VENTILATORY DYNAMICS AND EXERTIONAL DYSPNEA DURING RESPIRATORY CHALLENGES IN YOUNG ADULTS WITH ANXIETY

A Thesis
by
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Abstract

VENTILATORY DYNAMICS AND EXERTIONAL DYSPNEA DURING RESPIRATORY CHALLENGES IN YOUNG ADULTS WITH ANXIETY

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Background: In 2020, the Anxiety and Depression Association of America estimated that approximately 31% of adults will experience some form of anxiety in their lives. While regular exercise is an important component in the treatment of anxiety, anxious adults may be unwilling to exercise due to dyspnea on exertion (DOE). As a result, anxious adults may be less likely to participate in regular physical activity, diminishing their quality of living and potentially increasing their risk of cardiovascular disease and overall mortality. **Purpose:** The purpose of this study is to examine the relationships between trait anxiety, ventilatory dynamics, and exertional dyspnea in young adults. **Methods**: Healthy individuals, ages 18-25 years, will be categorized (Minimal, Mild-to-Severe Trait Anxiety) based on responses to the Generalized Anxiety Disorder (GAD-7) questionnaire. Subjects completed four cycling tests at 50% of their predetermined maximal aerobic capacity. During the exercise, dyspnea will be induced via 1) external dead space (DS), 2) resistance loading (RS), or 3) lessened via a heliox gas inspirate (HEL) and compared with control (CON). Ratings of perceived breathlessness (RPB) and unpleasantness of breathlessness (RPU) will be collected during exercise on a visual analog scale (VAS). After each trial, subjects will complete a modified dyspnea and VAS questionnaire describing their subjective emotions during maximum breathlessness. **Results:** There was no main effect by group for breathing patterns, operational lung volumes or perception of DOE ($p > 0.05$). The higher anxiety group did show a higher rating of 'anger' after exercising ($p = 0.037$). There was a main effect of challenge on breathing patterns, OLV, DOE and the affective dimensions ($p < 0.05$). **Discussion:** Although no main differences were exhibited between groups of different anxiety levels, the breathing challenges did show to have an effect on ventilatory dynamics and perceptions of dyspnea. Furthermore, there was an interaction during the DS challenge between groups, indicating differences in their OLV change in response to a chemical stimulus. Further investigation is warranted to determine a stronger relation between anxiety, breathing mechanics and DOE.

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Dedication

I would like to dedicate this project to my mother, Teresa Hufford, for all of her unconditional love and support in all of my endeavors. I would also like to dedicate this to my nieces and nephews: Isaiah, Julian, Tyson, Hayden, Remi, Raina, Lincoln and Marshall. They give me a reason to strive for greatness, and provide an endless amount of light in my life.

Table of Contents

List of Abbreviations and Symbols

AAQ-II	Acceptance and Action Questionnaire – II
AFVx	area under flow volume curve
ARDS	acute respiratory distress syndrome
ASI	Anxiety Sensitivity Index
ATPS	ambient temperature and pressure saturated
ATS	American Thoracic Society
BMI	body mass index
BTPS	body temperature and pressure saturated
C	compliance
CO_2	carbon dioxide
COPD	chronic obstructive pulmonary disease
DOE	dyspnea on exertion
DS	dead space
EELV	end-expiratory lung volume
EFL	expiratory flow limitation
EILV	end-inspiratory lung volume
ERS	European Respiratory Society
ERV	expiratory reserve volume
F	airflow
f_B	breathing frequency
FEV	forced expiratory volume
FEV_1	forced expiratory volume in one second
FFMQ	Five Facet Mindfulness Questionnaire
FRC	functional residual capacity

FVC	force vital capacity
GAD	generalized anxiety disorder
GAD-7	Generalized Anxiety Disorder 7-Item Scale
HADS	Hospital Anxiety Depression Scale
HEL	heliox
IC	inspiratory capacity
kPa	kilopascals
IFR	inspiratory flow reserve
IRV	inspiratory reserve volume
kg	kilogram
L	liters
$L\cdot s^{-1}$	liters per second
LLN	lower limit of normal
mFVL	maximum flow-volume loop
min	minute
MEF	maximal expiratory flow
MEP	maximal expiratory pressure
MIF	maximal inspiratory flow
MIP	maximal inspiratory pressure
MMEF	maximal mid-expiratory flow
MMIF	maximal mid-inspiratory flow
ms	milliseconds
MVV	maximum voluntary ventilation
NHANES III	Third National Health and Nutrition Examination Survey
O_2	oxygen
OLV	operational lung volume

P	pressure
Pe	expiratory pressure
Pi	inspiratory pressure
P_{atm}	atmospheric pressure
PCO_2	partial pressure of carbon dioxide
PFT	pulmonary function testing
PO_2	partial pressure of oxygen
PL	pressure in lung
P_{thorax}	pressure in thorax
Rb	resistance of bronchial tube
Rn	resistance of nasal area
rpm	revolutions per minute
RPB	rating of perceived breathlessness
RPE	rating of perceived exertion
RPU	rating of perceived unpleasantness of breathing
RS	resistance
Rt	resistance of trachea
R_{tot}	total resistance
RV	residual volume
s	seconds
SpO_2	blood oxygen saturation
sRaw	specific airway resistance
Raw	airway resistance
T	temperature
T_e	time duration of expiration
T_i	time duration of inspiration

T_{tot}	time duration of entire breath
T_{exp}	temperature expired
T_{insp}	temperature inspired
TLC	total lung capacity
ULN	upper limit of normal
V	volume
VAS	visual analog scale
VC	vital capacity
V_{exp}	volume expired
VFL	volume flow limited
V_{insp}	volume inspired
V_{O2max}	maximal oxygen consumption
V_E	ventilation
$\dot{V}_E$	ventilation per minute
V_T	tidal volume
VTG	thoracic gas volume
W	watts
WR	work rate
WoB	work of breathing

List of Tables

List of Figures

Chapter 1: Introduction

Background

According to a diagnostic interview from the National Institute of Mental Health (NIMH) in 2003, and estimated 19.1% of U.S. adults were diagnosed with an anxiety disorder that year or previously. When broken down into age groups, 22.3% of 18-29-year-old were diagnosed with anxiety. Age groups 30-44, 45-59 and 60+ reported 22.7%, 20.6% and 9.0% of diagnosed anxiety, respectively [1]. There are multiple variations of anxiety disorders, all of which have a negative impact on the day-to-day life of an individual. Those with generalized anxiety disorder (GAD) often exhibit symptoms of restlessness, fatigue, difficulty concentrating, irritability muscle tension, etc. Among these adults, impairment, as assessed by scores on the Sheehan Disability Scale [2], ranged from mild to severe. In this pool of subjects, approximately 22.8% had serious impairment; 33.7% and 43.5% experienced moderate and mild impairment, respectively. In 2020, the Anxiety and Depression Association of America estimate that 31% of adults will experience some form of anxiety disorder at some point, an 11% increase from the survey taken in 2003 [1].

It is commonly acknowledged that exercise brings many benefits to the quality of life, both physically and mentally. By increasing physical activity, more people can live a healthier lifestyle and reduce the risk for major diseases; particular cardiovascular diseases, which are considered the number one cause of death in the US. Many people do not exercise to the recommended guidelines for numerous reasons (time, money, access to equipment, etc.). One fairly common barrier is the discomfort that comes with exercise. Aside from sore muscles, breathlessness is a sensation that can bring about a great deal of discomfort to many individuals, which can come in many forms such a physical pain, anxiety, fear, depression, etc. The affective unpleasantness of dyspnea during exercise is associated with a greater burden and an overall reduction in health-related quality of life [3].

While regular exercise is an important component in the treatment of anxiety, anxious adults may be unwilling to exercise due to dyspnea on exertion (DOE). As a result, anxious adults may be less likely to participate in regular physical activity, diminishing their quality of living and potentially increasing their risk of cardiovascular disease and overall mortality. Therefore, DOE in adults who experience moderate-to-severe anxiety is a clinical concern and an obstacle to the prevention and treatment of coexisting comorbidities.

The relationship between the level of anxiety and exertional dyspnea is unclear. Further, it is unknown whether DOE in adults with moderate-to-severe anxiety is due to 1) respiratory limitations (i.e., anxiety-related changes in ventilatory mechanics) and or 2) exercise intolerance (i.e., cardiovascular deconditioning possibly the result of an anxiety-related decrease in functional capacity).

Statement of the Problem

DOE can be an uncomfortable sensation that discourages people from engaging in exercise, or even activities of daily living. Anxiety may have an impact on the level of breathlessness one experiences, but it is unclear what is actually causing the higher level of dyspnea that is typically associated with higher anxiety; whether that be ventilatory mechanics, exercise intolerance, or a number of other possibilities. By limiting exercise, there is an increased risk for exercise intolerance, cardiovascular disease and a host of other possibly health complications.

Purpose of the Study

The purpose of this study is to examine the relationships between trait-anxiety, ventilatory dynamics, and exertional dyspnea in young adults. Specifically, minimal and mild-to-severe anxiety levels in comparison to exertional dyspnea ratings, breathing frequency and operational lung volumes during exercise.

Research Questions

Are there differences in ventilatory dynamics, as indicated by breathing pattern and operational lung volumes, between individuals who are classified with minimal and mild-to-severe levels of trait-anxiety?

Are there differences in exertional dyspnea between individuals who are classified with minimal and mild-to-severe levels of trait-anxiety?

Are there differences in the affective dimensions of dyspnea between individuals who are classified with minimal and mild-to-severe levels of trait-anxiety?

Are there relationships between indicators of ventilatory dynamics and exertional dyspnea?

Hypotheses

<u>Hypothesis 1</u>: Breathing dynamics, as indicated by breathing pattern and operational lung volumes, will be significantly different in the minimal and mild-to-severe anxiety groups.

<u>Hypothesis 2</u>: Exertional dyspnea in the mild-to-severe anxiety group will be greater than that in the minimal anxiety groups.

<u>Hypothesis 3</u>: Indicators of the affective dimension of exertional dyspnea in the mild-to-severe anxiety group will be greater than that in the minimal anxiety group.

<u>Hypothesis 4</u>: There will be a relationship between indicators of ventilatory dynamics and exertional dyspnea.

Significance

This study is aimed to investigate the underlying mechanics that could be driving the increase in exertional dyspnea in people with higher trait-anxiety. The findings may aid in the development of future investigations to target these disturbances, which could lead to strategies that help alleviate the exertional dyspnea and improve exercise in anxious adults.

Delimitations

1. Individuals with any known cardiovascular, renal or metabolic diseases, or signs/symptoms of, will be excluded. These individuals would require medical clearance before participation, and the variables measured may be impacted by these diseases, thus normal responses to exercise may not be observed.
2. Individuals currently taking prescriptions drugs that influence the parasympathetic or sympathetic nervous system will be excluded because the measurements of interest in this study may be affected by these tapes of drugs.
3. Individuals currently receiving psychotherapy because the psychotherapy may explain the changes in anxiety and/or stress.
4. Individuals who regularly participate in regular vigorous conditioning, any form of aerobic training, two times per week will be excluded because the focus of this study is to examine untrained individuals and their exercise responses.
5. Individuals who are obese (BMI ≥ 30) will be excluded due to the role of obesity-related dyspnea.
6. The order of breathing challenges will be randomized for each subject to avoid any order effect.

Limitations

1. Dyspnea is only evaluated on exertion, not during daily living activities; meaning results can only be related to exercise states.
2. The participants were all recruited from the same area, there may be cultural influences applicable to the participant pool.

3. This study focused on college-aged individuals, meaning these results cannot be referred to the older population. Likewise, the participants were considered healthy, and not aerobically trained, so results cannot be directly related to an unhealthy or trained population.

Definition of Terms

Boyle's Law – $P1 \cdot V1 = P2 \cdot V2$ [4]

Compliance – a measure of elasticity of the respiratory system; determined by the ability of the pressure in the lung system of changing volume [$C = d(\Delta V)/dP$] [5]

Dyspnea – the term usually applied to sensations experienced by individuals complaining of unpleasant or uncomfortable respiratory sensations [6]

End-Expiratory Lung Volume (EELV) – functional residual capacity plus lung volume, increased by the applied positive end-expiratory pressure [7]

Expiratory Flow Limitation (EFL) – a functional condition in which expiratory flow cannot increase, and hence is maximal under the conditions at hand [8]

Forced expiratory volume in one second (FEV_1) – the largest volume displaced during the first second of a forced exhalation, starting at a maximal inspiratory level; influenced by both lung volume and the dimensions of the airways [9, 10]

Forced Vital Capacity (FVC) – the amount of air that can be forcibly exhaled from the lungs after taking the deepest breath possible, measured via spirometry [10]

FEV_1/VC – the ratio of the forced expiratory volume in the first second and the vital capacity. It is independent of lung size and measures airway obstruction [10]

$FEF_{25-75\%}$ - formerly called maximal mid-expiratory flow (MMEF), the mean expiratory flow during the middle of an FVC, an expression of forced expiration [10]

Functional Residual Capacity (FRC) – the volume of air present in the lungs at the end of a passive expiration [9, 10]

Maximal Expiratory Flow-Volume Curve (mFVL) – a graphical curve that represents a way of describing variation in lung function in health and disease [11]

Maximal Expiratory Pressure (MEP) – the greatest pressure which may be generated during a maximal expiration, a measure of the maximal strength of respiratory muscles [9]

Maximal Inspiratory Pressure (MIP) – the greatest pressure which may be generated during a maximal inspiration, a measure of the maximal strength of respiratory muscles [9]

Peak Expiratory Flow (PEF) – the most rapid airflow produced during a forced expiration with maximal effort, and starting from a maximal inspiratory level; a widely used parameter for the detection of airway obstruction [9]

Positive End-Expiratory Pressure (PEEP) – the pressure in the lungs above atmospheric pressure that exists at the end of expiration [7]

Residual Volume (RV) – the amount of air left in the lungs after a full exhalation [10]

Spirometry – test used to measure the volume of air displaced during either quiet or forced breathing [9]

Thoracic Gas Volume (VTG) – the volume of gas contained in the chest during body plethysmography; a rough estimate of the functional residual capacity of the lung [10]

Tidal Volume (V_T) – the volume of air displaced during spontaneous breathing [9]

Vital Capacity (VC) – the largest amount of air that an individual can displace by exhaling slowly or forcefully (FVC), starting at the maximal inspiratory level; and expression of lung size [9]

Chapter 2: Review of the Literature

Dyspnea

The term dyspnea is usually applied to sensations experienced by individuals complaining of unpleasant or uncomfortable respiratory sensations [6]. Multiple definitions have been provided: “difficult, labored, uncomfortable breathing”, “awareness of respiratory distress”, “sensation of feeling breathless or experiencing air hunger”, as well as “an uncomfortable sensation of breathing” [12]. The aforementioned definitions sometimes mix what the individual is feeling (true symptom), with the physical signs (what a physician observes about the patient) [12]. With this in mind, dyspnea can be seen as an individualized experience.

There is large interplay between physiological and behavioral factors that produce respiratory discomfort. Beyond any disease states, certain bio psychological factors are of particular importance when referring to the perception of dyspnea including psychological state (anxiety and depression), hormone status, sex, body weight (obesity) and general fitness level [13]. Likewise, there is a large spectrum of phrases that individuals use to describe these sensations; it’s a sensation that incorporates a variety of unpleasant respiratory sensation depending on the underlying cause and patient characteristics. The American Thoracic Society (ATS) suggests dyspnea as a term used to describe “a subjective experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity”. This experience stems from interactions of multiple physiological, psychological, social and environmental factors; which may induce secondary physiological and behavioral responses [12]. Recent investigations of the perception of breathlessness suggest multiple types of dyspnea, thus it is considered multidimensional.

Exertional Dyspnea

In normal, healthy, individuals, dyspnea intensifies as oxygen uptake and carbon dioxide output increases with physical activity, which is referred as exertional dyspnea [12]. Intensity of exertional dyspnea is common when ventilation is increased, or ventilatory capacity is reduced. Measurement of dyspnea on exertion (DOE) can be examined in relation to workload, power production, maximal oxygen uptake, or any interaction of respiratory-related variables [12]. Dyspnea can lead to the cessation of exercise, and the fear of this discomfort can discourage individuals from engaging in not only exercise, but daily activities. This could lead to reduced cardiovascular fitness and muscle strength, which then would increase the feeling of dyspnea, thus initiating and a spiral of decline in overall health. Dyspnea, especially upon exertion, is a common debilitating symptom, often associated with clinical anxiety/depression, in those with various disease [14].

Sensory vs Affective Dimensions of Dyspnea

Similar to pain, the sensory experience of dyspnea can result from a variety of interactions from numerous physiologic, psychological, social and environmental factors [15]. It is hypothesized that the affective dimensions of dyspnea (i.e. unpleasantness or emotional responses) is not necessarily tied to the intensity of dyspnea (i.e. the sensation itself) [16]. Leupoldt et al. show that with increasing dyspnea, perceived unpleasantness increased more so than the perceived intensity, which suggests that the sensory and affective dimension of dyspnea can be differentiated similar to the perception of pain [17]. These findings point to the multiple dimensions of dyspnea and highlight the role of psychological aspects in the processing of the sensation. With this in mind, negative affectivity has been shown to have an effect on the accuracy of perception [16].

Banzett et al. applied three different stimuli to healthy subjects to test whether the immediate unpleasantness would vary to the sensory intensity, depending the type underlying mechanism of dyspnea. Maximal hyperpnoea against inspiratory resistance initiated work and effort sensations with relatively low unpleasantness; hypercapnia with restricted ventilation led to similar dyspnea intensity ratings, by evoking air hunger, but produced significantly greater unpleasantness; while a further increase of maximal hypopnea evoked the highest intensity and unpleasantness ratings [18]. This provides evidence that the unpleasantness of dyspnea can vary independently from perceived intensity, which verifies that multiple dimensions of dyspnea exist and can be measured. The role of the psychological state of the patient may influence respiratory discomfort ratings. This can be investigated by determining whether a change in dyspnea reflects a change in the primary sensation, or the affective response. This information could help guide therapies to reduce the feelings of discomfort [16, 18].

Etiology of Dyspnea

There is no one unique peripheral site that elicits the sensation of dyspnea. The sensation of dyspnea originates with the activation of sensory systems involved with respiration, including: respiratory motor command signals, chest wall receptors, pulmonary vagal receptors, and chemoreceptors [12]. Sensory information is relayed to higher brain centers where the respiratory-related signals are processed and contextual, cognitive and behavioral influences create the ultimate expression of the sensation [12]. The understanding of these mechanisms come from studies utilizing a range of experimental conditions in animals, normal subjects, anesthetized subjects, and patients with cardiopulmonary and neurologic diseases [12].

A unifying theory of dyspnea suggests that it “results from a disassociation or mismatch between central respiratory motor activity and incoming afferent information from receptors in the airways, lungs, and chest wall structures” [12]. Afferent feedback from peripheral sensory receptors may allow the brain to assess the effectiveness of the motor commands that are issued to the ventilatory muscles; which would then determine the appropriate response for the command, in terms of flow and volume. When the changes in respiratory pressure, airflow or movement of the lungs and chest wall are do not follow suit with the outgoing motor command, this causes a heightened intensity of dyspnea [12]. In summary: disassociation in the command and response of the respiratory system can produce respiratory discomfort, along with accompanying sensations. As a result, breathing can become an unpleasant experience; this is more commonly seeing during exercise.

Assessment of Dyspnea

Dyspnea is mostly a “synthetic sensation”, meaning it often arises from multiple sources of information, rather than an individual neural receptor stimulation. Severity of dyspnea and the qualitative aspect of breathing unpleasantness varies widely among individuals [12]. As previously mentioned, interactions from numerous physiologic, psychological, social and environmental factors play a part in both the sensation and perception of dyspnea. Behavioral style and emotional state exert important influences on the expression of respiratory sensation; meaning it is important to take into consideration the psychological state (anxiety and depression), hormone status, sex, body weight (obesity) and general fitness level of an individual when assessing the perception of dyspnea, in particular upon exertion [13].

Assessment of dyspnea should measure both the intensity and quality of the sensation, as well as the emotional and behavior responses to the breathing discomfort [6, 16]. A consensus statement from the American Thoracic Society (ATS) has recently proposed that “instruments or section of instruments pertaining to dyspnea should be classified as addressing domains of sensory-perceptual experience, affective distress, or symptom/disease impact or burden”. Sensory-perceptual measures include ratings of intensity (real-time dyspnea measures) and sensory quality. Affective distress can pertain to either a perception of immediate unpleasantness or to a cognitive-evaluative response to or judgment about the possible consequence of what is perceived. Impact measures, although very important, do not directly assess what breathing feels like [12, 16]. Many researchers utilize the analogy of pain to better understand the dimensions of dyspnea, which has led to the categorization of this symptom in terms of its sensory (intensity) and affective (unpleasantness) domains [14].

There have been multiple attempts to unravel the way individuals use language to describe respiratory sensations, and how this can be related to specific descriptors of distinct pathophysiological states and respiratory pathophysiology [9, 19]. For example, chest tightness has been related to asthma and mild to moderate states of airway obstruction. Furthermore, a sense of effort or increased work of breathing is more related to stronger increases in airways resistance, decreases in compliance of the lungs or chest wall, or stronger mechanical load on the ventilatory muscles [9, 20]. Additionally, standard spirometry and lung volume measurements help distinguish healthy patients with those with potential restrictive pulmonary diseases and obstructive diseases, thus proving to be useful in assessing dyspnea in a patient.

A visual analog scale (VAS) is a psychometric measuring instrument utilized to describe and document characteristics of disease-related symptoms, and their subjective severities. This measurement can be utilized quickly and has been shown to be statistically measurable and reproducible [21]. They are referred to as a graphic ratting method; visual is used to represent the concrete nature of this scale, whereas analog refers to the infinite variable (i.e. it permits an infinite number of possible responses between the allotted space) [21]. Advantages of a VAS: high degree of interpretations so responses can be very fine-tuned, repeated measurements can show very slight changes in responses, answering the VAS scale itself is very simple – so room for error is small. Likewise, processing the answers is straight forward and has little possibility or subjective errors [21]. The VAS scale used in the ERPL lab at Appalachian State University uses a 10 cm scale, and answers are measured to the nearest millimeter, giving a possibility of 100 different responses. Disadvantages include the time it takes to measure the scale, possible error in logging in data points, and the requirements for the subjects to be able to see and write precisely.

Dyspnea is considered one singular sensation, but as previously mentioned it is multidimensional and can elicit multiple sensations. Simon et.al. (1990) developed a 15-statement questionnaire describing different sensations individuals may feel while experiencing dyspnea [22]. The list of statements originally consisted of 19 phrases describing sensations associated with breathlessness, and its unpleasantness among patients with lung and cardiac diseases [23]. The list was then revised (1990) to consist of only 15 of these statements that best described the sensations felt with dyspnea. In the aforementioned study, along with another completed by Mahler et. Al (1996), it was discovered that when patients experience breathlessness via different pathophysiological conditions, they also experience different qualitative sensations [19, 22]. Each condition associated with a different group of statements; although some statements were shared among conditions, no two conditions chose the exact set of sensations [22]. Likewise, in an earlier study by Simon et al. (1989) it was shown that 'normal subject', those without cardiopulmonary diseases, were able to distinguish different sensations, when dyspnea was induced using different stimuli [23]. These stimuli included: breath holding, CO2 inhalation, driven target ventilation (a target below that dictated by the chemical drive), resistive and elastic loads, altered patterns of breathing (decreased V_T and increased FRC), and exercise.

Respiratory System

Anatomy

Airways can be divided into upper and lower air ways. Upper airway consists of: nose, nasopharynx, oropharynx, hypopharynx and larynx. The lower airway is everything from the trachea to the alveolar ducts (bronchi/bronchioles, diaphragm, alveolar, intercostals) [9]. Larynx: is made up of thyroid, cricoid and arytenoid cartilage and contains the true and false vocal cords. One of its main functions is phonation. Narrowing of the larynx, as a result of certain pathologies, causes an increase in inspiratory resistance [9]. Trachea: is a 10-12cm tube made up of U-shaped cartilages that are connected by ligaments and banded together by smooth muscles. The trachea bifurcates into the left and right main bronchi. The right main bronchus then bifurcates into three lobar bronchi, while the left bifurcates into two lobar bronchi. This 'branching' continues into a

24th generation; where the bronchioles end at the alveoli. In the ‘conductive zone’ (1st – 16th generation) there is no exchange of oxygen and carbon dioxide; therefor, this part of the respiratory system is referred to as “anatomical dead space” [9].

Such as with the respiratory system as a whole, the ventilatory system is sub-divided into two parts: 1) conducting zone – the anatomical dead space, where no gas exchange occurs and the 2) transitional and respiratory zones – the respiratory zone is the site of gas exchange [9].

Respiratory Control/Drive

Breathing is regulated for both metabolic and homeostatic purposes by both central and peripheral chemoreceptors [24, 25]. Output from the respiratory centers is regulated by an autonomic metabolic control system in the brainstem, and also by higher neural centers that are under direct voluntary control [26]. Respiratory motor activity emanates from clusters of neurons in the medulla. Efferent respiratory signals activate the ventilatory muscles that expand the chest wall, inflate the lungs, and produce ventilation; which results in the regulation of oxygen and carbon dioxide tensions, as well as hydrogen ion concentration in the blood and body tissues. Central chemoreceptors in the medulla and peripheral chemoreceptors in the carotid and aortic bodies sense changes in partial pressure of both carbon dioxide and oxygen (P_{CO2} and P_{O2}, respectively). Signals from these chemoreceptors are transmitted back to brainstem respiratory centers that adjust breathing to maintain blood-gas and acid-base homeostasis [27-30].

In a similar fashion, mechanoreceptors in the airways, lungs, and chest wall are involved in the automatic regulation of the level and pattern of breathing [12, 31]. Breathing pattern is regulated by at least two interacting mechanisms: a central respiratory drive mechanism, and a “timing” mechanism in the respiratory center of the brainstem. The central respiratory drive is cyclically turned on and off by the aforementioned timing mechanism [27-30]. When inspiratory drive is enhanced, the mean inspiratory flow rate (V_t/T_i) is primarily effected, with only secondary effects on timing [32].

Stimulation of the aforementioned mechanoreceptors in the chest wall, lungs, airways, etc. can consciously alter breathing patterns. This action is a result of the sensory signals signaling the sensorimotor cortex within the respiratory system. Wolklove et al. (1981) assessed neurosensory feedback within the respiratory system by evaluating the conscious regulation of V_T. Results indicate that V_T is able to be controlled with precision, suggesting that respiratory mechanoreceptors are able to function with high degrees of sensitivity [25]. The mechanisms involved in the regulation of V_T are thought to play a role in preserving ventilation when lung mechanical functions are altered.

Anxiety

A panic attack can be described as intense, acute anxiety associated with certain physical symptoms, such as dyspnea, and cognitive fears (dying, suffocation, etc.) [33]. With panic attacks, individuals may develop a fear for these situations, and avoid them to the best of their ability (i.e. avoid stress, exercise, etc.). Dyspnea is a key symptom of respiratory illness, and a central feature of panic attacks. Likewise, panic attacks are often a component of dyspnea [33]. The symptom overlap brings about the question of whether respiratory physiology contributes to the pathophysiology of panic and/or anxiety.

There is now widespread clinical evidence of increased situations of anxiety and depression in individuals across a range of chronic conditions, including COPD, heart failure, pulmonary hypertension and late stage cancer [14]. The presence of these psychological comorbidities is associated with poorer health outcomes. It is unclear whether these associations are causative, however, it’s suggested that onset of anxiety and depression worsens the sensations of dyspnea [14, 34]. Managing dyspnea in patients with moderate COPD has been reported to improve depression and negative emotion [14, 35]. Numerous studies have shown cognitive behavioral therapy to have an effect on dyspnea sensation (a reduction of) in patients with COPD [14, 36]. Likewise, pulmonary rehabilitation often stresses the need for teaching relaxation and stress reduction techniques to help with dyspnea management in COPD and other chronic conditions [14, 37].

Dyspnea and Anxiety

In the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR; American Psychiatric Association, 2000), respiratory sensations are a key symptoms in the definition of panic disorder [38]. Panic anxiety can reflect underlying cardiopulmonary disease, and dyspnea can reflect an underlying anxiety disorder [33]. Additionally, psychological symptoms, such as fear of dying or anxiety are common feelings in patients complaining of dyspnea or a feeling of breathlessness. The contemporary learning model of panic [39] emphasizes the importance of respiratory symptoms in the etiology of panic disorder. During a complex conditioning process that occurs during initial spontaneous attacks, introspective cues, such as respiratory sensations, are conditioned as early indicators of upcoming panic attacks. Therefore, these sensations can be cues of anxious feelings that may eventually lead to a panic attack. All in all, respiratory sensations can become interceptive threat signals that elicit different mood states ranging from anxiety to full blown panic attacks [38, 39].

Tobin et al. (1983) state that the analysis of breathing patterns can be used for diagnostic discrimination for both healthy individuals and those with certain disease states [40]. Scano et al. (2013) compared the perceptual response to a resistive load in COPD patients with panic attack or disorders (PA and PD, respectively) and healthy subjects. The dyspnea rating increased linearly for all groups with increasing the resistive load, additionally, patients with PA or PD rated their level of dyspnea significantly higher than did other subjects. In addition, the higher the levels of depression between the groups, the greater the rating of dyspnea as the resistive load increased. This study indicated that the presence of PA or PD in patients with COPD may have an association with a heightened perception of dyspnea [16]. Conversely, other studies suggest that "defensive subjects" (i.e. those with panic disorders and/or anxiety) tend to impair accurate respiratory sensation [24, 41]. A review of 64 studies looking at patients with severe disease showed that the level of anxiety and depression in COPD patients was comparable to, or higher, than the levels shown in cancer, AIDS, renal and cardiac patients [16, 42]. This gives indication of a relationship between breathing patterns and feelings of anxiety and depression, however, the question with this, is whether or not anxiety/depression themselves intensify dyspnea more so than the actual limitation in cardiorespiratory function.

Emotional states can alter the quality and intensity of dyspnea, at a given level of respiration [16]. However, the exact underlying mechanism between the two is unclear, thus improving dyspnea and anxiety/depression remains uncertain. A proposed multidimensional model of dyspnea sensory focuses on multiple components: intensity and quality, as well as the affective components [16]. Sharma et al., (2015) found that in healthy subjects, experimentally induced positive mood states (invoked using pictures) were associated with lower dyspnea ratings (both intensity and unpleasantness) in comparison with negative mood states [14]. This same association was not found when comparing dyspnea ratings in response to leg fatigue. With these two findings in consideration, Sharma et al. suggest that dyspnea perceptions stem from complex central neural processing: cognitive/emotional events, then that for peripherally dependent perception of fatigue [14]. Therefore – strategies to improve dyspnea should focus on strategies aimed at improving mood. Another important finding from Sharma et al. is that the impact of mood was mostly directed at the intensity (sensory) rather than unpleasantness (affective dimension) of DOE, as found in exercising COPD patients, but different from resistive loading dyspnea in healthy subjects [14]. Affective responses, as previously mentioned, are the emotional aspects (i.e. unpleasantness) of dyspnea, and are what usually drive patients to seek treatment [16]. However, despite current findings, the negative association between anxiety/depression and dyspnea is not thought to provide proof of causality between these variables – further studies are needed to determine a specific cause-effect relationship [16].

It is important to investigate what causes anxiety upon breathlessness, and if there is a way to combat it. Breathing exercises and mental preparation can help alleviate anxiety, but a crucial factor to consider is what exactly is causing the affective dimensions of dyspnea during exercise. The study of the relationship between anxiety levels and respiratory parameters and between anxiety levels and sensation could assist the understanding of symptoms reported from patients [24]. All of these unclear correlations lead to the present study, observing dyspnea and its affective dimensions, between young, healthy individuals of varying levels of trait-anxiety.

Ventilatory Dynamics, at rest

Mechanical lung function relates to lung volumes, airflow through the respiratory system, and the pressure-volume and pressure-flow characteristics as an indication of elastic and resistive properties of the airways, lungs and chest wall [9]. In psychophysiology, as well as behavioral medicine, there seems to be possible associations between psychological or behavioral processes and mechanical lung function. Induced emotions, stress, and mood states have been linked to changes in resistive properties of the airways [9].

Pulmonary Function and Lung Volume Measurement

The basis of cardiopulmonary function is made relative to the person of interest, including the variables measured with pulmonary function testing [43]. Pulmonary function is most readily assessed via spirometry and utilizes: forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), and the FEV_1 to FVC ratio to determine if static lung function is within the scope of normal, based upon demographics and affiliated regression line established by the Third National Health and Nutrition Examination (NHANES III) survey [44]. Reference equations for the United States population have been appointed by the American Thoracic Society and European Respiratory Society (ATS and ERS, respectively) [45]. These equations are based upon the subjects' age, sex, weight, height and ethnicity.

Spirometry

The volume of gas within the lung that can be displaced by inspiration and expiration is usually measure at the mouth by the means of a spirometer (or via airflow, by a pneumotachograph) [9]. “Flow” is derived from measuring pressure drop over a fixed resistance [9]. Recording airflow during quiet, resting, breathing is used to measure tidal volume (V_T) (via integration of the flow signal). Maximal expiratory (MEF) and inspiratory flows (MIF) over the course of a forced respiratory maneuver (FVC) are utilized to detect airways obstructions, and are generally related to a fixed percentage of FVC in a flow-volume curve ($MEF_{75\%FVC}$, $MEF_{50\%FVC}$, $MEF_{25\%FVC}$). In healthy individuals, MEF over the first half of the FVC mostly reflect flow characteristics of larger airways (trachea and central airways); whereas the second half of FVC reflect the smaller intrathoracic airways [9, 46]. Forced expiration is accompanied by a compression of the central intrathoracic airways – the stronger the effort (larger pleural pressure), the more pronounced the compression up to a point [9]. In the further course of the expiration, MEF is effort independent (it can be affected by a possible flow-limitation), the effective driving pressure is the lung’s elastic recoil and the effective flow resistance of the upstream airways. Standard spirometry and lung volume measurements help distinguish healthy patients with those with potential restrictive pulmonary diseases and obstructive diseases, thus proving to be useful in assessing dyspnea in a patient.

Advantages of spirometry are its reliability, validity and widespread acceptance and availability as a tool. Limitations focus on the fact that it only provides indirect information on resistive properties of airways properties. Forced expiratory maneuvers may take several minutes, as they are dependent on subject’s effort and concentration, which have an effect on this measurement [9]. Lack of motivation, fatigue and deep relaxation may compromise the effort, thus results/reliability thereof. The directions and coaching of the breathing maneuver is important.

Body Plethysmography

This method measures airway resistance (Raw), which is mainly affected by the middle-sized airways with smooth muscles. Most commonly used method is the use of a “constant volume box”; the basic idea is the application of Boyle’s law ($P_1V_1 = P_2V_2$), stating that the volume of a gas varies inversely with its pressure [4]. This maneuver helps measure lung volumes.

The Maximum Expiratory Flow-Volume Curve

The maximum expiratory flow-volume loop (mFVL) provides data mainly on flow rates at different lung volumes – the most valuable being that at low lung volumes. Differences in the shape of the mFVL are linked with pathologies (obstructive and restrictive diseases), as well as physiological differences in normal individuals [11]. The mFVL measured via spirometry, and lung volumes obtained via body plethysmography are essential to describe operational lung volumes, as well as assessing breathing mechanics at rest and during exercise [47]. One can also achieve an estimate of ventilatory capacity by examining the shape of the mFVL and the pattern of breathing during exercise [48].

Ventilatory Dynamics, during exercise

Breathing mechanics during exercise incorporate the pressure generated, air flow and volume.

Volumes

Age, sex, weight, height and ethnicity are the main physiological determinants of static lung volumes and capacities.

The four, standard, static lung volumes consist of [10]: Tidal Volume (V_T): the volume of air that is inspired or expired during one cycle of respiration [9]; Inspiratory Reserve Volume (IRV): the amount of air that can be forcefully inspired beyond tidal inspiration [9]; Expiratory Reserve Volume (ERV): the amount of air that can be forcefully exhaled beyond tidal exhalation [9]; Residual Volume (RV): the amount of air that remains in the lungs after a full exhalation [9]

Likewise, the four, standard, lung capacities are:

Inspiratory Capacity (IC) [10]

$$IC = V_T + IRV$$

Functional Residual Capacity (FRC) [10]

$$FRC = RV + ERV$$

Vital Capacity (VC) [10]

$$VC = ERV + IRV + V_T$$

Total Lung Capacity (TLC) [10]

$$TLC = ERV + IRV + V_T + RLV$$

Dynamic Volumes:

Forced Vital Capacity (FVC): the amount of air that can be forcefully exhaled after a maximal inspiration [10]

Forced Expiratory Volume (FEV): the amount of air one can forcefully exhale

Forced Expiratory Volume in one second (FEV_1): amount of air forcefully exhaled after the first second [10]

Normal lung volumes and capacities can be predicted and used a referenced based on the previously mentioned physiological characteristics (age, sex, weight, height and ethnicity). When measured, the static lung volumes and capacities are described as a percent of the predicted value; 80% is considered the lower limit of normal (LLN) and 120% is considered upper limit of normal (ULN) [10].

Observing the operational lung volumes (OLV) during exercise can give insight as to how the participant is attempting to achieve an allosteric equilibrium. The analysis of OLV relies heavily on the end-expiratory lung volume (EELV). Measurements of EELV have been verified as the function:

$$EELV = TLC - IC$$

During exercise testing, subjects are instructed to perform an inspiratory capacity (IC) which is a fast and forceful breath to TLC, in which the difference of TLC and IC result in the estimated EELV [7, 49]. By default, the EILV can be concluded:

$$EILV = EELV + V_T$$

Assumptions for these equations rely on TLC being static [49]. With this in consideration: V_T increases. During exercise, changes in the OLV are necessary as a means to meet metabolic demands. In an otherwise healthy person, there will be an observed increase of EILV and a decrease of EELV from resting values [7, 50]. These changes have also been observed under different breathing challenges and intensities [51]. The result of this relationship is to maintain the lowest energy expenditure possible. By increasing EILV, additional work is required, as negative transpulmonary pressure is necessary and requires skeletal muscle work. In tidal breathing, expiration is a passive movement, requiring little to no work. It is produced by elastic forces which are developed in the chest and lung during inspiration and stored [52]. However, exercise requires additional work, especially in the expiration phase, to meet the decreased EELV. In these instances breathing frequency (fB) and volumes are increased with increasing workloads [52, 53]. This means that the volume of air expired surpasses FRC. Once FRC is reached, positive pressure of expiratory skeletal muscles is necessary to surpass it, thus requiring the similar work as inspiration [53]. Overall, there is an increased amount of work required to achieve the optimal amount of ventilation, but this is done in a way to expend the least amount of energy.

Ventilatory limitations during exercise are determined by measuring the exercise tidal flow-volume loops and plotting them according to the measured EELV within the mFVL. This gives rise to specific information regarding the sources and degree of ventilatory limitations. This information consists of: the extent of expiratory flow limitation (EFL), inspiratory flow reserve (IFR), changes in the regulation of EELV (i.e. dynamic hyperinflation), EILV in relation to TLC (V_T/IC). Of particular importance for analyzing breathing mechanics is the EFL [8]. $\dot{V}E$ in reference to maximum voluntary ventilation (MVV) is not as accurate a predictor of ventilatory constraints, as is EFL [48]. EFL occurs when the tidal breath increases to the point where it eventually becomes limited by the MEF of the lungs. An EFL is observed when a tidal breath is plotted with that mFVL and there is an overlap of the two loops [48, 54]. EFL can also be described by transpulmonary pressures, when certain pressures at given volumes do not increase flow [8]. The limitation in expiratory flow could lead to reduced IC and IRV, meaning there is an upward shift toward higher OLV, as well as the development of dynamic lung hyperinflation [54-56].

Timing Components/Flow

The respiratory cycle consists of an inspiration phase, followed by an expiration phase. There is sometimes a pause between the end of an inspiration, and onset of expiration, as well as the end of the expiration and onset of next inspiration. The parameters most commonly used to describe breathing patterns are depth and rate of breathing (f_B). Timing depends on the compliance of respiratory system and the resistance for the airflow. A component of flow is the time duration of a total breath (T_{tot}); both inspiration and expiration times (T_i and T_e, respectively) are measures observed in relation to the T_{tot} [5, 32, 57, 58]. The ratio T_i/T_{tot} is used to reflect constancy of the timing mechanism of breathing [27, 30, 32]. Breaths are expected to be longer in duration during the expiration phase, as this is a passive movement. As mentioned, when higher f_B is required, work is necessary, causing the duration of T_e to increase. In general, relative to T_{tot}, T_i is usually <0.50, and $T_e > 0.50$ at rest and high minute ventilation ($\dot{V}_E$) [5, 58]. However, with an increase in work rate (WR), T_i/T_{tot} and T_e /T_{tot} are seen to approach 0.50, indicating that T_i/T_e are equal [5]. Lind et al. (1984), suggests that the termination of inspiration during exercise is dependent on volume-related afferent feedback from the lungs and/or chest wall – not only in high, but also low volume range. Whereas, expiratory muscle activity occurs already at low exercise intensities combined with the aforementioned active control of expiratory flow, EELV and T_e increases as exercise hyperpnoea intensifies [57].

Minute ventilation ($\dot{V}E$) refers to total ventilation during a 1-min period [27]:

$$\dot{V}_E = f_B \cdot V_T$$

The contribution of drive and timing mechanisms upon ventilation can be assed with the expression [27]:

$$\dot{V}_E = f_B \cdot V_T = V_T/T_i \text{ x } T_i/T_{tot}$$

Where inspiratory flow rate ($V_T/_{Ti}$) is an index of the intensity of the central inspiratory drive mechanism [27, 30, 32].

Air moving through the respiratory tract undergoes both viscous and turbulent resistance. Airflow (F) is proportional to the change of volume (V) per time (t) [5]:

$$F = \Delta V/\Delta t$$

Total resistance (R_{tot}) is the sum of the single resistances along the air passages (nasal area, trachea tube, bronchial tube) [5]:

$$R_{tot} = Rn + Rt + Rb$$

The timing of the breathing cycle depends on compliance (C) and the resistance (R) to the airflow. Airflow can then be described as a function of pressure difference (ΔP) and tidal volume (ΔV_T = VVC - VFRC) [5]:

$$\Delta P - F \cdot R - \Delta V_T/C = 0$$

Pressures

Breathing, the inhaling and exhaling of gases, is controlled by pressure-volume conditions in the lungs. Pressure in the thorax (P_T) is often negative, while pressure in lung (P_L) (alveoli, in particular) is positive when inhaled and ~0 when exhaled. Pressure in lung-thorax

(P_{LT}) is dependent on time ($P_{LT} = P_L + P_T$). The lungs and chest wall are coupled in the way that the lungs sit inside an airtight system within the chest. The pressure between lungs and chest wall is referred to as intrapleural, or intrathoracic, pressure. As mentioned, pressure and volume are related, and this concept remains in the lung. The relation depends on the compliance (C), which is determined by the ability of the pressure in the lung system of changing volume: $C = d(\Delta V)/dP)$ [5].

