Acute Affective and Physiological Response to Different Exercise-Training

Protocols in Patients with Chronic Obstructive Pulmonary Disease (COPD)

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ABSTRACT

Acute Affective and Physiological Response to Different Exercise-Training Protocols in Patients with Chronic Obstructive Pulmonary Disease (COPD)

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Current pulmonary rehabilitation (PR) guidelines advocate high-intensity exercise training for individuals with chronic obstructive pulmonary disease (COPD), yet this approach has been shown to be unachievable in a large proportion of patients. Alternative approaches, such as training at the ventilatory threshold, have been proposed as more tolerable, less unpleasant, and thus possibly easier to comply with for this clientele. This assumption needs to be verified. The purpose of the present study was to compare, in COPD patients, the acute affective and physiological response to high-intensity training (CT80) versus training at the ventilatory threshold (CTVT). Thirteen subjects were randomly assigned to perform 40 minutes (including warm-up and cool-down) of either high-intensity exercise training at 80% of peak work rate (CT80) or training at the ventilatory threshold (CTVT) on a cycle ergometer. Affective response to the exercise bout was measured using the Positive and Negative Affect Schedule (PANAS) and the Global Vigor and Affect Instrument (GVA). Physiological response to the same bout was measured breath by breath with a portable metabolic system. Repeated-measures general linear models and mixed models were conducted using SAS. Positive affect scores from the PANAS increased from pre-, to end-, to post-exercise (time effect) (F=17.56, p=0.0005), but this increase was significant for the CTVT group only (time by intervention interaction) (F=5.85, p=0.02). No significant time

or interaction effect was observed for global affect or global vigor from the GVA. In addition, no significant difference in physiological response was observed between CT80 and CTVT. Results from this pilot study suggest that affect improves after an exercise-training bout in COPD patients, especially when the protocol used is CTVT. The acute physiological and symptomatic response to CT80 and CTVT appears to be similar.

Keywords: COPD, affective response, physiological response, exercise training.

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Be the change that you want to see in the world

-Mohandas Gandhi

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Author Contributions for the Manuscript

Amanda Rizk is the primary author of the manuscript included in this thesis. She is responsible for the literature review and assembly of the manuscript. In addition, she is responsible for the recruitment of patients, collection of data, and data analysis.

Véronique Pepin is the main supervisor to the primary author and oversaw assembly of the entire research project and manuscript. Dr. Pepin is responsible for the larger randomized control trial. As well, she is the primary editor of the manuscript ensuring its accurateness and completeness. Dr. Pepin has also made significant contributions to the display of results.

Simon L. Bacon is the co-supervisor to the primary author. Dr. Bacon has made substantial contributions to the manuscript including analysis and interpretation of the data, drafted the soon to be submitted article, and has revised it critically for important intellectual content.

Emilie Chan-Thim is responsible for aiding in data collection and ensuring patient safety during the research study.

Myriam De Lorimier is responsible for coordinating the larger randomized control trial which included patient recruitment and follow-up.

Kim L. Lavoie assessed general comprehensiveness of the manuscript.

CHAPTER I

1. Introduction

1.1 What is Chronic Obstructive Pulmonary Disease?

The term "chronic obstructive pulmonary disease" (COPD) represents a cluster of respiratory disorders which are preventable and manageable, associated with progressive and partially irreversible chronic airflow limitation [1-4]. The main symptoms of COPD, which typically appear in middle adulthood ($\geq$ 55 years), are shortness of breath, cough, and sputum production [5-9]. The two most common underlying disorders that lead to COPD are chronic bronchitis and emphysema [4]. Chronic bronchitis is clinically defined as the presence of cough and sputum production for at least 3 months in each of 2 consecutive years [1, 4]. Although chronic bronchitis is a main cause of COPD, it does not necessarily lead to chronic airflow limitation [1, 4]. Emphysema is characterized by the destruction of the gas exchanging surfaces of the lungs (alveoli) [1, 4]. Emphysema is a pathological term that is often used clinically to designate COPD; however, emphysema refers specifically to the destruction of the alveoli, which represents only one of many abnormalities associated with COPD [1]. In actuality, COPD is a combination of airway disease (bronchitis) and parenchymal destruction (emphysema) with the contributions of each varying from one patient to another [1].

1.2 Epidemiology:

1.2.1 Prevalence, Incidence and Economic Burden

COPD is currently the fourth leading cause of death in the world [5, 9]. Latest national estimates suggest that it is the fourth and fifth leading cause of death in Canadian men and women, respectively [10]. The province of Quebec has the second highest COPD-related mortality rate in the country after the Northwest Territories [6]. Close to 750,000 Canadians state that they have received a diagnosis of COPD from their physician, which accounts for approximately 4.4% of the population [3, 10]. The actual incidence and prevalence is probably higher since COPD is not diagnosed until clinically apparent and thus fairly advanced [6, 10]. The proportion of individuals affected by COPD increases steadily with age in men and women [6]. Hence, the total morbidity and mortality associated with this disease is expected to rise over the next two decades as the population ages [6, 8].

COPD imposes a heavy economic burden on the Canadian healthcare system. In 2004-05, respiratory diseases ranked third as a major cause of hospitalization in men and women, behind circulatory diseases and digestive disorders; among respiratory diseases, COPD ranked first in that category along with influenza/pneumonia [10]. In 2004-05, the average length of hospital stay for COPD was 9.6 days for individuals aged 55 and over [10]. Overall, respiratory diseases account for close to 7% ($8.63 billion) of total health care costs in Canada [10].

1.3 Risk Factors

1.3.1 Cigarette Smoking

The identification and understanding of the many risk factors of COPD is a crucial step towards developing treatment and preventative care aimed at this patient population. Cigarette smoking, through the inhalation of noxious particles or gases, is by far the strongest risk factor for this disease [5, 6, 9]; it is believed to be responsible for 80-90% of COPD cases [6]. In fact, in the Obstructive Lung Disease in North Sweden (OLIN) study, it was reported that approximately 50% of smokers eventually develop COPD, as defined by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines [11]. The risk of cigarette smoking is dose-dependent and is often represented as total pack-years smoked (calculated by multiplying the number of packs smoked per day by the number of years smoked) [1]. The discovery of smoking as a key risk factor has led to the incorporation of smoking cessation programs as a preventative treatment as well as an essential intervention for COPD patients [1]. Although smoking is the strongest and most-studied risk factor, it is possible for non-smokers to acquire this disease [1].

1.3.2 Genetic

The best documented genetic risk factor for COPD is a genetic deficiency of alpha-1-antitrypsin which predisposes individuals to emphysema [1]. This genetic deficiency affects approximately one in 2000-5000 individuals and is most commonly seen in individuals of Northern European decent [1, 12]. The main function of alpha-1-antitrypsin is to protect the lung from proteolytic damage from neutrophil elastase [12].

With a deficiency of alpha-1-antitrypsin, a greater secretion of neutrophil elastase occurs during inflammation [13]. Neutrophil elastase is an enzyme that promotes or leads to proteolysis (a breakdown of protein) thereby destroying bacteria and host tissue [13]. Individuals with this genetic component have a risk of developing emphysema and a decline in lung function [1]. This risk is amplified if individuals with this rare deficiency smoke, which clearly reveals the importance of the interaction between the genetic and environmental risk factors.

Other genes, which regulate the production of transforming growth factor beta 1 (TGF-β1) [14], microsomal epoxide hydrolase 1 (mEPHX1) [15], and tumor necrosis factor alpha (TNFα) [16], have also been associated with the pathogenesis of COPD. However, these findings have been largely inconsistent and further studies are needed to clarify the association of these genetic factors with the disease [1].

1.3.3 Occupational exposure to dusts and fumes

Occupational exposure to organic and inorganic dusts and chemicals (vapors, irritants, and fumes) are known to cause COPD, independent of smoking history [1]. In addition, they appear to act additively to smoking to increase the possibility of acquiring this disease [1]. According to the American Thoracic Society [17], occupational exposure accounts for up to 20% of all COPD cases. This risk varies depending on particle type, size, composition, and exposure time to these irritants [1].

1.3.4 Air pollution

Indoor and outdoor air pollution also contributes to the risk of developing COPD [1]. Although the risk of COPD due to air pollution is lesser than the risk due to cigarette smoking, it continues to remain an underestimated risk factor [1]. Indoor air pollution can be caused by the burning of wood, animal dung, crop residues, and coal in open fires and poorly operating stoves [1]. The risk of indoor air pollution caused by biomass cooking and heating continues to grow especially among women in developing countries who continue to use biomass and coal as their main source of energy for cooking and heating, among other household needs [1]. In addition, high levels of urban air pollution caused by fossil fuel combustion mainly from vehicle emissions is considered as a risk factor for COPD; however its role in causing this disease remains unclear [1]. Among the many questions needed to be answered includes the effect of short duration, high-peak exposures compared with long duration, low-level exposures [1].

1.3.5 Infection

Viral and bacterial infections may also contribute as a risk factor for COPD as well as play a major role in exacerbations [1]. A history of childhood respiratory tract infections is associated with increased respiratory symptoms and decreased lung function [1]. Childhood infections are also related to having a low birth weight, which is also associated with COPD [1]. Furthermore, HIV infection and a history of tuberculosis have also been associated with airflow obstruction in COPD patients [18, 19].

1.4 Pathology, Pathogenesis and Pathophysiology of COPD

1.4.1 Pathology and Pathogenesis

The chain of events leading to COPD begins with specific risk factors linked to this disease which trigger inflammatory cells such as lymphocytes (T CD4$^+$, T CD8$^+$), macrophages, and neutrophils. These cells can then potentially release certain inflammatory mediators such as lipid mediators (leukotriene B_4), chemokines (interleukin-8), cytokines (interleukin-1 beta, interleukin-6, tumor necrosis factor-alpha), and growth factors (transforming growth factor-beta) interacting with structural cells in the airways and lung parenchyma [1]. This interaction induces chronic inflammation in various regions of the lung and structural changes resulting from recurring tissue damage and repair [1]. In addition, chronic inflammation can be brought on by oxidative stress and an imbalance between proteases (which break down connective tissue) and antiproteases (which protect against this breakdown), at the favour of the former [1, 2]. For example, this imbalance may cause the breakdown of elastin to occur [2]. A breakdown of elastin diminishes the elastic ability of the lungs, which is a classic sign of emphysema [1, 2].

In general, pathological structural changes occur in four distinct regions of the lung: the proximal (central) airways, the peripheral airways, the lung parenchyma, and the pulmonary vasculature [1, 2]. The proximal airways refer to the trachea and bronchi with an internal diameter greater than 2 mm [1]. Structural changes occurring in this region include an increase in goblet cells, hypersecretion of mucus caused by enlarged submucosal glands, and squamous metaplasia of the epithelium (the reversible replacement of columnar epithelium with squamous epithelium thereby altering the normal homeostatic state) [1]. The peripheral airways include the bronchioles with an

internal diameter less than 2 mm [1]. Potential structural changes which may occur in this region include inflammation, thickening of the airway wall, narrowing of the airway, peribronchial fibrosis, and exudate, which is fluid accumulation in areas of inflammation [1]. Lung parenchyma consists of the respiratory bronchioles and alveoli [1]. Structural changes in this region caused by COPD include destruction of the alveolar wall and apoptosis (programmed death) of epithelial and endothelial cells [1]. The pulmonary vasculature refers to all the vessels (arteries, veins, and capillaries) found in the lungs, and possible structural changes in this region include an increase in smooth muscle mass, endothelial cell dysfunction accompanied with thickening of the intima, which can all lead to pulmonary hypertension [1]. It is important to note that the extent to which each region is affected varies from one COPD patient to another [2].

1.4.2 Pathophysiology

1.4.2.1 Expiratory flow limitation and Lung Hyperinflation

In order to comprehend the complexity of expiratory flow limitation and lung hyperinflation, which are classic features of COPD, it is important to first gain background knowledge of basic lung volumes, capacities, and flow rates. Figure 1 illustrates the basic lung volumes and capacities. There are four basic lung volumes as well as four basic lung capacities. When one is breathing normally, at rest, the regular inspiratory/expiratory cycle of breathing is termed tidal breathing [20]. The volume of air breathed in and out through each breath during tidal breathing is called tidal volume (V_T). Inspiratory reserve volume (IRV) is the maximum amount of additional air that can be inspired from the end of a normal inspiration, while expiratory reserve volume (ERV) is the maximum amount of additional air that can be expired from the end of a normal

expiration. Finally, residual volume (RV) is the amount of air remaining in the lungs after a maximal expiration [20]. In normal lungs, this point represents the relaxation of all respiratory muscles in addition to the balance of recoil pressures between the lungs and chest wall [20].

