The interaction between walking speed and depth of breathing post-stroke

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DEDICATION

A special thank you to my husband, Rafael Otfinowski, who guided me through this process, provided statistical and editorial assistance, but most importantly, gave me the strength and courage to persevere. This thesis is also dedicated to all of my parents, biological or through marriage, who have supported me financially, spiritually and with lots of love; you have made this process easier.

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PREFACE

Research combining two systems, respiratory and locomotor, is important in order to understand the interaction, the adaptations, and how they are affected by a stroke. Science questions tend to isolate problems but when that knowledge is translated to clinical practice, there are many unanswered questions, as clinicians observe the interactions between the systems more often than isolated problems.

Traditionally physiotherapy programs for individuals with stroke have focused on sensory and motor impairment. However, some individuals have experienced respiratory impairment in the form of shortness of breath, fatigue, reduced tolerance for rehabilitation programs and limited exercise capacity, impacting their ability to perform daily activities. Some studies indicate that respiratory impairment exists post-stroke and conversely, that individuals post-stroke improve exercise capacity and walking speed with aerobic exercise training but the mechanisms are poorly understood. Thus we were interested in studying the interaction between increased breathing depth on walking speed; and increased walking speed, or exercise, on depth of breathing, in individuals post-stroke.

This thesis is written in the conventional format. The first chapter, the introduction, includes an overview providing the rationale for the project, followed by the objectives and the hypotheses. The second chapter provides background information to the problem. Following that each chapter outlines the results, discussion and conclusion.

CONTRIBUTION OF AUTHORS

Cynthia Otfinowski was responsible for integration of the optoelectronic plethysmography (OEP) system to the pilot study protocol, applying for ethics, participant recruitment, training of research assistants, data collection and processing, statistical analysis and writing of the thesis. Dr. J. Spahija and Dr. J. Fung were responsible for the original project idea and experimental design, providing research assistants, and overall supervision of Cynthia Otfinowski and this project. Dr. J. Fung provided technical and office support assistance, laboratory space, and equipment for gait data (Vicon, self-paced treadmill, harness, virtual reality, treadmill cane), while Dr. J. Spahija provided respiratory equipment (pneumotachograph, OEP system and oximeter). Dr. Fung also provided funding from the Jewish Rehabilitation Hospital Foundation and partly from a CIHR grant (SensoriMotor Rehabilitation Research Team).

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LIST OF ABBREVIATIONS

6MWT: 6 minute walk test

ANOVA: analysis of variance

APA: anticipated postural adjustments

BMI: body mass index

CAREN: Computer Assisted Rehabilitation Environment

CIHR: Canadian Institute of Health Research

CMSA: Chedoke-McMaster Stroke Assessment

CO_2: carbon dioxide

COP: center of pressure

CRIR: Centre for Interdisciplinary Research in Rehabilitation of Greater Montreal

CVA / AVC: cerebrovascular accident / accident vasculaire cérébral

DC: deep breathing while walking at a comfortable pace

DF: deep breathing while walking at a fast pace

DLS: double limb support

DST: deep breathing, standing

EILV: end-inspiratory lung volume

FEV_1: forced expiratory volume in one second

FVC: forced vital capacity

IQR: interquartile range

MET: metabolic equivalent

n: number in group

OEP: optoelectronic plethysmography

p: P-value

$PaCO_2$: partial pressure of carbon dioxide in blood

PaO_2: partial pressure of oxygen in blood

PEF: peak expiratory flow

PFT: pulmonary function test

PIF: peak inspiratory flow

RC: regular breathing while walking at a comfortable pace

RF: regular breathing while walking at a fast pace

RPE: rating of perceived exertion

RR: respiratory rate

RST: regular breathing, standing

SLS: single limb support

SMA: supplementary motor area in the brain

SpO_2%: peripheral oxygen saturation in the blood

T_E: expiratory time

T_I: inspiratory time

T_{ToT}: total breath time

$T_I/T_{ToT:}$ duty cycle

VC: vital capacity

V_E: minute ventilation

VO_2: oxygen consumption

VCO_2: carbon dioxide production

V_T: tidal volume

V_T/T_E: mean expiratory flow

V_T/T_I: mean inspiratory flow

WD: walk distance

ABSTRACT

Rationale: Exercise capacity may be limited in individuals post-stroke. A hemi-paretic walking pattern is associated with higher oxygen cost; however, impaired diaphragm and chest wall movement post-stroke may reduce voluntary depth of breathing. Mild to moderate exercise increases tidal volume through automatic control of breathing mechanisms in healthy adults, however, it is unknown if this occurs post-stroke. Thus, fast walking may stimulate deeper breathing and increased ventilation may facilitate faster walking speed post-stroke.

Objectives: The purpose of this study was to determine: 1) if increased walking speed changes depth of breathing (i.e. tidal volume), or conversely, 2) if increased depth of breathing impacts walking speed in individuals post-stroke compared to a control group. Furthermore, we wanted to estimate if tidal volume was reduced during voluntary control of breathing (i.e. deep breathing) compared to automatic control of breathing pathways (i.e. exercise stimulus) in individuals post-stroke compared to the control group.

Relevance: Understanding the relationship between respiratory and walking impairments may provide insight into exercise limitations post-stroke.

Methods: Eleven participants in both groups performed one session of two standing and breathing (regular and deep) conditions as well as four randomized walking trials on a self-paced motorized treadmill at two paced (comfortable and fast) and breathing (regular and deep) conditions. Tidal volume and breathing pattern were measured with a pneumotachograph and walking speed and pattern were captured using the Vicon motion analysis system.

Analysis: The interaction between tidal volume and walking speed was analyzed using 2-way repeated measures Analysis of Variance (ANOVA) for both tidal volume and walking speed and for both groups. One-way repeated measures ANOVA was used to analyze the tidal volume response to deep breathing and exercise compared to standing and breathing regularly. The Mann-Whitney rank sum test was used to compare between groups.

Results: While walking fast compared to a comfortable pace, individuals post-stroke decreased tidal volume by 6% while breathing deeply, whereas the control group increased tidal volume by 22%, while breathing regularly. Comparing deep to regular breathing, individuals post-stroke increased comfortable walking speed by 25%, whereas the control group did not change walking

speed significantly. Between groups, tidal volumes are similar in standing but lower in individuals post-stroke with fast walking with either regular or deep breathing.

Conclusions: Walking and breathing pattern strategies may be influenced by locomotor-respiratory coupling while optimizing ventilatory response with postural stability. Deep breathing while walking at a comfortable pace may improve walking speed in individuals post-stroke and is an efficient and cost-effective potential therapy.

ABRÉGÉ

Exposé : La capacité de faire de l'exercice physique peut être limitée chez les individus qui ont subi un accident vasculaire cérébral (AVC). Un profil de marche hémiparétique est associé à une augmentation du coût de l'oxygène, cependant, une réduction de mouvement du diaphragme et de la cage thoracique post-AVC peuvent réduire la profondeur de la respiration volontaire. L'exercice léger à modérer augmente le volume pulmonaire grâce à un contrôle automatique des mécanismes respiratoires chez les adultes en bonne santé, mais on ignore si cela se produit aussi chez ceux qui sont en situation post-AVC. Ainsi, la marche rapide peut stimuler une respiration profonde et une augmention de respiration peut améliorer la vitesse de marche post-AVC.

Objectifs : Le but de cette étude était de déterminer : 1) si l'augmentation de la vitesse de marche affecte la profondeur de la respiration (par exemple, le volume courant); ou inversement, 2) si l'augmentation de la profondeur de la respiration entraîne un changement de la vitesse de marche chez les personnes qui ont subi un AVC, comparativement à un groupe témoin. En outre, nous voulions évaluer si le volume courant était réduit lors d'un contrôle volontaire de la respiration (par exemple, respiration en profondeur) comparativement à la commande automatique des voies respiratoires (par exemple : l'exercice modéré) chez les personnes post-AVC, le tout comparativement au groupe témoin.

Pertinence : Comprendre la relation entre la respiration et la marche peut fournir un nouveau regard sur les limites de l'exercice post-AVC.

Méthodes : Onze participants pour chacun des deux groupes ont pris part à une session de deux conditions respiratoires différentes (régulière et profonde) tout en se tenant debout aussi bien que quatre essais randomisés de marche sur un tapis roulant motorisé et auto-rythmé réglé à deux rythmes de marche (rapide et confortable) et de respiration (régulière et profonde). Le volume courant et le profile respiratoire furent mesurés avec un pneumotachograph et la vitesse et le profil de marche furent captés en utilisant le système d'analyse du mouvement Vicon.

Analyse : L'interaction entre le volume courant et la vitesse de marche furent étudiée en utilisant l'analyse de variance (ANOVA) par mesures répétées appliquées à deux facteurs, soit le volume courant et la vitesse de marche, et ce, pour chacun des deux groupes. Des mesures ANOVA à sens unique répétées servirent à analyser la réponse du volume courant à la respiration profonde

et à l'exercice comparé à la station debout et à la respiration régulière. Le test de Mann-Whitney a servi à comparer les groupes.

Résultats : Lors d'une marche rapide comparée à celle à un rythme confortable, les participants post-AVC ont vu leur volume courant diminuer de 6 % tout en respirant profondément, tandis que le volume courant du groupe témoin a augmenté de 22 %, tout en respirant régulièrement. Lors d'une respiration profonde comparée à celle à une respiration régulière, les participants qui avaient subi un AVC avaient augmenté leur vitesse de marche de 25%, tout en marchant à un rythme confortable alors que le groupe de contrôle n'a pas modifié de manière significative la vitesse de marche. Entre les groupes, les volumes courants étaient similaires en position debout, mais réduits au cours d'une marche plus rapide chez les personnes ayant subi un AVC, que ce soit avec une respiration régulière ou profonde.

Conclusions : Les stratégies de mode de respiration et la marche peuvent être influencées par le lien entre la respiration et la marche, tout en optimisant la réponse ventilatoire avec la stabilité posturale chez les personnes ayant subi un AVC. Respirer profondément tout en marchant à un rythme confortable peut améliorer la vitesse de marche post-AVC et s'avérer une thérapie économisant temps et argent.

CHAPTER 1.0: INTRODUCTION

1.1 Overview

The World Health Organization defines stroke as "rapidly developing clinical signs of focal (at times global) disturbance of cerebral function, lasting more than 24 h or leading to death with no apparent cause other than that of vascular origin" (Hatano, 1976). A stroke can lead to death, hospitalization and subsequent disability, or full recovery. According to statistics Canada in 2007, 11,276 deaths were due to stroke; however, silent strokes or deaths from stroke, having occurred outside of the hospital, were not taken into consideration (Government of Canada, 2011). A person post-stroke with a regular breathing pattern has a 10% chance of dying which increases to 66-100 % with a hyperventilation pattern of breathing (Vingerhoets & Bogousslavsky, 1994). Despite the fact that the number of hospitalizations and deaths due to stroke have been declining over time, in 2005, stroke was identified as the primary medical condition in 38,341 hospitalized Canadians, and as a medical complication in an additional 12,123 individuals (Government of Canada, 2011). In 2005/2006, 42% of individuals diagnosed with stroke were sent home, 40% were sent to another facility, and 18% died in hospital (Government of Canada, 2011).

For the majority of individuals post-stroke, rehabilitation is an essential part of recovery in every phase. In Laval, Quebec, the Jewish Rehabilitation Hospital is a center of excellence for sub-acute, medically stable patients who require intensive rehabilitation before being discharged.

Stroke is costly in terms of time and money for the healthcare system and families. Individuals post-stroke constitute an estimated 16% of admissions to Canadian rehabilitation facilities (Institut national d'excellence en santé et en services sociaux (INESSS), 2012). Of the individuals discharged home, many are left with impairments that can lead to reduced mobility and deconditioning. Normal rehabilitation post-stroke involves assessment of functional independence and mobility but rarely assesses respiratory function or cardiovascular capacity (Brooks et al., 2008). Brooks and colleagues (2008) reported that cardiorespiratory fitness could not be predicted based on conventional clinical tools used to assess mobility in individuals with sub-acute stroke.

Respiratory dysfunction has been observed in 18-88% of individuals post-stroke, which varies depending on the stage of recovery, as well as the location and severity of stroke (Rochester & Mohsenin, 2002). Respiratory dysfunction in individuals with a stroke above the brainstem is associated with hemi-paretic respiratory muscles, namely the diaphragm, intercostal and abdominal muscles (Annoni et al., 1990; Cohen et al., 1994; DeTroyer et al., 1981; Fluck, 1966; Vingerhoets & Bogousslavsky, 1994) but the mechanism is poorly understood. Lanini and colleagues (2003) demonstrated normal chest wall excursion during quiet breathing whereas the paretic chest wall had decreased expansion during deep breathing. Voluntary control of breathing, or deep breathing, may be impaired post-stroke whereas automatic control of breathing pathways, or regular breathing, may remain intact.

Hemi-paretic gait is common post-stroke and is associated with reduced walking speed and an asymmetric gait pattern (Olney & Richards, 1996). Motor impairments increase oxygen cost of walking in individuals with hemiparesis (Da Cunha-Filho et al., 2003; Olney & Richards, 1996), and ventilatory response is higher than controls while walking at similar speeds (Haas et al., 1967). In healthy young individuals, controlled inspiration cued by an auditory tone was shown to increase stepping rate indicating breathing pattern may affect walking pattern (Rassler & Kohl, 2000). It is unknown if deep breathing would affect walking speed in individuals post-stroke.

Exercise capacity in individuals with chronic stroke is estimated to be 55-75% that of age-, sex-, and activity level- matched healthy adults (Brooks et al., 2008). During exercise, individuals post-stroke increase both, respiratory rate and tidal volume, to meet ventilatory demands, whereas healthy adults increase tidal volume followed by respiratory rate (Chung et al., 1999; Narain & Puckree, 2002). Normally tidal volume increases with mild to moderate exercise by activating the diaphragm and respiratory muscles, through automatic control processes, such as chemoreceptors and through the raphe nucleus that project to the spinal cord and brainstem (Rochester & Mohensin, 2002). As mild to moderate exercise increases tidal volume in healthy adults and hemi-paretic gait has a higher oxygen cost requiring a greater ventilatory response, walking fast may increase tidal volume in individuals post-stroke.

Brooks and colleagues (2008) recommended treadmill walking to assess and treat cardiorespiratory fitness for its task-specificity to community ambulation. Furthermore, if this

dynamic interaction occurs in individuals post-stroke, deep breathing and fast walking may be used for gait rehabilitation and may improve exercise capacity.

1.2 Objectives

The objectives in this study were to estimate and compare, in individuals post-stroke and healthy controls:

1. The effect of exercise, and voluntary deep breathing on tidal volume.
2. How fast versus comfortable-paced walking affects tidal volume during regular and deep breathing.
3. How deep versus regular breathing affects gait speed during comfortable and fast pace walking.

1.3 Hypotheses

1. Voluntary control of breathing is impaired but automatic control of breathing pathways remains intact post stroke. Thus, the tidal volume will be lower in the post-stroke group compared to the control group during the condition of deep breathing and standing, but will remain similar during regular breathing while standing or walking fast.
2. As oxygen cost of walking is higher in individuals post-stroke, fast walking may stimulate increased ventilatory response (i.e. tidal volume), to maintain homeostasis. Thus, tidal volume will increase to a similar extent in individuals post-stroke (relative to the increase in walking speed) and healthy controls when walking speed is increased during regular breathing, but to a lesser extent in individuals post-stroke when walking speed is increased during deep breathing.
3. As breathing and walking are controlled by central pattern generators that may interact, and locomotor-respiratory coupling has been demonstrated in healthy adults, increased depth of breathing may increase walking speed in individuals post-stroke. Thus, individuals post-stroke and healthy controls will increase walking speed when depth of breathing changes from regular to deep.

CHAPTER 2.0: LITERATURE REVIEW

2.1 Control of Breathing

Breathing, which is under the control of the central nervous system, can be controlled automatically or voluntarily (Rochester & Mohsenin, 2002). Automatic or involuntary control of breathing originates in the pons and medulla, but also involves the limbic system (emotional responses) and the hypothalamus (temperature regulation) (Rochester & Mohsenin, 2002). Automatic control of breathing is based on metabolic demands and maintaining an acid-base homeostasis (Rochester & Mohsenin, 2002; Figure 1). In contrast, voluntary control of breathing, which is based on behavioral modification (i.e. breath holding), involves the cerebral cortex via the corticospinal tract (Howard et al., 2001; Figure 1). Emotional stimuli alter respiratory patterns via the limbic cortex and brain stem (Rochester & Mohsenin, 2002). Automatic and voluntary controls of breathing are functionally independent but interact with each other by neural redundancy and plasticity (Howard et al., 2001).

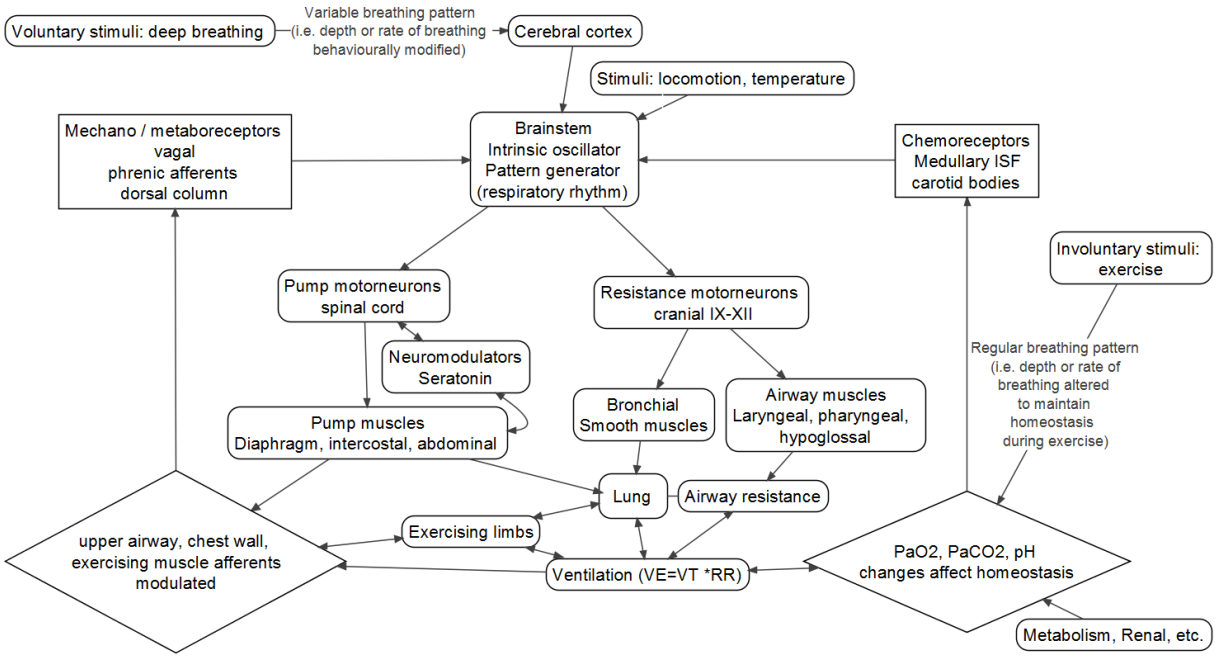

Figure 1: Ventilatory control mechanisms. Adapted from: Forster et al., (2012)

2.1.1 Automatic Control of Breathing

The medulla and pons located in the brainstem are responsible for automatic control of the respiratory rate (RR) and depth of breathing (tidal volume) (Rochester & Mohsenin, 2002). Sensory feedback from the stretch and irritant receptors in the lung, as well as the proprioceptors in the respiratory muscles and joints provide information to the brain for automatic modulation of the breathing pattern and respiratory drive (Wilmore & Costill, 1999). Central chemoreceptors on the ventral portion of the medulla, respond to hydrogen ion concentration in the extracellular fluid of the brain whereas peripheral chemoreceptors, located in carotid bodies, respond to decreased pH, partial pressure of oxygen (PaO_2) and carbon dioxide in blood ($PaCO_2$), and maintain acid-base homeostasis (Rochester & Mohsenin, 2002). When PaO_2 is normal, minute ventilation (V_E) increases by 2-3 L/min for every 1 mm/Hg rise in $PaCO_2$ (West, 2000). When PaO_2 is low, the response to the same rise in $PaCO_2$ will be greater (West, 2000). When automatic control of breathing is impaired, secondary to disturbance of central rhythm generators, abnormal respiratory rhythms may occur (Howard et al., 2001).

2.1.2 Voluntary Control of Breathing

Voluntary control of breathing involves intentional modulation of the breathing pattern such as during breath holding (inhibitory) or singing (excitatory). The primary motor cortex, supplementary motor area (SMA), and ventrolateral thalamus control voluntary inspiration, whereas the primary motor cortex, SMA, premotor cortex, and cerebellum control expiration (Shea, 1996). The primary motor cortex predominantly communicates contralaterally to the diaphragm via oligosynaptic pathways (Cohen et al., 1994; Gandevia & Rothwell, 1987; Kedr et al., 2000; Similowski et al., 1996). The intercostal muscles also have cortical representation communicating contralaterally and occasionally ipsilaterally (Maskill et al., 1991; Przedborski et al. 1988). When voluntary control of breathing is impaired, the breathing pattern becomes regular and invariable and the person is unable to volitionally alter breathing pattern (Howard et al., 2001). Integration of automatic and voluntary control of breathing occurs in the spinal cord through spinal reflexes, supraspinal inputs, and stimuli from ascending pathways (Rochester & Mohsenin, 2002).

2.2 Breathing patterns in individuals post-stroke compared to healthy adults

Abnormal breathing patterns have been reported in 18-88% of individuals post-stroke and may depend on whether individuals have cardiopulmonary disease, or are evaluated in the acute or chronic phase of stroke, as some issues may resolve with improved alertness (Rochester & Mohsenin, 2002). Severity of stroke or motor impairment, and location of stroke (Kedr et al., 2000; Santamaria-Ruiz et al., 1988; Similowski et al., 1996) may also contribute to the degree of inter-individual variation of respiratory patterns observed (Rochester & Mohsenin, 2002).

2.2.1 Lung function

Of the individuals post-stroke who are able to perform pulmonary function tests, 8%, 12%, and 64% have obstructive, restrictive and normal lung function, respectively (Teixeira-Salmela et al., 2005). Others have also noted restrictive, obstructive and mixed respiratory dysfunction based on pulmonary function tests in individuals post-stroke previously not diagnosed with lung disease (Kedr et al., 2000; Lanini et al., 2003, Sezer et al., 2004). Regarding lung volumes post-stroke compared to healthy individuals, residual volume has been reported to be higher than predicted (123%), and vital capacity is lower than predicted (79%). Total lung capacity and functional residual capacity are near normal (Cohen et al., 1994). Low lung volumes or high residual volumes suggest respiratory muscle weakness (Cohen, 1994).

