT) as independent variables, controlling for age, sex, and group.

	Dependent variables	C	HS	M	MUSS		CNSS CSAS		SAS
Step:	Independent variables:	Beta	P -value	Beta	P-value	Beta	P -value	Beta	P -value
1	TAS20-DIF <sup>1</sup>	0.23	0.001	0.14	0.01	0.25	0.001	0.16	0.001
	TAS20-DDF <sup>1</sup>	-0.20	0.001	-0.10	0.07	-0.19	0.001	-0.19	0.001
	TAS20-EOT	0.00	0.97	-0.13	0.01	-0.14	0.01	0.08	0.87
2	TAS20-DIF	0.12	0.01	0.06	0.23	0.18	0.001	0.09	0.09
	TAS20-DDF	-0.16	0.01	-0.08	0.14	-0.18	0.001	-0.16	0.003
	TAS20-EOT	0.01	0.83	-0.12	0.01	-0.12	0.01	0.02	0.66
	NAS	0.17	0.001	0.15	0.001	0.15	0.001	0.09	< 0.05
	Age	0.26	0.001	0.16	0.001	0.09	0.05	0.16	0.001
	Sex	0.13	0.001	0.06	0.18	0.05	0.23	0.12	0.01
3	TAS20-DIF	0.03	0.48	0.00	0.99	0.09	0.05	-0.03	0.38
	TAS20-DDF	-0.06	0.16	-0.02	0.74	-0.08	0.07	-0.04	0.26
	TAS20-EOT	0.04	0.26	-0.01	0.05	-0.09	0.05	0.06	0.05
	NAS	0.16	0.001	0.15	0.001	0.14	0.001	0.09	0.005
	Age	0.17	0.001	0.10	0.01	-0.01	0.78	0.03	0.23
	Sex	0.05	0.11	0.00	0.93	.0.02	0.49	0.02	0.46
	Population (1) vs patient sample (2)	0.57	0.001	0.39	0.001	0.58	0.001	0.74	0.001
Final model	Total adjusted R <sup>2</sup>	0.42	F=62.5 P < 0.001	0.22	F=23.4 P<0.001	0.41	F=57.3 P<0.001	0.56	F=109.4 P<0.001

TAS20-DIF: Difficulties identifying feelings; TAS20-DDF: Difficulties describing feelings; TAS20-EOT: externally oriented thinking:; NAS: Negative Affectivity Scale.

<sup>&</sup>lt;sup>1</sup>DIF and DDF were log-transformed due to skewed distributions.

#### **Discussion**

The aim of the present study was to test if two aspects of emotional inhibition: repressive coping and alexithymia, were associated with more severe self-reported chemical sensitivity, and if the association was moderated by stress.

# Repressive coping

While TMAS and MCSD were independently associated with the four descriptive MCS features, the repressive coping approach did not yield any significant results. This is in concordance with other studies unable to support the validity of the Weinberger construct [24]. Although we were unable to confirm the hypothesis of a role of repression, our results provide evidence for an influence of the somewhat broader concept of defensiveness in MCS [41]. Defensiveness as assessed by the MCSD has been investigated in two studies on MCS [42;43]. No differences were found in either study. In another study, using a subscale from the Minnesota Multiphasic Inventory (MMPI-2) as a measure of defensiveness, chemical sensitivity litigants were found to be more defensive about expressing distress and psychopathology and also scored higher on a measure of somatization [44]. The authors concluded that unauthenticated somatic symptoms may be exaggerated, suggesting malingering. While the last study may be seen as supportive of our findings, it should be noted that a different measure of defensiveness was used and the sample investigated were plaintiffs [44]. Despite more studies pointing to a role of trait anxiety in MCS [4;8], the role of defensiveness needs further investigation. It should also be noted that the MCSD-scale has been criticized for being unable to distinguish between other-deception and self-deception [45], and future studies of MCS should attempt to distinguish between these two aspects of social desirable responding.

## Alexithymia

Overall, the mean scores on the TAS-20 did not deviate from normative scores obtained in a community population sample [46]. We were only partly able to confirm our second hypothesis concerning alexithymia, since only one subscale, DIF, was independently associated with more severe self-reported reactions. In contrast, DDF was associated with less severe MCS scores, and no clear pattern was found for the EOT- subscale. We are aware of only one other study of alexithymia and MCS, which found no differences between MCS patients, individuals with asthma and controls [9]. Differences between the separate domains of TAS-20 and their relationships with symptomatology and other personality constructs have also been reported Kirmayer and Robbins, who argue that the

TAS-20 may measure psychometrically and conceptually separate states or traits [29]. This was partly supported by the results of our mediation analyses, which confirmed that negative affectivity acted as a mediator between the DIF-subscale and the CHS, MUSS, and CNSS. No difference was found when analyzing high and low stress individuals separately.

# Negative affectivity

The relatively strong association between negative affectivity and MCS confirmed our fourth hypothesis. In addition, the mediation analyses partly support our fifth hypothesis as negative affectivity acted as a significant partial mediator of the association between DIF and the CHS, MUSS, and CNSS. Associations between negative affectivity and somatic symptoms has been reported in more studies [16;47;48], but the mechanism is unclear. In a study of negative affectivity as a predictor of objective and subjective symptoms of respiratory viral infections, Cohen and colleagues attributed the association to cognitive bias rather than a pathophysiological response to infection [48]. Results from a study by Van Den Bergh and colleagues on respiratory symptom perception in persons with high and low negative affectivity suggest that negative affective cues or arousal may activate somatic memory in persons high in negative affectivity [49]. This process may lead to bias in the interpretation of bodily sensations and actual physiological responses, resulting in less interoceptive accuracy [49]. In line with these results, it has been suggested that negative affectivity is more likely to influence reports of vague, general symptoms (e.g., headache and fatigue) in conditions that are not clearly defined, whereas such symptoms are less likely to be incorporated in conditions with a specific symptom pattern [50]. It is not clear whether these suggested mechanisms also apply to MCS, and the current status of the MCS diagnosis makes the distinction between illness-specific symptoms and vague, general symptoms problematic. The causal relationship, i.e., whether negative affectivity influences an attribution of symptoms or vice versa, was not possible to determine in our cross-sectional study design. It may be important to note that negative affectivity was also a strong predictor of self-reported social consequences, which could suggest that individuals high in negative affectivity are more severely affected. The possible mechanisms underlying this association are clearly in need of further elaboration

# Methodological issues

Some methodological questions can be raised. The lack of consensus criteria for MCS leads to some uncertainty regarding the case definition. We investigated symptoms, symptom-inducing environmental odours, as well as social consequences as proxies for estimating subjectively reported severity. Although this severity classification may be scientifically inadequate in terms of defining pathophysiological mechanisms, it represents a pragmatic approach by describing the subjectively experienced manifestations. Due to the broad definition of MCS and the possibility that some respondents may interpret the reactions as indicative of other health problems, e.g., allergy or asthma, we cannot rule out classification or recall bias. Including a healthy control group could have strengthened our design by adding information regarding the influence of psychological features on the presence of MCS independent of severity. This research question, however, was not the objective of the present study.

#### **Conclusion**

In conclusion, we were unable to support he hypothesis that repressive coping is associated with MCS. While this was also the case for alexithymia, we did find evidence for an influence of one alexithymia domain: difficulties identifying feelings. Further analyses, however, indicated that this association could be mediated by negative affectivity, a conclusion which was further supported by our findings of relatively strong independent associations between negative affectivity and trait anxiety and the four descriptive factors of MCS. We also found evidence of a role of defensiveness. Further studies are needed to elucidate the possible interplay between negative emotional reactions, defensiveness, and difficulties identifying feelings in MCS, and our results may direct future therapeutic interventions towards focusing on increasing emotional awareness and functioning.

#### Acknowledgements

This study was supported by research grants from Aage Bangs Foundation. We thank Søren Vesterhauge, DMSc, ENT-consultant for valuable assistance in enrolling MCS patients.

#### References

- [1] Das-Munshi J, Rubin GJ, Wessely S: Multiple chemical sensitivities: review. Curr Opin Otolaryngol Head Neck Surg 2007;15:274-280.
- [2] Fink P, Toft T, Hansen MS, Ornbol E, Olesen F: Symptoms and syndromes of bodily distress: an exploratory study of 978 internal medical, neurological, and primary care patients. Psychosom Med 2007;69:30-39.
- [3] Bailer J, Witthoft M, Bayerl C, Rist F: Syndrome stability and psychological predictors of symptom severity in idiopathic environmental intolerance and somatoform disorders. Psychol Med 2007;37:271-281.
- [4] Bailer J, Witthoft M, Rist F: Psychological predictors of short- and medium term outcome in individuals with idiopathic environmental intolerance (IEI) and individuals with somatoform disorders. J Toxicol Environ Health A 2008;71:766-775.
- [5] Bornschein S, Hausteiner C, Zilker T, Bickel H, Forstl H: [Psychiatric and somatic morbidity of patients with suspected multiple chemical sensitivity syndrome (MCS)]. Nervenarzt 2000;71:737-744.
- [6] Bornschein S, Hausteiner C, Konrad F, Forstl H, Zilker T: Psychiatric morbidity and toxic burden in patients with environmental illness: a controlled study. Psychosom Med 2006;68:104-109.
- [7] Hausteiner C, Mergeay A, Bornschein S, Zilker T, Forstl H: New aspects of psychiatric morbidity in idiopathic environmental intolerances. J Occup Environ Med 2006;48:76-82.
- [8] Osterberg K, Persson R, Karlson B, Carlsson EF, Orbaek P: Personality, mental distress, and subjective health complaints among persons with environmental annoyance. Hum Exp Toxicol 2007;26:231-241.
- [9] Caccappolo-van VE, Kelly-McNeil K, Natelson B, Kipen H, Fiedler N: Anxiety sensitivity and depression in multiple chemical sensitivities and asthma. J Occup Environ Med 2002;44:890-901.
- [10] Witthoft M, Rist F, Bailer J: Evidence for a specific link between the personality trait of absorption and idiopathic environmental intolerance. J Toxicol Environ Health A 2008;71:795-802.
- [11] Hausteiner C, Bornschein S, Zilker T, Henningsen P, Forstl H: Dysfunctional cognitions in idiopathic environmental intolerances (IEI)--an integrative psychiatric perspective. Toxicol Lett 15-6-2007;171:1-9.
- [12] Simon GE, Daniell W, Stockbridge H, Claypoole K, Rosenstock L: Immunologic, psychological, and neuropsychological factors in multiple chemical sensitivity. A controlled study. Ann Intern Med 15-7-1993;119:97-103.

