OXYGEN UPTAKE KINETICS AT THE ONSET OF EXERCISE AND CARDIORESPIRATORY FITNESS IN FRAIL ELDERLY PEOPLE

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ABSTRACT

Introduction Current methods of measuring cardiorespiratory (CR) fitness are not appropriate for use with frail, older people primarily due to exercise intensity and mode. The lack of a direct/submaximal measurement creates problems with longitudinal monitoring and evaluation of interventions. A positive relationship between the rate of change of oxygen uptake at the onset of exercise (VO_2 kinetics) and CR fitness (VO_2max.) has previously been demonstrated; VO_2 kinetics in combination with a suitable exercise mode (self-paced walking) may provide the solution. The purpose of this thesis was two-fold. 1) To investigate VO_2 kinetics using a novel exercise mode (self-paced walking). 2) To examine VO_2 kinetics at the onset of self-paced walking as an indicator of an aspect of CR fitness in frail, older people using the following criteria: feasibility; validity; reproducibility; sensitivity to a physical training intervention.

Methods VO_2 and walking speed were measured during 3 minutes of comfortable self-paced walking in young (Y) (N=17; median age 23 (20-29) years) and healthy elderly (HE) (N=8; median age 80 (76-87) years) volunteers and groups of patients recovering from a hip fracture (HF) (N=15; median age 81 (72-91) years) or stroke (ST) (N=66; median age 74 (49-87) years). Each individual attempted 3 walks per study visit. Y, HE and HF groups were tested on two occasions. The ST group were allocated to exercise training (N=32) or relaxation classes (N=34). VO_2 kinetics were assessed 3 times (before, after and 4 months following a thrice weekly 12 week intervention). On study visits that achieved defined criteria, (3 walks of 3 minutes; constant walking speed; steady state VO_2 in the final 30s; moderate intensity exercise

(RER<1.0)) the ensemble average VO_2 response of the 2nd and 3rd walks was fitted with a monoexponential model to derive a time constant, Mean Response Time (MRT).

Results ***Feasibility*** On 214/277 study visits individuals completed 3 walks of 3 minutes (77%). Participants maintained a constant walking speed of moderate intensity and achieved steady state VO_2 conditions within 3 minutes on 127/214 visits. 114/127 visits (41% of 277) were adequately described using a monoexponential model (82% Y; 44% HE; 53% HF; 32% ST). ***Validity*** A group comparison of MRT demonstrated content validity (Y 20s; HE 37s; HF 52s; ST 42s, mean values, Visit 1). Criterion-related concurrent validity (MRT versus VO_2max. in Y and HE) and predictive validity of MRT were not demonstrated. ***Reproducibility*** There was no evidence of a significant systematic bias from Visit 1 to Visit 2 (Y, HE and HF). The Standard Error of the Measurement (SEM) of the MRT was 4.9s in the Y group, 4.4s in the HE group and 7.0s for the HF group. Limits of agreement of MRT for the HF group were -23 to 30s. ***Training intervention*** Poor tolerance of the study methodology in the frailer stroke patients compromised evaluation of the training intervention. A before and after training comparison of MRT was possible in 4 stroke patients. A training related reduction in MRT (49s to 35s (mean values, N=4)) was evident.

Conclusion As the measure was acceptable to 'fitter' patients (for whom current measures are unsuitable) the feasibility threshold for VO_2 kinetics testing has been lowered. However, the inability of frailer study participants to achieve feasibility criteria and inconclusive validity questions the applicability of this measure to those

for whom it is intended – frail, older people. A measure for the frailest frail still eludes us.

CONTENTS

LIST OF PUBLICATIONS

FULL PAPERS

GE Mead, CA Greig, I Cunningham, SJ Lewis, S Dinan, DH Saunders, C Fitzsimons, A Young. STARTER: STroke: A Randomised Trial of Exercise or Relaxation (in preparation for submission to British Medical Journal).

Claire F. Fitzsimons, A. Hamish R.W. Simpson, Archie Young, Carolyn A. Greig. Oxygen uptake kinetics measured at the onset of comfortable self-paced walking in elderly women after hip fracture (in preparation for submission to European Journal of Applied Physiology).

ABSTRACTS

Fitzsimons, C F, Carnwath, A, McLellan, S, Young, A, Greig, C A. The effect of exercise intensity on oxygen uptake kinetics in healthy young women. J Physiol. 565P, C36. 2005.

Fitzsimons CF, Simpson AHRW, Young A, Greig CA. Oxygen uptake kinetics in very elderly hip fracture survivors measured at the onset of comfortable self-paced walking. Journal of Aging and Physical Activity.12 (3): 411-412 (2004).

Fitzsimons, Claire F., Greig, Carolyn A., Forsythe, Lynsey, Saunders, David H., Young, Archie, Simpson, A. Hamish R.W. Is self-paced walking suitable for studies of oxygen uptake kinetics in frail elderly women? Proceedings of the 8th Annual Congress European College of Sport Science, July 2003, Salzburg, P10N-05.

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Declaration and Ethical Approval

I declare this thesis has been composed by myself and the books and papers cited were all consulted by me personally, except where otherwise stated.

I declare that the work described in this thesis is original work and has been performed solely by Claire Fitzsimons, with the exception of the STARTER trial. (See pages 93 & 94, Chapter 5 (Feasibility) & separate declaration in Appendix 5, page 242 for details of the Candidate's roles in the STARTER team).

I declare that the work included in this thesis has not been submitted for any other degree or professional qualification.

ETHICAL APPROVAL:

All studies in this thesis were conducted with the approval of the Lothian Research Ethics Committee and all volunteers gave written informed consent.

