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Negative affect is associated with development and persistence of chemical intolerance: A prospective population-based study

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ABSTRACT

Objective: Chemical intolerance (CI) is characterised by negative health effects attributed to a heightened responsiveness to common airborne chemicals. This longitudinal study explored the hypothesised role of negative affect in the development and persistence of CI in a general population.
Methods: A general population sample aged 19 to 72 years was examined in 2006–2008 and again in 2011–2012. Longitudinal data on CI were analysed with the purpose of examining baseline negative affect as a risk factor for having developed CI at 5-year follow-up and for reporting persistent CI. Participants were classified as reporting no signs of CI, having symptoms of CI and as being a likely CI case based on self-reported reactions to 11 common chemical exposures, symptoms related to chemical exposures and daily life adjustments attributed to reactions when exposed to chemicals.
Results: A total of 69.4% of the participants who had reported CI at baseline also reported CI at follow-up. In participants with no baseline CI, 15.5% reported CI at follow-up and 18.1% reported symptoms related to chemicals but no daily life adjustments. Baseline negative affect was positively and statistically significantly associated with both development and persistence of CI.
Conclusions: Initial reports of CI were found to be persistent over time, and a considerable proportion of the participants with no CI at baseline reported having developed CI after 5 years. The positive association between negative affect and CI at the 5-year follow-up supports negative affect as a possible risk factor for CI.

Introduction

Chemical intolerance (CI) is a term referring to negative health effects attributed to a heightened self-reported responsiveness to common airborne chemicals, e.g., fragranced products, freshly printed papers and evaporation from new furniture [1]. In severe forms, CI is also often referred to as multiple chemical sensitivity (MCS) [2]. CI is more common in women than in men and symptom reports often involve multiple organ systems without a clear symptom profile [3–5]. However, symptoms from the central nervous system (CNS) are commonly reported, and some studies suggest that CNS symptoms are associated with more severe states of CI [5,6]. The variability in estimates of the prevalence of CI is large with prevalence estimates from 9% to 33% in population-based studies [7–12]. Social and occupational changes attributed to reactions related to chemical exposures has been reported in a smaller proportion, i.e., 0.5%, in one study [12]. A likely contributing factor to the observed differences in prevalence is the absence of an internationally accepted case definition and thus different approaches to delimit CI is often applied [13]. Little is known about the course of CI, but there is some evidence to suggest that the symptoms are persistent in clinical populations [14,15]. Only one study has examined the 5-year persistence of symptoms in representative sample of 10.485 members of the general population [16]. The results showed that about half of the respondents, who reported symptoms of CI at baseline, continued to report such symptoms at follow-up. Despite the uncertainties surrounding the nature and course of CI, the impact on the quality of life in affected people may be considerable and there is thus a need to increase our understanding of the disorder through clinical and epidemiological studies.

Several theories have been suggested to explain the disease mechanisms in CI focusing on both physiological and psychological processes [3,17,18], but the availability of clinical data is still limited, and no

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definitive conclusions have yet been drawn. Recent studies have demonstrated signs of central sensitisation in terms of an enlarged area of capsaicin-induced secondary punctate hyperalgesia [19,20] and increased sensitivity to cold pressor pain in comparison with a healthy control group [20]. Central sensitisation can be defined as an amplification of neural signalling within the central nervous system that elicits pain hypersensitivity [21] and may also contribute to other disorders without identifiable structural pathology [21,22]. It has been suggested that the concept extends beyond pain sensitivity and may also include sensitivity to other sensory stimuli such as chemicals and noise [22]. However, whether sensitivity to exposure to common airborne chemicals is in fact a consequence of prolonged central sensitisation still needs to be investigated. In addition to symptoms from, e.g., mucosa and airways, CI is also characterised by fatigue, confusion and depression, suggesting that psychosocial factors may also be involved. It has, for example, been hypothesised that negative affect could be involved in various phases of CI, e.g., by facilitating development and contributing to the persistence of the disorder [18]. Findings of cognitive bias in CI [23,24], e.g., difficulty ignoring chemical stimuli whereby attentional priority is given to thoughts related to fear and somatic symptoms, support this hypothesis [25]. Furthermore, a recent study demonstrated elevated levels of pro-inflammatory cytokines in CI suggestive of chronic low-grade inflammation [26]. Inflammation, a possible risk factor for several diseases, has also been found associated with negative affect [27]. The neurobiological mechanisms linking negative affect and inflammation have not been established, but exaggerated neurobiological sensitivity to threat in the form of, e.g., cognitive bias, has been hypothesised as a possible model [27]. A likely role for negative affect in CI is further supported by studies showing a higher prevalence of anxiety disorders in CI patients compared with patients without CI [28,29], as well as findings from several studies showing associations between CI and both trait and state anxiety in clinical as well as non-patient groups [14,18,30,31]. Taken together, several studies point towards negative affect as a contributing factor in CI. However, the causal direction of the relationship has not been established. Neuroticism is another construct related to the experience of negative affect and closely associated with anxiety [32]. Neuroticism has also been found associated with CI [18] and is generally a more prominent feature in women than in men [33], which is also the case in CI. Measures of neuroticism are suggested to reflect reduced control over and increased self-referential evaluation of negatively valenced stimuli [33]. Negative affect can thus be viewed as a disposition to experience more negative emotions such as self-dissatisfaction, nervousness, tension and worry [34]. This does not necessarily imply an absence of ability to experience positive emotions but rather that a person is more likely, in any given situation and even in the absence of a major stressor, to experience negative emotions [34]. High negative affectivity may thus be taken to reflect reduced emotion regulatory abilities. Taken together, several lines of evidence point to negative affect as a likely factor in CI, but if we are to gain a deeper understanding of possible risk factors involved in the development and persistence of CI, there is a need for longitudinal, population-based data. The aims of the present study were therefore to test the following hypotheses in a population-based sample: 1) negative affect at baseline is associated with increased risk of reporting CI at 5-year follow-up in respondents with no signs of CI at baseline, and 2) negative affect at baseline is associated with reports of persistent or more severe states of CI at 5-year follow-up.