The faster the rate of inflation or deflation, the more dynamic pressure is required to overcome the resistance. A small amount of pressure overcomes tissue friction; the ratio $\Delta P_{dyn}/\Delta V'$ is called resistance to breathing and for the whole chest, amounts to 0.3 or 0.4kPa·1-1·s [9]. A portion of this pressure is dissipated in the airways and lungs, the remainder in the chest wall; P_{dyn} contributes to P_{stat}, which is needed to inflate the chest [9].

During inspiration, P_{Pl} decreases from −5 to −8 cmH_2O causing the intra-alveolar pressure (P_{alv}) to decrease one cmH_2O below atmospheric pressure (P_{atm}). This pressure change causes air to flow into the alveoli, following the pressure gradient. The drop of P_{Pl} also decreases the airways resistance by dilating the small airways, thus enhancing the air flow [10]. These events reverse during tidal expiration. When the inspiratory muscles relax, dimensions of the thoracic cage decrease, P_{Pl} rises from −8 back to −5 cmH_2O and P_{alv} increases 1 cmH_2O above P_{atm}, causing air to flow outside the alveoli. This is another explanation the for the passive process of tidal expiration [10].

When a greater inspiration is needed (one above the tidal limit), accessory respiratory muscles (i.e. diaphragm, trunk muscles and intercostals) are engaged. The thoracic cage has a greater expansion, causing a greater drop in P_{PI} and P_{alv}, delivering more air to the alveolar. Likewise, expiration below tidal level is no longer a passive process, and requires contraction of expiratory muscles (i.e. abdominals and intercostals), which compress the thoracic cage to its maximum. P_{PI} and P_{alv} rise above P_{atm}; but PALV continues to be greater than P_{PI} due to the elastic recoil pressure (P_{el}) of the alveolar wall [10].

Work of Breathing

There are two different approaches to measure the work of breathing (WoB): 1) estimation of the total energy cost of breathing by measuring the oxygen consumption of the breathing muscles, 2) estimation of the mechanical work done by the breathing muscles from measurements of the pressures developed and volumes displaced by them [59]. The work required to inhale and exhale is described as a function of change of the V_T. The amount of work is directly proportional to V_T, and the rate at which this work is done depends on the number of breaths per a unit of time [5].

The muscles associated with breathing work against three types of forces: elastic forces, which are developed in the lung and chest tissues whenever there is a change in volume; flow-resistive forces, which depend on the resistance from the airways to the flow of gas, and on the resistance offered by non-elastic deformation of tissue. The third force is inertial forces, these depend on the mass of tissue and gases [59]. Forces developed within the respiratory system are measured by pressure differences, whereas volume changes are used to express displacements. Total mechanical work during a respiratory cycle is the sum of: elastic work completed, work against gravity in both the inspiration and/or expiration, all flow-resistive work (negating that completed via stored elastic energy), as well as all negative work [59].

Similar to other skeletal muscles, those associated with respiration are evaluated by strength and/or endurance. Respiratory muscle strength is assessed by maximal inspiratory (PI_{max}) and expiratory (PE_{max}) mouth pressures; these are measured at RV and TLC, respectively. The endurance of respiratory muscles is measured based on the ability of the muscles to resist fatigue via tests that require maximal sustainable ventilation or breathing against added resistive or threshold elastic loads [60].

Indices of Drive: Autonomic Nervous System Regulation of Airways

As previously described, breathing is performed by the respiratory muscles. These muscles are controlled by the higher central nervous system, via the intercostal and phrenic nerves [9]. Most breathing is involuntary – it is controlled subconsciously. However, a person can also voluntarily change different aspects of their breathing – hold their breath, breath “deeper”, cough, sneeze, speak, sing, or use chest muscles to lift heavy objects. During physical work, an increase in both V_T and f_B contribute to a rise in V_E. Reflexes of the respiratory drive have been shown in the V_T-T_i relationship. Likewise, certain stimuli can alter respiratory drive [24].

Stimuli to alter breathing mechanics

Resistive Loads:

Added resistive loads create an extrinsic load to breathing that alters normal ventilatory parameters (e.g. the rate at which air flows to and from the lungs). Resistive loads (i.e. our use of resistance tubing) alter normal pulmonary pressure-flow relationships and mimic similar flow limitation experience by patients with obstructive lung disease [9]. The intention behind adding resistance is to increase the work of breathing. Intensities are determined in units of $kPa^{-1}\cdot s$, by passing air through the resistors at various known flows and simultaneously measuring the drop in pressure across the resistor that results [9].

Studying added loads in humans has two main goals: the regulation of ventilation (i.e. load compensation) and quantifying the relationship between mechanical alterations and respiratory sensations (i.e. load perception) [9, 19]. Those with an altered mechanical load on the respiratory system may have a dissociation between the efferent and afferent information during breathing [12]. This disassociation of neural activity and consequent mechanical or ventilatory outputs may contribute to the intensity of dyspnea under these conditions [12]. Although the ventilatory response to inspiratory loads is governed primarily by respiratory system mechanics and re-flexes, behavioral or cognitive factors may play a role in this response as well [16].

Dead Space

The airways where no exchange of carbon dioxide and oxygen takes place is considered the “conductive zone”, and referred to as anatomical dead space [9]. An increase in dead space will decrease the efficiency of CO_2 elimination. Anatomical dead space is greater at rest and during exercise in patients with pulmonary diseases due to ventilation-perfusion ($\dot{V}/\dot{Q}$) abnormalities [12]. In healthy individuals, the dead space normally declines from rest to peak exercise due to improvements in the $\dot{V}/\dot{Q}$ relationship [12]. This is not seen in diseased individuals because of any reduction or restriction in V_T response.

In an exercise testing setting, where ventilation is measured using equipment, external dead space is a factor to take into consideration, and in turn, can be altered. In these settings, dead space is known as the volume of gas common within the inspiratory and expiratory sides of the tubing a subject is breathing through [9]. It usually consists of a mouthpiece, a respiratory valve and any other equipment in between. Breathing through a tube does slightly increase dead space, but it can be tolerated if sufficient time is allotted for acclimation. In a normal, control setting, it is crucial to keep dead space as minimal as possible (less than 100 ml) [9]. Increases in ventilation (V) are required to compensate for any enlarged dead space [12]. This is seen in both parenchymal and pulmonary vascular diseases, but can also be mimicked in a laboratory setting by adding extra tubing to the ventilatory circuit. It is regularly observed, both in normal individuals and in patients with lung disease, that the intensity of the dyspnea increases progressively with the level of ventilation (V_E) during exercise [12].

Heliox

Heliox is the term used to describe an inert gas mixture of helium and oxygen. It is less dense than typical room air – which allows for less turbulent flow through airways, and ultimately less airway resistance [61]. Helium in oxygen is shown to relieve airway obstruction and lower the WoB [62]. The underlying mechanism of this response involves an increase of the threshold at which turbulent gas flow is induced [62, 63]. A combination of less turbulent and more laminar flow contributes to the lowered the WoB. During ventilation utilizing heliox, there is a lower demand for driving pressures to distribute oxygen to distal alveoli, in comparison with ventilation with oxygen [61].

Heliox therapies have been previously studied with the intentions of reducing symptoms of obstructive lung diseases, but results are inconsistent. For patients with COPD, several studies showed heliox breathing had benefits during exercise, but did not display an effect on lung mechanics and gas exchange at rest. When inhaling a heliox mixture while cycling, there was observed delays in dynamic hyperinflation, as well as respiratory mechanics. These alterations resulted in an increase in maximum ventilatory capacity, and greater exercise tolerance [63-65]. Likewise, EFL can be improved because the resistance to exhalation is reduced, thus reducing the operational lung volume [63]. Other studies, including one from Laude et al, show that breathing heliox both increased exercise performance and reduced dyspnea scores [63, 66]. A majority of studies involving heliox utilize a diseased population, meaning there is a gap in knowledge of potential heliox effects on physically-healthy individuals with what is considered normal lung function. Today, heliox is often used in clinical settings for patients with severe pulmonary disease, such as acute respiratory distress syndrome (ARDS) or COPD. In these settings, heliox is a mixture of helium with varying oxygen contents – but usually at least 21% [62, 67].

Breathing Mechanics Changes with Anxiety:

Emotions and respiration are very much linked: panting in fear and rage, yawning during boredom, as well as sighing in relief or distress. Likewise, everyday speech can include breathing expressions with direct emotional connotations: gasping, snorting, sobbing, sighing, etc. [32]. With this in mind, it is possible that these links between emotion and respiration can lead to the idea that different emotions can be associated with different respiratory patterns; and personality type can have an effect on respiration [32]. Humans breathe in various ways while in a resting state – which is referred to as "ventilation personality" [24, 31]. Additionally, breathing patterns in individuals with chronic anxiety often have irregularities of rhythm which were enhanced when angry [32]. Previous studies, by Masaoka et al., have shown that individual anxiety levels greatly influence f_B in particular [24, 31]. The aforementioned study did not find a correlation in between scores of subjective feelings and variables of breathing parameters during a physical load (isometric leg exercise); however, there were significant correlations between f_B and state-anxiety scores during the physical load – as well as a significant correlation between f_B and trait-anxiety scores during a mental stress test [31]. Masaoka et al. saw a similarity in most parameters comparing the high-state-anxiety and low-state-anxiety groups. However, the high-state-anxiety group showed a significant decrease in the end-tidal fraction of CO_2 (FET_{CO2}), likewise, T_i and T_e shortened. An interesting finding with this study is that with the increase of f_B during the physical load test, there was no correlation between T_i and state-anxiety scores, however, there was a correlation between T_e and state-anxiety scores [24]. This suggests that an increase in $\dot{V}_E$ can not only be related to metabolic demand, but also to a mental demand (i.e. anxiety). Additionally, it is important to point out that there were no observed significance differences between state- and trait-anxiety groups.

Furthermore, other studies have found increases in breathing activity during negative emotional states. Rehwoldt (1911) conducted a study asking subjects (n=3) to imagine different emotions: positive or negative, and calm, excited or tense effect. Excited negative affects led to an increase in f_B as well as increased depth of breathing. Tense affects, both positive and negative, were also associated with a higher f_B, but variable depth [32]. Ax (1953) induced fear and anger in subjects by creating an environment of alarm and confusion, as well as one of irritation and anger, f_B increased in both situations – fear and anger, but was greatest in the anger-induced situation [32]. These studies indicate that f_B can be greatly affected by one's emotional state; with a change in f_B, a host of other breathing parameters may be altered as a result. Controversially, Borges-Santos et al. (2015), found that breathing pattern parameters (i.e. V_T, f_B, T_i, T_e, and T_{tot}) were not influenced by either depression or anxiety during both rest and exercise [68]. This study suggests that the symptoms of anxiety and depression interfere with the sensation of dyspnea, in patients with COPD, but breathing parameters remained unaltered.

As previously described, limitation in expiratory flow could lead to reduced IC and IRV, indicating a higher OLV. Higher operating lung volumes has been shown to correlate with increased dyspnea sensations during bronchoconstriction at rest in asthma patients [54-56], as well as COPD [54, 69, 70] . Likewise, during exercise, patients with asthma that showed a lower IRV reported more intense dyspnea sensations, than those with larger IRV [54, 70]. However, it is not known if this same correlation occurs within healthy individuals, a gap in knowledge that the study at hand intends to address.

Chapter 3: Methods

Participants

For this study, participants were healthy individuals (between 18-25 years of age). College-aged students were the primary focus due to the high prevalence of anxiety, and its impact on the health and lifestyle of this particular group of people. This study consisted of two visits to the Exercise and Respiratory Physiology Laboratory at Appalachian State University.

Screening and Classification

Informed Consent and Anxiety Questionnaires

Participants completed the informed consent, and a series of questionnaires: Generalized Anxiety Disorder 7-item Scale (GAD-7) [71], Anxiety Sensitivity Index (ASI) [72], Hospital Anxiety Depression Scale (HADS) [73], Five Facet Mindfulness Questionnaire (FFMQ) [74], Acceptance and Action Questionnaire – II (AAQ-II) [75], Perceived Stress Scale[76], Marlowe-Crowne Scale [77], PANAS [78], Marteau [79]. Once completed, and the subject qualified for this study, each participant were placed into a category of either Minimal (MIN), or Mild-to-Severe (M-S) based on the scores of their GAD-7 survey. Spitzer et al., indicate that scores of '0-4' indicate the subject experiences minimal anxiety, while scores of 5-9 indicate mild anxiety, and 10-14/15+ indicate moderate and severe anxiety, respectively[71]. The results of the survey were not disclosed to the participant, unless they scored in the severe range, to which we were obligated to refer subjects to the school counseling department. Based on the number of subjects that completed the study, the data pool was split into these two groups: MIN and M-S. After all paperwork was finished, the participant completed a standardized body composition measurement, via air displacement plethysmography.

Pulmonary Function Testing

Following screening and the body composition test, the participants went through a series of pulmonary function testing (PFT). Participants were asked to perform three repeatable forced vital capacity (FVC) maneuvers. In order to be determined repeatable, less than 150 mL vital capacity difference between trials had to occur. After FVC maneuvers are completed, lung volumes were measured via body plethysmography. According to the American Thoracic Society (ATS), a minimum of three repeatable trials are required to determine participant lung volumes [4]. Participants had to perform three FRC trials, with values that were less than or equal to 5% of each other (the criteria to be considered repeatable).

The last test in this series was maximum voluntary ventilation (MVV). Subjects were asked to “breathe rapidly” with the goal to “move as much air as possible”. Researchers encouraged the subjects throughout this test (10 seconds of rapid breathing), giving prompts to rather “breathe faster” or “breathe deeper”, referring to a higher f_B or larger V_T, respectively. The participant was required to reach approximately 50% of vital capacity and a f_B around 90 Hz [47].

Maximal Aerobic Capacity Exercise Testing

The last measurement of this visit was a maximal aerobic capacity ($\dot{V}O_{2max}$) exercise test, performed on a cycle ergometer. The subsequent visit required a work rate based on a percentage of the individual's maximal oxygen uptake. This maximal test gave a value to utilize with the further testing.

Participants performed this test on a cycle ergometer (Lode, Groningen, Netherlands) while breathing through a low-resistance two-way valve (Hans Rudolph, Shawnee, KS). Expired air was analyzed for volume and gas fractions from a TrueOne 2400 metabolic cart (ParvoMedics, Salt Lake City, UT). Volumes was measured using a heated pneumotach calibrated with a 3L syringe (CareFusion, San Diego, CA). A gas analyzer measured Fe_{O2} using a paramagnet and Fe_{CO2} was measured via infrared sensor. Gas was calibrated via calibration gas with O_2 (15.96 %) and CO_2 (3.992 %). A heart rate strap (Polar, Bethpage, NY) was used to continuously measure heart rate; blood oxygen saturation (SpO_2) was monitored via a Nellcor™ forehead infrared sensor (Nellcor, Minneapolis, MN). Before testing began, subjects were familiarized with three different visual analog scales (VAS) to assess their breathing and exercise. The VAS was used to represent participant's subjective ratings of their perceived breathlessness, unpleasantness of their breathing, and (total-body) exertion. Breathing and unpleasantness of breathing were scored on scales 0-10, while exertion was scored on the traditional Borg scale from 6-20. Because subjects were on a mouthpiece, and prompted not to attempt to talk, the scales were held in front of the subjects face, and they were asked to point to the number on the scale that best described their perceptions of the aforementioned feelings. It was also explained that they will be asked to perform inspiratory capacity (IC) maneuvers at the last minute of rest and at each minute (around 40 sec) of exercise; the test facilitator prompted the participant when to do so. Prior to the exercise, each participant was asked to sit at rest on the cycle ergometer for six minutes. At this time resting values were collected and technicians ensured all equipment was working properly. After this rest period, the test began at 30 W for males and 20 W for females. The participant was prompted to pedal at 60-80 revolutions per minute (rpm). Each stage lasted 60 seconds, and the work rate increased by 30W or 20W for the sexes, respectively. At the end of every minute, subjects were asked to perform an IC; after this maneuver, they were asked to rate their perceived breathlessness, unpleasantness of breathing and perceived exertion on the previously mentioned VAS. This procedure continued until the participant voluntary ceased exercise, the test facilitators deemed they have reached their maximum aerobic threshold, based on the ACSM guidelines for cardiopulmonary exercise testing, or if/when legs slowed down to below the required 60rpm (ACSM's Guidelines for Exercise Testing and Prescription, 2017). Once exercise was completed, and the subject cooled down, they were prompted to fill out an additional two surveys: the VAS [12, 80], and a modified dyspnea survey. The VAS asked the participants to describe how much they felt different negative emotions (unpleasantness, depression, anxiety, frustration, anger, fear), in relation to their maximal breathlessness rating. The dyspnea survey included a list of fifteen statements describing different breathing sensations. Subjects were asked to pick the top three descriptors that described how they felt at their maximum breathlessness level, and rank them (1-3), with 1 being the statement that pertained the most with how they felt. The dyspnea questionnaire was modified into four different formats that differ in the ordering of the phrases, and were randomized for each subject.

Submaximal Exercise Testing with Breathing Challenges

Participants completed four, randomized, 5-min constant work rate cycling trials at 50% $\dot{V}O_{2max}$. One trial served as a control, with spontaneous breathing and no changes to the standard exercise testing set-up. During the other three cycling trials, participants were introduced to different ventilatory challenges: breathing with increased dead space (DS), breathing with added air flow resistance (RS), and breathing with decreased air flow resistance, using heliox (HEL), a gas mixture of helium and oxygen (20.92% O_2). Various factors of breathing pattern: f_B, $\dot{V}_E$, V_T, $PetCO_2$; as well as operational lung volume measurements: EELV, EILV and IC were examined during all cycling trials. Before testing began, subjects were reminded of the three different visual analog scales (VAS) used in the max test (visit 1). The VAS represented participant's perceived level of breathlessness, perceived unpleasantness of breathing, and their perceived (total-body) exertion. Breathing and unpleasantness of breathing were scored on scales of 0-10, while exertion was scored on the traditional Borg scale from 6-20. During the exercise, subjects were asked their subjective ratings on the VAS scale during the final minute of rest and after the fourth minute of the test. Because subjects were on a mouthpiece, and prompted not to attempt to talk, the scales were held in front of the subjects face, and they were asked to point to the number on the scale that best described their perceptions of the aforementioned feelings. It was explained that they would be asked to perform two inspiratory capacity (IC) maneuvers during the last minute of rest, and the fifth (final) minute of the exercise test; the test facilitator prompted the participant when to do so. An important factor to this visit was to assess the subjects' baseline mood before exercising using the Spielberger State-Trait Anxiety Inventory (Marteau) [14, 79]. Subjects filled out this questionnaire before each exercise test (four total). Likewise, subjects completed the PANAS questionnaire before the first exercise test (one time). Following the completion of each breathlessness challenge, subjects completed a modified dyspnea and VAS questionnaire [12, 80] describing their subjective emotions during maximum breathlessness. These are the same questionnaires completed after the maximal aerobic capacity test in Visit 1. The dyspnea survey was randomized for each subject, and each test. Each trial was separated by approximately 15-20 minutes of rest while the surveys were completed and technicians set up for the next test.

Data Analysis

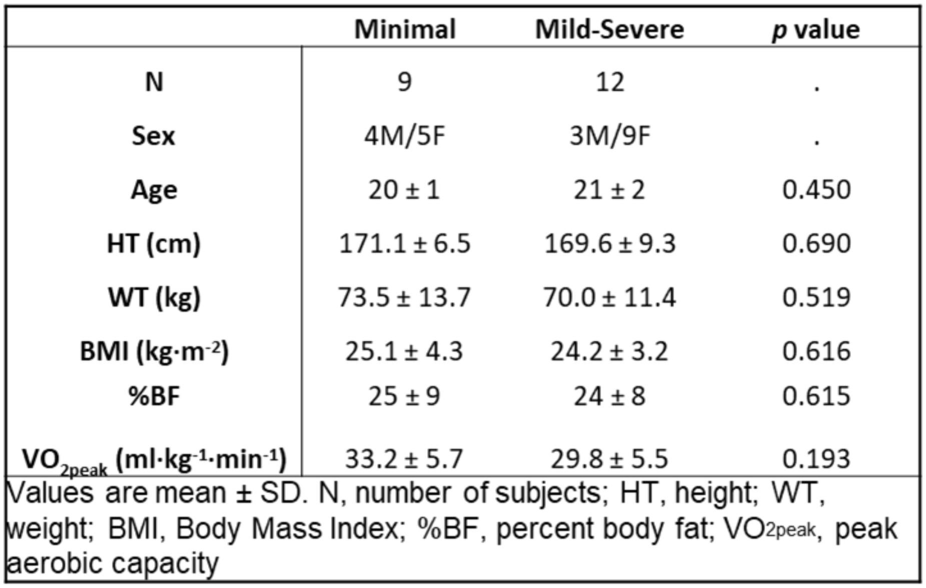
A mixed model analysis of variance was used, via SPSS data acquisition software, to identify any differences in RPB, RPU, RPE and VAS subjective ratings of negative emotions at maximum breathlessness between each breathing challenge. These results were compared by "group" and "challenge", and likewise by "group*challenge" to determine any interactions. A chi square was used to assess the frequency of descriptors (statements) selected by the subjects in the modified dyspnea questionnaire. These were also compared by "group" and by "challenge" and analyzed for any interactions between "group by challenge". Additional measurements of focus included aspects of ventilatory dynamics of interest: EELV, EILV, V_E, V_T, f_B, $\dot{V}_A$, $PetCO_2$, EstInspW and EstExpW. A mixed analysis of variance was used, via SPSS data acquisition software, to identify any difference between "group", "stage" (i.e. rest and exercise) and "challenge". "Group by challenge", "group by stage" "challenge by stage", "group by challenge by stage" interactions were also analyzed.

Chapter 4: Results:

Subject Characteristics

Twenty-one (n=21) healthy, young adults with varying levels of anxiety completed this study. Subject characteristics (age, height, weight, BMI and VO_2 peak) are shown in Table 1.

Table 1: Age, height, weight, BMI and $\dot{V}O_{2peak}$ were all similar between the two groups (*p*>0.05).



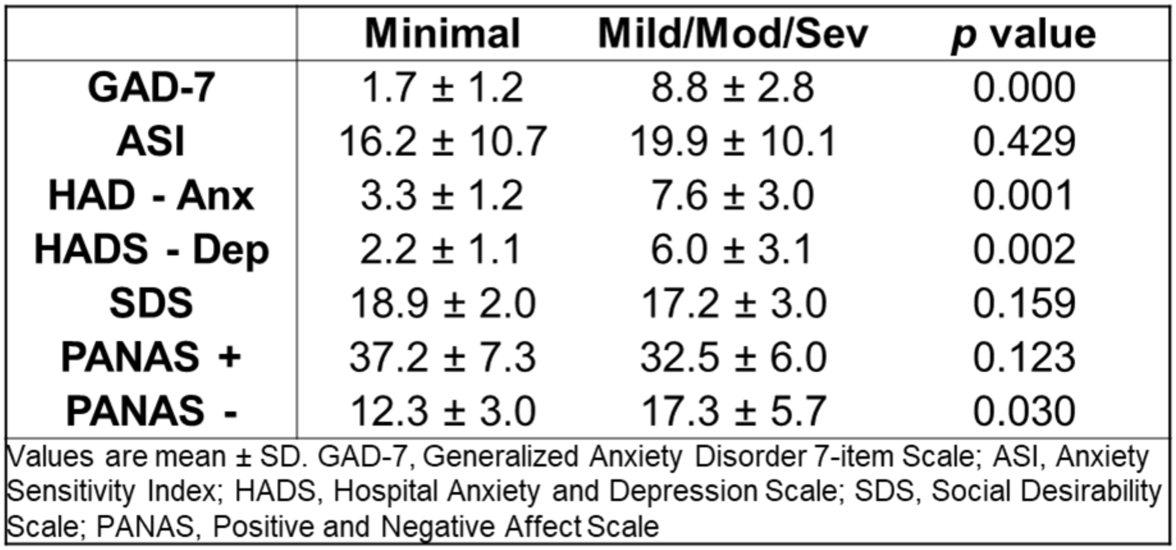
	Minimal	**Mild-Severe**	***p* value**
N	9	12	.
Sex	4M/5F	3M/9F	.
Age	20 ± 1	21 ± 2	0.450
HT (cm)	171.1 ± 6.5	169.6 ± 9.3	0.690
WT (kg)	73.5 ± 13.7	70.0 ± 11.4	0.519
BMI ($kg \cdot m^{-2}$)	25.1 ± 4.3	24.2 ± 3.2	0.616
%BF	25 ± 9	24 ± 8	0.615
VO_{2peak} ($ml \cdot kg^{-1} \cdot min^{-1}$)	33.2 ± 5.7	29.8 ± 5.5	0.193

Values are mean ± SD. N, number of subjects; HT, height; WT, weight; BMI, Body Mass Index; %BF, percent body fat; VO_{2peak}, peak aerobic capacity

Psychological Questionnaire Scores

Scores from each psychological questionnaire, from the initial visit/screening process, can be found in Table 2. As mentioned, subjects were divided in to two groups, either “Minimal” anxiety (MIN) or “Mild-to-Severe” anxiety (M-S), (or “With Anxiety”) based on their GAD-7 scores. Nine subjects scored in the 0-4 range, placing them in MIN; 12 subjects scored ≥5, placing them in the M-S. It is important to note that 9 subjects in the group scored within the “Mild” anxiety range, as depicted by GAD-7 scoring criteria. Likewise, 2 subjects scored in the “Moderate” range, and 1 subject scored in the “Severe” range (individual scores can be found in the Appendix). Subjects were consolidated into two groups to provide better statistical power during the analysis. The two groups were different in terms of their scores for the GAD-7 ($p<0.001$), HADS-Anxiety ($p=0.001$), HADS-Depression ($p=0.002$), and negative PANAS ($p=0.030$). Scores were similar between the two groups for ASI ($p = 0.429$), SDS ($p=0.159$), and positive PANAS ($p=0.123$).

Table 2: Psychological questionnaires within the two groups (N=21).



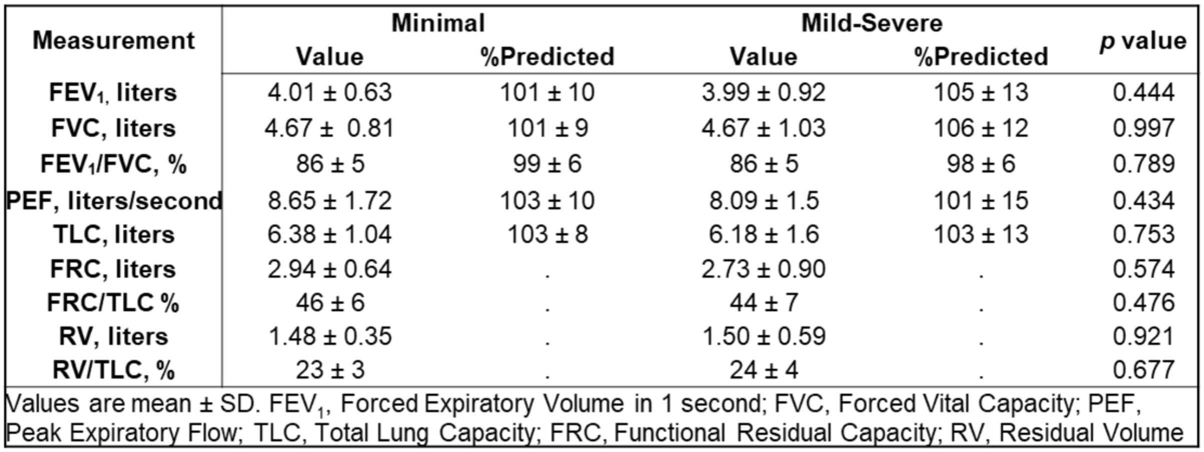
	Minimal	Mild/Mod/Sev	*p* value
GAD-7	1.7 ± 1.2	8.8 ± 2.8	0.000
ASI	16.2 ± 10.7	19.9 ± 10.1	0.429
HAD - Anx	3.3 ± 1.2	7.6 ± 3.0	0.001
HADS - Dep	2.2 ± 1.1	6.0 ± 3.1	0.002
SDS	18.9 ± 2.0	17.2 ± 3.0	0.159
PANAS +	37.2 ± 7.3	32.5 ± 6.0	0.123
PANAS -	12.3 ± 3.0	17.3 ± 5.7	0.030

Values are mean ± SD. GAD-7, Generalized Anxiety Disorder 7-item Scale; ASI, Anxiety Sensitivity Index; HADS, Hospital Anxiety and Depression Scale; SDS, Social Desirability Scale; PANAS, Positive and Negative Affect Scale

Pulmonary Function Testing

Results from pulmonary function testing are presented in Table 3 and demonstrate that subjects within both groups exhibited spirometry and lung volume measurements near predicted. Additionally, the two groups were not statistically different from one another in any measurement (all *p*>0.43).

Table 3: Pulmonary function within the two groups (N=21).



Measurement	Minimal		Mild-Severe		*p* value
	Value	%Predicted	Value	%Predicted	
FEV_1, liters	4.01 ± 0.63	101 ± 10	3.99 ± 0.92	105 ± 13	0.444
FVC, liters	4.67 ± 0.81	101 ± 9	4.67 ± 1.03	106 ± 12	0.997
FEV_1/FVC, %	86 ± 5	99 ± 6	86 ± 5	98 ± 6	0.789
PEF, liters/second	8.65 ± 1.72	103 ± 10	8.09 ± 1.5	101 ± 15	0.434
TLC, liters	6.38 ± 1.04	103 ± 8	6.18 ± 1.6	103 ± 13	0.753
FRC, liters	2.94 ± 0.64	.	2.73 ± 0.90	.	0.574
FRC/TLC %	46 ± 6	.	44 ± 7	.	0.476
RV, liters	1.48 ± 0.35	.	1.50 ± 0.59	.	0.921
RV/TLC, %	23 ± 3	.	24 ± 4	.	0.677

Values are mean ± SD. FEV_1, Forced Expiratory Volume in 1 second; FVC, Forced Vital Capacity; PEF, Peak Expiratory Flow; TLC, Total Lung Capacity; FRC, Functional Residual Capacity; RV, Residual Volume

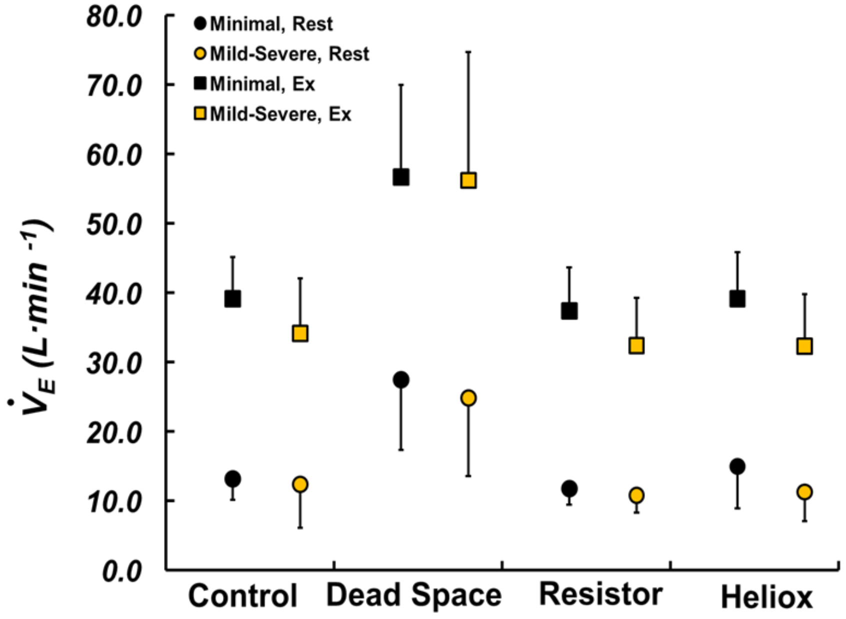
Submaximal Exercise

Subjects cycled at an external work rate of 80 W, which required a $\dot{V}O_2$ of 17 $mL\cdot kg^{-1}\cdot min^{-1}$ (~54% $\dot{V}O_{2peak}$). The work rate was held constant across the challenges, and no differences in $\dot{V}O_2$ were observed (*p*>0.05).

Exercise Ventilation and Breathing Pattern During Breathing Challenges

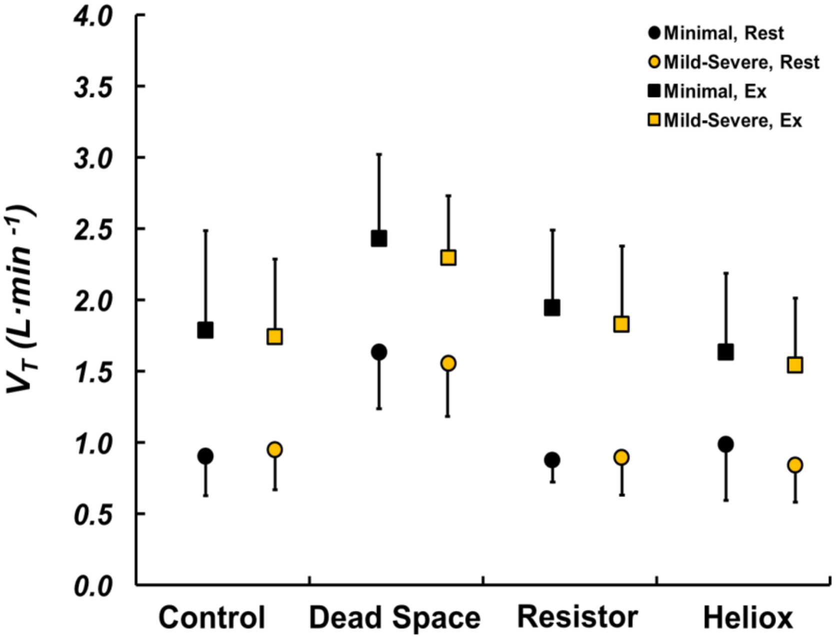
No interaction of group by challenge was observed for $\dot{V}_E$, V_T, and f_B (all $p>0.05$). Independent of group, $\dot{V}_E$ showed a main effect of challenge (Figure 1; $p<0.001$). $\dot{V}_E$ during DS was significantly greater than during all other challenges (all $p>0.01$). In contrast, $\dot{V}_E$ during RES was lower than during CON, DS, and HEL (all $p<0.01$). $\dot{V}_E$ during HEL was similar to that of CON ($p=0.79$).

Figure 1: Ventilation ($\dot{V}_E$) during DS was significantly greater than during all other challenges (mean ± SD, $p<0.01$). There was no main effect of group ($p>0.05$).



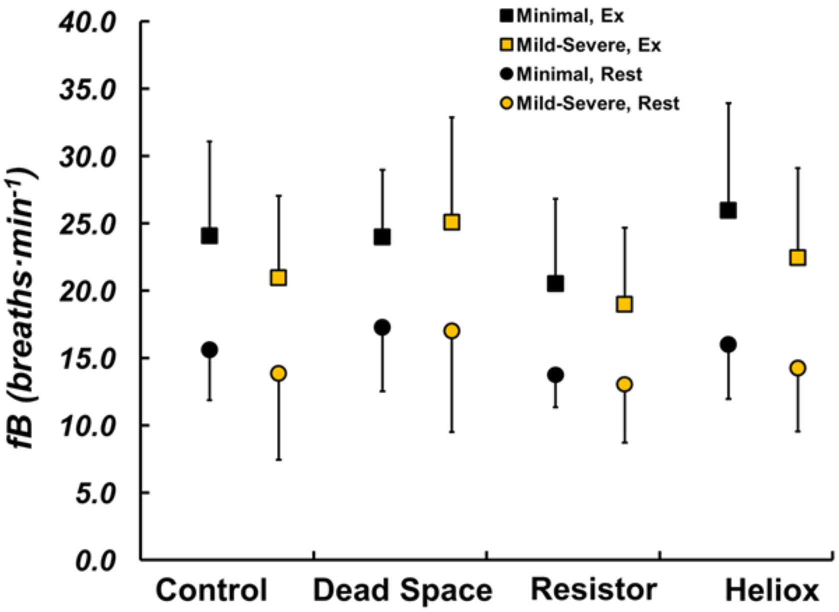
V_T showed a main effect of challenge (Figure 2; $p<0.001$). VT during DS was larger than during all other challenges (all $p<0.001$), and V_T during RES was larger than during HEL ($p<0.05$) but similar to CON ($p=0.045$). No difference was detected between CON and HEL for V_T ($p=0.08$).

Figure 2: Tidal Volume (V_T) during DS was significantly greater than during all other challenges (mean ± SD, $p<0.01$). There was no main effect of group ($p>0.05$).



f_B showed a main effect by challenge (Figure 3; $p<0.001$). f_B during DS was higher than during CON ($p=0.002$) and RES ($p<0.001$) but not HEL ($p=0.30$). f_B during RES was lower than in all other challenges (all $p\leq0.003$). No difference was detected between CON and HEL for f_B ($p=0.052$).

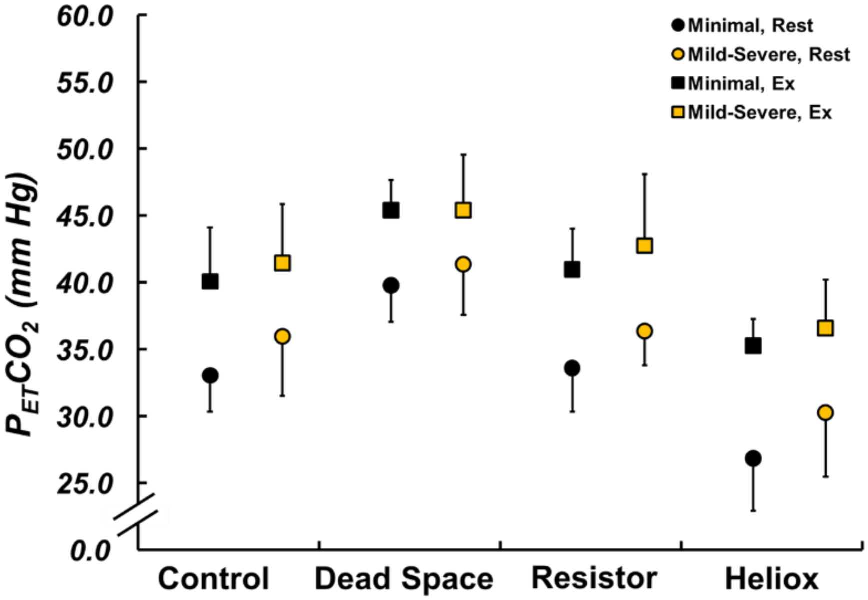
Figure 3: Breathing Frequency (f_B) during RES was lower than in all other challenges (mean ± SD, $p<0.001$). f_B during DS was significantly greater than CON and RES, but not HEL. There was no main effect of group ($p>0.050$).



Adequacy of Exercise Ventilation During Breathing Challenges

No interaction of group by challenge was observed for $P_{ET}CO_2$ (p>0.05). Independent of group, $P_{ET}CO_2$ showed a main effect of challenge (Figure 4; p<0.001). $P_{ET}CO_2$ was higher during DS than during all other challenges (all p<0.001). $P_{ET}CO_2$ was similar during the CON and RES challenges (p>0.05); however, it was lower during HEL compared with CON (p<0.001) and RES (p<0.001).

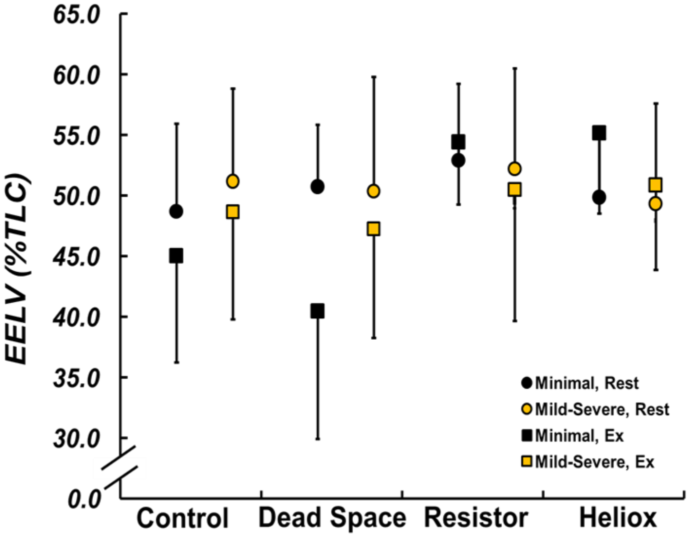
Figure 4: End-tidal CO_2 $P_{ET}CO_2$was higher during DS and lower during HEL (mean ± SD, p<0.001). There was no main effect of group (p>0.05).



OLV at Submaximal Exercise During Breathing Challenges

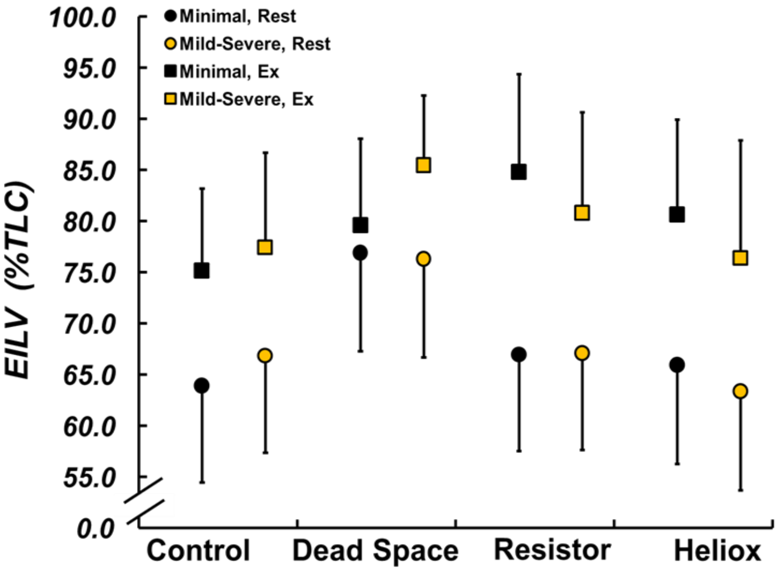
There was a significant challenge by stage by group interaction for EELV ($p=0.015$). Post hoc testing revealed that the MIN group exhibited a decrease in EELV from rest to exercise during the DS challenge (Figure 5; $p<0.001$), whereas the M-S group did not ($p=0.10$). Furthermore, EELV increased from rest to exercise during HEL in MIN group ($p=0.016$), but it stayed the same from rest to exercise in the M-S group ($p=0.367$). A significant challenge by stage interaction also was detected. EELV at rest was similar between CON, DS, and RES ($p>0.05$). EELV decreased from rest to exercise during CON ($p=0.014$) and DS ($p<0.001$), increased during HEL ($p=0.011$), but did not change during RES ($p=0.953$). As a result, exercise EELV during the RES challenge was higher than during CON and DS but not different from HEL. When comparing only the challenges independent of group and stage, EELV was significantly greater during RES than CON ($p<0.004$) and DS ($p<0.001$) but not HEL ($p=0.23$).