Lung capacities are composed of two or more lung volumes. Inspiratory capacity (IC) is the amount of air that can be inhaled forcefully subsequent to a normal expiration and corresponds to the sum of V_T and IRV [20]. At the end of a normal expiration, the volume of air contained in the lungs is termed the functional residual capacity (FRC) and corresponds to the sum of RV and ERV [20]. Vital capacity (FVC) is the amount of air that can be forcefully exhaled following a maximal inspiration and corresponds to the sum of ERV, V_T, and IRV [21]. Finally, total lung capacity (TLC) is the total volume of air that can be contained in the lungs at the end of a maximal inspiration and corresponds to the sum of all four basic lung volumes (RV, ERV, V_T, and IRV) [20].
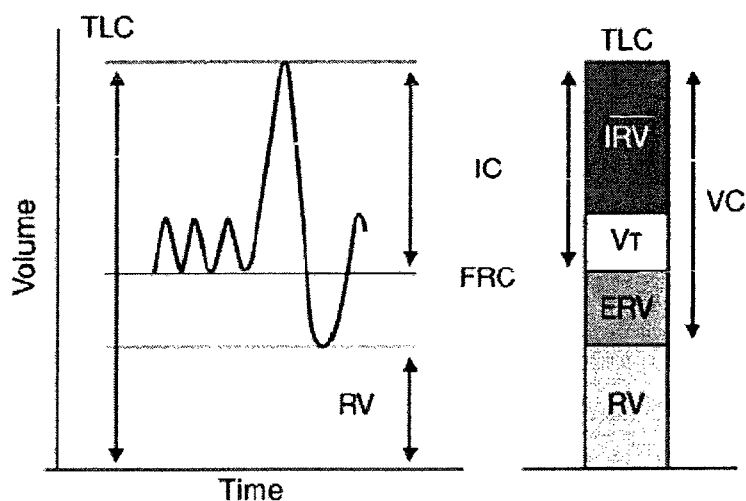
Figure 1.1 Basic lung volumes and capacities. TLC: total lung capacity; IC: inspiratory capacity; FRC: functional residual capacity; RV: residual volume; IRV: inspiratory reserve volume; V_T: tidal volume; ERV: expiratory reserve volume; RV: residual volume; VC: vital capacity.

Several flow rates can be measured, yet the two of greatest interest and clinical usefulness in COPD are forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC). Both of these measurements can be obtained through spirometry with a FVC manoeuvre, which requires patients to forcefully inspire and expire as much air as possible following certain standards [22]. FEV_1 represents the amount of air that is exhaled in the first second of the FVC manoeuvre [21]. Its value in litres and in percentage of the normal predicted value is pivotal in the classification of COPD disease severity. Likewise, the ratio of FEV_1 to FVC, which provides an indication of the proportion of FVC exhaled in the first second of expiration, is critical in the diagnosis of COPD [20].

The pathophysiology of COPD is not completely understood. However, the hallmark feature of this disease is expiratory flow limitation as shown by a reduction in the FEV_1 / FVC ratio often accompanied by a reduction in FEV_1 [23]. This outcome arises due to intrinsic and extrinsic factors that increase airway resistance [23]. Such factors include mucosal inflammation and oedema, secretions, extraluminal compression by adjacent overinflated alveoli, etc [23]. Emphysema further limits respiration by reducing the elastic recoil in the lungs thereby increasing the expiratory pressure making it progressively more difficult to expire [23]. Patients with COPD also often have an increased physiological dead space because of the destruction of alveolar wall integrity and concurrent loss of gas exchange surfaces [24]. Due to this physiological limitation, patients with COPD have an increased ventilatory requirement (V_E) for any given task [25]. In contrast to their healthy counter-parts, COPD patients often achieve levels of V_E that reach their predicted maximum voluntary ventilation (MVV) on exertion due to flow obstruction [26-28]. The ratio of V_E/MVV can therefore reach 100% in this patient population during exercise, whereas it rarely exceeds 80% in healthy individuals [27].

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This also means that V_E can be a limiting factor to exercise in COPD patients, which is not the case in healthy individuals.

Patients with COPD also often experience some degree of lung hyperinflation, also commonly known as air trapping, which is intimately linked to the sensation of dyspnoea [20]. Hyperinflation can be thought of as having two main components; static hyperinflation and dynamic hyperinflation. Static hyperinflation is caused by a loss of elasticity in the lung parenchyma (alveoli, alveolar duct, and bronchioles), thereby causing a reduced amount of recoil pressure from the lungs to counter the pressure exerted by the chest wall [20]. Static hyperinflation can be considered if values of resting functional residual capacity (FRC) or end-expiratory lung volume (EELV) are elevated above normal values (Figure 2) [20]. Dynamic hyperinflation refers to an elevation of EELV, which could be brought on by exercise or anything that would increase V_E (e.g., emotional stress) [29]. It is caused by additional air trapping within the lungs following each breath due to the patient being unable to completely empty their lungs upon exhalation, therefore causing disequilibrium between inspired and expired volumes [20]. Several factors could be associated with the degree of hyperinflation in COPD patients such as inflammation, increased mucus production, narrowed airways, and possible collapsing of the airways [20, 30]. Both the static and dynamic effects contribute to lung hyperinflation in this disease, yet dynamic hyperinflation typically occurs more frequently. Additionally, dynamic hyperinflation can occur independent of static hyperinflation [20]. Hyperinflation can cause several unfavourable effects, including an increase in the amount of work needed to breathe, an impairment in gas exchange between alveoli and blood vessels, and possible respiratory muscle dysfunction [20].

1.4.2.2 Gas Exchange Limitations

Several limitations exist concerning gas exchange in COPD patients. In an emphysematous lung, the destruction of alveoli inhibits oxygen (O_2) from entering the capillaries in order to reach the systemic circulation, and carbon dioxide (CO_2) from entering the alveoli so as to be expired upon exhalation. This leads to a lack of available O_2 in the systemic circulation as well as an abundance of trapped CO_2 in the lungs and circulation. This faulty mechanism thereby results in hypoxemia (a decreased partial pressure of O_2 in the blood) and hypercapnia (increased levels of CO_2 in the blood) [1]. In most cases, the transfer of gases worsens as disease severity progresses [1]. The arterial perfusion of oxygen, the ventilation to perfusion ratio (V_A/Q), and the partial pressure of oxygen in arterial blood (P_aO_2) are all indicators of emphysema severity [1].

1.4.2.3 Respiratory and Peripheral Muscle Dysfunction

Although COPD affects the lungs directly, significant systemic consequences may occur, such as respiratory and peripheral muscle dysfunction [1-4]. The extent to which respiratory muscles are affected in COPD patients siiii remains unclear, but some aspects have been described. More specifically, the diaphragm of COPD patients seems to be affected [31]. Due to the overload placed upon this respiratory muscle, the diaphragm initially shows a greater resistance to fatigue [31]. During the early stages of the disease, the inspiratory muscles of patients with COPD generate a greater force as compared to healthy individuals [31]. However, patients with COPD also experience hyperinflation, which places the respiratory muscles at a disadvantage (i.e. compromised inspiratory muscle strength and endurance) [31]. Due to this muscular disadvantage, the diaphragm begins to remodel itself to adapt to the physiological needs [31]. In a study

conducted by Levine et al. [32], the remodelling of the diaphragm was found to decrease its force due to adaptations occurring through fiber type transformation as well as adaptations taking place within each muscle fiber type [32]. Evidence suggests that the diaphragmatic fiber type switches from type II (glycolytic) to type I (oxidative) which is a fatigue-resistant fiber type as compared to type II fibers [32]. There also seems to be a competition for oxygen, in COPD patients during exercise, between the respiratory and peripheral muscles in favour of the respiratory muscles. This is known as the "steal" effect [1, 31, 33].

Peripheral muscle dysfunction has been identified as another important systemic consequence associated with this disease. The quadriceps, more specifically the vastus lateralis muscle, has been the most studied muscle group linked to peripheral muscle fatigue [34]. To date, muscle fatigue has been linked with specific peripheral muscle alterations, such as a switch in muscle fiber type to more fatigable fibers (switch from type I to type II fibers) [34], muscle atrophy and weakness [35], reduced oxidative capacity, and lactic acid build-up [36]. Peripheral muscle dysfunction has also shown to be a predictor of mortality [37].

1.4.2.4 Exercise Intolerance

Exercise intolerance is a complex consequence of COPD [27]. It is closely related to disability and impairment, and is a strong predictor of quality of life [27, 38]. Exercise intolerance can stem from a multitude of intricate mechanisms and interactions frequently present among patients with COPD. These include a reduced ventilatory capacity (reduced expiratory flow rates), a decreased exercise capacity (decrease in peak work rate, maximal VO_2 or endurance time to constant-load exercise), the

presence of dynamic hyperinflation (decrease in inspiratory capacity), symptom perception during exercise (dyspnoea and leg fatigue being reached at lower intensities), hypoxemia (oxygen desaturation), and peripheral muscle fatigue [27]. The contribution from each of these factors varies greatly from one individual to another [27].

During exercise, COPD patients will increase their minute ventilation, mostly via an increase in breathing frequency, to compensate for the increased ventilatory demand [30]. This increase in respiratory frequency will reduce the time between breaths, thus making it increasingly difficult to fully empty the lungs [30]. This vicious cycle will result in dynamic hyperinflation and could thus lead to premature exercise termination due to breathlessness [30].

Leg fatigue is another symptom often reported by patients with COPD as a limiting factor to exercise, prior to the occurrence of physiological limits of the body being attained (VO_2) [27]. A study conducted by Saey and colleagues [39] examined the relationship between muscle fatigue and exercise response and found that even after the administration of a bronchodilator, patients with greater susceptibility to leg fatigue did not obtain a significant improvement in exercise capacity with bronchodilation. This shows that peripheral muscle dysfunction may play a significant role in exercise intolerance among COPD patients [39]. It is important to note that the type of exercise modality chosen (e.g. walking versus cycling) seems to affect the degree and the source of exercise intolerance in this patient population [27, 40]. A study conducted by Pepin and coworkers [27], compared the response of COPD patients to a cycle endurance test to their response to an endurance shuttle walk test [37]. The cycling test was found to induce greater levels of perceived leg fatigue as compared to the walking test, whereas the shuttle walk test induced greater levels of dyspnoea [37].

1.4.2.5 Pulmonary Complications

Respiratory exacerbations are the most frequent pulmonary complication among COPD patients. According to the American Thoracic Society and European Respiratory Society [1, 2], an exacerbation of COPD is defined as "an event in the natural course of the disease characterised by a change in the patient's baseline dyspnoea, cough and/or sputum beyond day-to-day variability sufficient to warrant a change in management". On average, COPD patients experience two exacerbations per year and approximately half of all exacerbations are caused by acquiring an infection [3]. Management of an exacerbation should include careful assessment along with an increased dosage of inhaled short-acting beta$_2$-agonist and/or an anticholinergic drug [3]. Antibiotics and/or oral corticosteroids are also often prescribed during this time [3]. If severe enough, patients might also be prescribed oxygen therapy [3]. To date, there is no classification of exacerbations that has been established [1, 2]. However, several well known indicators exist such as the requirement of hospital admittance; the presence of a high-risk co-morbid condition, an obvious increase in dyspnoea, difficulty sleeping or eating, worsening hypoxaemia and/or hypercapnia, changes in mental status, uncertain diagnosis, inadequate home care, and the inability for the patient to care for them self [1, 2].

Aside from exacerbations, COPD patients can be faced with other pulmonary complications such as pulmonary hypertension [41]. Pulmonary hypertension evolves due to the constriction of pulmonary arteries, making it much more difficult for the right heart to pump blood through the lungs [42]. Eventually, this resistance in the lungs may result in vascular remodelling, such as thickening of the blood vessels (intimal hyperplasia) and smooth muscle hypertrophy [42]. In addition, as blood pressure rises within the lungs, the heart's right ventricle has to pump to a greater extent thereby

causing hypertrophy of the myocardium [42]. Due to the greater workload exerted on the heart, right heart failure could occur [1]. Right heart failure occurs when the right heart in unable to supply sufficient blood supply to the lungs in order for reoxygenation to occur; this then affects oxygenated blood supply to the left heart and subsequently to the rest of the body [42].

1.4.2.6 Anxiety and Depression

Like in many other chronic diseases, patients with COPD tend to present with both anxiety and depression [1]. However, they are the least-treated comorbidities of COPD [43]. In a systematic review [44] of 64 studies comparing rates of anxiety and depression in various diseases, the prevalence of depression in COPD patients was found to range from 37 to 71%, and that of anxiety from 50 to 75% which was comparable to other chronic diseases such as renal disease, heart disease, AIDS, and cancer. However high the prevalence rates are, less than one third of COPD patients receive appropriate treatment [45, 46]. If left untreated, depression and anxiety can have major implications such as increased number of consultations with their physician, increased frequency of hospital admission, prolonged hospital stay, lower treatment adherence, as well as poor quality of life and premature death [46]. Depression among COPD patients has also been found to predict dyspnoea, fatigue, and disability [47, 48]. Symptoms of depression include hopelessness, pessimism, difficulties concentrating, and social withdrawal [49]. Symptoms of anxiety include difficulties concentrating, sweating, tachycardia, and dyspnoea [43]. Possible treatments consist of pharmacotherapy and psychotherapy [43].

1.5 Clinical Assessment of COPD

1.5.1 Diagnosis

Individuals with the previously mentioned comorbidities as well as a history of a significant exposure to the potential risk factors should be considered for possible diagnosis [2]. Diagnosis of COPD requires that a spirometry test be performed [1, 2]. Spirometry is a common pulmonary function test that measures expiratory flow rates and three of the four lung volumes (all except RV) [1]. Patients must have a post-bronchodilator forced expiratory volume in one second (FEV_1) to forced vital capacity (FVC) ratio ≤ 0.7 to confirm the presence of airflow limitation that is not fully reversible [2]. Through the results of a spirometry test, disease severity can be classified into four stages (I through IV) (Table 1) [1]. It is recommended that a spirometry test be performed after a bronchodilator is administered (e.g. 400 μg salbutamol) [2]. Patients with airflow limitation in their 40's or 50's and especially those with a family history of COPD should also be tested for α-1-antitrypsin deficiency [1, 2].