2.2.2 Respiratory muscles

Maximum inspiratory and expiratory pressures represent inspiratory and expiratory muscle strength (Enright et al., 1994) and may be reduced in individuals with hemiplegia (Lanini et al., 2003; Nuzzo et al., 1999). Inspiratory and expiratory muscle dysfunction depends on the level of motor impairment and the muscles affected (Annoni et al., 1990; De Troyer et al., 1981; Fugyl-Meyer et al., 1983; Khedr et al., 2000; Similowski et al., 1996; Przedborski et al., 1988).

In healthy adults, the diaphragm is responsible for 70-80% of ventilation (Rochester & Mohsenin, 2002). The length-tension of the diaphragm is dependent on its position, the structure of the thorax, abdominal tone and the length-tension of other respiratory muscles such as intercostal and abdominal muscles (Rochester & Mohsenin, 2002). Therefore, if the hemi-diaphragm (De Troyer et al., 1981) or other respiratory muscles (Fluck, 1966; Jandt et al., 2010; MacKay-Lyons et al., 2005; Rochester & Mohsenin, 2002) are affected post-stroke, chest wall expansion (Lanini et al., 2003) and consequently tidal volume may also be reduced.

Decreased diaphragmatic excursion has been observed in individuals post-stroke. Houston and colleagues (1995) reported no significant difference in diaphragm excursion during quiet breathing, however, when individuals post-stroke began deep breathing, there was a significant decrease in bilateral excursion of the hemi-diaphragm (21 to 33%) compared to the control group. Contrary to other studies which demonstrate respiratory muscle impairment on the hemi-paretic side (De Troyer et al., 1981; Lanini et al., 2003; Przedborski et al. 1988), Houston et al. (1995), observed symmetrical reduction in diaphragmatic excursion in individuals post-stroke. The difference in diaphragmatic excursion between right and left sides is normally 0.5 to 1.6 mm (right to left excursions) (Houston et al., 1992). The ratios of right to left excursions post-stroke were within this range in the study conducted by Houston and colleagues (1995). The difference between bilateral compared to unilateral reductions in diaphragm function may be partly explained by the method of comparison. Some studies compare the paretic hemi-diaphragm in the group post-stroke to a control group (DeTroyer et al., 1981; Houston et al., 1995), and others compare between the paretic and non-paretic side within the individual post-stroke (Cohen et al., 1994, Lanini et al, 2003, Przedborski et al. 1988). In a study by Cohen et al. (1994) diaphragmatic function was decreased during deep breathing in 50% (number in group (n) =8) of individuals with hemiparesis. However, in this study, Cohen et al. (1994) defined diaphragmatic dysfunction as a reduction in hemi-diaphragm excursion on the paretic side to at least half of that observed on the non-paretic side.

2.2.3 Chest wall expansion

Impaired breathing mechanics occur because of decreased diaphragmatic excursion, respiratory muscle weakness, and decreased or paradoxical chest wall movement on the paretic side (MacKay-Lyons et al., 2006). Lanini et al. (2003) demonstrated that individuals post-stroke had significantly less expansion of the paretic chest wall compared to the non-paretic side during voluntary deep breathing. However, the paretic chest wall expanded equally at rest and more than the non-paretic side during carbon dioxide (CO_2) re-breathing trials. This demonstrates that the voluntary control of breathing has been damaged post-stroke, but the involuntary control of breathing pathways, that regulate acid-base homeostasis, may remain intact. Thus, with sufficient stimulation (i.e. elevated CO_2 blood levels), the paretic side is able to expand to the same degree as the non-paretic side. Tidal volume may be reduced post-stroke due to impaired respiratory

muscle strength, chest wall expansion, and voluntary control of breathing on the affected side, resulting in altered breathing patterns.

2.3 Breathing patterns in response to exercise

The normal response to exercise in healthy individuals involves an increase in: 1) oxygen transport to the mitochondria of the active muscles; 2) energy production by the muscles; and 3) force output (McKenzie, 2012). In general, the ventilatory response is to increase tidal volume (V_T) and then RR, thereby increasing V_E (Chung et al., 1999). Compared to resting conditions, V_E can increase 20-fold during heavy exercise (McKenzie, 2012). Thus, aerobic capacity is not usually limited by the ventilatory system (McKenzie, 2012).

Typically during exercise, ventilation matches metabolic demand, and is linearly related to both oxygen consumption (VO_2) and carbon dioxide production (VCO_2) at low to moderate exercise levels (Wilmore & Costill, 1999). Anaerobic metabolism increases blood lactate levels, decreases blood pH, and increases the ratio of VCO_2 to VO_2 (Waters & Mulroy, 1999), causing a disproportionate increase in pulmonary V_E relative to VO_2 (Waters & Mulroy, 1999; Wilmore & Costill, 1999). Chemoreceptors, stimulated by the increased CO_2 levels during exercise, increase V_E in order to reduce the hydrogen ion and CO_2 levels and maintain acid-base homeostasis (Wilmore & Costill, 1999). It has also been suggested that V_E increases at the onset of exercise, as a result of communication between suprapontine locomotor areas and spinal locomotor neurons as well as brainstem respiratory neurons (Waldrop et al., 1996; Forster et al., 2012). However, the exact mechanism that causes increased depth of breathing during exercise is unknown.

In order to increase V_T, the breathing pattern adjusts as the inspiratory muscles increase the end-inspiratory lung volume (EILV) slightly and the expiratory muscles decrease end-expiratory lung volume closer to the reserve volume (Dempsey et al., 2008; McKenzie, 2012). This ensures that EILV does not approximate total lung capacity, where the elastic resistance of lung expansion is higher. In this way, the oxygen cost and work of breathing are minimized (Dempsey et al., 2008). Tissue resistance is inversely proportional to RR, thus a high RR results in lower tissue resistance (West, 2000).

Individuals post-stroke have an exercise capacity of 55-75% of age-, sex- and physical activity level- matched healthy adults (Brooks et al., 2008). Hemiparesis is associated with a reduced motor neuron pool, resulting in reduced active muscles (McComas et al., 1973). Smaller muscle mass and biomechanical adaptations to hemiparesis while walking results in higher oxygen cost but exercise capacity is reduced (MacKay-Lyons et al., 2006). Metabolism during exercise is also affected. Individuals post-stroke use a higher percentage of glycolytic energy (Landin et al., 1977) and reach their anaerobic threshold levels faster than healthy adults (Chen et al, 2010). Peripherally, a change in muscle fiber type, from slow-twitch to fast-twitch, occurs post-stroke and has been associated with slower oxygen uptake in the muscles at the beginning of exercise, and a slower clearance of CO_2 after stopping exercise. This results in a build-up of lactate and use of anaerobic or glycolytic energy during exercise (Manns et al., 2010; Tomczak et al., 2008). Leg or general fatigue, and breathlessness have been reported as the main reasons for stopping exercise testing in individuals post-stroke (Brooks et al., 2008). Tomczak et al., (2008) suggested that exercise capacity, determined by VO_2, is reduced post-stroke secondary to reductions in cardiac output and V_E, while RR remains unchanged. Narrain & Puckree (2002) suggested that individuals post-stroke increase their RR and V_T simultaneously in response to exercise.

2.4 Energy cost and ventilation during walking

Metabolic costs can be as high as 75-88% of peak oxygen consumption (VO_2peak) during daily activities in individuals post-stroke compared to 42-45% in healthy adults (Bjuro et al., 1975), suggesting an increase in energy expenditure for daily activities (Waters & Mulroy, 1999) and compromised physical fitness (Manns et al., 2010). Aerobic energy sources are used during mild to moderate exercise workloads whereas anaerobic or glycolytic energy sources are needed for heavier workloads (55-65% of VO_2peak) (Waters & Mulroy, 1999).

As walking speed increases, VO_2 increases linearly up to 1.67 m/s, whereas oxygen cost of walking (VO_2 / walking speed) is greater at slower walking velocities, increasing curvilinearly at speeds < 0.67 m/s in healthy adults (Waters et al., 1988). Thus, with faster walking speeds, VO_2 increases but efficiency of walking improves at speeds >0.67 m/s. In healthy adults, fast and preferred walking speeds are typically selected above and below the anaerobic threshold level, respectively (Waters & Mulroy, 1999). The ability to perform aerobic walking activity post-stroke depends on the severity of gait impairment and the ability to meet oxygen demands.

Hemi-paretic gait, common post-stroke, increases oxygen consumption (Detrembleur et al., 2003; Micheal et al., 2005; Potempa et al., 1995), due to inefficiencies of walking related to the presence of spasticity (Waters & Mulroy, 1999), as well as increased mechanical muscle work for vertical displacement of the center of mass (Detrembleur et al., 2003; Stoquart et al., 2012) . Furthermore, metabolism is altered by changes in: muscle fibers (from slow to fast-twitch), mitochondria, and motor neuron pools affecting active tissue (Iseri et al., 1968; Landin et al., 1977; McComas et al., 1973).

Da Cunha-Filho and colleagues (2003) evaluated 20 individuals post-stroke (< 6 months since stroke) and 39 healthy controls. Differences in walking energy cost (oxygen consumption per distance walked in 5 minutes) were twice as high for persons with stroke (0.40 ml/kg*m) compared to healthy individuals (0.18 ml/kg*m); however, it was not significant due to the variability post-stroke (standard deviation = 0.52 in stroke and 0.02 in healthy) (Da Cunha-Filho et al., 2003). This variability may be explained by the observation that individuals post-stroke having preferred gait speeds greater than 0.7 m/s generate total mechanical muscle work during walking at an energy cost that is near to normal. In contrast, individuals who preferred a gait speed of less than 0.7 m/s had a total mechanical muscle work and energy cost of walking twice that of healthy adults (Detrembleur et al., 2003). In either case, the efficiency of walking (muscle work: energy cost) was near normal for individuals post-stroke (Detrembleur et al., 2003) because preferred gait speed is the most economical speed of walking (Waters & Mulroy, 1999). This suggests that individuals post-stroke adapt their stride frequency to reduce metabolic costs, as seen in healthy individuals (Holt et al., 1995; Waters & Mulroy, 1999).

In the past, stroke rehabilitation has focused on increasing gait symmetry in order to improve walking ability (Verma et al., 2012). Treadmill walking can be used as a strategy to increase gait symmetry however, Brouwer et al., (2009) reported that this resulted in higher metabolic costs compared to overground walking with an asymmetrical gait pattern. It is not clear if the higher metabolic costs resulted from walking on the treadmill itself or from the improved symmetry of the gait pattern. One interpretation is that individuals post-stroke adapt their gait pattern to be more energy-efficient while walking overground, despite the asymmetry.

To meet ventilatory requirements during exercise, individuals post-stroke tend to simultaneously increase their RR and tidal volumes (Narain & Puckree, 2002; Vingerhoets and Bogousslavsky,

1994) whereas healthy adults increase their tidal volumes first, followed by their RR (Chung et al., 1999). Therefore, although the ventilatory system is not limited in healthy individuals during exercise, whether or not, and the extent to which respiratory dysfunction (low tidal volumes and reduced diaphragmatic excursion) contributes to exercise limitation and reduced walking endurance and speed post-stroke, remains unknown.

2.5 Walking patterns in individuals post-stroke compared to healthy adults

In normal human gait, the stance phase generally comprises 60% of the gait cycle from initial contact to pre-swing period, whereas the swing phase comprises 40% of the gait cycle and continues from pre-swing to initial contact again. The relative proportions, however, can change, with the stance phase shortened and the swing phase lengthened, as walking speed increases. As well, single leg support occurs when the opposite foot is swinging and double leg support is when weight shift is occurring and both feet are in contact with the surface. Other than walking speed, common gait measures include step length and stride length. Step length is the distance covered by one foot (from initial contact of one foot to initial contact of the other foot) during the gait cycle (time from between initial contact periods of one foot) whereas stride length is the distance covered in one gait cycle (Koerner, 1986; Winter, 2009).

After a stroke, walking may be affected by muscle paresis (decreased muscle force generation), incoordination, spasticity, sensory-perceptual and balance impairments. Hemi-paretic gait pattern is common post-stroke affecting recovery, and is usually described by measuring spatiotemporal asymmetry, walking velocity and endurance (Patterson S. L. et al., 2008).

2.5.1 Gait asymmetry

Gait impairment is associated with decreased stance time and increased swing time on the paretic side, and the opposite is true for the non-paretic leg (Verma et al., 2012). Patterson K. K. et al. (2008) report a non-linear, negative correlation between overall temporal symmetry (ratio of paretic to non-paretic swing stance ratios) and comfortable walking velocity ($r=-0.586$). There is a higher correlation with slower speed (<0.6m/s) and severe temporal asymmetry (Patterson K. K. et al., 2008). In addition, individuals post-stroke are more likely to improve symmetry at faster speeds (Patterson K. K. et al., 2008). Temporal symmetry improved (50.9%), worsened (32.1%) or did not change (17%), in individuals post-stroke when walking velocity increased

from preferred to fast. In the study by Patterson et al., (2008), only 8/53 individuals were unable to increase their velocity from preferred to fast walking, whereas Lamontagne & Fung (2004) reported that individuals post-stroke were able to increase their pace by 2-3 fold more than their preferred walking velocity when walking with a safety harness to avoid the risk of falling. Furthermore, individuals with ankle-foot orthoses (AFO) show severe temporal asymmetry and slow walking velocity, although one person had a higher walking velocity than 0.6 m/s (Patterson K. K. et al., 2008).

Increased paretic stride length is commonly reported however, some individuals post-stroke increase non-paretic stride length (Verma et al., 2012). Balasubramanian et al. (2007) suggest this is related to propulsion of the paretic foot which was strongly, negatively correlated with step length ratio. Therefore, when paretic foot propulsion was weaker, equal or stronger than the non-paretic foot, the step length of the paretic side was longer, equal or shorter than the non-paretic side, respectively. Step length ratio was moderately correlated and could be predicted with severity of hemiparesis. Stroke impairments affected not only plantarflexion, but also hip flexion during early swing phase, and hip extension during terminal stance phase, which are major determinants of walking (Balasubramanian et al., 2007; Lamontagne et al., 2007).

Individuals with more severe hemiparesis tended to decrease weight-bearing on the paretic leg. People with longer paretic step length tended to increase cadence (steps/min) in order to increase walking velocity, and decrease the non-paretic step length. Other compensatory strategies to overcome decreased paretic foot propulsion included increased non-paretic foot propulsion and forward trunk lean (Balasubramanian et al., 2007). Compensatory strategies would require more muscle work production and therefore have higher energy costs. Energy cost of walking may be decreased at faster walking velocities secondary to improved temporal symmetry, coordination and inter- and intra-limb energy transfers (Lamontagne & Fung, 2004; Patterson et al., 2010).

2.5.2 Walking speed

On average, healthy adults in their 50s walk 1.40 m/s at a comfortable pace and 2.04 m/s at a fast pace (Bohannon, 1997). Walking speed is commonly reduced post-stroke, and has been associated with participation at the community level (Perry et al., 1995). A walking velocity of >0.8 m/s has been reported as a functional walking velocity for community ambulation (i.e. to cross an intersection) whereas <0.4 m/s suggests ambulation limited to the home (Cramer, 2011).

Lower-limb exercises and gait-related activities improve comfortable and fast walking velocity on average by 0.10 m/s and 0.20 m/s, respectively, in the first 6 months post-stroke (Veerbeek et al., 2011). Lamontagne and Fung (2004) suggest fast walking post-stroke elicits improvements in body and limb kinematics and muscle activation patterns. Adaptations when changing walking velocity from comfortable to fast include longer step lengths (m) and shorter cycle durations (stride/min) (Lamontagne & Fung, 2004). A home exercise program, including endurance exercise training has also been shown to increase walking velocity (Duncan et al., 2003), suggesting that walking speed may be limited, secondary to respiratory dysfunction or metabolic changes in the muscles post-stroke.

2.6 Interaction between breathing, posture and walking

2.6.1 Dual role of respiratory muscles for breathing and postural stability

During walking, one must maintain upright posture. Muscles of the thorax play a dual role by maintaining postural stability while meeting ventilatory demands. Hodges and Gandevia (2000a) reported that the diaphragm and transversus abdominis muscles have a dual role of contracting during respiration (phasic muscle activity) as well as to increase postural stability (tonic muscle activity) (Hodges and Gandevia, 2000a; Gandevia et al., 2002; Hodges et al., 2001). Rimmer et al., (1995) observed tonic muscle activity in the internal and external oblique muscles during thoracic rotation. However, internal intercostal muscle activity is inhibited when participants are asked to rotate and inhale whereas external intercostal muscle activity is enhanced with the combined task. Thus, they function differently depending on the task (Rimmer, 1995). Postural or tonic activity in respiratory muscles may act to stiffen the ribcage or the airway (Butler et al, 2007; Gandevia et al., 2006; Saboisky et al., 2007). As well, the diaphragm in conjunction with pelvic floor muscles and the transversus abdominis increase abdominal pressure and stabilize the spine (Hodges, 1999; Hodges et al., 2001; Sapsford et al., 2001; Shirley et al., 2003).

2.6.2 Optimization of muscles between respiratory and postural demands

One theory to explain the response to exercise by respiratory / postural muscles is the feedforward / feedback theory. Movement and posture may be regulated based on the central motor command and afferent feedback as well as integration from 1) vascular distention, 2) vestibular feedback, and 3) behaviour, arousal, and volitional control (Bell, 2006). Anticipated

postural adjustments (APAs) to movement are one example of a feedforward mechanism. Chemical afferents to maintain homeostasis during exercise are an example of a feedback mechanism. Thus, the ventilatory response, while maintaining postural stability, could be controlled based on a feedforward / feedback theory in response to an exercise stimulus.

A second theory by Poon and colleagues (2007), suggests that ventilatory and postural drives can be optimized to accommodate metabolic and behavioural needs to maintain posture while increasing walking speed. It has been demonstrated that increased ventilatory demand can override postural drive during hypercapnia in order to maintain homeostasis with rising CO_2 levels (Hodges et al., 2001). Hodges and colleagues (2001) suggested that a 'gating' phenomenon may occur where postural drive is attenuated at the phrenic motor neurons in order to increase V_E. This was demonstrated in reduced tonic activity of the diaphragm and transversus abdominis after one minute of hypercapnic breathing (Hodges et al., 2001). In contrast, postural drive can override respiratory drive while lifting (Lamberg et al., 2003). Thus prioritization or optimization of the respiratory and postural drives has been suggested to be task-specific and convergence of these two drives may occur at the spinal level (Butler, 2007). This also suggests that an interaction between walking and breathing cycles may occur at the spinal level and not be impaired post-stroke.

2.6.3 Factors influencing optimization

Breathing and walking perturb postural stability. The optimization between respiratory and postural demands may be influenced by depth of breathing, position, and speed of the movement. Hodges et al., (2002) studied the effect of mode of breathing on postural stability. They suggested that center of pressure (COP) was displaced backward on inspiration during deep breathing while movement amplitude increased at the neck and ankle to adjust for the postural perturbation in healthy adults. On the other hand, compensation from multi-segmental adjustments of the trunk, pelvis and lower limbs may result in minimal displacement of the COP during quiet (regular) breathing. They suggested that automatic control of breathing or quiet breathing may be more optimal for compensation of respiratory perturbation to postural control than deep breathing in healthy adults. Hodges et al., (2002) suggested that postural stability is affected by deep breathing in sitting more than standing because the hips and knees are unable to compensate for the perturbation of center of pressure backward during inspiration. In individuals

post-stroke, Lee et al., (2012) demonstrated that tidal volume and vital capacity significantly change between supine and sitting. However, it is unknown how posture affects depth of breathing in standing or how depth of breathing affects postural stability in individuals post-stroke.

APAs occur to maintain postural stability by increasing spinal stability in preparation for an internal perturbation such as voluntary movement (Massion, 1992). Erector spinae and rectus abdominis play a general role in stabilizing the trunk but are not modulated depending on the task (Hodges and Gandevia, 2000a) whereas the diaphragm, latissimus dorsi and external oblique muscles are modulated based on the task (Dickstein et al., 2004). Slow movements may not require APAs (Massion, 1992). For example, the transversus abdominis is not modulated when transitioning from walking to running, but is modulated with increased ventilatory demand in healthy adults (Saunders et al., 2004). The diaphragm is activated before limb movement (Gandevia et al., 2002; Hodges and Gandevia 2000a, 2000b) and the magnitude of muscular activity for postural stability increases as the velocity of the limb increases (Hodges and Gandevia 2000b).

Sensory and motor impairments affect the ability to maintain balance in individuals post-stroke, which may impact the optimization between respiratory and postural drives compared to healthy adults. In individuals post-stroke, the APAs are weak on the paretic side (Dickstein et al., 2004; Slijper et al., 2002) but similar to healthy adults on the non-paretic side. Time of onset of APA is slower in individuals post-stroke however recruitment sequence of muscles during the APA is similar to healthy adults (Dickstein et al., 2004; Horak et al., 1984).

Compensation for reduced APAs post-stroke may result in weight shift to the non-paretic leg to increase postural stability rather than modifying the APA (Slijper et al., 2002). Self-selected walking speed in 10 m has been correlated with the Berg Balance Scale and daily ambulatory activity (steps/day) (Micheal et al., 2005), suggesting balance deficits and sedentary lifestyle may impact walking speed. Combined with muscle weakness, and impaired postural and motor control, individuals post-stroke have difficulty maintaining their balance while walking (MacKay-Lyons et al., 2006).

In healthy individuals, the respiratory, neurological and orthopedic systems interact during walking. Biomechanical restraints and metabolic costs affect the speed at which a person walks. The cardiorespiratory system must supply oxygen to the heart and active muscles, whereas the orthopedic and neurological systems are responsible for biomechanical acts and coordination of breathing and walking cycles. Morin & Viala, (2002) demonstrated that the locomotor system can modulate the respiratory system, and Rassler & Kohl (2000) showed that paced breathing with an auditory tone can change stepping rate. As well, gait speed can influence V_E in healthy adults (Mercier et al., 1994).