Figure 5: End-expiratory lung volumes (EELV) were higher during RES (mean ± SD, $p<0.001$). A challenge by stage interaction indicates a change in EELV from rest to exercise during CON, DS and HEL ($p<0.05$). A challenge by stage by group interaction indicates a greater decrease in EELV for the MIN group during DS, and a great increase during HEL, from rest to exercise ($p<0.05$).. There was no main effect of group ($p>0.05$).



No challenge by stage by group interaction was observed for EILV (*p*=0.09). However, there was a significant challenge by stage interaction (Figure 6; *p*<0.001). EILV at rest was similar between CON, RES, and HEL (all *p*>0.05), but was elevated during DS compared with all other challenges (*p*<0.001). EILV increased from rest to exercise in every challenge (p<0.001). Exercise EILV was similar during DS and RES (*p*=0.90), but both were greater than during CON (both *p*≤0.001). Thus, EILV demonstrated a greater increase from rest to exercise during RES than in DS.

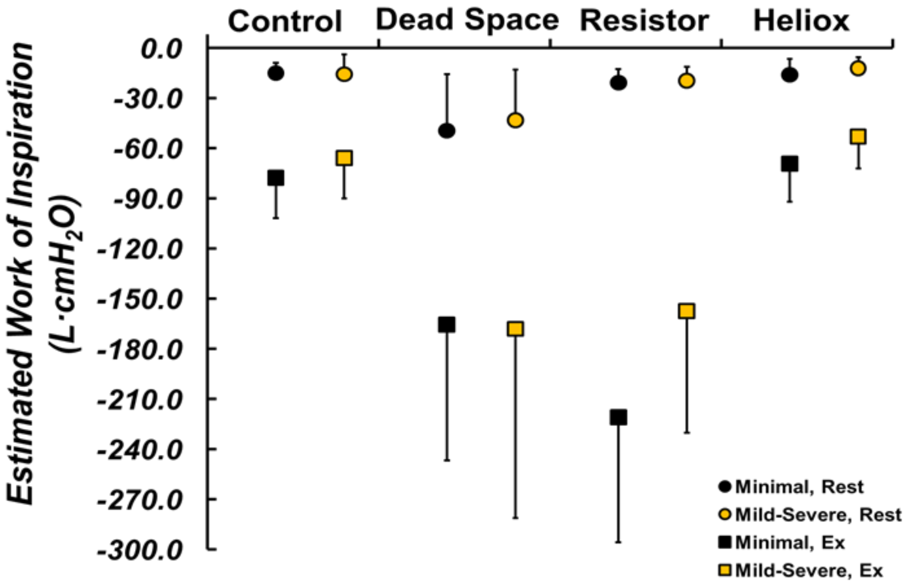
Figure 6: End-inspiratory lung volumes (EILV) were higher during DS and RES (mean ± SD*,* *p*<0.001). A challenge by stage interaction indicates a higher EILV at rest during DS; and at exercise during DS and RES (*p*=0.09). There was no main effect by group (*p*>0.05).



Estimated Work of Breathing During Breathing Challenges

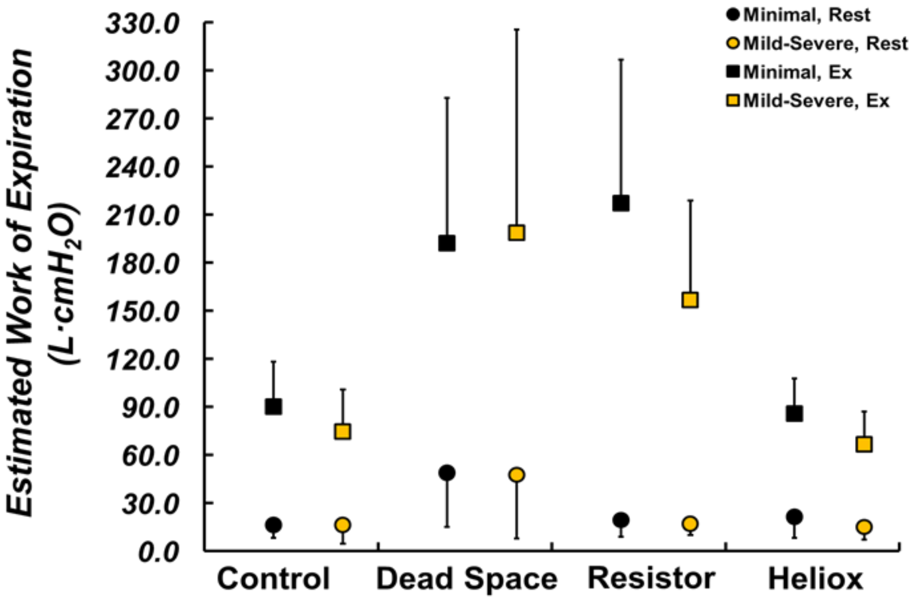
No significant challenge by stage by group interaction was detected for either of the estimated work of breathing during inspiration and expiration (*p*>0.05). However, significant challenge by stage interactions were detected for both (p<0.001). Estimated inspiratory work at rest was greater during DS than during all other challenges (Figure 7; all *p*≤0.001). Estimated inspiratory work at rest also was greater during RES than during CON (*p*=0.01) and HEL (*p*<0.001). No difference was detected between CON and HEL (*p*=0.453). Estimated inspiratory work significantly increased from rest to exercise during every challenge (all *p*<0.001). During exercise, estimated inspiratory work in the DS and RES challenges were similar (*p*=0.218), and greater than during CON and HEL (*p*<0.001), indicating that there was a larger change in inspiratory work from rest to exercise in RS compared with DS. Additionally, the estimated inspiratory work during exercise was less during HEL than during CON (*p*<0.001), demonstrating that inspiratory work changed the least from rest to exercise during HEL. The main effect of challenge revealed that the estimated inspiratory work during CON was greater than during HEL (*p*=0.001), both of which were less than that of DS and RES (all *p*≤0.001), which were not different from each other (*p*=0.859).

Figure 7: Estimated inspiratory work was greater during DS and RES (mean ± SD*, p*<0.001). DS was greater at rest, compared with CON, RES and HEL (p<0.001). There was no main effect of group (*p*>0.05).



Estimated expiratory work at rest was greater during DS than during all other challenges (Figure 8; all *p*≤0.001). No differences were detected between CON, RES, and HEL (all *p*>0.324). Estimated expiratory work significantly increased from rest to exercise during every challenge (all *p*<0.001). During exercise, estimated expiratory work in the DS and RES challenges were similar (*p*=0.679), and greater than during CON and HEL (*p*<0.001), indicating that there was a larger change in expiratory work from rest to exercise in RS compared with DS. Additionally, the estimated expiratory work during exercise was less during HEL than during CON (*p*<0.001), demonstrating that expiratory work changed the least from rest to exercise during HEL. The main effect of challenge revealed that the estimated expiratory work during CON and HEL were similar (*p*=0.095) and less than that of DS and RES (all *p*<0.001), which were not different from each other (*p*=0.153).

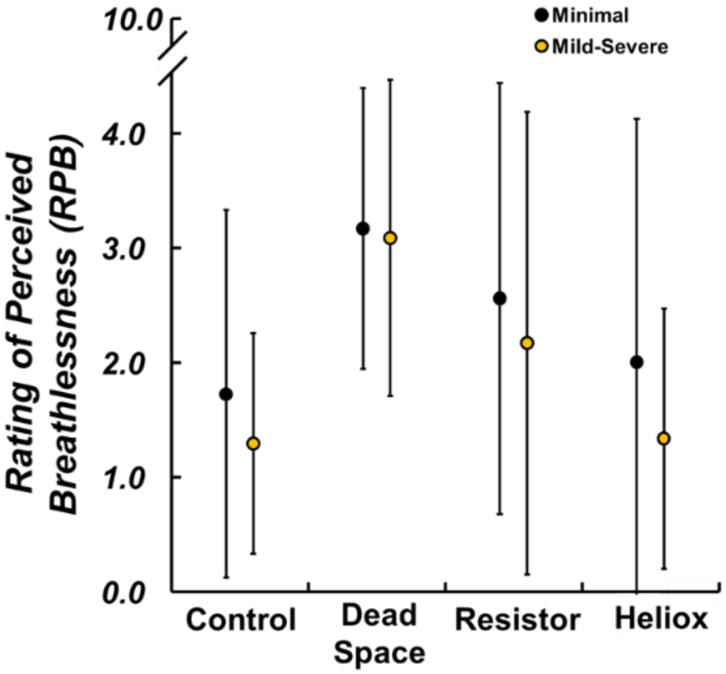
Figure 8. Estimated expiratory work was greater during DS and RES (mean ± SD*, p*<0.001). DS was greater at rest, compared with CON, RES and HEL (*p*<0.001). There was no main effect of group (*p*>0.05).



Perceptual Rating at Submaximal Exercise During Breathing Challenges

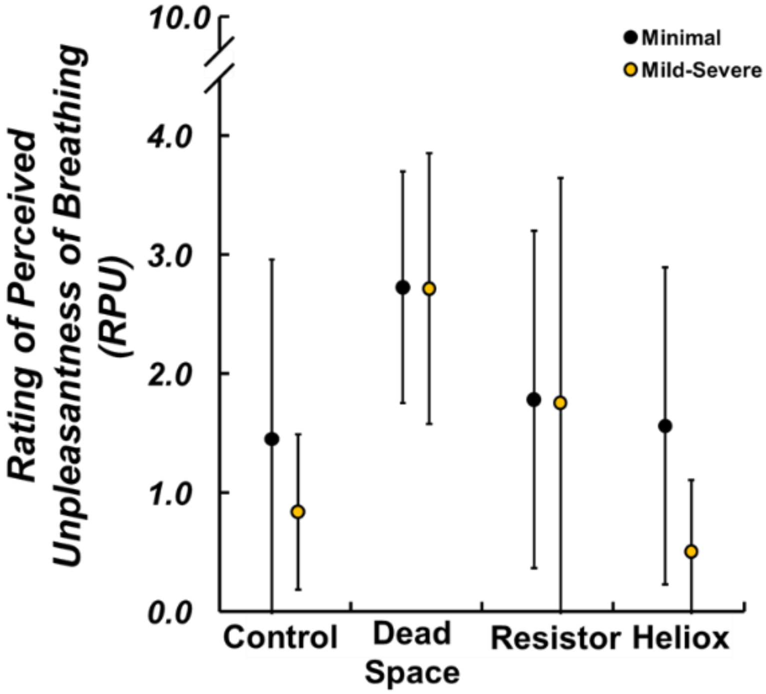
No interaction of group by challenge was observed for RPB. There was a main effect of challenge on RPB (Figure 9; CON: 1.48 ± 1.26, DS: 3.12 ± 1.28, RES: 2.33 ± 1.92, HEL: 1.62 ± 1.62; p=0.001). RPB was greater during DS than during all other challenges (all p<0.05). RPB also was greater during RS than during CON (p=0.011) and HEL (p=0.037).

Figure 9. Ratings of perceived breathlessness (RPB) during exercise (mean ± SD; main effect of group p<0.05). Significant difference during DS and RES and all challenges (p>0.01).



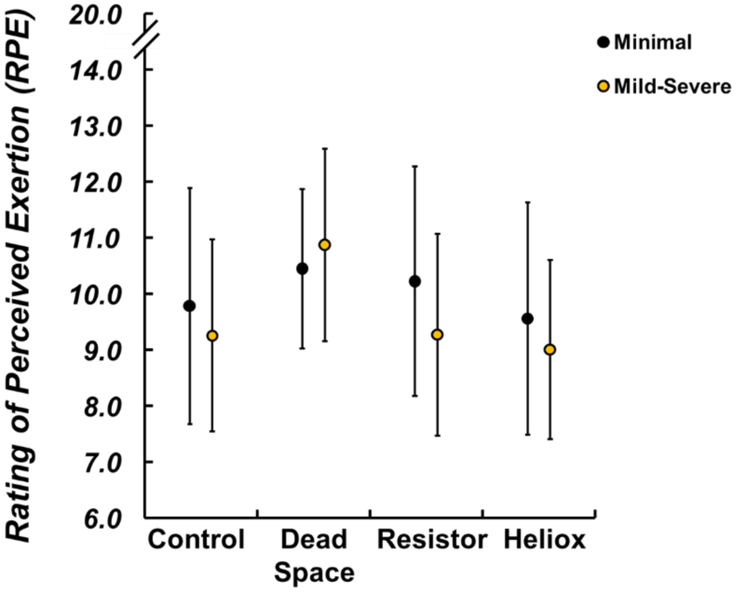
No interaction of group by challenge was observed for RPU. There was a main effect of challenge on RPU (Figure 10; CON: 1.10 ± 1.11, DS: 2.71 ± 1.04, RES: 1.76 ± 1.66, HEL: 0.95 ± 1.09; $p<0.001$). RPU was greater during DS than during all other challenges (all $p<0.03$).

Figure 10. Ratings of perceived unpleasantness of breathing (RPU) during exercise (mean ± SD; main effect of group $p<0.05$). Significant difference during DS and all challenges ($p>0.01$).



No interaction of group by challenge was observed for RPE. There was a main effect of challenge on RPE (Figure 11; CON: 9.48 ± 1.86, DS: 10.69 ± 1.57, RES: 9.68 ± 1.92, HEL: 9.24 ± 1.79; $p=0.003$). RPE during DS was greater than all other conditions (all $p \leq 0.012$). No other differences were detected.

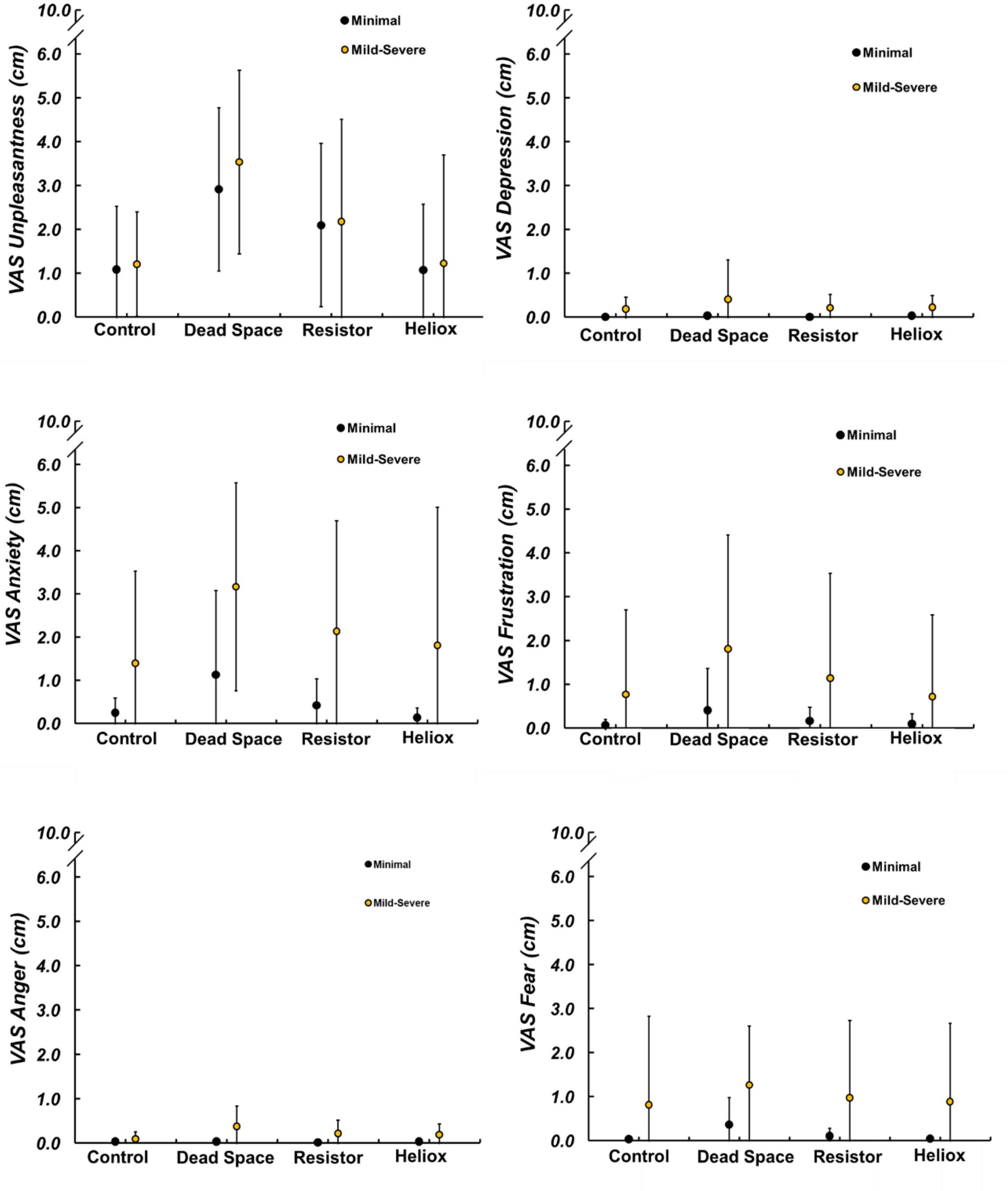
Figure 11. Ratings of perceived exertion (RPE) during exercise (mean ± SD; main effect of group $p<0.05$). Significant difference during DS and all challenges ($p>0.01$).



VAS Ratings at Submaximal Exercise During Breathing Challenges

No interaction of group by challenge was observed for VAS ratings of unpleasantness, depression, anxiety, frustration, anger, and fear (all $p>0.05$). Independent of challenge, VAS anger ratings were greater in the M-S group compared with the MIN group (0.03 ± 0.06 vs. 0.21 ± 0.32, $p=0.037$). While VAS ratings for unpleasantness ($p=0.735$), depression ($p=0.077$), anxiety ($p=0.062$), frustration ($p=0.195$), and fear ($p=0.138$) were similar between the two groups (Figure 12).

Figure 12. Visual Analog Scale (VAS) ratings for unpleasantness and anxiety were different amongst challenges (mean ± SD; main effect of challenge *p*>0.05). Whereas VAS ratings of anger were higher in M-S (main effect of group *p*>0.05; group*challenge interaction *p*>0.05).

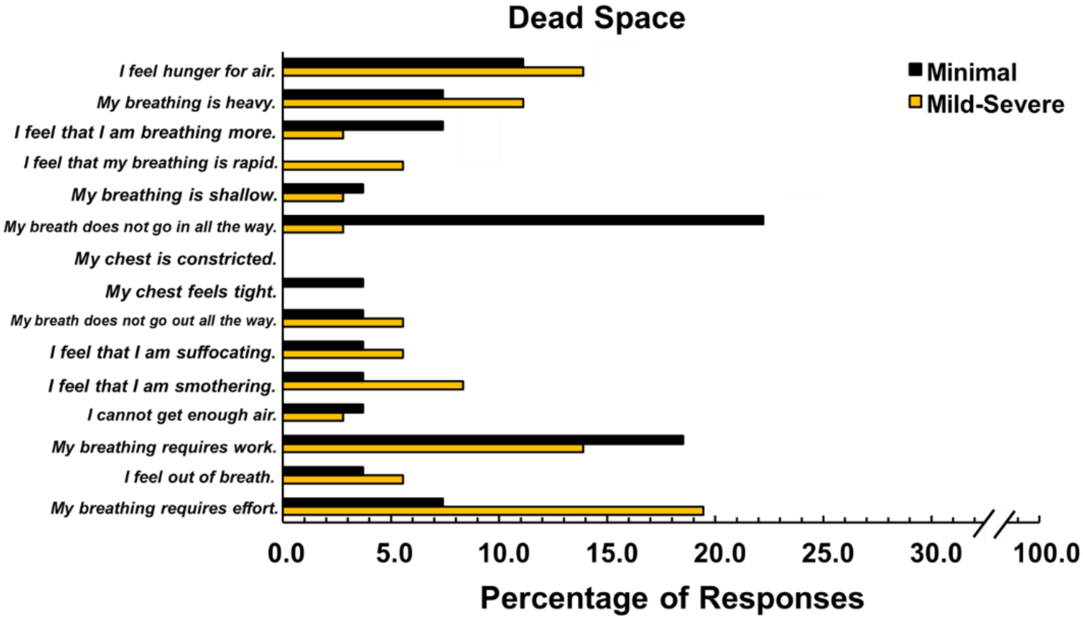


When subjects were pooled (i.e., independent of group), VAS ratings of unpleasantness (UNP: $p<0.000$) and anxiety (ANX: $p<0.001$) were significantly different between the challenges (UNP: CON: 1.15 ± 1.27 cm, DS: 3.27 ± 1.97 cm, RES: 2.13 ± 2.10, HEL: 1.15 ± 2.07; ANX: CON: 0.90 ± 1.70 cm, DS: 2.29 ± 2.40 cm, RES: 1.40 ± 2.13, HEL: 1.09 ± 2.53). Post hoc analyses indicated that DS was rated as being more unpleasant than CON, RES, and HEL (all $p<0.04$). Further, RES was rated more unpleasantly than CON and HEL. VAS ratings of depression were greater following the DS challenge than following all other challenges (all $p<0.001$). VAS ratings of depression, frustration, anger, and fear showed no main effect of challenge (all $p>0.05$).

Dyspnea Descriptors Following the Breathing Challenges

A chi-square analysis was used to analyze the frequency of statements (n=15) selected in the dyspnea questionnaire. Independent of group, subjects indicated statement #4 ("I feel hunger for air") more frequently after DS than after CON and RES. Likewise, independent of group, subjects indicated statement #3 ("I feel that I am breathing more") less frequently after DS than after CON, RES and HEL ($\chi^2(39) = 66.513$, $p=0.004$) (Figure 13). When analyzing the statement selections independent of challenge, both groups selected the same descriptors at a similar frequency ($\chi^2(13) = 7.564$, $p=0.8871$). Yet, while both groups indicated each descriptor with similar frequency when all challenges were pooled, the MIN group selected statement #1 ("My breath does not go in all the way") more frequently following the DS challenge than the M-S group ($\chi^2(13) = 11.804$, $p=0.544$).

Figure 13. The modified dyspnea questionnaire showed a higher frequency of statement #4 independent of group, and a lower frequency of statement #3. The MIN group selected statement #1 more frequently following the DS challenge than the M-S group.



Chapter 5: Discussion

The results of this study largely reveal that the presence of mild trait anxiety does not alter ventilatory dynamics and exertional dyspnea, including both the sensory and affective dimensions, during experimental challenges to breathing. This finding is supported by the lack of differences observed between the two groups for breathing strategy, indices of gas exchange, estimates of respiratory work, operational lung volumes, and ratings of the sensory and affective dimensions of dyspnea across various challenges to breathing, with few exceptions. However, our data do show that the presence of at least mild anxiety prevents a decrease in EELV from rest to exercise in the presence of a chemical stimulus (i.e., CO_2) and larger tidal volume requirement. Additionally, individuals with mild anxiety associate more anger with their DOE when breathing is challenged compared with individuals with minimal anxiety levels. While subjects included in the current study were classified as only having mild anxiety according to the mean GAD-7 score, as opposed to moderate or severe, our findings suggest that worsening anxiety levels will negatively impact operational lung volumes when ventilation is stimulated with CO_2 and/or requires a large V_T. Consequently, this could further amplify exertional dyspnea, especially in overlapping disease states such as chronic obstructive pulmonary disease or obstructive sleep apnea. Thus, it is important to elucidate the relationships between anxiety levels, ventilatory mechanics, and exertional dyspnea in order to design effective treatments and exercise training programs.

Subjects

We included young, healthy adults in both groups for the current investigation. Subjects within both groups were of similar height, weight, BMI and percent body fat. They also are similar to previous studies examining potential effects of anxiety in young adults [24, 31]. All subjects were free of any cardiovascular, metabolic, and pulmonary disease. This ensured that any potential differences we observed to breathing pattern, operational lung volumes, and exertional dyspnea would be attributed to an elevated anxiety level, and not an underlying condition. Our M-S group included more females than did the MIN. However, we do not believe this impacts the main findings of the study.

Psychological Questionnaires

By design, subjects were different in their classification and score on the GAD-7 questionnaire. This questionnaire is frequently used within clinical settings as a screening tool and severity measure for generalized anxiety disorder [71, 81]. Responses to the HADS questionnaire in terms of both anxiety and depression, were greater in the M-S group compared with the MIN group. This was expected given that 1) subjects were grouped based on their underlying trait anxiety levels, and 2) feelings of anxiety and depression are commonly expressed together [82, 83]. Thus, we expected that depression scores as assessed using the HADS could be elevated in the M-S group. However, though the two groups were statistically different in this regard, the mean HADS depression score for the M-S group still was considered normal. While we are unable to determine the potential impact of greater depressive feelings on results from our current subject pool, it can be noted that the comorbidity of the two disorders is a common experience and those who experience this should also be studied. Interestingly, the M-S also expressed greater negative affect, as assessed by the PANAS questionnaire, which could have impacted our findings. For example, affect / emotion / mood is known to affect the quality of dyspnea [14, 31]. Certainly, that the ratings of anger, independent of challenge, were higher in the M-S group could be a manifestation of this difference in the negative affect between the two groups.

Pulmonary Function

Spirometric measurements were not different between the subjects within the two groups. Additionally, all values were considered normal according to the percent predicted values. Thus, we are confident the participants represent otherwise healthy young adults free of respiratory dysfunction.

Exercise Ventilation and Breathing Pattern

The exercise work rate was set at approximately 50% $\dot{V}O_{2peak}$. This allowed us to examine perceptual response at the same relative exercise intensity, as this results in similar perceptual responses between individuals [84-86]. The external work rate did not change between challenges, and as a result, no differences were observed in the metabolic power (i.e., $\dot{V}O_2$) across the challenges. Certain breathing challenges (i.e. DS and RES) caused an alteration in breathing patterns, as indicated by the increase in V_T and $\dot{V}_E$ during DS, and decrease in $\dot{V}_E$ and f_B during RES. These results indicate the subjects were able to alter their breathing strategy in order to achieve effective ventilation necessary for the given $\dot{V}O_2$ that was required.

Operational Lung Volumes

At both rest and exercise, RES caused a higher EELV compared with all other challenges. It can be speculated that the use of the flow-restriction was causing inspiration and expiration to be a longer process, as evidenced by the lower f_B. Although a longer time is required for a full expiration, the respiratory command center has the potential to initiate inspiration after a certain time has elapsed, thus ending expiration prematurely [27-29]. This could prevent individuals from reaching a lower EELV during RES, so in essence, they end up breathing at higher lung volumes.

A reduction in EELV, from rest to exercise, is a normal response, as V_T increases [7, 50-52]. Controversially, HEL caused EELV to increase from rest to exercise, although V_T during exercise is similar in the HEL and CON challenges. This indicates that the HEL caused subjects to breathe at higher lung volumes, compared with CON, even without the need for a larger V_T. The cause for this change in OLV requires further investigation, but can be speculated that it is initiated by the reduction of turbulent flow throughout the airways, thus causing air to move more passively [62, 64].

All subjects indicated a normal increase to EILV with exercise [7, 50-52]. The significantly higher EILV during DS and RES indicated that these challenges caused subjects to shift V_T closer to TLC. This change in OLV is favorable, as it takes advantage of the elastic recoil in the lungs and chest wall, and conserves energy during expiration [52, 59]. As previously mentioned, DS forced subjects to breathe at higher V_T, even at rest; M-S subjects were shown to manipulate their EILV while keeping the exercise EELV similar to at rest. In contrast, the MIN subjects reduced their exercise EELV below resting levels. Thus, these results suggest that the presence of trait anxiety prevents the typically observed reduction in EELV that comes with exercise when CO_2 is presented as a ventilatory stimulus. That the perception of exertional dyspnea was not different between groups during DS despite this difference in OLV could suggest that breathing at a higher lung volume is a coping mechanism to minimize any disturbance to dyspnea. $\dot{V}_E$, breathing pattern, and the estimated WoB were similar between groups. Thus, the shift in OLV cannot be attributed to unique breathing strategies between groups. The group with higher anxiety adopted similar breathing patterns as have been seen in individuals with asthma or obstructive diseases [69, 87]. And this is an aspect to further investigate as these OLV are not energetically favorable and have been noticed to cause higher ratings of dyspnea in patients with asthma and COPD [69, 87].

Estimated Work of Breathing

We observed the estimated inspiratory and expiratory work during exercise was higher in the DS and RES challenges, as expected. This increase in work may be attributed to the evident increase in V_T and $\dot{V}_E$ during DS; as well as the increased flows (i.e., driving pressure) necessary to overcome the flow resistor during RES. However, the estimated WoB *at rest* during RES was similar with CON. At rest, subjects do not require a higher $\dot{V}_E$, so V_T can remain relatively low, and higher pressures are not yet needed to push the V_T through the flow resistors. Once exercise began, they were forced to drastically increase WoB to achieve proper $\dot{V}_E$. Interestingly, the WoB was similar between DS and RES, as well as between CON and HEL. Although the work required for breathing was expectedly reduced during HEL [63, 64]; subjects did not show an adjustment to WoB, in order to conserve energy.

Perceptual Responses

Though unintended, we observed that the estimated inspiratory and expiratory work during exercise was similar between the DS and RES challenges. This allows us to speculate on the components involved in the perceptual responses. Accordingly, we found that RPB and RPU was greater during DS than RES. That the DS challenge yielded greater $P_{ET}CO_2$ but comparable respiratory work indicates that the presence of CO_2 increases RPU and is additive to respiratory work in the elevated RPB. We also observed that RPB during RES was greater, but that RPU during RES was similar, compared with CON. These results suggest that the increased respiratory work does not alter the unpleasantness associated with dyspnea. It does, however, elevate the sensory aspect of exertional dyspnea. Additionally, RPE was greater during DS than all other challenges, which were otherwise similar. Thus, RPE is influenced by high levels of ventilation, but not respiratory work, and/or the unpleasantness associated with exertional dyspnea. In contrast to previous literature, perceptual ratings of DOE intensity did not differ between individuals with varying levels of anxiety [14, 16, 17, 38].

Conclusion

In conclusion, these results indicate that breathing challenges do not lead to differences in breathing patterns or perceptual ratings between young adults with varying levels of anxiety. However, we can support that breathing challenges cause an overall change in OLV, and the measurements mentioned above. The most profound finding of this study is that although DS and RES caused similar WoB, DS elicited higher perceptual ratings of breathlessness, unpleasantness of breathing and overall exertion. Which leads us to the idea that the addition of a chemical stimulus (i.e. increased blood-gas tension), individuals are more prone to discomfort and an increased sense of exertion. Further studies are warranted to investigate additional individuals with moderate-severe levels of anxiety; and further unravel the relationship between one's ventilatory dynamics, anxiety level and DOE.

Appendices

Subject Information/Demographics

Table 4: Subject information and demographics.

ID	GRP	RACE	AGE	DOB	SEX	HT (cm)	WT (kg)	WT:HT	BMI	%BF	HxDOE	snore-subjective	snore-objective	Hx Asth	Smoke HX	ExFreq (per/wk)	ExDuration (min)
2	Minimal	Hispanic/White	19	12/26/1997	M	165.9	88.4	0.533	32.1	.	Y	Y	Y	Y	N	.	.
3	Mild	White	25	12/13/1991	F	170.0	87.2	0.513	30.2	.	.	.	.	.	N	.	.
4	Mild	White	21	9/23/1996	F	163.2	59.0	0.362	22.2	30.40	.	.	.	.	N	.	.
5	Minimal	White	20	5/20/1997	F	175.5	60.5	0.345	19.6	22.20	.	.	.	.	N	.	.
6	Mild	Hispanic	20	5/25/1997	F	157.0	49.0	0.312	19.9	17.40	.	.	.	.	N	.	.
7	Minimal	Hispanic	20	12/18/1997	M	180.0	92.6	0.514	28.6	27.80	N	N	Y	N	N	2-3	
8	Moderate	Asian	21	7/29/1996	M	171.4	60.7	0.354	20.6	13.70	N	N	Y	Y	N	.	.
9	Moderate	White	21	7/30/1996	M	183.2	78.0	0.426	23.2	.	N	N	N	N	N	2	30.0
10	Mild	White	22	7/7/1995	F	160.7	68.0	0.423	26.3	36.40	N	Y	Y	N	N	2-3	20.0
11	Mild	White	23	12/21/1994	M	189.0	82.4	0.436	23.1	17.00	N	N	Y	N	N	3-4	60-90
12	Minimal	White	20	1/21/1999	F	170.0	84.8	0.499	29.3	40.20	N	N	N	N	N	1	45.0
13	Minimal	White	20	4/1/1998	F	162.0	57.4	0.354	21.9	31.40	N	N	N	N	N	1	.
14	Mild	White	19	12/23/1999	F	168.9	60.5	0.358	21.2	26.80	N	N	N	N	N	.	.
17	Mild	Asian/White	18	7/26/2000	F	165.4	64.7	0.391	23.7	26.00	N	N	N	N	N	3	60.0
18	Mild	White	19	5/21/1999	F	161.5	73.5	0.455	28.2	34.80	N	N	N	N	N	1	30.0
20	Mild	AA	19	3/29/2000	F	171.6	78.3	0.456	26.6	33.10	N	N	N	N	N	<1	30m
21	Severe	White	21	9/24/1998	F	173.3	78.5	0.453	26.1	31.40	N	Y	Y	N	N	.	.
22	Minimal	Hispanic	21	12/26/1997	F	166.2	57.1	0.344	20.7	21.40	N	N	N	N	N	1-2	30-40
25	Minimal	White	21	2/6/1998	M	180.0	75.5	0.419	23.3	15.00	N	N	N	N	N	5	20.0
26	Minimal	White	20	8/11/1999	F	167.0	66.5	0.398	23.9	26.40	N	N	N	N	N	3	60.0
28	Minimal	White	21	7/31/1998	M	173.0	79.4	0.459	26.5	12.80	N	N	N	N	N	3	60.0

Psychological Questionnaire Data

Table 5: Subjects psychological questionnaire scores.

ID	GRP	ASI	GAD-7	HADS - Anx	HADS - Dep	SDS	PANAS - PAS	PANAS - NAS
2	Minimal	8	0	2	2	19	28	10
3	Mild	17	5	7	5	19	.	.
4	Mild	3	7	2	2	12	34	15
5	Minimal	35	1	2	1	16	41	10
6	Mild	30	9	9	2	18	28	11
7	Minimal	17	4	5	4	20	32	18
8	Moderate	18	10	5	10	.	28	25
9	Moderate	10	11	10	5	16	36	13
10	Mild	15	7	5	4	19	29	13
11	Mild	11	6	7	4	22	37	23
12	Minimal	19	1	4	3	21	43	10
13	Minimal	14	2	2	3	19	38	11
14	Mild	29	9	9	11	15	24	15
17	Mild	35	8	9	9	15	28	28
18	Mild	22	8	7	5	17	41	17
20	Mild	34	9	14	6	15	42	18
21	Severe	15	16	7	9	21	30	12
22	Minimal	31	1	3	3	22	25	11
25	Minimal	8	1	4	2	18	43	11
26	Minimal	4	2	3	1	19	46	14
28	Minimal	10	3	5	1	16	39	16

Pulmonary Function Testing Data

Table 6: Subject FVC, FEV_1 results.

ID	GRP	AGE	HT (cm)	WT (kg)	SEX	SPIRO	FVC	FVC PP NHANES	FVC P Knudson	FVC PP Knudson	FEV1	FEV1 PP NHANES	FEV1 P Knudson	FEV1 PP Knudson	FEV1/FVC	FEV1/FVC PP Knudson	25-75%	25-75% PP
2	Minimal	19.0	165.9	88.4	M	Spiro	4.5	96.2	4.3	105.0	3.7	93.5	3.7	101.1	82.7	96.3	3.8	82.8
3	Mild	25.0	170.0	87.2	F	Spiro	5.1	123.9	3.9	131.0	4.5	127.4	3.3	134.8	87.7	102.9	5.7	150.5
4	Mild	21.0	163.2	59.0	F	Spiro	4.3	113.7	3.7	116.7	3.8	115.8	3.2	118.8	88.4	101.8	4.5	121.9
5	Minimal	20.0	175.5	60.5	F	Spiro	3.6	82.5	4.2	85.5	3.1	81.3	3.6	85.5	85.2	100.0	3.3	81.4
6	Mild	20.0	157.0	49.0	F	Spiro	3.9	108.1	3.5	112.6	3.4	107.6	3.0	112.0	87.7	99.5	3.7	97.9
7	Minimal	20.0	180.0	92.6	M	Spiro	5.8	100.0	5.2	110.5	4.6	92.1	4.5	101.2	79.0	91.6	4.2	77.2
8	Moderate	21.0	171.4	60.7	M	Spiro	4.4	86.0	4.8	92.7	3.7	86.1	4.1	90.7	84.2	97.8	4.4	93.8
9	Moderate	21.0	183.2	78.0	M	Spiro	6.5	110.1	5.5	119.5	6.2	125.2	4.7	130.6	94.3	109.3	7.8	152.9
10	Mild	22.0	160.7	68.0	F	Spiro	4.0	88.4	3.6	111.2	3.3	86.6	3.1	105.5	82.7	94.9	3.4	79.3
11	Mild	23.0	189.0	82.4	M	Spiro	6.8	106.6	6.0	113.3	5.3	101.7	5.2	102.6	78.3	90.6	4.8	91.2
12	Minimal	20.0	170.0	84.8	F	Spiro	4.6	112.4	4.0	114.9	4.0	111.4	3.4	116.4	87.0	101.2	4.6	116.9
13	Minimal	20.0	162.0	57.4	F	Spiro	4.0	107.2	3.7	109.6	3.3	100.9	3.2	104.1	82.8	95.0	3.4	91.2
14	Mild	19.0	168.9	60.5	F	Spiro	4.0	98.3	3.9	102.9	3.7	102.0	3.5	104.7	90.8	101.8	4.3	109.2
17	Mild	18.0	165.4	64.7	F	Spiro	4.0	103.6	3.7	109.2	3.6	103.2	3.3	107.8	88.1	98.8	4.6	117.9
18	Mild	19.0	161.5	73.5	F	Spiro	4.6	122.4	3.6	127.5	3.6	109.4	3.2	112.2	78.9	88.0	3.3	88.3
20	Mild	19.0	171.6	78.3	F	Spiro	3.5	94.1	4.0	86.6	2.9	91.3	3.6	81.6	83.9	94.2	3.6	91.5
21	Severe	21.0	173.3	78.5	F	Spiro	4.8	112.3	4.1	116.8	4.0	107.0	3.5	112.2	82.0	96.1	4.1	101.3
22	Minimal	21.0	166.2	57.1	F	Spiro	4.1	102.8	3.8	107.3	3.7	106.9	3.3	113.0	91.0	105.4	5.2	130.5
25	Minimal	21.0	180.0	75.5	M	Spiro	5.5	95.5	5.3	103.7	4.9	102.1	4.6	106.8	88.9	103.0	5.6	112.4
26	Minimal	20.0	167.0	66.5	F	Spiro	4.1	102.3	3.9	105.3	3.9	112.3	3.4	116.9	95.8	111.0	5.1	132.2
28	Minimal	21.0	173.0	79.4	M	Spiro	5.8	109.8	4.9	119.0	4.8	109.0	4.2	114.9	83.1	96.5	5.3	111.2

Table 7: Subjects PEF, MVV, fB, and FRC results.