Table 1.1 – Spirometry Classification of COPD Severity Based on Post-Bronchodilator FEV_1

Stage	Severity	FEV_1 % pred	Post-Bronchodilator FEV_1/FVC
I	Mild	≥ 80	<0.70
II	Moderate	50-80	<0.70
III	Severe	30-50	<0.70
IV	Very severe	< 30 or <50 plus chronic respiratory failure	<0.70

FEV_1: forced expiratory volume in one second; FVC: forced vital capacity; respiratory failure: arterial partial pressure of Oxygen (PaO_2) less than 8.0 kPa (60 mmHg) with or without arterial partial pressure of CO_2 ($PaCO_2$) greater than 6.7 kPa (50 mmHg) while breathing air at sea level.

Adapted from GOLD [1]

1.5.2 Investigations

Further investigations should include gathering a thorough medical history, performing a physical examination, and exercise testing if required [1]. A detailed history should be conducted for any patient suspected of having COPD and should include the following: medical history, family history of COPD, identification of risk factors and possibilities for reducing them, pattern of symptom development, history of previous exacerbations and hospitalizations, presence of comorbidities, appropriateness of current medical treatments, impact of disease on patient's life, and family/social support [1].

A physical assessment is important to detect any signs of COPD prior to disease progression. Physical signs are infrequently diagnostic in nature due to the fact that they are typically not apparent until significant impairment of lung function has already transpired [1]. During assessment, medical examiners should look for the following signs: central cyanosis (bluish color), chest wall abnormalities (horizontal ribs, barrel chest, protruding abdomen), flattening of the hemi-diaphragms, accelerated heart rate, shallow breathing, pursed-lip breathing, resting respiratory muscle activation while supine, and ankle/lower leg oedema [1]. In addition to an examination, a medical evaluator should palpitate surrounding areas in addition to listening for any wheezing or inspiratory crackles [1].

Cardiopulmonary exercise tests such as the six-minute shuttle walking test or an exercise test performed on a cycle ergometer or treadmill are often conducted in patients with COPD [1]. Indications for clinical exercise testing in this population include evaluating exercise capacity for prognosis, impairment/disability assessment and/or exercise prescription, identifying factors that contribute to exercise limitation, as well as

evaluating the impact of therapeutic interventions on exercise capacity and exercise response [38].

1.6 Management of COPD

COPD is a preventable and manageable disease [1, 3]. Although this disease cannot be cured with current available therapy, it is possible to slow down a patient's descent through the COPD downward spiral (figure 2) with modern management of the disease [5, 8]. Treatment should

Figure 1.2 COPD downward spiral. Adapted from la Clinique du Souffle la Solane, Osséja, France.

include a management strategy combining pharmacotherapy and non-pharmacotherapeutic interventions [3]. The goals of such interventions are to prevent disease progression, reduce the frequency and severity of exacerbations, improve health-status, improve health-related quality of life, and reduce mortality [3]. A comprehensive approach, as illustrated in Figure 3, has been suggested for optimal management of COPD [3].

1.6.1 Smoking Cessation

Tobacco is a highly addictive substance and tobacco smoking is considered a chronic relapsing disorder [2]. Smoking cessation programs are the single most effective and cost-effective strategy for preventing and treating those with COPD and should therefore be considered as the primary intervention [1, 3]. Approximately 41% of smokers try to quit smoking every year; however only 10% achieve and maintain this goal [3]. Thus, it is imperative that all smoking COPD patients or those at risk of
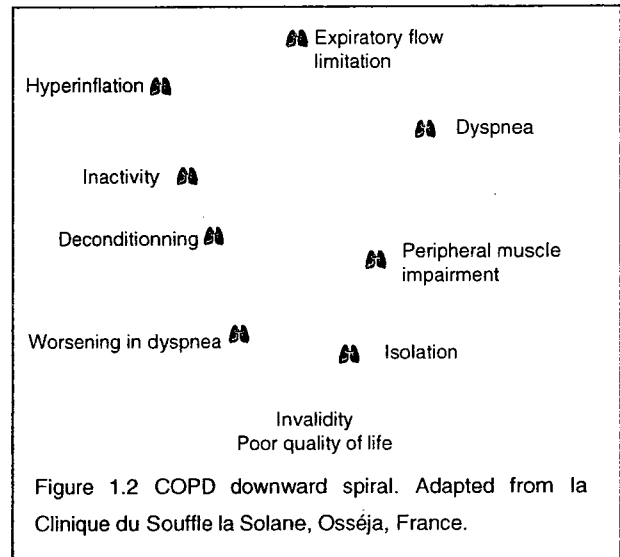
developing this disease be offered a smoking cessation intervention in order to increase

the chances of cessation [1, 3]. Effective interventions include counselling from
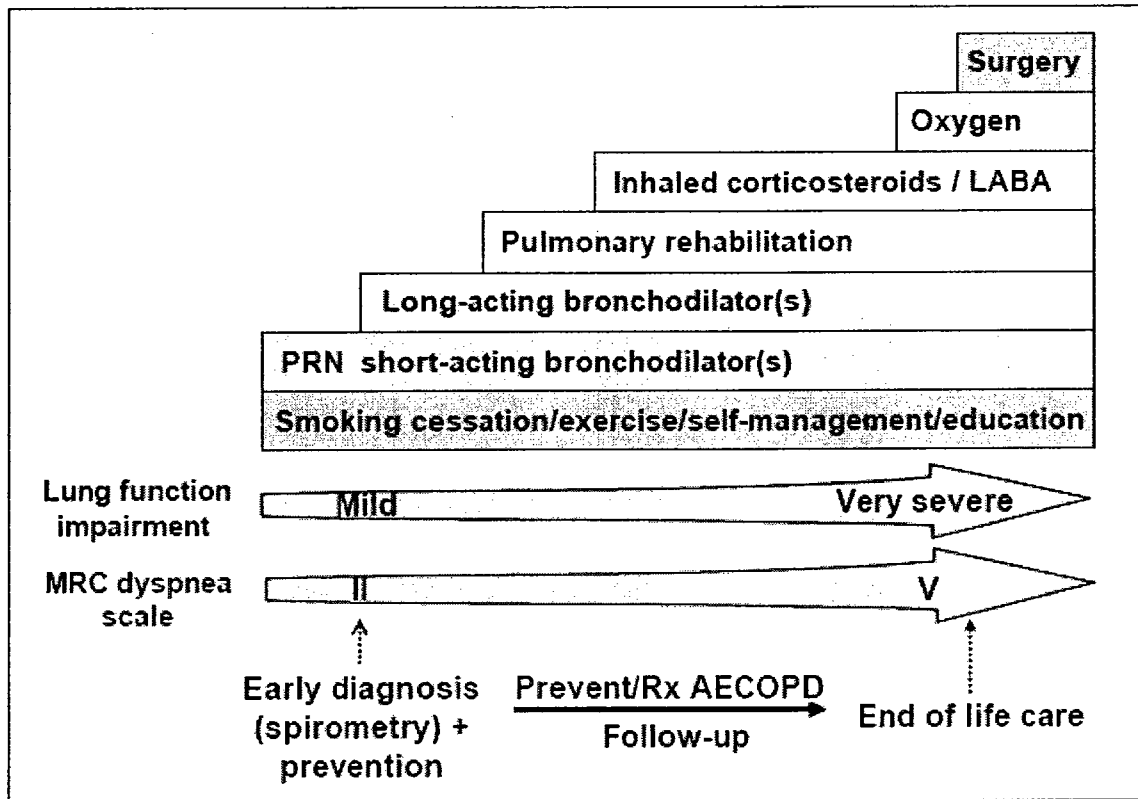
Figure 1.3 A comprehensive approach to the management of chronic obstructive pulmonary disease (COPD). AECOPD = Acute exacerbation of COPD; LABA = long-acting beta$_2$-agonist; MRC = medical research council; PRN = as needed; Rx = treatment.

Taken from CTS COPD Recommendations [23]

physicians and other health care professionals, self-help and community based

programs, as well as medications [1]. The use of medications such as nicotine

replacement therapy (gums, transdermal patches, and nasal sprays) and antidepressant

bupropion, approximately doubles smoking cessation rates [3]. Recent evidence has

also suggested that exercise training can be used as an aid to smoking cessation [50, 51].

1.6.2 Self-Management

Self-management plays an important role in COPD. According to Bourbeau et al. [52], self-management is a term used to describe "any patient education program aimed at teaching skills needed to carry out medical regimens specific to the disease, guide health behaviour change, and provide emotional support for patients to control their disease and live functional lives". The same authors conducted a multi-centered randomized controlled trial examining the impact of a self-management program on the use of hospital services and health outcomes among moderate to severe COPD patients [52]. The self-management program through disease specific education ("Living Well with COPD"), weekly and monthly follow-up phone calls, and the availability of case managers for advice and treatment supervision was shown to reduce hospital admissions, emergency department and unscheduled physician visits, and to improve health-related quality of life [52]. These results show the importance of self-management care among this patient population.

1.6.3 Pharmacotherapy

Pharmacotherapy is central to reduce symptoms and/or complications [5]. This form of treatment differs from one individual to another and is based on disease severity and frequency of exacerbations [3]. Three main types of pharmacotherapy treatments

are commonly prescribed for COPD patients: bronchodilators, anti-inflammatories, and vaccines.

Bronchodilators are a class of medications which relax smooth muscle around the airways thus improving expiratory flow rates and reducing hyperinflation [3]. Three common types of bronchodilators include: β-agonists, anticholinergic drugs, and mythelxanthines [3]. Bronchodilators are normally administered through an inhaler or nebulizer [3]. Short-acting bronchodilators, such as anticholinergics (e.g., ipratropium bromide) and $β_2$-agonists (e.g., albuterol), have been shown to improve dyspnoea, pulmonary function, and exercise tolerance in moderate to severe COPD patients [3]. Long-acting agents (e.g., salmeterol, tiotropium) are more effective than short-acting bronchodilators [3]; indeed, greater benefits in chronic dyspnoea, pulmonary function, and health-status have been observed with the long-acting agents in this patient population [3]. Common side-effects of bronchodilators include tachycardia, heart palpitations, irritability, insomnia, muscle cramps, and tremors [3]. Methylxanthines (e.g., theophylline) are another form of bronchodilator (weaker form) which is administered orally [2, 3]. This medication offers modest improvements in dyspnoea, pulmonary function, and exercise performance compared with other bronchodilators [3]. In general, patients on this medication should be prescribed the lowest possible dose (8-14 $µg·dL^{-1}$) due to inherent cardiovascular and neurological adverse effects [1, 3].

Anti-inflammatories, such as inhaled corticosteroids (ICSs), are also commonly prescribed to patients with COPD. The use of ICSs unaccompanied by other medications remains a controversial issue due to conflicting effects on a multitude of outcomes such as symptoms, pulmonary function, airway inflammation, frequency and severity of exacerbations, and health status [3]. Randomized controlled trials have yet to

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show significant results pertaining to the improvement in lung function through the use of this medication [3]. Side-effects include ecchymosis, dysphonia, oral candidiasis, cataracts, glaucoma, pneumonia, and a decrease in bone density [3]. However, combinations medications including bronchodilators and ICSs have proven to be effective [1-3].

Vaccines are highly recommended for patients with COPD to prevent acute exacerbations from occurring [3]. The two most common are influenza vaccines and pneumococcal vaccines [3]. It is recommended that patients receive one influenza vaccine per year whereas pneumococcal vaccines should be administered once every 5 to 10 years [3]. It has been shown that annual influenza shots reduce morbidity and mortality by 50% in elderly patients, and reduces hospitalizations by 39% in patients with chronic lung disease [3]. The specific benefits of pneumococcal vaccines are less understood and are therefore recommended to be administered less frequently [3].

It is important to note that none of the current medications has been shown to alter the decline in lung function that occurs over time in COPD patients [5]. In addition, the effects of COPD medications on exercise tolerance, peripheral muscle function, and quality of life are modest compared to those of certain non-pharmacological interventions, such as pulmonary rehabilitation [53].

1.6.4 Oxygen Therapy

Oxygen therapy is a form of treatment carried out through the administration of supplemental oxygen in hypoxemic patients. This form of treatment benefits the patient by increasing the supply of oxygen to the lungs, thereby increasing the amount of

oxygen available for the body tissues. The preferred methods to determine whether a patient requires this form of treatment are an arterial blood gas assessment (PaO_2) and surveillance of arterial oxygen saturation via pulse oximetry (SpO2) [2]. Physiological indications for oxygen therapy include having a resting arterial oxygen partial pressure (PaO_2) < 7.3 kPa (55 mmHg) as well as an SpO_2 < 88% [2]. Concerning arterial oxygen saturation, the goal through the use of this treatment is to maintain a SpO_2 > 90% during sleep, rest, and exertion [2]. It is possible for those who are physically active to require oxygen therapy only during exercise or physical activities; in such cases, a portable oxygen tank can be used [2]. It is equally possible for patients with COPD to be prescribed oxygen therapy only during exacerbations [2]. In this case, prescription of oxygen therapy needs to be re-evaluated 30-90 days afterward by rechecking arterial blood gas [2]. Sources of oxygen include gas, liquid, and concentrator [2]. Educating patients on this form of treatment is essential and has been shown to improve compliance rates [2].