The neuromuscular and respiratory impairments post-stroke can impact on exercise capacity. The respiratory and locomotor systems can adapt depending on the demand from each other. In healthy adults, a fast walking pace has been shown to occur above the anaerobic (ventilatory) threshold (Waters & Mulroy, 1999) and as such, could stimulate automatic control of breathing via chemoreceptors. Since individuals post-stroke have increased carbon dioxide production during aerobic activity, reach anaerobic threshold and use anaerobic muscular energy sources earlier (Chen et al., 2010), it is possible that fast walking in such individuals could similarly stimulate automatic control of breathing. Mitchell & Babb (2006) also suggested that serotonin may modulate the response of the diaphragm and respiratory muscles through raphe neurons which project to the spinal cord in the same area as respiratory motor neurons. Both of these mechanisms which stimulate automatic control of breathing, could lead to increased chest wall movement and diaphragmatic muscle activity, increasing tidal volume and V_E, leading to increased gait speed.

CHAPTER 3.0: STUDY DESIGN AND METHODS

3.1 Overview of the research design

This was a balanced Latin-square design study, with two walking speed conditions (comfortable and fast) and two breathing conditions (regular and deep), (Figure 2). There were two groups, individuals post-stroke and a neurologically-intact control group.

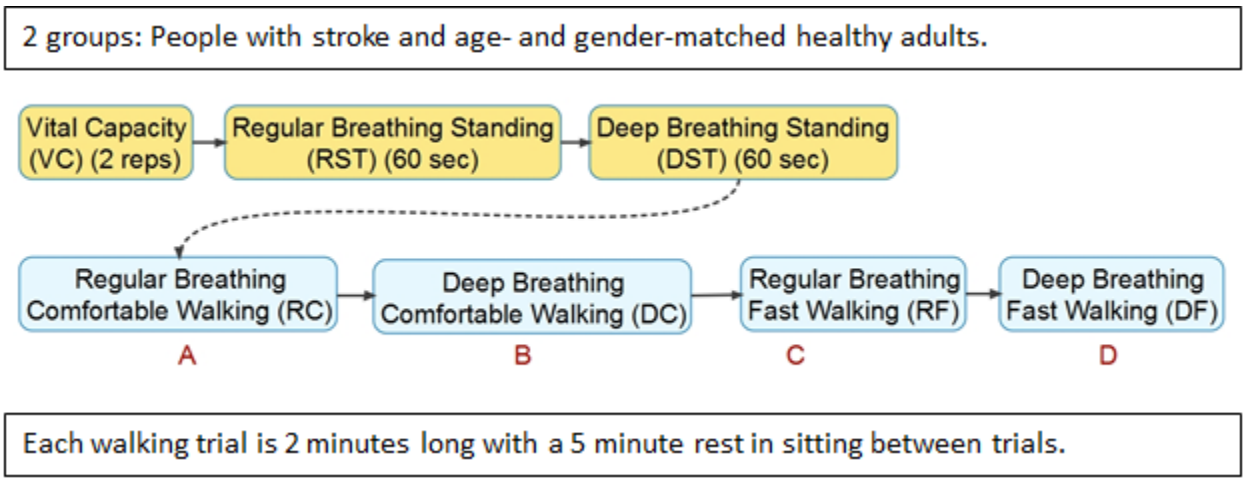

Figure 2: Experimental design.

Conditions A, B, C, D were randomized according to a balanced Latin-square design.

3.2 Ethics

The Centre for Interdisciplinary Research in Rehabilitation of Greater Montreal (CRIR) research ethics board approved the pilot study titled, "The Coupling between Respiratory and Locomotor Patterns Post-stroke" (CRIR 569-1210) and data were collected in the summer of 2011. CRIR research ethics board also approved the follow-up study titled, "The interaction between respiration, posture and walking post-stroke" in December 2011, which was later modified (Appendix I) to "The interaction between breathing and walking post-stroke" (CRIR 646-0811) in April 2013. Documents are protected and will be destroyed after 10 years.

3.3 Study Participants

Individuals aged 35 to 75 years with a chronic (>6 months), unilateral cerebrovascular accident (CVA) resulting in hemiparesis, who were able to walk independently for at least 2 minutes with or without a gait aid, were recruited. Healthy age- and sex-matched adults, who were able to

walk more than two minutes without a gait aid, were also recruited. Participants were excluded if they had: 1) obesity (body mass index (BMI) ≥31); 2) signs or symptoms related to heart or lung disease; 3) a brainstem, cerebellar, or bilateral stroke; or 4) moderate to severe cognitive impairment or were not able to follow instructions while completing two tasks at the same time.

Participants post-stroke were recruited via third-party involvement at the Jewish Rehabilitation Hospital, Laval, Quebec and from a databank of participants who have previously agreed to participate in future studies. The control participants, who met the eligibility criteria, were recruited through third-party involvement or through posted advertisements at the Jewish Rehabilitation Hospital or at the Cummings Centre, Montreal, Quebec. All participants gave their written informed consent prior to participation.

3.4 Study Procedures

3.4.1 Measures

3.4.1.1 Baseline measures

An interview was conducted to screen for exclusion criteria. Demographic data (age, gender), history of stroke (paretic side, date of CVA, and location of CVA), functional status (gait aid and orthotic used for mobility), medical disorders (cardiac or respiratory disorders and previous surgeries), and anthropometric data (height and weight) were collected.

3.4.1.1.1 Level of physical activity: was determined using the International Physical Activity Questionnaire (telephone-long in English or French) (Brown et al, 2004; Hagstromer et al., 2006).

3.4.1.1.2 Respiratory status: Participants underwent pulmonary function testing at the Jewish Rehabilitation Hospital consisting of spirometry for determination of forced expiratory volume in one second (FEV_1), forced vital capacity (FVC) and the ratio of FEV_1/FVC (Coates et al., 2013; Miller et al., 2005). A Winspiro Pro 5.0 spirometer with a FLOWMIR disposable turbine and cardboard mouthpiece was used with Winspiro PRO MIR version 5.0.101 software (Medical International Research, Rome, Italy).

3.4.1.1.3 Overground gait speed: As walking (or gait) speed is a determinant in recovery post-stroke, participants performed the 10-m gait speed test at comfortable and fast speeds, based on

the protocol outlined by Salbach and colleagues (2001). In a quiet corridor, two pylons were placed two meters before and after the 10 m testing area, in order to account for accelerating and decelerating speeds. The 10 m testing area was marked with masking tape on the floor to mark the start and stop lines. The researcher walked behind the participant and started and stopped the stopwatch when the participant's first foot crossed either the start or stop line, respectively. This test was repeated and the average value was recorded in m/s. This test has good reliability (Flansbjer et al., 2005) and validity (Taylor et al., 2006).

3.4.1.1.4 Endurance: The 6-minute walk test (6MWT) was conducted to determine participants' activity tolerance (Flansbjer et al., 2005; Kosak & Smith, 2005). The distance walked during the 6MWT is correlated with cardiovascular fitness, balance, paretic and non-paretic leg strength (Patterson et al., 2007). Participants were instructed to cover as much distance as possible in 6 minutes while walking with or without a gait aid. Two pylons were placed at a distance of 30 m apart in an unimpeded hallway and participants were instructed to turn after passing the pylon. The researcher demonstrated one lap and then stood halfway down the hall against the wall, stating standardized words of encouragement and the time after each minute (www.rehabmeasures.org) (i.e. "Keep up the good work. You have four minutes to go."). Participants were allowed to rest if needed. This test has good test-retest reliability (Flansbjer et al., 2005) and concurrent validity (Eng et al., 2002; Eng et al., 2004; Fulk et al., 2008; Kosak and Smith, 2005; Liu et al., 2008).

3.4.1.1.5 Motor impairment level: The Chedoke-McMaster Stroke Assessment (CMSA) Impairment Inventory (Gowland et al., 1993; Miller et al., 2008) was used to describe motor impairment. This scale grades motor impairment from 1-7 and starts with higher scores representing greater coordination, strength and range of motion. Subjects generally need stage 4 of the leg in order to be independent with walking. The CMSA Impairment Inventory has been validated (Gowland et al., 1993) and is a commonly used measure.

3.4.1.2 Primary outcome measures

3.4.1.2.1 Tidal volume (V_T): Coded as "respiration function" in the International Classification of Function (World Health Organization, 2001), the V_T refers to the volume of air inspired and exhaled during a breath and is ~500 ml during resting breathing (West, 2000). Multiplying V_T by the respiratory rate (RR) gives minute ventilation (V_E), a respiratory response that is task-

specific. V_T was chosen as the primary respiratory outcome measure because it may be reduced due to paretic muscles in individuals post-stroke and may be modulated by automatic and voluntary control of breathing pathways (Kedr et al., 2000; Przedborski et al., 1988).

3.4.1.2.2 Walking speed: Walking speed is an important indicator of recovery post-stroke (Fritz and Lusardi, 2012; Goldie et al., 1996; Salbach et al., 2001; Schmid et al., 2007) and functional walking speed tests are reliable (Flansbjer et al., 2005), valid (Taylor et al., 2006) and responsive to change (Goldie et al., 1996; Salbach et al., 2001). According to the International Classification of Function (Mudge & Stott, 2007; World Health Organization, 2001), impaired walking speed impacts levels of activity and participation. Walking speed has been used to classify individuals post-stroke into household or community ambulators (Perry et al., 1995). Thus, walking speed is frequently used as an outcome measure in both clinical and research settings.

Walking speed tests were originally designed for a cardiorespiratory population (Butland et al., 1982; Eng et al., 2002) but have recently been validated for individuals post-stroke (Perera et al., 2006). The difference between fast and comfortable walking speeds in individuals post-stroke has been shown to be correlated with peak oxygen consumption (Ovando et al., 2011). Correlations between other measures of cardiorespiratory fitness, heart rate and lactate levels, and walking speed have also been reported (Hesse et al., 2001). Thus, it seems reasonable to use walking speed as a response variable to increased depth of breathing while walking at a comfortable or fast pace.

Walking speed data were collected continuously per gait cycle while participants were walking on a self-paced treadmill using Vicon motion analysis system. Both self-selected and fast walking speeds were determined. For individuals post-stroke, Perera and colleagues (2006) suggested that a standard error of measurement for the 10 m walk test is 0.04 m/s and small and large meaningful changes are 0.05 m/s and 0.10 m/s, respectively. However, Tilson (2010) reported a minimally clinically important difference of 0.16 m/s for individuals with acute stroke. The normative value for the 10 m walk test in individuals post-stroke is 0.84 (0.3) m/s (Severinsen et al., 2011), whereas healthy adults in their 50s walk an average of 1.40 m/s at a comfortable pace or 2.04 m/s at a fast pace (Bohannon, 1997).

3.4.1.3 Other measures

3.4.1.3.1 Breathing pattern timing parameters: Total breath time (T_{TOT}) is composed of the inspiratory time (T_I), and the expiratory time (T_E) during a breath. Dividing 60 by the T_{TOT} gives the RR. Respiratory timing parameters, as well as mean and peak inspiratory and expiratory flow, were determined using the flow signal from the pneumotachograph.

3.4.1.3.2 Perceived exertion: Participants rated their level of perceived exertion and dyspnea using the modified Borg Scale (0-10 scale) (Borg, 1982) at baseline and at the end of each walking trial.

3.4.1.3.3 Gait pattern: Stride time was determined by adding the stance and swing times of one foot. Stance time was calculated by adding double limb support time (DLS) and single limb support time (SLS). Stride length is composed of the right and left step distances. Step velocity was determined by dividing the step length by the swing time for each foot. Cadence (gait cycles per minute) and the distance walked (WD) during the two minute trials were recorded.

3.4.2 Instrumentation

3.4.2.1 Respiratory data

3.4.2.1.1 Respiratory pattern: Airflow during inspiration and expiration was measured using a non-heated pneumotachograph (Hans Rudolph 4813, USA) with a differential force transducer, a bacterial filter, and a mouthpiece with a saliva trap (Hans Rudolph 9060 series, USA). The pneumotachograph was secured to the participant via an upper chest support for the initial five participants per group in 2011 and with a Hans Rudolph head support for the follow-up participants in 2013. See Figure 3 and Appendix I for details of differences between protocols in 2011 and 2013. Nose clips were worn throughout the experiment. Respiratory data were sampled at 60 Hz. The pneumotachograph was calibrated using a 3L syringe. Respiratory data were stored on the main computer for off-line analysis.

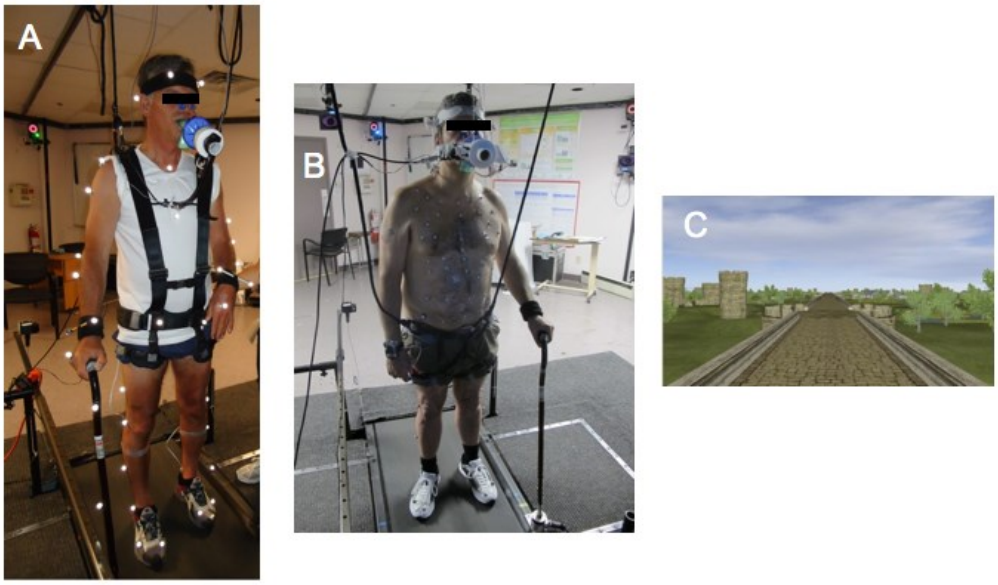

Figure 3: Lab set-up.

A) Equipment for initial data collection (CRIR 569-1210); B) equipment for follow-up data collection (CRIR 646-0811); C) virtual reality screen viewed by participants. Consent has been obtained from the participants for the photos to be used for research and educational purposes. CRIR: Centre for Interdisciplinary Research in Rehabilitation of Greater Montreal

3.4.2.2 Gait data

3.4.2.2.1 Walking pattern: Vicon MX motion analysis system (Oxfordmetrics Ltd, Oxford, UK) provides kinematic data on the gait parameters (walking and stepping speed, stride and step length, stride and swing time, cadence, stance time, single and double leg stance, and total distance walked). Six infrared LED Vicon MX cameras (Vicon, Oxford, UK) were placed around the treadmill where the participant walked and wore passive reflective markers on the body (Figure 3 and Appendix II). Placement of markers was performed by four physiotherapy students in 2011 and by a physiotherapist (CO) and an assistant in 2013, trained by the same physiotherapist (CP) with Vicon experience. However, in 2011 we placed 42 markers on the participants according to the plug-in gait full body model (Appendix II) and in 2013 we placed 7 markers on each leg as per the plug-in gait lower limb model. Five markers on the pelvis and seven markers on the thorax were replaced with opto-electronic plethysmography markers (for chest wall expansion motion) and markers originally placed on the arms (6 each arm) and head

(4) were absent. All trials were collected within the same session, minimizing error with marker placement.

Data were sampled at 120 Hz and the signal was stored on the computer using Nexus 1.8.3 software (Vicon, Oxford, UK) for off-line processing. Static and dynamic calibrations (Vicon) were performed before each participant.

3.4.3 Experimental protocol

The research was conducted at the Feil/Oberfeld CRIR Research Centre of the Jewish Rehabilitation Hospital in Laval, Quebec. Participants were habituated to the self-paced, motorized treadmill, while wearing a safety harness attached to an overhead suspension system, with a spotter beside them (Figure 3). An electropotentiometer is attached to the participant's pelvis while walking on the treadmill, where the linear change in distance of the pelvis can be detected instantaneously (Fung et al., 2006). This variable, along with its first derivative (velocity) computed by a micro-controller, is used to drive the treadmill motor with a proportional-integral-controller to enable voluntary self-pace control of the treadmill speed by the participant. A cane attached to a ball joint, which was fixed to the treadmill, was available for the participants' use (Perez and Fung, 2011). The virtual environment, "castle-walk" (Computer Assisted Rehabilitation ENvironment (CAREN) software (Motek Medical, Amsterdam) was synchronized with the speed of the self-paced treadmill and rear-projected onto a screen 1.5 m in front of it. Habituation to the self-paced treadmill was conducted until each participant could comfortably start and stop the treadmill and walk independently at both comfortable and fast walking speeds.

Preparation for kinematic data collection included measuring joint widths and leg lengths for the Vicon motion analysis system and placing passive markers on the body (Appendix II). Each person performed one session of two standing trials for 30 to 60 seconds and four randomized 2-minute walking trials. During the standing trials, participants performed two breathing trials: 1) regular breathing (RST); and 2) deep breathing (DST). After the initial pilot study was completed in 5 stroke participants and 5 healthy controls, a third standing trial was added where the participant performed a maximal inspiration and expiration twice (vital capacity or VC). Instructions for deep breathing were: 1) "put your hand on your chest and one on your stomach", 2) "slowly inhale through your mouth", 3) "as you inhale, feel your stomach expand with your

hand", followed by 4) "slowly exhale through your mouth". The participant practised deep breathing at rest before the standing and walking trials began. Instructions for vital capacity were "breathe in as much as possible" with encouragement such as "in, in, in" at the end of inspiration followed by "breathe out as much as possible" with encouragement at the end of the breath such as: "out, out, out". If needed, participants took a rest after the standing trials, followed by four walking trials: 1) walking at a comfortable pace and breathing regularly (RC) or 2) deeply (DC); or 3) walking at a fast pace and breathing regularly (RF) or 4) deeply (DF). There was a minimum 10 minute pause between each walking trial where participants sat for at least 5 minutes and heart rate and blood pressure returned to near baseline levels (Figure 2).

Signals from the pneumotachograph, Vicon and CAREN were acquired simultaneously and continuously on-line and could be viewed using NEXUS 1.8.3 software on the main computer. The participants started walking when indicated on the screen in front of them ("Allez-y") and after 3 meters of walking (ramp-up time) a timing pulse or spike was initiated by the CAREN software, to coordinate data from all instruments. A second spike was recorded two minutes after the first one and the participant was instructed to stop walking ("Arrêtez"; ramp-down). Heart rate, oxygen saturation, blood pressure and the Borg (0-10) scale for dyspnea and perceived exertion were taken between walking trials to ensure safety.

3.5 Data Analysis

Using a script written in C++ (Microsoft, Washington, USA), respiratory parameters were calculated from the airflow signal collected using the pneumotachograph. Tidal volume (V_T) was obtained by digital integration of the flow signal and used for calculation of minute ventilation (V_E). Mechanical timing parameters including the respiratory rate (RR), inspiratory time (T_I), expiratory time (T_E) and total breath time (T_{TOT}) were determined from the airflow signal. Mean and peak inspiratory and expiratory flows were also calculated. The physiotherapist (CO) who placed the markers on the participants in 2013 processed the kinematic data for the feet (great toe, lateral malleolus, and calcaneus) using NEXUS 1.8.3 from both 2011 and 2013 data in the fall of 2013. Using a customized script in C++, the gait parameters, including walking speed, were calculated per gait cycle.

The paretic leg and the left leg were used in the analysis to represent the group post-stroke and the control group respectively for the following variables: walking speed, stride length and time, cadence, two minute walk distance (2 minWD), stance time and double limb support (DLS). Analysing the paretic and non-paretic leg separately, and comparing them to the left leg of the control group, we also looked at single limb support (SLS), step length, swing time and step velocity. In the control group, data for the left foot was used as differences were minimal between right and left legs.

The respiratory and gait data were synchronized with an analog spike indicating the beginning and end of the two minute trial. Respiratory data were verified breath-by-breath and abnormal breaths were removed. Gait cycle data were also verified and abnormal steps were removed. Thus if an aberrant respiratory cycle was removed, the corresponding gait cycles were also removed from the analysis and vice versa.

For each participant, respiratory and gait parameters were calculated per breath or gait cycle, respectively, and the average was used. For group data, the median and interquartile range (75th-25th quartile) were reported as the distributions were non-normal (n=11 per group).

Percent change within a group was calculated based on the difference between conditions over the baseline condition (i.e. DF-RF/RF) within participants and the median was reported for the group. Change between groups was reported using the median difference.

3.6 Statistical Analysis

The participants were characterized with basic descriptive statistics. The Mann-Whitney Rank sum test was used to compare groups (stroke vs control). Sigmaplot (Systat software Inc., San Jose, CA) was used for statistical analysis.

A one-way repeated measures analysis of variance (ANOVA) was used to determine the main effect on V_T based on three conditions: 1) regular breathing while standing; 2) deep breathing while standing; and 3) regular breathing while walking fast (hypothesis 1). Normal distribution of data was tested using the Shapiro-Wilks Normality test. Repeated measures ANOVA with 2 within-participant factors (gait speed: comfortable vs fast; and breathing: regular vs deep) was used to determine the main effect due to gait speed on tidal volume (hypothesis 2) and the main

effect due to breathing on walking speed (hypothesis 3). A p-value (p) of <0.05 was considered significant. Data were transformed per test to normalize the distribution.

CHAPTER 4.0: RESULTS

4.1 Participants

Eleven participants post-stroke (six males: five females) and 11 healthy adults (seven males: four females) with a median age of 57 years (range =44-71) and 54 years (range =41-67) respectively, were included in the study (see recruitment flowchart, Figure 4). Five participants with chronic, unilateral, cortical stroke and five sex and age-matched healthy adults participated in a pilot study during the summer of 2011. Eleven more individuals post-stroke and 7 group sex-and age-matched healthy adults were recruited in a follow-up study in the summer of 2013.

Four participants post-stroke were excluded from the study based on: obesity (2), mild obstructive lung disease (1), and a Chedoke-McMaster Stroke Assessment score of the foot <3 (1). One participant post-stroke dropped out of the study after habituation to the self-paced treadmill. Due to scheduling issues, this participant did not return to complete the experiment. He used a quad cane and his comfortable (0.25 m/s) and fast (0.30 m/s) overground walking speeds in 10 meters were slower than any other participant in the study.

One person in the control group was dizzy which resolved once the trial was stopped and did not reoccur. Another person in the control group stepped off to the side of the treadmill, resulting in the harness catching her. No fall occurred and the person was not injured. This person was removed from all analyses because her fast walking speed (0.96 m/s) was slower than her comfortable walking speed (1.15 m/s) while breathing regularly. Since the trial in question was the first condition performed, the poor quality data were likely due to insufficient habituation to the self-paced treadmill.