Materials and methods

The present study used data from the Health2006 study and the 5-year follow-up. The Health2006 cohort has been described in detail in Thuesen BH et al. [35]. In brief, participants in the baseline Health2006 cohort were drawn as a random sample from the background population aged 18–69 years, living in 11 municipalities in the south-western part of suburban Copenhagen. A total of 3,471 individuals (44.7%) entered the study and participated in the health examination, which took place in 2006–2008. In 2011–2012, participants in the baseline Health2006 were invited for a 5-year follow-up examination including essentially the same study protocol [36]. The flow of participants from baseline to follow-up is presented in Fig. 1. All participants gave written informed consent before taking part in the study, which was approved by the ethics committee of the Capital Region of Denmark, Copenhagen (KA20060011).

Grouping of respondents

A baseline and at the 5-year follow-up examination participants completed a questionnaire on reactions when exposed to one or more of 11 categories of common airborne chemicals, e.g., fragranced products, motor vehicle exhaust fumes and cleaning agents, and responded to questions on symptoms attributed to the exposures, e.g., headache, fatigue or symptoms from the respiratory tract, skin, joints or muscles. Furthermore, participants were asked questions about the possible impact of their reactions on daily life, such as their choice of personal care products, use of public transportation or participation in social activities, absence from work or inability to work. The questionnaire was pilot tested prior to the baseline study for linguistic comprehension, reproducibility and relevance in a group of members from the Danish patient organisation for multiple chemical sensitivities (MCS). The procedure is described in detail in Berg ND et al. [12]. Based on baseline responses to these questions, participants were classified into three groups: 1) no CI, i.e., not bothered when exposed to common airborne chemicals; (2) symptoms of CI, i.e., reporting reacting to at least one of 11 common airborne chemicals and experiencing at least one symptom related to exposure; and 3) likely CI case, i.e., reporting adjustments in daily life attributed to reactions when exposed to common airborne chemicals in addition to experiencing symptoms. Group 3 was anticipated to resemble more severe states of CI the most because of reports of avoidant behaviour in addition to symptoms. Avoidant behaviour is characteristic for severe states of CI [37–39] and because of differences in reported behaviour when exposed to chemicals we decided to divide participants into three groups as described above.

As a measure of negative affect and the tendency to experience negative affect, the following self-report measures were included:

Anxiety: Symptom-Check-List-90 (SCL-90)

The SCL-90 is a widely used self-report rating scale for measuring the degree of different aspects of psychological distress experienced within the past week. The anxiety subscale of the SCL-90 consists of 10 items, including questions on the degree of nervousness or shakiness inside and trouble concentrating. Responses are rated on a 5-point Likert scale ranging from “not at all” to “extremely”. The anxiety subscale was used as a measure of anxiety. The SCL-90 has been psychometrically evaluated in a Danish population with item-response models and the psychometric properties of the anxiety subscale were found to be acceptable [40]. The internal consistency (Cronbach's α) of the anxiety scale in the baseline Health2006 study was 0.83.

Neuroticism: the NEO-Five Factor Inventory (NEO-FFI)

Neuroticism is part of the five factor model on personality and reflects the tendency to experience negative emotions, i.e., anxiety, anger, hostility, depression, self-consciousness, vulnerability and impulsiveness [33]. The measure of neuroticism included in the Health2006 study was part of the short form of the Revised NEO Personality Inventory, the NEO-FFI. The neuroticism subscale in the NEO-FFI consists of 12 items with 5-point Likert scale response options, ranging from “totally disagree” to “totally agree”. The internal consistency (Cronbach's α) of the neuroticism scale in the baseline Health2006 study was 0.85 [41].