

A twin study of perfume-related respiratory symptoms

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Abstract

Respiratory symptoms from environmental perfume exposure are main complaints in patients with multiple chemical sensitivities and often coincide with asthma and or eczema. In this population-based twin study we estimate the heritability of respiratory symptoms related to perfume and if co-occurrences of the symptoms in asthma, atopic dermatitis, hand eczema or contact allergy are influenced by environmental or genetic factors common with these diseases. In total 4,128 twin individuals (82%) responded to a questionnaire. The heritability of respiratory symptoms related to perfume is 0.35, 95%CI 0.14-0.54. Significant associations ($p < 0.05$) between perfume-related respiratory symptoms and asthma, atopic dermatitis, hand eczema or contact allergy are not attributable to shared genetic or shared environmental/familial factors, except possibly for atopic dermatitis where genetic pleiotropy with respiratory symptoms to perfume is suggested by an estimated genetic correlation of 0.39, 95%CI 0.09-0.72.

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Introduction

Environmental perfume exposure may cause respiratory symptoms such as discomfort, breathing problems or cough (Berg et al., 2008; Elberling et al., 2005a, 2006). The symptoms are mostly mild, but can be severe and affect daily life activities (Berg et al., 2008; Elberling et al., 2005a; Labarge and McCaffrey, 2000).

The pathophysiology of perfume-related respiratory symptoms is unclear; but IgE-mediated allergy is

unlikely (Elberling et al., 2005a, 2007). The symptoms are positively associated with asthma (Opiekun et al., 2003; Elberling et al., 2005a), as well as hand eczema (HE) and/or contact allergy (CA), independent of asthma, skin prick test reactivity to common aeroallergens, sex and psychological vulnerability (Elberling et al., 2004). Perfume-related respiratory symptoms are also a main complain in individuals with multiple chemical sensitivity (MCS) (Labarge and McCaffrey, 2000), a complex disorder with unknown etiology (Winder, 2002).

Possible explanations for the co-occurrence of perfume-related respiratory symptoms in HE, CA or asthma

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include 1) genetic factors 2) environmental factors 3) physiological factors associated with inflammation 4) increased general tendency to report symptoms.

In the attempt to elucidate the influence of genetic factors on respiratory symptoms it is relevant to include atopic dermatitis (AD), as AD influences both the development of asthma and HE (Dold et al., 1992; Meding and Swanbeck, 1989). Atopic dermatitis is a chronic skin conditions characterized by dry skin, inflammation and itch, and it is important to note that AD does not imply an IgE-antibody associated reaction. The development of AD is strongly influenced by mutations in the gene encoding the skin barrier protein filaggrin (Sandilands et al., 2007), and probably also influenced by several other genes (Morar et al., 2006). The development of asthma and HE are also influenced by genetic factors independent of AD (Los et al., 2001; Bryld et al., 2003), and it is uncertain to what extent genetic factors influence the development of contact allergies (Brasch et al., 2006).

Comparison of casewise concordances in monozygotic (MZ) and dizygotic (DZ) twins can be used to distinguish genetic from environmental causes of a certain phenotype (Martin et al., 1997), e.g. perfume-related respiratory symptoms. Polygenic modeling of quantitative genetics can be used to estimate the relative contribution of genetic and environmental factors to the observed data, by finding the model that best balances parsimony and goodness of fit with as few parameters as possible. Additionally, a co-twin control design is suitable to control for shared genetic and environmental factors, sex and age when associations between a phenotype and disease are investigated, in this case respiratory symptoms and inflammatory diseases in skin and airways (HE, AD, CA and asthma). Further, probandwise concordance rate analysis, i.e. comparisons between MZ and DZ pairs of combined categories of perfume-related respiratory symptoms and a disease conditional on the co-twin status may verify and detail if genetics are shared between the symptoms related to perfume and the diseases in question. Lastly, polygenic modeling allows investigating possible pleiotropy between traits, i.e. the effects of the same gene or set of genes on two different phenotypes.

We aimed to estimate the heritability of respiratory symptoms related to perfume and to investigate if perfume-related respiratory symptoms are influenced by genetic factors shared with asthma, HE, AD or CA.

Materials and methods

Study population

In 2005 a questionnaire focusing on diseases and symptoms in skin and airways was posted to 5048 twin

individuals. The twins had previously participated in a population-based questionnaire survey in 1996 and were randomly selected for that study (Bryld et al., 2000). All twins were born between 1953 and 1976 and were living on Zealand or neighboring Danish islands in 1996. Zygosity had been determined in a previous questionnaire study and was based on the similarity method (Kyvik et al., 1995). This method gives a reliable diagnosis of zygosity in more than 95% of all twin pairs (Christiansen et al., 2003). The cohort of twins comprised same-sex monozygotic (MZ) and dizygotic (DZ) twin pairs, a few triplets and quadruplets, and a minor group with unknown zygosity.

Questionnaire and definitions

The questionnaire included one question on self-reported perfume-related respiratory symptoms and one question on pollen-related respiratory symptoms used as reference in the statistical analysis. The questions were formulated in Danish and the questions in English reported here have not undergone any linguistic or cultural validation. Respiratory symptoms were defined in the questionnaire ahead of the two questions as an annoying experience, for example itching; sneezing, stinging, coughing or difficult in breathing. Then respondents were asked: “Have you within the last 12 months experienced symptoms from your eyes, nose, mouth, throat or lungs elicited by other people’s wearing of perfume, aftershave or deodorant?” Yes/ No, and “Have you within the last 12 months experienced symptoms from your eyes, nose, mouth, throat or lungs elicited by pollen from grass or trees?” Yes/No.

A history of hand eczema was determined by two validated questions from The Nordic Occupational Skin Questionnaire (NOSQ-2002) (Susitaival et al., 2003; Svensson et al., 2002), phrased: “Have you ever had hand eczema?” and the 1-year prevalence was estimated by asking about the time of last eruption? Atopic dermatitis was defined by questions from the UK working party criteria (Williams et al., 1994) as a history of an itchy skin condition plus a minimum 2 of 4 minor criteria: 1) a history of flexural involvement 2) a history of generalized dry skin 3) onset of rash under the age of 2 years 4) a history of asthma/ allergic-rhinitis. Contact allergy was defined as at least one self-reported positive patch test to nickel, preservatives, perfume, rubber, plants, chromate or other. Asthma and allergic rhinitis was determined by an affirmative answer to the questions, “Have you ever been told by a doctor that you have asthma?” and “Have you ever been told by a doctor that you have allergic rhinitis?” respectively. Included in the questionnaire were also questions on smoking habits.

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