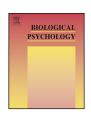
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## Airway reactivity in response to repeated emotional film clip presentation in asthma



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#### ABSTRACT

Emotional stimuli elicit airway constriction in individuals with asthma and in healthy individuals, but little is known about effects of repeated stimulation. We therefore explored the effect of repeated emotion induction on respiratory resistance ( $R_{rs}$ ) using unpleasant, high-arousal surgery films and investigated effects of respiration and emotional reactivity. Twenty-six participants (13 with asthma) watched a series of 12 short, 45-s surgery films followed by 2-min recovery periods.  $R_{rs}$  assessed with impulse oscillometry was significantly elevated during films in both groups compared to baseline and recovered quickly after that. No habituation of airway responses occurred.  $R_{rs}$  was higher in participants who felt more aroused and less in control when watching the films. Changes in  $R_{rs}$  remained significant when controlling for changes in respiration or emotional experience. Thus, although unpleasant stimuli lead to elevated  $R_{rs}$ , airway obstruction is not exacerbated with repeated stimulation due to a fast return to baseline after stimulation.

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#### 1. Introduction

Stress and negative affect contribute to the development and maintenance of asthma morbidity through a variety of mechanisms (Ritz, Meuret, Trueba, Fritzsche, & von Leupoldt, 2013). Stress and negative emotions have been shown to impact airway pathophysiology, including changes in inflammatory status and airway hypersensitivity (for review, see Chen & Miller, 2007; Marshall, 2004; Trueba & Ritz, 2013), which make the airways more sensitive to a variety of asthma triggers. Moreover, stress and negative emotions can be asthma triggers in their own right, as they can elicit increased contraction of airway smooth muscles, leading to emotion-induced airway constriction (Ritz, 2012). In individuals with asthma, the degree of emotion-induced airway constriction correlates with self-report of psychological triggers of asthma in daily life, suggesting that it is one of the major drivers for psychologically triggered asthma (Ritz, Steptoe, Bobb, Harris, & Edwards, 2006).

Induction of stress and negative emotions has an extensive history as a laboratory-based model of stress-induced airway constriction (Kotses, Westlund, & Creer, 1987; Levenson, 1979; Ritz & Steptoe, 2000). Using film clips or still images, these studies have

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consistently shown reactivity of the airways to materials that are high in arousal and negative valence, whereas studies that have used other stress-induction methods, such as mental arithmetic have shown less consistent effects on airway reactivity (for an overview, see Ritz, 2012). It has been hypothesized that stressors that elicit a passive coping responses (such as unpleasant film materials) as compared to elicitors of active coping responses (such as achievement-oriented challenges) may be more detrimental to the airways due to their association with cholinergic excitation that leads to airway constriction (Lehrer, 1998). The involvement of the cholinergic system in emotion-induced airway responses is further corroborated by a reduction of emotion-induced airway reactivity after inhalation of ipratropium bromide vs. a placebo substance (Ritz, Kullowatz, Goldman, & Smith et al., 2010). Alternative mechanisms have been proposed, including bronchoconstriction due to changes in breathing response similar to the bronchoconstrictive effects of exercise or normocapnic hyperventilation. However, previous studies have not found clear evidence for this proposed pathway (Ritz, 2012).

Emotion-induced airway constriction has been observed in individuals with asthma as well as in healthy control participants, although a larger effect has been observed in individuals with asthma compared to healthy controls (Ritz, 2012). Effects of allergic states on cholinergic neural signaling have been suggested as mechanisms explaining these differences in reactivity (Undem & Taylor-Clark, 2014). In individuals with asthma, these differences may furthermore occur during states in which the airways are

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already compromised, further adding to bronchoconstriction that is caused through other triggers or mechanisms or complications in asthma management (Janssens & Ritz, 2013).

Studies on emotion-induced airway reactivity have given only limited attention to the time course of changes in airway responses. Two exception can be found in the literature: one of the first studies on emotion-induced airway reactivity in asthma showed that airway obstruction increased during particularly arousing parts of negative film clips (Levenson, 1979). Furthermore, a recent study showed that during 4–5 min film clips the initial increase in respiratory impedance wears off after reaching a peak 1–2 min into the film clip (Ritz, Rosenfield, Wilhelm, & Roth, 2012).

So far, no studies have investigated the effects of repeated emotional stimulation on emotion-induced airway reactivity. Changes in airway reactivity in response to a repeated stressor may inform us about the mechanisms of emotion-induced airway reactivity. A first possibility is that over time, changes in emotional reactivity will occur, as participants habituate to the emotional content of the film clips or find different ways to cope with the emotional content of the film clips. Another possibility is that changes in airway reactivity occur irrespective of changes in emotional experience of the films, either due to habituation of physiological reactivity or due to changes in airway physiology that are related to (active) changes in breathing behavior. Yet another possibility could be a sensitization with increasingly stronger airway responses or an accumulation of constriction leading to sustained and/or enhanced airway obstruction. The occurrence of changes on these different levels would have different implications for the management of asthma.