- [13] Devriese S, Winters W, Stegen K, Van D, I, Veulemans H, Nemery B, Eelen P, Van de WK, Van den BO: Generalization of acquired somatic symptoms in response to odors: a pavlovian perspective on multiple chemical sensitivity. Psychosom Med 2000;62:751-759.
- [14] Pennebaker JW: Psychological bases of symptom reporting: perceptual and emotional aspects of chemical sensitivity. Toxicol Ind Health 1994;10:497-511.
- [15] de RD, Geenen R, Kuijer R, van MH: Psychological adjustment to chronic disease. Lancet 2008;372:246-255.
- [16] van MH, Lumley MA, Jacobs JW, van Doornen LJ, Bijlsma JW, Geenen R: Emotions and emotional approach and avoidance strategies in fibromyalgia. J Psychosom Res 2008;64:159-167.
- [17] Taylor SE, Stanton AL: Coping resources, coping processes, and mental health. Annu Rev Clin Psychol 2007;3:377-401.
- [18] Folkman S, Moskowitz JT: Coping: pitfalls and promise. Annu Rev Psychol 2004;55:745-74.
- [19] Weinberger DA. The construct validity of the repressive coping style. In: Singer J.L., editor.Repression and dissociation.Chicago: University of Chicago Press, 1990: 337-386. 1990.
- [20] Suls J, Fletcher B: The relative efficacy of avoidant and nonavoidant coping strategies: a meta-analysis. Health Psychol 1985;4:249-288.
- [21] Schwartz GE. Psychobiology of repression and health: A systems approach. In J.L.Singer (Ed.), *Repression and dissociation*. 405-434. 1995. Chicago: University of Chicago Press.
- [22] Derakshan N, Eysenck MW: Interpretive biases for one's own behavior and physiology in high-trait-anxious individuals and repressors. Journal of Personality and Social Psychology 1997;73:816-825.
- [23] Holmes DS. The evidence for repression: An examination of sixty years of research. In Singer, J.L. (ed) Repression and dissociation Implications for personality theory, psychopathology, and health. 85-102.1995. University of Chicago Press. Chicago. IL.
- [24] Jorgensen MM, Zachariae R: Repressive coping style and autonomic reactions to two experimental stressors in healthy men and women. Scand J Psychol 2006;47:137-148.
- [25] Nemiah JC, Sifneos PE: Affect and fantasy in patients with psychosomatic disorders. In:Hill OW, editor Modern trends in psychosomatic medicine London: Butterworths 1970;2:26-34.
- [26] Nemiah JC, Freyberger H, Sifneos PE: Alexithymia: a view of the psychosomatic process. In: Hill OW, editor Modern trends in psychosoamtic medicine London: Butterworhts 1976;3:430-439.

- [27] Jorgensen MM, Zachariae R, Skytthe A, Kyvik K: Genetic and environmental factors in alexithymia: a population-based study of 8,785 Danish twin pairs. Psychother Psychosom 2007;76:369-375.
- [28] Taylor GJ, Bagby RM, Parker JDA. *Disorders of affect regulation: Alexithymia in medical and psychiatric illness.* 1997. New York: Cambridge University Press.
- [29] Kirmayer LJ, Robbins JM: Cognitive and social correlates of the Toronto Alexithymia Scale. Psychosomatics 1993;34:41-52.
- [30] Berg ND, Linneberg A, Dirksen A, Elberling J: Prevalence of self-reported symptoms and consequences related to inhalation of airborne chemicals in a Danish general population. Int Arch Occup Environ Health 6-12-2007;...
- [31] Crowne DP, Marlowe D: A new scale of social desirability independent of psychopathology. J Consult Psychol 1960;24:349-354.
- [32] Bendig AW: The development of a short form of the manifest anxiety scale. J Consult Psychol 1956;20:384.
- [33] Bagby RM, Taylor GJ, Parker JD: The Twenty-item Toronto Alexithymia Scale--II. Convergent, discriminant, and concurrent validity. J Psychosom Res 1994;38:33-40.
- [34] Bagby RM, Parker JD, Taylor GJ: The twenty-item Toronto Alexithymia Scale--I. Item selection and cross-validation of the factor structure. J Psychosom Res 1994;38:23-32.
- [35] Taylor GJ, Bagby RM, Parker JD: The 20-Item Toronto Alexithymia Scale. IV. Reliability and factorial validity in different languages and cultures. J Psychosom Res 2003;55:277-283.
- [36] Cohen S, Tyrrell DA, Smith AP: Psychological stress and susceptibility to the common cold. N Engl J Med 1991;325:606-612.
- [37] Zevon MA, Tellegen A: The structure of mood change: An idiographic/nomothetic analysis. J Pers Soc Psychol 1982;43:111-122.
- [38] Watson D, Clark LA, Tellegen A: Development and validation of brief measures of positive and negative affect: the PANAS scales. J Pers Soc Psychol 1988;54:1063-1070.
- [39] Baron RM, Kenny DA: The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. J Pers Soc Psychol 1986;51:1173-1182.
- [40] Preacher KJ, Hayes AF: SPSS and SAS procedures for estimating indirect effects in simple mediation models. Behav Res Methods Instrum Comput 2004;36:717-731.

- [41] Garssen B: Repression: finding our way in the maze of concepts. J Behav Med 2007;30:471-481.
- [42] Bell IR, Miller CS, Schwartz GE, Peterson JM, Amend D: Neuropsychiatric and somatic characteristics of young adults with and without self-reported chemical odor intolerance and chemical sensitivity. Arch Environ Health 1996;51:9-21.
- [43] Bell IR, Peterson JM, Schwartz GE: Medical histories and psychological profiles of middle-aged women with and without self-reported illness from environmental chemicals. J Clin Psychiatry 1995;56:151-160.
- [44] Staudenmayer H, Phillips S: MMPI-2 validity, clinical and content scales, and the Fake Bad Scale for personal injury litigants claiming idiopathic environmental intolerance. J Psychosom Res 2007;62:61-72.
- [45] Paulhus DL: Two-component models of socially desirable responding. J Pers Soc Psychol 1984;46:598-609.
- [46] Parker JD, Taylor GJ, Bagby RM: The 20-Item Toronto Alexithymia Scale. III. Reliability and factorial validity in a community population. J Psychosom Res 2003;55:269-275.
- [47] Watson D, Pennebaker JW: Health complaints, stress, and distress: exploring the central role of negative affectivity. Psychol Rev 1989;96:234-254.
- [48] Cohen S, Doyle WJ, Skoner DP, Fireman P, Gwaltney JM, Jr., Newsom JT: State and trait negative affect as predictors of objective and subjective symptoms of respiratory viral infections. J Pers Soc Psychol 1995;68:159-169.
- [49] Van den BO, Winters W, Devriese S, Van Diest I, Vos G, de Peuter S: Accuracy of respiratory symptom perception in persons with high and low negative affectivity. Psychology & Health 2004;19:213-222.
- [50] Mora PA, Halm E, Leventhal H, Ceric F: Elucidating the relationship between negative affectivity and symptoms: the role of illness-specific affective responses. Ann Behav Med 2007;34:77-86.

# 10. Additional comments on the methodology and the validity of the results

The following section includes some additional comments on the methodology applied to the three studies and the validity of the results which has not already been discussed in the four manuscripts.

#### 10.1 Study 1: Questionnaire study: General practitioners

The study on experience with MCS among GPs included a random sample of Danish GPs. The questionnaire was pilot tested for relevance, comprehension and ease of completion by individual interviews with eight GPs; the response rate was high (69%). The limitations of this study concern the absence of diagnostic criteria, which may raise some concerns regarding the validity of the results and the extent to which they can be generalised. In order to respond to this problem we presented the GPs with a case description on the first page of the questionnaire, and the high response rate may imply that the patient group was recognized by the GPs. Unfortunately we had no information on non-respondents, who although speculative, may consist of GPs who are not familiar with this type of patient. Among the responding GPs 62.5% have seen a relevant patient within the last twelve months (n= 431/691). No differences in relation to sex and length of experience as a GP were found between these two groups. We chose to perform subsequent statistical analyses on the group who reported having seen a patient, and therefore this must be kept in mind when interpreting the results from this study.

# 10.2 Study 2: Focus group study: Individuals with self-reported MCS

The focus-group study provides an insight into the impact of MCS on everyday life in a selected group of affected individuals, and the strategies they applied in order to cope with the disorder. The study aimed at uncovering many different areas of everyday life which were hypothesized to be influenced by MCS, including daily activities, family, friends, other social relations, work and healthcare. Based on the data from the two focus-groups central problems and coping strategies were touched upon, and it may be argued that the study would have benefited from an elaboration of these themes in more groups in order to gain a deeper understanding. However, the overall purpose of this study was to gain knowledge of the importance of the aforementioned areas

and to include this in the questionnaire study on individuals with self-reported or doctor-diagnosed MCS.

# 10.3 Study 3: Questionnaire study: Individuals with self-reported or doctor-diagnosed MCS

The epidemiological study on MCS has produced knowledge of valuable associations that may form the basis for further epidemiological and clinical studies. Some consideration should be given to the possibility of epidemiological bias particularly because of the uncertainties surrounding a case definition. Apart from the group with doctor-diagnosed MCS, inclusion in the study was largely based on self-reported symptoms and consequences. The relatively broad inclusion criteria may increase the risk of selection bias [69] in terms of the possibility of including individuals whose symptoms are merely attributable to other conditions, e.g., allergy, asthma or somatoform disorders. This may have influenced the associations found between the four descriptive MCS factors and the psychological variables included in this study. Future studies would thus benefit from a more detailed inclusion procedure, optimally including a medical examination or a review of medical records, and a standardized psychiatric interview, e.g., Schedules for Clinical Assessment in Neuropsychiatry (SCAN). This would provide a more detailed description of study participants and a possibility to adjust for co-morbidity in subsequent data analyses.