1.6.5 Surgery

Few surgical treatments are available for COPD patients. One such treatment is lung volume reduction surgery [1]. This type of surgery involves the removal of parts of the lung. By removing the diseased lung tissue, the remaining healthier tissue can have an enhanced performance [1]. Lung volume reduction surgery has been shown to reduce hyperinflation, reduce the frequency of exacerbations, improve expiratory flow rates, increase maximal work capacity, and improve health-related quality of life [1]. This type of surgery is an expensive procedure and is only recommended for a select few [1].

In patients with very severe COPD, lung transplantation surgery has been shown to improve functional capacity and quality of life [1]. To be referred for such an intervention, patients must have the following criteria: $FEV_1 < 35\%$ predicted, $PaO_2 < 7.3 - 8.0$ kPa (55-60 mm Hg), $PaCO_2 > 6.7$ kPa (50 mm Hg), and secondary pulmonary hypertension [1]. Limitations for this type of surgery include shortage of donor lungs, possible complications (including death during surgery, acute rejection of donor lung, bronchiolitis obliterans), infection, and its cost (ranges from $110,000 to over $200,000 US) [1]. Individual risk factors are assessed through examination of patient history, physical examination, chest x-ray, and pulmonary function tests [1]. Surgery might be contraindicated for some patients, for example being at high risk of death due to poor lung function or experiencing an exacerbation pre-surgery [1].

1.6.6 Pulmonary Rehabilitation

Pulmonary Rehabilitation (PR), which combines exercise training, patient education and psychosocial support, has become widely recognized as a cornerstone in the management of COPD because it is the best available intervention to tackle the systemic consequences of the disease [5, 7, 8, 53, 54].

In a recent statement from the American Thoracic Society and European Thoracic Society [31], PR was defined as *"... an evidence-based, multidisciplinary, and comprehensive intervention for patients with chronic respiratory diseases who are symptomatic and often have decreased daily life activities."* The goals of PR are to reduce symptoms, optimize functional status, improve health-related quality of life (HRQL), and reduce health care costs [55, 56]. In a meta-analysis of 23 randomized controlled trials in COPD, PR was shown to significantly reduce dyspnoea, increase

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exercise tolerance, and improve HRQL compared with standard care [57]. Emerging evidence is also beginning to document its effectiveness in reducing respiratory exacerbations [58] and hospital days [59-63].

Exercise training is considered the key to successful PR because it is responsible for much of the benefits associated with this intervention [31, 59]. Exercise training has been shown to improve exercise tolerance (peak oxygen consumption (VO_{2peak}), peak work rate, or endurance time to constant-load exercise) in COPD patients despite the absence of improvement in resting lung function [59]. Improvements in exercise tolerance are mediated by several physiological mechanisms, including a reduction in minute ventilation for any given work rate [59], a desensitization to the sensation of dyspnoea [59], and an improvement in skeletal muscle strength [59] and oxidative capacity [59]. In the daily life of COPD patients, these physiological adaptations translate into less dyspnoea for any given task [59], a greater ability to perform various activities [59], and a better health-related quality of life [64]. After initial scepticism in the early 1980s [65], the therapeutic role of exercise training in COPD has now gained widespread acceptance, as evidenced by its inclusion in Canadian [31], American/ European [2], and World Health Organization [1] guidelines for the management of COPD.

1.7 Exercise Training in Pulmonary Rehabilitation: How Much Is Enough?

There is considerable variability worldwide in the way PR programs deliver their exercise component [53, 54]. This is largely attributable to the fact that the optimal exercise dose (intensity, duration, and frequency of training sessions) for PR has not been determined. As a result, the current guidelines for exercise training in PR are rather ambiguous. In their 2006 statement on PR [54], the American Thoracic Society and European Thoracic Society made the following recommendations with regards to the exercise dose: *"A minimum of 20 sessions should be given at least three times per week to achieve physiologic benefits; twice-weekly supervised plus one unsupervised home session may also be acceptable. High-intensity exercise produces greater physiologic benefits and should be encouraged; however, low-intensity training is also effective for those patients who cannot achieve this level of intensity. [...] The total effective training time should ideally exceed 30 minutes. However, for some patients, it may be difficult to achieve this target training time or intensity, even with close supervision."*

In reality, no systematic studies have been conducted to establish the optimal duration or frequency of training sessions in PR. Current guidelines regarding session duration are based on evidence obtained in healthy individuals [66], while recommendations for frequency of training sessions stem from clinical trials of PR versus usual care that were not designed to determine optimal training dose [67, 68]. Furthermore, the evidence favouring high-intensity over moderate- or low-intensity training in COPD patients is limited. The contention that *"high-intensity training produces greater physiologic benefits and should be encouraged"* [54] comes from one small (n = 19) randomized clinical trial from Casaburi and colleagues [69], in which the physiological training effects of a high training work rate (≈ 80% of peak work rate) were

compared to those of a low training work rate ($\approx$ 50% of peak work rate). At program

completion (week 8), the high training work rate was found to elicit greater physiological

adaptations (reductions in lactate levels and minute ventilation for a given work rate) and

larger gains in exercise tolerance and was therefore deemed optimal [69].

A major issue with the use of exercise training at 80% of peak work rate in PR is

that compliance to this training intensity has been shown to be problematic for COPD

patients [53, 70]. In a group of 42 patients enrolled in a 12-week program, this target

intensity was achieved by 0, 3, 5, and 5 patients at weeks 2, 4, 10, and 12, respectively

[70]. In light of this compliance issue, other approaches to exercise training, such as

training at the ventilatory threshold, have been proposed as more tolerable, less

unpleasant, and thus possibly easier to comply with for COPD patients. The ventilatory

threshold is commonly described as the breakpoint in the ventilatory response to

incremental exercise above which minute ventilation increases disproportionately in

response to increments in oxygen consumption [71]. This breakpoint does not occur at

the same percentage of peak capacity for all individuals, and thus needs to be

determined on an individual basis with incremental exercise testing. Training at the

ventilatory threshold is associated with tolerable levels of ventilation and dyspnoea, a

particularly valuable feature for a patient population limited by those two factors during

exercise [26, 28, 72]. The effectiveness of exercise training at the ventilatory threshold

was compared to that of training at a standardized moderate intensity (50% of heart rate

reserve) in 24 patients with moderate COPD [71]. Despite the fact that the mean training

intensity was similar between both groups, training at the ventilatory threshold led to

larger physiological adaptations (greater reductions in lactate levels, CO_2 excretion, and

minute ventilation for a given workload) than training at the standardized moderate

intensity [71]. This approach to training was also shown to be effective at improving

muscular strength and endurance in a subsequent study conducted by the same group [73].

The chronic effects of training at the ventilatory threshold (i.e. effects of several weeks or months of training) in COPD patients are therefore promising [25, 27, 71]. However, the contention that it is more tolerable, less unpleasant and easier to comply with than high-intensity exercise training has yet to be investigated. The affective response to this form of exercise has, to our knowledge, never been examined in COPD patients.

1.8 Affective Valence: Definition, Measurement, and Relationship with Exercise

1.8.1 Definition

According to Ekkekakis et al., the term "affect" is defined as "the most basic component of all valenced responses (i.e. positive or negative, pleasant or unpleasant), including, but not limited to, emotions and moods." [74] Affect is broader than an emotion, the main difference being that an emotion requires cognitive appraisal, which can generate positive or negative implications on one's ambitions or well-being [74]. According to Lazarus et al. [75], "emotions are generated and controlled by the personal implications for well-being conveyed by relationships with the environment and comprehended through an appraisal process which draws heavily on evolved intelligence and knowledge." In other words, individuals decide what to feel after interpreting or explaining what has happened. Moods, on the other hand, are also thought to have a cognitive origin. In comparison with emotions, moods are not responses to specific events; they are responses to how we view the world [76]. Simply stated, affect is a broader feeling than an emotion or mood. Essentially, it is the difference between a pleasant versus an unpleasant feeling.

Within exercise psychology, there has been much deliberation on how to best define affective response in relation to exercise [77]. Thus far, researchers have made use of categorical as well as dimensional approaches. Watson, Clark and Tellegen [78] declared that affect is composed of two primary dimensions termed positive affect (PA) and negative affect (NA). This would be classified as a categorical approach which organizes affective responses into distinct categories [79]. On the other hand, the dimensional approach is "based on the assumption that affective states are interrelated

and can be understood by a parsimonious set of underlying dimensions" [79]. These dimensions include positive and negative affect as well as high and low arousal. Positive affect (PA) includes feelings such as active, enthusiastic, and alert [78]. The negative affect (NA) dimension reflects feelings such as anger, disgust, guilt, and fear [78]. Furthermore, several dimensions exist within PA and NA. High/low PA or high/low NA describes the level of arousal felt by the participant.

1.8.2 Measurement of Affective Response

The measurement of affect is a highly controversial issue [80]. The dilemma on whether to use a categorical measurement versus a dimensional measurement is at the heart of this controversy [80]. Current views advocate that both approaches possess advantages and limitations, which will depend on the specific research question needing to be answered [76]. Researchers interested in examining specific emotions (positive and negative affect) should choose a categorical approach whereas researchers wanting to examine basic affect (positive and negative affect as well as high and low arousal) should select a dimensional approach [81]. To date, various measurement tools have been used to measure affective response. Table 2 presents an overview of some of these tools.

Table 1.2 - Overview of Some Self-Reported Measures of Affect

Reference	Measure	Construct	No. Of Items
McNair et al. [82]	POMS	Mood	65 adjectives
Gauvin & Rejeski [83]	EFI	Exercise- induced feeling	12
Watson, Clark & Tellegen [84]	PANAS	Positive and Negative Affect	20
Spielberger, Gorsuch & Lushene [85]	STAI	Anxiety	12
Zuckerman & Lubin [86]	MAACL	Affective response during exercise	132 adjectives
Thayer [87]	AD-ACL	Various transitory arousal states	4
Kendzierski & DeCarlo [88]	PACES	Exercise enjoyment	7
Mackay et al. [89]	SACL	Stress and Arousal	20
McAuley & Courneya [90]	SEES	Exercise-induced feeling states	3
Lox et al. [91]	PAAS	Feeling state	16
Monk [92]	VAS (GVA specific)	Global vigor and affect	8

POMS = Profile of Mood States, EFI = Exercise-Induced Feeling Inventory, PANAS = Positive and Negative Affect Schedule, STAI = State-Trait Anxiety Inventory, FS = Feeling Scale, MAACL = Multiple Affect Adjective Checklist, AD-ACL = Activation Deactivation Adjective Checklist, PACES = Physical Activity Enjoyment Scale, SACL = Stress/Arousal Adjective Checklist, SEES = Subjective Exercise Experiences Scale, PASS = positive affect/sensation-seeking measure, VAS = Visual Analogue Scale, GVA = Global Vigor and Affect Instrument.

1.8.3 Affective Response and its Relationship to Acute Exercise

Reviewing the literature on the exercise-affect relationship is a difficult and a challenging task [93]. Variations in methodology, mainly in the measurement of affect,

definition of intensity, and the choice of exercise dose, make it difficult to formulate any direct comparisons among studies [80].

To date, a common belief has been that acute exercise is usually associated with unpleasant feelings, which might explain why few individuals exercise or adhere to an exercise program [80]. As well, in the realm of the exercise-affect relationship, a common belief has been that exercise performed at moderate-intensities, versus low or high intensities, leads to acute positive affective responses and should therefore be prescribed to all individuals involved in an exercise program [80]. Based on these traditional assumptions, researchers have attempted to provide clarification on the mechanisms involved in the relationship between exercise intensity and adherence through the study of affective response [74]. Currently, this area of research is expanding and studies have shown that exercise intensity is negatively related to acute pleasure responses [80] and long-term adherence [94, 95] to an exercise program .

A large extent of research has focused on the dose-response relationship between acute exercise and affect [80, 96]. The reason for this interest has been based on the notion that a specific exercise intensity and duration will elicit a certain affective response. Thus far, the common beliefs for exercise have been that moderate intensity elicits positive affective changes [97-99], low intensity is suspect to bring about any changes in affect (76-80), and high intensity is likely to be unpleasant [97-100]. However, researchers have argued that this relationship in an acute condition is possibly dependent on inter-individual differences and therefore cannot be generalized to the entire population [101]. Possible inter-individual differences suggested include; the individual's personal goals and objectives from exercising, initial aerobic fitness, the physical and social environment, how the individual perceives the exercise stimulus, as

well as the psychological state of the individual [80]. As well, exercise duration of single bouts have not been shown to have an impact on affective changes [102, 103]. Furthermore, it has been shown that affect during acute exercise is negatively correlated with physiological responses of metabolic strain, such as heart rate, respiratory rate, oxygen consumption, and blood lactate levels [104, 105].

1.8.4 Affective Response to Acute Exercise Among COPD Patients

To date, few studies have looked at affective response to acute exercise training among COPD patients. A study performed by Carrieri-Kohlman et al. [106], examined whether patients with COPD at rest and during acute exercise could make the distinction between affective response to dyspnoea and perceived shortness of breath [106]. This study defined affective response as distress and anxiety experienced from dyspnoea [106]. They used several visual analogue scales to measure breathing effort, shortness of breath, as well as distress and anxiety associated with dyspnoea [106]. Results indicated that COPD patients exercising in acute conditions can, in fact, differentiate the sensation of dyspnoea from affective response [106].

