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Daily respiratory training with large intrathoracic pressures, but not large lung volumes, lowers blood pressure in normotensive adults

Jennifer R. Vranish, E.Fiona Bailey*

Department of Physiology, College of Medicine, University of Arizona, Tucson, AZ 85721-0093, USA

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ABSTRACT

Inspiratory muscle training holds promise as a non-pharmacologic treatment that can improve respiratory muscle strength, reduce blood pressure, and improve autonomic balance in hypertensive patients. There is a gap in knowledge regarding the specific respiratory stimulus that gives rise to these favorable outcomes. We implemented five respiratory training protocols that differed in the magnitude and direction of the lung volumes and/or intrathoracic pressures generated by subjects in training. Normotensive adults were randomly assigned to each group and trained daily for 6 weeks. Pre-post and weekly measures of blood pressure showed significant declines in systolic [−8.96 mmHg (95% CI, 7.39–10.53)] and diastolic [−5.25 mmHg (95% CI, 3.67–6.83)] blood pressures for subjects who trained with large positive or negative intrathoracic pressures. Subjects who trained with modest intrathoracic pressures or large lung volumes saw no improvement in blood pressure ($P > 0.3$). Large intra-thoracic pressures are the specific respiratory stimulus underpinning breathing training related improvements in blood pressure.

1. Introduction

As the prevalence of hypertension grows worldwide, novel approaches are needed to combat what may become a public health epidemic (Brook et al., 2013; Mancia et al., 2013). Of the non-pharmacologic treatments available, a long-time respiratory strength training protocol (Abelson & Brewer, 1987; Aldrich et al., 1989) has yielded surprising results including improved blood pressure and autonomic balance in hypertensive patients (Ferreira et al., 2013) and improved baroreflex sensitivity in a rodent model of heart failure (Jaenisch et al., 2011). Despite the important secondary benefits of inspiratory muscle training (IMT) on cardiovascular health, the respiratory mechanisms responsible for the reported improvements in blood pressure and autonomic balance are not known. Accordingly, our purpose in this study was to determine if 6 weeks IMT can lower blood pressure in normotensive adults and second, to identify the specific respiratory stimulus underpinning that result.

From the standpoint of respiratory mechanics, IMT requires that a subject generate large negative (i.e., inspiratory) intrathoracic pressures with attendant large increases in lung volume and chest wall excursion. Thus, it is unclear whether the large negative intrathoracic pressures and/or large lung volumes contribute to the lowering of blood pressure. In order to identify the stimulus, we devised five training groups that differed from one another in regard to the magnitude and direction of the lung volumes and/or intrathoracic pressures generated by the subject in the course of training. Individuals in Group 1 served as the positive control and performed standard IMT (Griffiths and Mcconnell, 2007; Held and Pendergast, 2014; Kellerman et al., 2000; Sapienza et al., 2011; Tzelepis et al., 1994; Volianitis et al., 2001; Weiner et al., 2003) to verify the effects of training on respiratory strength and to assess its secondary effect on blood pressure in healthy adults. Individuals in Group 2 trained with large positive intrathoracic pressures and large lung volumes. Individuals in Group 3 trained with large negative intrathoracic pressures and minimal lung volume excursion. Individuals in Group 4 trained with large lung volumes but modest intrathoracic pressures and those in Group 5 trained with modest intrathoracic pressures and lung volume excursion comparable to tidal breathing, and served as the placebo control. By separating respiratory-related pressures from respiratory-related volume events we sought to assess the effects of each separately and determine their significance in the long-term modulation of blood pressure. Based on previous work (Jaenisch et al., 2011) we hypothesized that large lung volumes (and chest wall excursions) would be the principle stimulus contributing to the lowering of blood pressure.

* Corresponding author.
E-mail address: ebailey@email.arizona.edu (E.Fiona Bailey).

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Table 1
Sex and anthropomorphic data of subjects in each of the training groups. Values are displayed as averages (± SEM).

Training group	Sex	Age (yrs)	Height(cm)	Weight (kg)	
	Male/Female			Pre	Post
Group 1(n = 10)	4/6	21.1 ± 0.4	170.8 ± 2.3	68.1 ± 3.8	68.1 ± 3.9
Group 2(n = 10)	6/4	22.0 ± 0.8	174.7 ± 1.9	67.0 ± 5.2	67.1 ± 5.0
Group 3(n = 10)	4/6	21.1 ± 0.6	173.7 ± 2.4	74.4 ± 5.8	74.1 ± 5.6
Group 4(n = 10)	5/5	20.8 ± 0.5	172.9 ± 2.1	68.4 ± 3.4	68.3 ± 3.4
Group 5(n = 10)	6/4	19.8 ± 0.2	170.3 ± 2.6	66.7 ± 4.4	67.7 ± 4.3

2. Methods

We recruited 50 healthy young adults (25 women and 25 men, age 21.0 ± 0.3 years; height 172.5 ± 1.4 cm; weight 68.9 ± 2.0 kg; BMI 22.9 ± 0.4) to participate in a 6 week training protocol (Table 1). Subjects were nonsmokers, without history of hypertension, respiratory, neuromuscular, or cardiovascular disease and forced expiratory volume in 1.0 sec ($FEV_{1.0}$), expressed relative to forced vital capacity ($FEV_{1.0}$/FVC) was greater than 80% predicted in all cases. All experimental procedures were approved by the Human Subjects Protection Program at The University of Arizona and subjects gave their written informed consent prior to participation.