When conducting the mediation analyses in manuscript 4, *Repressive coping and alexithymia in multiple chemical sensitivity*, the four analytical steps necessary to establish mediation defined by Baron and Kenny were used [70]. In detail the four steps include: 1) The independent variable should be a significant predictor of the dependent variable; 2) The independent variable should predict the mediator; 3) The mediator should predict the dependent variable, when controlling for the independent variable; and 4) The association between the independent variable and the dependent variable should be reduced, when controlling for the mediator. Complete mediation of the independent variable-dependent variable-dependent variable association is reduced to zero when controlling for the mediator. Partial mediation requires the association to be reduced to a nontrivial amount but not to zero.

The questionnaire used in this study was to a large degree composed of the Danish translation of scales that have been extensively used and validated within psychological research, which is one way to ensure quality and comparability of the data. Details on the psychometric properties of these scales have been described in manuscripts 3 and 4 and will not be further discussed here. The questions on symptoms attributed to environmental odours, symptom eliciting chemical agents and so-cial consequences were modified from questions used in a previous population-based questionnaire

study among 6000, 18-69-year old individuals randomly drawn from the Danish Civil Registration System [10]. Based on principal components analysis, values obtained from these questions were summarized in continuous scores on four scales; the Chemical Hypersensitivity Scale (CHS), the Mucosal Symptoms Scale (MUSS), the CNS Symptoms Scale (CNSS) and the Consequences for Social Activities Scale (CSAS). The four scales were subsequently used as dependent variables in multiple, hierarchical linear regression analysis. Ideally, we should have conducted a pilot-study including a number of items relevant for MCS and then have performed a factor analysis before using the scales in a new sample. There is clearly a need for an internationally accepted and validated measure of MCS [71] to ensure comparability of data across studies and to provide better insight into the strength of associations between MCS and measures of personality traits and psychopathology.

#### 11. General discussion

MCS is most likely a complex disorder and as such cannot be embraced in an entirely biomedical disease model. Qualitative and quantitative research methods provide different opportunities for studying the complexities of MCS and to gain insight into the psychosocial aspects of this disorder.

The study on GPs' experiences with provision of healthcare to patients with self-reported MCS generally suggests a pragmatic approach to this group of patients. The majority of the GPs perceive the cause to be multi-factorial and recommend either partial or complete avoidance of exposure to common environmental odours. Nevertheless, many GPs find it difficult to meet the expectations for healthcare expressed by these patients, which is a well established problem in consultations with patients who report subjective health complaints in general [35;72;73]. A great need for evidence-based guidelines and diagnostic tools in relation to this patient group was expressed by the majority of the GPs.

The emergent themes in the focus group discussions were overall the social and occupational disruptions following MCS, the strategies applied in order to cope with the disorder and the feelings of unfulfilled healthcare needs. The most prominent coping strategy was avoidance of being exposed to common environmental odours. Initially this strategy may appear to be the most optimal for managing the disorder but it can be speculated whether in persisting states avoidance may eventually lead to increased disability levels. This remains to be seen, however. Because of the qualitative study design the findings from the focus group study cannot be generalized; nevertheless, the discussions suggest that MCS may have a severe impact on central aspects of everyday life.

The associations derived from the multiple, hierarchical linear regression analyses between the psychological variables and the four descriptive factors of MCS reported in the epidemiological study were generally modest. Nonetheless, the results support the existing evidence on psychological vulnerability in individuals with MCS and the association with personality traits involved in the perception and maintenance of symptoms. It has been speculated that the use of differential perceptual strategies between women and men may explain the sex differences seen in MCS [74]. Women tend to be especially sensitive to situational cues whereas men are more liable to focus on physiological cues. However, whether differences in perceptual strategies can explain

the sex differences in MCS is a question for future studies. Significant univariate associations were found between trait anxiety (TMAS) and the four descriptive MCS factors (mucosal and CNS symptoms, number of chemical and odourous exposures and social consequences), and strong asso-

ciations were also seen between trait negative affectivity (NAS) and MCS. Trait negative affectivity is basically identical with other dispositional constructs, such as trait anxiety, and reflects individual differences in mood and self-concept [74]. Individuals who are high in this trait are believed to experience higher levels of distress over time and across different situations and to report more somatic symptoms than low negative affect individuals in the absence of differences in objective health status [74-77]. The role of negative affectivity in terms of symptom formation and reports warrants further examination. Evidence suggests that negative affectivity is a heritable trait [78], which may imply that it is a potential inherited risk factor in the development of MCS. While the question of identifying potential risk factors in the development of MCS is best studied in a prospective study design, it may currently be argued that negative affectivity needs to be assessed when symptom severity and the consequences of MCS are evaluated among researchers.

Sensitisation and conditioning processes have been suggested as mechanisms in the acquisition and maintenance of self-reported symptoms of MCS [29;30;67;68;79-81]. Sensitisation and conditioning are distinct but interactive processes [80], whereas sensitisation requires an initial exposure to a stimulus conditioning does not [30]. Sensitisation has been described as a non-associative learning mechanism involving a progressive amplification of responsivity to repeated, intermittent exposures [80]. Sensitisation covers reactions at multiple levels in the organism involving, e.g., the neuronal level and higher psychological functions such as attentional or cognitive bias [31;82]. Signs of increased sensitization after repeated chemical exposure accompanied by alterations in central cognitive responses in chemically sensitive individuals have been reported in a recent study by Andersson and colleagues [68]. In order to examine performance on tasks assessing cognitive variables Witthöft and colleagues compared a group of individuals with IEI with a somatoform group and a healthy control group [67]. Attentional bias was reported for the IEI group in terms of enhanced attention allocation to symptom words, e.g., headache and fatigue, in response to an emotional stroop task. While no evidence was reported regarding attentional bias towards words describing symptom eliciting agents in IEI, e.g., perfume and paint smell, the IEI group produced more negative emotional ratings of these words than the other two groups. Enhanced attention to "internal information" supports the theory of somato-sensory amplification as a mechanism of symptom maintenance in IEI. Witthöft and colleagues replicated these findings in a corresponding study design after one year [79]. Personality traits such as negative affectivity may influence both conditioning and sensitization processes as individuals who are high on this trait may be more vulnerable to learning symptoms [29-31].

Given the prevalence of co-occurring mental disorders in MCS and the individual consequences, it has been argued that attention should be given to the possibility of psychiatric co-morbidity in clinical encounters with these patients [5;62;83]. This is supported by the results from a study on 295 patients attending an environmental outpatient clinic where the environmental complaints could be explained by a current psychiatric disorder in the majority of the patients [84]. The reason why only a few per cent of the GPs in our study reported having referred to either psychiatric or other specialists, including psychology, can only be speculative. Fear of stigmatizing the patients may cause reluctance to suggest psychiatric referrals [85], which may offer some explanation. In general, studies on patients with other medically unexplained disorders suggest that experiences with physicians who ascribe a psychological explanation for the symptoms cause distress [86-88], which was also experienced by the participants in our focus-group study. To manage the possibility of co-occurring mental disorders without causing additional distress to the patients is thus not straightforward, and furthermore it is well established that absence of diagnostic possibilities, treatment and preventive strategies may predict dissatisfaction with consultations among both GPs and patients [73;86;89]. The patient's initial understanding of the symptoms and their implications on the patient's life is another factor that has been identified as central for satisfaction with a consultation [73]. In theory the content of an individual's understanding of illness is comprised of five themes: identity, timeline, consequences, causes, and perceived control [90]. In particular, uncertainty about the nature of the health problem, high levels of emotional distress and perceived low personal control have been identified as important factors in the patient's evaluation and satisfaction with a consultation [73]. Examining the understanding of MCS among affected individuals may thus be one step in optimizing healthcare management in terms of improving doctor-patient communication. In terms of research, an understanding of illness perceptions may also direct future intervention studies using, e.g., cognitive therapy or mindfulness-based cognitive therapy strategies aimed at reducing emotional distress and improving coping strategies in individuals with MCS. Clinical studies on the effect of therapeutic interventions are needed [62], and if there is an effect of such interventions, it would provide both the patient and GPs with a treatment option.

In 2002, medically unexplained symptoms or functional somatic symptoms accounted for 10-15% of all disability pensions in Denmark [91], and it has been argued that failure to diagnose and treat

these disorders may have severe individual and societal consequences [47]. MCS has been associated with occupational restraints and job loss and since avoiding common environmental odours may be difficult in a work setting it is likely that even mildly affected individuals experience some level of difficulty with workplace exposures, e.g., colleagues wearing fragranced products, or newly printed materials. The number of individuals who receive disability pensions because of MCS has not been estimated, but in general obtaining a disability pension based on functional somatic symptoms can be difficult since such disorders are not acknowledged by the social security system [92]. Knowledge of how individuals with MCS cope with workplace exposures is limited but identifying important strategies for preventing occupational consequences in terms of job loss may be a question for future research within this field.

#### 12. Conclusion

With regard to the aims of the thesis presented in chapter 4, the following conclusions can be drawn:

- Many GPs find it difficult to fulfil the healthcare needs expressed by patients with self-reported MCS, and there is a demand for evidence-based guidelines and diagnostic tools in relation to the management of this patient group. At present most GPs recommend either partial or complete avoidance of exposure to common environmental odours.
- Self-reported MCS may severely influence everyday life by limiting individual possibilities for performing normal daily activities including shopping, participating in social activities and using public transportation; avoidance is a prominent coping strategy. Healthcare needs were experienced as unfulfilled.
- The personality traits of somato-sensory amplification and autonomic perception were significantly associated with individual reports of multiple mucosal and CNS symptoms attributed to MCS. There was some evidence to suggest that these traits were also associated with higher numbers of symptom-inducing odours and social consequences. In contrast no evidence of a role of the personality trait of absorption was revealed.
- The hypotheses that repressive coping and the personality trait of alexithymia are associated with MCS were not supported. Although there was evidence of a role of one alexithymia domain: difficulties identifying feelings. The association was, however, mediated by negative affectivity. An association was also seen between defensiveness and MCS. Further studies are needed to elucidate the possible interplay between negative emotional reactions, defensiveness, and difficulties in identifying feelings in MCS.

#### 13. Future studies

Future studies on MCS could be aimed at:

- exploring the influence of perceptual factors in symptom generation and maintenance, and the role of sex in perceptual strategies
- o exploring the influence of trait negative affectivity on the initiation and course of MCS
- o exploring the influence of depression on the initiation and course of MCS
- testing the effect of either group-based or individual therapeutic interventions such as mindfulness-based cognitive therapy or individual cognitive therapy
- examining illness-perceptions among individuals with MCS in order to provide a basis for more optimal communication between patients and healthcare professionals, and to guide therapeutic interventions
- o formulating evidence-based guidelines on MCS for GPs and other health care professionals
- methodological development in terms of standardized and validated tools for research in MCS.