Another study performed by Carrieri-Kohlman et al. [107] looked at dyspnoea and affective response during long-term exercise training in subjects with COPD. This randomized clinical trial included 45 dyspnoea-limited patients with COPD who underwent a 12-week exercise training program with and without nurse coaching [107]. The 12 week program was divided into 4 weeks of supervised treadmill training and 8 weeks of home walking [107]. This study defined affective response as simply dyspnoea-related anxiety and used a visual analogue scale and the state-trait anxiety inventory as measurement tools [107]. The objectives of the study were to compare

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dyspnoea intensity, dyspnoea-related anxiety, and exercise performance [107]. Results showed that dyspnoea-related anxiety rapidly decreased within the first 4 sessions despite constant levels of dyspnoea intensity [107]. Further investigation revealed that exercise training with coaching is as effective when compared to exercise training alone in improving exercise performance, dyspnoea, anxiety, and distress [107].

Finally, a study performed by Gayle et al. [108], examined psychological change among 15 COPD patients undergoing an exercise program. The treatment group underwent psychological and physiological assessments followed by 28 weeks of exercise training [108]. The control group, in contrast, did not participate in the initial 14 weeks of exercise training [108]. This study did not define affect directly, but measured anxiety and depression using the state-trait anxiety inventory (STAI) and the Self-Rating Depression Scale [108]. Contrary to other studies, results indicated that exercise did not have any significant impact on anxiety or depression [108].

In summary, the evidence regarding the relationship between affect and exercise in COPD patients is scarce and inconsistent. Furthermore, prior investigations have used surrogate rather than direct measures of affect, such that the affective response to an acute bout of exercise in COPD patients remains unknown.

1.9 Acute Physiological Response to Exercise Training Among COPD Patients

Thus far, few researchers have attempted to investigate the acute physiological response to an exercise-training bout among COPD patients. Most researchers have investigated long-term physiological adaptations to exercise programs [60, 71]. Sabapathy et al. [109] have specifically examined the acute physiological response to single exercise bouts of continuous high-intensity training (70% of peak VO_2) and interval training. Results showed that high-intensity training was found to induce higher levels of ventilation, lung hyperinflation and dyspnoea than interval training which resulted in patients performing a reduced total amount of work [110].

A study conducted by Maltais et al. [70] examined the physiological response in moderate to severe COPD patients undergoing a pulmonary rehabilitation program. Forty-eight COPD patients were asked to perform 25-30 minute exercise sessions on a calibrated ergocycle [70]. These exercise sessions were held 3 times per week for a total of 12 weeks with a target intensity of 80% Wmax [70]. Results showed that although most participants were unable to tolerate high-intensity exercise, physiological changes did occur with the exception of resting pulmonary function [70]. Participants were shown to have significant ($p<0.0002$) increases in VO_2max and Wmax, reductions in lactic acid and V_E, and significant ($p<0.004$) decreases in submaximal heart rate [70].

CHAPTER II

Rational and Clinical Significance

Current PR guidelines advocate high-intensity exercise training (at $\approx 80\%$ of peak work rate) for patients with COPD. However, this training intensity has been shown to be unachievable in a large proportion of patients. Alternative approaches to exercise training, including training at the ventilatory threshold, have thus been proposed as more tolerable, less unpleasant, and thus possibly easier to comply with in this patient population. However, this belief has yet to be investigated by comparing the acute affective and physiological response to different exercise-training protocols in COPD patients. To date, few studies have examined the relationship between exercise and affect in patients with COPD undergoing exercise training. In addition, to our knowledge, no study has simultaneously assessed both affective and physiological responses to an exercise-training bout in COPD patients.

The general aim of the present study was to identify which protocol, between high-intensity training and training at the ventilatory threshold, is more pleasurable and tolerable for COPD patients. The proposed research project will improve our understanding of the affective response to different exercise training protocols among COPD patients undergoing a PR program. Clinically, the significance of this study is to determine which protocol patients find more pleasant/unpleasant, with the rationale that acute responses may subsequently influence long-term exercise adherence and program effectiveness.

CHAPTER III

Research Objectives and Hypotheses

The purpose of the present study was to compare, in COPD patients, the acute affective and physiological response to a single bout of exercise-training performed using the following protocols: i) high intensity training at 80% of peak work rate (CT80) and ii) training at the ventilatory threshold (CTVT). More specifically, our primary research objective was to compare the acute affective response (i.e. pleasant versus unpleasant feelings), as measured by the PANAS, to a single bout of exercise-training for CT80 and CTVT to determine if the latter approach is in fact perceived as less unpleasant for COPD patients. The secondary objectives were to: i) compare the acute affective response, as measured by the GVA, between CT80 and CTVT, and ii) to compare the acute physiological response to both training protocols.

Our research hypotheses were that: 1) training at the ventilatory threshold would be associated with greater positive affective response compared to the high-intensity exercise-training group (as measured by the PANAS and GVA instrument); and 2) high-intensity exercise would induce higher levels of VO_2, VE, HR, dynamic hyperinflation ($\downarrow$IC), dyspnoea and leg fatigue compared to training at the ventilatory threshold.

CHAPTER IV

Acute Affective and Physiological Response to Exercise Training in Chronic Obstructive

Pulmonary Disease: A Pilot Study

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Abstract

Purpose: Pulmonary rehabilitation (PR) guidelines advocate high-intensity exercise training for patients with chronic obstructive pulmonary disease (COPD) yet this approach is unachievable for a large proportion of patients. Alternative approaches, such as training at the ventilatory threshold, have been proposed as more tolerable, less unpleasant, and thus possibly easier to comply with for the COPD clientele. This assumption remains to be verified. The study aim was to compare, in COPD patients, the acute affective and physiological response to high-intensity training (CT80) versus training at the ventilatory threshold (CTVT). **Methods:** Subjects were randomly assigned to perform a bout of either CT80 or CTVT on a cycle ergometer. Affective response to the exercise bout was measured using the Positive and Negative Affect Schedule (PANAS) and the Global Vigor and Affect Instrument (GVA). Physiological response to the same bout was measured breath by breath using portable equipment. **Results:** Thirteen subjects (CT80 = 7; CTVT = 6) completed all assessments. Positive affect scores from the PANAS increased from pre-, to end-, to post-exercise (time effect)(F=17.56, p=0.0005), but this increase was significant for the CTVT group only (time by intervention interaction)(F=5.85, p=0.02). No significant time or interaction effect was observed for global affect or global vigor from the GVA. In addition, no significant difference in physiological response was observed between CT80 and CTVT. **Conclusion:** The main finding from this pilot study is that affect seems to improve after an exercise-training bout in COPD patients, especially when the protocol used is training at the ventilatory threshold.

Keywords: COPD, affective response, physiological response, exercise training

Introduction

Pulmonary rehabilitation (PR), which combines exercise training, patient education and psychosocial support, has become widely recognized as a cornerstone in the management of COPD because it is the best available intervention to tackle the systemic consequences of the disease [5, 7, 8, 53, 54]. Exercise training is considered the key to successful PR because it is responsible for much of the benefits associated with this intervention [8, 53, 54]. Exercise training has been shown to improve exercise tolerance in COPD patients despite the absence of improvement in resting lung function [111]. Improvements in exercise tolerance are mediated by several physiological mechanisms, including a reduction in minute ventilation for any given work rate [69], a desensitization to the sensation of dyspnoea [112], and an improvement in skeletal muscle strength [112] and oxidative capacity [69, 113]. In the daily life of COPD patients, these physiological adaptations translate into less dyspnoea for any given task [114], a greater ability to perform various activities [115], and a better health-related quality of life [111]. After initial scepticism in the early 1980s [65], the therapeutic role of exercise training in COPD has now gained widespread acceptance, as evidenced by its inclusion in Canadian [8], American/ European [7], and World Health Organization [5] guidelines for the management of COPD.

There is considerable variability worldwide in the way PR programs deliver their exercise component [53, 54]. Current PR guidelines advocate high-intensity exercise training [7, 8]. Yet, the evidence favouring high-intensity over moderate- or low-intensity training in COPD patients is limited [17]. A major issue with the use of high-intensity exercise training in PR is that compliance to this training intensity has been shown to be problematic for COPD patients [53, 70]. In light of this compliance issue, other approaches to exercise training have been proposed as more tolerable, less unpleasant,

and thus possibly easier to comply with for COPD patients. Exercise training at the ventilatory threshold has been suggested as one of these alternatives to high-intensity training [24, 25]. The ventilatory threshold is commonly described as the breakpoint in the ventilatory response to incremental exercise above which minute ventilation increases disproportionately in response to increments in oxygen consumption [71]. In clinical trials, the chronic effects of training at the ventilatory threshold in COPD patients have been promising [24, 26]. However, the belief that this form of training is more tolerable, less unpleasant, and easier to comply with for COPD patients than high-intensity training has yet to be verified.

Very few studies have compared the acute physiological response to different exercise-training protocols in COPD patients. Training at the ventilatory threshold has been shown to be associated with tolerable levels of ventilation and dyspnoea, a particularly valuable feature for a patient population limited by those two factors during exercise [26, 28, 72]. However, its acute physiological effects have yet to be directly compared to those of high-intensity exercise training.

Even fewer studies have examined the acute affective response to exercise training in COPD patients. The term "affect" can be defined as "the most basic component of all valenced responses (i.e. positive or negative, pleasant or unpleasant), including, but not limited to, emotions and moods" [74]. Simply stated, it is the differentiation between a pleasant and an unpleasant feeling. To date, a common belief has been that acute exercise is associated with unpleasant feelings, which would explain why few individuals undertake or adhere to an exercise program [80]. As well, in the realm of the exercise-affect relationship, a common belief has been that exercise performed at moderate intensities, versus low or high intensities, leads to acute positive

affective responses and should therefore be prescribed to all individuals involved in an exercise program [80]. In healthy individuals, studies have shown that exercise intensity is negatively related to acute pleasure responses [80] and to long-term adherence to an exercise program [94, 95]. However, the acute affective response to different exercise-training protocols in COPD patients has yet to be examined.

The primary research objective of the present study was to compare, in individuals with COPD, the acute affective response to a single bout of exercise training performed using the following protocols: i) high intensity training at 80% of peak work rate (CT80) and ii) training at the ventilatory threshold (CTVT). The secondary objective was to compare the acute physiological response to both training protocols. The ultimate aim of the study was to verify whether CTVT is, in fact, more pleasant (affectively) and more tolerable (physiologically) than CT80 for individuals with COPD.

Methods

Subjects

Thirteen subjects were recruited from a pool of individuals who previously agreed to participate in the larger pulmonary rehabilitation trial at the Hôpital du Sacré-Coeur de Montréal. Eligibility was ascertained according to the following criteria: *Inclusion criteria*: 1) clinically stable COPD; 2) age 40 years or older; 3) smoking history of at least 10 American pack-years (20 cigarettes per pack); 4) post-bronchodilation forced expiratory volume in one second (FEV_1) less than 80% of the predicted normal value; and 5) FEV_1 to forced vital capacity (FVC) ratio less than 0.7. *Exclusion criteria*: 1) exacerbation of respiratory symptoms in the past 4 weeks (change in dyspnoea or volume/colour of

sputum, need for antibiotic treatment, or need for hospitalization); 2) any contraindication to exercise testing based on guidelines from the American Thoracic Society [116]; 3) any active condition other than COPD that can influence exercise tolerance (asthma, unstable coronary heart disease, left congestive heart failure, neoplasia, severe claudication, severe arthritis, etc.); 4) oxygen therapy; 5) participation in a PR program in the past year; 6) inability to complete baseline evaluations (including the achievement of a ventilatory threshold on the incremental cycling exercise test). These eligibility criteria were mostly meant to differentiate COPD from other respiratory diseases and to ensure clinical stability and patient safety. Figure 4.1 illustrates the flow of participants through each stage of the study.

Study Design and Procedure

The present pilot study was a sub-study to a larger randomized, parallel-group clinical trial (RCT) comparing the chronic effects of different exercise training protocols on various pulmonary rehabilitation program outcomes. As part of the larger RCT, patients who met the eligibility criteria and accepted to participate completed a thorough baseline evaluation and were then randomly assigned in blocks of six to one of three training protocols. Each subject trained three times per week for 12 weeks, for a total of 36 exercise sessions. Session duration was adjusted such that the total amount of work performed per session was identical across the different protocols.

As a sub-study to the larger RCT, the present study followed the same design, that is a randomized, parallel-group design. The specific objective of the present sub-study was to compare the acute affective and physiological response to a single bout of exercise training performed according to one of two different protocols which were part

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of the larger RCT: CT80 and CTVT. Both exercise protocols were performed on a cycle ergometer where patients were asked to perform quiet breathing for 3 minutes, followed by 5 minutes of unloaded pedalling (warm-up), followed by 25 minutes or more at the target intensity, followed by 5 minutes of cool-down. Subjects who agreed to participate in this sub-study accepted to be monitored closely and to complete additional evaluations in the initial phase of their rehabilitation program. Further details regarding baseline measurements from the RCT and additional measurements taken for this sub-study are provided below.