ABBREVIATIONS

[ ]	denotes concentration
31P-NMRS	31P-nuclear magnetic resonance spectroscopy
95% C.I.	95% Confidence Interval
A1	amplitude of the VO_2 response
ATP	adenosine triphosphate
$C_{(a-v)}O_2$	arteriovenous oxygen content difference
C_{aO_2}	oxygen content of arterial blood
C_{MvO_2}	oxygen content of muscle venous blood
COPD	chronic obstructive pulmonary disease
COV	Coefficient of Variation
E.C.G.	Electrocardiogram
EMS	Elderly Mobility Scale
FIM	Functional Independence Measure
IQR	inter quartile range
MRT	Mean Response Time
mVO_2	skeletal muscle oxygen consumption
NIRS	Near Infrared Spectroscopy
O_2def	oxygen deficit
P_aO_2	arterial oxygen tension, or partial pressure
PCO_2	partial pressure of carbon dioxide
PCr	phosphocreatine
PO_2	partial pressure of oxygen

PO_2m	microvascular oxygen pressure
$PvCO_2$	carbon dioxide tension of mixed venous blood
PvO_2	oxygen tension of mixed venous blood
Q	blood flow
Q_M	muscle blood flow
RER	respiratory exchange ratio
RM ANOVA	Repeated measures Analysis of Variance
SD	Standard Deviation
SEM	Standard error of the measurement
Sy.x	standard deviation of the residuals
τ	Tau
VCO_2	carbon dioxide production/min corrected for TPD conditions
V_E	Expired volume/min
VO_2	oxygen consumption/min corrected for STPD conditions
VO_2B	baseline VO_2 value
$VO_2max.$	Maximum oxygen uptake
$\Delta VO_2(ss)$	steady state increment of VO_2

CHAPTER 1: Introduction

Requirement of an acceptable measure of cardiorespiratory fitness for frail older people

Unsuitability of conventional measures of cardiorespiratory fitness

Potential to use self-paced walking as a mode of exercise

Oxygen Uptake Kinetics

Scotland's population is growing older. As a result, the number of individuals with chronic disease and disabilities will increase dramatically. The development of effective interventions for the maintenance of physical independence in frail elderly people is therefore crucial both in terms of alleviating the burden of health care and maintaining/improving quality of life. Physical fitness training represents one such intervention, but there are few data available for the frailest and oldest members of our community, (particularly for cardiorespiratory training). One reason for the lack of information is the lack of an appropriate test with which to assess the effectiveness of cardiorespiratory training or changes in cardiorespiratory fitness. Cardiorespiratory fitness is related to the ability of the body to take in and deliver oxygen. Performance of such exercise therefore depends on the functional state of the respiratory, cardiovascular and skeletal muscle systems (Balady et al, 2000).

Three significant concerns exist when considering the application of current methodologies for measuring cardiorespiratory fitness to frail older people.

a) The gold standard measurement of cardiorespiratory fitness is maximum oxygen uptake (VO_2max.) obtained during exhaustive exercise using continuous progressively increasing work rates. "Maximal" exercise may not provide a reliable measure of cardiorespiratory fitness because of such factors as volunteer motivation and the criteria used to terminate the test (Greig, 2002). The intensity of exercise required may render this procedure uncomfortable.

Many daily functional tasks do not require that an individual utilize their maximum oxygen uptake, and therefore a submaximal measure of an aspect of cardiorespiratory fitness may better reflect the true exertion required for daily functional tasks.

b) Current methodologies make use of cycle or treadmill ergometry, which may be unfamiliar to many older people. It is impractical to subject many frail, older men and women to treadmill testing, especially if they use walking aids or suffer from musculoskeletal comorbidity or mobility problems.

c) The increased prevalence of chronotropic medications invalidates heart-rate based methods for evaluating cardiorespiratory fitness. The prevalence of atrial fibrillation in old age also makes heart-rate based methods less useful. A further argument against heart-rate based predictors of VO_2max. is the high inter-individual variability of maximal heart rate.

The problem of how to measure cardiorespiratory fitness in frail individuals in a way which does not necessarily involve maximal exercise but which still allows for both intra- and inter- individual comparisons, still remains. Current measures have two main problems – firstly the method/mode of exercise and secondly the outcome measure.

1. The Method/Mode of Exercise

As the most frequently used modes of exercise testing (treadmill/cycle ergometry) are unsuitable, a different exercise mode is needed. An alternative exercise mode that has been used in previous research is self-paced walking. Bassey et al., 1976 used self-paced walking as a mode of exercise for fitness testing in both young (19-21 years) and elderly (64-66 years) men. The variation in lap-by-lap walking speed was not greater than +/-6%. It is not clear if self-paced walking would serve as a suitable exercise mode for frailer, older individuals, such as those after a hip fracture or stroke. Self-paced walking does however offer an appealing mode of exercise – it may involve submaximal exercise; does not require sustained high intensity exercise (and is ethically reassuring that comfortable self-paced walking does not require any higher exercise intensity than used in every day life); traditional laboratory settings and equipment are avoided and individuals may use their usual walking aids.

2. The Outcome Measure

While self-paced walking as a mode of exercise is appealing with regard to older people, unfortunately the outcome measure Bassey et al used isn't (the relationship between walking speed and heart rate while walking was defined by linear regression and individual standardized heart rates obtained by interpolation). An alternative outcome measure is needed. Recent advances in lightweight, breath-by-breath portable gas analysers have allowed the measurement of oxygen uptake within more functionally relevant environments. As portable breath-by-breath gas analysers enable gas exchange to easily be measured during non-steady state conditions the rate of oxygen uptake at the onset of exercise (oxygen uptake (VO_2) kinetics) can be investigated.

There is a growing body of literature relating to the measurement of oxygen uptake kinetic response to exercise in young, healthy elderly and clinical populations using standard ergometry as the mode of exercise. All individuals for whom standard ergometry is unsuitable are excluded from such measurements.

