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Acute and chronic responses of the upper airway to inspiratory loading in healthy awake humans: An MRI study

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Abstract

We assessed upper airway responses to acute and chronic inspiratory loading. In Experiment I, 11 healthy subjects underwent T_2-weighted magnetic resonance imaging (MRI) of upper airway dilator muscles (genioglossus and geniohyoid) before and up to 10 min after a single bout of pressure threshold inspiratory muscle training (IMT) at 60% maximal inspiratory mouth pressure (MIP). T_2 values for genioglossus and geniohyoid were increased versus control ($p < 0.001$), suggesting that these airway dilator muscles are activated in response to acute IMT. In Experiment II, nine subjects underwent 2D-Flash sequence MRI of the upper airway during quiet breathing and while performing single inspirations against resistive loads (10%, 30% and 50% MIP); this procedure was repeated after 6 weeks of IMT. Lateral narrowing of the upper airway occurred at all loads, whilst anteroposterior narrowing occurred at the level of the laryngopharynx at loads ≥30% MIP. Changes in upper airway morphology and narrowing after IMT were undetectable using MRI.

Keywords: Upper airway; Inspiratory muscle training; MRI

1. Introduction

During inspiration, contraction of the thoracic inspiratory muscles creates a negative pressure within the intra- and extrathoracic airways. To prevent upper airway collapse during inspiration, the pharyngeal muscles contract prior to the onset of neural activity to the thoracic inspiratory muscles (Strohl et al., 1980). According to the "balance of pressures" concept, upper airway occlusion occurs when the positive dilating pressure from the upper airway musculature is unable to resist the negative intraluminal pressure caused by inspiratory effort (Brouillette and Thach, 1979). Another approach to understanding airway collapse has been to consider the airway as a collapsible tube. According to this model, the intrinsic properties of the pharyngeal wall determine the collapsibility of the airway (Isono et al., 1997). It is known that chronic training increases the passive stiffness of locomotor muscles, independent of increases in either muscle mass or force output (Lindstedt et al., 2002). Thus, if it were possible to impose a training stimulus upon the upper airway dilator muscles, it is reasonable to suppose that there would be a reduced tendency of the upper airway to collapse due to an increase in the active (neural) tone, an increase in the passive (intrinsic) stiffness of the pharyngeal dilators, or both.

Pressure threshold inspiratory muscle training (IMT) is a method of applying a quantifiable external load to the inspiratory muscles. When applied daily over a period of up to 6 weeks, IMT has been shown to improve the function of the thoracic inspiratory muscles (Romer and McConnell, 2003) and to stimulate adaptive changes, including an increase in the percentage of fatigue resistant Type I fibres and an increase in the size of Type II fibres (Ramirez-Sarmiento et al., 2002). We propose that the skeletal muscles regulating the upper airway are also subjected to a training stimulus during IMT. Specific evidence in support of this postulate is twofold. First, electromyographic (EMG) activity of genioglossus (GG) is increased during inspiratory flow resistive loading (Malhotra et al., 2000; Pillar et al., 2001) and when a negative pressure is applied externally to the upper airway (Aronson et al., 1989; Horner et al., 1991; Pillar et al., 2001). Second, in rodents the hyperpnoea of exercise training has been shown to elicit a fast to slow shift in myosin heavy chain phenotype, and an increase in oxidative and antioxidant capacity, in both the diaphragm and upper airway muscles (Vincent et al., 2002).

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There are three pieces of evidence in support of the notion that IMT may enhance the function of the upper airway dilator muscles. First, 4 weeks of voluntary isocapnic hyperpnoea training was found to reduce the incidence of snoring in otherwise healthy subjects (Furrer et al., 1998), whilst 4 months of didgeridoo playing improved sleep-related outcomes in patients with obstructive sleep apnoea (OSA; Puhan et al., 2006). In addition, 8 weeks of tongue-muscle training by intraoral electrical neurostimulation was found to reduce the incidence of snoring in patients with OSA (Randerath et al., 2004). Finally, a number of case study reports show that pressure threshold IMT is effective in treating vocal cord dysfunction (Sapienza et al., 1999; Baker et al., 2003a,b; Mathers-Schmidt and Brilla, 2005). These findings suggest that IMT activates the upper airway muscles in a way that enhances function.

In light of these observations we aimed to quantify the acute and chronic responses of the upper airway to inspiratory loading in healthy awake subjects, before and after 6 weeks of IMT. In Experiment I, we measured the nuclear magnetic resonance (MR) transverse relaxation time (T_2) of muscle water (Fleckenstein et al., 1988; Patten et al., 2003) to determine whether specific upper airway dilator muscles are activated in response to an acute bout of pressure threshold IMT. The GG and geniohyoid (GH) were chosen due to their putative role in maintaining upper airway patency (Series, 2002) and because they can be identified clearly on MR images (Ryan et al., 1991; Schotland et al., 1996). In Experiment II, we determined whether there was a dose–response relationship between the magnitude of inspiratory loading and narrowing of the upper airway as assessed using 2D-Flash MR imaging. In addition, we examined the effect of 6 weeks of IMT on this relationship. We hypothesised that a dose–response relationship would be present, whereby larger negative pressures would result in greater narrowing of the airway. Further, we predicted that after IMT, airway narrowing would be attenuated at each level of inspiratory loading.

