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Asthma and odors: The role of risk perception in asthma exacerbation

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ABSTRACT

Objective: Fragrances and strong odors have been characterized as putative triggers that may exacerbate asthma symptoms and many asthmatics readily avoid odors and fragranced products. However, the mechanism by which exposure to pure, non-irritating odorants can elicit an adverse reaction in asthmatic patients is still unclear and may involve both physiological and psychological processes. The aim of this study was to investigate how beliefs about an odor's relationship to asthmatic symptoms could affect the physiological and psychological responses of asthmatics.
Methods: Asthmatics classified as 'moderate-persistent', according to NIH criteria, were exposed for 15 min to a fragrance which was described either as eliciting or alleviating asthma symptoms. During exposure, participants were asked to rate odor intensity, perceived irritation and subjective annoyance while physiological parameters such as electrocardiogram, respiratory rate, and end tidal carbon dioxide ($etCO_2$) were recorded. Before, immediately after, and at 2 and 24 h post-exposure, participants were required to subjectively assess their asthma symptom status using a standardized questionnaire. We also measured asthma status at each of those time points using objective parameters of broncho-constriction (spirometry) and measures of airway inflammation (exhaled nitric oxide, FeNO).
Results: Predictably, manipulations of perceived risk altered both the quality ratings of the fragrance as well as the reported levels of asthma symptoms. Perceived risk also modulated the inflammatory airway response.
Conclusions: Expectations elicited by smelling a perceived harmful odor may affect airway physiology and impact asthma exacerbations.

Introduction

Asthma, a chronic inflammatory disorder of the respiratory tract, affects approximately 17 million Americans. Asthma poses significant challenges to an individual's quality of life, results in lost productivity due to work or school absences and imposes significant financial burdens from chronic medical care. Epidemiologic studies frequently associate exposures to airborne chemicals with asthma exacerbations [1], yet, controlled studies to determine the doses that may trigger symptoms or the mechanisms underlying those symptoms often fail to support the epidemiology [2]. Based on a paucity of data, guidelines for residential and occupational exposures to airborne chemicals are often set or adjusted even though little scientific evidence is available to determine whether such adjustments are adequately protective or necessary.

Many asthmatics report airway symptoms upon exposure to fragrances and odorants, however, the mechanisms underlying these adverse responses are likely to be varied and may involve both physiological and psychological processes. Interestingly, many odor-averse asthmatics identify a subset of odors which do not cause them to perceive symptoms or concern (unpublished data from focus groups & [3]). Because the airways are under the control of the autonomic nervous system (ANS), activation of the ANS or variation in autonomic regulation may contribute to or amplify the bronchoconstriction that asthmatics experience when an attack is triggered [4]. This may in part be due to the fact that people with asthma commonly express concerns about the possible impact of airborne chemical exposures on their health, and these concerns escalate when airborne emissions are odorous.

Most odorants at sufficiently high concentrations can activate two different sensory systems in the nose: the olfactory system (via Cranial Nerve I) and the trigeminal system (via Cranial Nerve V) [5]. Cranial nerve I is the olfactory nerve that provides neural information from odorant receptors. Cranial nerve V is the trigeminal nerve, an unmyelinated free nerve distributed throughout the nasal, ocular and oral mucosa that responds to irritant vapors and leads to chemesthetic irritant sensations such as burning, tingling, prickling, and cooling. Trigeminal stimulation from volatile chemicals can give rise to the release of neuropeptide mediators such as substance P (SP) and calcitonin-gene-related peptides. The release of these neuropeptides can affect a variety of physiological functions including respiration, vasodilation and glandular secretions in the airways and can potentially trigger the onset of asthma symptoms [6]. For this reason, when studying the role of fragrance

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perception among asthmatics, it is critically important to evaluate whether the stimulus is capable of activating trigeminal fibers in the respiratory system in order to separate trigeminally-induced adverse responses from those induced merely by the perception of an odor.

Chen and Miller [7] have formally considered the role of psychological variables such as health beliefs or expectations in their model of stress induced asthma exacerbation (Fig. 1). The model posits that perception of an odor deemed potentially harmful can initiate cognitive and emotional events which, for an asthmatic, can culminate in the interpretation and appraisal of an uncontrolled health threat. The emotional state induced by threat perception can affect biological pathways initiating a cascade of events, which can lead to changes in smooth muscle tone (bronchoconstriction), airway inflammation and increases in airway sensitivity to inhaled agents. In short, a threat can stimulate both arms of the autonomic nervous system (ANS): the sympathetic and the parasympathetic branches. It will also stimulate the hypothalamic–pituitary–adrenal (HPA) cortex and the sympathetic–adrenal–medullary axes (SAM). Bronchoconstriction may occur by the activation of the parasympathetic system [8,9], while inflammation will be regulated among other things through the interplay of the different hormones such as cortisol, epinephrine, norepinephrine and their effects in the immune system [7,9–11].