Oxygen uptake kinetics

The oxygen uptake response to constant-load exercise

At the onset of submaximal constant work rate exercise, the oxygen uptake during the transition from rest to exercise follows a pattern of increase that is usually completed within several minutes and has been shown to increase exponentially (Linnarsson, 1974; Whipp, 1971; Whipp & Wasserman, 1972). The oxygen uptake response to comfortable self-paced walking is shown for a young, healthy woman in Figure 1a (walking began at time 0 on the x axis). Although work-rate, and therefore energy demand increase immediately in a square wave fashion, there is a delay before steady state oxygen uptake is achieved.

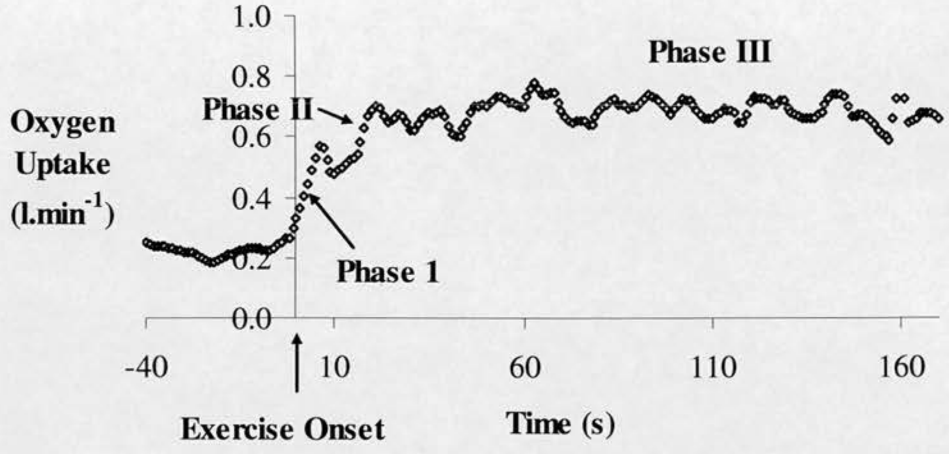


Figure 1a. Oxygen Uptake response to self-paced walking

When oxygen uptake is measured at the onset and during exercise at the lungs, three distinct phases of the gas exchange process have been identified. The first phase (Phase I) is an abrupt increase in oxygen consumption, typically within the first one or two breaths after exercise begins, which gives way after 15-20 seconds to a subsequent Phase II, an exponential increase in oxygen consumption which lasts two to three minutes, and finally Phase III, a steady state or slow drift upwards of oxygen consumption depending on whether the exercise is below or above the anaerobic threshold (Linnarsson, 1974; Whipp et al., 1982; Sietsema et al., 1986; Whipp and Ward, 1990; Brunner-La Rocca et al., 1999). Oxygen uptake increases rapidly in the first one or two breaths due mainly to an increase in cardiac output that pumps mixed venous blood towards the lungs. Deoxygenated blood from the exercising muscles has not yet reached the lungs. Phase I is therefore thought to be 'cardiodynamically' mediated. This was first suggested in 1913 by Krogh and Lindhard (see also Linnarsson, 1974; Whipp et al., 1982; Reybrouck, 2000). Following the short transit delay from the exercising muscles (Phase I), venous blood with a lower oxygen content arrives at the lungs. This lower oxygen content signals the initiation of Phase II (Behnke et al., 2005, page 142). Oxygen consumption then increases exponentially to meet the energy demands of the work-load until steady state (Phase III) conditions are achieved (if the exercise is of moderate intensity).

The dynamics of Phase II (that is the time constant/tau value of Phase II) are thought to closely reflect oxygen consumption at the level of the muscle. Evidence for this was provided by Barstow and Mole´ (1987) who used computer simulations of leg muscle blood flow and oxygen consumption to illustrate that pulmonary VO_2 would increase in 2 phases after the start of exercise. They concluded that in humans, the VO_2 kinetics during Phase II could be used to estimate the kinetics of muscle oxygen consumption. There was still however, a lack of 'real' human evidence that this assumption was correct.

Oxygen consumption of the muscle can be described using the Fick principle (Jones and Poole, 2005, page 13; Koga et al., 2005, page 53; Ward, 1999, pages 117-119). The Fick principle provides one way of measuring muscle oxygen consumption by measuring muscle blood flow and the difference between the oxygen contents of arterial and venous blood (Koga et al., 2005, page 53). The Fick principle is described using the equation -

$VO_2 = Q_T \times (CaO_2 - CvO_2)$ (Jones and Poole, 2005, page 13)

where Q_T corresponds to tissue blood flow, CaO_2 arterial oxygen content and CvO_2 venous oxygen content. Tissue blood flow, Q_T will depend on cardiac output, the amount of vasodilation, and also the pressure difference across the muscle tissue (Jones and Poole, 2005, page 13). The difference between $CaO_2 - CvO_2$, (that is arterial oxygen content minus venous oxygen content) gives a measure of the amount of oxygen that has been removed from arterial blood for use by the muscle. Blood flow can be measured by the thermodilution method or by Doppler ultrasound. The difference in oxygen content between arterial and venous blood can be determined by analysis of the oxygen content of samples of both arterial and venous blood.

Grassi et al., 1996 used the Fick principle in humans to compare oxygen consumption of the leg with that measured at the mouth. By using constant infusion thermodilution techniques to measure leg blood flow, along with measurements of arteriovenous oxygen content difference across the leg, Grassi et al. were able to measure the oxygen consumption of the leg. Following an initial short delay of 10-15 seconds when VO_2leg increased only slightly, VO_2leg then increased exponentially. Similarly, when oxygen uptake was measured at the lungs, there was an initial delay phase which was followed by an exponential increase of oxygen uptake towards steady state. Grassi et al concluded that in the transition from light to moderate exercise, VO_2leg kinetics and VO_2 kinetics as measured at the lungs showed similar temporal profiles. Bangsbo et al., 2000 used a similar approach to Grassi et al., 1996 to measure muscle oxygen kinetics, also in humans. Although the exercise was of higher intensity the findings of Bangsbo et al., 2000 supported the work of Grassi et al., 1996 with oxygen consumption of the exercising muscles shown to increase after a short delay.