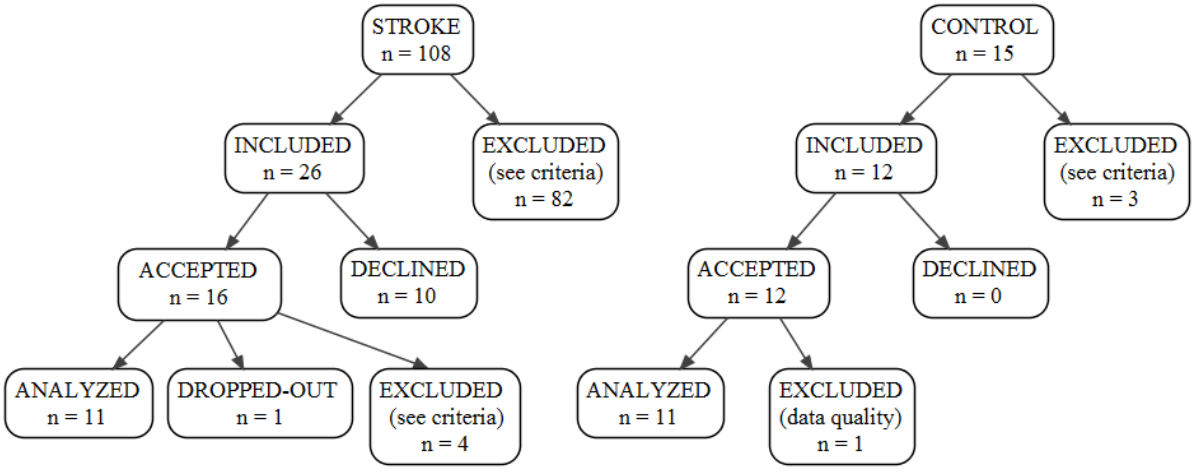

Figure 4: Flow chart of participant recruitment.

Baseline information on the participants is found in Table 1. For the pilot study, we do not have information on smoking, lung function, physical activity scores or the 6 minute walk test (6 MWT). One person in the control group was a current smoker (45 pack*years) but due to equipment malfunction, we were unable to assess this individual's spirometry. The participant reported no respiratory symptoms or history of respiratory disease. As well, one control participant did not perform the 10 m gait speed test at a fast pace.

Table 1: Participant characteristics.

Variables	Stroke		Control	
	Median (range)	n	Median (range)	n
Age, years	57 (44-71)	11	54 (41-67)	11
Gender, M/F	6/5	11	7/4	11
BMI, kg/m^2	27 (21-30)	11	22 (19-30)	11
FEV_1 , % predicted	91 (57-121)	6	102 (87-107)	5*
FVC , % predicted	87 (55-129)	6	99 (87-114)	5*
FEV_1/FVC, %	80 (75-94)	6	83 (73-84)	5*
Smoking history, pack-years	10 (0-57)	6	0 (0-45)	6
Current smoker, yes/no	0/6	6	1/5	6
IPAQ, MET*minutes/week	1402 (281 - 14536)	6	2172 (660-13311)	6
10 m gait speed: Comfortable pace, m/s	0.58 (0.32-1.30)	11	1.47 (1.12-1.90)	11
10 m gait speed Fast pace, m/s	0.66 (0.40-1.73)	11	2.06 (1.75-2.63)	10 *
6MWT, m	322 (106-525)	6	632 (483-775)	6
Gait aid (cane), yes/no	7/4	11	0/11	11
Orthosis	3 ankle foot 2 ankle supporting	11	0	11
Paretic side, R/L	8/3	11	n/a	-
Time since stroke, months	24 (8-200)	11	n/a	-
CMSA, leg/ foot	(3-6) / (3-5)	6	n/a	-

* missing data. BMI: body mass index; FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity; IPAQ: International Physical Activity Questionnaire; MET: metabolic equivalent; MWT: minute walk test; CMSA: Chedoke-McMaster Stroke Assessment; n: number in group.

4.2 Volitional control but not automatic control of breathing is impaired post-stroke (Hypothesis 1)

Compared to the control group, individuals post-stroke did not have significantly different tidal volumes (V_T) during regular and deep breathing in standing (Figure 5). In contrast, V_T was lower in individuals post-stroke when breathing regularly and walking fast (median difference =0.29 L; p=0.026; Figure 5). For comparison to maximal respiration in standing, vital capacity was 2.85 (2.03) L and 2.89 (1.19) L for the participants post-stroke (n=6) and healthy adults (n=6) respectively.

To estimate the response of V_T to exercise and deep breathing, a one way repeated measure ANOVA was used. The three conditions: 1) regular (RST) and 2) deep breathing while standing (DST); and 3) regular breathing while walking fast (RF), were significantly different for both groups ($p<0.001$ for ANOVA) (Figure 5). Post-hoc tests revealed that V_T increased from regular breathing while standing (RST) to deep breathing while standing (DST) in the control group by 96% and in the group post-stroke by 93% (Figure 5). V_T was also increased with regular breathing while walking at a fast pace (RF) in the control group by 52% and in the group post-stroke by 42% (see Appendix III for % change in respiratory parameters).

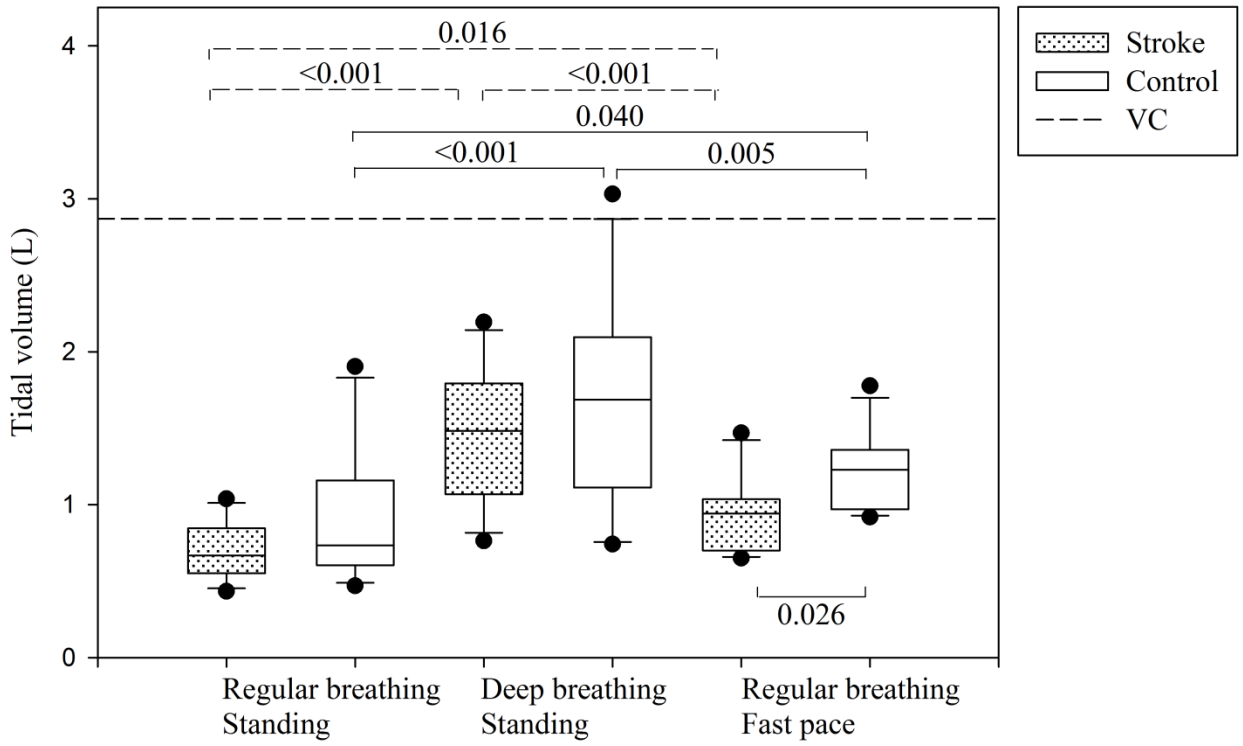

Figure 5: Tidal volume response to exercise and deep breathing.

Boxplots showing the median values and interquartile range (IQR) for the tidal volume (V_T) responses to exercise and voluntary deep breathing, compared to automatic regular breathing, in 11 individuals post-stroke and 11 healthy controls. Significant post-hoc test comparisons within groups are shown above and rank sum test comparison between groups is shown below. As vital capacity was similar between groups (n=6), the average (2.87 L) was provided for comparison.

4.3 Respiratory pattern modifications in response to increased ventilatory drive with faster walking speed (Hypothesis 2)

4.3.1 Tidal volume (V_T)

Ventilatory drive may be increased both voluntarily, by breathing deeply, or automatically, with exercise. Two factors, breathing (regular and deep) and walking (comfortable and fast pace), were included in the two way repeated measures ANOVA analysis. Data for the control group were log transformed but no transformation was required for the group post-stroke. V_T increased from regular to deep breathing while walking at a comfortable or fast pace in both the control group ($p<0.001$ ANOVA) and the group post-stroke ($p=0.011$ ANOVA). The main effect on V_T due to walking speed was significant for the control group ($p=0.036$ ANOVA) but not for individuals post-stroke ($p=0.138$ ANOVA). However, an interaction effect on V_T with increased gait speed occurs for the control group ($p=0.019$ ANOVA) and individuals post-stroke ($p=0.014$ ANOVA).

Post-hoc tests revealed that the control group increased V_T from 1.01 to 1.23 L (change=22%) from comfortable to fast walking speed while breathing regularly, whereas the group post-stroke decreased V_T from 1.45 to 1.00 L (change = -6%) with increased gait speed while breathing deeply (Figure 6). On the contrary, both groups did not significantly increase V_T while increasing gait speed from comfortable to fast, while breathing deeply for the control group (2%; from 2.08L to 2.16L) and regularly for the group post-stroke (5%; from 0.91L to 0.94L; Figure 6).

Between groups, V_T were not significantly different while walking at a comfortable pace and breathing regularly or deeply, however, individuals post-stroke trend toward lower V_T compared to the control group while breathing deeply (median difference = 0.63 L; $p=0.088$). In contrast, V_T were lower with either regular (median difference =0.29 L; $p=0.026$) or deep (median difference =1.17 L; $p=0.042$) breathing while walking fast in the group post-stroke (Figure 6).

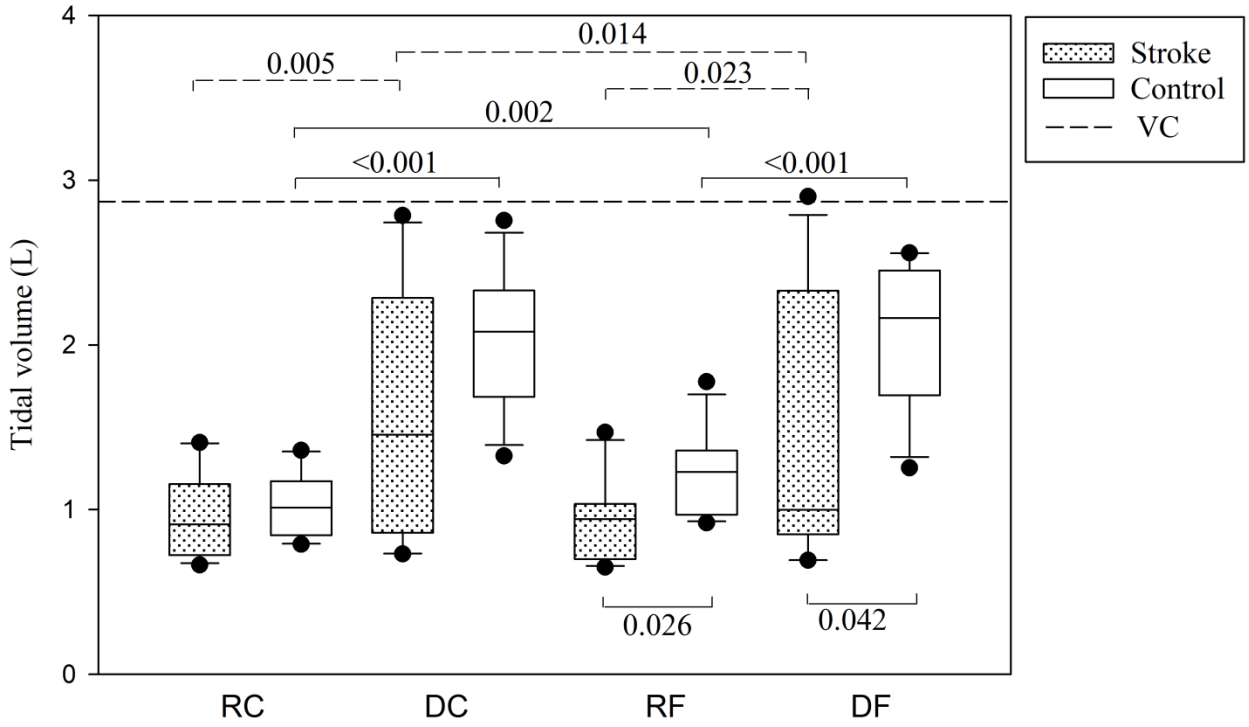

Figure 6: Tidal volume responses to walking faster and breathing deeper.

Boxplots showing the median values and interquartile range (IQR) for the tidal volume (V_T) responses to increased walking speed and/or depth of breathing in 11 individuals post-stroke and 11 healthy controls. Significant post-hoc test comparisons within groups (dashed lines = group post-stroke and solid lines = control group) are shown above and rank sum test comparison between groups is shown below. As vital capacity was similar between groups (n=6), the average was provided for comparison. Participants in both groups increased V_T with deeper breathing. With faster walking, V_T decreased in the group post-stroke while breathing deeply and increased in the control group while breathing regularly.

4.3.2 Other breathing pattern responses

Although V_T is the primary outcome of interest, other ventilatory parameters may help understand the respiratory modifications to increased walking speed. The ratio of respiratory rate (RR) to V_T indicates the relative proportion of RR to V_T in order to modify minute ventilation (V_E). The ratio RR/V_T was higher in individuals post-stroke in all conditions compared to the control group (Figure 7). However, V_E, a product of RR and V_T, was only significantly different between groups while walking fast and breathing deeply (stroke= 26.5 (6.3) L/min; control= 39.2 (13.7) L/min; p= 0.036; Figure 8). V_E increases with walking speed in individuals post-stroke, whereas it increases with walking speed and deep breathing in the control group. In Figure 9, the control group increases V_T (from 1.01 to 1.23 L; p=0.002) and RR (from 20.8 to 22.9

breaths/min; p=0.009) with increased walking speed from comfortable to fast while breathing regularly (Table 2), but individuals post-stroke mainly increase RR from 24.3 to 28.7 breaths/min (Table 3; Figure 9; p<0.001). While breathing deeply and increasing walking speed, both groups mainly increase RR, however, the group post-stroke reduces V_T from 1.45 to 1.00 L (Figure 9; p=0.014).

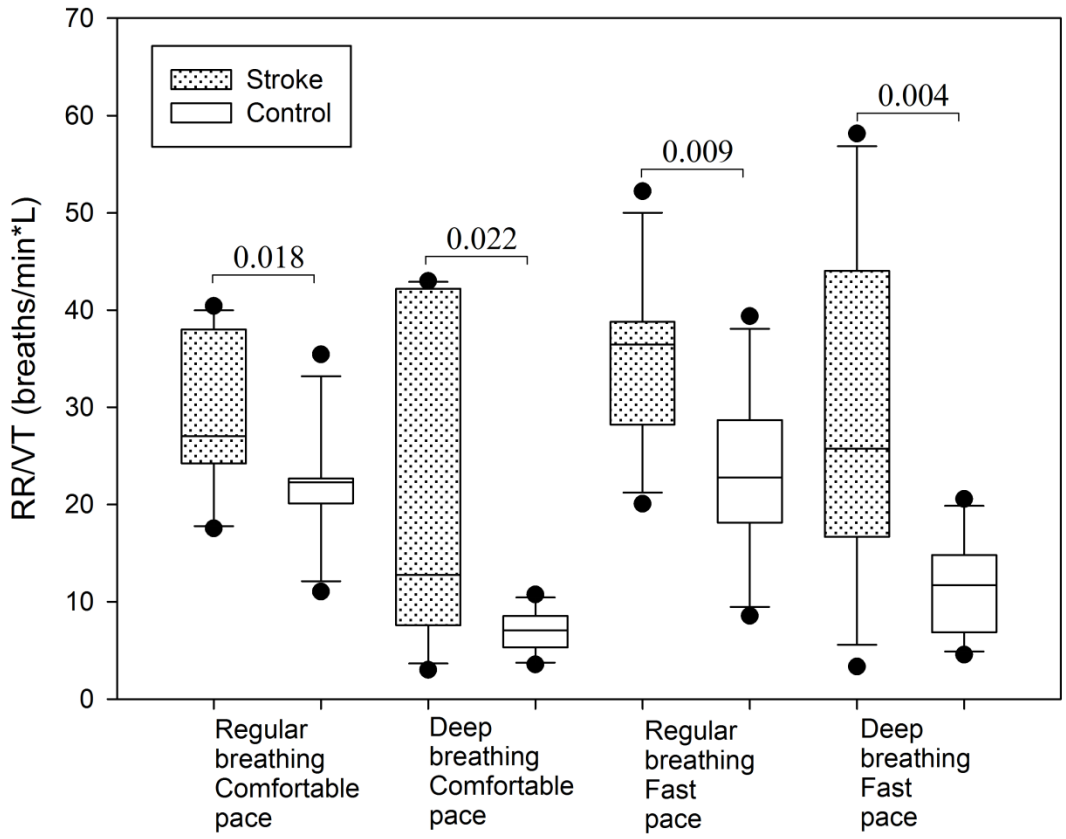

Figure 7: Ratio of respiratory rate (RR) to tidal volume (V_T).

Boxplots illustrate the median and interquartile range (IQR) of V_T while walking, with outliers represented by the points, in 11 individuals post-stroke and 11 healthy controls. The ratio of RR to V_T indicates that individuals post-stroke have higher respiratory rates relative to V_T while walking compared to the control group. The p-values from the rank sum tests between groups are shown.

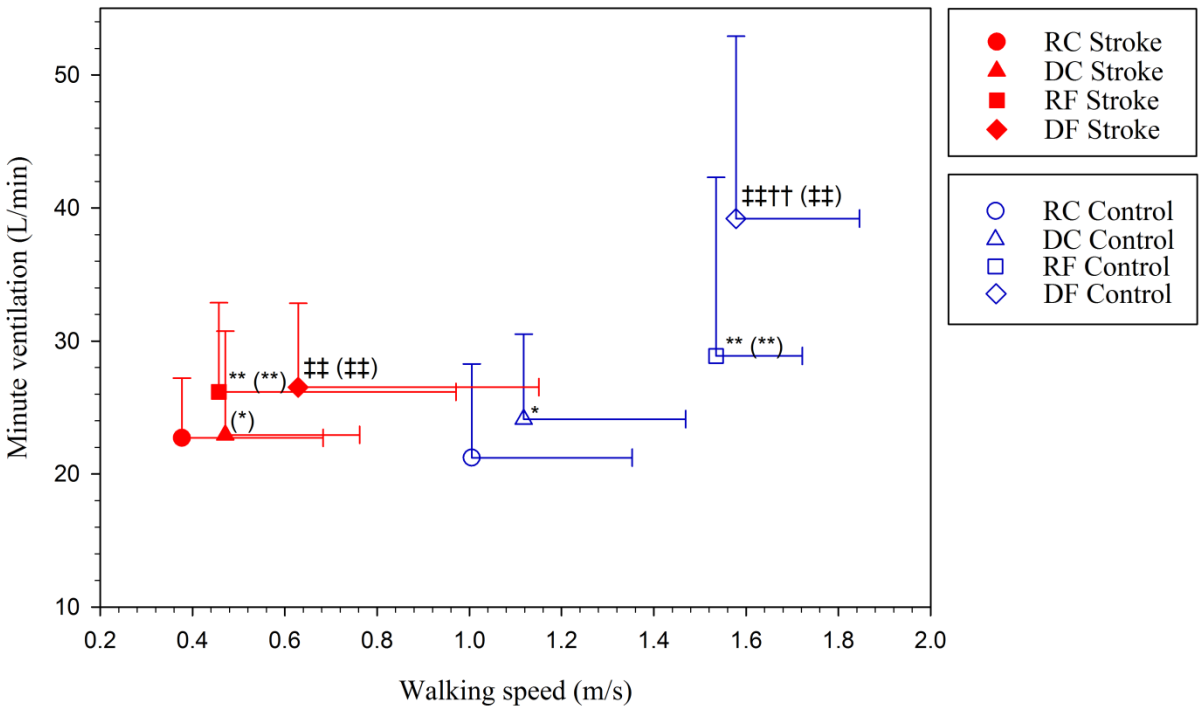

Figure 8: Minute ventilation response to increased walking speed.

Scatterplot showing the median values and interquartile range (IQR) for the minute ventilation (V_E) responses relative to walking speed, in 11 individuals post-stroke and 11 healthy controls. RC: regular breathing, comfortable pace (walking); RF: regular breathing, fast pace; DC: deep breathing, comfortable pace; and DF: deep breathing, fast pace. Posthoc contrasts within groups: Compared to RC *p<0.05, ** p<0.01; compared to RF † p<0.05, †† p<0.01; compared to DC ‡ p<0.05; ‡‡ p<0.01. Significant differences for V_E are indicated first outside of brackets, followed by gait speed within brackets. Rank sum tests indicate that V_E was only significantly different between groups while walking fast and breathing deeply. V_E increases with walking speed in individuals post-stroke, whereas it increases with walking speed and deep breathing in the control group. Walking speed increases as predicted with increased walking speed in both groups, although the group post-stroke also increases walking speed with deep compared to regular breathing and walking at a comfortable pace.