Assessments

Baseline assessments

As mentioned earlier, baseline measurements were taken as part of the larger RCT. These measurements included pulmonary function tests, exercise tests, a quality of life questionnaire, a series of psychological questionnaires and a battery of cognitive function tests. Of the above mentioned measures, pulmonary function tests and one exercise test were used for the present study.

Pulmonary Function Testing

Spirometry, lung volumes, and lung diffusion capacity for carbon monoxide (D_LCO) were obtained at the time of enrolment according to recommended techniques [117]. Values were compared to predicted normal values from the European Community for Coal and Steel/European Respiratory Society [118].

<u>Exercise Testing</u>

A symptom-limited incremental cycling exercise test was performed at baseline to rule out the presence of cardiovascular co-morbidities and to determine the work rate at peak effort and at the ventilatory threshold for subsequent exercise prescription. Subjects were seated on an electromagnetically braked cycle ergometer (Ergometrics 800, SensorMedics, Yorba Linda, CA) and connected to an electrocardiogram and to a respiratory circuit through a mouthpiece. The respiratory circuit consisted of a pneumotachograph, O_2 and CO_2 analyzers, and a mixing chamber (Vmax Encore, SensorMedics, Yorba Linda, CA). After five minutes of rest and three minutes of unloaded pedalling, the workload was increased in a stepwise manner up to the individual's maximal capacity. Each step lasted one minute and increments of 5 or 10 watts were used. This protocol is frequently used in respirology [119]. Gas exchange parameters (minute ventilation, O_2 uptake, CO_2 excretion) and heart rate were measured at rest and during exercise on a breath-by-breath basis. Dyspnoea and leg fatigue was evaluated at rest and every other minute during the test with the modified 10-point Borg scale [120]. The ventilatory threshold was determined using the V-slope method [121], a computerized approach to identify the breakpoint in the VCO_2-VO_2 relationship. Peak work rate was defined as the highest work rate maintained at a pedalling speed of at least 50 revolutions per minute for a minimum of 30 seconds.

Measurements taken during training

To answer our specific research question, affective response, a series of physiological parameters, and symptoms (dyspnoea and leg fatigue) were measured during a single exercise training session in the initial phase of the rehabilitation program.

More specifically, these measures were collected either before the beginning of the training program or during one of the three weekly exercise sessions within the first two weeks of program initiation. This timeframe was chosen i) to capture the acute response to the training protocols before adaptations occur, and ii) to allow for a reasonable window to obtain these measurements in as many subjects as possible from the larger RCT. These measurements are described in detail below and the timeline of the experimental design is depicted in Figure 4.2.

Affective Response

The acute affective response to exercise training was assessed using two different scales: the Positive and Negative Affect Schedule (PANAS) and the Global Vigor and Affect (GVA) instrument.

Positive and Negative Affect Schedule (PANAS): Subjects completed the PANAS at rest, at completion of the exercise bout, and half an hour after the completion of the exercise session. The PANAS, developed by Watson, Clark, and Tellegen [84], is a brief and easy to administer questionnaire which provides measures on positive and negative affect. More specifically, this questionnaire consists of 20 questions related to affect, 10 of which deal with positive affect responses (interested, excited, strong, enthusiastic, proud, alert, inspired, determined, attentive, and active) and the remaining 10 dealing with negative affect responses (distressed, upset, guilty, scared, hostile, irritable, ashamed, nervous, jittery, and afraid) [122]. Its structure is consistent with the two-dimensional circumflex model and has been shown to have excellent reliability [123] and validity [122]. In addition, it has been shown to be highly internally consistent and largely

uncorrelated [122]. Various time-frames have been used for the PANAS, yet the chosen time-frame for the current study was "in the moment". This scale is a 5 point scale where 1 represents "very slightly or not at all", 2 represents "a little", 3 represents "moderately", 4 represents "quite a bit", and 5 represents "extremely". Individuals are asked to circle one of the points on the scale to indicate to what extent they feel a given sentiment or emotion in the moment. The final outcome is obtained in two separate scores: one for positive affect and the other for negative affect. These scores can be calculated by simply adding the chosen numbers for each. Scores can range from 10 to 50 for each affective response.

Global Vigor and Affect (GVA) Instrument: At rest (pre-exercise), at the beginning of the exercise bout (0%), halfway through the exercise bout (50%), at completion (100%), and half an hour after the completion of the PR session (post-exercise), participants were asked to rate their global affect and vigor using the GVA instrument which is composed of several visual analogue scales. Visual analogue scales have an extended history in the measurement of mood [124, 125] and have been shown to be highly reliable and valid in assessing both global vigor and global affect [126, 127]. This scale is a simple and frequently used measure which has been included in several studies to assess a wide range of subjective phenomena such as dyspnoea, pain, fatigue, sleep loss, among many others [126]. Each visual analogue scale is a 100 millimetre line separating opposite extremes of the mood or state of arousal [126]. Subjects are asked to place a mark on these continuums to demonstrate their overall affective state and state of arousal for that particular moment [126]. The mark placed on this continuum, ranging from 0 to 100, is then measured using a ruler. Four of the visual analogue scales are related to global affect and the remaining four are related to global vigor. Each score is

then entered into a separate equation revealing a global affect and vigor score ranging from 0 to 100. The equations are the following:

$$GV = [(alert) + 300 - (sleepy) - (effort) - (weary)] / 4$$

and

$$GA = [(happy) + (calm) + 200 - (sad) - (tense)] / 4$$

Physiological Response

Physiological measurements were obtained with a wireless portable metabolic system (Oxycon Mobile, Jaeger, Viasys Healthcare GmbH, Germany). The system consists of a lightweight, battery-operated portable system mounted on the subjects' body via a vest. It records breath-by-breath data through a facemask and subsequently sends it to a host computer system through wireless transmission. Oxygen uptake (VO_2), carbon dioxide excretion (CO_2), minute ventilation (V_E), heart rate (HR), breathing frequency (BF), and oxygen saturation (SpO_2) were measured on a breath-by-breath basis through the use of this portable system throughout the training session. In addition, inspiratory capacities (IC) were measured at 5 minute intervals.

Symptoms and Compliance

Dyspnoea and leg fatigue, the main two symptoms which limit exercise in COPD patients [128], were measured at rest, at the beginning of the training session, every 5 minutes during training, at the completion of training, and half an hour after the completion of the PR session. Symptoms were measured using the modified 10-point Borg scale [120]. Compliance to the training protocol was defined as the percent time

spent at the prescribed training intensity during the single exercise-training bout. As such, measured HR was compared to target HR for every minute of the exercise bout. If measured heart rate was within ± 5 beats of target HR, the subject was considered compliant for that minute. The final compliance rate was obtained by calculating the following:

$$\frac{\text{Time spent at target HR (min)}}{\text{Total time of intensity phase (min)}} \quad \text{X } 100$$

Statistical Analyses

To assess the effects of the different exercise protocols on PANAS and GVA, four repeated-measures general linear models were conducted. These models used the exercise protocol (CT80 or CTVT) as the between-factor independent variable and assessment points as the within-factor repeated measure independent variable (3 levels for the PANAS and 5 levels for the GVA). For the assessment of the physiological changes that occurred during the testing sessions, a series of repeated measures mixed models were conducted. This analysis strategy was utilized due to the magnitude of measures for each variable, thus increasing the likelihood of violating the regression assumption of independence. In these analyses the exercise protocol was the only between factor effect assessed. All analyses were conducted using SAS (v9.2, SAS Institute, Cary NC).

For the purpose of this study, affective response was defined as any change in self-reported pleasure or displeasure and took into account the various dimensions which compose affect.

Results

Subjects

A total of thirteen subjects completed the present study, seven of which were in the CT80 group and six of which were in the CTVT group. The baseline characteristics of the study group are presented in Table 4.1, and are typical of COPD samples in terms of age and BMI. Participants had, on average, stage II to stage III COPD according to the GOLD classification, which is indicative of moderate to severe airflow obstruction [1]. Subjects had a wide range of peak exercise capacities, as indicated by the wide range of peak work rates and peak VO_2.

Acute Affective Response to Exercise

Results from the PANAS questionnaire revealed a significant time effect (F=17.56, p=0.0005) as well as a time by intervention interaction (F=5.85, p=0.02) for positive affect scores. As shown in Figure 4.3, positive affect increased from rest to end-exercise to post-exercise in both groups combined (time effect), but this increase was significant for the CTVT group only (time x intervention interaction). In contrast, no significant changes in negative affect scores were obtained (Figure 4.3). Likewise, results from the GVA questionnaire revealed no significant time or interaction effect for global vigor (level of alertness) or global affect. Although not statistically significant, the changes in GVA scores observed were in the same direction as those obtained with the PANAS (Figure 4.4), meaning it had a tendency to increase from rest to post-exercise.

Acute Physiological Response to Exercise

The mean physiological responses at the target intensity during the single exercise training-bout for CT80 and CTVT are found in Table 4.2. In addition, the time course for $\dot{V}O_2$, $\dot{V}E$, heart rate, and inspiratory capacity is depicted in Figure 4.5. As illustrated, $\dot{V}O_2$, $\dot{V}E$, and heart rate were higher in the CT80 group than in the CTVT group at most exercise time points, possibly suggesting a greater physiological demand from the CT80 protocol. Likewise, inspiratory capacity was lower for CT80 than CTVT at all time points, indicating greater lung hyperinflation (air trapping) in the CT80 group. However, despite these subtle differences, the interaction between the exercise protocol and time was not significant for any of the four parameters. Our results thus suggest that the CT80 and the CTVT protocols are similarly physiologically tolerable.

Acute Symptomatic Response and Compliance to Exercise

The symptomatic response to CT80 and CTVT is illustrated in Figure 4.6. As clearly shown in this figure and confirmed by statistical analyses, the perceived levels of dyspnoea and leg fatigue were comparable between the two groups. Mean compliance rates to the single bout of exercise were 88% for the CT80 group and 82% for the CTVT group. These values were not significantly different.

Discussion

The present study compared, in COPD patients, the acute affective and physiological response to different exercise training protocols (high-intensity training

versus training at the ventilatory threshold) during a single exercise training bout. Our findings suggest that affect improves after a single bout of exercise in this patient population, especially if the protocol used is training at the ventilatory threshold. As well, the acute physiological response to both CT80 and CTVT protocols do not appear to differ significantly.

Reviewing the literature on the exercise-affect relationship is a difficult and a challenging task [93]. Variations in methodology, mainly in the measurement of affect, definition of intensity, and the choice of exercise dose, make it difficult to formulate any direct comparisons among studies [80]. Previous investigations, in healthy individuals, state that a common belief has been that acute exercise is associated with unpleasant feelings, which could explain why few individuals take part or adhere to an exercise program [80]. This belief is somewhat inconsistent with our findings which demonstrate that a change in affect is possible after a single bout of exercise. However, results from the GVA did indicate a dip in both global affect and global vigor halfway through the exercise bout, but this dip was not statistically significant, possibly because of our small sample size. This belief stemming from previous literature will therefore have to be confirmed with a larger trial.

The current study also found an increase in positive affect from pre-exercise to post-exercise using the PANAS. This change was especially true with the CTVT protocol, which exposed subjects to an intensity that can be considered moderate. This finding is consistent with the previous literature suggesting that exercise performed at moderate intensities, versus low or high intensities, leads to acute positive affective responses [80]. As well, in studies conducted in healthy individuals, exercise intensity has been shown to be negatively related to acute pleasure responses [80]. The fact that,

in the present study, positive affect increased in CTVT (moderate intensity), but not in CT80 (high intensity) is in line with these previous investigations. However, the fact that we found statistically significant findings with the PANAS but not with the GVA warrants further investigation. The sensitivity of the GVA questionnaire during exercise will need to be verified.

No studies, to our knowledge, have investigated the acute physiological response to training at the ventilatory threshold. However, the acute physiological response to continuous high-intensity training has been documented [109]. Sabapathy and coworkers have reported on the acute physiological response to single exercise bouts of continuous high-intensity training at 70% of peak VO_2 in 10 individuals with moderate COPD [109]. These investigators reported a significant degree of dynamic lung hyperinflation (i.e. a significant drop in inspiratory capacity) with this form of exercise [109]. The present study findings are not consistent with this observation from Sabapathy et al. since inspiratory capacity did not decrease significantly with CT80. A potential reason for our finding may be that subjects from the CT80 group were not truly working at an intensity corresponding to 80% of their peak work rate, thereby not eliciting the expected physiological response. This would have occurred if the exercise test performed at baseline was not a true peak test. This aspect was not verified, but if an underestimation of peak work rate occurred at baseline, it would have affected the CT80 group only, since the CT80 intensity is relative to peak work rate while CTVT intensity is independent of it. Caution is warranted, however, at this point, with respect to the conclusions to draw from this finding given our small sample size.

Dyspnoea upon physical exertion can be a major deterrent for COPD patients to engage in physical activity, thereby reducing compliance [129]. The present study found

no differences in symptomatic responses (i.e. dyspnoea and leg fatigue) between the two exercise-training protocols. The finding regarding dyspnoea coincides with our results for inspiratory capacity, where no statistically differences were found between the CT80 and CTVT group. Inspiratory capacity is a physiological marker of dynamic hyperinflation (i.e. air trapping), which is highly correlated with dyspnoea [130]. It is therefore not surprising that no differences in dyspnoea was observed since no statistically significant differences were found for inspiratory capacity between both groups. As stated previously, if the exercise test performed at baseline was not a true peak test and subjects were therefore not working at an intensity corresponding to 80% of their peak work rate, this may be another potential reason why no differences were found in subjective measurements of dyspnoea and leg fatigue between groups.