Although oxygen consumption of the muscle can be measured using the Fick principle, this approach is invasive, uncomfortable to the volunteers and may not include all the muscle involved in a given exercise (Ward, 1999, page 117). In addition, no insight is gained into levels of metabolic controls, for example phosphocreatine (PCr). In 1968 Piiper et al. measured oxygen consumption of the gastronemius muscle of dogs with intact blood supplies in combination with phosphate levels. Piiper et al. successfully demonstrated a close correlation between a fall in PCr levels and an increase in the level of muscle oxygen consumption in dogs. Additionally, in 1985 Mahler demonstrated oxygen consumption of frog tetanised muscle was monoexponential and changed in parallel with levels of Cr and PCr.

The direct proportionality between the fall of PCr levels and muscle oxygen consumption in animals provided the basis for similar experiments in humans using a technique called ^{31}P-MRS (Magnetic Resonance Spectroscopy) to measure the in vivo breakdown of phosphocreatine (PCr) in the muscle. After the onset of exercise, limited ATP stores are maintained by PCr breakdown by both the creatine kinase pathway and by oxidative phosphorylation (Jones and Poole, 2005 page 4; Rossiter et al., 1999). Investigation of PCr breakdown therefore provides an indirect measure of skeletal muscle oxygen consumption. Rossiter et al. (1999) reported the first study which utilised a non-invasive technique to investigate the relationship between oxygen consumption measured at the mouth and changing phosphate levels in humans in the same muscle group. Using a whole body NMR (Nuclear Magnetic Resonance) spectrometer, Rossiter et al., 1999 were able to simultaneously measure both the kinetics of the decrease in PCr in the muscle and the kinetics of pulmonary oxygen uptake. This group found the decrease in PCr was monoexponential with no delay (the mean time constant was 35 seconds (range 20 – 64 seconds, N=6)). The increase in oxygen uptake towards steady state measured at the lungs had two phases. When Phase II only was modelled, the time constant was found to match the time constant of the PCr breakdown in the muscle (mean time constant of pulmonary VO_2 was 36 seconds, range 20 – 68 seconds). On the basis of these data, Rossiter et al., 1999 proposed that the kinetics of the Phase II VO_2 response measured at the lungs correspond to those of PCr breakdown and therefore reflect the kinetics of muscle oxygen consumption.

Another methodology that has been used to study skeletal muscle oxygen uptake in animals is to use an intravascular phosphorescence quenching technique to measure the microvascular oxygen pressure (PO_2m) directly, i.e. the oxygen response within a contracting muscle. Behnke et al., 2001 used this approach to determine PO_2m in rat muscle. Following the delivery of an electrical stimulation, PO_2m decreased exponentially (time constant 22 seconds), after a delay of ~19 seconds. As this quenching technique cannot be used in humans, DeLorey et al., 2003 and Grassi et al., 2003 used a further means to investigate muscle oxygen consumption directly. They used the technique of near-infrared spectroscopy (NIRS) which enabled the sampling of deoxyhemoglobin, oxyhemoglobin and total haemoglobin and myoglobin levels each second. NIRS measures the changes in oxygen content of the blood and therefore provides an estimation of changes in intramuscular oxygenation status and oxygen extraction (and unlike ^{31}P-MRS can be used at rest or during aerobic or ischemic exercise). DeLorey et al., 2003 compared gas exchange measurements made at the mouth during constant work rate moderate intensity cycling exercise, with local muscle deoxygenation in the quadriceps muscles using NIRS. After an initial delay of approximately 13 seconds after exercise onset, muscle deoxygenation increased to a new exercise steady state level. The time constant of deoxyhemoglobin (10 +/- 3 seconds after 13 seconds delay) was notably faster than the time constant of pulmonary VO_2 (30 +/- 8 seconds). Similarly, Grassi et al., 2003 found the Phase II VO_2 time constant correlated significantly with a MRT (time constant plus delay) of the changes in deoxygenated haemoglobin and myoglobin concentration.

The current evidence therefore suggests that the Phase II time constant of oxygen uptake measured at the lungs correlates with indicators of muscle oxygen consumption (levels of phosphates; markers of blood oxygenation levels e.g. deoxyhaemoglobin). Thus pulmonary VO_2 kinetics (Phase II) may be used as an indicator of skeletal muscle VO_2 kinetics.

The entire ventilatory response will be closely regulated to ensure adequate oxygen levels in exercising muscles and also to ensure the waste products of metabolism are removed. Ventilation is closely regulated by the acidity of the blood as the result of metabolism (Wasserman et al., 1999, page 42). Ventilation increases to remove the CO_2 added by metabolism and therefore maintain pH homeostasis. For moderate intensity exercise, increased ventilation regulates arterial PCO_2 and pH at approximately resting values. The ventilatory increase is usually achieved at low or moderate work rates by an increase in tidal volume and also, to a lesser extent, by breathing frequency.

Exponential modelling of VO_2

The exponential time course of pulmonary VO_2 in response to moderate intensity exercise can be characterised using nonlinear regression techniques by the following regression equation (Whipp et al., 1982):

$$Y = VO_2(b) + A1 * (1\text{-}e^{-[(t\text{-TD1})/\text{K1}]})$$

where Y is VO_2 at a time t; $VO_2(b)$ is the baseline VO_2 value; A1 is the asymptotic amplitude for the exponential response; TD1 and K1 are the time delay of the response and the time constant respectively.