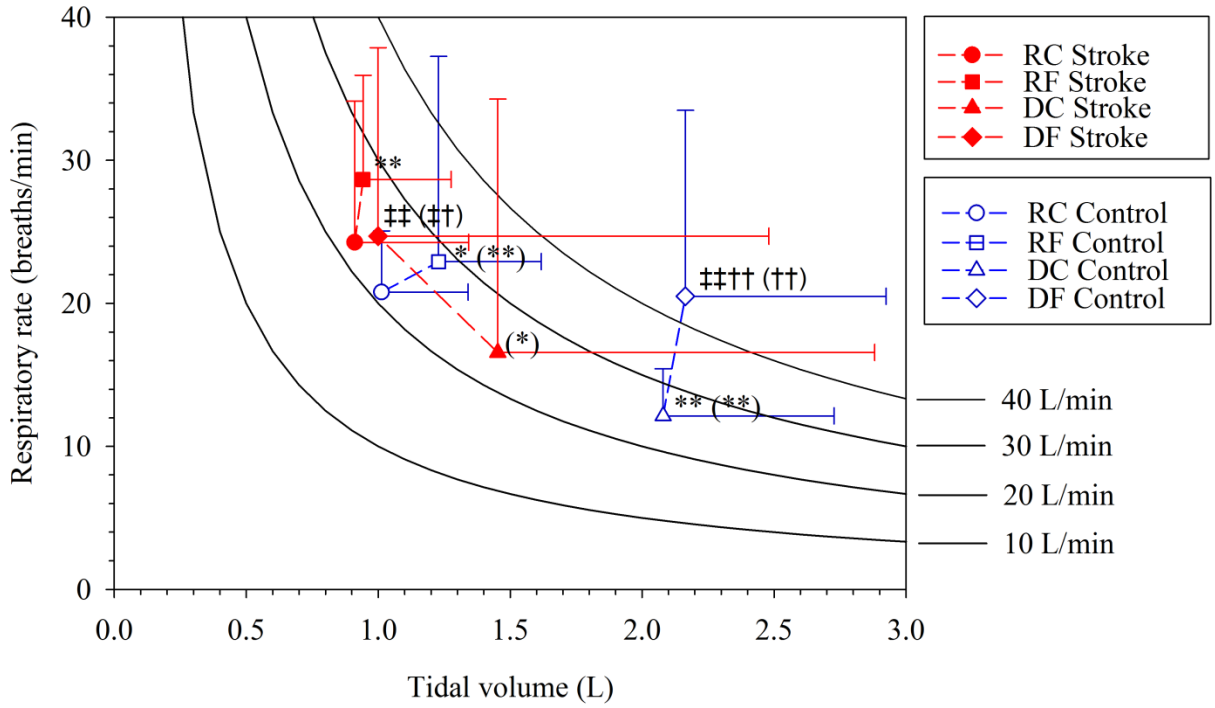

Figure 9: Respiratory responses to increased walking speed.

Minute ventilation (L/min isopleth lines) is the product of respiratory rate (y-axis) and tidal volume (x-axis). RC: regular breathing, comfortable pace (walking); RF: regular breathing, fast pace; DC: deep breathing, comfortable pace; and DF: deep breathing, fast pace. Posthoc contrasts within groups: Compared to RC *p<0.05, ** p<0.01; compared to RF † p<0.05, †† p<0.01; compared to DC ‡ p<0.05; ‡‡ p<0.01. Significant differences for respiratory rate (RR) are indicated first outside of brackets, followed by tidal volume (V_T) within brackets. Individuals post-stroke increased RR to increase minute ventilation (V_E) while breathing regularly and increasing walking speed from comfortable to fast, whereas the control group increased both V_T and respiratory rate. Individuals post-stroke decreased V_T and increased RR while breathing deeply and increasing walking speed and V_E, whereas the control group increased RR to increase V_E.

Table 2: Respiratory responses in the control group.

Variable	RC	DC	RF	DF	P-value	P-value	P-value
					R vs. D	C vs. F	interaction
V_T	1.01 (0.33)	2.08 (0.65)**	1.23 (0.32)**	2.16 (0.57)††	<0.001	0.036	0.019
RR	20.8 (4.27)	12.1 (3.3)**	22.9 (11.0)*	20.5 (10.4)‡‡††	<0.001	0.001	0.095
V_E	21.2 (7.0)	24.1 (6.4)*	28.9 (12.4)**	39.2 (12.5)‡‡††	<0.001	<0.001	0.330

R: regular breathing; D: deep breathing; C: comfortable pace; F: fast pace; V_T: tidal volume; RR: respiratory rate; V_E: minute ventilation. Posthoc contrasts within groups: Compared to RC *p<0.05, ** p<0.01; compared to RF † p<0.05, †† p<0.01; compared to DC ‡ p<0.05; ‡‡ p<0.01.); V_T and V_E data were log transformed.

Table 3: Respiratory responses in participants post-stroke.

Variable	RC	DC	RF	DF	P-value	P-value	P-value
					R vs. D	C vs. F	interaction
V_T	0.91 (0.43)	1.45 (1.43)*	0.94 (0.33)	1.00 (1.48)‡†	0.011	0.138	0.014
RR	24.3 (9.9)	16.6 (17.7)	28.7 (7.3)**	24.7 (13.2)‡‡	0.078	<0.001	0.347
V_E	22.7 (4.5)	22.9 (7.8)	26.2 (6.7)**	26.5 (6.3)‡‡	0.054	<0.001	0.602

R: regular breathing; D: deep breathing; C: comfortable pace; F: fast pace; V_T: tidal volume; RR: respiratory rate; V_E: minute ventilation. Posthoc contrasts within groups: Compared to RC *p<0.05, ** p<0.01; compared to RF † p<0.05, †† p<0.01; compared to DC ‡ p<0.05; ‡‡ p<0.01.); V_E data was log transformed.

Peripheral oxygen saturation (SpO_2%), as well as the Borg rating of perceived exertion (RPE) and dyspnea scales (0-10) were taken at the end of each trial for the individuals who participated in the study in 2013 (n=6). The median SpO_2% readings for individuals post-stroke were: 96% (regular breathing, comfortable pace (RC)), 97% (deep breathing, comfortable pace (DC)), 97% (regular breathing, fast pace (RF)) and 95% (deep breathing, fast pace (DF)). Values were similar for the control group: 94% (RC), 98% (DC), 96% (RF) and 95% (DF). Values ranged from 91% to 99% in the group post-stroke and from 93% to 98% in the control group. The median RPE scores for individuals post-stroke were: 2.5 (RC), 3 (DC), 4 (RF) and 4 (DF). Scores for the control group were: 0.5 (RC), 1.5 (DC), 2 (RF) and 3 (DF). Scores ranged from 0.5 to 7 in the group post-stroke and from 0 to 7 in the control group. The median dyspnea scores for individuals post-stroke were: 1.5 (RC), 2 (DC), 2 (RF) and 2.5 (DF). Scores for the control

group were: 0 (RC), 0 (DC), 1.5 (RF) and 0 (DF). Scores ranged from 0 to 6 in the group post-stroke and from 0 to 7 in the control group.

4.4 Gait adaptations in response to locomotor-respiratory coupling relative to the control group (Hypothesis 3)

4.4.1 Walking speed

Gait speed may be increased both voluntarily, by walking faster, or through automatic processes (i.e. locomotor-respiratory coupling) with increased depth of breathing. Two factors, breathing (regular and deep) and walking (comfortable and fast pace), were included in the two way repeated measures ANOVA analysis. Data were log transformed for the group post-stroke and the control group data were squared to meet the normality criteria. When participants were asked to walk faster, gait speed increased while breathing regularly or deeply in both the control group (Table 4) and the group post-stroke (Table 5). The main effect on gait speed due to increased depth of breathing was significant for individuals post-stroke ($p=0.030$) but not for the control group. The interaction was not significant for either group. Post-hoc tests revealed that individuals post-stroke increased walking speed by 25% (0.07 m/s difference) with increased depth of breathing, while walking at a comfortable pace ($p=0.015$) but not while walking fast. Overall, the control individuals walked faster and were able to increase walking speed more than individuals post-stroke ($p<0.001$) for all four conditions (Figure 10).

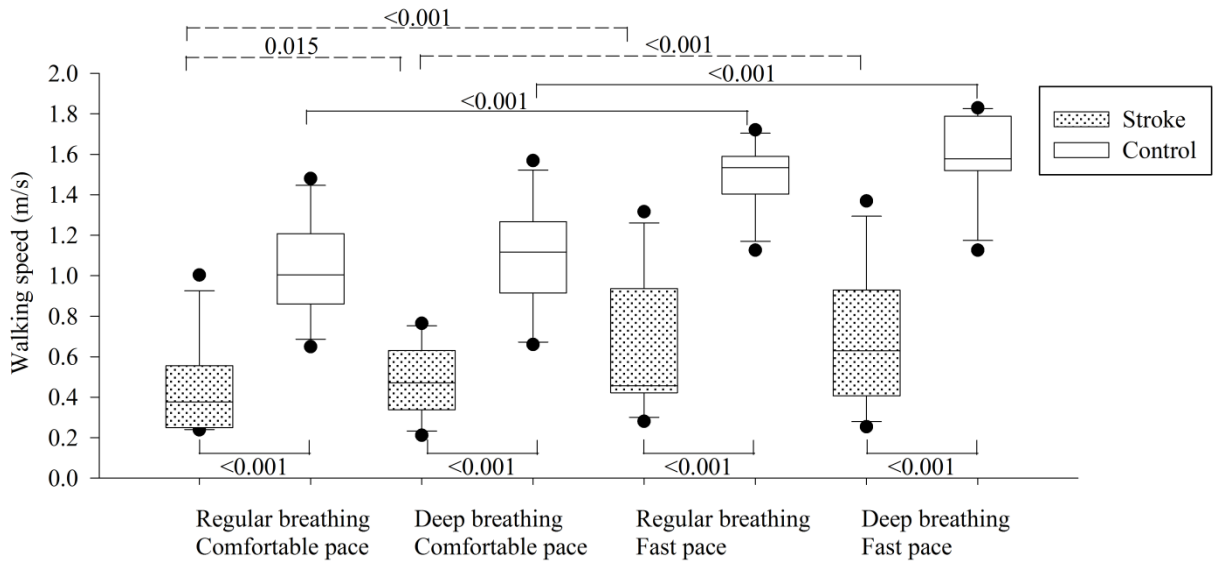

Figure 10: Walking speed in all conditions.

Boxplots showing the median values and interquartile range (IQR) for the changes to walking speed with increased walking speed and/or depth of breathing in 11 individuals post-stroke and 11 healthy controls. Significant post-hoc test comparisons within groups (dashed lines = group post-stroke and solid lines = control group) are shown above and rank sum test comparison between groups is shown below. Individuals post-stroke have slower walking speeds than healthy adults. Both groups increased walking speed from comfortable to fast. The group post-stroke also increased walking speed with deeper breathing while walking at a comfortable pace.

Table 4: Gait adaptations in response to locomotor-respiratory coupling in healthy adults.

Variable	RC	DC	RF	DF	P-value R vs. D	P-value C vs. F	P-value interaction
Gait speed	1.01 (0.35)	1.12 (0.35)	1.54 (0.19)**	1.58 (0.27)‡‡	0.249	<0.001	0.374
Cadence	52.69 (7.38)	55.17 (4.47)	65.45 (7.02)**	64.87 (8.54)‡‡	0.276	<0.001	0.512
Stride length	1.19 (0.30)	1.19 (0.25)	1.39 (0.22)**	1.48 (0.24)‡‡	0.506	0.001	0.888

R: regular breathing; D: deep breathing; C: comfortable pace; F: fast pace. Posthoc contrasts within groups: Compared to RC *p<0.05, ** p<0.01; compared to RF † p<0.05, †† p<0.01; compared to DC ‡ p<0.05; ‡‡ p<0.01; Gait speed data were transformed by the power of two and stride length was transformed by the power of three and inversed.

Table 5: Gait adaptations in response to locomotor-respiratory coupling post-stroke

Variable	RC	DC	RF	DF	P-value R vs. D	P-value C vs. F	P-value interaction
Gait speed	0.38 (0.31)	0.47 (0.29)*	0.46 (0.51)**	0.63 (0.52)‡‡	0.030	<0.001	0.286
Cadence	38.13 (8.91)	40.25 (10.40)	44.95 (11.09)**	44.62 (12.63)‡‡	0.09	<0.001	0.079
Stride length	0.61 (0.40)	0.66 (0.29)	0.76 (0.53)**	0.79 (0.47)‡‡	0.056	<0.001	0.948

R: regular breathing; D: deep breathing; C: comfortable pace; F: fast pace. Posthoc contrasts within groups: Compared to RC *p<0.05, ** p<0.01; compared to RF † p<0.05, †† p<0.01; compared to DC ‡ p<0.05; ‡‡ p<0.01; Gait speed and cadence data were log transformed.

4.4.2 Other gait parameters

While walking at a comfortable pace and increasing depth of breathing from regular to deep, stride length increased by 16%, as stride time decreased by 3%, increasing cadence by 3% and walking speed by 25% in individuals post-stroke (Figure 11). Stepping velocity increased by 14% in the paretic compared to 16% in the non-paretic leg, which was mainly due to increased step length of 9% and 19% in the paretic and non-paretic leg respectively. Swing time did not change (paretic=-1%; non-paretic=0%). Single limb support decreased by 7% and 11% in the paretic and non-paretic limbs respectively; and double limb support decreased by 8% (paretic limb) (Appendix IV). Distance walked in two minutes increased by 25% (see Appendix IV for percent change in gait parameters).

In contrast, the control group increased walking speed by 5% based on a change of stride distance of 3%, stride time of -1% and cadence by 1% (Figure 11). Step velocity increased by 4% and step length by 3% while walking at a comfortable pace. Swing time did not change (0%) with increasing V_T. Distance walked increased by 5%.

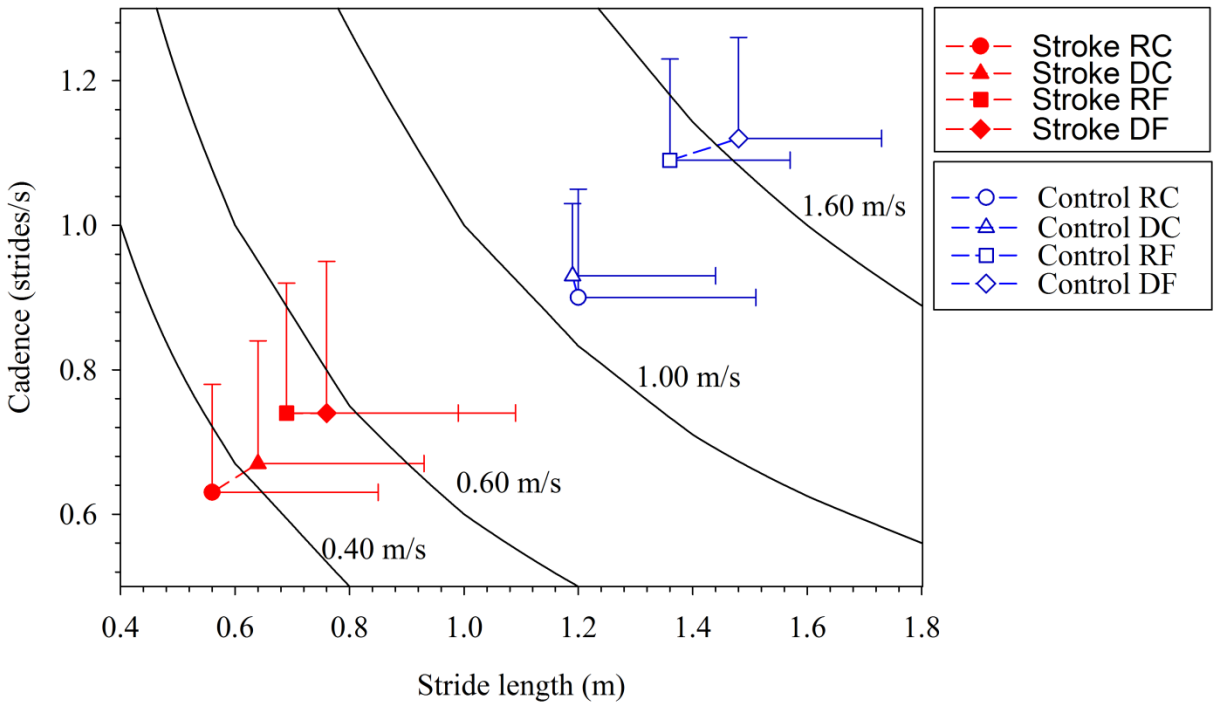

Figure 11: Walking adaptation to increased depth of breathing.

Gait speed is indicated by the curved lines and increases as cadence and stride length increase.*Sample size=10 for both groups as outliers (Control4, Stroke7) were removed to illustrate the percent changes or trend in walking pattern. RC: regular breathing, comfortable pace (walking); RF: regular breathing, fast pace; DC: deep breathing, comfortable pace; and DF: deep breathing, fast pace. Individuals post-stroke increase walking speed with deeper breathing at a comfortable pace.

In individuals post-stroke, changes were minimal while walking fast and increasing depth of breathing. Walking speed increased by 4% as stride length increased by 5% and stride time and cadence did not change (Figure 11). Stepping velocity increased by 1% in the paretic compared to 5% in the non-paretic leg, which was mainly due to increased step length of 4% and 5% in the paretic and non-paretic leg respectively. Swing time increased slightly by 2% in both the paretic and non-paretic legs. Single limb support decreased by 4% and 3% in the paretic and non-paretic limbs respectively (Appendix IV).

In contrast, the control group increased walking speed by 12% based on a change of stride length of 6% and stride time of -4% while cadence increased by 4% (Figure 11). Step velocity increased by 8% and step length by 5% m while walking at a comfortable pace. Double and single limb support decreased by 12% and 13% respectively (Appendix IV).

4.5 Interaction between walking speed and depth of breathing

As participants post-stroke vary in their response to the breathing and walking conditions, it is valuable to look at their individual responses compared to the control group. The following four figures represent the four possible combinations of breathing (regular and deep) and walking (comfortable and fast pace) conditions with the primary outcome measures (tidal volume and gait speed) for both groups (stroke and control).

While increasing walking speed from comfortable to fast and breathing regularly (RC to RF), 9/11 individuals increased tidal volume (V_T) and walking speed in the control group, whereas 7/11 individuals post-stroke increased V_T and walking speed. One person did not change and one person increased walking speed while decreasing V_T in the control group, whereas 3/11 individuals decreased V_T while increasing walking speed in the group post-stroke.

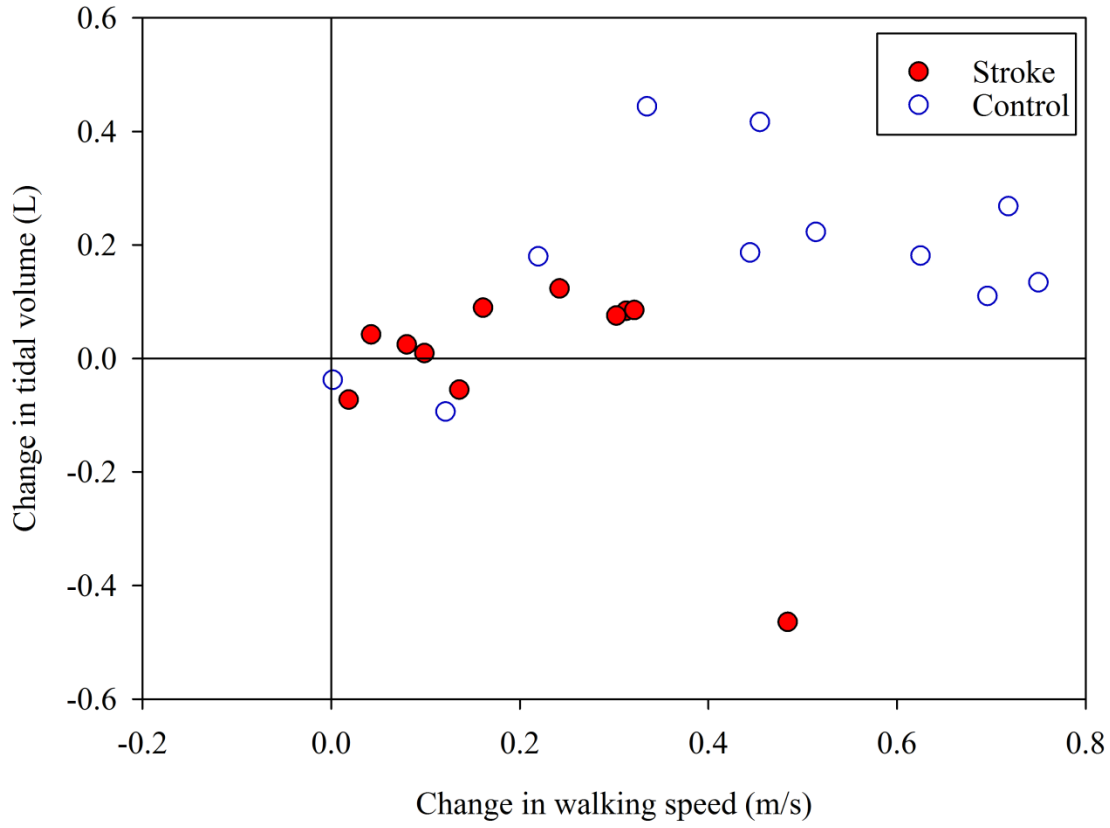

Figure 12: Change in tidal volume while breathing regularly and walking faster.

Eleven participants in each group increased walking speed from comfortable (RC) to fast (RF), while breathing regularly.

While increasing walking speed from comfortable to fast and breathing deeply (DC to DF), V_T and walking speed were increased in 6/11 individuals in the control group, whereas only 2/11 individuals increased both walking speed and depth of breathing in the group post-stroke.

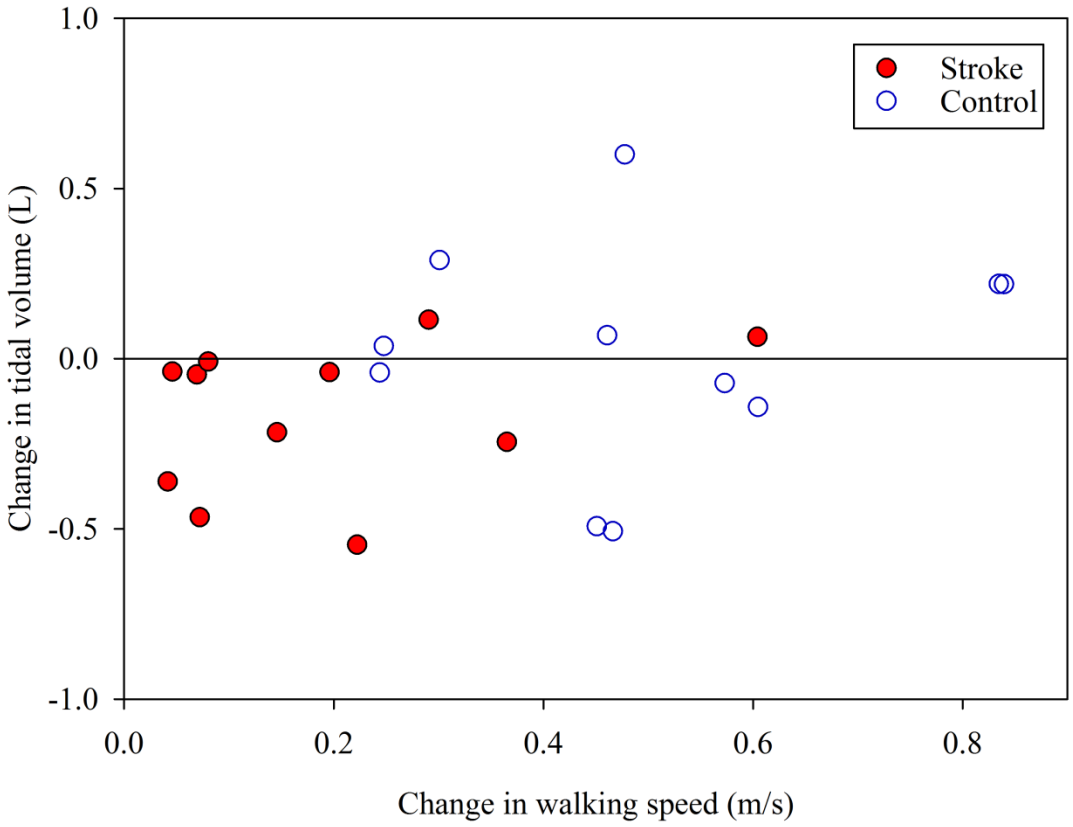

Figure 13: Change in tidal volume while breathing deeply and walking faster.