Finally, no differences in the compliance rates to the single bout of exercise were obtained between the two groups. Subsequent compliance to the rest of the PR program would give us more information about the effect of acute affective response to the training protocol on long-term compliance. This aspect will have to be examined in a future study.

In summary, the present study indicates that affect improves after a single exercise-training bout in COPD patients. This seems especially true when the protocol used is CTVT. The acute physiological response to both protocols did not differ significantly. These preliminary results suggest that CTVT increases positive affect to a greater degree than CT80, but is similarly tolerable than CT80 for the COPD clientele.

Legends for Figures

Figure 4.1 Flow of Participants Through Each Stage of the Study

Figure 4.2 Timeline of the experimental design.

Figure 4.3 Positive and negative affect, as measured by the PANAS, for the CT80 (closed circles) and CTVT (open circles) groups. Values are mean ± SD.

Figure 4.4 Global affect and global vigor, as measured by the GVA, for the CT80 (closed circles) and CTVT (open circles) groups. Values are mean ± SD.

Figure 4.5 Time course and end-exercise values for $\dot{V}O_2$ (A), $\dot{V}E$ (B), heart rate (C), and inspiratory capacity (D) for the CT80 (closed circles) and CTVT (open circles). Values are mean ± SD. Data is missing for inspiratory capacity in one individual.

Figure 4.6 Dyspnoea and leg fatigue perception using the modified 10-point Borg scale for the CT80 (closed circles) and CTVT (open circles) groups. Values are mean ± SD.

TABLES

Table 4.1 Characteristics of the Study Group

	CT80	CTVT
Male/Female, n	2/5	2/4
Age, years	64.6 ± 7.9	72.3± 8.9
BMI, kg·m^{-2}	28.3 ± 4.1	25.8 ± 5.7
FEV$_1$, L	1.57 ± 0.32	1.40 ± 0.23
FEV$_1$, % predicted	66.7 ± 15.5	64.2 ± 17.2
FEV$_1$/FVC, %	40.4 ± 19.7	50.5 ± 12.1
Peak Work Rate, W	65.7 ± 20.5	70.8 ± 27.6
VO$_2$peak, L·min^{-1}	1.09 ± 0.21	1.00 ± 0.31

Values presented are Mean ± SD.
BMI, Body Mass Index; FEV$_1$, Forced Expiratory Volume in 1 second; FVC, Force Vital Capacity; VO$_2$peak, peak O_2 Uptake.

## Table 4.2 Mean Physiological Response to the Target Intensity for CT80 and CTVT

	CT80	CTVT
Time at Target Intensity, min	25 ± 0	29.67 ± 2.58
VO_2, L/min	0.74 ± 0.14	0.69 ± 0.192
V_E, L/min	30.67 ± 5.84	26.43 ± 8.18
HR, b/min	115.26 ± 16.89	92.77 ± 17.94
Δ IC, L	-0.065 ± 0.071	-0.005 ± 0.284
Dyspnoea, Borg	3.4 ± 1.49	3.7 ± 2.36
Leg Fatigue, Borg	3.3 ± 1.59	3.3 ± 1.65