MRT value

If the exponential model is constrained to fit the VO_2 data from the beginning of exercise (i.e. Phase I and II; TD1=0), having as its baseline the resting value and as its asymptote the end exercise VO_2 value, then the time constant is known as the Mean Response Time (MRT) (Whipp & Ward, 1990). The MRT characterises the relative rate at which the Phase III steady state of VO_2 is attained. The MRT is therefore the time taken to achieve 63% of the overall VO_2 response (Linnarsson, 1974).

Oxygen Deficit

As the MRT is determined from the entire non steady state oxygen uptake response and is constrained to begin at the start of exercise, it provides a measure of the total oxygen actually utilised and therefore can be used to calculate the oxygen deficit for exercise of moderate intensity (Whipp, 1971). Figure 1b shows the oxygen uptake response and corresponding oxygen deficit in response to comfortable self-paced walking. The area between the dashed line and the VO_2 uptake profile represents the oxygen deficit.

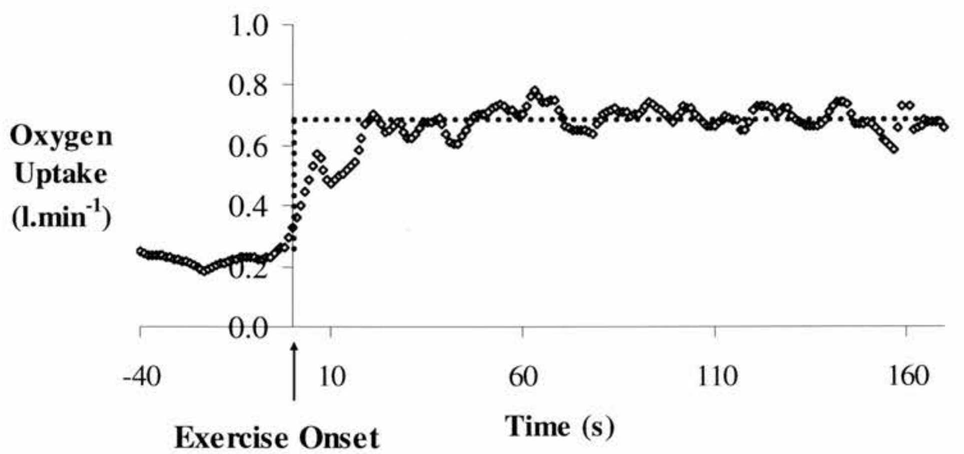


Figure 1b. Oxygen uptake response to self-paced walking and the oxygen deficit

The MRT of oxygen uptake and the steady state increment of VO_2 from the pre-exercise levels to Phase III levels ($\Delta VO_2(ss)$) can be used to calculate the oxygen deficit:

$$O_2def = \Delta VO_2(ss) \cdot MRT \qquad \text{(Whipp, 1971)}$$

If VO_2 kinetics slow (i.e. larger MRT) a larger oxygen deficit occurs and therefore a greater degree of disturbance within cells (increased lactic acid, decreased PCr, accumulation of lactate and protons and a greater utilisation of the intramuscular glycogen reserves, all factors which result in reduced exercise tolerance) (Jones and Poole, 2005, page 20). Faster VO_2 kinetics and lower oxygen deficit will result in less muscle fatigue and will improve exercise tolerance.

Tau value

An alternative approach to modelling the oxygen uptake response to constant load exercise is to exclude the Phase I proportion of the response (i.e. exclude the first 15-20s). In this instance the time constant is known as a tau (τ) value (i.e. 63% of the Phase II VO_2 response). While the MRT provides a measure of total oxygen utilised, the tau value (Phase II only) permits insight into oxygen consumption at the level of the muscle as it excludes the 'cardiodynamic' Phase I portion of the VO_2 response.

Goodness of Fit of the monoexponential model to the oxygen uptake data

Variations in breathing from breath to breath can produce fluctuations in gas exchange. Lamarra et al (1987) stated "The kinetic response to exercise can be viewed as the sum of two components: 1) an underlying physiological signal and 2) "noise" whose magnitude proves to be much greater in some subjects than in others". A large amount of 'noise' can make it difficult to estimate the kinetic parameters. Before modelling the oxygen uptake data the physiological signal can be enhanced and the amount of noise reduced by removing any anomalous or unusual breaths (Lamarra et al., 1987). Lamarra et al., 1987 recommended the removal of any breath whose oxygen uptake was greater than +/- 3 standard deviations from the local mean and Rossiter et al., 2000 recommended the removal of any values greater than +/- 4 standard deviations of the local mean. This process removes any breaths caused by swallowing, coughing, sighing etc. which are considered not to be reflective of underlying kinetics (Lamarra et al., 1987). The individual breath by breath responses for the exercise repetitions should then be interpolated on a second by second basis and time aligned to the onset of exercise. Interpolating the data on a second by second basis enables a further method of enhancing the physiological signal to be incorporated into the modelling process - ensemble averaging the oxygen uptake response from more than one exercise bout. The ensemble average response produces an overall response for each individual, again reducing noise, and increasing the confidence of parameter estimation (Ozyener et al., 2001).

How well the monoexponential model fits the oxygen uptake data can be assessed by four methods: R^2 values; Sy.x values, the signal to noise ratio and 95% confidence intervals (95% C.I.).

R^2 values

R^2 provides an indication of how well a model fits data. As it is a fraction between 0.0 and 1.0 it has no units. R^2 is obtained from the sum of the squares of the distances of the points from the exponential curve fitted through the data (www.graphpad.com). When R^2 is 1.0 the model fits the data well and the curve fitted through the data comes very close to all the data points (www.graphpad.com; Bland, 2000).

Sy.x values

Sy.x is the standard deviation of the vertical distances of the data points from the best-fit line (www.graphpad.com). The distance of a point from the best-fit line is called a residual. Sy.x is therefore the standard deviation of the residuals (www.graphpad.com). The units of Sy.x are the same units as for the y axis (i.e. $l.min^{-1}$).