# 14. References

- [1] Skovbjerg S, Brorson S, Rasmussen A, Johansen J.D, Elberling J: Impact of self-reported multiple chemical sensitivity on everyday life: A qualitative study. Scand J Public Health 2009; doi:10.1177/1403494809105430.
- [2] Schottenfeld RS, Cullen MR: Recognition of occupation-induced posttraumatic stress disorders. J Occup Med 1986;28:365-369.
- [3] Cullen MR: The worker with multiple chemical sensitivities: an overview. Occup Med 1987;2:655-661.
- [4] Multiple chemical sensitivity: a 1999 consensus. Arch Environ Health 1999;54:147-149.
- [5] Lacour M, Zunder T, Schmidtke K, Vaith P, Scheidt C: Multiple chemical sensitivity syndrome (MCS)--suggestions for an extension of the U.S. MCS-case definition. Int J Hyg Environ Health 2005;208:141-151.
- [6] Kreutzer R: Idiopathic environmental intolerance: case definition issues. Occup Med 2000;15:511-517.
- [7] Bailer J, Witthoft M, Paul C, Bayerl C, Rist F: Evidence for overlap between idiopathic environmental intolerance and somatoform disorders. Psychosom Med 2005;67:921-929.
- [8] Bailer J, Witthoft M, Bayerl C, Rist F: Syndrome stability and psychological predictors of symptom severity in idiopathic environmental intolerance and somatoform disorders. Psychol Med 2007;37:271-281.
- [9] Bailer J, Witthoft M, Rist F: Psychological predictors of short- and medium term outcome in individuals with idiopathic environmental intolerance (IEI) and individuals with somatoform disorders. J Toxicol Environ Health A 2008;71:766-775.
- [10] Berg ND, Linneberg A, Dirksen A, Elberling J: Prevalence of self-reported symptoms and consequences related to inhalation of airborne chemicals in a Danish general population. Int Arch Occup Environ Health 2008;81:881-887.
- [11] Berg ND, Linneberg A, Dirksen A, Elberling J: Phenotypes of individuals affected by airborne chemicals in the general population. Int Arch Occup Environ Health 2008;82:509-517.
- [12] Hausteiner C, Bornschein S, Hansen J, Zilker T, Forstl H: Self-reported chemical sensitivity in Germany: a population-based survey. Int J Hyg Environ Health 2005;208:271-278.
- [13] Carlsson F, Karlson B, Orbaek P, Osterberg K, Ostergren PO: Prevalence of annoyance attributed to electrical equipment and smells in a Swedish population, and relationship with subjective health and daily functioning. Public Health 2005;119:568-577.

- [14] Osterberg K, Persson R, Karlson B, Carlsson EF, Orbaek P: Personality, mental distress, and subjective health complaints among persons with environmental annoyance. Hum Exp Toxicol 2007;26:231-241.
- [15] International Programme on Chemical Safety/World Health Organisation (IPCS/WHO), 1996. Conclusions and recommendations of a workshop on multiple chemical sensitivities (MCS). Geneva, Switzerland. Regul Toxicol Pharmacol 1996;24:188-189.
- [16] Johansson A, Bramerson A, Millqvist E, Nordin S, Bende M: Prevalence and risk factors for self-reported odour intolerance: the Skovde population-based study. Int Arch Occup Environ Health 2005;78:559-564.
- [17] Kreutzer R, Neutra RR, Lashuay N: Prevalence of people reporting sensitivities to chemicals in a population-based survey. Am J Epidemiol 1999;150:1-12.
- [18] Caress SM, Steinemann AC: Prevalence of multiple chemical sensitivities: a population-based study in the southeastern United States. Am J Public Health 2004;94:746-747.
- [19] Caress SM, Steinemann AC: A national population study of the prevalence of multiple chemical sensitivity. Arch Environ Health 2004;59:300-305.
- [20] Black DW, Okiishi C, Schlosser S: The Iowa follow-up of chemically sensitive persons. Ann N Y Acad Sci 2001;933:48-56.:48-56.
- [21] Graveling RA, Pilkington A, George JP, Butler MP, Tannahill SN: A review of multiple chemical sensitivity. Occup Environ Med 1999;56:73-85.
- [22] Bell IR, Miller CS, Schwartz GE: An olfactory-limbic model of multiple chemical sensitivity syndrome: possible relationships to kindling and affective spectrum disorders. Biol Psychiatry 1992;32:218-242.
- [23] Yunus MB: Central sensitivity syndromes: a new paradigm and group nosology for fibromyalgia and overlapping conditions, and the related issue of disease versus illness. Semin Arthritis Rheum 2008;37:339-352.
- [24] Fink P, Toft T, Hansen MS, Ornbol E, Olesen F: Symptoms and syndromes of bodily distress: an exploratory study of 978 internal medical, neurological, and primary care patients. Psychosom Med 2007;69:30-39.
- [25] Elberling J, Linneberg A, Dirksen A, Johansen JD, Frolund L, Madsen F, Nielsen NH, Mosbech H: Mucosal symptoms elicited by fragrance products in a population-based sample in relation to atopy and bronchial hyper-reactivity. Clin Exp Allergy 2005;35:75-81.
- [26] Elberling J, Lerbaek A, Kyvik KO, Hjelmborg J. A twin study of perfume-related respiratory symptoms. Int.J.Hyg.Environ.Health 2009;doi:10.1016/j.ijheh.2009.05.001.

- [27] Das-Munshi J, Rubin GJ, Wessely S: Multiple chemical sensitivities: A systematic review of provocation studies. J Allergy Clin Immunol 2006;118:1257-1264.
- [28] Zachariae R, Paulsen K, Mehlsen M, Jensen AB, Johansson A, von der MH: Anticipatory nausea: the role of individual differences related to sensory perception and autonomic reactivity. Ann Behav Med 2007;33:69-79.
- [29] Devriese S, Winters W, Stegen K, Van D, I, Veulemans H, Nemery B, Eelen P, Van de WK, Van den BO: Generalization of acquired somatic symptoms in response to odors: a pavlovian perspective on multiple chemical sensitivity. Psychosom Med 2000;62:751-759.
- [30] Van den BO, Devriese S, Winters W, Veulemans H, Nemery B, Eelen P, Van de Woestijne KP: Acquiring symptoms in response to odors: a learning perspective on multiple chemical sensitivity. Ann N Y Acad Sci 2001;933:278-290.
- [31] Brosschot JF: Cognitive-emotional sensitization and somatic health complaints. Scand J Psychol 2002;43:113-121.
- [32] Barsky AJ, Goodson JD, Lane RS, Cleary PD: The amplification of somatic symptoms. Psychosom Med 1988;50:510-519.
- [33] Nakao M, Barsky AJ, Kumano H, Kuboki T: Relationship between somatosensory amplification and alexithymia in a Japanese psychosomatic clinic. Psychosomatics 2002;43:55-60.
- [34] Caress SM, Steinemann AC: A review of a two-phase population study of multiple chemical sensitivities. Environ Health Perspect 2003;111:1490-1497.
- [35] Eriksen HR, Ursin H: Subjective health complaints, sensitization, and sustained cognitive activation (stress). J Psychosom Res 2004;56:445-448.
- [36] Buchwald D, Garrity D: Comparison of patients with chronic fatigue syndrome, fibromyalgia, and multiple chemical sensitivities. Arch Intern Med 26-9-1994;154:2049-2053.
- [37] Eek F, Merlo J, Gerdtham U, Lithman T: Health care utilisation and attitudes towards healthcare in subjects reporting environmental annoyance from electricity and chemicals. Journal of Environmental and Public Health 2009;2009.
- [38] Carlsson F, Persson R, Osterberg B, Hansen K, Hansen AM, Garde AH, Orbaek P: Salivary cortisol and self-reported stress among persons with environmental annoyance. Scand J Work Environ Health 2006;32:109-120.
- [39] Hausteiner C, Mergeay A, Bornschein S, Zilker T, Forstl H: New aspects of psychiatric morbidity in idiopathic environmental intolerances. J Occup Environ Med 2006;48:76-82.
- [40] Black DW, Okiishi C, Schlosser S: A nine-year follow-up of people diagnosed with multiple chemical sensitivities. Psychosomatics 2000;41:253-261.

- [41] Caccappolo-van VE, Kelly-McNeil K, Natelson B, Kipen H, Fiedler N: Anxiety sensitivity and depression in multiple chemical sensitivities and asthma. J Occup Environ Med 2002;44:890-901.
- [42] Papo D, Eberlein-Konig B, Berresheim HW, Huss-Marp J, Grimm V, Ring J, Behrendt H, Winneke G: Chemosensory function and psychological profile in patients with multiple chemical sensitivity: Comparison with odor-sensitive and asymptomatic controls. J Psychosom Res 2006;60:199-209.
- [43] Bolt HM, Kiesswetter E: Is multiple chemical sensitivity a clinically defined entity? Toxicol Lett 2002;128:99-106.
- [44] Ørbaek P, Persson R, Österberg K: Impact of trait anxiety and social conformity on responses to experimental chemical challenge. Environ Toxicol Pharmacol 2005;19:659-664.
- [45] Witthoft M, Rist F, Bailer J: Evidence for a specific link between the personality trait of absorption and idiopathic environmental intolerance. J Toxicol Environ Health A 2008;71:795-802.
- [46] Lowe B, Mundt C, Herzog W, Brunner R, Backenstrass M, Kronmuller K, Henningsen P: Validity of current somatoform disorder diagnoses: perspectives for classification in DSM-V and ICD-11. Psychopathology 2008;41:4-9.
- [47] Fink P, Rosendal M, Olesen F: Classification of somatization and functional somatic symptoms in primary care. Aust N Z J Psychiatry 2005;39:772-781.
- [48] Bell IR, Peterson JM, Schwartz GE: Medical histories and psychological profiles of middle-aged women with and without self-reported illness from environmental chemicals. J Clin Psychiatry 1995;56:151-160.
- [49] Tellegen A, Atkinson G: Openness to absorbing and self-altering experiences ("absorption"), a trait related to hypnotic susceptibility. J Abnorm Psychol 1974;83:268-277.
- [50] Roche SM, McConkey KM: Absorption: Nature, Assessment, and Correlates. Journal of Personality and Social Psychology 1990;59:91-101.
- [51] Zachariae R, Jorgensen MM, Bjerring P, Svendsen G: Autonomic and psychological responses to an acute psychological stressor and relaxation: the influence of hypnotizability and absorption. Int J Clin Exp Hypn 2000;48:388-403.
- [52] Nemiah JC, Sifneos PE: Affect and fantasy in patients with psychosomatic disorders. In:Hill OW, editor Modern trends in psychosomatic medicine London: Butterworths 1970;2:26-34.
- [53] Nemiah JC, Freyberger H, Sifneos PE: Alexithymia: a view of the psychosomatic process. In: Hill OW, editor Modern trends in psychosoamtic medicine London: Butterworhts 1976;3:430-439.
- [54] Jorgensen MM, Zachariae R, Skytthe A, Kyvik K: Genetic and environmental factors in alexithymia: a population-based study of 8,785 Danish twin pairs. Psychother Psychosom 2007;76:369-375.