ID	GRP	PEF	PEF PP	FET100%	MVV	MVV PP	fb	TLC	TLC P G/B	TLC PP G/B	TLC P ATS/ERS	TLC PP ATS/ERS	Vtg	FRC PL	FRC %TLC	Pred FRC %TLC	PP FRC %TLC	FRC Pred G/B	FRC PP G/B	FRC P ATS/ERS	FRC PP ATS/ERS
2	Minimal	9.9	112.0	8.1	185.0	110.8	110.0	6.0	6.1	98.3	6.2	97.8	2.7	2.3	37.3	47.8	78.1	2.7	83.1	3.0	76.0
3	Mild	10.2	137.4	8.1	147.0	103.5	130.0	6.6	5.7	115.0	5.4	121.6	2.4	2.2	33.1	49.1	67.3	2.8	78.3	2.8	77.1
4	Mild	7.6	110.7	9.5	146.0	109.8	95.0	5.7	5.2	109.5	5.0	115.1	3.4	2.7	46.5	48.5	95.9	2.9	91.7	2.7	99.6
5	Minimal	7.6	100.3	4.1	.	.	.	.	6.2	.	5.8	.	.	.	.	48.3	.	3.5	.	3.0	.
6	Mild	6.3	95.9	7.1	104.0	81.9	110.0	5.2	4.8	109.8	4.6	114.2	2.9	2.5	47.8	48.3	98.9	2.7	90.7	2.5	98.3
7	Minimal	9.0	83.9	7.7	145.0	73.2	100.0	7.5	7.5	101.2	7.3	103.3	3.9	3.2	42.2	48.0	87.9	3.6	88.1	3.3	96.4
8	Moderate	9.9	104.3	7.7	195.0	112.7	110.0	6.3	6.6	94.9	6.6	95.1	3.4	2.9	45.6	48.2	94.6	3.7	77.0	3.1	92.3
9	Moderate	10.3	97.7	10.9	133.0	67.5	130.0	9.5	7.7	122.2	7.6	125.1	5.4	4.7	50.1	48.2	104.0	4.2	114.0	3.4	140.0
10	Mild	7.8	90.9	8.0	108.0	71.1	90.0	5.1	5.0	102.1	4.8	106.7	2.4	1.7	33.1	48.6	68.1	2.6	64.8	2.6	64.8
11	Mild	9.4	83.7	7.4	180.0	86.5	100.0	9.0	8.3	109.4	8.0	112.6	4.5	4.0	44.2	48.6	91.0	4.5	89.4	3.5	112.9
12	Minimal	7.7	105.6	7.1	130.0	90.3	105.0	5.7	5.8	98.7	5.4	105.0	3.6	3.0	52.7	48.3	109.1	2.8	106.3	2.8	106.3
13	Minimal	7.5	109.9	7.3	131.0	99.2	70.0	5.3	5.1	102.6	4.9	107.7	2.5	2.3	42.8	48.3	88.6	2.9	78.7	2.6	85.3
14	Mild	8.1	113.2	7.2	96.0	67.1	105.0	5.5	5.7	95.9	5.4	102.1	2.7	2.7	48.5	48.1	100.8	3.2	83.3	2.8	94.7
17	Mild	7.2	104.2	9.5	131.0	95.6	105.0	4.9	5.4	89.9	5.1	95.3	2.9	2.6	53.2	48.0	110.8	2.9	88.7	2.7	95.4
18	Mild	7.1	105.5	7.2	125.0	94.7	100.0	5.7	5.1	111.0	4.9	116.7	3.0	2.5	44.8	48.1	93.1	2.6	99.1	2.6	96.6
20	Mild	6.5	87.1	10.7	117.0	90.7	105.0	4.5	5.9	75.2	5.5	80.4	1.9	1.4	30.9	48.1	64.2	3.0	45.5	2.9	48.0
21	Severe	6.5	86.7	10.8	161.0	108.1	85.0	6.2	6.0	102.6	5.6	109.6	3.4	2.9	46.9	48.5	96.7	3.1	93.3	2.9	100.0
22	Minimal	6.8	94.6	7.1	128.0	91.4	100.0	5.6	5.5	102.8	5.2	108.6	3.2	2.6	45.7	48.5	94.4	3.1	83.1	2.7	93.8
25	Minimal	11.1	108.0	7.2	217.0	113.6	105.0	7.2	7.4	96.3	7.3	98.1	4.4	4.1	56.6	48.2	117.4	4.0	101.6	3.3	122.4
26	Minimal	7.0	98.9	7.2	135.0	96.4	80.0	5.7	5.5	102.2	5.2	108.3	3.3	2.6	46.1	48.3	95.4	3.0	87.6	2.8	94.5
28	Minimal	11.3	116.1	10.6	184.0	104.0	105.0	8.0	6.8	118.4	6.7	119.1	4.1	3.6	44.5	48.2	92.3	3.4	105.1	3.1	113.6

Table 8: Subjects lung volume and pressure results.

ID	GRP	ERV	RV	RV P ATS/ERS	RV PP ATS/ERS	RV/TLC	VC	VC PP	IC	IC P ATS/ERS	IC PP ATS/ERS	Raw	Raw PP	Gaw	Gaw PP	sRaw	sRaw PP	sGaw	sGaw PP
2	Minimal	1.0	1.3	1.4	93.0	21.0	4.8	101.5	3.8	3.2	117.8	1.8	104.9	0.6	85.0	4.8	99.9	0.2	100.5
3	Mild	0.7	1.5	1.5	99.1	22.2	5.1	123.9	4.4	2.6	170.2	0.8	56.4	1.3	193.5	466.8	12221.0	0.5	209.4
4	Mild	1.1	1.5	1.3	117.3	26.4	4.2	111.1	3.1	2.3	133.1	1.7	133.3	0.6	86.1	5.7	149.3	0.2	68.4
5	Minimal	1.6	.	1.5	.	.	.	.	2.7	2.8	95.4	.	.	.	.	.	.	.	.
6	Mild	0.9	1.5	1.2	130.8	29.1	3.7	102.8	2.7	2.0	134.0	1.2	86.5	0.8	126.8	3.5	90.9	0.3	110.8
7	Minimal	1.0	2.0	1.6	130.1	27.1	5.5	95.5	4.4	4.0	108.9	1.8	152.5	0.6	63.1	6.9	154.8	0.1	65.0
8	Moderate	1.2	1.5	1.5	104.2	24.5	4.8	92.2	3.4	3.5	97.6	1.9	152.9	0.6	64.3	6.3	142.4	0.2	73.6
9	Moderate	1.5	3.0	1.6	181.2	31.3	6.5	109.4	4.7	4.2	113.1	0.5	52.1	1.8	186.0	2.9	68.1	0.3	147.9
10	Mild	0.4	1.1	1.3	89.4	21.9	4.0	89.1	3.4	2.2	156.6	1.3	74.5	0.8	120.6	3.1	64.2	0.3	157.5
11	Mild	1.6	2.3	1.8	129.8	25.2	6.8	106.6	5.0	4.5	112.4	1.7	174.7	0.6	56.0	7.5	174.5	0.1	57.5
12	Minimal	1.6	1.3	1.4	96.1	23.5	4.4	106.3	2.7	2.6	103.6	2.1	164.8	0.5	73.3	7.7	202.2	0.1	52.2
13	Minimal	1.1	1.1	1.3	86.2	20.5	4.2	112.0	3.0	2.3	134.0	3.2	247.8	0.3	44.8	8.1	212.8	0.1	47.4
14	Mild	1.2	1.5	1.4	107.3	26.7	4.0	98.0	2.8	2.6	110.2	2.9	243.9	0.4	46.7	7.6	201.5	0.1	50.4
17	Mild	1.6	1.0	1.3	74.4	19.5	3.9	101.0	2.3	2.4	95.1	1.5	73.2	0.7	480.0	4.4	75.2	0.2	133.3
18	Mild	1.4	1.1	1.2	88.8	19.2	4.6	122.4	3.1	2.2	140.4	2.6	177.9	0.4	62.0	7.8	203.7	0.1	49.7
20	Mild	0.5	0.9	1.4	60.3	19.1	3.6	97.3	3.1	2.7	115.0	2.5	195.2	0.4	57.2	4.7	123.6	0.2	85.6
21	Severe	1.6	1.2	1.5	83.0	19.7	5.0	115.6	3.3	2.7	119.9	2.4	197.5	0.4	56.6	8.0	210.8	0.1	48.1
22	Minimal	1.1	1.4	1.3	101.7	24.3	4.3	106.5	3.1	2.4	125.4	1.2	101.9	0.8	109.0	3.9	103.4	0.3	98.8
25	Minimal	2.6	1.3	1.6	81.8	18.2	5.9	102.1	3.1	4.0	77.8	1.5	135.2	0.7	71.3	6.5	148.2	0.2	68.1
26	Minimal	1.1	1.4	1.3	105.5	25.0	4.3	106.3	3.1	2.5	123.7	1.3	104.8	0.8	108.6	4.4	115.0	0.2	90.2
28	Minimal	1.4	2.0	1.5	132.1	24.7	6.1	114.6	4.5	3.6	123.9	3.1	237.2	0.4	47.1	12.4	274.1	0.1	42.6

Incremental Exercise Testing Data (Aerobic Capacity Test)

Table 9: Subject (2-4) aerobic capacity test results.

ID	Stage	Power	V_E IET	V_T IET	f_B IET	VO_2 IET	VO_2 ml/kg IET	Peak VO_2 IET	VCO_2 IET	RER IET	HR IET	RPB IET	RPU IET	RPE IET
2	Rest	0.0	11.9	0.7	16.3	0.4	4.2	2.8	0.3	0.7	69.0	.	.	.
2	Average	0.0	11.7	0.7	16.1	0.4	4.0	2.8	0.3	0.7	67.7	0.0	0.0	.
2	60W	60.0	26.7	0.9	28.7	1.0	10.9	2.8	0.7	0.7	110.0	0.0	0.0	6.0
2	120W	120.0	45.0	1.3	33.5	1.6	17.6	2.8	1.3	0.8	150.0	0.5	1.0	9.0
2	Max	240.0	113.6	2.4	47.1	2.8	31.1	2.8	3.2	1.2	188.0	7.0	7.0	17.0
3	Rest	0.0	9.5	0.7	13.8	0.3	3.9	2.2	0.2	0.7	80.0	.	.	.
3	Average	0.0	14.4	0.9	16.3	0.4	4.8	2.2	0.3	0.8	83.5	2.0	0.0	.
3	60W	60.0	20.8	1.1	18.7	0.8	9.0	2.2	0.6	0.8	114.0	2.0	0.0	7.0
3	120W	120.0	35.6	1.7	21.0	1.4	16.3	2.2	1.2	0.8	150.0	3.0	0.0	12.0
3	Max	180.0	78.5	2.3	34.7	2.2	25.5	2.2	2.3	1.0	188.0	9.0	3.0	18.0
4	Rest	0.0	6.7	0.8	8.1	0.2	4.1	2.0	0.2	0.8	81.5	.	.	.
4	Average	0.0	7.4	0.9	8.2	0.3	4.7	2.0	0.2	0.8	84.8	0.0	0.0	6.0
4	60W	60.0	23.1	1.3	17.5	0.9	15.7	2.0	0.8	0.8	130.0	0.0	0.0	7.0
4	120W	120.0	42.5	2.0	21.6	1.4	23.9	2.0	1.5	1.1	166.0	3.0	1.0	12.0
4	Max	180.0	76.0	2.2	34.3	2.0	33.5	2.0	2.4	1.2	187.5	7.0	4.0	18.0

Table 10: Subject (5-7) aerobic capacity test results.

ID	Stage	Power	V_E IET	V_T IET	f_B IET	VO_2 IET	VO_2 ml/kg IET	Peak VO_2 IET	VCO_2 IET	RER IET	HR IET	RPB IET	RPU IET	RPE IET
5	Rest	0.0	12.4	0.8	15.8	0.4	6.0	1.8	0.3	0.9	.	.	.	.
5	Average	0.0	11.7	0.7	17.8	0.3	5.3	1.8	0.3	0.9	.	0.5	0.5	.
5	60W	60.0	21.3	1.2	17.4	0.8	12.8	1.8	0.7	0.8	.	1.0	1.0	9.0
5	120W	120.0	37.8	1.6	24.1	1.3	20.9	1.8	1.3	1.0	.	4.0	4.0	14.0
5	Max	180.0	64.8	1.8	35.7	1.8	29.8	1.8	2.1	1.1	.	9.0	9.0	19.0
6	Rest	0.0	6.4	0.7	9.6	0.2	4.4	1.6	0.2	0.8	93.0	.	.	.
6	Average	0.0	7.5	0.6	12.1	0.3	5.4	1.6	0.2	0.7	96.0	0.0	0.0	.
6	60W	60.0	17.6	1.0	18.2	0.7	14.7	1.6	0.5	0.7	127.0	0.5	0.0	7.0
6	120W	120.0	37.3	1.4	26.9	1.3	25.9	1.6	1.3	1.0	166.0	2.0	2.0	11.0
6	Max	160.0	59.0	1.7	35.4	1.6	33.3	1.6	1.9	1.2	181.0	7.0	6.0	17.0
7	Rest	0.0	12.1	0.9	14.2	0.4	4.3	2.7	0.3	0.8	84.5	.	.	.
7	Average	0.0	12.3	0.8	14.8	0.4	4.4	2.7	0.3	0.8	86.8	.	.	.
7	60W	60.0	26.2	1.1	23.3	1.0	10.5	2.7	0.8	0.8	110.0	0.5	0.5	6.0
7	120W	120.0	37.7	1.6	24.0	1.4	15.2	2.7	1.2	0.9	123.0	1.0	1.0	8.0
7	Max	240.0	94.8	2.7	35.7	2.7	29.4	2.7	3.0	1.1	183.0	5.0	6.0	13.0

Table 11: Subject (8-10) aerobic capacity test results.

ID	Stage	Power	V_E IET	V_T IET	f_B IET	VO_2 IET	VO_2 ml/kg IET	Peak VO_2 IET	VCO_2 IET	RER IET	HR IET	RPB IET	RPU IET	RPE IET
8	Rest	0.0	8.0	0.5	15.6	0.2	3.4	1.9	0.2	0.8	67.0	.	.	.
8	Average	0.0	9.5	0.6	16.2	0.3	4.4	1.9	0.2	0.7	69.3	0.0	0.0	.
8	60W	60.0	27.1	1.1	25.5	0.9	14.5	1.9	0.7	0.8	103.5	0.5	0.5	9.0
8	120W	120.0	54.3	1.6	33.7	1.4	23.6	1.9	1.5	1.1	133.0	3.0	1.0	8.0
8	Max	180.0	86.8	1.8	49.1	1.9	30.7	1.9	2.1	1.1	159.0	5.0	5.0	15.0
9	Rest	0.0	12.9	0.6	20.7	0.3	4.4	3.1	0.2	0.7	82.0	.	.	.
9	Average	0.0	12.6	1.2	9.2	0.3	4.4	3.1	0.3	0.8	85.3	0.0	0.0	.
9	60W	60.0	26.0	1.0	25.3	1.0	13.0	3.1	0.7	0.7	109.0	1.0	1.0	9.0
9	120W	120.0	39.2	1.5	26.6	1.7	21.3	3.1	1.3	0.8	129.0	2.0	2.0	10.0
9	Max	240.0	103.8	2.4	43.8	3.1	39.9	3.1	3.4	1.1	156.0	9.0	10.0	18.0
10	Rest	0.0	3.6	0.5	7.1	0.1	2.0	1.7	0.1	0.8	81.0	.	.	.
10	Average	0.0	3.8	0.5	8.4	0.1	2.1	1.7	0.1	0.8	81.3	3.0	3.0	.
10	60W	60.0	17.5	0.9	19.1	0.7	10.0	1.7	0.5	0.8	113.0	5.0	5.0	13.0
10	120W	120.0	36.4	1.4	25.2	1.3	19.6	1.7	1.3	1.0	151.0	7.0	7.0	17.0
10	Max	180.0	60.2	1.9	32.3	1.7	25.5	1.7	1.9	1.1	182.0	10.0	10.0	20.0

Table 12: Subject (11-13) aerobic capacity test results.

ID	Stage	Power	V_E IET	V_T IET	f_B IET	VO_2 IET	VO_2 ml/kg IET	Peak VO_2 IET	VCO_2 IET	RER IET	HR IET	RPB IET	RPU IET	RPE IET
11	**Rest**	0.0	10.8	1.2	8.9	0.4	4.5	3.1	0.3	0.8	88.0	.	.	.
11	**Average**	0.0	17.5	1.6	10.7	0.6	7.1	3.1	0.5	0.8	97.0	0.0	0.0	.
11	**60W**	60.0	30.3	1.8	16.9	1.3	15.5	3.1	1.0	0.8	114.0	0.0	0.0	6.0
11	**120W**	120.0	43.7	2.1	20.3	1.6	19.9	3.1	1.5	0.9	135.0	0.5	0.5	7.0
11	**Max**	240.0	139.2	3.2	43.9	3.1	38.1	3.1	3.9	1.2	181.0	10.0	10.0	20.0
12	**Rest**	0.0	13.3	1.2	11.4	0.5	5.4	2.1	0.4	0.8	102.5	.	.	.
12	**Average**	0.0	11.2	1.0	10.9	0.3	4.0	2.1	0.3	0.9	103.3	3.0	0.0	.
12	**60W**	60.0	24.0	1.1	22.0	1.0	12.1	2.1	0.7	0.7	191.5	3.0	0.5	8.0
12	**120W**	120.0	42.0	1.5	27.5	1.6	18.3	2.1	1.5	1.0	171.0	3.0	1.0	9.0
12	**Max**	160.0	65.1	1.8	35.6	2.1	24.6	2.1	2.3	1.1	213.0	2.0	5.0	13.0
13	**Rest**	0.0	7.9	0.7	10.5	0.0	-0.1	2.1	0.0	0.2	0.0	.	.	.
13	**Average**	0.0	7.7	0.7	10.5	0.0	-0.1	2.1	0.0	0.2	0.0	0.0	0.0	.
13	**60W**	60.0	23.2	0.9	25.1	0.9	15.2	2.1	0.7	0.8	60.0	0.5	0.5	8.0
13	**120W**	120.0	42.2	1.3	32.4	1.4	24.7	2.1	1.4	1.0	120.0	2.0	2.0	11.0
13	**Max**	180.0	75.9	1.7	45.2	2.1	36.6	2.1	2.4	1.1	179.9	8.0	8.0	17.0

Table 13: Subject (14-18) aerobic capacity test results.

ID	Stage	Power	V_E IET	V_T IET	f_B IET	VO_2 IET	VO_2 ml/kg IET	Peak VO_2 IET	VCO_2 IET	RER IET	HR IET	RPB IET	RPU IET	RPE IET
14	**Rest**	0.0	11.6	0.9	12.8	0.3	4.4	2.1	0.3	1.1	101.5	.	.	.
14	**Average**	0.0	11.0	0.9	12.5	0.3	4.3	2.1	0.3	1.0	101.7	0.0	0.0	.
14	**60W**	60.0	19.0	1.1	17.7	0.8	12.5	2.1	0.6	0.8	129.0	2.0	2.0	11.0
14	**120W**	120.0	39.1	1.4	28.9	1.3	21.9	2.1	1.3	1.0	160.0	4.0	4.0	13.0
14	**Max**	200.0	63.6	1.5	43.3	1.5	24.2	2.1	1.8	1.2	180.0	8.0	7.0	17.0
17	**Rest**	0.0	9.7	0.7	13.7	0.3	4.9	1.7	0.3	0.8	75.0	.	.	.
17	**Average**	0.0	9.3	0.7	13.4	0.3	4.6	1.7	0.3	0.9	75.0	1.0	0.0	.
17	**60W**	60.0	22.5	1.2	18.9	0.9	14.4	1.7	0.8	0.8	114.0	2.0	1.0	8.0
17	**120W**	120.0	39.8	1.7	24.0	1.4	20.9	1.7	1.4	1.1	156.0	3.0	2.0	10.0
17	**Max**	160.0	61.8	1.9	31.9	1.7	27.0	1.7	2.0	1.2	177.0	5.0	4.0	15.0
18	**Rest**	0.0	8.6	0.5	17.3	0.3	3.5	1.7	0.2	0.7	71.0	.	.	.
18	**Average**	0.0	9.0	0.5	18.0	0.3	3.7	1.7	0.2	0.7	74.7	2.0	2.0	.
18	**60W**	60.0	23.7	1.2	20.4	0.9	12.1	1.7	0.7	0.8	88.0	4.0	3.0	12.0
18	**120W**	120.0	47.0	1.5	30.9	1.3	18.3	1.7	1.3	1.0	29.0	7.0	6.0	161.0
18	**Max**	140.0	63.7	1.8	34.6	1.7	22.5	1.7	1.7	1.0	29.0	10.0	8.0	19.0

Table 14: Subject (20-22) aerobic capacity test results.

ID	Stage	Power	V_E IET	V_T IET	f_B IET	VO_2 IET	VO_2 ml/kg IET	Peak VO_2 IET	VCO_2 IET	RER IET	HR IET	RPB IET	RPU IET	RPE IET
20	**Rest**	0.0	9.6	0.4	21.8	0.3	3.7	2.4	0.3	0.9	77.0	.	.	.
20	**Average**	0.0	9.4	0.4	21.1	0.3	3.2	2.4	0.2	1.0	77.0	0.0	0.0	.
20	**60W**	60.0	28.2	1.3	22.3	1.1	13.8	2.4	0.9	0.8	77.0	4.0	4.0	12.0
20	**120W**	120.0	37.7	1.4	26.5	1.3	16.2	2.4	1.3	1.0	77.0	.	.	.
20	**Max**	180.0	100.2	2.1	47.7	2.4	30.9	2.4	3.0	1.2	92.0	2.0	9.0	18.0
21	**Rest**	0.0	20.2	1.6	12.3	0.3	3.2	2.1	0.4	1.6	95.5	.	.	.
21	**Average**	0.0	18.3	1.4	13.5	0.3	3.4	2.1	0.4	1.4	96.2	0.5	0.5	.
21	**60W**	60.0	37.8	2.1	17.8	1.3	15.9	2.1	1.1	0.8	123.5	0.5	0.5	7.0
21	**120W**	120.0	68.5	2.3	29.5	2.0	25.3	2.1	2.1	1.0	163.0	3.0	1.0	13.0
21	**Max**	140.0	81.8	2.5	33.2	2.1	27.2	2.1	2.4	1.1	172.0	5.0	2.0	15.0
22	**Rest**	0.0	6.8	0.6	14.9	0.3	5.3	2.2	0.2	0.6	70.0	.	.	.
22	**Average**	0.0	7.5	0.7	14.2	0.3	5.2	2.2	0.2	0.7	67.3	0.0	0.0	.
22	**60W**	60.0	19.8	1.1	18.1	0.9	15.3	2.2	0.6	0.7	97.0	0.0	0.0	7.0
22	**120W**	120.0	32.8	1.3	25.1	1.4	25.3	2.2	1.1	0.8	136.0	1.0	0.0	10.0
22	**Max**	200.0	73.0	2.0	36.7	2.2	39.1	2.2	2.4	1.1	173.0	6.0	7.0	12.0

Table 15: Subject (25-28) aerobic capacity test results.

ID	Stage	Power	V_E IET	V_T IET	f_B IET	VO_2 IET	VO_2 ml/kg IET	Peak VO_2 IET	VCO_2 IET	RER IET	HR IET	RPB IET	RPU IET	RPE IET
25	**Rest**	0.0	9.5	0.7	0.8	0.3	3.9	2.7	0.2	0.8	87.0	.	.	.
25	**Average**	0.0	10.9	0.8	0.8	0.3	4.5	2.7	0.3	0.8	86.7	0.0	0.0	.
25	**60W**	60.0	28.0	1.8	0.8	1.1	14.9	2.7	0.9	0.8	120.5	0.5	0.0	7.0
25	**120W**	120.0	39.8	2.3	0.9	1.5	19.6	2.7	1.3	0.9	133.0	1.0	0.5	8.0
25	**120W**	120.0	50.7	2.8	0.9	2.0	26.1	2.7	1.8	0.9	154.0	4.0	3.0	11.0
25	**Max**	160.0	74.6	3.2	1.0	2.7	36.3	2.7	2.7	1.0	181.0	9.0	8.0	20.0
26	**Rest**	0.0	12.3	0.9	0.9	0.4	5.6	2.0	0.3	0.9	94.0	.	.	.
26	**Average**	0.0	10.9	0.9	0.9	0.3	5.0	2.0	0.3	0.9	93.7	1.0	0.0	.
26	**60W**	60.0	25.2	1.6	0.9	0.9	13.4	2.0	0.8	0.9	113.5	3.0	2.0	11.0
26	**120W**	120.0	42.0	1.8	1.0	1.4	21.0	2.0	1.3	1.0	141.5	5.0	5.0	16.0
26	**Max**	160.0	64.5	1.9	1.0	2.0	29.4	2.0	2.0	1.0	171.0	9.0	8.0	17.0
28	**Rest**	0.0	11.8	0.9	12.5	0.4	4.5	3.4	0.3	0.8	81.8	.	.	.
28	**Average**	0.0	11.7	1.0	12.1	0.4	4.6	3.4	0.3	0.8	80.4	3.0	2.0	.
28	**60W**	60.0	24.4	1.4	17.9	1.0	13.1	3.4	0.7	0.7	102.3	3.0	2.0	8.0
28	**120W**	120.0	36.1	2.0	17.7	1.6	20.0	3.4	1.2	0.7	111.8	4.0	3.0	10.0
28	**Max**	270.0	101.9	2.9	35.3	3.4	42.4	3.4	3.4	1.0	177.2	10.0	10.0	20.0

Submaximal Exercise Testing Data – Control

Table 16: Subject (2-8) metabolic, dyspnea and ventilation, during control challenge, results.

ID	Stage	VO_2 ml/kg 50%	RER 50%	HR 50%	RPB 50%	RPU 50%	RPE 50%	MinVi Mech 50%	MinVe Mech 50%	V_T Mech 50%	fB Mech 50%	IC Mech 50%	EELV %TLC 50%	EILV %TLC 50%
2	MeanRest	3.8	1.0	55.5	0.0	0.0	6.0	-20.9	20.2	1.3	16.8	3.1	48.0	69.9
2	MeanEx	15.1	1.0	134.5	0.0	0.0	7.0	-43.9	44.3	1.3	34.9	3.4	43.7	64.8
3	MeanRest	3.3	0.8	80.3	0.5	0.0	.	-11.1	10.9	0.9	12.5	3.7	44.0	57.5
3	MeanEx	12.5	0.8	121.3	1.0	0.0	7.0	-28.2	28.0	1.7	17.2	3.7	43.2	68.8
4	MeanRest	2.2	0.8	102.8	0.0	0.0	.	-8.1	8.1	0.9	8.9	2.0	64.8	80.4
4	MeanEx	16.0	1.0	139.0	0.5	0.0	9.0	-32.5	32.7	1.5	21.1	2.4	57.5	84.5
5	MeanRest	2.4	0.8	94.0	.	.	.	-13.0	12.7	0.7	18.8	1.9	.	.
5	MeanEx	11.8	0.9	127.5	.	.	.	-29.5	29.0	1.3	22.7	2.3	.	.
6	MeanRest	4.7	0.7	91.8	0.0	0.0	.	-9.8	10.0	0.8	11.7	2.5	52.2	68.4
6	MeanEx	17.9	0.9	138.0	0.5	0.5	9.0	-26.6	26.6	1.3	20.7	2.5	52.6	77.3
7	MeanRest	4.3	0.7	85.0	0.0	0.0	6.0	-12.7	12.7	0.9	14.2	4.3	42.5	54.4
7	MeanEx	17.2	0.9	135.0	1.0	1.0	8.0	-43.7	43.9	2.0	21.8	4.1	45.9	72.8
8	MeanRest	4.3	0.8	63.7	0.0	0.0	.	-11.5	11.8	0.7	17.1	2.7	57.4	68.4
8	MeanEx	17.5	1.0	99.4	2.0	2.0	11.0	-42.3	42.6	1.5	29.0	2.6	58.5	82.0

Table 17: Subject (9-17) metabolic, dyspnea and ventilation, during control challenge, results.

ID	Stage	VO_2 ml/kg 50%	RER 50%	HR 50%	RPB 50%	RPU 50%	RPE 50%	MinVi Mech 50%	MinVe Mech 50%	V_T Mech 50%	fB Mech 50%	IC Mech 50%	EELV %TLC 50%	EILV %TLC 50%
9	MeanRest	7.6	0.8	70.7	0.5	1.0	.	-31.0	31.3	1.1	29.5	4.1	56.1	67.6
9	MeanEx	21.1	1.0	117.2	1.0	1.0	9.0	-47.8	47.8	1.6	30.0	3.9	58.3	75.1
10	MeanRest	2.2	0.8	80.0	3.0	0.0	.	-9.6	9.7	1.0	9.8	2.8	45.2	64.7
10	MeanEx	11.0	0.9	126.5	3.0	0.5	11.0	-26.6	26.1	1.4	19.5	2.6	48.6	75.2
11	MeanRest	4.2	0.8	83.8	0.0	0.0	.	-10.2	10.3	1.3	8.0	4.4	50.7	65.3
11	MeanEx	20.5	0.9	124.0	0.5	0.5	7.0	-39.2	39.5	2.8	14.4	4.5	50.3	80.9
12	MeanRest	3.5	0.9	100.7	5.0	1.0	.	-13.2	13.1	0.7	19.9	3.0	47.5	59.3
12	MeanEx	14.6	1.0	140.8	5.0	3.0	12.0	-36.8	36.7	1.3	27.5	3.1	46.4	69.8
13	MeanRest	5.5	0.8	.	0.0	0.0	,	-12.8	12.7	0.6	20.4	2.7	48.5	60.3
13	MeanEx	23.1	0.9	.	2.0	1.0	12.0	-42.4	42.7	1.3	32.6	2.9	44.5	69.4
14	MeanRest	4.6	0.9	101.3	0.0	0.0	.	-10.0	10.0	1.2	8.4	2.2	59.2	81.0
14	MeanEx	18.5	0.9	150.3	2.0	2.0	11.0	-31.1	30.5	1.8	17.6	2.4	55.4	87.6
17	MeanRest	4.3	0.8	106.3	0.5	0.5	.	-8.9	9.0	0.9	9.9	2.2	55.6	74.9
17	MeanEx	15.7	0.9	153.5	0.5	0.5	7.0	-24.1	24.3	2.1	11.5	2.5	48.4	91.9

Table 18: Subject (18-28) metabolic, dyspnea and ventilation, during control challenge, results.

ID	Stage	VO_2 ml/kg 50%	RER 50%	HR 50%	RPB 50%	RPU 50%	RPE 50%	MinVi Mech 50%	MinVe Mech 50%	V_T Mech 50%	fB Mech 50%	IC Mech 50%	EELV %TLC 50%	EILV %TLC 50%
18	MeanRest	3.2	0.8	82.0	0.5	1.0	.	-10.5	10.1	0.6	17.6	3.4	40.0	50.1
18	MeanEx	12.3	0.9	114.2	.	1.0	8.0	-30.7	30.7	1.1	26.7	3.2	43.7	64.0
20	MeanRest	2.5	1.0	81.7	4.0	0.0	.	-11.2	11.0	0.5	21.2	2.6	42.7	54.4
20	MeanEx	14.0	0.9	126.5	3.0	1.0	11.0	-35.9	36.1	1.3	27.3	3.1	31.2	60.9
21	MeanRest	2.9	1.2	99.7	0.0	0.0	.	-16.1	16.1	1.4	11.3	3.4	45.9	69.1
21	MeanEx	17.3	0.8	133.0	1.0	1.0	11.0	-44.1	44.8	2.8	16.2	4.0	35.6	80.7
22	MeanRest	4.1	1.4	68.5	0.0	0.0	.	-10.2	10.6	0.9	12.3	2.3	59.3	74.4
22	MeanEx	22.2	1.2	114.8	0.0	0.0	11.0	-33.1	33.5	1.4	23.2	2.5	55.6	81.3
25	MeanRest	5.1	0.8	90.8	0.0	0.0	.	-14.3	14.5	1.4	10.5	3.3	53.9	73.3
25	MeanEx	19.1	0.9	127.5	0.5	0.0	7.0	-37.9	38.0	3.2	12.1	3.9	45.4	89.9
26	MeanRest	4.0	0.8	77.7	1.0	1.0	.	-9.1	9.6	0.9	11.1	2.6	53.8	69.1
26	MeanEx	18.3	0.8	122.5	3.0	4.0	12.0	-35.9	36.4	1.5	23.7	2.7	52.8	79.9
28	MeanRest	4.6	0.7	83.2	0.0	0.0	.	-11.6	11.9	0.8	16.2	3.6	36.0	50.3
28	MeanEx	25.3	0.8	128.3	2.0	3.0	9.0	-47.8	47.6	2.7	17.9	4.2	25.9	73.0

Table 19: Subject (2-8) breathing mechanics, during control challenge, results.

ID	Stage	Ti Mech 50%	Te Mech 50%	Ti/T tot Mech 50%	PetCO2 Mech 50%	Avg Pi Mech 50%	Avg Pe Mech 50%	EstInspWork	EstExpWork	P_P/VT	PaCO2	PAO2	VD	VD/VT	VA	VA/VO2	VA/VCO2
2	MeanRest	1.7	2.1	45.0	28.7	-1.3	1.6	-29.8	35.9	2.5	29.1	101.7	0.7	0.5	9.6	26.9	29.6
2	MeanEx	0.8	1.0	44.4	38.1	-2.0	2.3	-91.0	102.3	4.0	35.9	96.2	0.4	0.3	30.1	23.2	24.0
3	MeanRest	1.6	3.3	33.8	37.1	-1.9	1.6	-20.9	17.5	4.5	35.1	89.1	0.4	0.4	6.3	18.6	24.6
3	MeanEx	1.6	2.0	43.7	42.7	-2.5	2.3	-71.3	65.8	3.4	39.2	85.4	0.6	0.3	18.5	17.2	22.0
4	MeanRest	1.7	5.2	25.5	35.0	-1.3	1.4	-10.4	10.9	3.7	33.7	91.8	0.6	0.7	2.5	20.4	25.6
4	MeanEx	1.2	1.7	40.7	39.5	-2.0	1.9	-66.2	61.1	3.0	36.9	94.3	0.6	0.4	20.8	22.5	23.4
5	MeanRest	1.1	2.3	32.6	30.3	-0.8	1.6	-10.0	20.3	4.2	30.3	97.8	0.5	0.7	3.6	22.8	28.5
5	MeanEx	1.1	1.7	39.9	37.4	-1.3	2.3	-37.5	68.2	3.1	35.4	94.5	0.5	0.4	17.6	21.3	24.4
6	MeanRest	1.8	3.4	34.4	35.9	-1.1	1.5	-10.9	14.6	3.5	34.3	87.2	0.5	0.6	4.1	17.7	25.2
6	MeanEx	1.3	1.7	43.3	41.4	-1.5	1.8	-40.5	47.4	2.9	38.3	90.4	0.4	0.3	18.3	19.8	22.5
7	MeanRest	1.5	2.8	34.4	36.8	-1.2	1.0	-15.3	12.3	2.6	35.0	86.8	0.3	0.3	8.3	17.5	24.7
7	MeanEx	1.2	1.6	42.2	40.1	-2.2	2.2	-96.3	94.7	2.4	37.3	91.7	0.6	0.3	30.7	20.3	23.1
8	MeanRest	1.1	2.4	31.7	34.9	-1.1	0.9	-13.6	11.3	3.4	33.6	89.0	0.4	0.6	5.1	19.1	25.7
8	MeanEx	0.9	1.2	42.7	35.4	-2.0	2.5	-86.2	106.3	3.9	33.9	96.3	0.6	0.4	26.3	24.1	25.4

Table 20: Subject (9-17) breathing mechanics, during control challenge, results.

ID	Stage	Ti Mech 50%	Te Mech 50%	Ti/T tot Mech 50%	PetCO2 Mech 50%	Avg Pi Mech 50%	Avg Pe Mech 50%	EstInspWork	EstExpWork	P_P/VT	PaCO2	PAO2	VD	VD/VT	VA	VA/VO2	VA/VCO2
9	MeanRest	0.9	1.1	45.7	37.9	-1.6	1.6	-50.9	50.4	3.4	35.7	92.3	0.7	0.7	10.3	20.1	24.2
9	MeanEx	0.9	1.1	46.9	41.4	-2.1	2.3	-102.0	109.4	3.0	38.2	95.4	0.4	0.2	36.7	22.4	22.6
10	MeanRest	2.7	3.6	43.3	36.6	-0.9	0.9	-9.0	8.9	2.1	34.8	90.5	0.7	0.7	2.8	19.3	24.8
10	MeanEx	1.5	1.7	46.8	39.4	-1.4	1.6	-37.2	42.1	2.5	36.8	91.9	0.6	0.4	14.9	20.3	23.5
11	MeanRest	2.2	5.8	28.2	35.7	-0.9	0.9	-10.0	9.7	1.5	34.2	90.6	0.4	0.3	7.1	19.6	25.2
11	MeanEx	1.9	2.3	44.6	41.7	-1.8	2.1	-70.4	82.8	1.6	38.4	88.8	0.6	0.2	31.4	19.1	22.4
12	MeanRest	1.3	1.8	41.0	31.2	-1.1	1.2	-15.4	16.2	3.8	31.0	97.4	0.3	0.4	7.5	23.5	27.9
12	MeanEx	0.9	1.3	42.1	38.0	-1.9	2.2	-68.8	80.6	3.3	35.8	96.4	0.3	0.2	29.2	23.4	24.1
13	MeanRest	1.2	1.8	38.7	33.4	-1.0	1.0	-13.2	13.1	4.1	32.5	92.8	0.3	0.5	6.3	20.7	26.5
13	MeanEx	0.9	1.0	47.7	35.3	-1.8	2.3	-76.1	98.3	3.7	33.9	95.4	0.4	0.3	31.3	22.7	25.4
14	MeanRest	3.5	3.8	47.7	36.2	-1.2	1.4	-12.4	14.3	3.2	34.5	95.2	0.4	0.3	6.8	22.3	25.0
14	MeanEx	1.7	1.8	47.8	48.0	-1.8	2.2	-54.5	69.8	2.6	42.9	87.2	0.6	0.4	19.8	18.5	20.1
17	MeanRest	2.1	4.3	33.0	43.9	-1.3	1.1	-12.0	9.9	2.8	40.0	84.0	0.5	0.5	4.2	16.7	21.6
17	MeanEx	2.2	3.1	41.6	49.0	-1.7	2.2	-40.8	54.9	2.2	43.7	83.0	0.7	0.3	16.3	16.5	19.7

Table 21: Subject (18-28) breathing mechanics, during control challenge, results.

ID	Stage	Ti Mech 50%	Te Mech 50%	Ti/T tot Mech 50%	PetCO2 Mech 50%	Avg Pi Mech 50%	Avg Pe Mech 50%	EstInspWork	EstExpWork	P_P/VT	PaCO2	PAO2	VD	VD/VT	VA	VA/VO2	VA/VCO2
18	MeanRest	1.4	2.1	40.0	35.7	-0.9	0.9	-9.3	9.0	3.9	34.2	89.1	0.3	0.5	4.9	18.0	25.2
18	MeanEx	1.0	1.2	44.9	38.0	-1.5	1.9	-46.9	57.7	4.0	35.8	95.5	0.4	0.3	20.7	21.8	24.1
20	MeanRest	1.2	1.6	43.1	38.4	-0.9	1.1	-10.2	12.6	4.7	36.1	100.1	0.3	0.5	5.3	24.7	23.9
20	MeanEx	1.0	1.2	43.4	45.3	-1.9	2.0	-67.0	73.7	3.2	41.1	91.2	0.5	0.4	21.5	19.2	21.0
21	MeanRest	2.3	3.0	43.0	24.0	-1.5	1.5	-23.6	23.9	2.4	25.8	111.0	0.2	0.2	13.4	37.5	33.5
21	MeanEx	1.7	2.1	44.5	35.3	-2.4	2.7	-110.7	123.4	2.2	33.9	92.8	1.0	0.4	28.6	19.7	25.5
22	MeanRest	2.1	2.8	43.1	32.1	-1.0	1.0	-10.3	11.0	2.5	31.6	109.8	0.2	0.3	7.9	39.6	27.3
22	MeanEx	1.1	1.5	43.5	41.6	-1.6	1.7	-53.1	58.4	2.6	38.4	100.3	0.1	0.1	30.9	27.1	22.5
25	MeanRest	2.3	3.5	39.2	35.2	-1.2	0.9	-18.3	13.3	1.7	33.8	93.9	0.6	0.4	8.6	19.8	25.5
25	MeanEx	2.0	3.1	39.2	46.6	-2.4	2.0	-91.5	77.1	1.8	42.0	88.4	1.1	0.3	25.1	17.8	20.6
26	MeanRest	1.8	3.7	33.5	33.7	-1.1	1.0	-10.3	9.5	2.8	32.7	96.3	0.3	0.4	5.9	20.6	26.4
26	MeanEx	1.0	1.5	41.4	36.8	-2.0	2.0	-72.0	74.3	2.9	35.0	94.5	0.5	0.3	24.0	19.8	24.7
28	MeanRest	1.6	2.5	39.2	35.8	-1.2	1.1	-15.4	14.4	4.5	34.2	88.4	0.4	0.5	6.5	17.8	25.2
28	MeanEx	1.5	1.8	45.5	46.3	-2.4	3.2	-116.9	154.8	2.3	41.7	84.7	0.9	0.3	32.3	16.9	20.7

Submaximal Exercise Testing Data – Dead Space

Table 22: Subject (2-8) metabolic, dyspnea and ventilation, during dead space challenge, results.

ID	Stage	VO_2 ml/kg 50%	RER 50%	HR 50%	RPB 50%	RPU 50%	RPE 50%	MinVi Mech 50%	MinVe Mech 50%	V_T Mech 50%	fB Mech 50%	IC Mech 50%	EELV %TLC 50%	EILV %TLC 50%
2	MeanRest	3.8	0.7	83.8	0.5	0.5	6.0	-33.3	33.4	1.8	18.5	3.4	43.9	74.5
2	MeanEx	16.4	0.9	146.0	2.0	2.0	11.0	-85.2	85.5	3.0	28.9	4.7	22.1	71.6
3	MeanRest	2.2	0.7	81.7	3.0	2.0	.	-22.2	22.2	1.4	15.5	4.2	36.7	58.5
3	MeanEx	13.2	0.8	131.0	3.0	3.0	12.0	-43.0	43.0	2.4	18.3	4.1	38.3	74.3
4	MeanRest	2.2	0.8	91.0	0.0	0.0	.	-18.6	18.4	1.4	13.2	2.2	62.5	87.4
4	MeanEx	15.2	1.0	145.0	1.0	0.5	.	-51.9	52.0	2.3	23.2	2.7	53.3	93.0
6	MeanRest	3.8	0.6	97.5	2.0	2.0	.	-20.7	20.7	1.2	17.2	2.2	57.4	80.7
6	MeanEx	19.6	0.8	145.5	4.0	4.0	9.0	-47.9	48.1	1.9	25.6	2.3	55.4	91.5
7	MeanRest	3.1	0.6	90.0	0.5	0.5	6.0	-28.4	28.4	1.6	17.5	3.7	50.6	72.1
7	MeanEx	16.4	0.9	137.5	4.0	3.0	10.0	-67.5	67.6	2.7	25.2	4.5	40.5	76.4
8	MeanRest	3.6	0.6	81.5	3.0	1.0	.	-40.9	41.3	1.5	28.3	2.6	59.0	82.2
8	MeanEx	17.7	0.9	118.5	2.0	4.0	11.0	-88.5	88.5	2.3	38.8	3.1	50.7	87.0

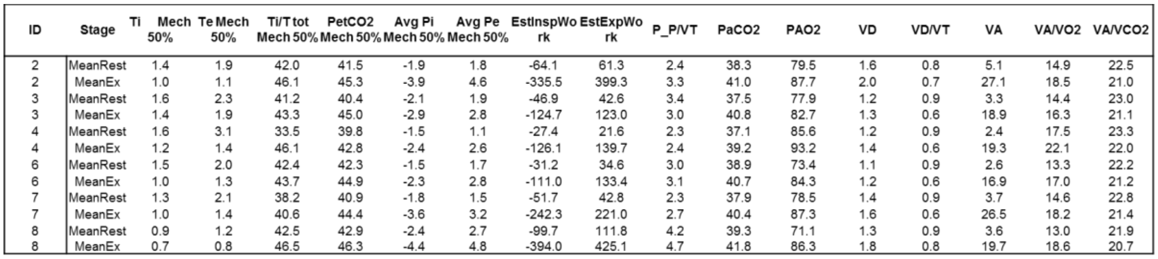
Table 23: Subject (9-17) metabolic, dyspnea and ventilation, during dead space challenge, results.