2. Methods

2.1. Subjects

Eleven healthy subjects volunteered for Experiment I and nine individuals volunteered for Experiment II, including five of the subjects from Experiment I. The local Research Ethics Committee approved all experimental procedures and each subject provided written informed consent. All of the subjects had pulmonary function within normal limits, as inferred from maximum flow-volume loops. Descriptive characteristics of the subjects are shown in Table 1.

Table 1
Descriptive characteristics of the subjects

Parameter	Experiment I	Experiment II	
	Baseline	Baseline	Post-IMT
n (male/female)	8/3	5/4	
Age (y)	29 ± 7	25.2 ± 4.7	–
Stature (m)	1.74 ± 0.09	1.76 ± 0.11	–
Body mass (kg)	72.5 ± 14.5	69.0 ± 14.2	–
$FEV_{1.0}$ (L)	4.0 ± 0.8	4.5 ± 0.8	4.4 ± 0.8
FVC (L)	5.1 ± 0.9	5.3 ± 0.8	5.2 ± 0.9
$FEV_{1.0}$/FVC	82.0 ± 4.7	84.7 ± 2.7	85.0 ± 2.7
$FEF_{25–75}$ ($L\,s^{-1}$)	4.1 ± 1.0	4.7 ± 1.2	4.6 ± 1.3
PIF ($L\,s^{-1}$)	8.0 ± 1.6	8.2 ± 2.7	8.4 ± 2.0
MIP at RV supine (cm H_2O)	−112 ± 28	–	–
MIP at RV standing (cm H_2O)	–	−96 ± 18	−126 ± 24***
MIP at FRC supine (cm H_2O)	–	−55 ± 10	−72 ± 14***
MEP (cm H_2O)	–	156 ± 46	155 ± 45

$FEV_{1.0}$, forced expiratory volume in 1.0 s; FVC, forced vital capacity; $FEF_{25–75}$, forced expiratory flow between 25% and 75% of FVC; PIF, peak inspiratory flow; MIP, maximum inspiratory mouth pressure at either residual volume (RV) or functional residual capacity (FRC); MEP, maximum expiratory mouth pressure. All pulmonary function values were within normal limits (Quanjer et al., 1993). *** $p < 0.001$, significantly different from baseline. Values are mean ± S.D.

2.2. Procedures

2.2.1. Pulmonary function

Maximum flow-volume loops were assessed at baseline (Experiments I and II) and after 6 weeks of IMT (Experiment II) using an online spirometer (Oxycon Pro, Jaeger, Hoechberg, Germany). All measurements were performed and interpreted according to European Respiratory Society/American Thoracic Society guidelines (Pellegrino et al., 2005).

2.2.2. Respiratory muscle function

Inspiratory muscle strength was assessed in order to set inspiratory loads (Experiments I and II) and to monitor IMT effectiveness (Experiment II). Expiratory muscle strength was assessed in order to control for learning effects (Experiment II). In Experiment I, subjects lay supine whilst maximum inspiratory mouth pressure (MIP) was determined from residual volume (RV). In Experiment II, MIP was assessed in two positions. First, MIP was assessed from RV whilst standing in order to monitor changes in inspiratory muscle strength due to IMT. Second, MIP was measured from RFC whilst subjects were supine in order to set the acute inspiratory loads. Maximum expiratory mouth pressure (MEP) was determined from total lung capacity (TLC). Measurements from FRC were made using an arrangement similar to that described for the MR imaging protocol in Experiment II (see Section 2.2.5). Specifically, subjects performed a maximal inspiratory manoeuvre via a semi-occluded mouthpiece attached to a length of polyethylene tubing that was connected at its distal end to the pressure meter. The mouthpiece was linked to a wedge spirometer (Spirotrac II, Vitalograph Ltd., Buckingham, UK) via a two-way non-rebreathing valve arrangement, which ensured that all inspiratory manoeuvres were performed from FRC. All pressures were measured using a digital mouth pressure meter (Micro RPM, Micro Medical Ltd., Chatham, Kent, UK). MIP and MEP were defined as the highest pressure averaged over 1 s from three manoeuvres that varied by less than 10% (ATS/ERS, 2002).

2.2.3. Magnetic resonance (MR) imaging

Measurements were performed using a 3.0 T MR scanner (Siemens Trio, Siemens AG, Erlangen, Germany) with a circular