2.1. Assessment measures

Height and weight were recorded at intake and at the completion of 6 weeks training. A pre-assessment questionnaire recorded typical levels of physical activity which subjects were required to maintain throughout the 6 week training period. Tests of pulmonary function, respiratory muscle strength, and blood pressure were performed at study intake, at the beginning of each week prior to that day's training, and at completion of the study, 24 h after the final training session of week six.

Standard spirometric measures including $FEV_{1.0}$, FVC, forced inspiratory volume in 1.0 s ($FIV_{1.0}$), $FEV_{1.0}$/FVC, $FIV_{1.0}$/FIVC, peak expiratory flow (PEF), and peak inspiratory flow (PIF) were performed in accordance with the guidelines of The American Thoracic Society (Miller et al., 2005). To assess respiratory muscle strength, subjects were required to generate maximal inspiratory (PI_{max}) and expiratory pressures (PE_{max}) by inspiring or expiring against a constant resistance (Black and Hyatt, 1969; Kellerman et al., 2000). PI_{max} and PE_{max} were measured via a pressure transducer (Omegadyne Inc., Sunbury, OH) and determined from the average of the three largest pressure values generated by the subject. Blood pressure was determined via sphygmomanometer and stethoscope at the brachial artery and measurement was performed in accordance with current guidelines (Mancia et al., 2013; Pickering et al., 2005). As such, subjects rested for 5 min prior to measurements, with back and arms supported. Measures were taken in triplicate, on alternating arms, and averaged to obtain the individual's systolic and diastolic blood pressures. All measures were obtained at the same time and day each week by a certified emergency medical technician blind to subject training group.

2.2. Respiratory training protocols

Subjects were randomly assigned to one of the five training groups using selection of de-identified subject codes by a third party. Subjects were blind to the existence of multiple training groups and to the purpose of the study. As depicted in Fig. 1,

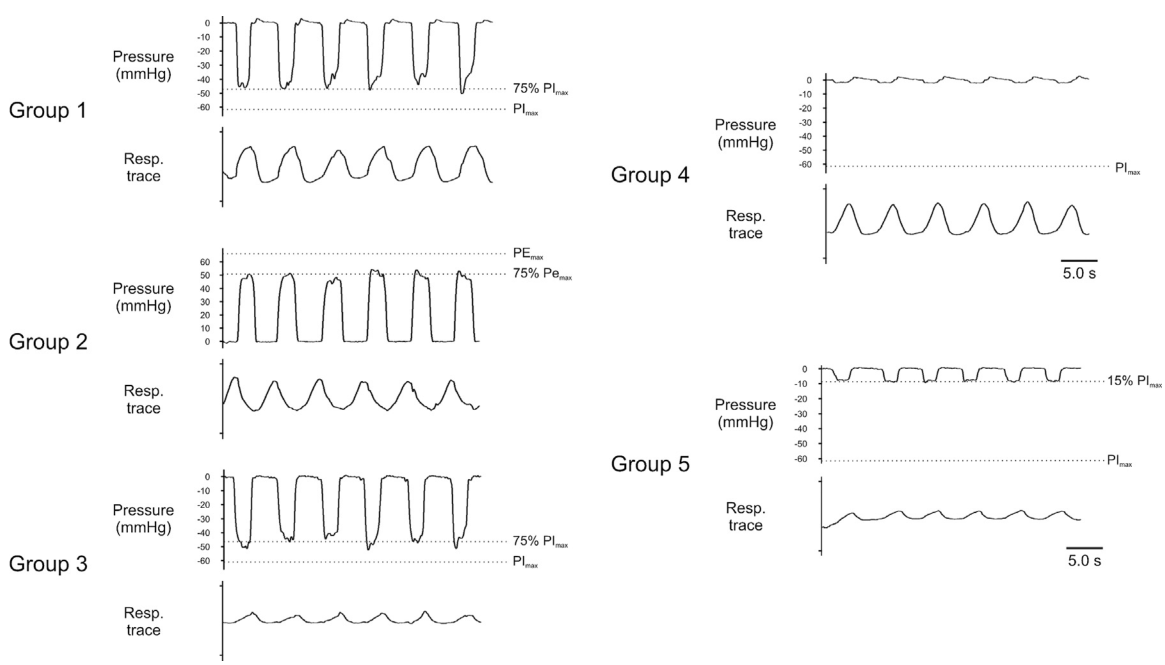

Fig. 1. Training groups. Schematic depiction of the respiratory parameters manipulated for each the training group. All individuals trained on the same device and all training was performed under supervision. Groups differed in regard to the end-inspiratory volume and/or intrathoracic pressure generated during training. Individuals in Group 1 generated large end-inspiratory lung volumes and large negative (inspiratory) intrathoracic pressures. Individuals in Group 2 generated large end-inspiratory lung volumes and large positive (expiratory) intrathoracic pressures. Individuals in Group 3 generated large negative intrathoracic pressures in the absence of lung volume expansion. Individuals in Group 4 generated large end-inspiratory volumes alone, and those in the placebo training Group 5 generated modest volumes and pressures typical of rest breathing.