ID	Stage	VO_2 ml/kg 50%	RER 50%	HR 50%	RPB 50%	RPU 50%	RPE 50%	MinVi Mech 50%	MinVe Mech 50%	V_T Mech 50%	fB Mech 50%	IC Mech 50%	EELV %TLC 50%	EILV %TLC 50%
9	MeanRest	4.4	0.7	90.3	1.0	1.0	.	-51.8	51.7	1.9	28.0	4.0	57.6	77.4
9	MeanEx	19.8	0.8	131.2	4.0	3.0	12.0	-96.8	96.4	2.7	36.5	3.8	59.8	87.9
10	MeanRest	3.5	0.7	84.7	4.0	0.5	.	-12.8	12.7	2.0	6.3	3.0	42.5	82.3
10	MeanEx	13.4	0.8	128.0	5.0	3.0	13.0	-50.4	50.7	1.7	30.2	2.6	48.7	81.4
11	MeanRest	4.3	0.7	76.3	2.0	3.0	.	-19.6	19.9	2.0	10.0	3.5	60.8	83.1
11	MeanEx	19.7	0.9	125.5	4.0	4.0	12.0	-59.6	59.4	2.7	22.3	3.8	58.0	87.6
12	MeanRest	2.8	0.7	87.7	4.0	2.0	.	-51.5	51.7	2.1	25.2	3.2	44.2	80.2
12	MeanEx	12.6	0.9	150.0	4.0	3.0	11.0	-51.6	51.9	2.1	25.2	3.2	44.7	80.8
13	MeanRest	4.6	0.6	93.8	0.0	0.0	.	-23.2	23.1	1.0	22.8	2.7	48.0	67.2
13	MeanEx	24.4	0.9	151.0	4.0	3.0	12.0	-61.4	61.4	1.9	31.9	3.8	28.8	65.3
14	MeanRest	3.0	0.6	98.3	2.0	2.0	.	-20.1	19.0	1.1	18.7	2.4	56.9	76.7
14	MeanEx	16.8	0.9	141.6	3.0	3.0	12.0	-41.1	40.8	2.0	19.9	2.8	48.4	85.9
17	MeanRest	4.7	0.7	74.7	1.0	1.0	.	-14.8	14.8	2.1	7.1	2.7	44.9	87.5
17	MeanEx	15.6	0.8	128.3	1.0	1.0	7.0	-32.9	33.0	2.5	13.3	2.7	45.3	96.4

Table 24: Subject (18-28) metabolic, dyspnea and ventilation, during dead space challenge, results.

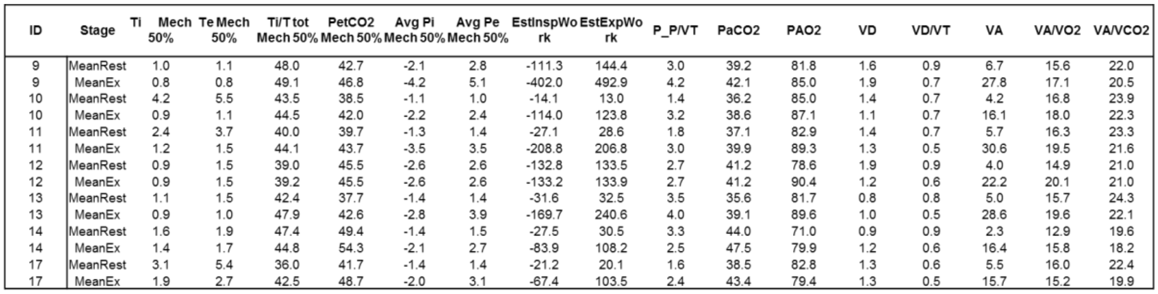
ID	Stage	VO_2 ml/kg 50%	RER 50%	HR 50%	RPB 50%	RPU 50%	RPE 50%	MinVi Mech 50%	MinVe Mech 50%	V_T Mech 50%	fB Mech 50%	IC Mech 50%	EELV %TLC 50%	EILV %TLC 50%
18	MeanRest	3.5	0.7	83.0	0.0	0.0	.	-30.5	30.5	1.3	23.5	3.2	43.0	65.8
18	MeanEx	12.5	0.9	110.4	2.0	2.0	10.0	-52.8	52.6	1.8	29.0	3.3	41.9	74.0
20	MeanRest	2.3	1.2	85.3	3.0	0.0	.	-24.2	24.2	1.1	22.7	2.7	39.4	63.4
20	MeanEx	16.2	1.1	134.5	2.0	2.0	12.0	-57.1	57.6	2.1	27.5	2.9	34.2	81.3
21	MeanRest	4.0	1.1	111.3	0.5	0.5	.	-22.1	22.2	1.7	13.3	3.5	43.2	70.3
21	MeanEx	16.5	1.0	139.0	5.0	3.0	11.0	-51.3	51.7	3.2	16.1	4.2	32.7	85.2
22	MeanRest	3.2	1.5	66.8	2.0	2.0	.	-19.8	19.8	1.2	16.3	2.7	52.7	74.5
22	MeanEx	19.9	1.3	112.0	3.0	3.0	11.0	-45.0	44.8	2.0	22.9	3.0	46.9	81.8
25	MeanRest	6.2	0.8	91.0	0.0	0.0	.	-25.1	25.2	1.9	13.4	3.5	51.6	78.5
25	MeanEx	20.2	0.9	135.0	0.5	0.5	7.0	-53.7	53.6	3.2	16.8	4.4	37.9	82.5
26	MeanRest	4.4	0.9	76.8	3.0	0.0	.	-17.9	18.3	1.5	12.4	2.4	57.5	84.2
26	MeanEx	18.2	0.9	131.0	4.0	3.0	11.0	-49.5	49.1	2.0	24.4	2.8	50.2	85.8
28	MeanRest	5.3	0.8	81.8	0.5	0.0	.	-23.2	23.1	2.2	10.6	3.5	56.9	84.0
28	MeanEx	24.0	0.8	126.3	4.0	3.0	11.0	-53.6	53.4	3.2	16.6	3.8	52.4	92.5

Table 25: Subject (2-8) breathing mechanics, during dead space challenge, results.



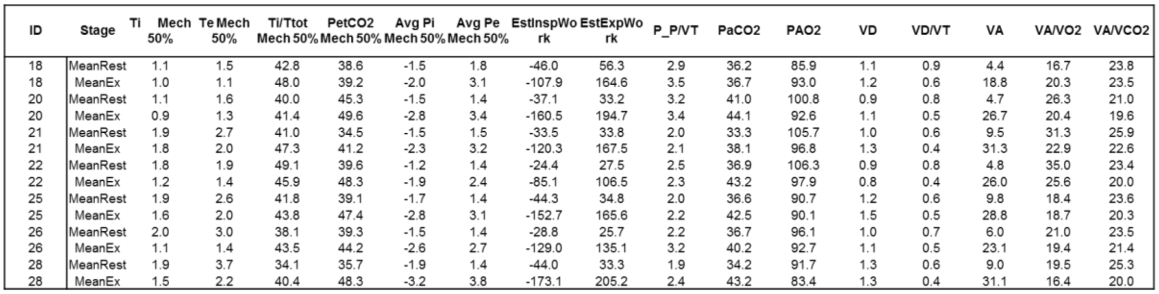
ID	Stage	Ti Mech 50%	Te Mech 50%	Ti/T tot Mech 50%	PetCO2 Mech 50%	Avg Pi Mech 50%	Avg Pe Mech 50%	EstInspWork	EstExpWork	P_P/VT	PaCO2	PAO2	VD	VD/VT	VA	VA/VO2	VA/VCO2
2	MeanRest	1.4	1.9	42.0	41.5	-1.9	1.8	-64.1	61.3	2.4	38.3	79.5	1.6	0.8	5.1	14.9	22.5
2	MeanEx	1.0	1.1	46.1	45.3	-3.9	4.6	-335.5	399.3	3.3	41.0	87.7	2.0	0.7	27.1	18.5	21.0
3	MeanRest	1.6	2.3	41.2	40.4	-2.1	1.9	-46.9	42.6	3.4	37.5	77.9	1.2	0.9	3.3	14.4	23.0
3	MeanEx	1.4	1.9	43.3	45.0	-2.9	2.8	-124.7	123.0	3.0	40.8	82.7	1.3	0.6	18.9	16.3	21.1
4	MeanRest	1.6	3.1	33.5	39.8	-1.5	1.1	-27.4	21.6	2.3	37.1	85.6	1.2	0.9	2.4	17.5	23.3
4	MeanEx	1.2	1.4	46.1	42.8	-2.4	2.6	-126.1	139.7	2.4	39.2	93.2	1.4	0.6	19.3	22.1	22.0
6	MeanRest	1.5	2.0	42.4	42.3	-1.5	1.7	-31.2	34.6	3.0	38.9	73.4	1.1	0.9	2.6	13.3	22.2
6	MeanEx	1.0	1.3	43.7	44.9	-2.3	2.8	-111.0	133.4	3.1	40.7	84.3	1.2	0.6	16.9	17.0	21.2
7	MeanRest	1.3	2.1	38.2	40.9	-1.8	1.5	-51.7	42.8	2.3	37.9	78.5	1.4	0.9	3.7	14.6	22.8
7	MeanEx	1.0	1.4	40.6	44.4	-3.6	3.2	-242.3	221.0	2.7	40.4	87.3	1.6	0.6	26.5	18.2	21.4
8	MeanRest	0.9	1.2	42.5	42.9	-2.4	2.7	-99.7	111.8	4.2	39.3	71.1	1.3	0.9	3.6	13.0	21.9
8	MeanEx	0.7	0.8	46.5	46.3	-4.4	4.8	-394.0	425.1	4.7	41.8	86.3	1.8	0.8	19.7	18.6	20.7

Table 26: Subject (9-17) breathing mechanics, during dead space challenge, results.



ID	Stage	Ti Mech 50%	Te Mech 50%	Ti/T tot Mech 50%	PetCO2 Mech 50%	Avg Pi Mech 50%	Avg Pe Mech 50%	EstInspWork	EstExpWork	P_P/VT	PaCO2	PAO2	VD	VD/VT	VA	VA/VO2	VA/VCO2
9	MeanRest	1.0	1.1	48.0	42.7	-2.1	2.8	-111.3	144.4	3.0	39.2	81.8	1.6	0.9	6.7	15.6	22.0
9	MeanEx	0.8	0.8	49.1	46.8	-4.2	5.1	-402.0	492.9	4.2	42.1	85.0	1.9	0.7	27.8	17.1	20.5
10	MeanRest	4.2	5.5	43.5	38.5	-1.1	1.0	-14.1	13.0	1.4	36.2	85.0	1.4	0.7	4.2	16.8	23.9
10	MeanEx	0.9	1.1	44.5	42.0	-2.2	2.4	-114.0	123.8	3.2	38.6	87.1	1.1	0.7	16.1	18.0	22.3
11	MeanRest	2.4	3.7	40.0	39.7	-1.3	1.4	-27.1	28.6	1.8	37.1	82.9	1.4	0.7	5.7	16.3	23.3
11	MeanEx	1.2	1.5	44.1	43.7	-3.5	3.5	-208.8	206.8	3.0	39.9	89.3	1.3	0.5	30.6	19.5	21.6
12	MeanRest	0.9	1.5	39.0	45.5	-2.6	2.6	-132.8	133.5	2.7	41.2	78.6	1.9	0.9	4.0	14.9	21.0
12	MeanEx	0.9	1.5	39.2	45.5	-2.6	2.6	-133.2	133.9	2.7	41.2	90.4	1.2	0.6	22.2	20.1	21.0
13	MeanRest	1.1	1.5	42.4	37.7	-1.4	1.4	-31.6	32.5	3.5	35.6	81.7	0.8	0.8	5.0	15.7	24.3
13	MeanEx	0.9	1.0	47.9	42.6	-2.8	3.9	-169.7	240.6	4.0	39.1	89.6	1.0	0.5	28.6	19.6	22.1
14	MeanRest	1.6	1.9	47.4	49.4	-1.4	1.5	-27.5	30.5	3.3	44.0	71.0	0.9	0.9	2.3	12.9	19.6
14	MeanEx	1.4	1.7	44.8	54.3	-2.1	2.7	-83.9	108.2	2.5	47.5	79.9	1.2	0.6	16.4	15.8	18.2
17	MeanRest	3.1	5.4	36.0	41.7	-1.4	1.4	-21.2	20.1	1.6	38.5	82.8	1.3	0.6	5.5	16.0	22.4
17	MeanEx	1.9	2.7	42.5	48.7	-2.0	3.1	-67.4	103.5	2.4	43.4	79.4	1.3	0.5	15.7	15.2	19.9

Table 27: Subject (18-28) breathing mechanics, during dead space challenge, results.



ID	Stage	Ti Mech 50%	Te Mech 50%	Ti/Ttot Mech 50%	PetCO2 Mech 50%	Avg Pi Mech 50%	Avg Pe Mech 50%	EstInspWork	EstExpWork	P_P/VT	PaCO2	PAO2	VD	VD/VT	VA	VA/VO2	VA/VCO2
18	MeanRest	1.1	1.5	42.8	38.6	-1.5	1.8	-46.0	56.3	2.9	36.2	85.9	1.1	0.9	4.4	16.7	23.8
18	MeanEx	1.0	1.1	48.0	39.2	-2.0	3.1	-107.9	164.6	3.5	36.7	93.0	1.2	0.6	18.8	20.3	23.5
20	MeanRest	1.1	1.6	40.0	45.3	-1.5	1.4	-37.1	33.2	3.2	41.0	100.8	0.9	0.8	4.7	26.3	21.0
20	MeanEx	0.9	1.3	41.4	49.6	-2.8	3.4	-160.5	194.7	3.4	44.1	92.6	1.1	0.5	26.7	20.4	19.6
21	MeanRest	1.9	2.7	41.0	34.5	-1.5	1.5	-33.5	33.8	2.0	33.3	105.7	1.0	0.6	9.5	31.3	25.9
21	MeanEx	1.8	2.0	47.3	41.2	-2.3	3.2	-120.3	167.5	2.1	38.1	96.8	1.3	0.4	31.3	22.9	22.6
22	MeanRest	1.8	1.9	49.1	39.6	-1.2	1.4	-24.4	27.5	2.5	36.9	106.3	0.9	0.8	4.8	35.0	23.4
22	MeanEx	1.2	1.4	45.9	48.3	-1.9	2.4	-85.1	106.5	2.3	43.2	97.9	0.8	0.4	26.0	25.6	20.0
25	MeanRest	1.9	2.6	41.8	39.1	-1.7	1.4	-44.3	34.8	2.0	36.6	90.7	1.2	0.6	9.8	18.4	23.6
25	MeanEx	1.6	2.0	43.8	47.4	-2.8	3.1	-152.7	165.6	2.2	42.5	90.1	1.5	0.5	28.8	18.7	20.3
26	MeanRest	2.0	3.0	38.1	39.3	-1.5	1.4	-28.8	25.7	2.2	36.7	96.1	1.0	0.7	6.0	21.0	23.5
26	MeanEx	1.1	1.4	43.5	44.2	-2.6	2.7	-129.0	135.1	3.2	40.2	92.7	1.1	0.5	23.1	19.4	21.4
28	MeanRest	1.9	3.7	34.1	35.7	-1.9	1.4	-44.0	33.3	1.9	34.2	91.7	1.3	0.6	9.0	19.5	25.3
28	MeanEx	1.5	2.2	40.4	48.3	-3.2	3.8	-173.1	205.2	2.4	43.2	83.4	1.3	0.4	31.1	16.4	20.0

Submaximal Exercise Testing Data – Resistor

Table 28: Subject (2-8) metabolic, dyspnea and ventilation, during resistor challenge, results.

ID	Stage	VO_2 ml/kg 50%	RER 50%	HR 50%	RPB 50%	RPU 50%	RPE 50%	MinVi Mech 50%	MinVe Mech 50%	V_T Mech 50%	fB Mech 50%	IC Mech 50%	EELV %TLC 50%	EILV %TLC 50%
2	MeanRest	4.0	0.8	67.5	0.0	0.0	6.0	-11.0	10.6	1.0	10.8	3.4	44.1	60.6
2	MeanEx	15.9	1.0	134.0	0.5	0.5	8.0	-40.7	41.7	1.7	25.0	2.6	56.5	84.2
3	MeanRest	3.9	0.8	82.7	2.0	0.5	.	-10.5	10.7	0.8	14.3	3.8	41.7	53.2
3	MeanEx	13.9	0.8	126.5	3.0	2.0	11.0	-27.0	26.8	1.7	16.0	3.8	41.7	67.5
4	MeanRest	2.3	0.8	103.0	0.0	0.0	.	-9.4	9.6	0.9	10.8	2.4	58.7	74.4
4	MeanEx	15.9	1.0	145.0	0.5	0.5	.	-30.4	29.7	1.7	17.9	2.1	64.2	94.6
6	MeanRest	5.5	0.7	92.2	0.5	0.5	.	-9.4	9.2	0.8	12.4	2.1	59.0	73.4
6	MeanEx	19.3	0.8	139.5	2.0	2.0	8.0	-26.2	25.6	1.3	19.2	2.6	50.3	75.9
7	MeanRest	3.8	0.7	79.8	0.0	0.0	6.0	-12.7	12.9	0.8	17.3	3.8	49.2	59.1
7	MeanEx	17.2	0.9	131.8	.	.	.	-41.7	41.5	1.8	23.2	3.9	48.8	72.5
8	MeanRest	4.5	0.8	67.3	0.0	0.0	.	-10.3	10.2	0.7	15.0	2.2	65.0	75.9
8	MeanEx	18.4	1.0	113.5	0.5	0.5	7.0	-37.0	37.2	1.4	26.5	2.2	65.1	87.5

Table 29: Subject (9-17) metabolic, dyspnea and ventilation, during resistor challenge, results.

ID	Stage	VO_2 ml/kg 50%	RER 50%	HR 50%	RPB 50%	RPU 50%	RPE 50%	MinVi Mech 50%	MinVe Mech 50%	V_T Mech 50%	fB Mech 50%	IC Mech 50%	EELV %TLC 50%	EILV %TLC 50%
9	MeanRest	5.3	0.8	92.7	0.0	0.5	.	-17.2	17.3	0.8	21.1	4.1	56.3	65.1
9	MeanEx	20.2	0.9	114.0	2.0	2.0	10.0	-45.8	46.2	1.7	26.8	3.8	60.2	78.5
10	MeanRest	3.6	0.8	87.5	3.0	0.0	.	-7.7	7.7	0.8	9.6	2.8	46.2	62.4
10	MeanEx	12.9	0.9	129.5	4.0	0.0	11.0	-30.4	30.2	1.5	20.8	2.5	52.3	80.8
11	MeanRest	2.3	0.8	85.5	0.0	0.0	.	-10.5	10.3	1.4	7.6	4.3	52.1	67.2
11	MeanEx	17.1	0.9	123.0	1.0	1.0	9.0	-35.9	35.8	3.0	12.1	4.2	54.0	86.9
12	MeanRest	.	.	.	5.0	1.0	.	-12.0	12.5	0.9	14.4	2.9	49.1	64.5
12	MeanEx	.	.	.	5.0	2.0	11.0	-39.0	39.2	1.6	25.2	3.2	44.5	72.1
13	MeanRest	3.7	0.8	85.5	0.0	0.0	.	-11.2	11.1	0.7	15.8	2.7	48.2	61.6
13	MeanEx	22.5	1.0	143.0	2.0	2.0	12.0	-45.7	46.5	1.5	31.2	2.4	54.4	82.7
14	MeanRest	4.5	0.9	93.5	0.0	0.0	.	-10.5	10.9	1.2	9.1	2.1	61.2	83.3
14	MeanEx	18.1	0.9	147.0	1.0	2.0	10.0	-24.6	24.0	1.9	13.1	2.2	60.0	94.1
17	MeanRest	4.5	0.8	73.0	0.5	0.5	.	-8.3	9.8	1.0	10.3	2.2	54.4	74.7
17	MeanEx	15.6	0.8	125.0	0.5	0.5	7.0	-24.2	24.1	2.1	11.4	2.9	41.5	85.2

Table 29: Subject (18-28) metabolic, dyspnea and ventilation, during resistor challenge, results.

ID	Stage	VO_2 ml/kg 50%	RER 50%	HR 50%	RPB 50%	RPU 50%	RPE 50%	MinVi Mech 50%	MinVe Mech 50%	V_T Mech 50%	fB Mech 50%	IC Mech 50%	EELV %TLC 50%	EILV %TLC 50%
18	MeanRest	3.0	0.8	79.0	0.0	0.0	.	-8.7	8.6	0.6	15.2	2.9	49.2	59.4
18	MeanEx	13.0	0.9	112.2	0.5	0.5	7.0	-31.5	31.8	1.2	25.7	3.1	46.1	68.1
20	MeanRest	3.6	1.0	82.5	0.0	0.0	.	-11.8	11.5	0.6	20.4	2.6	40.9	53.7
20	MeanEx	17.5	0.9	129.0	7.0	7.0	11.0	-36.8	36.3	1.6	23.4	3.1	30.9	65.8
21	MeanRest	3.7	1.0	99.0	0.5	0.5	.	-13.4	13.2	1.3	10.5	3.6	41.5	61.9
21	MeanEx	16.6	0.9	135.5	4.0	3.0	12.0	-40.1	40.2	2.8	14.5	3.8	39.2	84.4
22	MeanRest	3.8	1.5	68.2	0.0	0.0	.	-9.4	9.2	0.8	12.2	2.2	61.4	75.0
22	MeanEx	22.0	1.2	117.0	0.0	0.0	11.0	-32.0	31.9	1.5	21.6	2.4	56.5	82.9
25	MeanRest	5.2	0.8	90.0	0.0	0.0	.	-13.3	13.4	1.1	12.5	2.8	61.3	76.2
25	MeanEx	19.8	0.8	126.0	0.0	0.0	7.0	-34.7	35.0	2.9	12.3	2.9	59.5	99.3
26	MeanRest	3.8	0.8	81.2	1.0	1.0	.	-8.6	8.5	0.8	10.3	2.6	53.9	68.6
26	MeanEx	18.4	0.8	128.0	4.0	4.0	12.0	-30.3	31.2	1.9	16.6	2.3	59.2	92.5
28	MeanRest	5.3	1.0	83.8	1.0	0.0	.	-16.5	16.1	1.1	14.5	3.6	55.7	69.8
28	MeanEx	24.3	0.8	125.3	4.0	3.0	11.0	-41.8	41.7	2.9	14.4	3.5	55.9	92.0

Table 30: Subject (2-8) breathing mechanics, during resistor challenge, results.

ID	Stage	Ti Mech 50%	Te Mech 50%	Ti/T tot Mech 50%	PetCO2 Mech 50%	Avg Pi Mech 50%	Avg Pe Mech 50%	EstInspWork	EstExpWork	P_P/VT	PaCO2	PAO2	VD	VD/VT	VA	VA/VO2	VA/VCO2
2	MeanRest	2.7	3.0	47.2	37.6	-1.6	1.5	-16.7	15.9	3.6	35.5	94.1	0.3	0.3	6.9	21.6	24.3
2	MeanEx	1.1	1.3	44.0	41.6	-5.3	5.6	-221.1	233.6	7.7	38.4	93.9	0.4	0.2	31.6	21.9	22.5
3	MeanRest	1.6	2.7	36.7	36.1	-2.3	1.9	-25.3	20.0	6.3	34.5	.	.	.	.	.	.
3	MeanEx	1.7	2.1	44.0	41.8	-4.5	4.8	-123.0	131.1	7.5	38.5	83.5	0.4	0.3	20.1	16.4	22.4
4	MeanRest	1.8	4.2	32.1	35.1	-2.2	1.5	-21.0	14.4	5.0	33.7	91.9	0.7	0.7	2.6	20.4	25.6
4	MeanEx	1.5	1.9	44.5	40.9	-4.9	3.8	-152.1	118.3	7.5	37.9	94.5	0.5	0.3	21.1	22.8	22.8
6	MeanRest	1.8	3.1	36.3	35.6	-1.5	1.5	-14.3	14.0	4.9	34.1	88.2	0.3	0.4	5.2	18.1	25.3
6	MeanEx	1.6	1.6	49.9	42.0	-3.1	3.1	-78.7	80.5	5.1	38.7	87.4	0.5	0.3	16.9	18.2	22.3
7	MeanRest	1.2	2.3	35.0	36.6	-1.9	1.4	-24.7	18.4	5.2	34.8	88.9	0.4	0.5	6.5	18.4	24.8
7	MeanEx	1.1	1.5	43.7	41.9	-6.7	6.3	-278.7	260.8	7.9	38.6	91.2	0.4	0.2	31.5	20.1	22.4
8	MeanRest	1.4	2.7	34.9	36.3	-2.2	1.7	-22.5	17.3	6.3	34.6	89.2	0.4	0.5	4.8	19.4	25.0
8	MeanEx	1.0	1.3	42.6	38.2	-5.6	5.0	-209.3	185.1	9.3	35.9	96.7	0.4	0.3	27.2	24.8	24.0

Table 31: Subject (9-18) breathing mechanics, during resistor challenge, results.

ID	Stage	Ti Mech 50%	Te Mech 50%	Ti/T tot Mech 50%	PetCO2 Mech 50%	Avg Pi Mech 50%	Avg Pe Mech 50%	EstInspWork	EstExpWork	P_P/VT	PaCO2	PAO2	VD	VD/VT	VA	VA/VO2	VA/VCO2
9	MeanRest	1.1	1.7	40.1	38.8	-2.2	2.0	-39.0	35.3	6.9	36.4	92.7	0.4	0.5	8.0	20.4	23.7
9	MeanEx	1.0	1.2	44.9	41.7	-6.4	6.0	-294.0	275.8	8.2	38.5	92.2	0.5	0.3	32.8	20.3	22.4
10	MeanRest	3.1	3.5	45.5	35.5	-1.1	1.1	-9.2	9.1	3.5	34.1	92.6	0.3	0.4	4.9	20.4	25.3
10	MeanEx	1.4	1.5	46.5	38.3	-3.5	3.5	-107.4	106.5	5.6	36.0	95.5	0.5	0.4	19.6	22.6	24.0
11	MeanRest	2.4	5.6	30.3	36.1	-1.7	1.2	-17.1	12.5	2.4	34.5	91.0	0.9	0.7	3.5	19.9	25.0
11	MeanEx	2.3	2.7	46.4	43.8	-4.9	4.6	-176.1	164.0	3.9	40.0	88.4	0.9	0.3	25.2	19.0	21.6
12	MeanRest	1.7	2.5	40.0	33.2	-1.7	1.4	-21.2	17.3	4.1	32.4	.	.	.	.	.	.
12	MeanEx	1.0	1.4	42.2	38.9	-5.3	4.6	-208.9	180.9	7.7	36.4	.	.	.	.	.	.
13	MeanRest	1.5	2.3	40.4	35.4	-1.6	1.2	-18.2	13.9	5.0	33.9	91.7	0.4	0.5	5.6	20.2	25.4
13	MeanEx	0.9	1.1	45.2	36.4	-6.9	7.8	-322.5	362.9	11.9	34.7	98.2	0.4	0.3	34.5	25.2	24.9
14	MeanRest	3.1	3.8	44.6	38.2	-1.6	1.5	-17.7	16.5	3.1	36.0	93.4	0.6	0.5	5.6	21.3	24.0
14	MeanEx	2.2	2.4	47.7	55.9	-3.4	4.1	-82.8	100.6	4.7	48.7	80.7	0.5	0.3	17.2	16.2	17.7
17	MeanRest	2.3	3.8	36.6	37.5	-1.5	1.3	-15.1	13.6	4.2	35.4	89.7	0.5	0.5	4.8	18.8	24.3
17	MeanEx	2.3	3.1	42.4	48.1	-4.0	4.7	-97.3	114.3	5.4	43.0	82.5	0.7	0.3	16.2	16.3	20.1
18	MeanRest	1.4	2.6	36.1	37.0	-1.3	1.1	-11.2	9.4	4.8	35.1	89.7	0.3	0.5	3.9	18.4	24.6
18	MeanEx	1.1	1.2	47.8	37.8	-3.4	4.6	-108.9	148.2	9.0	35.7	94.8	0.4	0.4	20.6	21.3	24.2

Table 32: Subject (20-28) breathing mechanics, during resistor challenge, results.

ID	Stage	Ti Mech 50%	Te Mech 50%	Ti/T tot Mech 50%	PetCO2 Mech 50%	Avg Pi Mech 50%	Avg Pe Mech 50%	EstInspWork	EstExpWork	P_P/VT	PaCO2	PAO2	VD	VD/VT	VA	VA/VO2	VA/VCO2
20	MeanRest	1.2	1.8	41.4	39.8	-1.4	1.4	-16.3	16.1	6.2	37.1	97.1	0.2	0.4	6.7	22.4	23.3
20	MeanEx	1.1	1.4	44.3	46.4	-5.2	5.3	-188.2	191.8	8.7	41.8	89.0	0.5	0.3	25.2	18.2	20.6
21	MeanRest	2.6	3.2	44.9	29.7	-2.2	1.9	-29.5	24.7	3.9	29.8	103.0	0.4	0.3	9.4	27.0	28.9
21	MeanEx	2.1	2.1	50.5	37.6	-6.8	6.4	-275.2	261.0	5.9	35.6	94.1	0.8	0.3	28.5	20.7	24.3
22	MeanRest	2.4	2.5	48.8	30.0	-1.2	1.3	-11.3	12.1	4.0	30.1	112.6	0.0	0.0	8.8	46.5	28.7
22	MeanEx	1.3	1.5	47.1	42.0	-4.1	3.7	-132.9	119.0	6.0	38.7	99.6	0.1	0.1	29.8	26.4	22.3
25	MeanRest	1.9	3.0	38.7	36.3	-2.0	1.2	-27.1	16.1	3.7	34.6	93.0	0.5	0.5	6.6	19.4	24.9
25	MeanEx	2.1	2.7	44.0	46.0	-7.1	4.4	-248.7	154.1	4.8	41.5	87.4	0.8	0.3	25.4	17.3	20.8
26	MeanRest	2.3	3.6	38.5	33.9	-1.5	1.1	-13.2	9.4	3.7	32.9	98.0	0.3	0.3	5.7	21.7	26.3
26	MeanEx	1.7	2.0	45.1	41.0	-5.1	3.6	-160.9	112.5	5.9	38.0	89.4	0.6	0.3	21.5	17.5	22.7
28	MeanRest	2.1	2.1	50.2	28.1	-2.4	2.7	-38.7	45.0	6.0	28.7	106.8	0.2	0.2	12.9	32.3	30.0
28	MeanEx	1.9	2.2	46.8	43.6	-7.3	8.1	-305.1	336.7	6.2	39.8	85.4	0.8	0.3	30.8	17.0	21.7

Submaximal Exercise Testing Data – Heliox

Table 33: Subject (2-8) metabolic, dyspnea and ventilation, during heliox challenge, results.

ID	Stage	VO_2 ml/kg 50%	RER 50%	HR 50%	RPB 50%	RPU 50%	RPE 50%	MinVi Mech 50%	MinVe Mech 50%	V_T Mech 50%	fB Mech 50%	IC Mech 50%	EELV %TLC 50%	EILV %TLC 50%
2	MeanRest	2.5	0.2	84.7	0.0	0.0	6.0	-25.3	26.8	1.3	20.7	3.0	49.7	71.3
2	MeanEx	13.5	0.3	141.0	0.0	0.0	7.0	-46.3	47.2	1.2	40.2	3.4	44.5	64.0
3	MeanRest	.	.	.	0.5	.	.	-10.0	10.0	0.6	16.5	4.4	32.7	41.9
3	MeanEx	7.0	0.2	128.5	2.0	0.0	8.0	-27.4	27.3	1.3	21.3	4.1	38.6	58.3
4	MeanRest	4.5	0.7	102.7	0.0	0.0	.	-7.5	7.8	1.0	7.9	2.4	58.7	76.2
4	MeanEx	25.3	0.7	141.5	0.0	0.5	10.0	-29.8	29.4	1.7	17.6	2.1	63.7	93.1
6	MeanRest	6.1	0.6	102.5	0.0	0.0	.	-7.6	7.6	0.7	10.4	2.4	53.8	67.9
6	MeanEx	28.3	0.7	149.5	0.0	0.5	9.0	-28.1	28.1	1.2	23.6	2.4	53.5	76.3
7	MeanRest	5.4	0.6	89.8	0.0	0.0	6.0	-13.7	13.1	0.7	18.1	4.2	43.8	53.7
7	MeanEx	25.3	0.7	136.3	1.0	1.0	8.0	-42.8	42.9	1.8	23.3	3.6	52.3	76.7
8	MeanRest	6.9	0.6	65.0	0.0	0.0	.	-12.8	12.6	0.8	16.5	2.7	57.4	69.8
8	MeanEx	26.6	0.7	100.0	2.0	1.0	9.0	-36.3	35.0	1.4	25.7	2.9	53.9	75.5

Table 34: Subject (9-17) metabolic, dyspnea and ventilation, during heliox challenge, results.

ID	Stage	VO_2 ml/kg 50%	RER 50%	HR 50%	RPB 50%	RPU 50%	RPE 50%	MinVi Mech 50%	MinVe Mech 50%	V_T Mech 50%	fB Mech 50%	IC Mech 50%	EELV %TLC 50%	EILV %TLC 50%
9	MeanRest	6.7	0.7	91.7	0.0	0.5	.	-20.2	18.3	0.9	21.7	4.2	55.5	64.6
9	MeanEx	28.6	0.7	132.8	1.0	2.0	10.0	-49.8	49.8	1.4	35.3	4.0	58.0	73.1
10	MeanRest	5.9	0.7	82.7	3.0	0.0	.	-10.8	10.8	1.2	9.3	2.8	44.9	67.5
10	MeanEx	19.8	0.6	125.0	3.0	0.0	9.0	-26.7	26.6	1.1	25.3	2.6	49.5	70.1
11	MeanRest	4.2	0.4	83.5	0.0	0.0	.	-12.9	11.9	0.9	13.1	4.5	50.2	60.4
11	MeanEx	20.3	0.5	120.3	0.0	0.0	7.0	-39.7	39.8	2.3	17.7	4.6	49.1	74.6
12	MeanRest	5.5	0.7	97.5	6.0	2.0	.	-14.2	14.0	1.0	15.1	3.1	44.9	61.7
12	MeanEx	20.6	0.7	147.5	6.0	3.0	12.0	-42.4	42.2	1.3	32.8	2.9	48.3	71.1
13	MeanRest	5.7	0.7	102.7	0.0	0.0	.	-11.0	10.9	0.5	21.2	2.5	52.2	61.8
13	MeanEx	25.2	1.1	141.5	3.0	2.0	12.0	-38.3	38.8	1.2	33.3	1.8	65.2	87.4
14	MeanRest	3.3	1.2	82.5	0.0	0.0	.	-8.8	8.7	0.9	10.5	2.4	56.9	72.5
14	MeanEx	27.7	0.7	148.0	2.0	0.5	9.0	-27.2	27.0	2.1	13.0	2.4	56.7	95.1
17	MeanRest	5.3	0.6	74.7	0.5	0.5	.	-7.7	7.6	0.6	12.0	2.6	47.4	60.5
17	MeanEx	21.9	0.6	121.5	0.5	0.5	7.0	-25.4	24.7	1.5	16.7	2.4	50.1	81.6

Table 35: Subject (18-28) metabolic, dyspnea and ventilation, during heliox challenge, results.

ID	Stage	VO_2 ml/kg 50%	RER 50%	HR 50%	RPB 50%	RPU 50%	RPE 50%	MinVi Mech 50%	MinVe Mech 50%	V_T Mech 50%	fB Mech 50%	IC Mech 50%	EELV %TLC 50%	EILV %TLC 50%
18	MeanRest	4.3	0.6	88.0	0.0	0.0	.	-8.4	8.6	0.7	14.9	2.6	53.5	65.4
18	MeanEx	17.6	0.7	119.2	0.5	0.0	7.0	-26.7	26.5	1.0	25.6	3.2	43.1	61.4
20	MeanRest	2.9	0.6	79.5	3.0	0.0	.	-10.6	10.2	0.5	23.0	2.7	38.5	48.6
20	MeanEx	18.1	0.6	132.3	3.0	0.0	11.0	-35.8	35.6	1.1	31.3	2.5	43.4	69.0
21	MeanRest	.	.	106.5	0.5	0.5	.	-20.7	20.6	1.4	14.8	3.6	42.1	64.6
21	MeanEx	.	.	133.5	2.0	1.0	12.0	-37.6	37.5	2.4	16.0	3.1	50.3	88.3
22	MeanRest	6.1	1.3	74.0	0.0	0.5	.	-13.8	13.8	0.9	15.4	2.5	56.4	72.5
22	MeanEx	31.5	1.0	121.5	0.0	1.0	10.0	-31.2	31.5	1.2	26.3	2.2	60.2	81.7
25	MeanRest	6.9	0.8	89.3	0.0	0.0	.	-15.7	15.3	1.1	15.4	3.6	49.5	64.5
25	MeanEx	27.0	0.7	126.5	0.0	0.0	7.0	-39.5	40.0	2.4	17.1	3.0	57.8	91.1
26	MeanRest	5.1	0.6	77.5	1.0	1.0	.	-8.2	7.8	1.0	8.3	3.1	45.3	62.2
26	MeanEx	25.7	0.6	124.0	4.0	4.0	12.0	-32.5	33.7	1.5	22.8	2.4	58.0	84.4
28	MeanRest	7.2	0.8	82.2	0.0	0.0	.	-22.4	22.6	1.8	12.2	3.5	56.7	79.4
28	MeanEx	34.3	0.7	128.0	3.0	1.0	9.0	-48.2	47.2	2.7	17.6	3.6	54.9	88.3

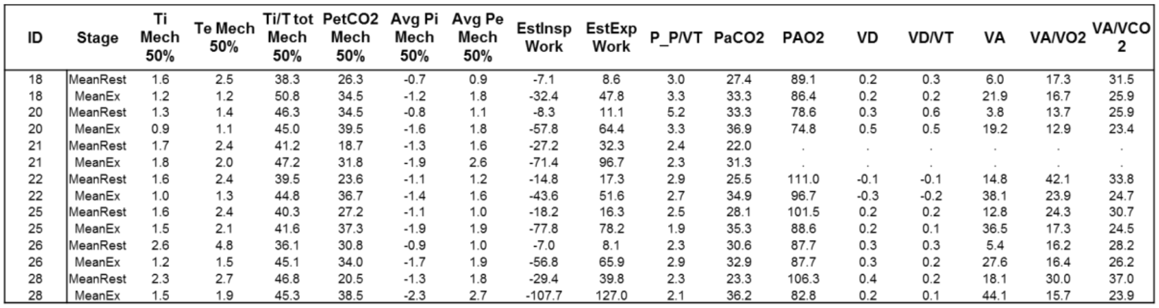
Table 36: Subject (2-8) breathing mechanics, during heliox challenge, results.

ID	Stage	Ti Mech 50%	Te Mech 50%	Ti/T tot Mech 50%	PetCO2 Mech 50%	Avg Pi Mech 50%	Avg Pe Mech 50%	EstInsp Work	EstExp Work	P_P/VT	PaCO2	PAO2	VD	VD/VT	VA	VA/VO2	VA/VCO 2
2	MeanRest	1.4	1.5	48.0	23.1	-1.3	1.8	-33.9	47.4	2.7	25.2	39.5	1.2	0.9	2.1	7.7	34.3
2	MeanEx	0.7	0.8	44.2	33.3	-1.9	2.2	-88.1	105.0	4.0	32.5	43.1	0.9	0.8	10.0	8.2	26.6
3	MeanRest	1.2	2.5	33.5	31.2	-1.2	2.1	-11.7	21.0	6.1	31.0	.	.	.	.	.	.
3	MeanEx	1.2	1.6	43.4	36.0	-1.3	2.3	-36.7	64.6	3.7	34.4	2.5	1.1	0.9	3.6	5.5	25.1
4	MeanRest	3.1	4.9	39.4	32.0	-1.4	1.5	-10.9	12.3	3.9	31.5	88.4	0.5	0.5	3.8	18.3	27.4
4	MeanEx	1.6	1.9	44.9	35.8	-2.0	2.1	-59.1	61.4	2.8	34.2	84.6	0.3	0.2	23.5	16.8	25.2
6	MeanRest	2.1	3.8	35.8	32.9	-1.2	1.5	-9.3	11.8	4.4	32.2	87.6	0.3	0.4	4.5	17.6	26.8
6	MeanEx	1.2	1.4	45.3	35.1	-1.7	2.1	-46.5	58.2	3.5	33.7	87.2	0.2	0.2	23.2	17.6	25.6
7	MeanRest	1.2	2.2	35.3	32.4	-1.1	1.0	-14.3	13.7	3.3	31.8	81.3	0.4	0.5	6.3	15.1	27.1
7	MeanEx	1.1	1.5	41.1	36.3	-1.9	2.1	-80.5	90.3	2.3	34.6	85.1	0.2	0.1	39.2	16.7	24.9
8	MeanRest	1.5	2.2	40.6	28.0	-1.2	1.1	-15.7	13.6	4.2	28.7	85.2	0.3	0.4	7.9	16.8	30.1
8	MeanEx	1.0	1.4	41.2	33.0	-1.7	1.9	-60.9	67.3	3.3	32.2	88.1	0.2	0.1	30.8	18.5	26.8

Table 37: Subject (9-17) breathing mechanics, during heliox challenge, results.