Eleven participants in each group increased walking speed from comfortable (DC) to fast (DF), while breathing deeply.

While walking at a comfortable pace and increasing depth of breathing (RC to DC), 6/11 individuals post-stroke and 8/11 healthy adults increased both V_T and gait speed. Additionally, in the group post-stroke, 3/11 individuals maintained V_T with increased gait speed, and 2/11 individuals decreased walking speed with increasing V_T. In the control group, 3/11 individuals decreased walking speed with increasing V_T.

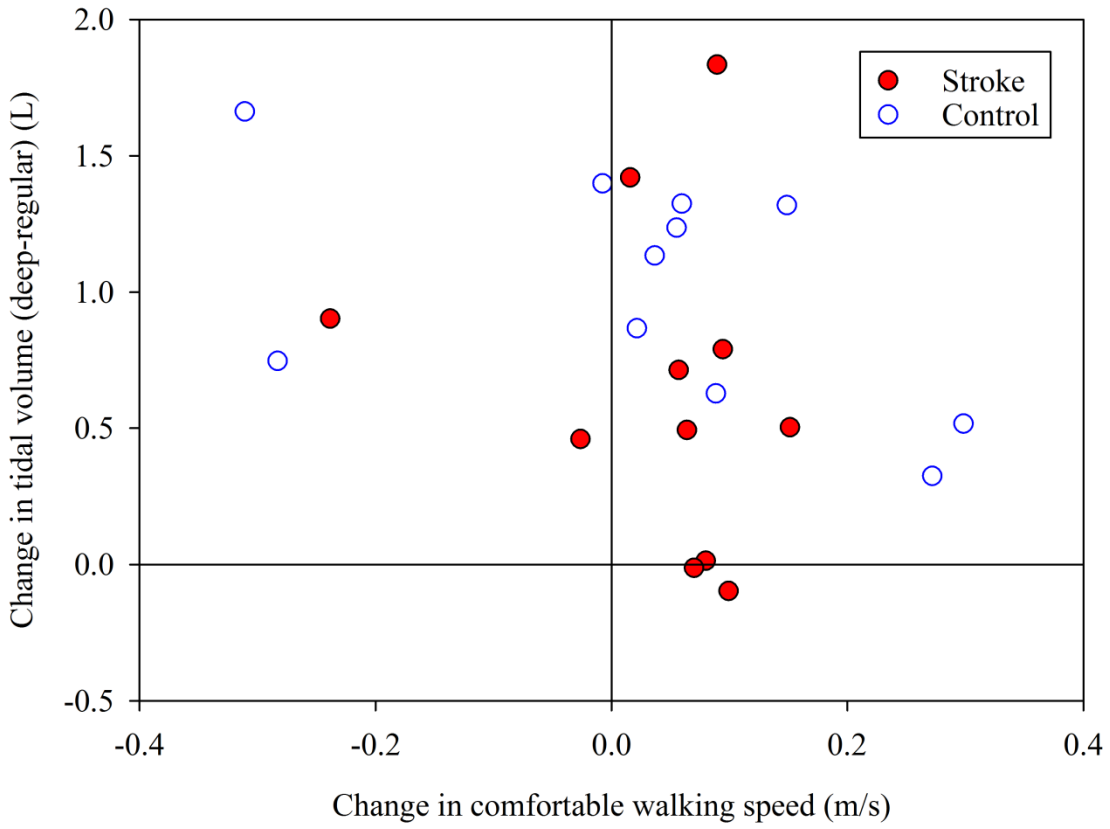

Figure 14: Change in comfortable walking speed with increased depth of breathing.
Eleven participants in each group increased depth of breathing from regular (RC) to deep (DC), while walking at a a comfortable pace.

While walking fast and increasing depth of breathing from regular to deep (RF to DF), the response was more variable in the group post-stroke. Six participants (6/11) increased both V_T and gait speed and one person (1/11) increased gait speed and decreased V_T. As well, while decreasing gait speed, V_T was increased (2/11) or decreased (1/11); and one person (1/11) did not change either gait speed or V_T. In the control group, 8/11 individuals increased both V_T and gait speed, whereas 3/11 individuals decreased gait speed while increasing V_T.

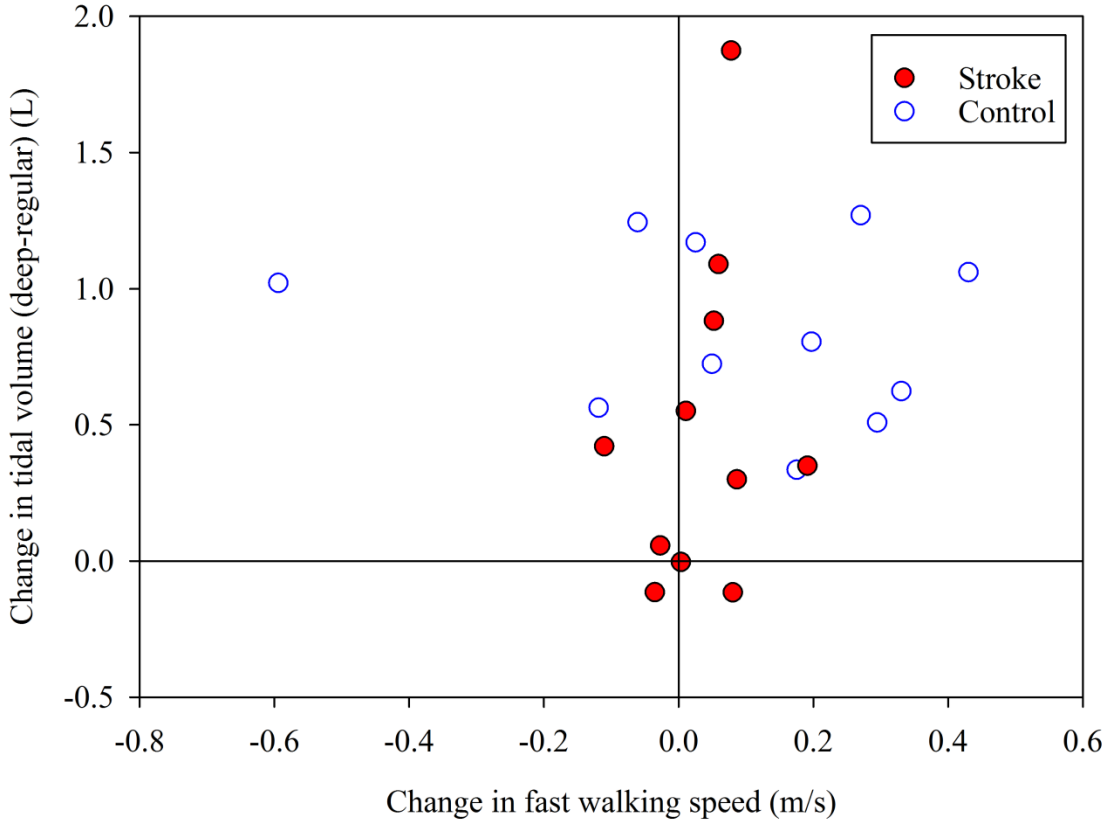

Figure 15: Change in fast walking speed with increased depth of breathing

All participants in the control group and 8/11 participants in the group post-stroke, increased depth of breathing from regular (RF) to deep (DF), while walking at a fast pace.

CHAPTER 5: DISCUSSION

5.1 Participants

5.1.1 Lung function

Pulmonary function tests demonstrated inter-individual variability among participants post-stroke. When we conducted pulmonary function tests (PFT) in 2013, 3/7 individuals post-stroke were found to have a restrictive lung function pattern whereas everyone in the control group (n=5) had normal lung function. Two of these participants with stroke, Stroke2 and Stroke8, were not able to increase tidal volume (V_T) from regular to deep breathing while walking at a comfortable (Stroke2=2% and Stroke8=-2% change) or fast pace (Stroke2=-14% and Stroke8=-1% change), but they were able to increase V_T while standing (Stroke2=154% and Stroke8=94% change). A pulmonary function test was not available for another participant who was unable to change his V_T while walking at a comfortable pace (Stroke11=-10% change) or fast pace (Stroke11=-12 % change). One person in our study was excluded due to an obstructive lung disease pattern that was observed on pulmonary function testing.

Teixeira-Salmela et al., (2005) performed PFT's on 30 individuals with chronic stroke and no previous diagnosis of respiratory disease. From this group, five individuals were not able to perform the test; three had restrictive lung function, four had obstructive lung function, and two individuals had mixed ventilatory dysfunction. From the 16 individuals who had normal lung function, maximal inspiratory and expiratory pressures were 21% ($p<0.01$) and 10% ($p=0.01$) lower than the control group, respectively.

Despite the research suggesting that individuals post-stroke have respiratory impairment, inter-individual variability exists in many studies in which symmetrical impairment of the intercostal muscles and diaphragm (Houston et al., 1995; Similowski et al, 1996) or no diaphragm muscle impairment (Cohen et al., 1994) has been reported. In a study by Houston et al. (1995), individuals with an acute stroke were reported to have a similar diaphragm excursion during quiet breathing as healthy controls, whereas maximum diaphragm excursion was reduced bilaterally with deep breathing in individuals post-stroke. However, it was not stated if reduced diaphragmatic excursion resulted in a significant decrease in V_T. Cohen et al. (1994) reported that 50% (4/8) of participants post-stroke had diaphragmatic hemiparesis, which correlated with

a reduction in V_T. However this also means that 50% had relatively normal diaphragmatic excursion. Compensation with increased movement by the non-paretic hemi-diaphragm has also been observed, maintaining V_T near normal (Cohen et al., 1994). Upon testing, respiratory impairment may be present in individuals post-stroke, not previously diagnosed, but it may not be evident until they perform moderate to heavy intensity exercise (Cohen et al., 1994; Sezer et al., 2004).

5.1.2 Hemiparetic gait

Walking speed is known to be slower in individuals post-stroke compared to healthy adults (Perry et al., 1995). During the 10 m walk test, the median walking speeds at a comfortable and fast pace were 1.47 m/s and 2.06 m/s for the control group (Table 1). The group post-stroke walked less than half that speed, at 0.58 m/s (comfortable pace) and 0.66 m/s (fast pace). These are comparable to comfortable walking speeds published by Titianova and colleagues (2003) for both groups. Eng et al., (2004) noted that self-selected treadmill speed was on average 60% of the comfortable walking speed overground and in our group post-stroke, treadmill speed was 66% (0.38 m/s/ 0.58 m/s).

The 6 minute walk test (6 MWT) measures endurance and is correlated with cardiovascular fitness, balance, paretic and non-paretic leg strength (Patterson et al., 2007) as well as walking speed and motor impairments post-stroke (Eng et al., 2002). On average the group post-stroke walked 322 m (106 to 525 m) whereas the control group walked 632 m (483 to 775 m).

5.2 Volitional control but not automatic control of breathing is impaired post-stroke (Hypothesis 1)

Individuals post-stroke have been reported to have respiratory impairment while deep breathing compared to regular breathing or hypercapnic ventilation (CO_2 re-breathing condition) (DeTroyer, 1981; Lanini et al., 2003; Przedborski et al., 1988). Thus, we hypothesized that voluntary control of breathing was impaired post-stroke, but automatic control of breathing remained intact. We expected individuals post-stroke to have similar V_T to the control group while standing and breathing regularly but lower V_T with deep breathing. We also expected that V_T would increase with exercise (i.e. walking fast and breathing regularly). In response, automatic control of breathing would increase minute ventilation (V_E) to maintain homeostasis.

5.2.1 Voluntary control of breathing

Contrary to our expectations, individuals post-stroke were able to increase depth of breathing voluntarily, similar to the control group, during regular (median difference=0.066 L; p=0.212) and deep breathing (median difference=0.205 L; p=0.325) while standing (Figure 5).

This finding is in contrast with Lanini's study (2003) which suggested that voluntary control of breathing or deep breathing may be compromised post-stroke. The difference in results may be due to the position of the participants. In Lanini's study, the participants were sitting but in our study they were standing or walking. Compensation for postural perturbation of breathing may be nearly complete during regular breathing in sitting or standing. However, multi-segmental movements of the hip and knee may be required during deep breathing which is compromised in sitting but not in standing (Bouisset and Duchene, 1994; Hodges et al., 2002). Thus, the participants in Lanini's study may have reduced V_T while breathing deeply because of increased postural demand on the respiratory muscles rather than a neurological impairment in the voluntary control of breathing. V_T while deep breathing and standing was not compromised in our participants and the difference between studies may be due to positioning (Narain & Puckeree, 2002). Alternatively, differences may also have been due to participant characteristics. Participants in Lanini's study had acute stroke whereas our participants had a stroke more than 6 months prior to the study. Mobility characteristics were also not mentioned in the description of their participants.

5.2.2 Automatic control of breathing

Automatic control of breathing which responds to metabolic needs during exercise should not be impaired in the group post-stroke because all participants had strokes above the brainstem where the respiratory control center is located. As expected, V_Ts were similar in standing while breathing regularly (RST) between groups (Figure 5) and V_T increased with onset of exercise from standing (RST) to fast walking (RF) while breathing regularly in both groups (Figure 5).

Tomczak et al. (2008) studied 10 individuals with chronic stroke with an average walking speed similar to our participants (0.71 m/s (range 0.35 to 1.2 m/s), however they included one person with chronic obstructive pulmonary disease and we excluded them. Similar to our study, they reported that V_T between groups were similar at rest but significantly lower during peak exercise for individuals post-stroke. However, resting values were lower in Tomczak's study and may

have been related to positioning (sitting vs standing). As well, the V_T for the control group during peak exercise were higher in Tomczak's study than our participants while walking fast and breathing regularly, which may suggest that our control participants did not reach peak exercise. However, they significantly increased V_T with increased walking speed and breathing regularly suggesting that our protocol was sufficient to increase V_T with fast walking.

Tidal volume response may be task-specific as it was lower while walking fast and breathing regularly (RF) compared to standing and breathing deeply (DST) in both groups (stroke: $p<0.001$; control: $p=0.005$). During our experiment, respiratory drive would be prioritized when participants were asked to take deep breaths while standing. Reciprocally, the postural drive would be prioritized in individuals post-stroke when walking fast and breathing regularly.

5.3 Respiratory pattern modifications in response to increased ventilatory drive relative to the control group (Hypothesis 2)

As oxygen cost of walking is higher with hemiparetic gait, fast walking may stimulate increased depth of breathing to meet metabolic requirements. As well, gait initiation may excite spinal locomotor neurons and brainstem respiratory neurons to increase minute ventilation. We expected V_T to increase while walking faster, relative to their ability to increase walking speed, while breathing regularly but to a lesser extent when breathing deeply in individuals post-stroke.

We propose two main factors that may explain the results of this study: 1) oxygen cost of walking and breathing; and the 2) dual role of thoracic muscles in optimizing ventilatory response and postural stability.

5.3.1 Respiratory response to fast walking while breathing regularly

Respiratory pattern strategies differed between groups while breathing regularly and increasing walking speed from comfortable (RC) to fast (RF). To meet ventilatory demand, the control group increased V_T and respiratory rate (RR) as expected (Pearson and Cunningham, 1973), whereas the group post-stroke maintained V_T and increased RR to increase V_E (Haas et al., 1967) (Figure 9).

Individuals post-stroke in Lanini and colleagues' study (2002) demonstrated a similar change in V_T / $PaCO_2$ as the control group during hypercapnic / hyperoxic conditions but the inspiratory

effort was greater as dynamic elastance and inspiratory motor output was higher. This suggests that individuals post-stroke would either need to increase inspiratory flow for comparable tidal volumes or have lower tidal volumes for a similar effort.

To reduce work of breathing and oxygen cost, respiratory rates may increase to meet ventilatory demand as V_T remains unchanged (Ainsworth et al., 1989; Johnson et al., 1999). In contrast to Lanini's results (2002), the participants post-stroke in our study have a higher ratio of RR/ V_T (Figure 7), which is a less efficient pattern of breathing but requires less effort. A restrictive ventilatory defect was present in 3/7 individual's post-stroke in our study which may have contributed to lower V_T and higher respiratory rates.

In Lanini's study (2002) increased inspiratory motor output may have compensated for respiratory muscle paresis but change in V_T / $PaCO_2$ was similar to the control group (Lanini et al., 2002). Thus, despite respiratory muscle weakness, similar tidal volumes between groups is possible. This is demonstrated in our study when individuals post-stroke are standing but not while walking fast. Respiratory muscle weakness may play a role but since individuals post-stroke demonstrate greater tidal volumes while standing, optimization between postural stability and increasing depth of breathing may better explain the results.

In our study, both, healthy adults and individuals post-stroke achieved similar V_E (median difference=2.7 L/min) while walking fast and breathing regularly, despite different strategies. Individuals post-stroke have a slower comfortable walking speed than healthy adults which has been shown to have similar oxygen cost of walking (Da Cunha-Filho et al., 2003). Thus, it is possible that individuals post-stroke may have lower V_T with similar oxygen cost of breathing.

5.3.2 Respiratory response to fast walking while breathing deeply

Optimization of postural stability and ventilatory demand is task-specific. The conditions of deep breathing and fast walking disturb postural stability. In healthy adults, tonic activation of respiratory muscles increases ribcage stiffness and abdominal support to maintain equilibrium when balance is perturbed (Hodges et al., 2001; Kenyon et al., 1997). In contrast, to meet increased ventilatory demand, the diaphragm and transversus abdominis muscles increase dynamic activity (Gandevia et al., 2002; Hodges et al., 2001). As well, Kolar and colleagues (2010) demonstrated that V_T is lower with greater diaphragmatic excursion during lower

extremity exercise than upper extremity exercise or rest. This suggests that increased postural demand during lower extremity exercise may reduce the ability to increase V_T more than necessary. Thus, when considering the dual role of respiratory muscles, the optimal balance between postural and ventilatory drives is likely different between groups based on their ability to maintain balance while meeting their metabolic requirements.

Respiratory pattern strategies differed between groups while breathing deeply and increasing walking speed from comfortable to fast. To meet ventilatory demand, the control group maintained V_T while increasing RR (RR/V_T= from 7.1 to 11.7 breaths/min/L; Figure 7) and V_E (from 24.1 to 39.2 L/min; Figure 9). This strategy is a reasonable response to an increased exercise stimulus as V_T was already elevated with deep breathing and thus higher V_E was achieved by increasing RR. On the contrary, the group post-stroke reduced V_T and increased RR (RR/V_T= from 22.9 to 26.5 breaths/min/L; Figure 7) increasing V_E (from 22.9 (DC) to 26.5 L/min (DF); Figure 9).

Although individuals post-stroke decreased V_T from comfortable to fast walking while breathing deeply (from 1.45 L to 1.00 L), metabolic needs are likely met as V_E was similar while walking fast and breathing either regularly (26.2 L/min) or deeply (26.5 L/min; Figure 9). While breathing deeply and walking fast (DF), the group post-stroke may have increased the RR/V_T ratio, from 12.8 to 25.7 breaths/min*L, compared to deep breathing and walking at a comfortable pace (DC), and minimizing the postural disturbance and work of breathing. Thus the optimal balance between respiratory and postural drives may be different between groups affecting V_T with increasing postural challenging tasks.

Optimizing oxygen cost could explain the difference in V_T while walking fast and breathing regularly but it does not explain the difference in V_T while breathing deeply. With instructions, individuals post-stroke increased gait speed and depth of breathing, although it may not be cost-efficient. V_T increased from regular (RF) to deep breathing (DF) while walking fast in individuals post-stroke ($p=0.024$) and the control group ($p<0.001$), although V_T was significantly less in individuals post-stroke than the healthy adults (median difference=1.165 L; $p=0.042$) while walking fast and breathing deeply (DF). Thus, it is possible that although the group post-stroke increased V_T it was still within a margin of optimization.

Optimization is likely task-specific and strategies employed vary between individuals. In the control group, V_T increased (6/11) or decreased (5/11) when walking speed was increased from comfortable to fast (Figure 13). In the group post-stroke, V_T was mostly decreased (8/11), with one person who maintained, and two individuals who increased V_T with increasing walking speed.

5.3.3 Tidal volume comparison between groups

Between groups, V_T while walking fast and breathing regularly (RF) was significantly lower in the group post-stroke (median difference=0.286 L; p=0.026). If this difference was due to motor impairment or incoordination of the hemi-paretic respiratory muscles, then V_T while standing and breathing deeply (DST) would be significantly lower in the group post-stroke compared to the control group, which was not supported by our finding (median difference=0.205 L). Thus, reduced V_T, while walking fast, was not likely due to impaired voluntary control of breathing after a stroke.

The difference between groups in V_T while walking fast could be due to the dual role respiratory muscles have to increase V_T as well as maintain postural stability. The magnitude of muscle response for postural stability is associated with velocity of limb movement (Gandevia et al., 2002; Hodges and Gandevia 2000a, 2000b). As tonic activity increases in respiratory muscles to maintain postural stability, rib cage stiffness will also increase and reduce chest wall expansion and V_T. This may explain why V_T was lower in individuals post-stroke while walking fast compared to the control group.