- [55] Taylor GJ, Bagby RM, Parker JDA. *Disorders of affect regulation: Alexithymia in medical and psychiatric illness.* 1997. New York: Cambridge University Press.
- [56] Black DW: The relationship of mental disorders and idiopathic environmental intolerance. Occup Med 2000;15:557-570.
- [57] Simon GE, Katon WJ, Sparks PJ: Allergic to life: psychological factors in environmental illness. Am J Psychiatry 1990;147:901-906.
- [58] Dietel A, Jordan L, Muhlinghaus T, Eikmann TF, Herr CE, Nowak D, Pedrosa GF, Podoll K, Wiesmuller GA, Eis D: [Psychiatric disorders of environmental outpatients-results of the standardized psychiatric interview (CIDI) from the German multi-center study on Multiple Chemical Sensitivity (MCS)]. Psychother Psychosom Med Psychol 2006;56:162-171.
- [59] Simon GE: Psychiatric symptoms in multiple chemical sensitivity. Toxicol Ind Health 1994;10:487-496.
- [60] Simon GE, Daniell W, Stockbridge H, Claypoole K, Rosenstock L: Immunologic, psychological, and neuropsychological factors in multiple chemical sensitivity. A controlled study. Ann Intern Med 1993;119:97-103.
- [61] Davidoff AL, Fogarty L, Keyl PM: Psychiatric inferences from data on psychologic/psychiatric symptoms in multiple chemical sensitivities syndrome. Arch Environ Health 2000;55:165-175.
- [62] Das-Munshi J, Rubin GJ, Wessely S: Multiple chemical sensitivities: review. Curr Opin Otolaryngol Head Neck Surg 2007;15:274-280.
- [63] Sharpe M, Mayou R, Walker J: Bodily symptoms: new approaches to classification. J Psychosom Res 2006;60:353-356.
- [64] Mayou R, Kirmayer LJ, Simon G, Kroenke K, Sharpe M: Somatoform disorders: time for a new approach in DSM-V. Am J Psychiatry 2005;162:847-855.
- [65] Bell IR, Baldwin CM, Fernandez M, Schwartz GE: Neural sensitization model for multiple chemical sensitivity: overview of theory and empirical evidence. Toxicol Ind Health 1999;15:295-304.
- [66] Van HB, Luyten P: Central Sensitivity Syndromes: Stress System Failure May Explain the Whole Picture. Semin Arthritis Rheum 2008; doi: 10.1016/j.semarthrit.2008.08.008
- [67] Witthoft M, Gerlach AL, Bailer J: Selective attention, memory bias, and symptom perception in idiopathic environmental intolerance and somatoform disorders. J Abnorm Psychol 2006;115:397-407.
- [68] Andersson L, Bende M, Millqvist E, Nordin S: Attention bias and sensitization in chemical sensitivity. J Psychosom Res 2009;66:407-416.

- [69] Rothman kj: Biases in study design; in Epidemiology, an introduction: Oxford University Press, Inc., 2002, pp 94-112.
- [70] Baron RM, Kenny DA: The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. J Pers Soc Psychol 1986;51:1173-1182.
- [71] Andersson MJ, Andersson L, Bende M, Millqvist E, Nordin S: The Idiopathic Environmental Intolerance Symptom Inventory: Development, Evaluation, and Application. J Occup Environ Med 2009;51:838-847.
- [72] Dowrick CF, Ring A, Humphris GM, Salmon P: Normalisation of unexplained symptoms by general practitioners: a functional typology. Br J Gen Pract 2004;54:165-170.
- [73] Frostholm L, Fink P, Oernboel E, Christensen KS, Toft T, Olesen F, Weinman J: The uncertain consultation and patient satisfaction: the impact of patients' illness perceptions and a randomized controlled trial on the training of physicians' communication skills. Psychosom Med 2005;67:897-905.
- [74] Pennebaker JW: Psychological bases of symptom reporting: perceptual and emotional aspects of chemical sensitivity. Toxicol Ind Health 1994;10:497-511.
- [75] Watson D, Pennebaker JW: Health complaints, stress, and distress: exploring the central role of negative affectivity. Psychol Rev 1989;96:234-254.
- [76] Cohen S, Doyle WJ, Skoner DP, Fireman P, Gwaltney JM, Jr., Newsom JT: State and trait negative affect as predictors of objective and subjective symptoms of respiratory viral infections. J Pers Soc Psychol 1995;68:159-169.
- [77] van MH, Lumley MA, Jacobs JW, van Doornen LJ, Bijlsma JW, Geenen R: Emotions and emotional approach and avoidance strategies in fibromyalgia. J Psychosom Res 2008;64:159-167.
- [78] Rose RJ, Koskenvuo M, Kaprio J, Sarna S, Langinvainio H: Shared genes, shared experiences, and similarity of personality: data from 14,288 adult Finnish co-twins. J Pers Soc Psychol 1988;54:161-171.
- [79] Witthoft M, Rist F, Bailer J: Abnormalities in cognitive-emotional information processing in idiopathic environmental intolerance and somatoform disorders. J Behav Ther Exp Psychiatry 2009;40:70-84.
- [80] Bell IR, Schwartz GE, Baldwin CM, Hardin EE, Klimas NG, Kline JP, Patarca R, Song ZY: Individual differences in neural sensitization and the role of context in illness from low-level environmental chemical exposures. Environ Health Perspect 1997;105 Suppl 2:457-466.
- [81] Dalton P, Wysocki CJ, Brody MJ, Lawley HJ: The influence of cognitive bias on the perceived odor, irritation and health symptoms from chemical exposure. Int Arch Occup Environ Health 1997;69:407-417.

- [82] Ursin H, Eriksen HR: Sensitization, subjective health complaints, and sustained arousal. Ann N Y Acad Sci 2001;933:119-129.
- [83] Sparks PJ, Daniell W, Black DW, Kipen HM, Altman LC, Simon GE, Terr AI: Multiple chemical sensitivity syndrome: a clinical perspective. II. Evaluation, diagnostic testing, treatment, and social considerations. J Occup Med 1994;36:731-737.
- [84] Hausteiner C, Bornschein S, Bickel H, Zilker T, Forstl H: Psychiatric morbidity and low self-attentiveness in patients with environmental illness. J Nerv Ment Dis 2003;191:50-55.
- [85] Scambler G: Stigma and disease: changing paradigms. Lancet 26-9-1998;352:1054-1055.
- [86] Werner A, Malterud K: It is hard work behaving as a credible patient: encounters between women with chronic pain and their doctors. Soc Sci Med 2003;57:1409-1419.
- [87] Asbring P, Narvanen AL: Women's experiences of stigma in relation to chronic fatigue syndrome and fibromyalgia. Qual Health Res 2002;12:148-160.
- [88] Ware, Norma C: Suffering and the Social Construction of illness: The Delegitimation of illness Experience in Chronic Fatigue Syndrome. Medical Anthropology Quarterly 1992;6:347-361.
- [89] Asbring P, Narvanen AL: Ideal versus reality: physicians perspectives on patients with chronic fatigue syndrome (CFS) and fibromyalgia. Soc Sci Med 2003;57:711-720.
- [90] Leventhal H, Benyamini Y, Brownlee S, Diefenbach M, Leventhal EA, Patrick-Miller L, Robitaille C. Illness Representations; Theoretical Foundations. Petrie K J and Weinman J A. 19-46. 1997. Amsterdam B.V, Harwood Academic Publishers.
- [91] Stenager EN, Svendsen MA, Stenager E: [Disability retirement pension for patients with syndrome diagnoses. A registry study on the basis of data from the Social Appeal Board]. Ugeskr Laeger 2003;165:469-474.
- [92] Fink P, Rosendal M: Recent developments in the understanding and management of functional somatic symptoms in primary care. Curr Opin Psychiatry 2008;21:182-188.

# 15. Appendices

- 1. Questionnaire on GP's experiences with multiple chemical sensitivity
- 2. The Chemical Sensitivity Scale for Sensory Hyper reactivity (CSS-SHR)
- 3. The Somato-Sensory Amplification Scale (SSAS)
- 4. The Autonomic Perception Questionnaire (APQ)
- 5. The Tellegen Absorption Scale (TAS)
- 6. The Negative Affectivity Scale (NAS)
- 7. The Toronto Alexithymia Scale (TAS-20)
- 8. The Bendig 20-item version of the Taylor Manifest Anxiety Scale (TMAS) and The Marlowe-Crowne Social Desirability Scale (MCSD)
- 9. Recent life events (RLE)

1. Er du?  Mand	romer .
2. Hvor mange år har du været i praksisår  I det følgende stilles 9 spørgsmål om de patienter som <u>primært</u> henvender sig pga. sympt relateret til indånding af almindeligt forekommende dufte og kemikalier (f.eks. fra parfum	romer
Hvor mange år har du været i praksisår  I det følgende stilles 9 spørgsmål om de patienter som <u>primært</u> henvender sig pga. sympt relateret til indånding af almindeligt forekommende dufte og kemikalier (f.eks. fra parfum	romer 1
I det følgende stilles 9 spørgsmål om de patienter som <u>primært</u> henvender sig pga. sympt relateret til indånding af almindeligt forekommende dufte og kemikalier (f.eks. fra parfum	tomer
relateret til indånding af almindeligt forekommende dufte og kemikalier (f.eks. fra parfum	omer
<ol> <li>Omtrent hvor mange patienter med symptomer relateret til ovenstående dufte og k er, har du set i din praksis <u>inden for det sidste år?</u></li> </ol>	cemikali-
Ingen	
Mindre end 5 patienter	
Omtrent 5 – 10 patienter	
> 11 patienter	
4. Omtrent hvor mange konsultationer har du med hver af disse patienter?	
5. Har du på noget tidspunkt viderehenvist nogle af disse patienter?	
Nej, aldrig	
Ja, og til specialet: Sæt gerne flere kryds  Medicinsk allergologi	
Lungemedicin	
Øre- Næse- Hals	
Dermatologi	
Arbejds – og miljømedicin	
Neurologi	
Psykiatri	
Andre specialister, da hvilke?	
6. Ordinerer du medicin på grund af symptomer over for dufte og kemikalier? Nej, aldrig	
Ja, jeg ordinerer: Ordineret præparattype	VEND