ID	Stage	Ti Mech 50%	Te Mech 50%	Ti/T tot Mech 50%	PetCO2 Mech 50%	Avg Pi Mech 50%	Avg Pe Mech 50%	EstInsp Work	EstExp Work	P_P/VT	PaCO2	PAO2	VD	VD/VT	VA	VA/VO2	VA/VCO 2
9	MeanRest	1.0	1.9	34.4	29.6	-1.3	1.4	-24.1	26.7	3.8	29.8	87.8	0.4	0.4	10.8	17.2	28.9
9	MeanEx	0.8	0.9	46.1	34.7	-1.9	2.2	-95.2	110.3	3.2	33.5	87.6	0.3	0.2	40.1	17.4	25.8
10	MeanRest	2.9	3.6	44.5	27.2	-0.9	1.0	-9.2	10.5	1.7	28.1	93.3	0.3	0.2	8.4	20.1	30.7
10	MeanEx	1.0	1.4	42.9	34.4	-1.3	1.4	-35.1	38.7	3.0	33.2	85.1	0.2	0.2	21.8	16.6	26.0
11	MeanRest	1.4	3.3	30.5	32.1	-1.1	1.0	-12.9	12.2	2.6	31.6	54.2	0.7	0.7	3.5	9.5	27.3
11	MeanEx	1.5	2.0	43.8	38.2	-1.7	1.9	-69.0	78.7	1.7	35.9	62.7	1.2	0.5	19.5	10.9	24.0
12	MeanRest	2.0	2.3	45.9	25.4	-0.9	1.3	-13.1	18.5	3.5	26.8	98.2	0.2	0.2	10.8	23.4	32.2
12	MeanEx	0.9	1.0	46.7	32.5	-1.7	2.2	-72.2	93.8	3.5	31.8	92.0	0.2	0.1	36.1	19.9	27.1
13	MeanRest	1.1	1.7	40.3	30.2	-0.9	1.1	-9.4	12.3	5.6	30.3	90.5	0.3	0.5	5.3	19.1	28.5
13	MeanEx	0.9	0.9	48.1	34.0	-1.7	2.2	-66.9	84.7	3.9	33.0	108.6	0.2	0.2	32.0	40.0	26.2
14	MeanRest	3.0	3.0	49.3	32.9	-0.9	1.2	-8.0	11.1	3.3	32.2	104.3	0.2	0.3	6.4	31.2	26.8
14	MeanEx	2.5	2.2	53.0	44.2	-1.5	2.2	-40.4	60.5	2.0	40.3	82.1	0.4	0.2	22.1	16.1	21.4
17	MeanRest	1.6	3.4	32.0	37.1	-0.9	0.9	-6.5	6.8	3.2	35.2	82.5	0.3	0.4	4.4	15.7	24.6
17	MeanEx	1.6	2.2	42.4	41.4	-1.4	1.9	-35.6	48.0	2.5	38.3	77.8	0.3	0.2	20.0	14.3	22.6

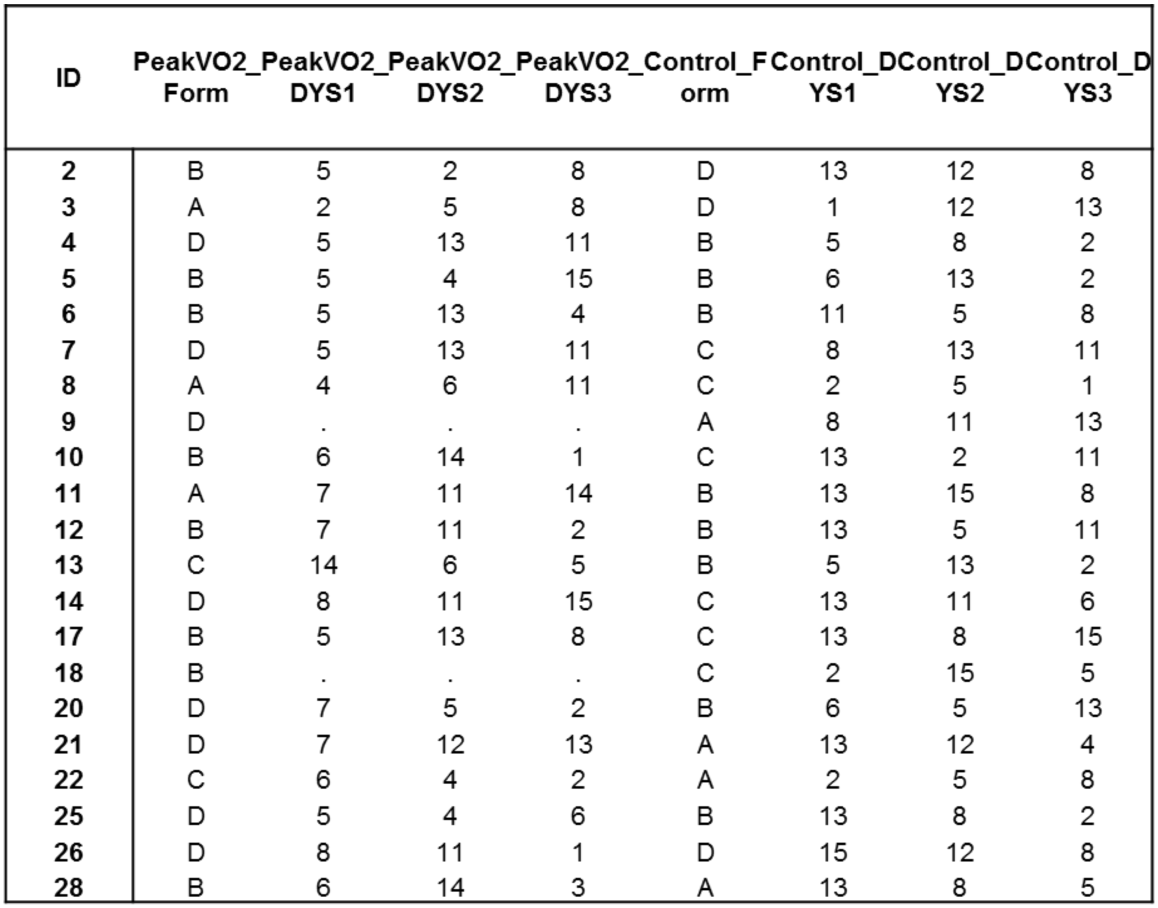
Table 38: Subject (18-28) breathing mechanics, during heliox challenge, results.



ID	Stage	Ti Mech 50%	Te Mech 50%	Ti/T tot Mech 50%	PetCO2 Mech 50%	Avg Pi Mech 50%	Avg Pe Mech 50%	EstInsp Work	EstExp Work	P_P/VT	PaCO2	PAO2	VD	VD/VT	VA	VA/VO2	VA/VCO2
18	MeanRest	1.6	2.5	38.3	26.3	-0.7	0.9	-7.1	8.6	3.0	27.4	89.1	0.2	0.3	6.0	17.3	31.5
18	MeanEx	1.2	1.2	50.8	34.5	-1.2	1.8	-32.4	47.8	3.3	33.3	86.4	0.2	0.2	21.9	16.7	25.9
20	MeanRest	1.3	1.4	46.3	34.5	-0.8	1.1	-8.3	11.1	5.2	33.3	78.6	0.3	0.6	3.8	13.7	25.9
20	MeanEx	0.9	1.1	45.0	39.5	-1.6	1.8	-57.8	64.4	3.3	36.9	74.8	0.5	0.5	19.2	12.9	23.4
21	MeanRest	1.7	2.4	41.2	18.7	-1.3	1.6	-27.2	32.3	2.4	22.0	.	.	.	.	.	.
21	MeanEx	1.8	2.0	47.2	31.8	-1.9	2.6	-71.4	96.7	2.3	31.3	.	.	.	.	.	.
22	MeanRest	1.6	2.4	39.5	23.6	-1.1	1.2	-14.8	17.3	2.9	25.5	111.0	-0.1	-0.1	14.8	42.1	33.8
22	MeanEx	1.0	1.3	44.8	36.7	-1.4	1.6	-43.6	51.6	2.7	34.9	96.7	-0.3	-0.2	38.1	23.9	24.7
25	MeanRest	1.6	2.4	40.3	27.2	-1.1	1.0	-18.2	16.3	2.5	28.1	101.5	0.2	0.2	12.8	24.3	30.7
25	MeanEx	1.5	2.1	41.6	37.3	-1.9	1.9	-77.8	78.2	1.9	35.3	88.6	0.2	0.1	36.5	17.3	24.5
26	MeanRest	2.6	4.8	36.1	30.8	-0.9	1.0	-7.0	8.1	2.3	30.6	87.7	0.3	0.3	5.4	16.2	28.2
26	MeanEx	1.2	1.5	45.1	34.0	-1.7	1.9	-56.8	65.9	2.9	32.9	87.7	0.3	0.2	27.6	16.4	26.2
28	MeanRest	2.3	2.7	46.8	20.5	-1.3	1.8	-29.4	39.8	2.3	23.3	106.3	0.4	0.2	18.1	30.0	37.0
28	MeanEx	1.5	1.9	45.3	38.5	-2.3	2.7	-107.7	127.0	2.1	36.2	82.8	0.2	0.1	44.1	15.7	23.9

Dyspnea Questionnaire

Table 39: Dyspnea questionnaire results from peak aerobic capacity and control submaximal exercise tests.



ID	PeakVO2_Form	PeakVO2_DYS1	PeakVO2_DYS2	PeakVO2_DYS3	Control_Form	Control_DYS1	Control_DYS2	Control_DYS3
2	B	5	2	8	D	13	12	8
3	A	2	5	8	D	1	12	13
4	D	5	13	11	B	5	8	2
5	B	5	4	15	B	6	13	2
6	B	5	13	4	B	11	5	8
7	D	5	13	11	C	8	13	11
8	A	4	6	11	C	2	5	1
9	D	.	.	.	A	8	11	13
10	B	6	14	1	C	13	2	11
11	A	7	11	14	B	13	15	8
12	B	7	11	2	B	13	5	11
13	C	14	6	5	B	5	13	2
14	D	8	11	15	C	13	11	6
17	B	5	13	8	C	13	8	15
18	B	.	.	.	C	2	15	5
20	D	7	5	2	B	6	5	13
21	D	7	12	13	A	13	12	4
22	C	6	4	2	A	2	5	8
25	D	5	4	6	B	13	8	2
26	D	8	11	1	D	15	12	8
28	B	6	14	3	A	13	8	5

Table 40: Dyspnea questionnaire results from dead space, resistor and heliox submaximal exercise tests.

ID	DeadSpace_Form	DeadSpace_DYS1	DeadSpace_DYS2	DeadSpace_DYS3	Resistor_Form	Resistor_DYS1	Resistor_DYS2	Resistor_DYS3	Heliox_Form	Heliox_DYS1	Heliox_DYS2	Heliox_DYS3
2	D	4	1	8	B	13	1	8	A	13	8	1
3	C	8	2	5	D	2	15	13	C	13	15	8
4	C	8	2	5	A	2	5	8	D	8	5	2
5	D	7	2	6	C	8	2	5	A	2	7	13
6	C	4	2	9	B	11	8	1	D	5	13	11
7	B	5	13	8	B	13	12	2	C	2	13	5
8	C	14	3	6	A	1	3	13	B	5	13	2
9	D	4	2	6	D	8	5	13	B	11	8	2
10	D	1	2	11	C	13	5	1	A	8	11	13
11	D	4	4	5	B	2	8	13	B	13	15	8
12	C	12	15	1	C	15	13	5	A	13	5	4
13	C	8	2	5	D	8	13	2	B	5	13	2
14	D	8	11	15	D	15	8	13	B	13	11	5
17	A	8	2	4	C	13	8	2	C	2	8	13
18	B	13	15	8	D	12	15	2	C	1	15	13
20	D	3	5	9	D	5	7	13	B	1	12	13
21	A	2	3	12	D	7	2	12	A	2	13	11
22	B	8	1	4	A	8	13	15	D	2	8	3
25	D	4	1	9	C	8	2	13	C	1	13	7
26	A	13	1	3	B	8	7	14	C	15	2	12
28	D	14	8	1	D	8	15	2	D	11	.	.

Visual Analog Scale

Table 41: Visual analog scale (VAS) results from peak aerobic capacity and control submaximal exercise tests.

ID	PeakVO2_VAS1_UNPLEA	PeakVO2_VAS2a_DEPR	PeakVO2_VAS2b_ANX	PeakVO2_VAS2c_FRUS	PeakVO2_VAS2d_ANGER	PeakVO2_VAS2e_FEAR	Control_VAS1_UNPLEA	Control_VAS2a_DEPR	Control_VAS2b_ANX	Control_VAS2c_FRUS	Control_VAS2d_ANGER	Control_VAS2e_FEAR
2	8.4	0.0	0.0	3.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
3	1.4	0.8	9.1	7.2	6.1	4.9	0.0	0.0	0.0	0.0	0.0	0.0
4	5.6	0.0	0.0	0.0	0.0	0.0	0.3	0.0	0.0	0.0	0.0	0.0
5	7.6	0.2	2.2	4.1	0.2	0.1	0.9	0.0	0.3	0.0	0.0	0.0
6	6.0	0.2	6.6	2.5	0.6	1.6	0.2	0.1	1.9	0.0	0.1	0.3
7	6.7	0.4	1.1	1.9	0.6	0.6	0.7	0.0	0.7	0.4	0.1	0.1
8	6.2	0.0	7.1	6.3	1.6	0.3	2.9	0.0	2.8	0.4	0.0	0.0
9	4.8	0.8	3.2	4.0	2.8	0.7	2.4	0.9	1.1	1.2	0.5	1.1
10	7.6	2.8	6.6	5.4	3.6	2.5	0.4	0.3	0.4	0.3	0.3	0.3
11	8.4	0.0	0.0	2.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
12	4.6	0.0	5.0	6.4	0.0	0.0	0.1	0.0	0.9	0.0	0.1	0.1
13	6.5	0.0	1.5	1.0	0.0	0.0	0.4	0.0	0.3	0.0	0.0	0.0
14	6.9	5.4	7.6	8.2	1.4	0.6	1.3	0.0	0.6	0.0	0.0	0.4
17	4.4	2.6	5.5	1.5	1.6	1.2	0.4	0.4	0.3	0.3	0.2	0.4
18	8.8	0.0	6.9	0.0	0.0	3.1	0.9	0.0	0.2	0.0	0.0	0.0
20	7.9	0.1	7.1	4.6	0.1	4.8	2.6	0.3	7.5	6.8	0.0	7.1
21	2.0	0.0	7.9	5.8	0.5	0.4	3.0	0.2	1.9	0.1	0.0	0.1
22	5.6	0.0	1.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
25	5.8	0.1	0.1	8.8	8.3	0.3	0.5	0.0	0.0	0.1	0.1	0.1
26	6.8	0.0	0.7	0.6	0.0	1.8	3.5	0.0	0.0	0.0	0.0	0.0
28	9.4	0.2	3.6	3.6	0.1	0.1	3.6	0.0	0.0	0.0	0.0	0.0

Table 42: Visual analog scale (VAS) results from dead space, resistor, and heliox submaximal exercise tests.

ID	DeadSpace_VAS1_UNPLEA	DeadSpace_VAS2a_DEPR	DeadSpace_VAS2b_ANX	DeadSpace_VAS2c_FRUS	DeadSpace_VAS2d_ANGER	DeadSpace_VAS2e_FEAR	Resistor_VAS1_UNPLEA	Resistor_VAS2a_DEPR	Resistor_VAS2b_ANX	Resistor_VAS2c_FRUS	Resistor_VAS2d_ANGER	Resistor_VAS2e_FEAR	Heliox_VAS1_UNPLEA	Heliox_VAS2a_DEPR	Heliox_VAS2b_ANX	Heliox_VAS2c_FRUS	Heliox_VAS2d_ANGER	Heliox_VAS2e_FEAR
2	2.0	0.0	0.0	0.0	0.0	0.0	1.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
3	2.9	0.0	1.9	1.1	0.0	0.7	1.8	0.0	1.3	0.9	0.0	0.6	0.0	0.0	0.0	0.0	0.0	0.0
4	0.5	0.0	0.1	0.0	0.0	0.0	0.2	0.0	0.0	0.0	0.0	0.1	0.2	0.0	0.0	0.0	0.0	0.0
5	6.2	0.1	6.1	0.2	0.0	1.2	5.2	0.0	1.9	0.0	0.0	0.4	0.3	0.0	0.0	0.0	0.0	0.0
6	3.8	0.1	3.1	0.1	0.1	1.6	0.4	0.1	4.9	0.1	0.1	2.5	0.4	0.1	0.3	0.3	0.3	0.4
7	0.9	0.1	0.6	0.1	0.2	0.2	1.1	0.0	0.6	0.9	0.1	0.1	0.2	0.1	0.4	0.0	0.0	0.1
8	4.7	0.0	4.9	1.2	0.0	0.5	4.1	0.0	3.2	0.5	0.2	0.0	2.3	0.0	2.6	0.0	0.0	0.0
9	3.6	0.5	2.3	1.1	0.9	0.8	2.7	0.7	0.8	0.9	0.9	0.8	1.8	0.7	0.8	0.8	0.8	0.9
10	4.4	0.2	1.4	0.2	0.2	0.2	2.7	0.2	0.3	0.3	0.3	0.2	0.3	0.3	0.3	0.3	0.3	0.2
11	3.0	0.0	3.5	2.1	0.6	0.0	0.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
12	3.4	0.1	1.2	2.9	0.1	0.2	2.5	0.0	0.3	0.4	0.0	0.0	0.7	0.1	0.1	0.7	0.1	0.2
13	1.8	0.0	0.8	0.0	0.0	0.0	0.9	0.0	0.2	0.0	0.0	0.0	0.9	0.0	0.6	0.0	0.0	0.0
14	4.4	0.0	3.4	0.3	0.0	2.6	0.6	0.0	1.3	0.4	0.0	0.8	0.0	0.0	0.2	0.0	0.0	0.0
17	0.3	0.4	1.2	1.1	0.7	1.2	0.3	0.3	0.6	0.3	0.7	0.4	0.3	0.4	0.5	0.3	0.2	0.6
18	1.5	0.0	1.1	0.0	0.0	0.4	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
20	5.9	0.4	7.6	6.9	0.5	4.3	6.0	0.3	7.3	8.6	0.2	6.1	0.6	0.6	7.7	6.6	0.3	6.1
21	7.4	3.2	7.4	7.5	1.4	2.8	6.7	0.9	5.9	1.6	0.1	0.1	8.7	0.5	9.2	0.2	0.3	2.3
22	3.0	0.0	0.0	0.0	0.0	1.6	0.0	0.0	0.0	0.0	0.0	0.0	2.7	0.0	0.0	0.0	0.0	0.0
25	0.6	0.0	0.0	0.0	0.0	0.0	0.2	0.0	0.0	0.1	0.0	0.0	0.0	0.1	0.1	0.1	0.2	0.1
26	3.1	0.0	0.0	0.4	0.0	0.0	3.7	0.0	0.0	0.0	0.0	0.4	4.4	0.0	0.0	0.0	0.0	0.0
28	5.2	0.0	1.4	0.0	0.0	0.0	4.1	0.0	0.7	0.0	0.0	0.0	0.4	0.0	0.0	0.0	0.0	0.0

Ratings of Perceived Breathlessness, Unpleasantness and Exertion

Table 43: Ratings of perceived breathlessness, unpleasantness of breathing, and exertion at submaximal exercise during various breathing challenges.

ID	Control_RPB	Control_RPU	Control_RPE	DS_RPB	DS_RPU	DS_RPE	Resistor_RPB	Resistor_RPU	Resistor_RPE	Heliox_RPB	Heliox_RPU	Heliox_RPE
2	0.0	0.0	7.0	2.0	2.0	11.0	1.0	0.5	7.0	0.0	0.0	7.0
3	1.0	0.0	7.0	3.0	3.0	12.0	3.0	2.0	11.0	2.0	0.0	8.0
4	0.5	0.0	9.0	1.0	0.5	9.4	0.5	0.5	8.2	0.0	0.5	10.0
5	2.0	1.0	10.0	3.0	4.0	10.0	4.0	3.0	12.0	1.0	2.0	9.0
6	0.5	0.5	9.0	4.0	4.0	9.0	2.0	2.0	8.0	0.0	0.5	9.0
7	1.0	1.0	8.0	4.0	3.0	10.0	3.0	2.0	9.0	1.0	1.0	8.0
8	2.0	2.0	11.0	2.0	4.0	11.0	0.5	0.5	7.0	2.0	1.0	9.0
9	1.0	1.0	9.0	4.0	3.0	12.0	2.0	2.0	10.0	1.0	2.0	10.0
10	3.0	0.5	11.0	5.0	3.0	13.0	4.0	0.0	11.0	3.0	0.0	9.0
11	0.5	0.5	7.0	4.0	4.0	12.0	1.0	1.0	9.0	0.0	0.0	7.0
12	5.0	3.0	12.0	4.0	3.0	11.0	5.0	2.0	11.0	6.0	3.0	12.0
13	2.0	1.0	12.0	4.0	3.0	12.0	2.0	1.5	12.0	3.0	2.0	12.0
14	2.0	2.0	11.0	3.0	3.0	12.0	1.0	2.0	10.0	2.0	0.5	9.0
17	0.5	0.5	7.0	1.0	1.0	7.0	0.5	0.5	7.0	0.5	0.5	7.0
18	0.5	1.0	8.0	2.0	2.0	10.0	0.5	0.5	7.0	0.5	0.0	7.0
20	3.0	1.0	11.0	3.0	2.0	12.0	7.0	7.0	11.0	3.0	0.0	11.0
21	1.0	1.0	11.0	5.0	3.0	11.0	4.0	3.0	12.0	2.0	1.0	12.0
22	0.0	0.0	11.0	3.0	3.0	11.0	0.0	0.0	11.0	0.0	1.0	10.0
25	0.5	0.0	7.0	0.5	0.5	7.0	0.0	0.0	7.0	0.0	0.0	7.0
26	3.0	4.0	12.0	4.0	3.0	11.0	4.0	4.0	12.0	4.0	4.0	12.0
28	2.0	3.0	9.0	4.0	3.0	11.0	4.0	3.0	11.0	3.0	1.0	9.0

Borg Scales

Table 44: Borg scale for ratings of perceived breathlessness (RPB)

Rate Your Breathing

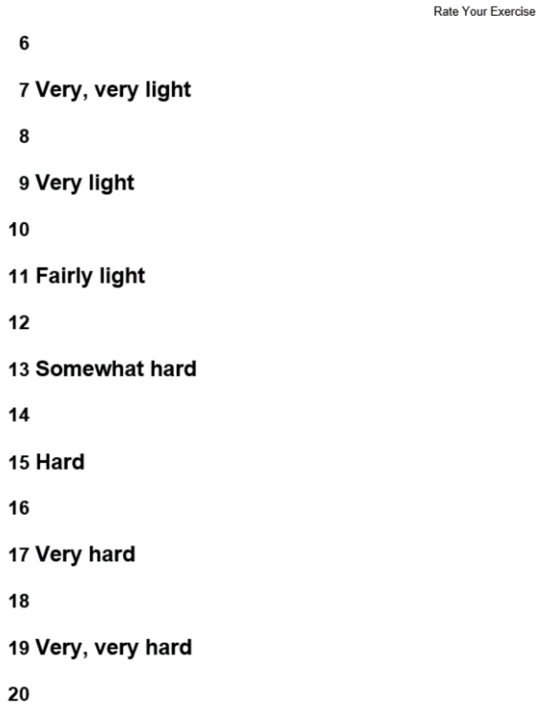
0	**Nothing at all**
0.5	**Very, very weak (Just Noticeable)**
1	**Very Weak**
2	**Weak (Light)**
3	**Moderate**
4	**Somewhat Strong**
5	**Strong (Heavy)**
6	
7	**Very Strong**
8	
9	
10	**Very, very strong (Almost max)** **Maximal**

Table 45: Borg scale for ratings of perceived unpleasantness of breathing (RPU)

Rate Unpleasantness of your Breathing

0	**Not Unpleasant**
0.5	**Very, very weak (Just Noticeable)**
1	**Very Weak Unpleasantness**
2	**Weak (Light) Unpleasantness**
3	**Moderate Unpleasantness**
4	**Somewhat Strong Unpleasantness**
5	**Strong (Heavy) Unpleasantness**
6	
7	**Very Unpleasant**
8	
9	
10	**Maximal Imaginable Unpleasantness**

Table 46: Borg scale for ratings of perceived exertion (RPE)



Rate Your Exercise

6

7 Very, very light

8

9 Very light

10

11 Fairly light

12

13 Somewhat hard

14

15 Hard

16

17 Very hard

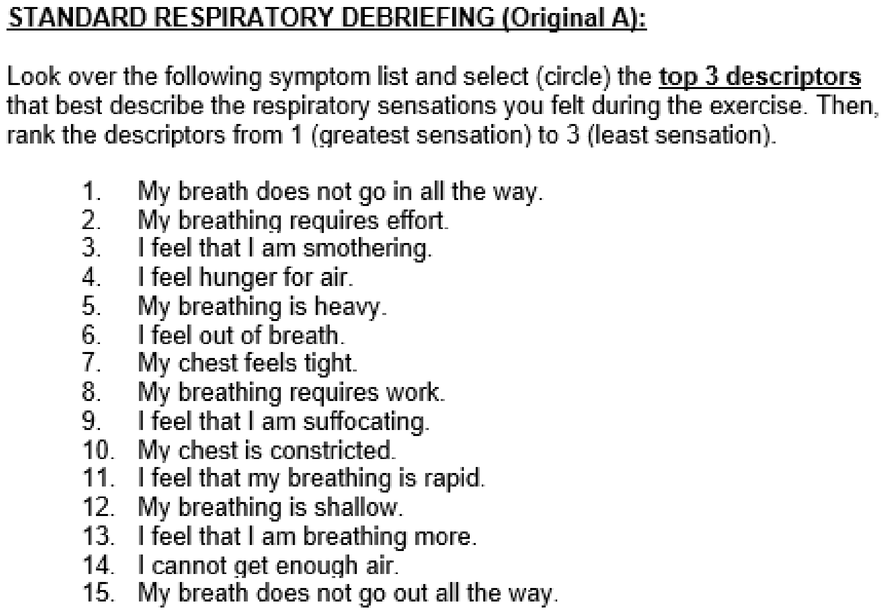
18

19 Very, very hard

20

Dyspnea Questionnaires (Post-Exercise)

Table 47: Modified dyspnea questionnaire (version A)

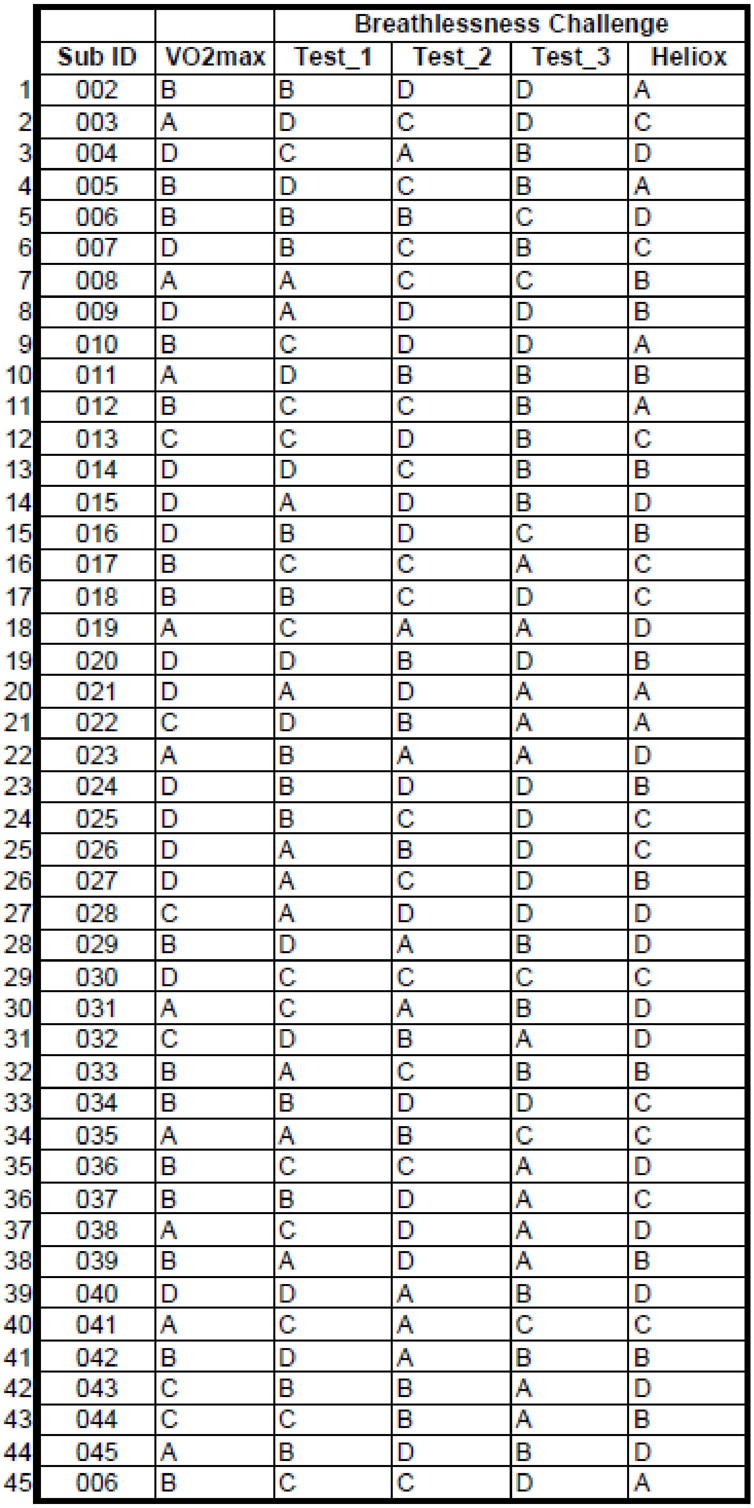


STANDARD RESPIRATORY DEBRIEFING (Original A):

Look over the following symptom list and select (circle) the **top 3 descriptors** that best describe the respiratory sensations you felt during the exercise. Then, rank the descriptors from 1 (greatest sensation) to 3 (least sensation).

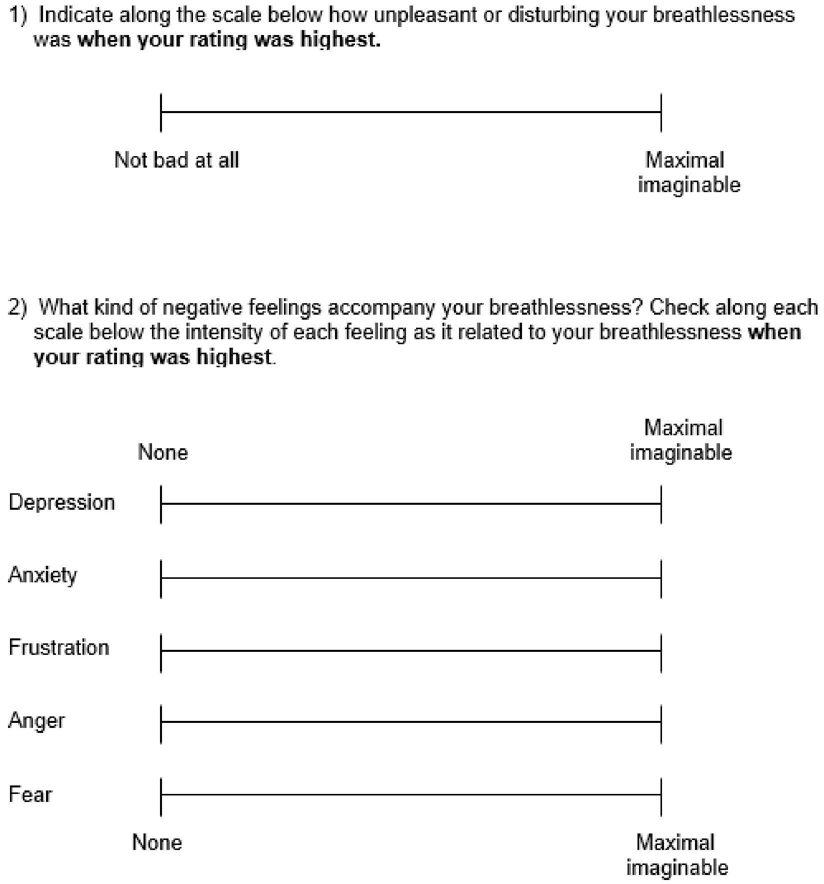
1. My breath does not go in all the way.
2. My breathing requires effort.
3. I feel that I am smothering.
4. I feel hunger for air.
5. My breathing is heavy.
6. I feel out of breath.
7. My chest feels tight.
8. My breathing requires work.
9. I feel that I am suffocating.
10. My chest is constricted.
11. I feel that my breathing is rapid.
12. My breathing is shallow.
13. I feel that I am breathing more.
14. I cannot get enough air.
15. My breath does not go out all the way.

Table 48: Randomization for dyspnea questionnaire



			Breathlessness Challenge			
	Sub ID	VO2max	Test_1	Test_2	Test_3	Heliox
1	002	B	B	D	D	A
2	003	A	D	C	D	C
3	004	D	C	A	B	D
4	005	B	D	C	B	A
5	006	B	B	B	C	D
6	007	D	B	C	B	C
7	008	A	A	C	C	B
8	009	D	A	D	D	B
9	010	B	C	D	D	A
10	011	A	D	B	B	B
11	012	B	C	C	B	A
12	013	C	C	D	B	C
13	014	D	D	C	B	B
14	015	D	A	D	B	D
15	016	D	B	D	C	B
16	017	B	C	C	A	C
17	018	B	B	C	D	C
18	019	A	C	A	A	D
19	020	D	D	B	D	B
20	021	D	A	D	A	A
21	022	C	D	B	A	A
22	023	A	B	A	A	D
23	024	D	B	D	D	B
24	025	D	B	C	D	C
25	026	D	A	B	D	C
26	027	D	A	C	D	B
27	028	C	A	D	D	D
28	029	B	D	A	B	D
29	030	D	C	C	C	C
30	031	A	C	A	B	D
31	032	C	D	B	A	D
32	033	B	A	C	B	B
33	034	B	B	D	D	C
34	035	A	A	B	C	C
35	036	B	C	C	A	D
36	037	B	B	D	A	C
37	038	A	C	D	A	D
38	039	B	A	D	A	B
39	040	D	D	A	B	D
40	041	A	C	A	C	C
41	042	B	D	A	B	B
42	043	C	B	B	A	D
43	044	C	C	B	A	B
44	045	A	B	D	B	D
45	006	B	C	C	D	A

Table 49: Visual analog scale (VAS) questionnaire



1) Indicate along the scale below how unpleasant or disturbing your breathlessness was **when your rating was highest.**

Not bad at all

Maximal imaginable

2) What kind of negative feelings accompany your breathlessness? Check along each scale below the intensity of each feeling as it related to your breathlessness **when your rating was highest**.

None

Maximal imaginable

Depression

Anxiety

Frustration

Anger

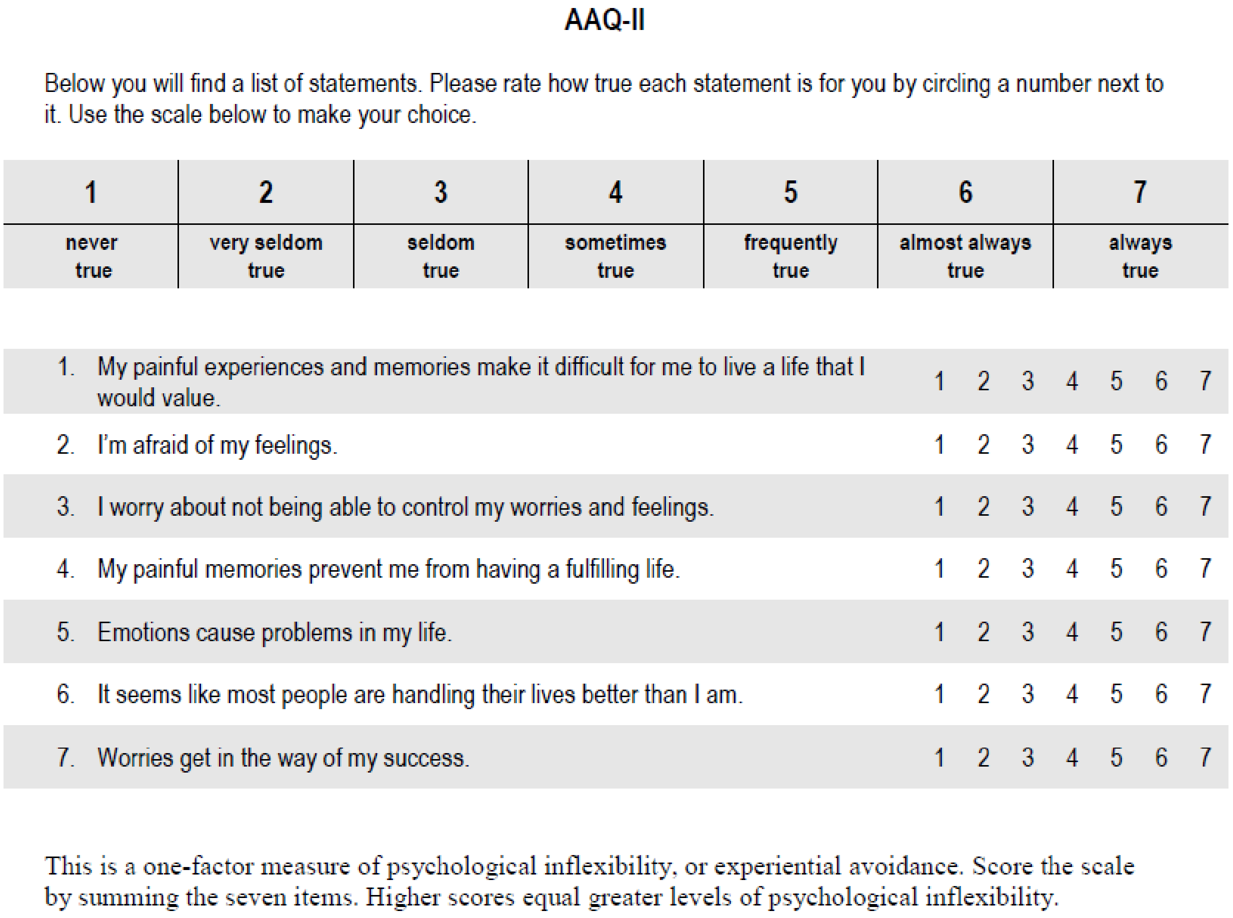
Fear

None

Maximal imaginable

Psychological Questionnaires (Visit 1)

Table 50: Acceptance and Action Questionnaire – II



AAQ-II

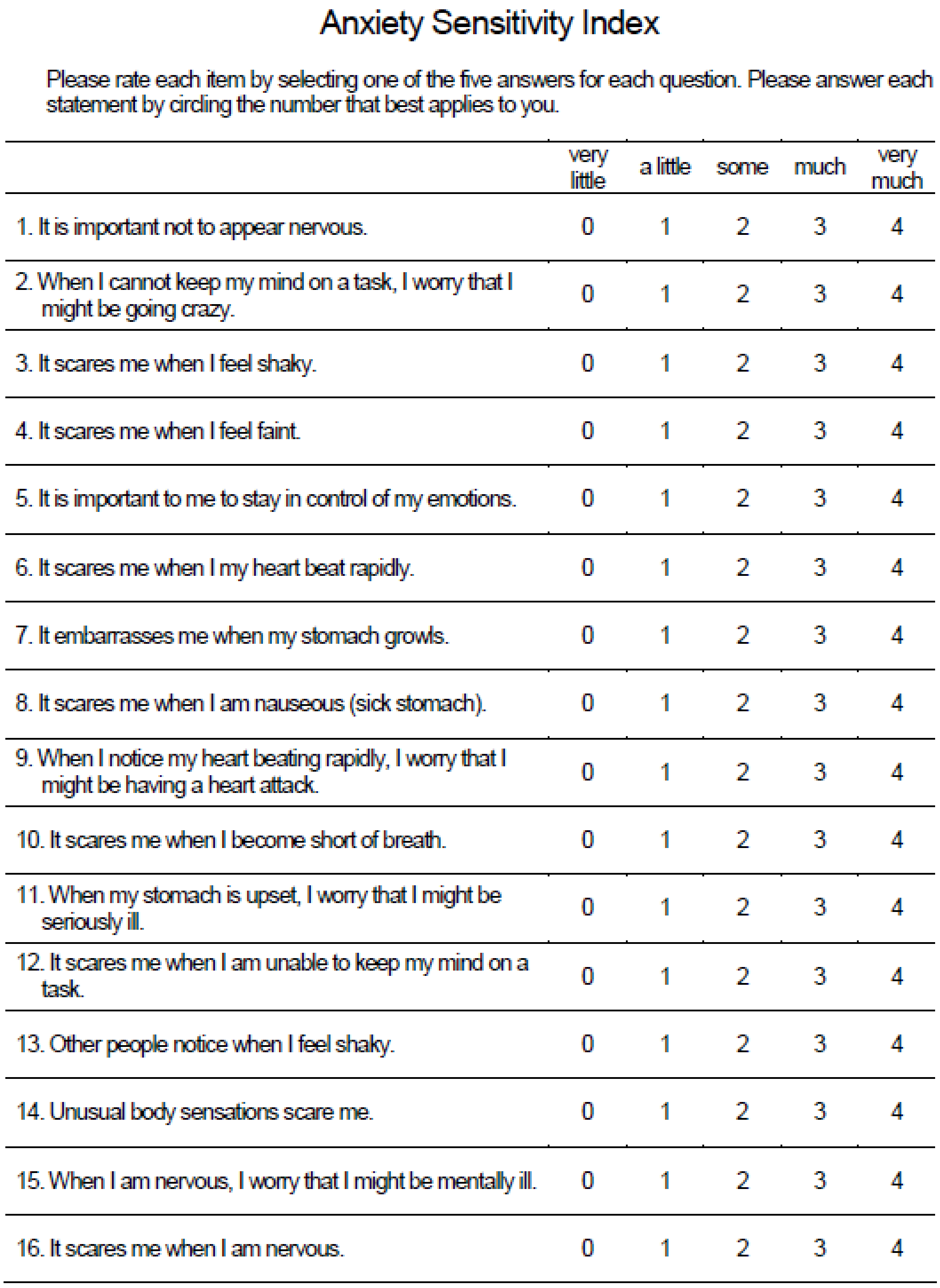
Below you will find a list of statements. Please rate how true each statement is for you by circling a number next to it. Use the scale below to make your choice.

1	2	3	4	5	6	7
never true	very seldom true	seldom true	sometimes true	frequently true	almost always true	always true

1. My painful experiences and memories make it difficult for me to live a life that I would value.	1	2	3	4	5	6	7
2. I'm afraid of my feelings.	1	2	3	4	5	6	7
3. I worry about not being able to control my worries and feelings.	1	2	3	4	5	6	7
4. My painful memories prevent me from having a fulfilling life.	1	2	3	4	5	6	7
5. Emotions cause problems in my life.	1	2	3	4	5	6	7
6. It seems like most people are handling their lives better than I am.	1	2	3	4	5	6	7
7. Worries get in the way of my success.	1	2	3	4	5	6	7

This is a one-factor measure of psychological inflexibility, or experiential avoidance. Score the scale by summing the seven items. Higher scores equal greater levels of psychological inflexibility.