Signal to Noise Ratio

The fit of the model can be assessed with percentage signal to noise ratios, i.e. the standard deviation of the residual values (Sy.x) divided by the amplitude of the VO_2 response x 100 (Lamarra et al., 1987). The signal to noise ratio can be increased by either increasing the signal (i.e. increasing the amplitude of the oxygen uptake response) or by decreasing the noise. Removing errant breaths and ensemble averaging of more than one exercise repetition will also help to decrease noise.

95% Confidence Intervals

Confidence in the estimation of the parameter values can be characterised by a 95% confidence interval, i.e. a range of values for a parameter estimate which have 95% probability of containing the true value of the parameter (Lamarra et al., 1987 Rossiter et al., 1999).

The combination of self-paced walking as a mode/method of exercise testing with VO_2 kinetics as the outcome measure may provide an indicator of an aspect of cardiorespiratory fitness (i.e. a functional evaluation of oxidative metabolism) for use with frail, older people. This approach may therefore enable an aspect of cardiorespiratory fitness to be assessed in individuals for whom all current measures are unsuitable.

Aims

The aims of this thesis are to: 1) Investigate VO_2 kinetics using a novel exercise mode (self-paced walking); 2) Examine VO_2 kinetics at the onset of self-paced walking as an indicator of an aspect of cardiorespiratory fitness in frail, older people after a hip fracture or stroke. To address these aims five research questions have been investigated.

Research Questions

1. Are oxygen uptake kinetics at the onset of exercise **intensity independent** within a range of 'moderate' exercise intensities?

2. Is the measurement of a time constant of oxygen uptake at the onset of 'comfortable' self-paced walking a **feasible** measure in healthy young and elderly volunteers and in frail patient groups?

3. Is the measurement of a time constant of oxygen uptake at the onset of 'comfortable' self-paced walking a **valid** measure of an aspect of cardiorespiratory fitness?

4. Is the measurement of a time constant of oxygen uptake at the onset of 'comfortable' self-paced walking a **reproducible** measurement?

5. Is the measurement of a time constant of oxygen uptake at the onset of 'comfortable' self-paced walking sensitive to a **physical training intervention** in frail individuals?

CHAPTER 2: Volunteers

Volunteer groups – pilot study, young, healthy elderly, hip fracture and stroke

Preliminary Volunteers:

Two women (aged 41 years (height 165cm, weight 64kg); aged 23 years (height 165cm, weight 65kg) and one man (aged 36 years (height 178cm, weight 70kg)

Pilot Volunteers:

		N	Age (years)	Height (cm)	Mass (kg)
Women	Young	**5**	22 (19-23)	168 (162-177)	61 (54-65)
Women	Healthy Elderly	**5**	78 (77-80)	157 (153-164)	55 (47-59)

Moderate Intensity Study volunteers:

	N	Age (years)	Height (cm)	Mass (kg)
Women	**6**	23 (21-24)	165.5 (160-169)	60.5 (56-69)

Group One – Young men and women:

	N	Age (years)	Height (cm)	Mass (kg)
	17	23.0 (20-29)	170.5 (161-195)	63.0 (54-101)
Women	11	23.0 (20-29)	168 (161-173)	61.0 (54-75)
Men	6	22.5 (20-26)	181.8 (178-195)	74.6 (69-101)

Group Two - Healthy Elderly men and women:

	N	Age (years)	Height (cm)	Mass (kg)
	8	79.5 (76-87)	168.8 (159-180)	71.3 (63-85)
Women	4	78.5 (76-85)	167 (159-169)	66.5 (63-73)
Men	4	80.5 (78-87)	174 (167.5-180)	74 (73-85)

Group Three - Hip Fracture:

	N	Age (years)	Height (cm)	Mass (kg)
Women	**15**	81.0 (72-91)	159.0 (149-170)	59.0 (43-75)

Group Four – Stroke:

	N	Age (years)	Mass (kg)
	66	73.9 (49-87)	69.5 (45-120)
Women	30	74.1 (54-87)	64.8 (50-94)
Men	36	71.5 (49-85)	74.8 (45-120)

Values are presented as median (range)

CHAPTER 3: Preliminary and Pilot Work

Volunteers

Methodology

1. What effect upon the kinetics of oxygen uptake will a seated/standing start to the walking test have?
2. How long does a volunteer need to recover from a walking repeat?
3. How long should the walking test be for steady state oxygen uptake conditions to be achieved?
4. Can self-paced 'free' walking be described as 'constant load' exercise in young and healthy elderly volunteers?
5. Is the amplitude of the oxygen uptake response from self-paced walking sufficient to be modelled using conventional moderate intensity exponential modelling techniques?
6. What is the minimum number of walking repeats necessary to optimise the physiological signal?

Discussion

Summary

Before the main research questions of the thesis were addressed preliminary and pilot studies were conducted. The preliminary study investigated how to approach the measurement of oxygen uptake kinetics at the onset of self-paced walking. Preliminary data were collected from three volunteers (N=3) to explore practical, experimental and modelling considerations in relation to self-paced walking and oxygen uptake kinetics.

On the basis of the findings of the preliminary study a methodology was suggested. The preliminary findings were from young volunteers. Older individuals may not have responded in a comparable manner. A pilot study was carried out to enable the methodology to be considered (practical, experimental, modelling considerations) in a group of older women. The methodology was investigated in five healthy elderly women (over 75 years) and also in a group of five healthy young women prior to the main research questions of the thesis being addressed.

The preliminary study is presented first in its entirety and then the findings of the pilot study are presented.

A) Preliminary Study

Introduction

Objectives of Preliminary Study

- **Practical Considerations**

i) Seated or standing start?