7.	Hvad er din opfattelse af de mulige årsager til symptomerne?	
	Symptomerne har overvejende en somatisk forklaring.	Sæt kun et krvds
	Symptomerne har overvejende en psykisk forklaring.	
	Symptomerne er et samspil mellem begge ovenstående faktorer.	
		_
8.	Hvad er din erfaring med prognosen for disse symptomer?	Sæt kun et kryds
	Symptomerne er sjældent kroniske.	
	Symptomerne er kroniske.	
	Jeg har ingen erfaring med, hvordan symptomerne udvikler sig.	
9.	Hvordan er dine muligheder for at indfri patientens forventninger til konsu	ıltationen? <u>Sæt kun et kryds</u>
	Jeq oplever, at jeq ofte kan indfri forventningerne hos patienten.	
	Jeg oplever, at jeg sjældent kan indfri forventningerne hos patienten.	
	Ved ikke.	
10.	Hvilken information giver du patienten?	
	Jeg anbefaler, at patienten:	Sæt kun et kryds
	- så vidt muligt undgår de dufte og kemikalier, der kan fremkalde en reaktion	ı. 🗆
	- så vidt muligt undgår <u>al eksponering</u> for dufte – og kemikalier.	
	- ikke bevidst forsøger at undgå dufte og kemikalier i hverdagen.	
	Jeq qiver generelt ingen anbefalinger ved sådanne symptomer.	
11.	Er der redskaber, som du mener på sigt kunne bidrage til arbejdet med pa Ja,	tientgruppen?
		t gerne flere kryds
	Viden om symptomernes patofysiologi	
	Diagnostiske værktøjer	
	Andet, da hvilke:	
	Nej, jeg mangler ingen af ovenstående redskaber.	

Tak for din hjælp

# BETYDNING AF DUFTE OG KEMISKE LUGTE I MILJØET

l det følgende afsnit stilles en række spørgsmål om hvordan du oplever almindeligt forekommende dufte og kemiske lugte i det omgivende miljø.

dufte og kemiske lugte i det omgivende miljø.
23. Læs venligst hvert af følgende udsagn omhyggeligt og sæt kryds udfor den svarmulighed som passer bedst til dig. Det er vigtigt at du markerer efter alle udsagn.
Jeg ville ikke have noget imod at bo på en vej, hvor der var meget udstødning, så længe at de var en god bolig, jeg havde.
O Fuldstændigt rigtigt
Overvejende rigtigt
O Det er nok rigtigt
O Det er nok forkert
Overvejende forkert
O Fuldstændigt forkert
Jeg er i dag mere opmærksom på dufte eller kemiske lugte, end jeg har været tidligere.
O Fuldstændigt rigtigt
Overvejende rigtigt
O Det er nok rigtigt
O Det er nok forkert
Overvejende forkert
O Fuldstændigt forkert
På offentlige steder, f.eks. i biografen, bliver jeg forstyrret af andre menneskers parfume eller aftershave.
O Fuldstændigt rigtigt
Overvejende rigtigt
O Det er nok rigtigt
O Det er nok forkert
Overvejende forkert
O Fuldstændigt forkert

O Ful	dstændigt rigtigt
	ervejende rigtigt
O De	t er nok rigtigt
O De	t er nok forkert
O 0v	ervejende forkert
○ Ful	dstændigt forkert
Jeg ha	r let ved at vænne mig til dufte eller kemiske lugte.
O Ful	dstændigt rigtigt
O 0v	ervejende rigtigt
O De	t er nok rigtigt
O De	t er nok forkert
O 0v	ervejende forkert
○ Ful	dstændigt forkert
	stor en betydning ville det have for dit valg af bolig, hvis der i nærheden af din drø å en ildelugtende virksomhed?
ОМе	get stor betydning
O Rir	nelig stor betydning
O En	vis betydning
O Ku	n ringe betydning
O Ful	dstændigt ligegyldigt
Jeg er	ligeglad med, at der lugter af tobaksrøg på offentlige steder.
O Ful	dstændigt rigtigt
O 0v	ervejende rigtigt
O De	t er nok rigtigt
O De	t er nok forkert
O 0v	ervejende forkert
O Ful	dstændigt forkert

_	
	Fuldstændigt rigtigt
	Overvejende rigtigt
	Det er nok rigtigt
_	Det er nok forkert
	Overvejende forkert
O	Fuldstændigt forkert
Jeg	har svært ved at slappe af på steder, hvor der forekommer dufte eller kemiske lug
0	Fuldstændigt rigtigt
0	Overvejende rigtigt
0	Det er nok rigtigt
0	Det er nok forkert
0	Overvejende forkert
0	Fuldstændigt forkert
Jeg	har intet imod at bo i en lejlighed, som har en svag lugt.
0	Fuldstændigt rigtigt
0	Overvejende rigtigt
0	Det er nok rigtigt
0	Det er nok forkert
0	Overvejende forkert
0	Fuldstændigt forkert
Jeg	er følsom over for dufte og kemiske lugte.
0	Fuldstændigt rigtigt
0	Overvejende rigtigt
0	Det er nok rigtigt
0	Det er nok forkert
0	Overvejende forkert
0	Fuldstændigt forkert

24.	Nedenfor er 10 sætninger. Læs hver sætning grundigt og angiv i hvor høj grad du mener, at den
	pågældende sætning bekriver dig generelt. Tegn en cirkel om det tal fra $1$ til $5$ som passer bedst til
	din oplevelse.

1 = Passer slet ikke på mig

2 = Passer en smule på mig

3 = Passer delvis på mig

4 = Passer godt på mig

5 = Passer fuldstændig på mig

Når en anden person hoster, kommer jeg også til at hoste	1	2	3	4	5
Jeg kan ikke udstå røg, os eller forurenet luft	1	2	3	4	5
Jeg er ofte opmærksom på forskellige ting, der foregår i min krop	1	2	3	4	5
Når jeg slår mig, kan man se mærkerne i lang tid efter	1	2	3	4	5
Pludselige høje lyde generer mig meget	1	2	3	4	5
Jeg kan somme tider høre min puls eller mit hjerteslag dunke i mit øre	1	2	3	4	5
Jeg hader at have det for koldt eller for varmt	1	2	3	4	5
Jeg mærker hurtigt sultfornemmelser i min mave	1	2	3	4	5
Selv mindre ting, f.eks. et mygstik eller en splint, generer mig meget	1	2	3	4	5
Jeg har en lav smertetærskel	1	2	3	4	5

## FYSISKE REAKTIONER I FORBINDELSE MED STRESS

Det følgende afsnit indeholder en række spørgsmål om fysiske reaktioner i forbindelse med stress

48.	Følgende spørgsmål omhandler en række forskellige kropslige fornemmelser, som vi alle kan opleve
	fra tid til anden. Med udgangspunkt i en konkret situation – som du selv har oplevet – vil vi bede dig
	vurdere, i hvor høj grad den efterfølgende række af udsagn passer på din oplevelse af, hvordan du
	reagerer, når du er bange/nervøs.

Brug først lidt tid på at tænke tilbage på en bestemt situation, hvor du har været bange/nervøs. Angiv med nogle få generelle stikord, hvilken situation, du tænker på. Stikordene behøver ikke være særligt detaljerede:

49. Besvar, med udgangspunkt i den pågældende situation, de følgende spørgsmål, og vurdér i hvor høj grad det pågældende udsagn passer på dig på en skala fra 1 til 9, hvor "1" betyder, at det slet ikke passer på dig, "5" betyder at det passer delvis på dig, og hvor "9" betyder, at det passer præcis på dig.

Når jeg bliver bange/nervøs	Passer slet ikk på mig	e			Passei delvis				Passer præcis på mig	
Bliver jeg varm i ansigtet	1	2	3	4	5	6	7	8	9	
Bliver mine hænder kolde	1	2	3	4	5	6	7	8	9	
Sveder jeg	1	2	3	4	5	6	7	8	9	
Bliver jeg tør i munden	1	2	3	4	5	6	7	8	9	
Kan jeg fornemme øgede muskelspændinger i kroppen	1	2	3	4	5	6	7	8	9	
Får jeg hovedpine	1	2	3	4	5	6	7	8	9	
Bliver mit åndedræt mere overfladisk	1	2	3	4	5	6	7	8	9	
Kan jeg føle mit hjerte slå hurtigere	1	2	3	4	5	6	7	8	9	
Slår mit hjerte kraftigere	1	2	3	4	5	6	7	8	9	
Bliver jeg ofte opmærksom på ændringer i mit åndedræt	1	2	3	4	5	6	7	8	9	
Bliver jeg mere stakåndet	1	2	3	4	5	6	7	8	9	

## 49. (fortsat)

Når jeg bliver bange/nervøs	Passer slet ikk på mig	e			Passe delvis				Passer præcis på mig
Bliver jeg opmærksom på ændringer i min hjert- erytme	1	2	3	4	5	6	7	8	9
Føles det som om blodet løber mig til hovedet	1	2	3	4	5	6	7	8	9
Føler jeg en klump i halsen eller en "kvælende" fornemmelse	1	2	3	4	5	6	7	8	9
Får jeg maveproblemer	1	2	3	4	5	6	7	8	9
Får jeg en tung fornemmelse i maven	1	2	3	4	5	6	7	8	9
Får jeg vanskeligheder med at tale	1	2	3	4	5	6	7	8	9
Får jeg kuldefornemmelser	1	2	3	4	5	6	7	8	9
Løber mine øjne i vand eller bliver fugtige	1	2	3	4	5	6	7	8	9
Føler jeg, at mine sanser svækkes	1	2	3	4	5	6	7	8	9
Føler jeg mig svag og usikker på benene	1	2	3	4	5	6	7	8	9
Får jeg kvalme	1	2	3	4	5	6	7	8	9
Får jeg svedige hænder	1	2	3	4	5	6	7	8	9
Bliver jeg rastløs	1	2	3	4	5	6	7	8	9
Skal jeg oftere lade mit vand eller føler oftere, at jeg har brug for at lade mit vand	1	2	3	4	5	6	7	8	9
Føles mit ansigt koldt og blegt	1	2	3	4	5	6	7	8	9
Får jeg en tung fornemmelse eller føler en knude i brystet	1	2	3	4	5	6	7	8	9
Får jeg gåsehud	1	2	3	4	5	6	7	8	9
Føler jeg mig svag og svimmel	1	2	3	4	5	6	7	8	9
Får jeg en flimrende følelse i brystkassen	1	2	3	4	5	6	7	8	9

Undersøg venligst, om du har besvaret alle spørgsmål.