Table 51: Anxiety Sensitivity Index

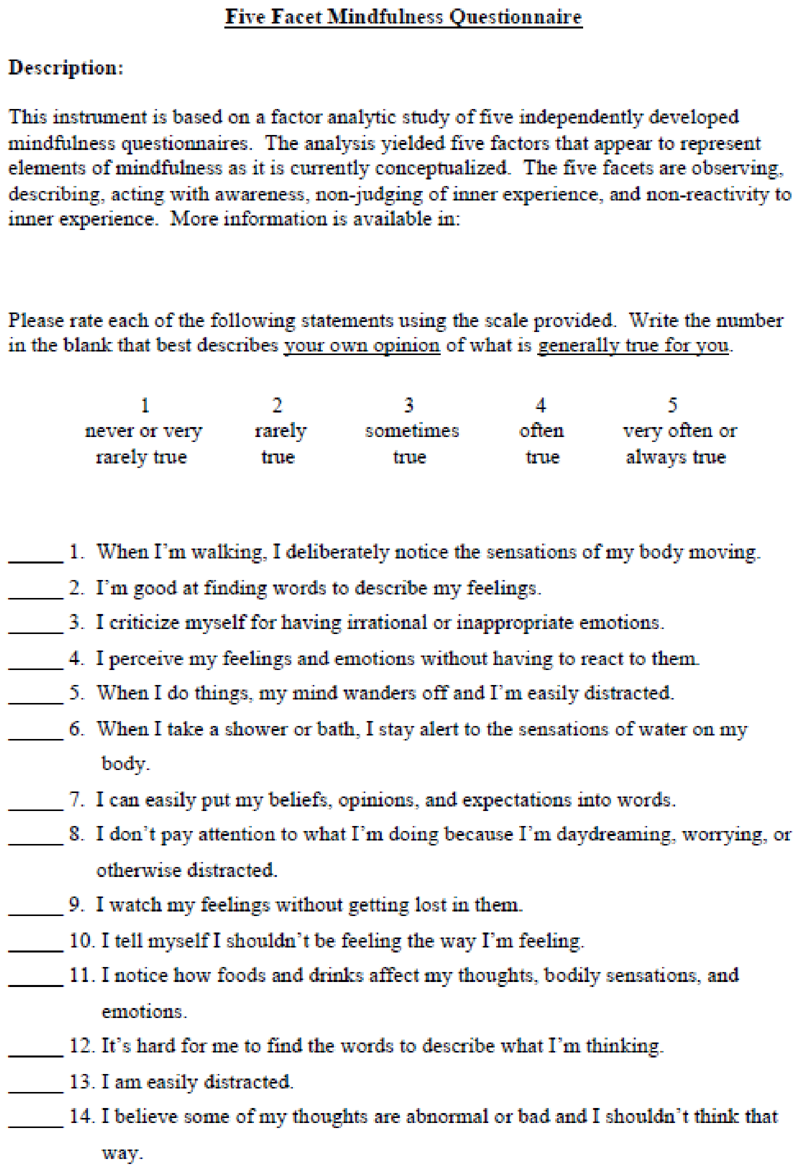


Anxiety Sensitivity Index

Please rate each item by selecting one of the five answers for each question. Please answer each statement by circling the number that best applies to you.

	very little	a little	some	much	very much
1. It is important not to appear nervous.	0	1	2	3	4
2. When I cannot keep my mind on a task, I worry that I might be going crazy.	0	1	2	3	4
3. It scares me when I feel shaky.	0	1	2	3	4
4. It scares me when I feel faint.	0	1	2	3	4
5. It is important to me to stay in control of my emotions.	0	1	2	3	4
6. It scares me when I my heart beat rapidly.	0	1	2	3	4
7. It embarrasses me when my stomach growls.	0	1	2	3	4
8. It scares me when I am nauseous (sick stomach).	0	1	2	3	4
9. When I notice my heart beating rapidly, I worry that I might be having a heart attack.	0	1	2	3	4
10. It scares me when I become short of breath.	0	1	2	3	4
11. When my stomach is upset, I worry that I might be seriously ill.	0	1	2	3	4
12. It scares me when I am unable to keep my mind on a task.	0	1	2	3	4
13. Other people notice when I feel shaky.	0	1	2	3	4
14. Unusual body sensations scare me.	0	1	2	3	4
15. When I am nervous, I worry that I might be mentally ill.	0	1	2	3	4
16. It scares me when I am nervous.	0	1	2	3	4

Table 52: Five Facet Mindfulness Questionnaire



Five Facet Mindfulness Questionnaire

Description:

This instrument is based on a factor analytic study of five independently developed mindfulness questionnaires. The analysis yielded five factors that appear to represent elements of mindfulness as it is currently conceptualized. The five facets are observing, describing, acting with awareness, non-judging of inner experience, and non-reactivity to inner experience. More information is available in:

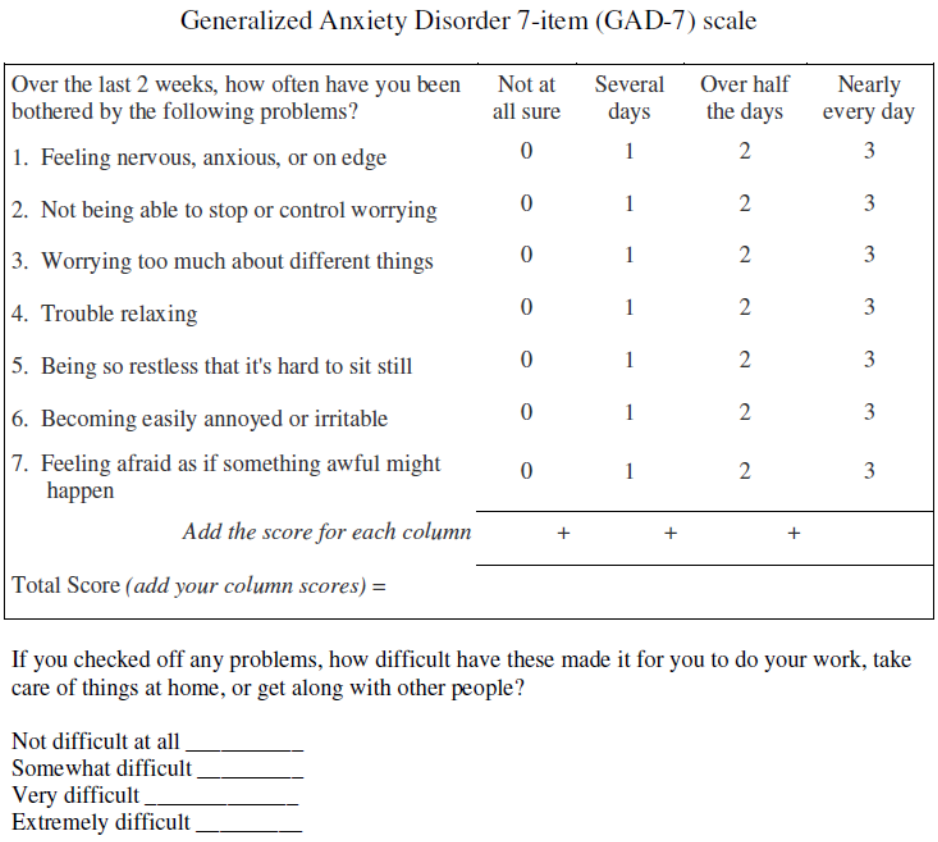
Please rate each of the following statements using the scale provided. Write the number in the blank that best describes your own opinion of what is generally true for you.

1	2	3	4	5
never or very rarely true	rarely true	sometimes true	often true	very often or always true

_____ 1. When I'm walking, I deliberately notice the sensations of my body moving.
_____ 2. I'm good at finding words to describe my feelings.
_____ 3. I criticize myself for having irrational or inappropriate emotions.
_____ 4. I perceive my feelings and emotions without having to react to them.
_____ 5. When I do things, my mind wanders off and I'm easily distracted.
_____ 6. When I take a shower or bath, I stay alert to the sensations of water on my body.
_____ 7. I can easily put my beliefs, opinions, and expectations into words.
_____ 8. I don't pay attention to what I'm doing because I'm daydreaming, worrying, or otherwise distracted.
_____ 9. I watch my feelings without getting lost in them.
_____ 10. I tell myself I shouldn't be feeling the way I'm feeling.
_____ 11. I notice how foods and drinks affect my thoughts, bodily sensations, and emotions.
_____ 12. It's hard for me to find the words to describe what I'm thinking.
_____ 13. I am easily distracted.
_____ 14. I believe some of my thoughts are abnormal or bad and I shouldn't think that way.

______ 15. I pay attention to sensations, such as the wind in my hair or sun on my face.
______ 16. I have trouble thinking of the right words to express how I feel about things
______ 17. I make judgments about whether my thoughts are good or bad.
______ 18. I find it difficult to stay focused on what's happening in the present.
______ 19. When I have distressing thoughts or images, I "step back" and am aware of the thought or image without getting taken over by it.
______ 20. I pay attention to sounds, such as clocks ticking, birds chirping, or cars passing.
______ 21. In difficult situations, I can pause without immediately reacting.
______ 22. When I have a sensation in my body, it's difficult for me to describe it because I can't find the right words.
______ 23. It seems I am "running on automatic" without much awareness of what I'm doing.
______24. When I have distressing thoughts or images, I feel calm soon after.
______ 25. I tell myself that I shouldn't be thinking the way I'm thinking.
______ 26. I notice the smells and aromas of things.
______ 27. Even when I'm feeling terribly upset, I can find a way to put it into words.
______ 28. I rush through activities without being really attentive to them.
______ 29. When I have distressing thoughts or images I am able just to notice them without reacting.
______ 30. I think some of my emotions are bad or inappropriate and I shouldn't feel them.
______ 31. I notice visual elements in art or nature, such as colors, shapes, textures, or patterns of light and shadow.
______ 32. My natural tendency is to put my experiences into words.
______ 33. When I have distressing thoughts or images, I just notice them and let them go.
______ 34. I do jobs or tasks automatically without being aware of what I'm doing.
______ 35. When I have distressing thoughts or images, I judge myself as good or bad, depending what the thought/image is about.
______ 36. I pay attention to how my emotions affect my thoughts and behavior.
______ 37. I can usually describe how I feel at the moment in considerable detail.
______ 38. I find myself doing things without paying attention.
______ 39. I disapprove of myself when I have irrational ideas.

Table 53: Generalized Anxiety Disorder 7-Item Scale (GAD-7)



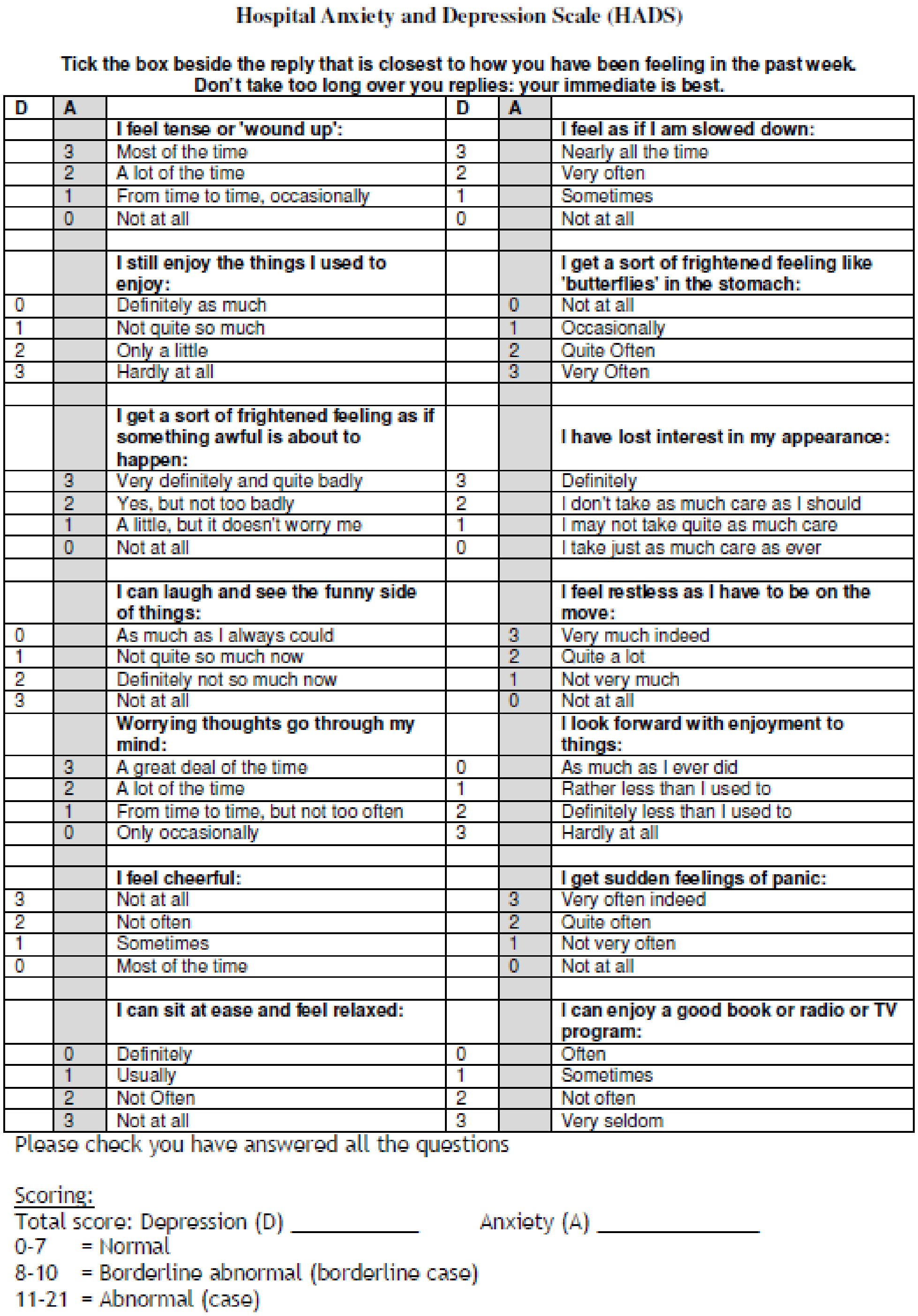
Generalized Anxiety Disorder 7-item (GAD-7) scale

Over the last 2 weeks, how often have you been bothered by the following problems?	Not at all sure	Several days	Over half the days	Nearly every day
1. Feeling nervous, anxious, or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it's hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
7. Feeling afraid as if something awful might happen	0	1	2	3
Add the score for each column	+	+	+	
Total Score *(add your column scores) =*				

If you checked off any problems, how difficult have these made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all __________
Somewhat difficult _________
Very difficult _____________
Extremely difficult _________

Table 54: Hospital Anxiety and Depression Scale (HADS)



Hospital Anxiety and Depression Scale (HADS)

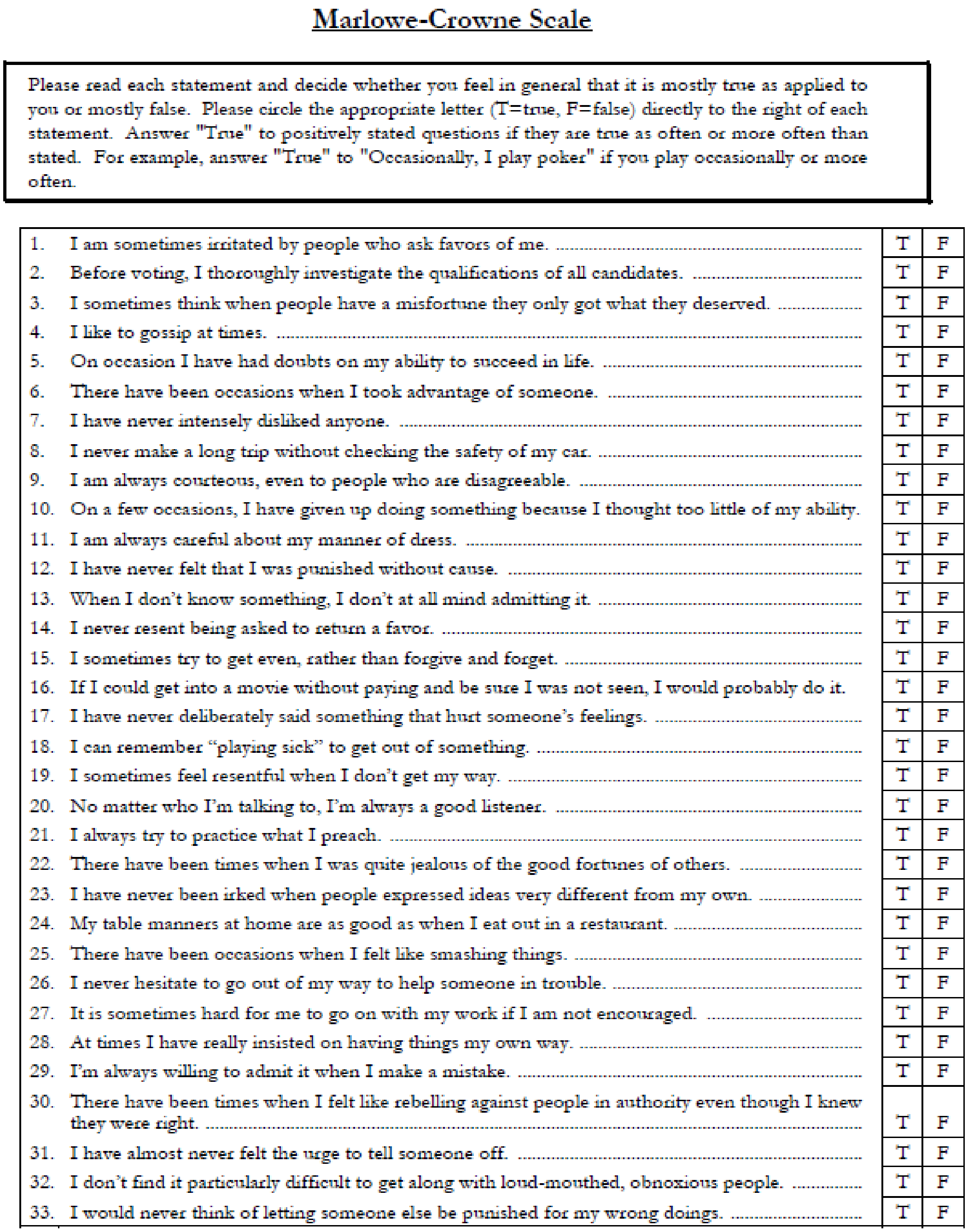
Tick the box beside the reply that is closest to how you have been feeling in the past week.
Don't take too long over you replies: your immediate is best.

D	A		D	A	
		I feel tense or 'wound up':			**I feel as if I am slowed down:**
	3	Most of the time	3		Nearly all the time
	2	A lot of the time	2		Very often
	1	From time to time, occasionally	1		Sometimes
	0	Not at all	0		Not at all
		I still enjoy the things I used to enjoy:			**I get a sort of frightened feeling like 'butterflies' in the stomach:**
0		Definitely as much		0	Not at all
1		Not quite so much		1	Occasionally
2		Only a little		2	Quite Often
3		Hardly at all		3	Very Often
		I get a sort of frightened feeling as if something awful is about to happen:			**I have lost interest in my appearance:**
	3	Very definitely and quite badly	3		Definitely
	2	Yes, but not too badly	2		I don't take as much care as I should
	1	A little, but it doesn't worry me	1		I may not take quite as much care
	0	Not at all	0		I take just as much care as ever
		I can laugh and see the funny side of things:			**I feel restless as I have to be on the move:**
0		As much as I always could		3	Very much indeed
1		Not quite so much now		2	Quite a lot
2		Definitely not so much now		1	Not very much
3		Not at all		0	Not at all
		Worrying thoughts go through my mind:			**I look forward with enjoyment to things:**
	3	A great deal of the time	0		As much as I ever did
	2	A lot of the time	1		Rather less than I used to
	1	From time to time, but not too often	2		Definitely less than I used to
	0	Only occasionally	3		Hardly at all
		I feel cheerful:			**I get sudden feelings of panic:**
3		Not at all		3	Very often indeed
2		Not often		2	Quite often
1		Sometimes		1	Not very often
0		Most of the time		0	Not at all
		I can sit at ease and feel relaxed:			**I can enjoy a good book or radio or TV program:**
	0	Definitely	0		Often
	1	Usually	1		Sometimes
	2	Not Often	2		Not often
	3	Not at all	3		Very seldom

Please check you have answered all the questions

Scoring:
Total score: Depression (D) ____________ Anxiety (A) _______________
0-7 = Normal
8-10 = Borderline abnormal (borderline case)
11-21 = Abnormal (case)

Table 55: Marlow-Crowne Scale

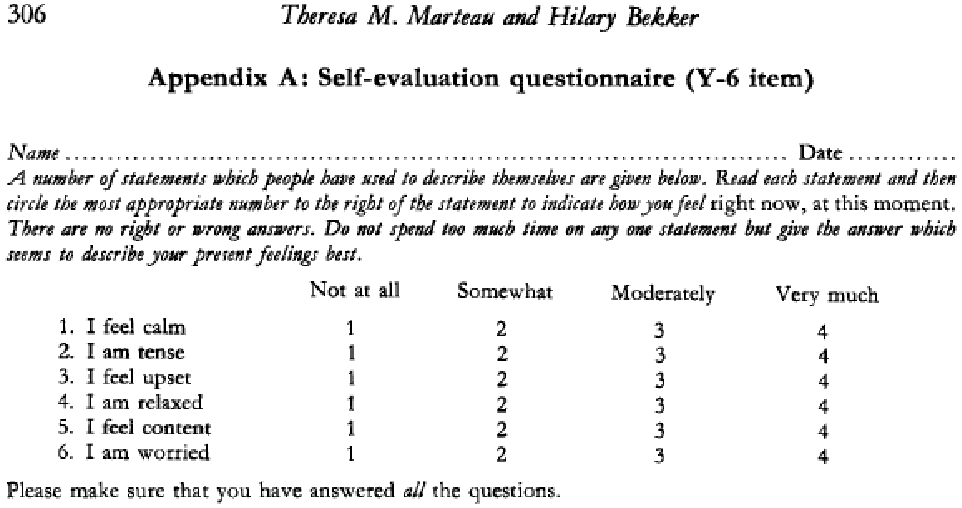


Marlowe-Crowne Scale

Please read each statement and decide whether you feel in general that it is mostly true as applied to you or mostly false. Please circle the appropriate letter (T=true, F=false) directly to the right of each statement. Answer "True" to positively stated questions if they are true as often or more often than stated. For example, answer "True" to "Occasionally, I play poker" if you play occasionally or more often.

1.	I am sometimes irritated by people who ask favors of me.	T	F
2.	Before voting, I thoroughly investigate the qualifications of all candidates.	T	F
3.	I sometimes think when people have a misfortune they only got what they deserved.	T	F
4.	I like to gossip at times.	T	F
5.	On occasion I have had doubts on my ability to succeed in life.	T	F
6.	There have been occasions when I took advantage of someone.	T	F
7.	I have never intensely disliked anyone.	T	F
8.	I never make a long trip without checking the safety of my car.	T	F
9.	I am always courteous, even to people who are disagreeable.	T	F
10.	On a few occasions, I have given up doing something because I thought too little of my ability.	T	F
11.	I am always careful about my manner of dress.	T	F
12.	I have never felt that I was punished without cause.	T	F
13.	When I don't know something, I don't at all mind admitting it.	T	F
14.	I never resent being asked to return a favor.	T	F
15.	I sometimes try to get even, rather than forgive and forget.	T	F
16.	If I could get into a movie without paying and be sure I was not seen, I would probably do it.	T	F
17.	I have never deliberately said something that hurt someone's feelings.	T	F
18.	I can remember "playing sick" to get out of something.	T	F
19.	I sometimes feel resentful when I don't get my way.	T	F
20.	No matter who I'm talking to, I'm always a good listener.	T	F
21.	I always try to practice what I preach.	T	F
22.	There have been times when I was quite jealous of the good fortunes of others.	T	F
23.	I have never been irked when people expressed ideas very different from my own.	T	F
24.	My table manners at home are as good as when I eat out in a restaurant.	T	F
25.	There have been occasions when I felt like smashing things.	T	F
26.	I never hesitate to go out of my way to help someone in trouble.	T	F
27.	It is sometimes hard for me to go on with my work if I am not encouraged.	T	F
28.	At times I have really insisted on having things my own way.	T	F
29.	I'm always willing to admit it when I make a mistake.	T	F
30.	There have been times when I felt like rebelling against people in authority even though I knew they were right.	T	F
31.	I have almost never felt the urge to tell someone off.	T	F
32.	I don't find it particularly difficult to get along with loud-mouthed, obnoxious people.	T	F
33.	I would never think of letting someone else be punished for my wrong doings.	T	F

Table 56: Marteau Self-Evaluation Questionnaire



Appendix A: Self-evaluation questionnaire (Y-6 item)

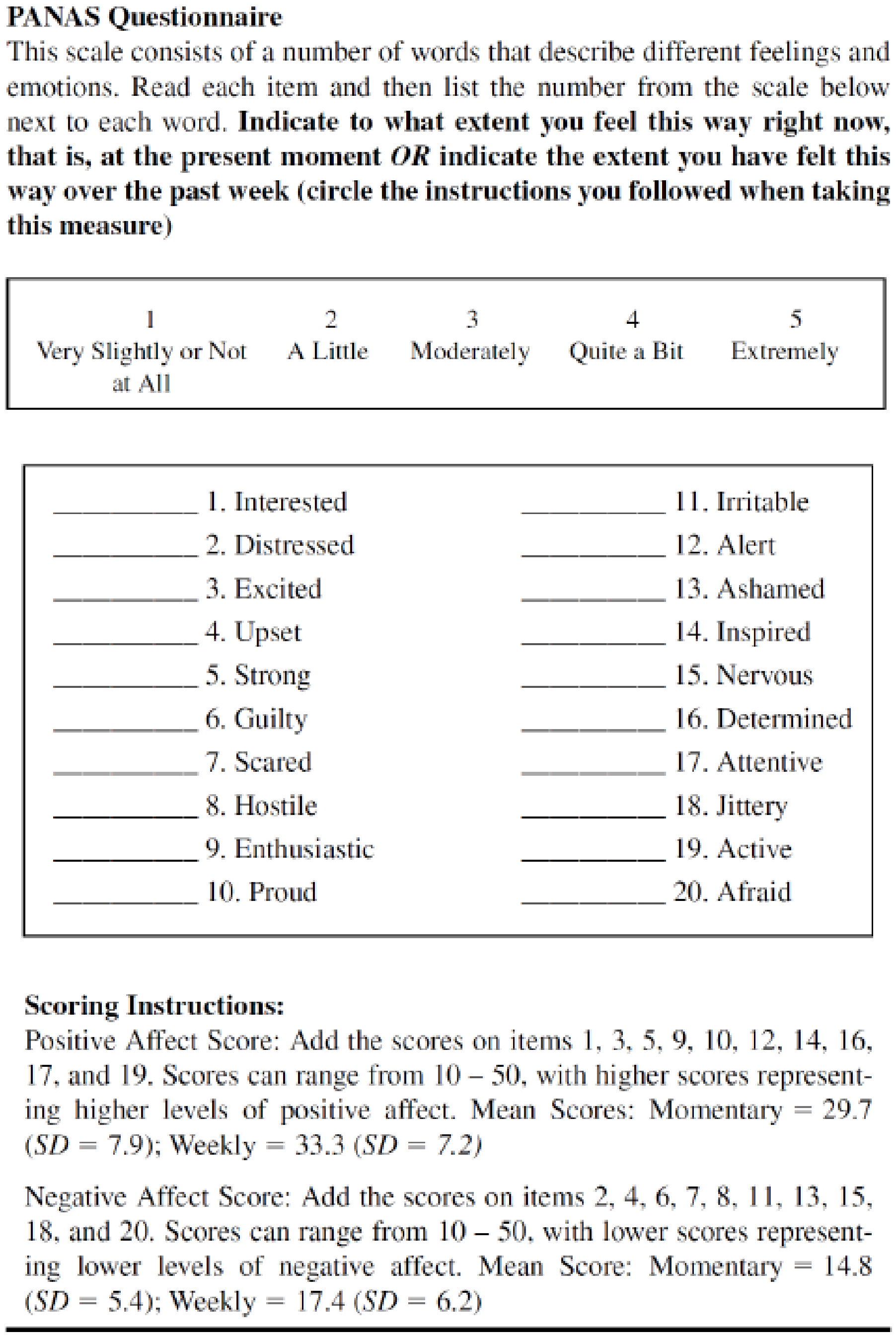
Name .... Date ....

A number of statements which people have used to describe themselves are given below. Read each statement and then circle the most appropriate number to the right of the statement to indicate how you feel right now, at this moment. *There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe your present feelings best.*

	Not at all	Somewhat	Moderately	Very much
1. I feel calm	1	2	3	4
2. I am tense	1	2	3	4
3. I feel upset	1	2	3	4
4. I am relaxed	1	2	3	4
5. I feel content	1	2	3	4
6. I am worried	1	2	3	4

Please make sure that you have answered *all* the questions.

Table 58: PANAS Questionnaire



PANAS Questionnaire

This scale consists of a number of words that describe different feelings and emotions. Read each item and then list the number from the scale below next to each word. **Indicate to what extent you feel this way right now, that is, at the present moment *OR* indicate the extent you have felt this way over the past week (circle the instructions you followed when taking this measure)**

1	2	3	4	5
Very Slightly or Not at All	A Little	Moderately	Quite a Bit	Extremely

__________ 1. Interested

__________ 2. Distressed

__________ 3. Excited

__________ 4. Upset

__________ 5. Strong

__________ 6. Guilty

__________ 7. Scared

__________ 8. Hostile

__________ 9. Enthusiastic

__________ 10. Proud

__________ 11. Irritable

__________ 12. Alert

__________ 13. Ashamed

__________ 14. Inspired

__________ 15. Nervous

__________ 16. Determined

__________ 17. Attentive

__________ 18. Jittery

__________ 19. Active

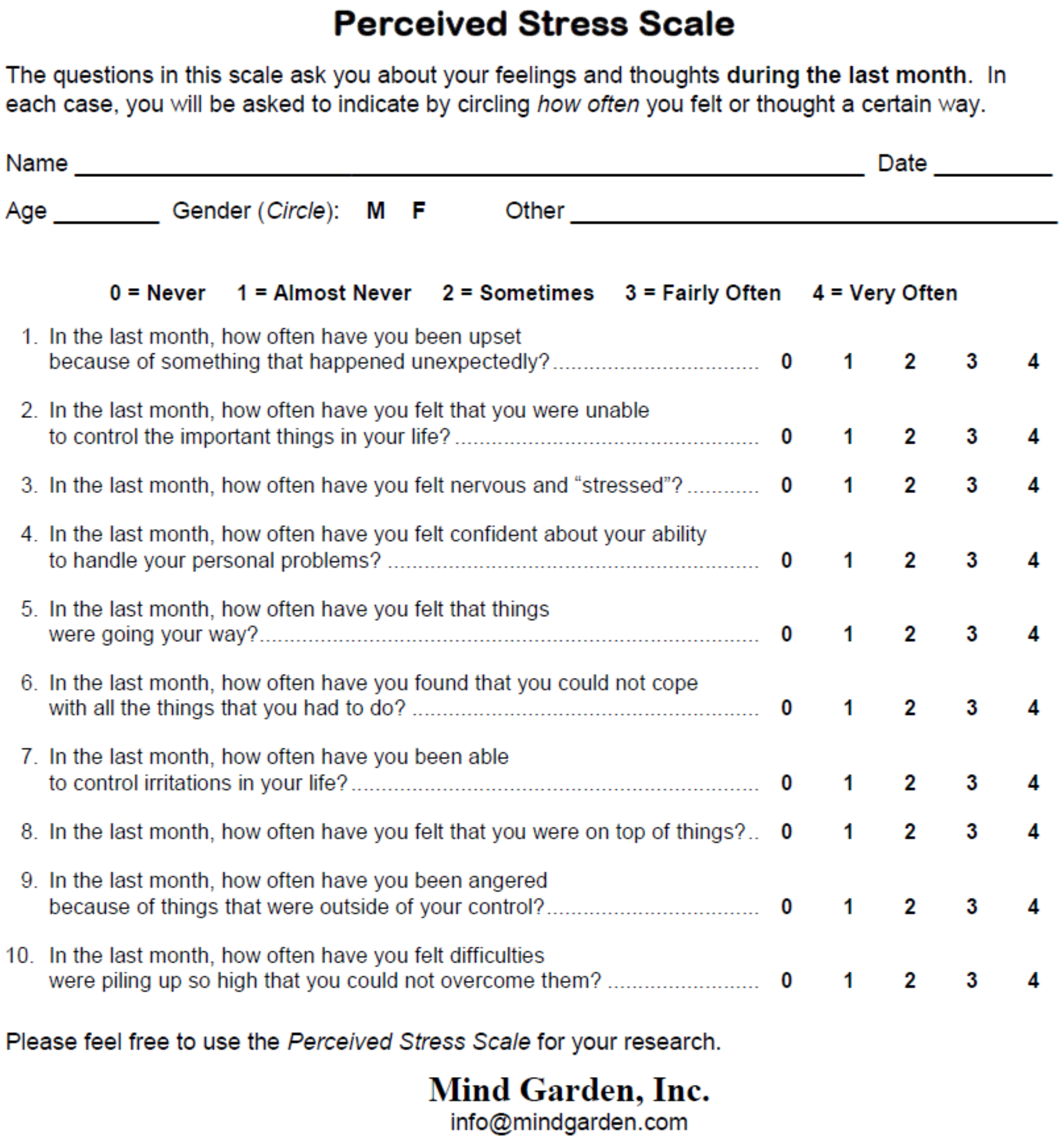
__________ 20. Afraid

Scoring Instructions:

Positive Affect Score: Add the scores on items 1, 3, 5, 9, 10, 12, 14, 16, 17, and 19. Scores can range from 10 – 50, with higher scores representing higher levels of positive affect. Mean Scores: Momentary = 29.7 (*SD* = 7.9); Weekly = 33.3 (*SD = 7.2)*

Negative Affect Score: Add the scores on items 2, 4, 6, 7, 8, 11, 13, 15, 18, and 20. Scores can range from 10 – 50, with lower scores representing lower levels of negative affect. Mean Score: Momentary = 14.8 (*SD* = 5.4); Weekly = 17.4 (*SD* = 6.2)

Table 59: Perceived Stress Scale



Perceived Stress Scale

The questions in this scale ask you about your feelings and thoughts **during the last month**. In each case, you will be asked to indicate by circling *how often* you felt or thought a certain way.

Name ______________________________ Date __________

Age ________ Gender (*Circle*): **M** **F** Other ______________________________

0 = Never 1 = Almost Never 2 = Sometimes 3 = Fairly Often 4 = Very Often

1. In the last month, how often have you been upset because of something that happened unexpectedly?	**0**	**1**	**2**	**3**	**4**
2. In the last month, how often have you felt that you were unable to control the important things in your life?	**0**	**1**	**2**	**3**	**4**
3. In the last month, how often have you felt nervous and "stressed"?	**0**	**1**	**2**	**3**	**4**
4. In the last month, how often have you felt confident about your ability to handle your personal problems?	**0**	**1**	**2**	**3**	**4**
5. In the last month, how often have you felt that things were going your way?	**0**	**1**	**2**	**3**	**4**
6. In the last month, how often have you found that you could not cope with all the things that you had to do?	**0**	**1**	**2**	**3**	**4**
7. In the last month, how often have you been able to control irritations in your life?	**0**	**1**	**2**	**3**	**4**
8. In the last month, how often have you felt that you were on top of things?	**0**	**1**	**2**	**3**	**4**
9. In the last month, how often have you been angered because of things that were outside of your control?	**0**	**1**	**2**	**3**	**4**
10. In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?	**0**	**1**	**2**	**3**	**4**

Please feel free to use the *Perceived Stress Scale* for your research.

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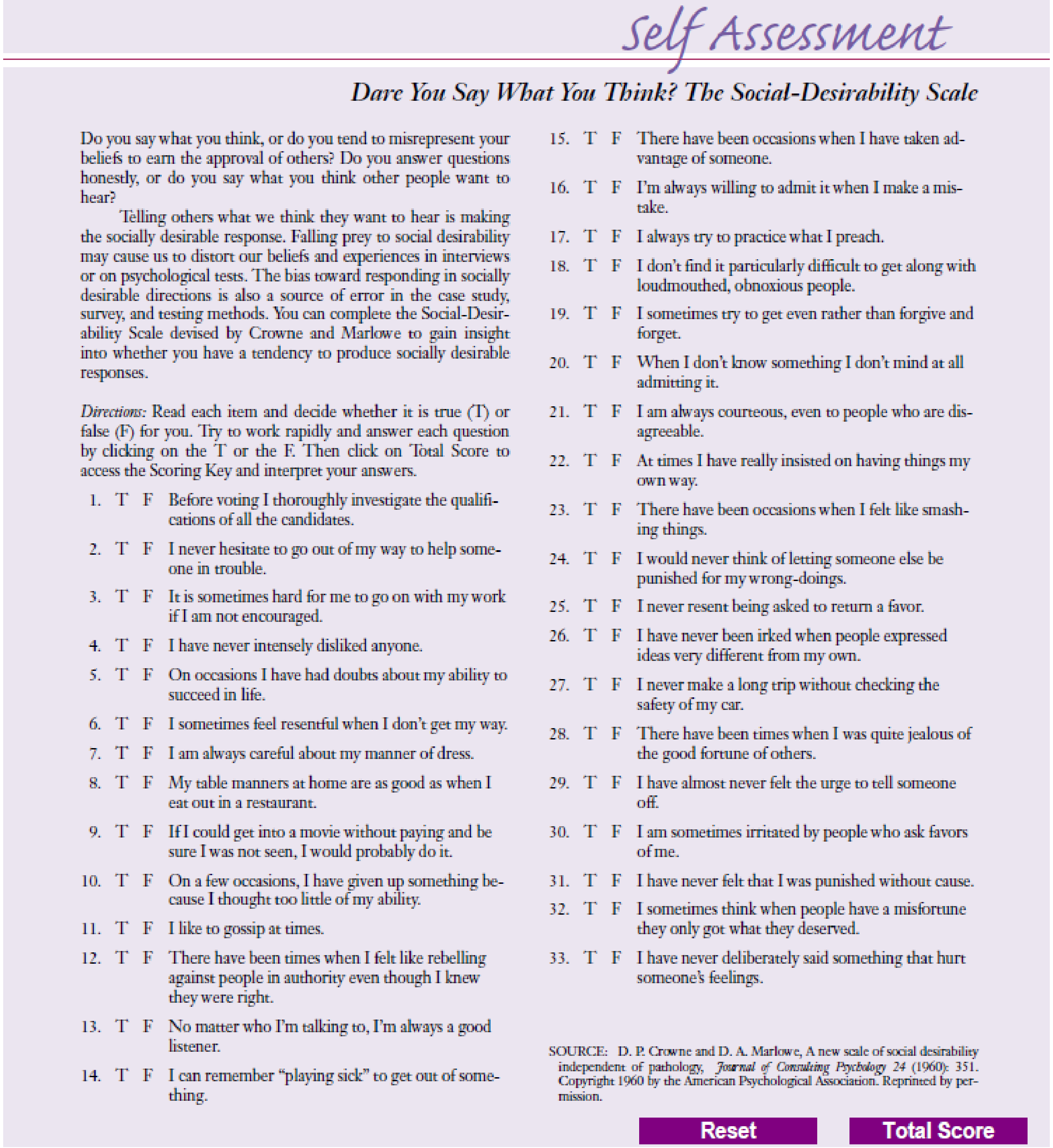
info@mindgarden.com

Table 60: Social Desirability Scale



Self Assessment

Dare You Say What You Think? The Social-Desirability Scale

Do you say what you think, or do you tend to misrepresent your beliefs to earn the approval of others? Do you answer questions honestly, or do you say what you think other people want to hear?

Telling others what we think they want to hear is making the socially desirable response. Falling prey to social desirability may cause us to distort our beliefs and experiences in interviews or on psychological tests. The bias toward responding in socially desirable directions is also a source of error in the case study, survey, and testing methods. You can complete the Social-Desirability Scale devised by Crowne and Marlowe to gain insight into whether you have a tendency to produce socially desirable responses.

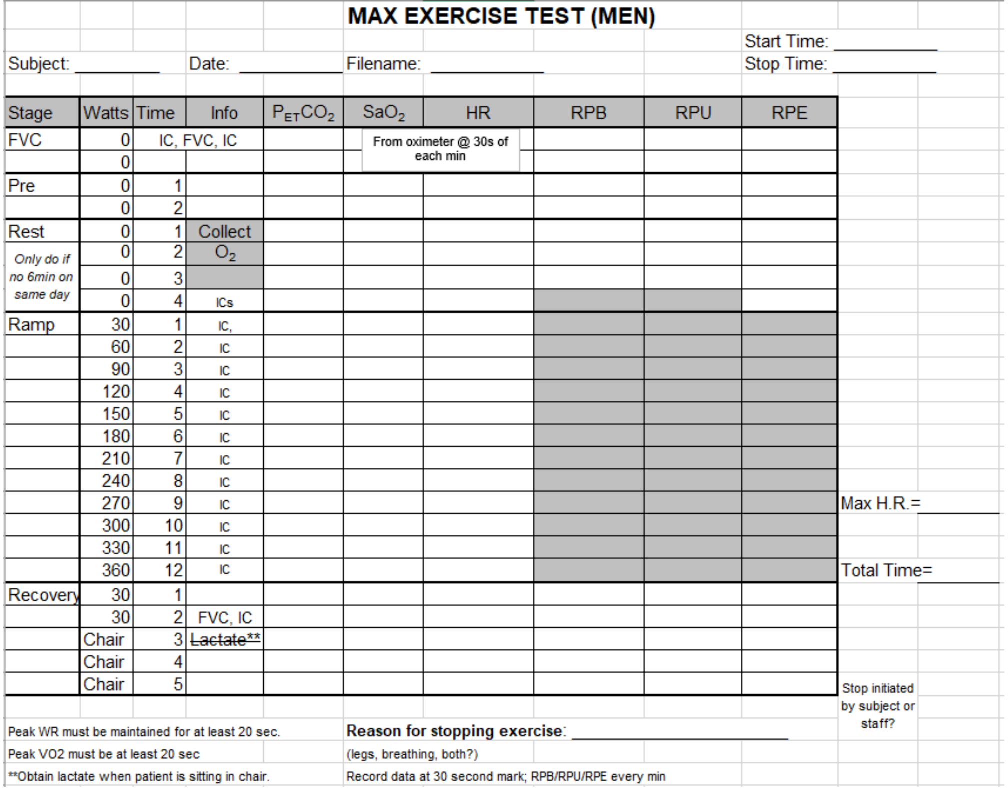
Directions: Read each item and decide whether it is true (T) or false (F) for you. Try to work rapidly and answer each question by clicking on the T or the F. Then click on Total Score to access the Scoring Key and interpret your answers.