The condition, deep breathing while walking fast, may have been more challenging than all the other conditions. As individuals post-stroke may have difficulty with dual-tasking it is possible that deep breathing while walking fast may have been too difficult. However, individuals post-stroke significantly increased walking speed from comfortable to fast, or depth of breathing from regular to deep, when asked. Canning et al., (2006) found that stride length, step length, and cadence are reduced with dual and triple-tasking, which was not evident in these participants as gait speed did not decrease with deep breathing (0.63 (0.52) m/s) compared to regular breathing (0.46 (0.51) m/s) while walking fast. Stride length (paretic=5 (20) %), step length (paretic=4 (17) %, non-paretic=5 (20) % change) and cadence (paretic=0 (6) %) were increased or maintained

with deep compared to regular breathing while walking fast. Thus, dual tasking or cognition was not likely the source of reduced V_T.

In healthy adults, mean inspiratory flow increases with increasing exercise intensity to achieve a higher tidal volume (Neder et al., 2003; Babb & Rodarte, 1991). If inspiratory or expiratory flow is compromised due to respiratory muscle weakness, work of breathing may increase, resulting in lower tidal volume and higher respiratory rate to meet ventilatory demands. Although it is possible that behaviour of dynamic lung volumes may impact tidal volume, individuals post-stroke had similar tidal volumes while standing, and while walking a comfortable pace.

Furthermore if metabolic demand is different between groups, then ventilatory response may also differ. As individuals post-stroke have been reported to have decreased muscle fiber recruitment and motor control, as well as changes in fiber composition on the paretic side (McKay-Lyons, 2006; Voyvoda, 2012), which may contribute to reduced tidal volume. However, Lanini et al. (2002) demonstrated similar changes in $V_T/PaCO_2$ during hypercapnic / hyperoxic conditions between a group post-stroke and healthy adults despite increased dynamic elastance by compensating with increased motor output during inspiration. Thus, individuals post-stroke are able to increase tidal volume similarly to the control group, as demonstrated during standing conditions, despite metabolic changes and decreased respiratory muscle strength.

5.3.4 Minute ventilation in response to walking speed

Individuals post-stroke with a hemi-paretic gait pattern have a slower comfortable walking pace but higher energy cost (Brouwer et al., 2009) and V_E compared to healthy adults (Da Cunha-Filho et al., 2003). In our study, individuals post-stroke walked slower than the control group, but V_E was similar between groups except while walking fast and breathing deeply (Figure 8). In healthy adults, oxygen consumption increases as walking speed increases (Waters et al., 1988). This was also demonstrated in Figure 8 as V_E increased from comfortable to fast paced walking for both groups. However, V_E increased significantly in the control group ($p<0.001$) when increasing depth of breathing, but the same trend did not reach significance in individuals post-stroke ($p=0.054$).

Although metabolic parameters may be different between individuals post-stroke and healthy adults resulting in higher oxygen cost of walking for individuals post-stroke, the energy

expenditure may be similar (Da Cunha-Filho et al., 2003). In the study conducted by da Cunha-Filho (2003), gait energy expenditure was defined as 'average rate of oxygen consumed during the 5-minute-walk' whereas the oxygen cost was the 'average amount of oxygen consumed per unit distance travelled during the 5-minute walk'. Thus, the rate of oxygen consumption per unit of time may be similar between groups but the amount of oxygen consumed for the equivalent distance is not the same. If we assume that the ventilatory demand is based on the rate of oxygen consumed per unit of time (i.e. 2 minute walking trial), then it is appropriate to compare ventilatory responses between groups. In our study, individuals post-stroke performed tasks for the same amount of time as the control group but were not expected to cover the same distance, as their walking speed was slower.

5.4 Gait adaptations in response to locomotor-respiratory coupling relative to the control group (Hypothesis 3)

As breathing and walking are controlled by central pattern generators that may interact, and locomotor-respiratory coupling has been demonstrated in healthy adults, increased depth of breathing may increase walking speed in individuals post-stroke. We expected walking speed to increase with deeper breathing similarly between groups while walking at a comfortable or fast pace.

5.4.1 Fast compared to comfortable walking speed

When referring to the "comfortable walking speed", we asked the participants to walk at their "normal pace" with respect to their preferred or self-selected pace. The fast walking speed was the "fastest the participant could walk safely". Walking speed correlates with cadence, stride time, stride length, paretic stance time, non-paretic stance time, and double limb support (DLS) time (Roth et al., 1997). With faster walking speeds, Lamontagne and Fung (2004) reported that stride length and cadence increase, while stance time and double limb support time decrease in individuals post-stroke, which was also illustrated in our study. Participants in both groups increased walking speed, as instructed by increasing stride length and decreasing stance time (Figure 11). Cadence (gait cycles/min) increased by 19% in both groups while breathing regularly and by 15% and 19% in the group post-stroke and the control group respectively while breathing deeply (Appendix IV).

5.4.2 Walking pattern response to deep breathing while walking at comfortable pace

Locomotor-respiratory coupling is associated with a fixed cadence to RR ratio (Bramble and Carrier, 1983), while adjusting V_T and stride length. Thus, increasing depth of breathing may increase stride length in order to increase walking speed. As expected, walking speed significantly increased with deep (DC) compared to regular (RC) breathing while walking at a comfortable pace in individuals post-stroke (25% change) but not in the control group (5% change). In order to increase walking speed, individuals post-stroke modified their stride length more than their cadence (16 and 3% increase, respectively; Figure 11), whereas the control group did not change walking pattern. Step velocity increased by 14% and 16% in the paretic and non-paretic foot respectively, while step length increased by 9% and 19%. Thus, increasing V_T may have led to an increase in walking speed, while walking at a comfortable pace.

Furthermore, while walking at a comfortable pace and increasing depth of breathing, we believe the ventilatory drive, enabling deeper breathing, would take priority over the postural drive, as slower walking velocities are associated with greater stability (England et al., 2007).

Thus we suggest that, at a self-selected speed, individuals post-stroke may benefit from deep breathing. To our knowledge, this was the first study to compare depth of breathing and walking in individuals post-stroke. As well, this study consisted of one session of testing, unlike other training programs that provide a program for several weeks. Thus, we note an improvement of 25% increase in walking speed, and a median change of 0.07 m/s. Although it is debatable whether 0.07 m/s constitutes a meaningful change in walking speed (Fritz and Lusardi, 2007; Perrera et al., 2006), the difference may be sufficient to conduct a follow-up study with a training protocol. Teixeira-Salmela et al., (1999) conducted an aerobic training program for 10 weeks, three times per week for 60 to 90 minutes per session and reported a 28.3% change in walking speed (from 0.78 m/s to 0.99 m/s). The percent change is similar to our results although the absolute change is much greater. However, their treatment program is costly in time and money and requires equipment. Conversely, deep breathing as an adjunct to therapy is safe, cost effective, time efficient, and easy to administer with no equipment required (Fritz and Lusardi, 2007). Efficacy could be tested using standardized gait speed tests before and after treatment.

5.4.3 Walking pattern response to deep breathing while walking fast

When comparing regular to deep breathing while walking fast (RF to DF), walking speed did not significantly increase with deep breathing (4% change) in individuals post-stroke or the control group (12% change). In the group post-stroke, considerable variability in individual response (interquartile range (IQR)=27%; range=-11% to 42% change) was observed (Figure 15).

In particular, 4/5 participants in the pilot study increased walking speed with deep breathing while walking fast, whereas 3/6 participants in the subsequent study improved. Differences between the groups include: 1) the harness used for safety on the treadmill; and 2) the range in gait speed of the participants.

In the pilot study, the body harness configuration included the pelvis and the trunk with attachments at the shoulders to the ceiling support, whereas in the subsequent study the harness configuration included only the pelvis, and attachments were near the anterior mid-line and anterior superior iliac spine on the right (Figure 3). The bar that attached the harness to the ceiling support was widened from 44 cm to 85 cm (point of attachment) to avoid interference of the ropes with the pneumotachograph and opto-electronic plethysmography markers on the thorax. This may have had an influence on the perception of support, although no body weight support was given in either experimental set-up and participants were re-assured that the harness would support them if they fell. As well, the ropes attached to the pelvis or the shoulders may have acted as a small perturbation to balance while participants walked fast. However, 8/11 individuals post-stroke had previous experience walking on the treadmill in the virtual environment prior to this study. In addition, despite questioning the validity of the gait speed of two participants, (Control4, Stroke7) on the first walking trial, habituation to the treadmill or novel environment is unlikely the source of the variability as most participants had previous experience on the treadmill.

Although not statistically significant, the control group alters gait pattern more while walking fast and increasing depth of breathing from regular to deep. One person (Control4) had an exaggerated response to increased depth of breathing. For example he decreased gait speed from 0.97 m/s in regular to 0.66 m/s (-0.31 m/s difference) with deep breathing while walking at a comfortable pace, and from 1.72 m/s to 1.13 m/s (-0.59 m/s difference) while walking at a fast pace. This response was more than what was expected by deep breathing. The first condition in

the series was deep breathing while walking fast where his gait speed was slightly faster than regular breathing while walking at a comfortable pace. Thus, this result may be due to poor habituation to the treadmill or his bias of the outcome of the experiment. If removed, the main effect of breathing becomes significant (p=0.010; n=10), as well as the change in fast walking speed with increased depth of breathing (DF-RF; p=0.002; n=10). The comfortable walking speed with increased depth of breathing was not significant (DC-RC; p=0.293; n=10) with this outlier removed. As these outliers made it more difficult to find significant results, the findings we have reported are likely robust.

Walking speed is related to balance deficits and motor impairment. The participants post-stroke who did not improve with deep breathing (n=3/4) walked ≤0.41 m/s, and may optimize postural stability more than chest wall expansion if metabolic needs are being met. Kolar et al., (2010) reported increased diaphragmatic excursion with a reduction in V_T with lower extremity exercise, and Hodges and Gandevia (2000b), suggest that velocity of limbs increases tonic or postural activity of the diaphragm. Thus, postural stability may be challenged by walking fast and breathing deeply, and may be prioritized over any increase in walking speed. If cadence and RR are coupled, but the diaphragm activity is used equally for postural stabilization and inspiratory drive, V_T may not increase sufficiently to stimulate an increase in stride length or walking speed. However, one more participant post-stroke who did not improve fast walking speed with deep breathing, walked 0.93 m/s and had an ankle-supporting orthosis with left hemi-paresis. He increased V_T by 0.42 L but decreased walking speed by 0.11 m/s.

As oxygen consumption increases with walking speed, individuals who walk faster than 0.7 m/s may need greater increases in oxygen supply to increase walking speed (Waters et al., 1988). As depth of breathing increased from regular to deep, the median difference in V_T while walking fast was only 0.06 L (RF to DF), whereas it was 0.50 L while walking at a comfortable pace (RC to DC). It is possible that 0.06 L, although statistically significant, was not sufficient to induce a change in walking speed with deep breathing, whereas 0.50 L was sufficient to increase walking speed at a comfortable pace. Of the participants post-stroke that increased fast walking speed with deep breathing (n=7/11), V_T increased > 0.30 L in six individuals, whereas it decreased in one person. Of the participants post-stroke that decreased or maintained fast walking speed with

deep breathing (n=4/11), V_T increased > 0.30 L in one person, whereas it decreased in three individuals.

CHAPTER 6.0: SUMMARY AND CONCLUSION

6.1 Summary and conclusion

The first hypothesis was that individuals post-stroke may be limited in voluntary or deep breathing compared to our control group, whereas automatic control of breathing or regular breathing would remain intact. Our results suggest that voluntary control of breathing was not impaired in our participants post-stroke as they were able to increase their tidal volume while standing. Tidal volume was increased with the onset of exercise, from standing to fast walking, in both groups however it was significantly lower in the group post-stroke compared to the control group while walking fast.

The second hypothesis was that individuals post-stroke would increase their depth of breathing in response to an exercise stimulus, from comfortable to fast walking, while breathing regularly or deeply. In our study, the control group increased or maintained tidal volume while breathing regularly or deeply, respectively. In contrast, the participants with stroke maintained or decreased tidal volume while breathing regularly or deeply, respectively. Despite different breathing pattern strategies, minute ventilation (V_E) was similar between groups except while walking fast and breathing deeply.

The third hypothesis was that individuals post-stroke would increase walking speed with increased depth of breathing due to locomotor-respiratory coupling. Walking speed did not increase significantly in the control group, while walking either a comfortable or fast pace. However, if the outlier was removed from analysis, the control group improved walking speed with deeper breathing while walking fast. In contrast, the group post-stroke increased walking speed with deeper breathing while walking at a comfortable pace.

Oxygen cost of walking is higher for individuals post-stroke with hemi-paresis leading to a slower preferred walking speed compared to neurologically intact adults. We suggest tidal volumes may also be lower in individuals post-stroke for similar effort in breathing. Compensation for a lower tidal volume results in higher respiratory rates, to maintain V_E and meet metabolic requirements. Comfortable walking speed increases in individuals post-stroke with deep breathing, suggesting that increased tidal volume may influence stride length, resulting in a significant increase in walking speed.

Participants with stroke may prioritize postural stability while meeting metabolic demands, resulting in slower walking speeds and lower tidal volumes compared to the control group while walking at a fast pace. The finding that tidal volume decreases between comfortable and fast walking while breathing deeply suggests that the thoracic muscles may be recruited for stiffening the ribcage as walking speed increased, resulting in decreased chest wall expansion and tidal volume.

It is also possible that if individuals post-stroke were not able to increase depth of breathing and walking speed in order to walk fast while breathing deeply (DF), that they chose to do one or the other. According to the data, two individuals may have chosen this strategy when increasing depth of breathing from regular to deep, while walking fast. As well, 8/11 individuals post-stroke decreased tidal volume when increasing walking speed from comfortable to fast, while breathing deeply.

In conclusion, deep breathing while walking at a comfortable pace (DC) may assist in increasing walking speed in individuals post-stroke. It is a treatment that is quick, easy and does not add to cost or time of rehabilitation programs. Efficacy can be easily monitored with standardized gait speed tests that are commonly used in hospitals and clinics.

6.2 Study limitations

A small sample size was obtained due to strict inclusion and exclusion criteria and difficulty in recruitment for both the experimental and control group. Despite the criteria, the group post-stroke were variable in age, gender, as well as location, time and severity of stroke. However, information on location of stroke was not available for the participants who had previously agreed to be contacted for future research projects. An age and gender-matched control group was recruited to limit the effect of the variability on the results but due to a small sample size the inter-individual variability while walking at a comfortable pace and breathing deeply, disguises a potentially significant result for lower tidal volumes in individuals post-stroke compared to the control group. In addition, a small sample size limits the generalizability of the study as individuals with chronic stroke vary widely in function. This study does not include individuals with obstructive lung disease or individuals who are not ambulatory. In addition, the participants

who were recruited were willing to travel and may be a biased subset of the general population as a whole.

Despite habituation, unfamiliar laboratory equipment and setting may have affected our results. For example we included two individuals (one per group) that may have lower walking speeds during the first walking condition tested. One person in each group had a walking speed in the first walking condition that appears different than the range of walking speeds in the other three conditions. However, the difference was not a clear methodological error to justify removing them from the analysis.

One person in the group post-stroke, Stroke7, walks slower while walking at a comfortable pace and breathing deeply (DC=0.76 m/s) than for any other walking condition (regular breathing, comfortable pace (RC)=1.00 m/s; regular breathing, fast pace (RF)=1.32 m/s; and DF=1.37 m/s). Since this was his first walking condition, it is possible that habituation to the self-paced treadmill was insufficient.

A limitation to this study is that metabolic parameters (oxygen consumption and carbon dioxide production) were not measured, and thus we cannot determine if anaerobic (ventilatory) threshold was reached or comparable between groups in relation to tidal volume or minute ventilation. This makes it difficult to compare ventilatory demand between groups

Furthermore, it would have been helpful to have 1) static lung volumes and capacities, 2) respiratory muscle strength, 3) dynamic operating lung volumes, and 4) the activity of inspiratory and expiratory muscles during exercise testing. This would have helped disclose underlying disease, respiratory muscle weakness, and its functional consequences.

As well, information on tonic and dynamic muscle activity using electromyography on postural muscles would have been useful to determine if tidal volume was affected by increased postural drive while walking fast and breathing deeply.

6.3 Significance and clinical implications

Deep breathing while walking is a technique that is commonly used with surgical patients in the hospital to improve tidal volume during their hospital stay. Stroke rehabilitation has only started to incorporate aerobic exercise training but historically, it has not included assessment or

treatment of the respiratory status. The participants post-stroke in this study live in the community and were not participating in a rehabilitation program. Walking speed is associated with community ambulation (Perry et al., 1995) thus increased walking speed may facilitate an increase in physical activity and community ambulation (Lord et al., 2004). Deep breathing is a technique that is easy to teach and an exercise that individuals can continue at home or in the community after rehabilitation has ended. Walking speed is easy to measure, and can be used to monitor the effectiveness of the treatment.

This research also highlights that individuals post-stroke in our study were not limited with deep breathing while standing, but difficulty with deep breathing increased with the speed of walking. Thus, tidal volumes were lower in individuals post-stroke while walking fast compared to the control group.

6.4 Future research

Results from this study indicate that further research in this area is justified. Firstly, muscle activity (electromyography) information regarding postural muscles while walking in conjunction with respiratory data would provide insight into the optimization between ventilatory and postural drives in individuals post-stroke. Secondly, this study could also be repeated while on a stationary bike compared to treadmill walking to minimize postural instability and increase ventilatory response. As many individuals in stroke rehabilitation use a stationary bike, this could provide useful information regarding respiratory response to exercise based on mode of exercise. Lastly, a study could be conducted in the clinic using standardized 10-m gait speed tests and a training protocol for deep breathing while walking either at comfortable or fast pace. In this way, every person with a stroke participating in a rehabilitation program could be tested, although the sensitivity of the test would be lower than the laboratory equipment used in this study.

CHAPTER 7.0: BIBLIOGRAPHY

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Appendix I: Ethics modifications

Protocol differences between 2011 (CRIR 569-1210) and 2013 (CRIR 646-0811)

CRIR 569-1210 Protocol:	**CRIR 646-0811** Protocol:
standing trials for 30 sec	standing trials for 60 sec
	Vital capacity condition (2 breaths) added
Pneumotachograph – chest mounted	Pneumotachograph – head mounted with light elastic support to ceiling
No OEP	89 OEP markers on thorax
Foot switches in shoes with wires at the back	no foot switches
Vicon markers on entire body according to Plug-In gait model	Vicon markers on lower limbs; pelvis markers (RASI, LASI, RPSI, LPSI) overlap with OEP markers
Vicon processing and analysis for lower limbs	Vicon processing and analysis for feet (2011 (re-analysed) & 2013 participants)
Supporting harness on pelvis and chest and attached to ceiling bar from shoulders (ceiling bar 50 cm long / 44 cm between right and left harness attachments)	Supporting harness on pelvis only and attached to ceiling bar from pelvis (ceiling bar 90 cm long / 85 cm between right and left harness attachments)
Total time for experiment (2.5 hours)	Total time for experiment (3.5 hours)

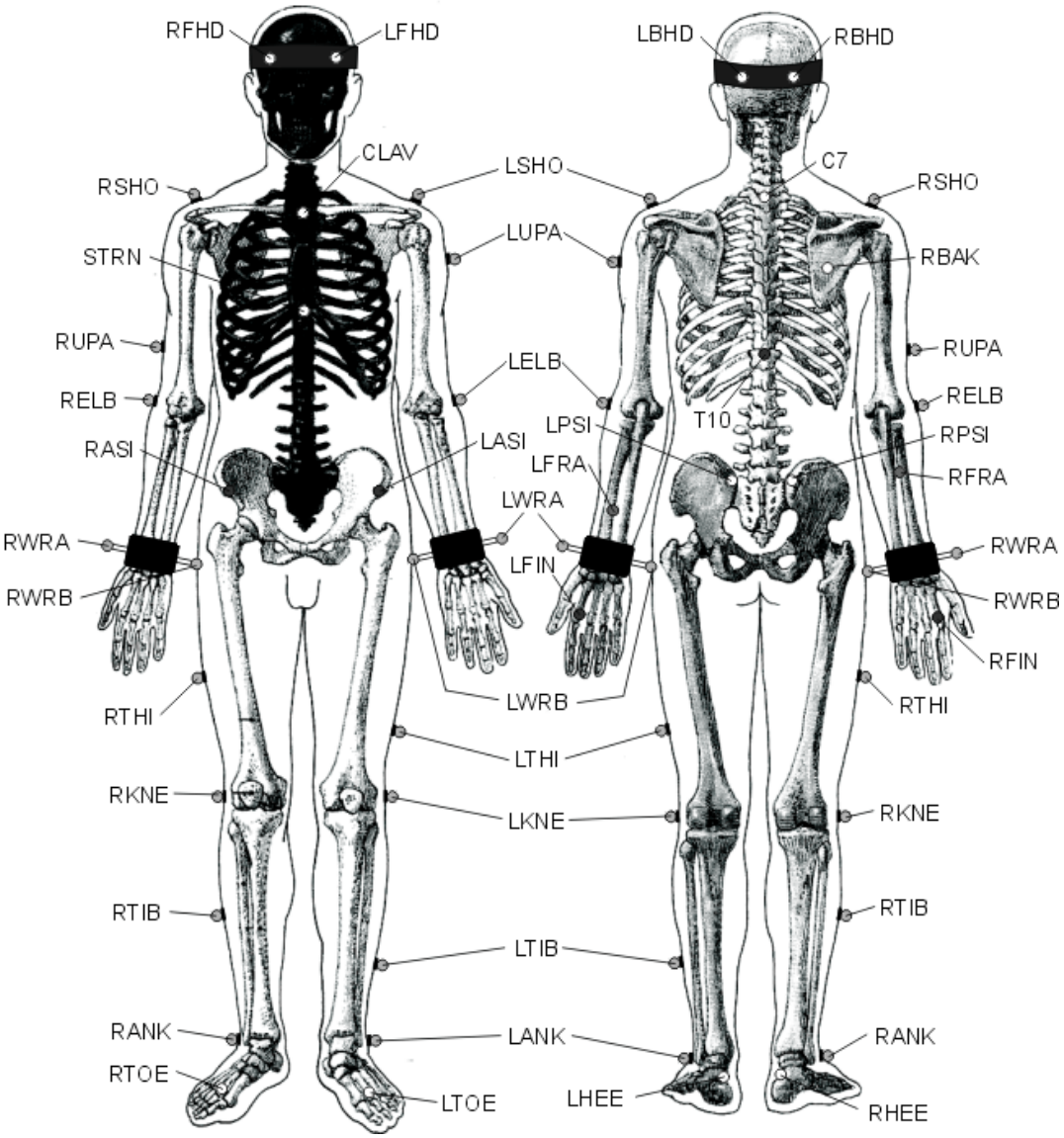
CRIR: Centre for Interdisciplinary Research in Rehabilitation of Greater Montreal; OEP: optoelectronic plethysmography