51.	Nedenfor finder du en række udsagn, som en person kunne tænkes at anvende til at beskrive sig
	selv, sine holdninger, interesser og andre karakteristika. Læs hvert udsagn og sæt kryds i den
	svarmulighed, der bedst passer til dig som person.

Vær venlig at besvare alle spørgsmål, også selvom du ikke er helt sikker på hvilken svarmulighed, der passer bedst på dig. Læs hvert udsagn grundigt, men brug ikke for meget tid på at bestemme dig for hvilket svar, du skal give.

Ja	Nej	
0	0	Nogle gange føler jeg og oplever ting, ligesom jeg gjorde, da jeg var barn
0	0	Jeg kan blive meget bevæget af elegant eller poetisk tale
0	0	Mens jeg ser en film eller et teaterstykke, kan jeg nogle gange blive så optaget af det jeg ser og hører, at jeg glemmer mig selv og mine omgivelser og oplever historien, som om den var virkelig, og at jeg selv tog del i den
0	0	Hvis jeg stirrer på et billede og derefter kigger væk, kan jeg nogle gange "se" billedet for mig, næsten som om jeg stadig kiggede på det
0	0	Nogle gange føler jeg, som om mine tanker kan omfatte hele verden
0	0	Jeg kan godt lide at betragte skyerne ændre form på himlen
0	0	Hvis jeg vil, kan jeg forestille mig (eller dagdrømme om) ting så tydeligt, at de kan holde min opmærksomhed fanget ligeså godt som en god historie eller film
0	0	Jeg føler, at jeg virkelig ved, hvad folk mener, når de taler om mystiske eller æteriske oplevelser
0	0	Nogle gange kan jeg træde udenfor mit sædvanlige jeg og opleve en helt anden virkelighed
0	0	Fornemmelsen af overflader, f.eks. fornemmelsen af uld, sand eller træ, kan nogle gange minde mig om farver eller musik
0	0	Nogle gange kan jeg opleve ting, som om de var dobbelt så virkelige
0	0	Når jeg lytter til musik, kan jeg blive så indfanget af det, at jeg ikke lægger mærke til noget som helst andet
0	0	Hvis jeg vil, kan jeg forestille mig min krop så tung, at jeg ikke ville være i stand til at bevæge den, selvom jeg ville
0	0	Jeg kan nogle gange fornemme tilstedeværelsen af en anden person, før jeg faktisk ser eller hører ham/hende
0	0	En kaminilds flammer og knitren stimulerer min fantasi
0	0	Det er nogle gange muligt for mig at blive fuldstændig opslugt af naturen eller kunst og føle mig som om hele min bevidsthed er blevet forandret på en eller anden måde

51. (fortsat)		
Ja	Nej	
0	0	Forskellige farver har helt særlige betydninger for mig
0	0	Mens jeg foretager mig en rutineopgave, er jeg i stand til at glide ind i mine egne tanker, for så at opdage nogle minutter senere at jeg er færdig med op- gaven
0	0	Nogle gange kan jeg genkalde mig ting, jeg tidligere har oplevet, så tydeligt og klart, at det er næsten som at genopleve disse begivenheder
0	0	Ting, som virker meningsløse for andre, giver ofte mening for mig
0	0	Mens jeg har spillet en rolle i et teterstykke, kunne jeg virkelig mærke perso- nens følelser og "være" denne person i et stykke tid, mens jeg glemte alt om mig selv og tilskuerne
0	0	Mine tanker er oftere som billeder end som ord
0	0	Jeg bliver ofte fascineret af små ting, f.eks. den form, der dukker op, når man skærer et æble midt over, eller farverne i sæbebobler
0	0	Når jeg lytter til orgelmusik eller anden kraftfuld musik, kan jeg nogle gange føle det som om jeg nærmest bliver løftet op i luften
0	0	Nogle gange kan jeg ved at lytte til støj ændre det, så det virker som musik
0	0	Nogle af mine mest tyderlige erindringer bliver fremkaldt af lugte og dufte
0	0	Nogle musikstykker minder mig om billeder eller farvemønstre
0	0	Jeg ved ofte, hvad en person vil sige, før han/hun faktisk siger det
0	0	Jeg har ofte "fysiske" erindringer, f.eks. at jeg kan føle det, som om jeg stadig e i vandet efter jeg har svømmet
0	0	En stemme kan nogle gange virke så fascinerende at jeg bliver ved med at lytte til den
0	0	Nogle gange kan jeg føle tilstedeværelsen af en person, som ikke fysisk er til stede
0	0	Nogle gange kan jeg opleve, at tanker og billeder dukker op, uden at jeg behøver at anstrenge mig det mindste
0	0	Jeg oplever at forskellige dufte har forskellige farver
0	0	Jeg kan blive stærkt bevæget af en solnedgang

35.	. Nedenfor er en liste af ord, som beskriver følelser. Vær venlig at læse hvert ord grundigt. Sæt	der-
	efter ét (og kun ét) kryds ved det svar, som svarer bedst til hvordan du har følt dig i den forløb	one
	uge, inklusive dagen i dag.	

I hvor høj grad har du indenfor den sidste uge følt dig:

		100	^	meges	
3	Sler itte	noger,	Or. Texn	Theget has	92.
	16	4/6	od.	36×	30
Stresset	0	0	0	0	0
Nervøs	0	0	0	0	0
Trist	0	0	0	0	0
Vred	0	0	0	0	0
Utilfreds med dig selv	0	0	0	0	0
Rolig	0	0	0	0	0
Haft skyldfølelser	0	0	0	0	0
Bange	0	0	0	0	0
Vred på dig selv	0	0	0	0	0
Ude af balance	0	0	0	0	0
Irriteret	0	0	0	0	0
Deprimeret	0	0	0	0	0
Fjendtlig	0	0	0	0	0
Usikker	0	0	0	0	0
Tilfreds	0	0	0	0	0

52. De følgende udsagn beskriver tanker og følelser, mennesker kan opleve. Læs hver sætning grundigt og angiv derefter i hvor høj grad den pågældende sætning passer på dig som person. Der findes ingen rigtige eller forkerte svar. Besvar venligst alle spørgsmål.

ASSE OF THE PROPERTY OF THE PR	Passer en si	Passer de Nule	Pass en her	er i haj g	
	CX 1440 SI	nule de	Phis ne	dela	Tay
Jeg er ofte usikker på, hvad det er for en følelse, jeg oplever	0	0	0	0	0
Det er vanskeligt for mig at finde de rigtige ord for mine følelser	0	0	0	0	0
Jeg oplever fysiske fornemmelser, som selv læger ikke kan forstå	0	0	0	0	0
Jeg har let ved at beskrive mine følelser	0	0	0	0	0
Jeg foretrækker at analysere problemer, fremfor blot at beskrive den	n O	0	0	0	0
Når jeg er oprevet, ved jeg ikke om jeg er ked af det, bange eller vre	d O	0	0	0	0
Jeg undrer mig ofte over fysiske fornemmelser i min krop	0	0	0	0	0
Jeg foretrækker at lade tingene ske, fremfor at ville forstå, hvorfor de sker	e O	0	0	0	0
Jeg har følelser, som jeg ikke helt kan identificere	0	0	0	0	0
Jeg mener, det er vigtigt, at man er i kontakt med sine følelser	0	0	0	0	0
Jeg har svært ved at beskrive, hvad jeg føler for andre	0	0	0	0	0
Andre beder mig som regel om at beskrive mine følelser mere præci	st O	0	0	0	0
Jeg ved ikke, hvad der foregår inden i mig	0	0	0	0	0
Ofte ved jeg ikke, hvorfor jeg er vred	0	0	0	0	0
Jeg foretrækker at tale med andre om deres daglige gøremål, fremfo at tale om deres følelser	r O	0	0	0	0
Jeg foretrækker at se lettere underholdningsprogrammer på TV - frei for psykologiske dramaer	m- ()	0	0	0	0
Jeg har vanskeligt ved at fortælle om mine inderste følelser, selv ove for nære venner	er- O	0	0	0	0
Jeg kan føle nærhed til en anden, selv i tavse øjeblikke	0	0	0	0	0
Jeg oplever, at det kan være en hjælp at mærke efter, hvad jeg føler når jeg skal løse et problem	, 0	0	0	0	0
Jeg mener, det ødelægger fornøjelsen, hvis man leder efter skjulte betydninger i film eller teaterstykker	0	0	0	0	0

50. Nedenfor er en række udsagn, der vedrører personlige holdninger og måder at være på. Læs hvert udsagn og vurder hvorvidt udsagnet er sandt eller falsk for dig som person. Hvis udsagnet overvejende er sandt for dig personligt, sætter du en cirkel om "S". Hvis udsagnet overvejende er falsk for dig personligt, sætter du en cirkel om "F".

Vær venlig at besvare alle spørgsmål, også selvom du ikke er helt sikker på hvilken svarmulighed, der passer bedst på dig.