Despite numerous claims to the contrary, many experimental chamber studies to evaluate odorous asthma triggers fail to substantiate the epidemiological or anecdotal evidence [2]. In addition, the number and quality of the studies investigating the role of odorous chemicals in triggering respiratory symptoms in asthmatics are often low. Shim and Williams [12] examined the effect of cologne and a saline placebo challenge on the expiratory volume of four patients with self-reported sensitivity to cologne. They reported an approximate decline from baseline in Forced Expiratory Volume in one second (FEV_1) of 18–58% during the 10-minute challenge period, but during the next 20 min, the FEV_1 gradually increased. The authors could not discard a psychological component involved in the response to the cologne, since the study was not blinded to the participants. Kumar et al. [13] studied the effects of exposure to commercial perfume-scented strips on 29 asthmatic and 13 non- asthmatic control adults. They reported significant declines of FEV_1 in asthmatic subjects when compared to controls, but no significant decline was observed after the saline (placebo) challenge in the asthmatic subjects. The percent decline in FEV_1 was greatest in severe asthmatics (15–20%) as compared to those with moderate (~11%) and mild asthma (~3–6%). In 1996, a study by Millqvist and Lowhagen [14] examined 9 non-smoking patients reporting respiratory symptoms following exposure to stimuli such as cigarette smoke, house paint, flower scents and perfumes. Each patient underwent a single-blind 30-minute provocation test with a musk-like perfume or saline (placebo) in a special exposure chamber and was asked to record respiratory and sensory symptoms. In almost all cases, patients evaluated the total strength of reaction to the perfume stronger than the saline. This was true whether or not a carbon filter face mask was worn. Participants wore a nasal clamp to eliminate odor cues, and breathed through the mouth and through a facial mask, which sometimes contained a carbon filter.

Furthermore, the mean symptom score in the perfume condition increased throughout the 30-minute provocation period. The authors concluded that symptoms suggestive of respiratory hyperreactivity and asthma could be provoked by perfume in the absence of bronchial obstruction. The authors reasoned that odor cues did not contribute as the subjects wore nasal clips throughout the exposure.

Following a review of these studies, the Institute of Medicine (2000) [15] concluded that it is difficult to draw conclusions regarding the direct role of chemical odors/fragrances in eliciting respiratory symptoms or asthma because many studies fail to control for the possible influence of odor perception among individuals reporting odor sensitivity. Those studies that did attempt to control for odor provide limited or only suggestive evidence of an association between exposure to certain fragrances and the manifestation of respiratory symptoms in asthmatics reportedly sensitive to such exposures. Moreover, the use of nose clips as a control for odor cues, forces subjects to breathe orally and expose their lungs in ways that normal oro-nasal breathing would not. It should also be noted that none of the studies to date have evaluated whether any exposure fragrances were at levels capable of eliciting airway irritation via stimulation of trigeminal free-nerve endings. For example, many commercial perfumes are ethanol- based, so any inflammatory effects in the respiratory system could be subsequent to trigeminal activation from ethanol.

Thus, the pathophysiologic mechanisms of odor-induced asthma remain to be elucidated, but may include some or all of the following: (1) immunological reactions with a secondary chemical mediator release or neural reflex, (2) direct irritant effects on the trigeminal somatosensory system, mediated by transient receptor potential channels (TRP) [16], in the upper or lower airways, or (3) psychologically-mediated reactions stemming from prior beliefs, expectations or conditioned responses.

It is now generally accepted that asthma is a chronic multifactorial disease with acute episodes that may be precipitated by a complex

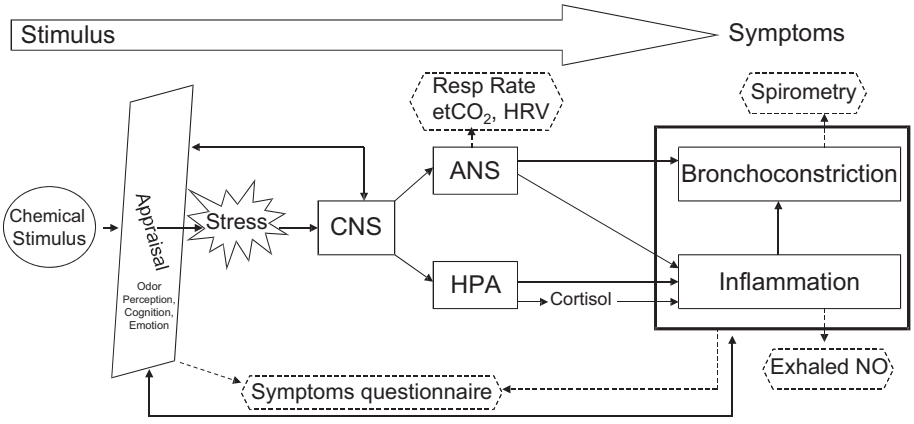

Fig. 1. Biophysical model of stress-induced asthma exacerbation. Perception of an odor deemed potentially harmful can start cognitive and emotional events which, for an asthmatic, can culminate in the interpretation and appraisal of an uncontrolled health threat. This threat can affect biological pathways initiating a cascade of events, which can lead to changes in smooth muscle tone (bronchoconstriction), airway inflammation and increases in airway sensitivity to inhaled agents. The Central Nervous System (CNS), the Autonomic Nervous System (ANS), and the Hypothalamic–Pituitary–Adrenal (HPA) axis are involved in the muscle tone control and airways inflammation. Solid arrows indicate the interactions among the different components; broken line hexagonal boxes indicate the end-points measured in this study.
Adapted from Chen and Miller [7].