When the exercise mode is self-paced walking the opportunity exists to starts the exercise bout from either a seated or standing start. There are practical reasons to begin from a standing start: A frail, older person may have difficulty getting out of a chair, subsequently the oxygen cost would be high. A frail individual may suffer postural hypotension and vestibular problems, which may prevent or make unsafe immediate walking from a seated position. Alternatively, if the exercise begins from a seated start, the test is easier as the volunteer spends less time on their feet. The first practical objective of the preliminary work was therefore to investigate the impact of a transfer from seated to standing on VO_2 (the magnitude of the VO_2 disturbance; the time an individual would need to stand to enable VO_2 to return to pre-exercise VO_2 levels; the ease with which a healthy, young individual could stand for the required duration for VO_2 levels to stabilise).

ii) Recovery between walking bouts

The time taken for recovery between walking bouts on a study visit is an important factor when the feasibility and length of test session is considered. The second practical objective of the preliminary work was to determine the time taken for ventilation, gas exchange and heart rate to return to pre-exercise levels following a bout of comfortable walking.

- **Experimental Considerations**

i) 'Constant-load' exercise

In an attempt to replicate the conventional exercise mode for investigation of gas exchange kinetics (square wave exercise transitions created under laboratory ergometry conditions), self-paced walking was required to be of constant pace. The ability of the volunteers to achieve 'constant-load' exercise conditions was assessed by calculation of the coefficient of variation, % (COV) of individual lap speeds, thus providing a measure of the extent of variation in walking speed within each exercise bout. Bassey et al., 1976 used self-paced walking as a mode of exercise for fitness testing in both young (19-21 years) and elderly (64-66 years) men. The variation in lap-by-lap walking speed was not greater than +/-6%. The first experimental objective of the preliminary work was to investigate the variability between individual lap speeds.

ii) Duration of walking exercise

A necessary prerequisite of the modelling process is the achievement of steady state oxygen uptake conditions within an exercise bout. The oxygen uptake data at the end of exercise should be no longer correlated with time (Mettauer et al., 2000). By minimising the duration of the walking test, the feasibility of the measure with frail, older people is maximised. The second experimental objective was to assess the required duration of the walking test in order to achieve steady state oxygen uptake.

- **Modelling Considerations**

The preliminary data were analysed using a conventional moderate intensity monoexponential model. This represents the most basic approach to exponential modelling of gas exchange kinetics.

i) Amplitude of the VO_2 response

As VO_2 kinetics at the onset of self-paced walking haven't been considered before, it was unknown if the oxygen uptake response to walking would be sufficient for mathematical modelling. The first modelling objective of the preliminary study was to assess if the amplitude of the oxygen uptake response to self-paced walking was sufficient to be modelled.

ii) Ensemble Averaging

Averaging of the oxygen uptake response to two or more exercise bouts has been shown to reduce 'noise' and increase the confidence of parameter estimation (Ozyener et al., 2001). A balance was needed between optimum number of repeats needed to enhance the physiological signal while ensuring the protocol was not too long for the volunteers' tolerance.

Volunteers

The **preliminary study** volunteers (Table 3a) were defined as 'healthy' (Health Questionnaire, Appendix 2, page 218) according to previously described exclusion criteria (Greig et al., 1994, Appendix 2, page 222) which were designed both for safety and to define freedom from diseases which might alter exercise performance data interpretation. None of the volunteers was involved in regular physical training (defined as any planned, structured and repetitive bodily movement done to improve or maintain one or more component of physical fitness (U.S. Department Health and Human Services (USDHHS) Report, 1996)). Informed consent was obtained prior to participating in the study (Appendix 2, page 224).

Volunteers	Sex	Age	Height (cm)	Mass (kg)
1	F	41	165	64
2	F	23	165	65
3	M	36	178	70

Table 3a. Characteristics of **preliminary study** volunteers (N=3)

Methodology

Preliminary volunteers were tested on three separate occasions (Visits 1, 2 and 3).

The purpose of the first visit was to assess whether the walking test should commence from a seated or standing start. Each volunteer was asked to sit comfortably while wearing the Metamax 3B system for two minutes. When instructed, the individual was asked to stand and remain standing for one minute.

This procedure was repeated three times (a total of four measurements). Ventilatory rate and fractional concentrations of oxygen and carbon dioxide were measured on a breath-by-breath basis using a Metamax 3B ambulatory metabolic measurement system, (Cortex Biophysik).

On Visits Two and Three each volunteer was asked to walk around a 33.3m elliptical marked course for three minutes in response to a standard instruction asking them to walk at their 'comfortable' pace. The volunteer was asked to sit quietly for three minutes, then stand for two minutes, walk comfortably for three minutes and then stand again for two minutes. This series was repeated three times (with rest periods of three minutes between each walk), on each of two separate occasions (i.e. four walks on each visit).Ventilation and gas exchange were measured continuously. Heart rate was recorded continuously using a Polar heart rate monitor. The time taken to complete each lap of the circuit was recorded. Walking speed and the coefficient of variation of the individual lap speeds were calculated retrospectively.

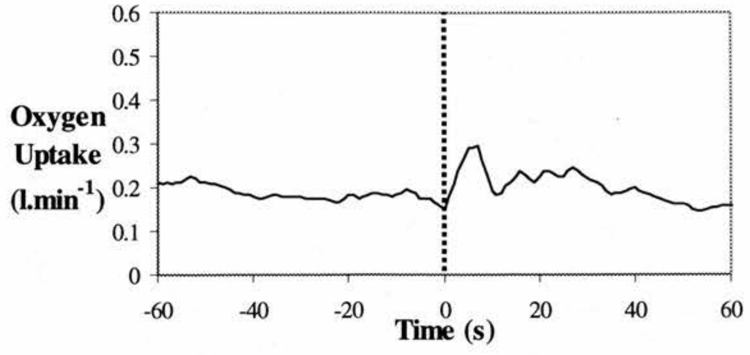
Results

- **Practical Considerations**

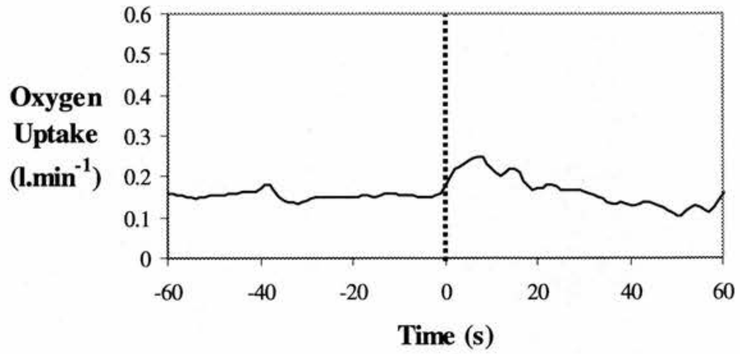
i) Seated or standing start?