	Sandt	Falsk
Jeg synes jeg har svært ved at koncentrere mig om en aktivitet eller en arbejdsopgave	S	F
Jeg bliver sommetider irriteret på folk, der beder mig om tjenester	S	F
Jeg er glad det meste af tiden	S	F
Inden jeg stemmer ved et valg, undersøger jeg kandidaternes kvalifikationer grundigt.	S	F
Jeg tror ikke, at jeg er mere nervøs end de fleste andre	S	F
Når folk har modgang, tænker jeg sommetider, at det blot er gået dem som fortjent	S	F
Jeg er mere følsom end de fleste andre	S	F
Til tider kan jeg godt lide at høre og videregive sladder om andre	S	F
En gang imellem har jeg været i tvivl om min evne til at klare mig her i livet	S	F
Der har været situationer, hvor jeg har udnyttet en anden for at opnå en fordel	S	F
Jeg har et nervøst temperament	S	F
Jeg har aldrig følt en intens modvilje mod nogen	S	F
Jeg kan ikke koncentrere mig om noget	S	F
Jeg tager aldrig på en længere køretur uden at sikre mig, at bilens sik- kerhedsudstyr (lygter, bremser m.v.) er i orden	S	F
Jeg har perioder, hvor jeg er så rastløs, at jeg ikke kan sidde i en stol ret længe ad gangen	S	F
Jeg er altid høflig, selv overfor folk, der er ubehagelige	S	F

rtsat)	Sandt	Fals
Ved nogle lejligheder har jeg opgivet et forehavende, fordi jeg følte at mine evner var for ringe	, S	F
Jeg er altid omhyggelig med min påklædning	S	F
Til tider føler jeg, at jeg slet ikke er noget værd	S	F
Jeg har aldrig følt, at jeg er blevet straffet uden grund	S	F
Når der er noget, jeg ikke ved, har jeg overhovedet ikke noget imo at indrømme det	d S	F
Jeg er almindeligvis rolig og svær at bringe ud af fatning	S	F
Jeg bliver aldrig irriteret, når nogen beder mig gengælde en tjenest	e S	F
Jeg er ikke specielt optaget af, hvordan jeg virker på andre	S	F
Jeg forsøger sommetider at gøre gengæld, frem for at tilgive og lad sket være sket	e S	F
Hvis jeg kunne slippe ind i en biograf uden at betale - og være sik- ker på ikke at blive opdaget - ville jeg sandsynligvis gøre det	S	F
Jeg føler mig presset i min hverdag	S	F
Jeg har aldrig bevidst sagt noget for at såre en andens følelser	S	F
Jeg kan mindes at have "spillet syg" for at slippe for noget	S	F
Jeg er tilbøjelig til at tage tingene tungt	S	F
Jeg bliver nogle gange fortørnet, hvis jeg ikke får min vilje	S	F
Livet er en anstrengelse for mig det meste af tiden	S	F
Uanset, hvem jeg taler med, er jeg altid en god lytter	S	F
Ind imellem kan jeg bestemt få den følelse, at jeg ikke dur til noget	S	F
Jeg prøver til enhver tid at handle efter de principper, som jeg selv er fortaler for	S	F
Jeg har nogle gange været temmelig misundelig på andres fremgang og succes	S	F
Jeg føler sommetider, at jeg er lige ved at gå op i limningen	S	F
Jeg er aldrig blevet irriteret, når folk udtrykte tanker, der var mege forskellige fra mine egne	s S	F

50. (	fortsat)	Sandt	Falsk
	Mine bordmanerer derhjemme er lige så gode, som når jeg er ude at spise på restaurant	S	F
	Det er sket, at jeg har haft lyst til at smadre noget	S	F
	Jeg har sommetider følt, at vanskelighederne hobede sig så meget op at jeg ikke kunne overkomme dem	S	F
	Jeg tøver aldrig med at smide, hvad jeg har i hænderne, for at hjælpe én, der er i knibe	S	F
	Det er sommetider svært for mig at komme videre med det, jeg arbejder med, hvis jeg ikke bliver opmuntret til det	S	F
	Til tider har jeg virkelig insisteret på, at tingene skulle foregå efter mit hoved	S	F
	Jeg er ængstelig for noget eller nogen nærmest hele tiden	S	F
	Jeg er altid villig til at indrømme det, når jeg begår en fejl	S	F
	Der har været tidspunkter, hvor jeg havde lyst til at gøre oprør mod autoritetspersoner, selvom jeg vidste, at de havde ret	S	F
	Jeg griber jævnligt mig selv i at være bekymret over noget	S	F
	Jeg har stort set aldrig haft lyst til at bede nogen om at gå ad H til	S	F
	Jeg "kryber i et musehul", når jeg konfronteres med kriser og van- skeligheder	S	F
	Jeg synes ikke, det er specielt svært at omgås højrøstede og ube- hagelige personer	S	F
	Jeg mangler helt bestemt selvtillid	S	F
	Jeg kunne aldrig finde på at lade en anden blive straffet for noget, jeg havde gjort galt	S	F

36. I det følgende er en liste med begivenheder, som kan indtræffe for hvilken som helst person indenfor et år. Du kan have oplevet nogle af dem. Mens du læser hver begivenhed på listen, tænk tilbage på dit liv indenfor de sidste 12 måneder og sæt et kryds for hver af de nævnte begivenheder, du har oplevet i den periode. Nogle af spørgsmålene handler om begivenheder, som en person, du er tæt på, kan have oplevet. Vi vil også gerne vide noget om disse begivenheder. For hver begivenhed, du har været ude for, vil vi desuden bede dig om at vurdere, hvorvidt den pågældende begivenhed har haft en negativ indflydelse pa dit liv og din livskvalitet.

	Har du oplevet den pågældende begivenhed?		Hvis ja, har begivenheden haft en negativ indflydelse på din livskvalitet?		
	Ja	Nej	Ja	Nej	
SYGDOM, SKADE ELLER ULYKKE					
Du har været ude for en alvorlig ulykke	0	0	0	0	
Du har haft en alvorlig sygdom eller skade	0	0	0	0	
En nærtstående person har været ude for langvarig og/eller alvorlig sygdom	0	0	0	0	
Din ægtefælle eller partner har været ude for langvarig og/eller alvorlig sygdom	0	0	0	0	
Du har haft et barn med langvarig og/eller alvorlig sygdom	0	0	0	0	
Din far eller mor har været ude for langvarig og/eller alvorlig sygdom	0	0	0	0	
Du har været ude for en mindre sygdom eller skade	0	0	0	0	
Du har været igennem en fysisk forandring (f.eks. overgangsalderen)	0	0	0	0	
TAB					
Dit barn døde	0	0	0	0	
Din ægtefælle eller partner døde	0	0	0	0	
En nær slægtning eller ven døde	0	0	0	0	
GRAVIDITET ELLER FØDSEL					
Du blev gravid	0	0	0	0	
Du fødte et barn	0	0	0	0	
Du fik en (frivillig eller ufrivillig) abort	0	0	0	0	
Du fødte et dødfødt barn	0	0	0	0	
Du adopterede et barn	0	0	0	0	
			1		

6. (fortsat)		Har du Hvis ja, ha oplevet den pågældende begivenhed? Hvis ja, ha begivenhed begivenhed? Hvis ja, ha begivenhed begivenhed?		
	Ja	Nej	Ja	Ne
ÆNDRINGER I FORHOLDET TIL ANDRE				
Du blev forlovet eller etablerede et nyt forhold	0	0	0	0
Du blev gift	0	0	0	0
Du genetablerede et forhold efter skilsmisse/ seperation	0	0	0	0
Du har oplevet en stigning i antallet af alvorlige uoverens- stemmelser med din ægtefælle/partner	0	0	0	0
Du har oplevet en stigning i antallet af alvorlige uoverens- stemmelser med en person, du bor sammen med	0	0	0	0
Du har oplevet alvorlige uoverensstemmelser/problemer med en nær ven, slægtning, nabo eller anden person, du ikke bor sammen med	0	0	0	0
Du påbegyndte en affære (udenfor dit parforhold/ægteskab)	0	0	0	0
Din mand/hustru/partner påbegyndte en affære	0	0	0	0
Din ægtefælles/partners opførsel har været et problem for dig	0	0	0	0
Et af dine børns opførsel har været et problem for dig	0	0	0	0
Du afsluttede et forhold	0	0	0	0
Du oplevede seksuelle problemer	0	0	0	0
ADSKILLELSE				
Du afbrød et fast forhold	0	0	0	0
Du var adskilt fra din partner i en længere periode	0	0	0	0
Du blev skilt	0	0	0	0
Dit barn blev forlovet, gift eller flyttede sammen med en partner	0	0	0	0
Dit barn forlod hjemmet af andre grunde	0	0	0	0
Du blev adskilt fra en anden nærtstående person	0	0	0	0
ÆNDRINGER I BOLIGFORHOLD				
Du flyttede til din nuværende bolig	0	0	0	0
En ny person flyttede ind i dit hjem	0	0	0	0

36. (fortsat)		u et den Idende enhed?	Hvis ja, har begivenheden haft en negativ indflydelse på din livskvalitet?	
	Ja	Nej	Ja	Nej
SKOLE/STUDIER				
Du påbegyndte en ny uddannelse	0	0	0	0
Du afsluttede en uddannelse	0	0	0	0
Du sprang fra en uddannelse	0	0	0	0
Du dumpede til en eksamen	0	0	0	0
ARBEJDSSITUATION				
Du har været eller er arbejdsløs	0	0	0	0
Du blev forflyttet til et andet arbejde	0	0	0	0
Du blev fyret	0	0	0	0
Der har været mange forandringer på din arbejdsplads	0	0	0	0
Du havde meget overarbejde	0	0	0	0
Du havde meget vanskelige arbejdsopgaver	0	0	0	0
Du blev pensioneret	0	0	0	0
Du har oplevet trusler om nedskæringer, fyringer eller lign. på din arbejdsplads	0	0	0	0
Din egen virksomhed gik fallit/blev lukket	0	0	0	0
Du har haft uoverensstemmelser med andre på din arbejd- splads	0	0	0	0
ØKONOMI OG RETSLIGE PROBLEMER				
Du har haft vedvarede økonomiske problemer	0	0	0	0
Du har haft forbigående økonomiske problemer	0	0	0	0
Du har tabt/fået stjålet noget som var værdifuldt for dig	0	0	0	0
Du har haft problemer med politiet, toldvæsenet eller lign.	0	0	0	0
Du har været i fængsel	0	0	0	0
Du har været i retten i forbindelse med skilsmisse, forældremyndighed, gæld eller lign.	0	0	0	0
ANDET				
Du har oplevet en stor skuffelse indenfor de sidste 12 måneder	0	0	0	0
Du har oplevet et andet større problem eller bekymring af et par måneders varighed eller længere	0	0	0	0