1. T F Before voting I thoroughly investigate the qualifications of all the candidates.
2. T F I never hesitate to go out of my way to help someone in trouble.
3. T F It is sometimes hard for me to go on with my work if I am not encouraged.
4. T F I have never intensely disliked anyone.
5. T F On occasions I have had doubts about my ability to succeed in life.
6. T F I sometimes feel resentful when I don't get my way.
7. T F I am always careful about my manner of dress.
8. T F My table manners at home are as good as when I eat out in a restaurant.
9. T F If I could get into a movie without paying and be sure I was not seen, I would probably do it.
10. T F On a few occasions, I have given up something because I thought too little of my ability.
11. T F I like to gossip at times.
12. T F There have been times when I felt like rebelling against people in authority even though I knew they were right.
13. T F No matter who I'm talking to, I'm always a good listener.
14. T F I can remember "playing sick" to get out of something.
15. T F There have been occasions when I have taken advantage of someone.
16. T F I'm always willing to admit it when I make a mistake.
17. T F I always try to practice what I preach.
18. T F I don't find it particularly difficult to get along with loudmouthed, obnoxious people.
19. T F I sometimes try to get even rather than forgive and forget.
20. T F When I don't know something I don't mind at all admitting it.
21. T F I am always courteous, even to people who are disagreeable.
22. T F At times I have really insisted on having things my own way.
23. T F There have been occasions when I felt like smashing things.
24. T F I would never think of letting someone else be punished for my wrong-doings.
25. T F I never resent being asked to return a favor.
26. T F I have never been irked when people expressed ideas very different from my own.
27. T F I never make a long trip without checking the safety of my car.
28. T F There have been times when I was quite jealous of the good fortune of others.
29. T F I have almost never felt the urge to tell someone off.
30. T F I am sometimes irritated by people who ask favors of me.
31. T F I have never felt that I was punished without cause.
32. T F I sometimes think when people have a misfortune they only got what they deserved.
33. T F I have never deliberately said something that hurt someone's feelings.

SOURCE: D. P. Crowne and D. A. Marlowe, A new scale of social desirability independent of pathology, *Journal of Consulting Psychology* 24 (1960): 351. Copyright 1960 by the American Psychological Association. Reprinted by permission.

Exercise Test Data Collection

Table 61: Maximal aerobic capacity test (male) data sheet



MAX EXERCISE TEST (MEN)

Start Time: ___________
Subject: _________ Date: ___________ Filename: ___________
Stop Time: ___________

Stage	Watts	Time	Info	$P_{ET}CO_2$	SaO_2	HR	RPB	RPU	RPE
FVC	0		IC, FVC, IC		From oximeter @ 30s of each min				
	0								
Pre	0	1							
	0	2							
Rest	0	1	Collect						
Only do if no 6min on same day	0	2	O_2						
	0	3							
	0	4	ICs						
Ramp	30	1	IC,						
	60	2	IC						
	90	3	IC						
	120	4	IC						
	150	5	IC						
	180	6	IC						
	210	7	IC						
	240	8	IC						
	270	9	IC						
	300	10	IC						
	330	11	IC						
	360	12	IC						
Recovery	30	1							
	30	2	FVC, IC						
	Chair	3	~~Lactate**~~						
	Chair	4							
	Chair	5							

Max H.R.= ________

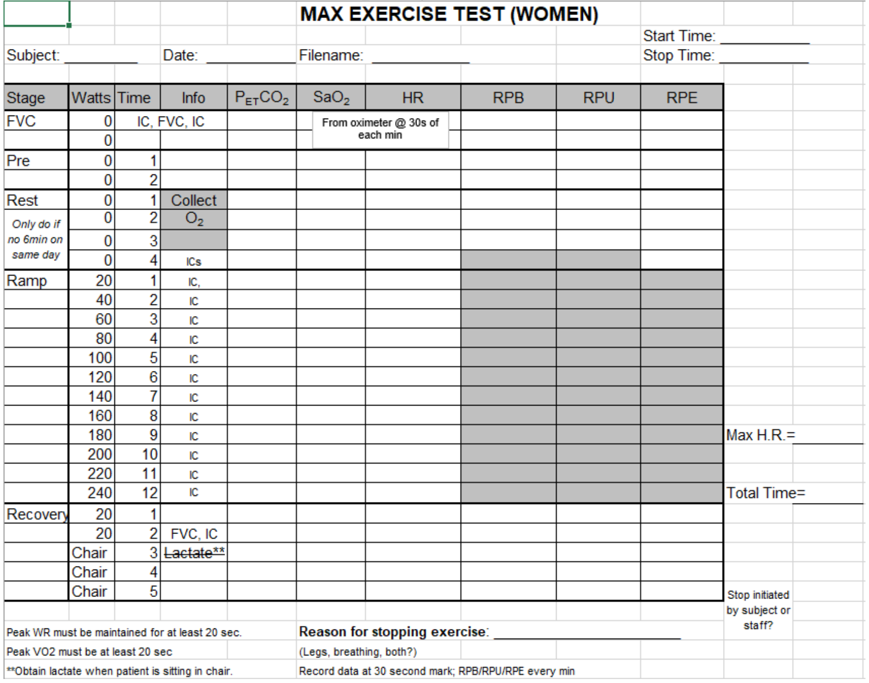
Total Time= ________

Stop initiated by subject or staff?

Peak WR must be maintained for at least 20 sec.
Peak VO2 must be at least 20 sec
**Obtain lactate when patient is sitting in chair.

Reason for stopping exercise: ______________________
(legs, breathing, both?)
Record data at 30 second mark; RPB/RPU/RPE every min

Table 62: Maximal aerobic capacity test (female) data sheet



MAX EXERCISE TEST (WOMEN)

Start Time: ___________
Subject: _________ Date: ___________ Filename: ___________
Stop Time: ___________

Stage	Watts	Time	Info	$P_{ET}CO_2$	SaO_2	HR	RPB	RPU	RPE
FVC	0		IC, FVC, IC		From oximeter @ 30s of each min				
	0								
Pre	0	1							
	0	2							
Rest	0	1	Collect						
Only do if no 6min on same day	0	2	O_2						
	0	3							
	0	4	ICs						
Ramp	20	1	IC,						
	40	2	IC						
	60	3	IC						
	80	4	IC						
	100	5	IC						
	120	6	IC						
	140	7	IC						
	160	8	IC						
	180	9	IC						
	200	10	IC						
	220	11	IC						
	240	12	IC						
Recovery	20	1							
	20	2	FVC, IC						
	Chair	3	~~Lactate**~~						
	Chair	4							
	Chair	5							

Max H.R.= ________

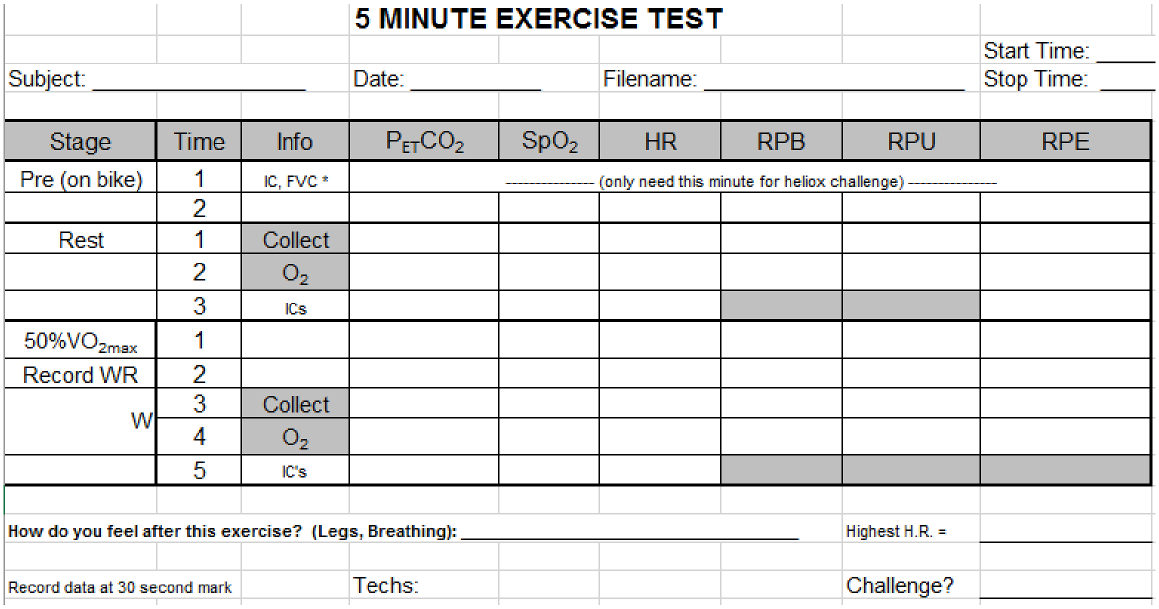
Total Time= ________

Stop initiated by subject or staff?

Peak WR must be maintained for at least 20 sec.
Peak VO2 must be at least 20 sec
**Obtain lactate when patient is sitting in chair.

Reason for stopping exercise: ______________________
(Legs, breathing, both?)
Record data at 30 second mark; RPB/RPU/RPE every min

Table 63: 5-Minute exercise test date sheet



5 MINUTE EXERCISE TEST

Start Time: _____

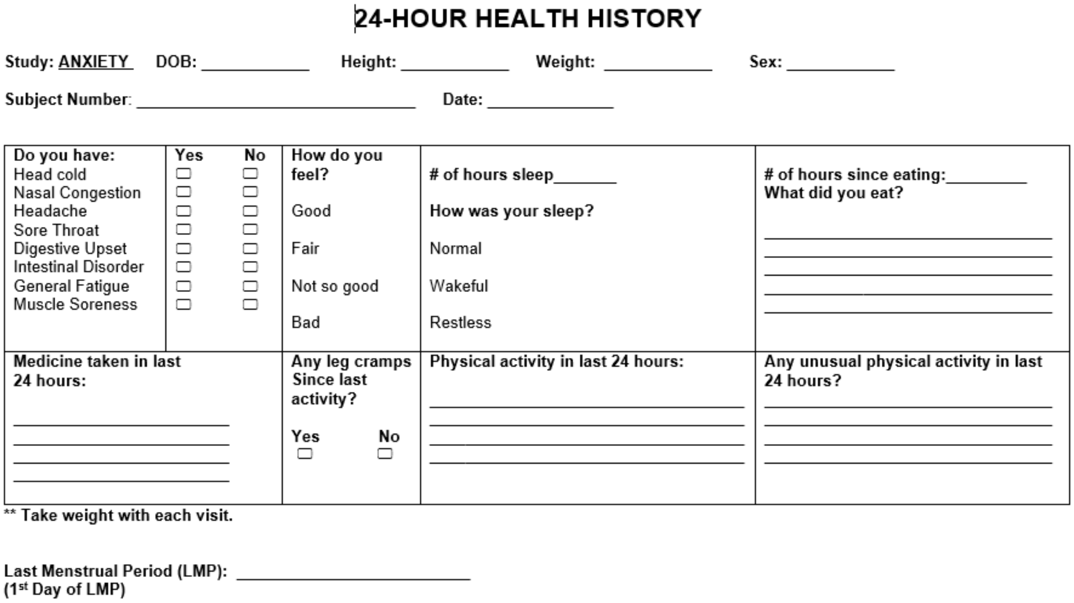
Subject: ____________________ Date: ____________ Filename: ________________________ Stop Time: _____

Stage	Time	Info	$P_{ET}CO_2$	SpO_2	HR	RPB	RPU	RPE
Pre (on bike)	1	IC, FVC *	--------------- (only need this minute for heliox challenge) ---------------					
	2							
Rest	1	Collect						
	2	O_2						
	3	ICs				▨	▨	
50%VO_{2max}	1							
Record WR	2							
W	3	Collect						
	4	O_2						
	5	IC's				▨	▨	▨

How do you feel after this exercise? (Legs, Breathing): ________________________________ Highest H.R. = ____________

Record data at 30 second mark Techs: Challenge? ____________

Table 64: 24-Hour health history form



24-HOUR HEALTH HISTORY

Study: **ANXIETY** **DOB:** ___________ **Height:** ___________ **Weight:** ___________ **Sex:** ___________

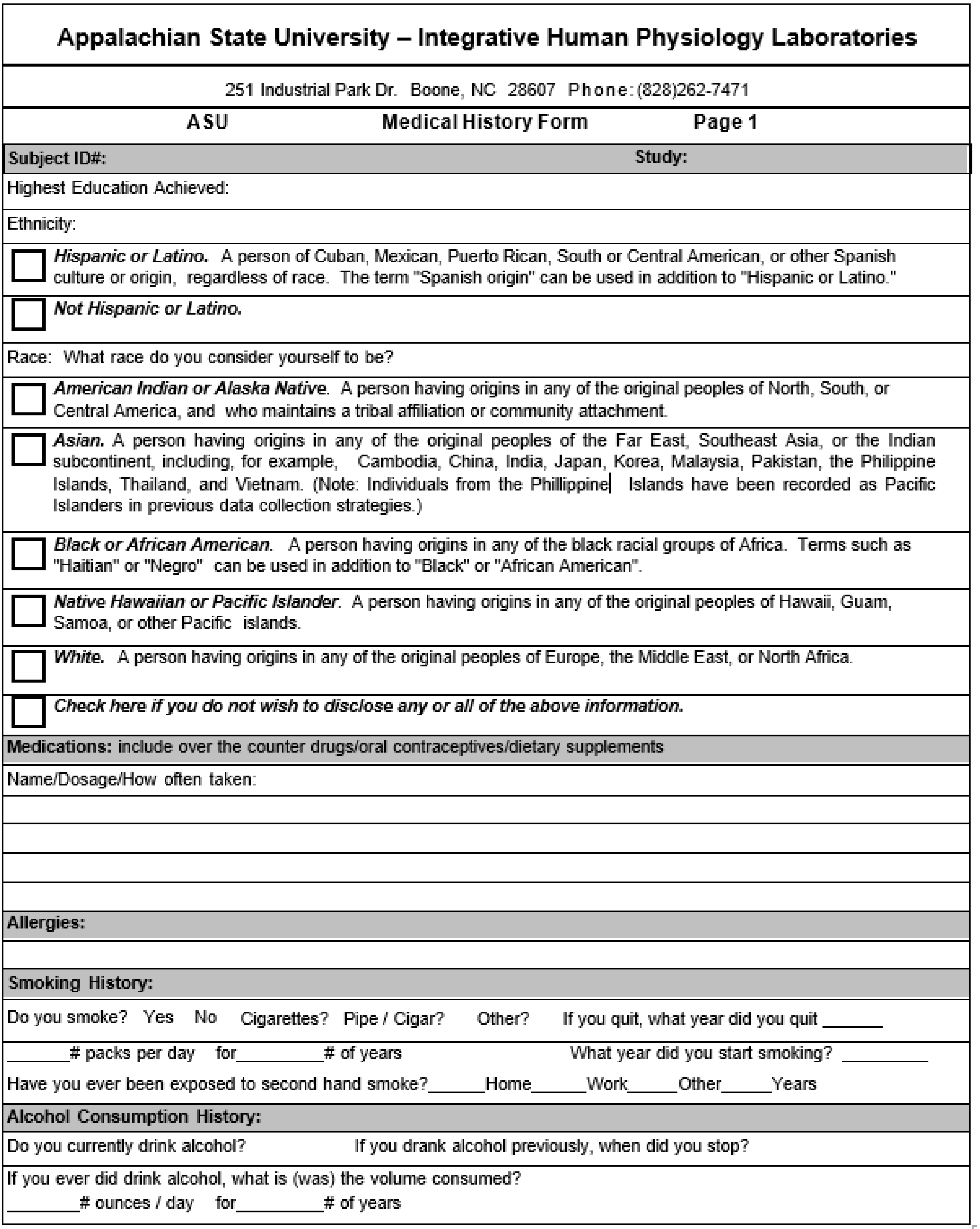
Subject Number: ___________________________ **Date:** ____________

Do you have: Head cold Nasal Congestion Headache Sore Throat Digestive Upset Intestinal Disorder General Fatigue Muscle Soreness	**Yes** ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐	**No** ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐	**How do you feel?** Good Fair Not so good Bad	**# of hours sleep**_______ **How was your sleep?** Normal Wakeful Restless	**# of hours since eating:**_________ **What did you eat?** ______________________ ______________________ ______________________ ______________________ ______________________
Medicine taken in last 24 hours: ____________________ ____________________ ____________________ ____________________			**Any leg cramps Since last activity?** **Yes** ☐ **No** ☐	**Physical activity in last 24 hours:** ______________________ ______________________ ______________________ ______________________	**Any unusual physical activity in last 24 hours?** ______________________ ______________________ ______________________ ______________________

**** Take weight with each visit.**

Last Menstrual Period (LMP): ______________________
(1st Day of LMP)

Table 65: Medical history form



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ASU **Medical History Form** **Page 1**

Subject ID#: **Study:**

Highest Education Achieved:

Ethnicity:

☐ ***Hispanic or Latino.*** A person of Cuban, Mexican, Puerto Rican, South or Central American, or other Spanish culture or origin, regardless of race. The term "Spanish origin" can be used in addition to "Hispanic or Latino."

☐ ***Not Hispanic or Latino.***

Race: What race do you consider yourself to be?

☐ ***American Indian or Alaska Native.*** A person having origins in any of the original peoples of North, South, or Central America, and who maintains a tribal affiliation or community attachment.

☐ ***Asian.*** A person having origins in any of the original peoples of the Far East, Southeast Asia, or the Indian subcontinent, including, for example, Cambodia, China, India, Japan, Korea, Malaysia, Pakistan, the Philippine Islands, Thailand, and Vietnam. (Note: Individuals from the Phillippine Islands have been recorded as Pacific Islanders in previous data collection strategies.)

☐ ***Black or African American.*** A person having origins in any of the black racial groups of Africa. Terms such as "Haitian" or "Negro" can be used in addition to "Black" or "African American".

☐ ***Native Hawaiian or Pacific Islander.*** A person having origins in any of the original peoples of Hawaii, Guam, Samoa, or other Pacific islands.

☐ ***White.*** A person having origins in any of the original peoples of Europe, the Middle East, or North Africa.

☐ ***Check here if you do not wish to disclose any or all of the above information.***

Medications: include over the counter drugs/oral contraceptives/dietary supplements

Name/Dosage/How often taken:

Allergies:

Smoking History:

Do you smoke? Yes No Cigarettes? Pipe / Cigar? Other? If you quit, what year did you quit ______

______# packs per day for________# of years What year did you start smoking? _________

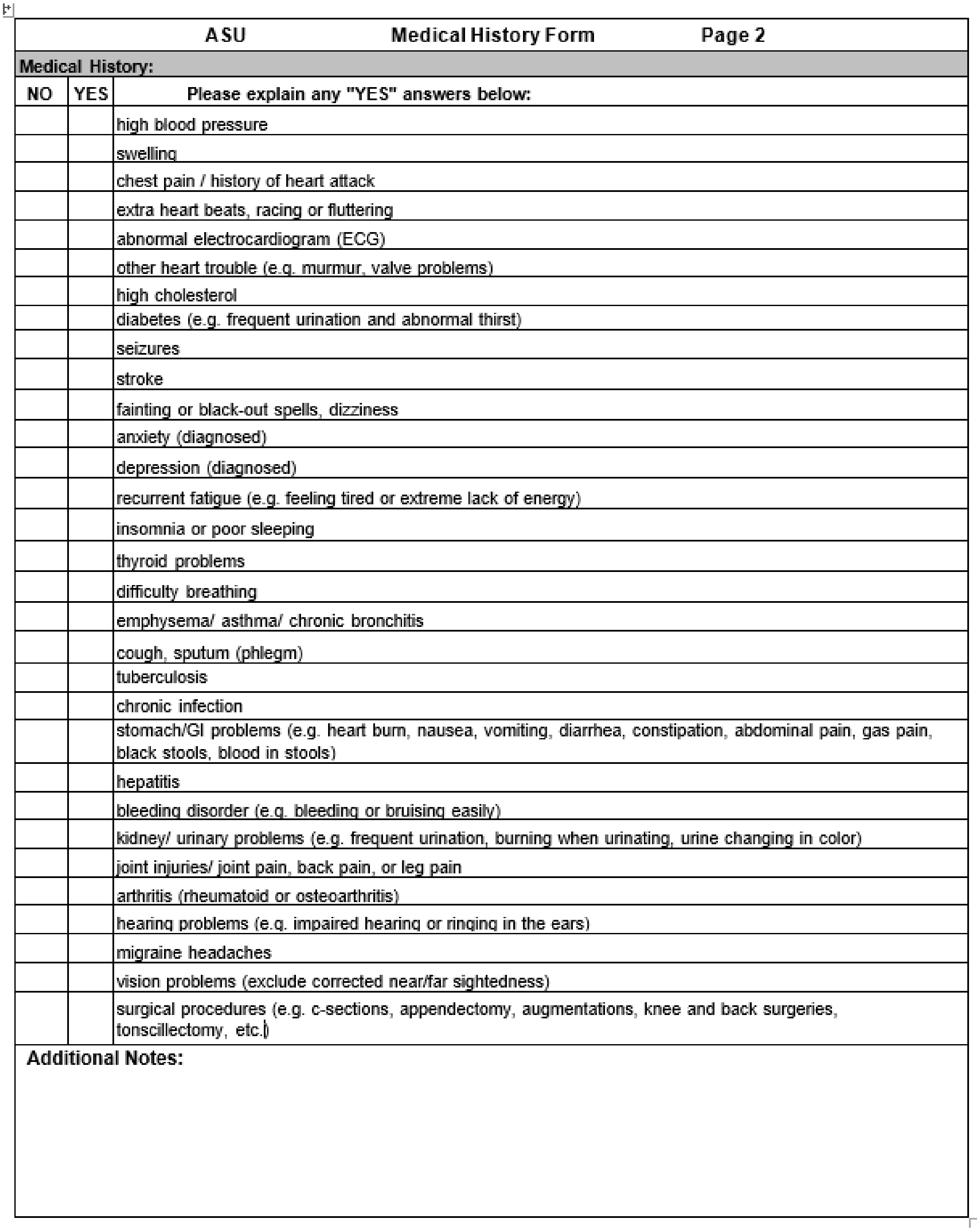
Have you ever been exposed to second hand smoke?_____Home_____Work_____Other_____Years

Alcohol Consumption History:

Do you currently drink alcohol? If you drank alcohol previously, when did you stop?

If you ever did drink alcohol, what is (was) the volume consumed?

_______# ounces / day for_________# of years



ASU **Medical History Form** **Page 2**

Medical History:

NO	YES	Please explain any "YES" answers below:
		high blood pressure
		swelling
		chest pain / history of heart attack
		extra heart beats, racing or fluttering
		abnormal electrocardiogram (ECG)
		other heart trouble (e.g. murmur, valve problems)
		high cholesterol
		diabetes (e.g. frequent urination and abnormal thirst)
		seizures
		stroke
		fainting or black-out spells, dizziness
		anxiety (diagnosed)
		depression (diagnosed)
		recurrent fatigue (e.g. feeling tired or extreme lack of energy)
		insomnia or poor sleeping
		thyroid problems
		difficulty breathing
		emphysema/ asthma/ chronic bronchitis
		cough, sputum (phlegm)
		tuberculosis
		chronic infection
		stomach/GI problems (e.g. heart burn, nausea, vomiting, diarrhea, constipation, abdominal pain, gas pain, black stools, blood in stools)
		hepatitis
		bleeding disorder (e.g. bleeding or bruising easily)
		kidney/ urinary problems (e.g. frequent urination, burning when urinating, urine changing in color)
		joint injuries/ joint pain, back pain, or leg pain
		arthritis (rheumatoid or osteoarthritis)
		hearing problems (e.g. impaired hearing or ringing in the ears)
		migraine headaches
		vision problems (exclude corrected near/far sightedness)
		surgical procedures (e.g. c-sections, appendectomy, augmentations, knee and back surgeries, tonscillectomy, etc.)

Additional Notes:

ASU Medical History Form Page 3

Exercise History:		
Do you currently exercise aerobically?	How many years?	Duration:
	Types of Exercise:	Frequency:
Do you compete in endurance events?	How many years?	Frequency:
	What events?	Athlete in college? Yes No
Any other types of exercise?	How many years?	Duration:
	Types of Exercise:	Frequency:
If you are currently sedentary, when did you last exercise?	How many years?	Duration:
	Types of Exercise:	Frequency:
Weight History:		
If overweight, how long have you been overweight?	Were you overweight as a child?	By how much?
	How many times has your weight changed?	

Any events that led up to your obesity? (E.g. Pregnancy, injury) Yes No If yes, how may events? 1 2 3 4 5 >5

Sleep History:		
Have you ever been diagnosed with a sleep disorder?	Yes	No
Do you use CPAP/BIPAP at night?	Yes	No
Do you snore at night?	Yes	No
Has someone ever told you that you snore at night?	Yes	No
Do you have daytime sleepiness?	Yes	No

Women Only:

Menstrual history: Age begin_____________ Regular? ☐ Yes ☐ No

☐ Heavy ☐ Medium ☐ Light

If your periods are irregular or associated with excessive bleeding or unusual discharge please elaborate:

Number of days between periods:________days Usual duration of period:________days

At what age did menopause occur, if applicable?

Number of pregnancies?________Number of births?________Explain any complications with pregnancy: _______________

Authorization to Release Information - Please check all that applies and sign/date.

	I authorize Appalachian State University to collect and save the above protected health information on me for purposes of research. I understand that all information is private and confidential.
	I authorize Appalachian State University to keep this information and any information gained from my participation in their studies in a database so that they may contact me.
	The above information is correct and complete to the best of my knowledge.

Signature **Date**

References

1. Kessler, R.C., et al., *Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication.* Arch Gen Psychiatry, 2005. **62**(6): p. 617-27.
2. Leon, A.C., et al., *Assessing psychiatric impairment in primary care with the Sheehan Disability Scale.* Int J Psychiatry Med, 1997. **27**(2): p. 93-105.
3. Von Leupoldt, A., et al., *The impact of emotion on respiratory-related evoked potentials.* Psychophysiology, 2010. **47**(3): p. 579-586.
4. Wanger, J., et al., *Standardisation of the measurement of lung volumes.* Eur Respir J, 2005. **26**(3): p. 511-22.
5. *Physics of Breathing*, in *Physics in Medicine*. 2003, University of Notre Dame. p. 90-123.
6. Parshall, M.B., et al., *An official American Thoracic Society statement: update on the mechanisms, assessment, and management of dyspnea.* Am J Respir Crit Care Med, 2012. **185**(4): p. 435-52.
7. Guenette, J.A., et al., *Inspiratory Capacity during Exercise: Measurement, Analysis, and Interpretation.* Pulm.Med., 2013. **2013**: p. 956081.
8. Hyatt, R.E., *Expiratory flow limitation.* J Appl Physiol Respir Environ Exerc Physiol, 1983. **55**(1 Pt 1): p. 1-7.
9. Ritz, T., et al., *Guidelines for mechanical lung function measurements in psychophysiology.* Psychophysiology, 2002. **39**(5): p. 546-67.
10. Lutfi, M.F., *The physiological basis and clinical significance of lung volume measurements.* Multidiscip Respir Med, 2017. **12**: p. 3.
11. Kapp, M.C., et al., *The shape of the maximum expiratory flow volume curve.* Chest, 1988. **94**(4): p. 799-806.
12. *Dyspnea. Mechanisms, assessment, and management: a consensus statement. American Thoracic Society.* Am J Respir Crit Care Med, 1999. **159**(1): p. 321-40.

13. Hayen, A., M. Herigstad, and K.T. Pattinson, *Understanding dyspnea as a complex individual experience.* Maturitas, 2013. **76**(1): p. 45-50.

14. Sharma, P., N.R. Morris, and L. Adams, *Effect of experimental modulation of mood on perception of exertional dyspnea in healthy subjects.* J Appl Physiol (1985), 2016. **120**(2): p. 114-20.

15. Von Leupoldt, A. and B. Dahme, *Emotions and airway resistance in asthma: Study with whole body plethysmography.* Psychophysiology, 2005. **42**(1): p. 92-97.

16. Scano, G., et al., *Dyspnea and emotional states in health and disease.* Respir Med, 2013. **107**(5): p. 649-55.

17. von Leupoldt, A., et al., *The impact of emotions on the sensory and affective dimension of perceived dyspnea.* Psychophysiology, 2006. **43**(4): p. 382-6.

18. Banzett, R.B., et al., *The affective dimension of laboratory dyspnea: air hunger is more unpleasant than work/effort.* Am J Respir Crit Care Med, 2008. **177**(12): p. 1384-90.

19. Mahler, D.A., et al., *Descriptors of breathlessness in cardiorespiratory diseases.* Am J Respir Crit Care Med, 1996. **154**(5): p. 1357-63.

20. Manning, H.L. and R.M. Schwartzstein, *Respiratory sensations in asthma: physiological and clinical implications.* J Asthma, 2001. **38**(6): p. 447-60.

21. Klimek, L., et al., *Visual analogue scales (VAS): Measuring instruments for the documentation of symptoms and therapy monitoring in cases of allergic rhinitis in everyday health care: Position Paper of the German Society of Allergology (AeDA) and the German Society of Allergy and Clinical Immunology (DGAKI), ENT Section, in collaboration with the working group on Clinical Immunology, Allergology and Environmental Medicine of the German Society of Otorhinolaryngology, Head and Neck Surgery (DGHNOKHC).* Allergo J Int, 2017. **26**(1): p. 16-24.

22. Simon, P.M., et al., *Distinguishable types of dyspnea in patients with shortness of breath.* Am Rev Respir Dis, 1990. **142**(5): p. 1009-14.

23. Simon, P.M., et al., *Distinguishable sensations of breathlessness induced in normal volunteers.* Am Rev Respir Dis, 1989. **140**(4): p. 1021-7.

24. Masaoka, Y. and I. Homma, *Expiratory time determined by individual anxiety levels in humans.* J Appl Physiol (1985), 1999. **86**(4): p. 1329-36.

25. Wolkove, N., et al., *Perception of changes in breathing in normal human subjects.* J Appl Physiol Respir Environ Exerc Physiol, 1981. **50**(1): p. 78-83.

26. Mador, M.J. and M.J. Tobin, *Effect of alterations in mental activity on the breathing pattern in healthy subjects.* Am Rev Respir Dis, 1991. **144**(3 Pt 1): p. 481-7.

27. Milic-Emili, J. and M.M. Grunstein, *Drive and timing components of ventilation.* Chest, 1976. **70**(1 Suppl): p. 131-3.

28. von Euler, C., *The functional organization of the respiratory phase-switching mechanisms.* Fed Proc, 1977. **36**(10): p. 2375-80.

29. Bradley, G.W., *Control of the breathing pattern.* Int Rev Physiol, 1977. **14**: p. 185-217.

30. Gautier, H., *Control of the pattern of breathing.* Clin Sci (Lond), 1980. **58**(5): p. 343-8.

31. Masaoka, Y. and I. Homma, *Anxiety and respiratory patterns: their relationship during mental stress and physical load.* Int J Psychophysiol, 1997. **27**(2): p. 153-9.

32. Boiten, F.A., N.H. Frijda, and C.J. Wientjes, *Emotions and respiratory patterns: review and critical analysis.* Int J Psychophysiol, 1994. **17**(2): p. 103-28.

33. Smoller, J.W., et al., *Panic anxiety, dyspnea, and respiratory disease. Theoretical and clinical considerations.* Am J Respir Crit Care Med, 1996. **154**(1): p. 6-17.

34. Neuman, A., et al., *Dyspnea in relation to symptoms of anxiety and depression: A prospective population study.* Respir Med, 2006. **100**(10): p. 1843-9.

35. Nguyen, H.Q. and V. Carrieri-Kohlman, *Dyspnea self-management in patients with chronic obstructive pulmonary disease: moderating effects of depressed mood.* Psychosomatics, 2005. **46**(5): p. 402-10.

36. Norweg, A. and E.G. Collins, *Evidence for cognitive-behavioral strategies improving dyspnea and related distress in COPD.* Int J Chron Obstruct Pulmon Dis, 2013. **8**: p. 439-51.

37. Nici, L. and R.L. ZuWallack, *Pulmonary rehabilitation: future directions.* Clin Chest Med, 2014. **35**(2): p. 439-44.

38. Alius, M.G., et al., *Induction of dyspnea evokes increased anxiety and maladaptive breathing in individuals with high anxiety sensitivity and suffocation fear.* Psychophysiology, 2013. **50**(5): p. 488-97.

39. Bouton, M.E., S. Mineka, and D.H. Barlow, *A modern learning theory perspective on the etiology of panic disorder.* Psychol Rev, 2001. **108**(1): p. 4-32.

40. Tobin, M.J., et al., *Breathing patterns. 2. Diseased subjects.* Chest, 1983. **84**(3): p. 286-94.

41. Isenberg, S., P. Lehrer, and S. Hochron, *Defensiveness and perception of external inspiratory resistive loads in asthma.* J Behav Med, 1997. **20**(5): p. 461-72.

42. Solano, J.P., B. Gomes, and I.J. Higginson, *A comparison of symptom prevalence in far advanced cancer, AIDS, heart disease, chronic obstructive pulmonary disease and renal disease.* J Pain Symptom Manage, 2006. **31**(1): p. 58-69.

43. Choudhary, S.S. and S. Choudhary, *Exercise testing in assessment and management of patients in clinical practice - present situation.* Lung India, 2008. **25**(3): p. 111-7.

44. *National Health and Nutrition Examination Survey Data*, N.C.f.H.S. (NCHS), Editor., Centers for Disease Control and Prevention (CDC): Hyattsville, MD.

45. Redlich, C.A., et al., *Official American Thoracic Society technical standards: spirometry in the occupational setting.* Am J Respir Crit Care Med, 2014. **189**(8): p. 983-93.

46. Quanjer, P.H., et al., *Lung volumes and forced ventilatory flows. Report Working Party Standardization of Lung Function Tests, European Community for Steel and Coal.*

Official Statement of the European Respiratory Society. Eur Respir J Suppl, 1993. **16**: p. 5-40.

47. Miller, M.R., et al., *Standardisation of spirometry.* Eur Respir J, 2005. **26**(2): p. 319-38.
48. Johnson, B.D., et al., *Emerging concepts in the evaluation of ventilatory limitation during exercise: the exercise tidal flow-volume loop.* Chest, 1999. **116**(2): p. 488-503.
49. Babb, T.G. and J.R. Rodarte, *Lung volumes during low-intensity steady-state cycling.* Journal of Applied Physiology: Respiratory, Environmental & Exercise Physiology, 1991. **70**: p. 934-937.
50. Sheel, A.W. and J.A. Guenette, *Mechanics of breathing during exercise in men and women: sex versus body size differences?* Exerc Sport Sci Rev, 2008. **36**(3): p. 128-34.
51. Henke, K.G., et al., *Regulation of end-expiratory lung volume during exercise.* J Appl Physiol, 1988. **64**(1): p. 135-46.
52. Otis, A.B., W.O. Fenn, and H. Rahn, *Mechanics of breathing in man.* J Appl Physiol, 1950. **2**(11): p. 592-607.
53. Welch, J.F., S. Kipp, and A.W. Sheel, *Respiratory muscles during exercise: mechanics, energetics, and fatigue.* Current Opinions in Physiology, 2019. **10**: p. 102-109.
54. Moore, L.E., et al., *Exertional dyspnea and operating lung volumes in asthma.* J Appl Physiol (1985), 2018. **125**(3): p. 870-877.
55. Lougheed, M.D., T. Fisher, and D.E. O'Donnell, *Dynamic hyperinflation during bronchoconstriction in asthma: implications for symptom perception.* Chest, 2006. **130**(4): p. 1072-81.
56. Lougheed, M.D., et al., *Breathlessness during acute bronchoconstriction in asthma. Pathophysiologic mechanisms.* Am Rev Respir Dis, 1993. **148**(6 Pt 1): p. 1452-9.
57. Lind, F.G., *Respiratory drive and breathing pattern during exercise in man.* Acta Physiol Scand Suppl, 1984. **533**: p. 1-47.

58. Clark, J.M., F.C. Hagerman, and R. Gelfand, *Breathing patterns during submaximal and maximal exercise in elite oarsmen.* J Appl Physiol Respir Environ Exerc Physiol, 1983. **55**(2): p. 440-6.

59. Otis, A.B., *The work of breathing.* Physiol Rev, 1954. **34**(3): p. 449-58.

60. Weiner, P., et al., *Efficiency of the respiratory muscles in healthy individuals.* Am Rev Respir Dis, 1989. **140**(2): p. 392-6.

61. Beurskens, C.J., et al., *Heliox Improves Carbon Dioxide Removal during Lung Protective Mechanical Ventilation.* Crit Care Res Pract, 2014. **2014**: p. 954814.

62. Hess, D.R., et al., *The history and physics of heliox.* Respir Care, 2006. **51**(6): p. 608-12.

63. Haussermann, S., et al., *Effects of a helium/oxygen mixture on individuals' lung function and metabolic cost during submaximal exercise for participants with obstructive lung diseases.* Int J Chron Obstruct Pulmon Dis, 2015. **10**: p. 1987-97.

64. Palange, P., et al., *Effect of heliox on lung dynamic hyperinflation, dyspnea, and exercise endurance capacity in COPD patients.* J Appl Physiol (1985), 2004. **97**(5): p. 1637-42.

65. Eves, N.D., et al., *Helium-hyperoxia, exercise, and respiratory mechanics in chronic obstructive pulmonary disease.* Am J Respir Crit Care Med, 2006. **174**(7): p. 763-71.

66. Laude, E.A., et al., *The effect of helium and oxygen on exercise performance in chronic obstructive pulmonary disease: a randomized crossover trial.* Am J Respir Crit Care Med, 2006. **173**(8): p. 865-70.

67. Allan, P.F., et al., *Feasibility study of noninvasive ventilation with helium-oxygen gas flow for chronic obstructive pulmonary disease during exercise.* Respir Care, 2009. **54**(9): p. 1175-82.

68. Borges-Santos, E., et al., *Anxiety and depression are related to dyspnea and clinical control but not with thoracoabdominal mechanics in patients with COPD.* Respir Physiol Neurobiol, 2015. **210**: p. 1-6.

69. O'Donnell, D.E. and K.A. Webb, *Exertional breathlessness in patients with chronic airflow limitation. The role of lung hyperinflation.* Am Rev Respir Dis, 1993. **148**(5): p. 1351-7.

70. Laveneziana, P., et al., *Tidal volume inflection and its sensory consequences during exercise in patients with stable asthma.* Respir Physiol Neurobiol, 2013. **185**(2): p. 374-9.

71. Spitzer, R.L., et al., *A brief measure for assessing generalized anxiety disorder: the GAD-7.* Arch Intern Med, 2006. **166**(10): p. 1092-7.

72. Reiss, S., et al., *Anxiety sensitivity, anxiety frequency and the prediction of fearfulness.* Behav Res Ther, 1986. **24**(1): p. 1-8.

73. Zigmond, A.S. and R.P. Snaith, *The hospital anxiety and depression scale.* Acta Psychiatr Scand, 1983. **67**(6): p. 361-70.

74. Baer, R.A., et al., *Using self-report assessment methods to explore facets of mindfulness.* Assessment, 2006. **13**(1): p. 27-45.

75. Bond, F.W., et al., *Preliminary psychometric properties of the Acceptance and Action Questionnaire-II: a revised measure of psychological inflexibility and experiential avoidance.* Behav Ther, 2011. **42**(4): p. 676-88.

76. Cohen, S., T. Kamarck, and R. Mermelstein, *A global measure of perceived stress.* J Health Soc Behav, 1983. **24**(4): p. 385-96.

77. Crowne, D.P. and D. Marlowe, *A new scale of social desirability independent of psychopathology.* J Consult Psychol, 1960. **24**: p. 349-54.

78. Watson, D., L.A. Clark, and A. Tellegen, *Development and validation of brief measures of positive and negative affect: the PANAS scales.* J Pers Soc Psychol, 1988. **54**(6): p. 1063-70.

79. Marteau, T.M. and H. Bekker, *The development of a six-item short-form of the state scale of the Spielberger State-Trait Anxiety Inventory (STAI).* Br J Clin Psychol, 1992. **31**(3): p. 301-6.

80. Wade, J.B., et al., *Assessing the stages of pain processing: a multivariate analytical approach.* Pain, 1996. **68**(1): p. 157-67.

81. Swinson, R.P., *The GAD-7 scale was accurate for diagnosing generalised anxiety disorder.* Evid Based Med, 2006. **11**(6): p. 184.

82. Brady, E.U. and P.C. Kendall, *Comorbidity of anxiety and depression in children and adolescents.* Psychol Bull, 1992. **111**(2): p. 244-55.

83. Aina, Y. and J.L. Susman, *Understanding comorbidity with depression and anxiety disorders.* J Am Osteopath Assoc, 2006. **106**(5 Suppl 2): p. S9-14.

84. Garcin, M., M. Danel, and V. Billat, *Perceptual responses in free vs. constant pace exercise.* Int J Sports Med, 2008. **29**(6): p. 453-9.

85. Kang, J., et al., *Metabolic and perceptual responses during Spinning cycle exercise.* Med Sci Sports Exerc, 2005. **37**(5): p. 853-9.

86. Price, M. and P. Moss, *The effects of work:rest duration on physiological and perceptual responses during intermittent exercise and performance.* J Sports Sci, 2007. **25**(14): p. 1613-21.

87. O'Donnell, D.E., *Hyperinflation, dyspnea, and exercise intolerance in chronic obstructive pulmonary disease.* Proc Am Thorac Soc, 2006. **3**(2): p. 180-4.

Vita

Valesha Maria Province was born in Tiffin, Ohio to Teresa (Hufford) Province. She graduated from Tiffin Columbian High School in June 2015. The following autumn, she entered Denison University to major in Health, Exercise and Sport Studies and minor in Biology. In May 2019, she was awarded a Bachelor of Arts degree. In the fall of 2019, she accepted a research assistantship in both cardiovascular* and respiratory physiology laboratories at Appalachian State University and began her study toward a Master of Science degree. The M.S. is intended to be awarded in May 2021. Ms. Province currently resides in Boone, North Carolina and is moving to Winston-Salem, North Carolina to continue working in the research field as a Clinical Studies Coordinator I in the Pulmonary and Critical Care Unit at Wake Forest Baptist Health.