Values presented are mean ± SD.
VO_2: oxygen consumption; V_E: minute ventilation; HR: heart rate; Δ IC: change in inspiratory capacity.
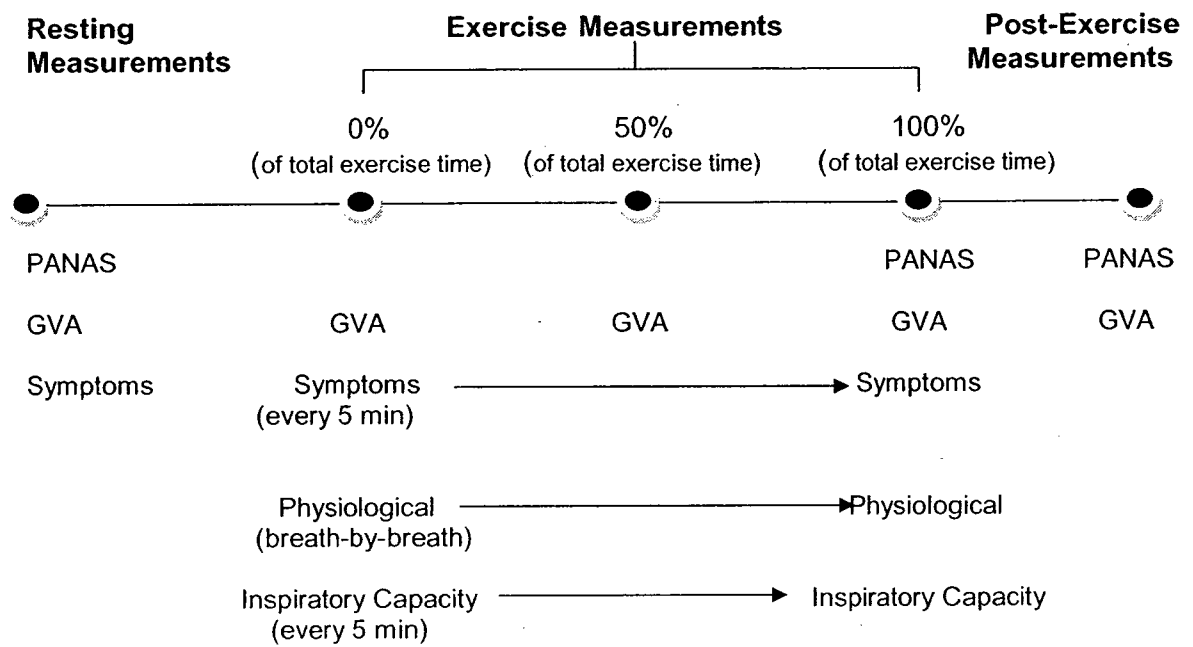
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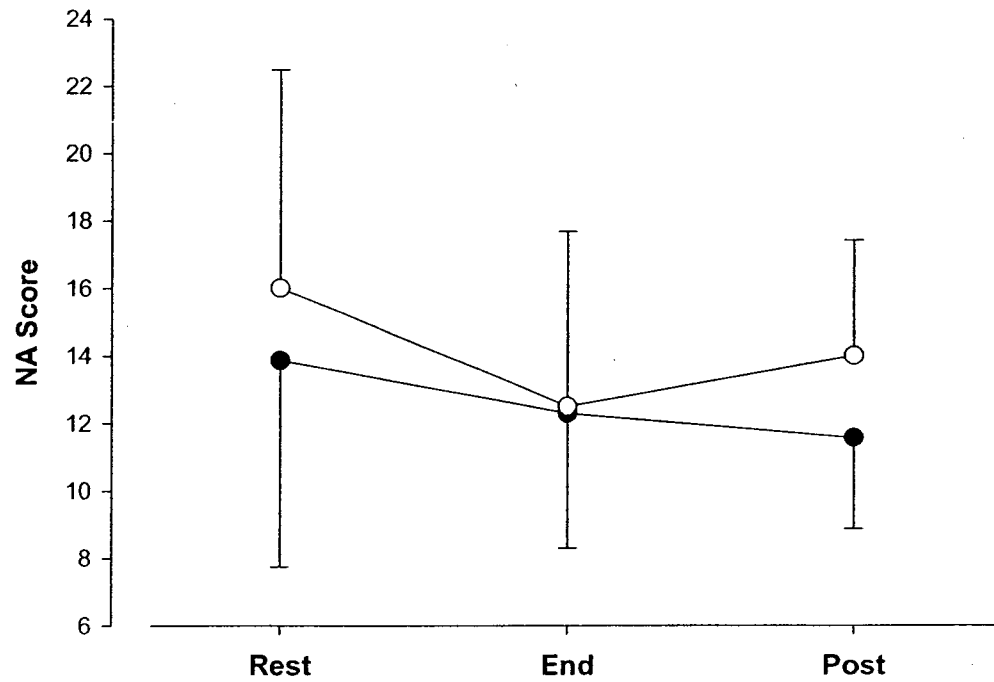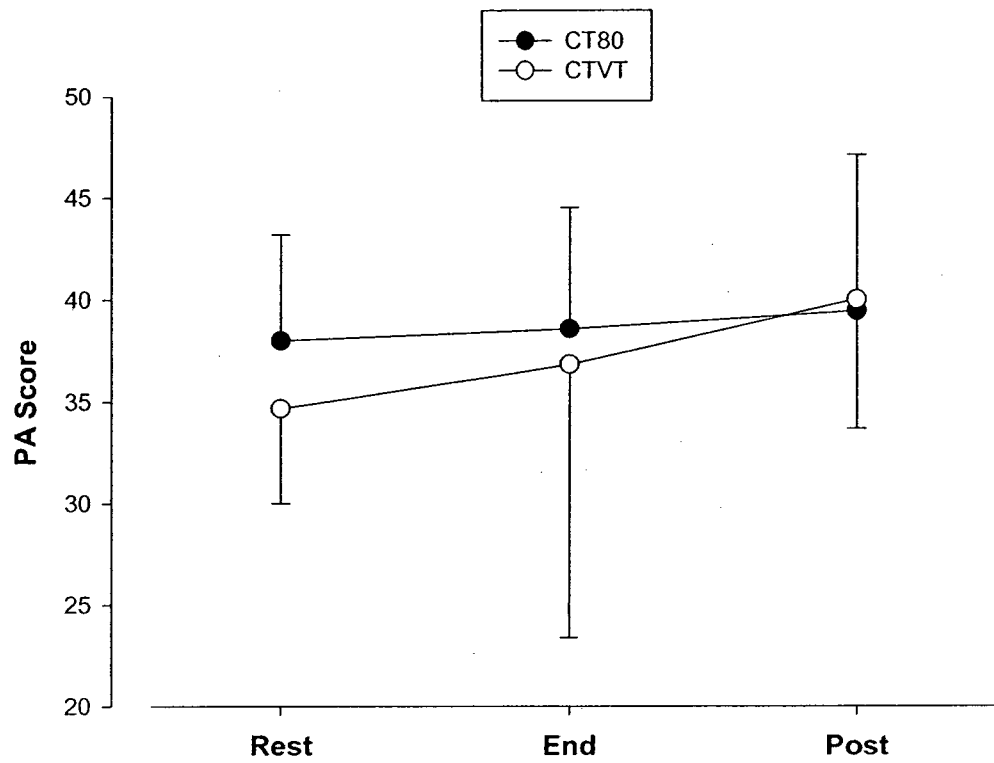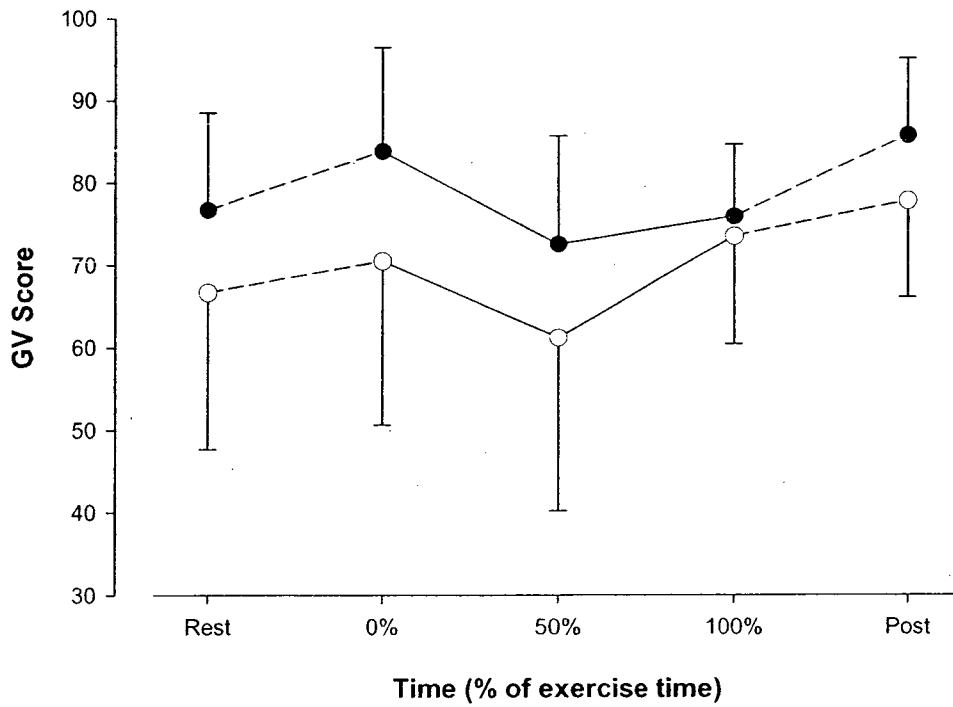
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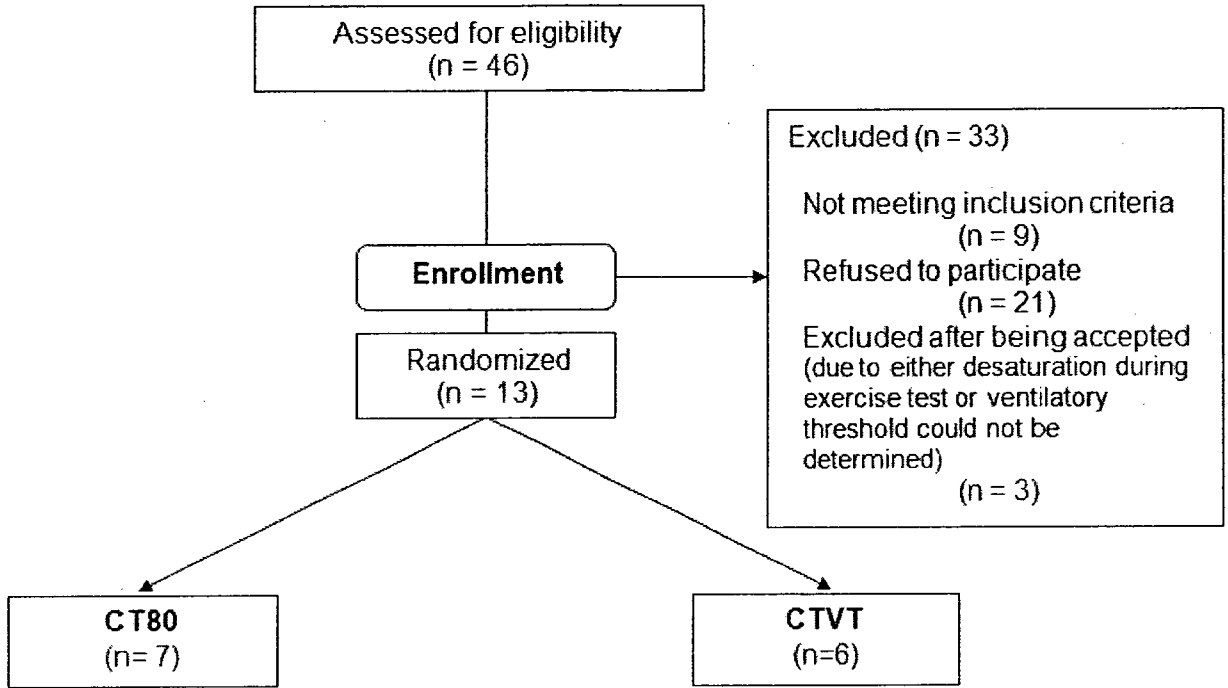
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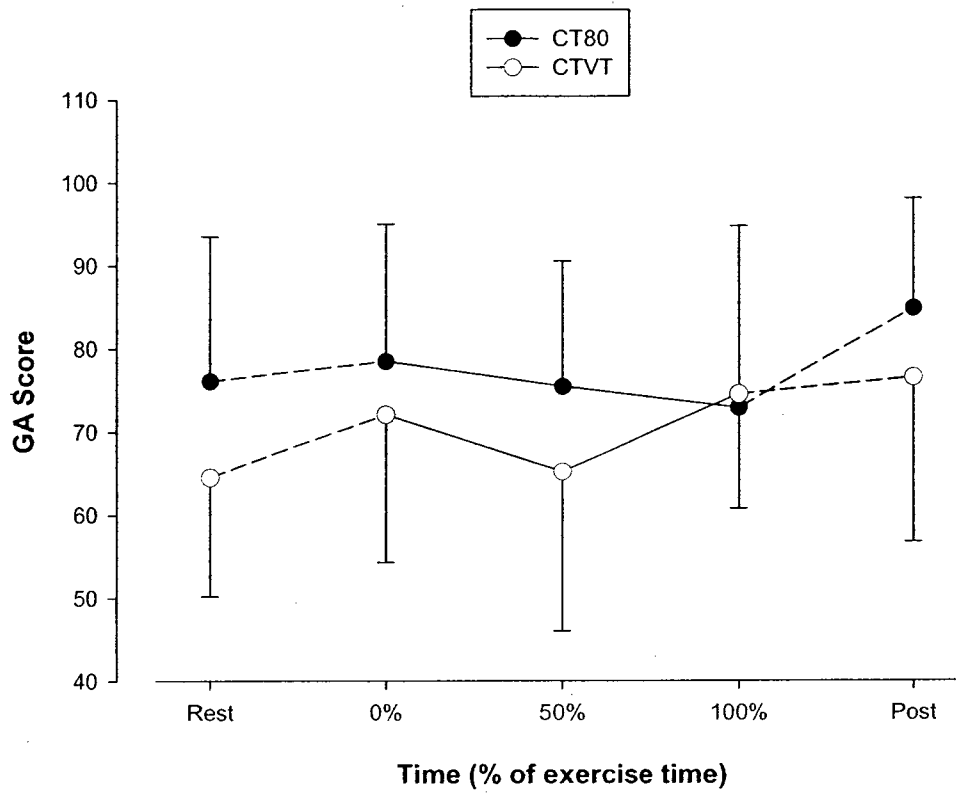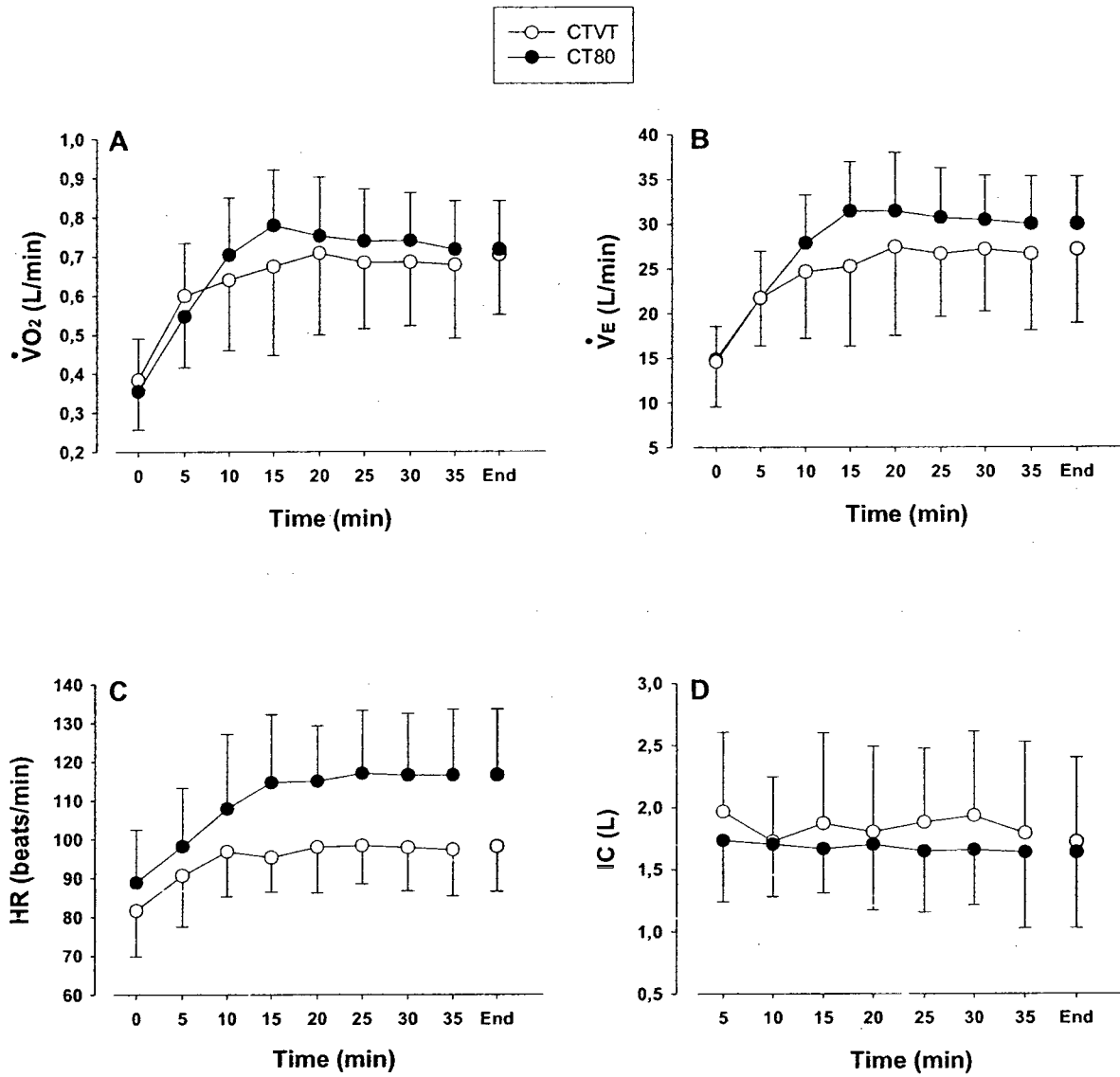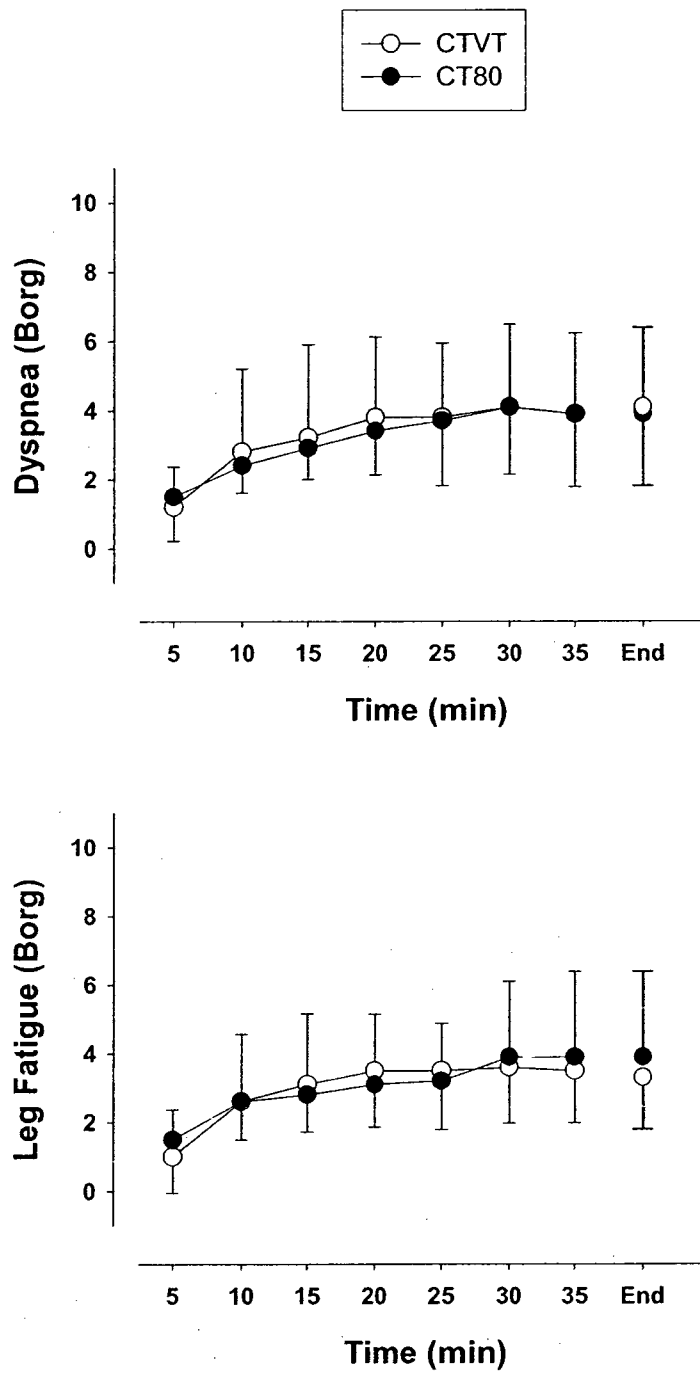
Figure 4.3

Figure 4.4

Figure 4.5

FIGURE 4.6

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APPENDIX

PANAS

Directions

This scale consists of a number of words that describe the different feelings and emotions. Read each item and then circle the appropriate answer next to that word. Indicate to what extent you feel these sentiments or emotions **in this moment**. Use the following scale to record your answers.

	Very slightly or not at all	A little	Moderately	Quite a bit	Extremely
1. Interested	1	2	3	4	5
2. Distressed	1	2	3	4	5
3. Excited	1	2	3	4	5
4. Upset	1	2	3	4	5
5. Strong	1	2	3	4	5
6. Guilty	1	2	3	4	5
7. Scared	1	2	3	4	5
8. Hostile	1	2	3	4	5
9. Enthousiastic	1	2	3	4	5
10. Proud	1	2	3	4	5
11. Irritable	1	2	3	4	5
12. Alert	1	2	3	4	5
13. Ashamed	1	2	3	4	5
14. Inspired	1	2	3	4	5
15. Nervous	1	2	3	4	5
16. Determined	1	2	3	4	5
17. Attentive	1	2	3	4	5
18. Jittery	1	2	3	4	5
19. Active	1	2	3	4	5
20. Afraid	1	2	3	4	5

Global Vigor and Affect (GVA) Instrument

Name _____ Day _____ Date ___ / ___ / ___ Time _____

How alert do you feel?
Very little————————————————————————— very much

How sad do you feel?
Very little————————————————————————— very much

How tense do you feel?
Very little————————————————————————— very much

How much of an effort is it to do anything?
Very little————————————————————————— very much

How happy do you feel?
Very little————————————————————————— very much

How weary do you feel?
Very little————————————————————————— very much

How calm do you feel?
Very little————————————————————————— very much

How sleepy do you feel?
Very little————————————————————————— very much