Ethics modifications approved April, 2013 (CRIR 646-0811)

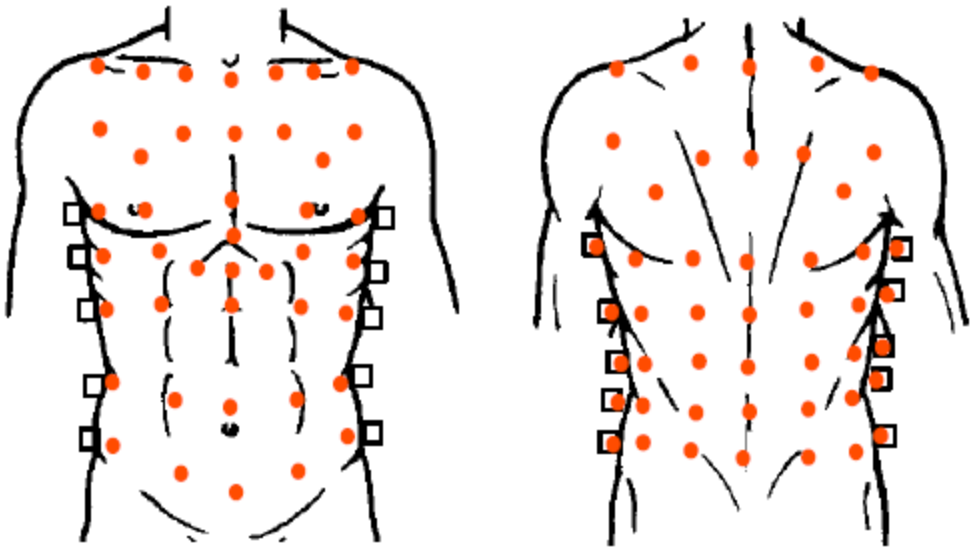
	CRIR 569-1210 accepted May 19, 2011	**CRIR 646-0811 accepted April, 2013**
Title of project:	The Coupling between Respiratory and Locomotor Patterns Post-stroke.	The interaction between breathing and walking post-stroke.
Sample size:	10	16
Inclusion criteria:	Age of participants: 45-75	Age of participants: 35-75
Exclusion criteria:		Body Mass Index (BMI) > 30 added
Baseline measures:	Interview with participant: Age, type and anatomical location of stroke (if available), time since stroke onset, the use of walking aids	Interview and chart review of participant: Age, type and anatomical location of stroke (if available), time since stroke onset, the use of walking aids, and previous scores on functional baseline measures such as 6 minute walk test, 10 m walk test, and Chedoke-McMaster leg and foot Impairment.
	Resting heart rate and resting blood pressure	Resting heart rate and resting blood pressure, pulse oximetry and Borg rating of perceived exertion and dyspnea scale (added).
		Pulmonary function test (added)
		6 minute walk test (added)
		Chedoke-McMaster leg and foot Impairment if not recently done or available from the chart (added)
		International Physical Activity Questionnaire (added)

CRIR: Centre for Interdisciplinary Research in Rehabilitation of Greater Montreal

Appendix II: Marker placement



Plug-in-Gait model for Vicon motion analysis system (2011=whole body; 2013=lower limbs and pelvis). Thoracic markers: CLAV= clavicle; STRN=sternum; Cervical7, T10= Cervical7 and T10 spinous process; RBAK= right shoulder blade. The following markers have an equivalent left side: RFHD= Right front of head; RBHD=right back of head; RSHO=right shoulder; RUPA= right upper arm; RELB= right elbow; RFRA= right forearm; RWRA, RWRB=right wrist (A) and (B); RFIN= right finger; (pelvis) RASI, RPSI= right anterior and posterior superior iliac spine; (lower limbs) RTHI=right thigh; RKNE=right knee; RTIB=right tibia; RANK= right ankle; RTOE=right great toe; RHEE= right heel. Only the RANK, RTOE, and RHEE were analysed.



Optoelectronic plethysmography (OEP) marker placement (BTS SpA, 2011).The OEP is used to measure the motion of the chest wall and to calculate regional lung volumes. Although this data was collected in 2013, it was not processed or analyzed for the purpose of this thesis. Markers along the bottom of the torso overlap with the Vicon lower limb model. The Vicon and OEP motion analysis systems both use passive reflective markers.

Appendix III: Respiratory parameters

Respiratory Parameters: absolute values in standing conditions

Variables	Regular breathing (RST)		Deep breathing (DST)		Vital capacity (VC)	
	Stroke	**Control**	**Stroke**	**Control**	**Stroke**	**Control**
V_T, L	0.67 (0.30)	0.73 (0.55)	1.48 (0.72)	1.69 (0.99)	2.85 (2.03)	2.89 (1.19)
RR, cycles/min	20.4 (6.0)	15.4 (8.1)	11.7 (6.4)	9.5 (4.5)	6.4 (2.6)	5.8 (1.8)
V_E, L/min	12.1 (7.6)	11.7 (3.8)	17.4 (10.6)	17.7 (10.9)	16.7 (14.5)	16.9 (7.2)
T_I (s)	1.29 (0.26)	1.70 (0.94)	2.23 (0.69)	2.50 (1.29)	3.92 (2.65)	4.46 (1.87)
T_E (s)	1.69 (0.61)	2.32 (1.47)	2.94 (2.47)	3.71 (1.55)	5.81 (1.69)	5.63 (2.09)
T_{TOT}, s	2.97 (0.91	3.99 (2.29)	5.21 (3.03)	6.32 (2.66)	9.53 (4.05)	10.31 (2.80)
V_T/T_I, L/s	0.47 (0.26)	0.49 (0.14)	0.70 (0.40)	0.63 (0.12)	0.66 (0.82)	0.60 (0.20)
V_T/T_E, L/s	-0.33 (0.23)	-0.35 (0.11)	-0.49 (0.34)	-0.51 (0.50)	-0.49 (0.36)	-0.48 (0.36)
PIF, L/s	0.65 (0.29)	0.69 (0.15)	0.93 (0.47)	0.99 (0.56)	1.34 (1.19)	1.65 (0.97)
PEF, L/s	-0.52 (0.29)	-0.63 (0.37)	-0.91 (0.33)	-1.00 (0.66)	-1.38 (0.76)	-2.63 (1.75)
Duty cycle	0.42 (0.03)	0.40 (0.07)	0.43 (0.08)	0.45 (0.09)	0.42 (0.11)	0.42 (0.16)

V_T: tidal volume; RR: respiratory rate; V_E: minute ventilation; T_I: inspiratory time; T_E: expiratory time; T_{TOT}: total breath time; V_T/T_I: mean inspiratory flow; V_T/T_E: mean expiratory flow; PIF: peak inspiratory flow; PEF: peak expiratory flow; RST: regular breathing, standing; DST: deep breathing, standing; VC: vital capacity.

Respiratory Parameters: absolute values in walking conditions for individuals post-stroke

	Stroke			
Variables	**RC**	**DC**	**RF**	**DF**
V_T, L	0.91 (0.43)	1.45 (1.43)	0.94 (0.33)	1.00 (1.48)
RR, cycles/min	24.3 (9.9)	16.6 (17.7)	28.7 (7.3)	24.7 (13.2)
V_E, L/min	22.7 (4.5)	22.9 (7.8)	26.2 (6.7)	26.5 (6.3)
T_I, s	1.00 (0.39)	1.95 (1.46)	0.90 (0.20)	1.27 (0.56)
T_E, s	1.48 (0.60)	2.08 (2.08)	1.21 (0.36)	1.44 (0.82)
T_{TOT}, s	2.48 (1.02)	4.17 (3.56)	2.15 (0.51)	2.47 (1.51)
V_T/T_I, L/s	0.88 (0.20)	0.89 (0.45)	1.04 (0.31)	0.99 (0.60)
V_T/T_E, L/s	-0.62 (0.16)	-0.66 (0.21)	0.72 (0.16)	0.74 (0.26)
PIF, L/s	1.18 (0.23)	1.34 (0.52)	1.37 (0.40)	1.45 (1.12)
PEF, L/s	-0.93 (0.30)	-1.22 (0.27)	1.05 (0.35)	1.23 (0.70)
Duty cycle	0.41 (0.02)	0.44 (0.03)	0.41 (0.04)	0.43 (0.04)

V_T: tidal volume; RR: respiratory rate; V_E: minute ventilation; T_I: inspiratory time; T_E: expiratory time; T_{TOT}: total breath time; V_T/T_I: mean inspiratory flow; V_T/T_E: mean expiratory flow; PIF: peak inspiratory flow; PEF: peak expiratory flow; RC: regular breathing, comfortable pace; RF: regular breathing, fast pace; DC: deep breathing, comfortable pace; DF: deep breathing, fast pace.

Respiratory Parameters: absolute values in walking conditions for the control group

	Control			
Variables	**RC**	**DC**	**RF**	**DF**
V_T, L	1.01 (0.33)	2.08 (0.65)	1.23 (0.32)	2.16 (0.57)
RR, cycles/min	20.8 (4.27)	12.1 (3.3)	22.9 (11.0)	20.5 (10.4)
V_E, L/min	21.2 (7.0)	24.1 (6.4)	28.9 (12.4)	39.2 (12.5)
T_I (s)	1.32 (0.27)	2.17 (0.61)	1.07 (0.53)	1.39 (0.51)
T_E (s)	1.72 (0.39)	2.84 (1.16)	1.40 (0.67)	1.79 (0.83)
T_{ToT}, s	2.96 (0.63)	5.31 (1.52)	2.67 (1.18)	3.08 (1.81)
V_T /T_I, L/s	0.77 (0.24)	0.93 (0.30)	1.11 (0.42)	1.22 (0.45)
V_T /T_E, L/s	-0.58 (0.22)	-0.71 (0.37)	-0.84 (0.37)	-1.25 (0.45)
PIF, L/s	1.03 (0.34)	1.32 (0.63)	1.48 (0.53)	1.77 (0.76)
PEF, L/s	-0.91 (0.49)	-1.49 (0.64)	-1.47 (0.58)	-2.27 (0.92)
Duty cycle	0.43 (0.05)	0.43 (0.06)	0.44 (0.04)	0.46 (0.05)

V_T: tidal volume; RR: respiratory rate; V_E: minute ventilation; T_I: inspiratory time; T_E: expiratory time; T_{TOT}: total breath time; V_T/T_I: mean inspiratory flow; V_T/T_E: mean expiratory flow; PIF: peak inspiratory flow; PEF: peak expiratory flow; RC: regular breathing, comfortable pace; RF: regular breathing, fast pace; DC: deep breathing, comfortable pace; DF: deep breathing, fast pace.

Percent change in respiratory parameters with deep (DST) compared to regular (RST) breathing while standing; and standing (RST) compared to fast walking (RF) while breathing regularly.

	Stroke		**Control**	
Variables	**(DST-RST)/RST**	**(RF-RST)/RST**	**(DST-RST)/RST**	**(RF-RST)/RST**
V_T	93 (78) %	42 (45) %	96 (62) %	52 (100) %
RR	-44 (40) %	40 (36) %	-30 (38) %	76 (98) %
V_E	25 (68) %	116 (67) %	32 (91) %	165 (117) %
T_I	73 (76) %	-31 (16) %	45 (62) %	-37 (38) %
T_E	67 (72) %	-30 (14) %	33 (60) %	-46 (30) %
T_{ToT}	80 (74) %	-31 (14) %	41 (67) %	-43 (32) %
V_T / T_I	14 (61) %	111 (70) %	31 (56) %	137 (114) %
V_T / T_E	33 (92) %	113 (64) %	34 (118) %	166 (127) %
PIF	43 (32) %	113 (60) %	54 (65) %	109 (101) %
PEF	60 (53) %	106 (54) %	34 (95) %	112 (69) %
Duty cycle	2 (19) %	1 (3) %	6 (14) %	6 (8) %

V_T: tidal volume; RR: respiratory rate; V_E: minute ventilation; T_I: inspiratory time; T_E: expiratory time; T_{TOT}: total breath time; V_T/T_I: mean inspiratory flow; V_T/T_E: mean expiratory flow; PIF: peak inspiratory flow; PEF: peak expiratory flow; RST: regular breathing, standing; RF: regular breathing, fast pace; DST: deep breathing, standing. The percent change in respiratory parameter was calculated by the formulas above.

Percent change of respiratory parameters for the group post-stroke while walking

Stroke				
Variables	**(RF-RC)/RC**	**(DF-DC)/DC**	**(DC-RC)/RC**	**(DF-RF)/RF**
V_T	5 (15) %	-6 (28) %	65 (117) %	45 (61) %
RR	15 (16) %	25 (64) %	-24 (48) %	-14 (36) %
V_E	20 (14) %	20 (27) %	11 (31) %	4 (13) %
T_I	-12 (19) %	-24 (41) %	55 (96) %	26 (65) %
T_E	-14 (8) %	-22 (33) %	23 (90) %	18 (73) %
T_{ToT}	-12 (13) %	-21 (30) %	35 (114) %	25 (60) %
V_T / T_I	15 (19) %	20 (26) %	3 (37) %	4 (23) %
V_T / T_E	18 (19) %	17 (26) %	27 (33) %	2 (23) %
PIF	19 (16) %	16 (11) %	11 (27) %	15 (30) %
PEF	15 (15) %	7 (39) %	34 (28) %	20 (39) %
Duty cycle	0 (6) %	-1 (9) %	7 (16) %	-1 (16) %

V_T: tidal volume; RR: respiratory rate; V_E: minute ventilation; T_I: inspiratory time; T_E: expiratory time; T_{TOT}: total breath time; V_T/T_I: mean inspiratory flow; V_T/T_E: mean expiratory flow; PIF: peak inspiratory flow; PEF: peak expiratory flow; RC: regular breathing, comfortable pace; RF: regular breathing, fast pace; DC: deep breathing, comfortable pace; DF: deep breathing, fast pace. The percent changes in respiratory parameters were calculated by the formulas above.

Percent change of respiratory parameters for the control group while walking

Control				
Variables	**(RF-RC)/RC**	**(DF-DC)/DC**	**(DC-RC)/RC**	**(DF-RF)/RF**
V_T	22 (14) %	2 (18) %	110 (78) %	75 (51) %
RR	20 (39) %	50 (52) %	-44 (33) %	-23 (26) %
V_E	38 (21) %	62 (47) %	19 (24) %	29 (27) %
T_I	-9 (39) %	-28 (19) %	76 (77) %	41 (46) %
T_E	-21 (24) %	-30 (26) %	51 (114) %	30 (37) %
T_{ToT}	-16 (27) %	-32 (23) %	78 (88) %	35 (37) %
V_T/T_I	32 (17) %	51 (44) %	16 (16) %	27 (30) %
V_T/T_E	46 (29) %	55 (58) %	24 (48) %	40 (26) %
PIF	35 (19) %	28 (34) %	29 (44) %	33 (40) %
PEF	40 (18) %	38 (31) %	57 (42) %	66 (33) %
Duty cycle	7 (12) %	4 (9) %	4 (20) %	3 (9) %

V_T: tidal volume; RR: respiratory rate; V_E: minute ventilation; T_I: inspiratory time; T_E: expiratory time; T_{TOT}: total breath time; V_T/T_I: mean inspiratory flow; V_T/T_E: mean expiratory flow; PIF: peak inspiratory flow; PEF: peak expiratory flow; RC: regular breathing, comfortable pace; RF: regular breathing, fast pace; DC: deep breathing, comfortable pace; DF: deep breathing, fast pace. The percent changes in respiratory parameters were calculated by the formulas above.

Appendix IV: Gait parameters

Gait parameters: absolute values in walking conditions for the group post-stroke

	Stroke (paretic)			
Variables	**RC**	**DC**	**RF**	**DF**
Gait speed, m/s	0.38 (0.31)	0.47 (0.29)	0.46 (0.51)	0.63 (0.52)
Stride length, m	0.61 (0.40)	0.66 (0.29)	0.76 (0.53)	0.79 (0.47)
Stride time, s	1.58 (0.39)	1.50 (0.43)	1.34 (0.33)	1.35 (0.39)
Cadence, cycles/min	38.13 (8.91)	40.25 (10.40)	44.95 (11.09)	44.62 (12.63)
2 min WD, m	45 (37)	56 (35)	55 (62)	75 (62)
Stance time, s	1.14 (0.35)	1.05 (0.36)	0.92 (0.32)	0.86 (0.34)
DLS, s	0.73 (0.28)	0.66 (0.31)	0.49 (0.29)	0.49 (0.28)
SLS, s	0.35 (0.21)	0.33 (0.20)	0.25 (0.20)	0.22 (0.17)
Step velocity, m/s	0.92 (0.49)	1.05 (0.38)	1.05 (0.53)	1.16 (0.45)
Step length, m	0.45 (0.18)	0.47 (0.12)	0.50 (0.26)	0.52 (0.22)
Swing time, s	0.46 (0.08)	0.45 (0.10)	0.43 (0.10)	0.42 (0.12)
	Stroke (non-paretic)			
Variables	**RC**	**DC**	**RF**	**DF**
SLS, s	0.36 (0.13)	0.33 (0.11)	0.25 (0.10)	0.25 (0.11)
Step velocity, m/s	0.89 (0.58)	1.09 (0.44)	1.26 (0.93)	1.38 (0.83
Step length, m	0.40 (0.23)	0.42 (0.20)	0.51 (0.34)	0.55 (0.28)
Swing time, s	0.41 (0.05)	0.39 (0.04)	0.36 (0.04)	0.38 (0.03)

WD: walk distance; DLS: double limb support; SLS: single limb support; RC: regular breathing, comfortable pace; RF: regular breathing, fast pace; DC: deep breathing, comfortable pace; DF: deep breathing, fast pace.

Gait parameters: absolute values in walking conditions for the control group

	Control (left)			
Variables	**RC**	**DC**	**RF**	**DF**
Gait speed, m/s	1.01 (0.35)	1.12 (0.35)	1.54 (0.19)	1.58 (0.27)
Stride length, m	1.19 (0.30)	1.19 (0.25)	1.39 (0.22)	1.48 (0.24)
Stride time, s	1.14 (0.16)	1.09 (0.09)	0.92 (0.10)	0.93 (0.11)
Cadence, cycles/min	52.69 (7.38)	55.17 (4.47)	65.45 (7.02)	64.87 (8.54)
2 min WD, m	120 (42)	134 (43)	184 (23)	189 (33)
Stance time, s	0.76 (0.11)	0.70 (0.07)	0.58 (0.05)	0.59 (0.10)
DLS, s	0.36 (0.09)	0.32 (0.08)	0.25 (0.04)	0.25 (0.08)
SLS, s	0.18 (0.05)	0.16 (0.05)	0.12 (0.01)	0.12 (0.04)
Step velocity, m/s	1.91 (0.31)	1.87 (0.54)	2.42 (0.25)	2.60 (0.35)
Step length, m	0.71 (0.16)	0.72 (0.13)	0.83 (0.11)	0.87 (0.12)
Swing time, s	0.39 (0.04)	0.38 (0.05)	0.34 (0.04)	0.33 (0.02)

WD: walk distance; DLS: double limb support; SLS: single limb support; RC: regular breathing, comfortable pace; RF: regular breathing, fast pace; DC: deep breathing, comfortable pace; DF: deep breathing, fast pace.

Percent change of gait parameters between conditions in individuals post-stroke (paretic and non-paretic legs)

Stroke (paretic)				
Variables	(DC-RC)/RC	(DF-RF)/RF	(RF-RC)/RC	(DF-DC)/DC
Gait speed	25 (26) %	4 (27) %	52 (37) %	29 (39) %
Stride length	16 (24) %	5 (20) %	26 (28) %	12 (28) %
Stride time	-3 (11) %	0 (6) %	-16 (10) %	-13 (11) %
Cadence	3 (12) %	0 (6) %	19 (14) %	15 (15) %
2 min WD	25 (26) %	4 (26) %	53 (37) %	30 (39) %
Stance time	-5 (13) %	-1 (8) %	-18 (10) %	-15 (13) %
DLS	-8 (15) %	-1 (14) %	-24 (15) %	-20 (17) %
SLS	-7 (18) %	-4 (17) %	-28 (21) %	-20 (18) %
Step velocity	14 (15) %	1 (13) %	20 (29) %	14 (20) %
Step length	9 (15) %	4 (17) %	14 (24) %	5 (18) %
Swing time	-1 (6) %	2 (4) %	-6 (6) %	-7 (5) %
Stroke (non-paretic)				
Variables	(DC-RC)/RC	(DF-RF)/RF	(RF-RC)/RC	(DF-DC)/DC
SLS	-11 (15) %	-3 (12) %	-24 (20) %	-21 (19) %
Step velocity	16 (22) %	5 (19) %	35 (25) %	21 (30) %
Step length	19 (26) %	5 (20) %	24 (20) %	10 (27) %
Swing time	0 (5) %	2 (2) %	-6 (6) %	-6 (5) %

WD: walk distance; DLS: double limb support; SLS: single limb support; RC: regular breathing, comfortable pace; RF: regular breathing, fast pace; DC: deep breathing, comfortable pace; DF: deep breathing, fast pace. The percent changes in gait parameters were calculated by the formulas above.

Percent change of gait parameters between conditions in healthy individuals (left leg).

Control (left)				
Variables	(DC-RC)/RC	(DF-RF)/RF	(RF-RC)/RC	(DF-DC)/DC
Gait speed	5 (8) %	12 (25) %	46 (61) %	49 (47) %
Stride length	3 (18) %	6 (12) %	30 (33) %	26 (22) %
Stride time	-1 (3) %	-4 (13) %	-16 (12) %	,-16 (13) %
Cadence	1 (3) %	4 (13) %	19 (16) %	19 (18) %
2 min WD	5 (18) %	12 (25) %	46 (61) %	50 (47) %
Stance time	-2 (2) %	-6 (13) %	-17 (14) %	-19 (14) %
DLS	-4 (4) %	-12 (18) %	-25 (18) %	-28 (21) %
SLS	-3 (9) %	-13 (22) %	-24 (16) %	-29 (17) %
Step velocity	4 (15) %	8 (17) %	30 (46) %	35 (33) %
Step length	3 (15) %	5 (10) %	23 (25) %	21 (15) %
Swing time	0 (4) %	-1 (11) %	-12 (8) %	-11 (12) %

WD: walk distance; DLS: double limb support; SLS: single limb support; RC: regular breathing, comfortable pace; RF: regular breathing, fast pace; DC: deep breathing, comfortable pace; DF: deep breathing, fast pace. The percent changes in gait parameters were calculated by the formulas above.