Information about changes in airway reactivity over time also has practical implications for further studies on emotioninduced airway reactivity, especially if reactivity is dependent upon repeated presentation of stimuli. For example, functional Magnetic Resonance Imaging (fMRI) studies on brain correlates of emotioninduced airway reactivity may benefit from accurate information about a decline in reactivity over repeated presentations of stimulus material, in order to maximize effect sizes of the effects that are under investigation. Additionally, with studies increasingly indicating a role for the small airways in asthma (Takeda et al., 2009; van den Berge, ten Hacken, Cohen, Douma, & Postma, 2011), we were interested in further studying differences in central versus peripheral airway response to repeated stimulus presentation. The multiple frequency forced oscillation technique has been used to identify small airway complications and we utilized a version of this technique, impulse oscillometry (Smith, Reinhold, & Goldman, 2005), for this purpose.

In this study, our aims were to investigate the effect of repeated presentation of short emotional film clips on changes in central and peripheral airway reactivity in individuals with asthma, and to explore if changes in emotional reactivity or breathing behavior contribute to these changes in respiratory resistance. In line with previous research, we expected a greater impact of emotional film clips in individuals with asthma compared to control participants. We held no specific hypotheses regarding the pattern of habituation versus sensitization of airway reactivity during repeated film clip presentation, but expected that, if changes were observed at all, they would more likely indicate habituation, similar to earlier work that found habituation during longer presentations of emotional films (Ritz et al., 2012).

#### 2. Methods

#### 2.1. Participants

Participants were undergraduate students or members of the greater university community. They participated in exchange for

extra course credit or monetary compensation (\$35). Potential participants were pre-screened prior to participation: Inclusion criteria were a self-reported physician confirmed diagnosis of asthma (asthma group), or an absence of any lung disease (control group). Furthermore, inclusion criteria were non-smoking status for at least 6 months and a lifetime smoking history of less than 6 pack-years. Participants had stable mental and physical health, with no reported history of cardiovascular disease, diabetes, neurological or endocrine disorders; no indications of a history of mania, psychosis, no current indications of depression or substance abuse. Furthermore, participants were excluded if there were indications of blood, injury, or injection phobia. The SMU Institutional Review Board approved the study, and written informed consent was gathered from all participants.

Prior to participation, participants were instructed to continue inhaled corticosteroid use as usual, but to discontinue short-acting bronchodilator use for 6 h, long-acting beta-agonist use for 12 h, antihistamines for 24 h, and leukotriene inhibitors for 3 days prior to participation. Participants were also asked not to eat or drink anything (except water) for one hour prior to their appointment (except for either a power bar, granola bar, or candy bar).

#### 2.2. Materials & measures

Surgery film clips were short 45-s film clips taken from videos depicting close ups of different surgical procedures (7 heart surgery, 3 foot surgery, 2 stent graft). The use of surgery films was based on previous success of this type of film to elicit sustained increases in respiratory resistance ( $R_{\rm rs}$ ) (Ritz et al., 2012). The 12 film clips were selected based on pilot data showing similar levels of arousal and unpleasantness across the individual film clips (film clips are available upon request).

 $R_{rs}$  was measured using impulse oscillometry (IOS Master-Screen, Jaeger, Hoechberg, Germany) (Goldman et al., 2002; Meraz et al., 2011). The pneumotachograph of the device was calibrated daily with a 3-l syringe. The pneumotachograph was also used to perform spirometry (forced expiratory volume in 1s, FEV<sub>1</sub>, was extracted as a variable of interest), as well as to extract measurements of tidal volume ( $V_T$ ) and respiration rate (RR).

As a common indicator of airway inflammation we also determined by the fraction of exhaled nitric oxide (FeNO, in ppb) (Barnes, 2010; Dweik et al., 2011), using an electrochemical analyzer (NIOXmino; Aerocrine; Solna, Sweden).

Emotional valence (pleasant-unpleasant), arousal (excited-calm), and dominance (controlled-in control) was measured using the Self-Assessment Manikin (SAM) scales, which are nine point (1–9) pictorial rating scales (Bradley & Lang, 1994).

In addition, individuals with asthma completed the Asthma Control Test (Schatz et al., 2006), a 5-item questionnaire that is used to assess asthma control as an indicator of successful asthma management. Total scores range from 5 to 25, with a score of 25 indicating perfect control over manifestations of asthma, and scores of 20 or above indicating well-controlled asthma.

#### 2.3. Procedure

Participants received verbal information about the experiment and read the consent form. After giving written informed consent, participants proceeded with filling out a questionnaire package. This was followed by baseline FeNO and impulse oscillometry tests.

Subsequently, participants were administered 4 trial blocks of films and recovery periods. Each trial block consisted of three 45-s surgery film clips, with each film clip followed by a 2-min recovery period. Impulse oscillometry was performed during surgery film clips and during the first 80 s of each recovery period. After each trial block, participants completed the rating scales that measured

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