VO_2 increased on standing from a seated position. Figure 3a presents the increase in oxygen uptake when the individual was asked to stand (preliminary volunteer 1 – A; 2 – B; 3 – C). The oxygen uptake data are presented as an average of four sit to stand repetitions for each volunteer. The duration of the standing effect was approximately 10-12 seconds.

A)



B)



C)

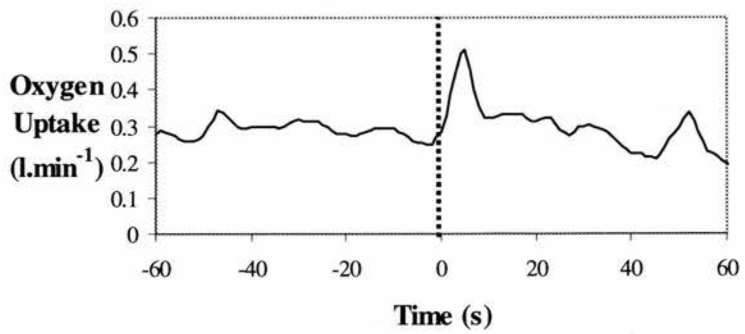


Figure 3a. Oxygen Cost ($l.min^{-1}$) of standing presented as an average of four sit to stand repeats for preliminary volunteers 1 (A), 2 (B) and 3 (C). The dashed line represents when the volunteer was asked to stand.

ii) Recovery between walking bouts

On the second and third visits preliminary volunteers performed the walking tests. Ventilation and gas exchange and heart rate had returned to pre-exercise levels within three minutes of seated rest between walking bouts. Two minutes of standing was reported as "uncomfortable" and "more difficult than walking for three minutes".

- **Experimental Considerations**

i) 'Constant-load' exercise

The ability of preliminary study volunteers to achieve and maintain an invariant walking pace was considered on Visits One and Two. The coefficient of variation, % (COV) for individual lap speeds was calculated. The median (and range) COV for the three preliminary study volunteers is presented in Table 3b for Visits One and Two.

		Preliminary Study		
		Volunteer One	**Volunteer Two**	**Volunteer Three**
COV (%)				
Visit One	Median	1.5	2.4	3.6
	Range	1.2 – 1.9	2.2 – 4.3	1.8 – 8.4
Visit Two	Median	1.3	2.6	3.0
	Range	1.1 – 3.9	2.0 – 6.2	1.5 – 3.4

Table 3b. Coefficient of Variation (%) of individual lap speeds for preliminary study volunteers

ii) Duration of walking exercise

Would steady state oxygen uptake conditions to be achieved in three minutes?

The ability of the volunteers to achieve steady state oxygen uptake during a necessarily short exercise bout (3 minutes) was considered by calculating the slope of the final 30 seconds of oxygen uptake data for each of four walks on two occasions for the three preliminary study volunteers. The slope of the final 30 seconds of oxygen uptake data did not differ significantly from zero indicating steady state oxygen uptake conditions were achieved within three minutes (Table 3c).

	Volunteer	1		2		3	
	Visit	1	2	1	2	1	2
Walk	Mean VO_2 of last 30s ($l.min^{-1}$)	0.74	0.63	0.72	0.99	0.51	0.56
1	B value ($l.min^{-1}.sec^{-1}$)	0.000	-0.001	0.002	0.001	0.000	0.000
	No. of data points	13	13	9	9	11	12
	p value	0.93	0.63	0.41	0.79	0.87	0.61
	Mean VO_2 of last 30s ($l.min^{-1}$)	0.71	0.64	0.71	0.98	0.49	0.53
2	B value ($l.min^{-1}.sec^{-1}$)	0.000	-0.001	-0.006	0.006	0.000	-0.001
	No. of data points	14	14	9	10	12	12
	p value	0.99	0.53	0.11	0.21	0.86	0.64
	Mean VO_2 of last 30s ($l.min^{-1}$)	0.65	0.62	0.77	1.02	0.51	0.54
3	B value ($l.min^{-1}.sec^{-1}$)	-0.001	-0.006	0.003	0.002	0.000	0.000
	No. of data points	14	13	9	10	11	11
	p value	0.59	0.14	0.28	0.29	0.76	1.00
	Mean VO_2 of last 30s ($l.min^{-1}$)	0.69	0.66	0.75	0.95	0.46	0.55
4	B value ($l.min^{-1}.sec^{-1}$)	0.000	-0.002	0.000	-0.001	0.000	0.000
	No. of data points	14	14	8	10	11	12
	p value	0.91	0.44	0.99	0.48	0.84	0.72

Table 3c. Mean VO_2, slope (B value, $l.min^{-1}.sec^{-1}$), number of data points and p value (to assess if the slope differs significantly from zero) of the final 30 seconds of oxygen uptake for each of the preliminary study volunteers on walks 1-4

- **Modelling Considerations**

i) Amplitude of the VO_2 response

Figure 3b shows the amplitude of the VO_2 response to self-paced walking was sufficient to be fitted with a monoexponential model.

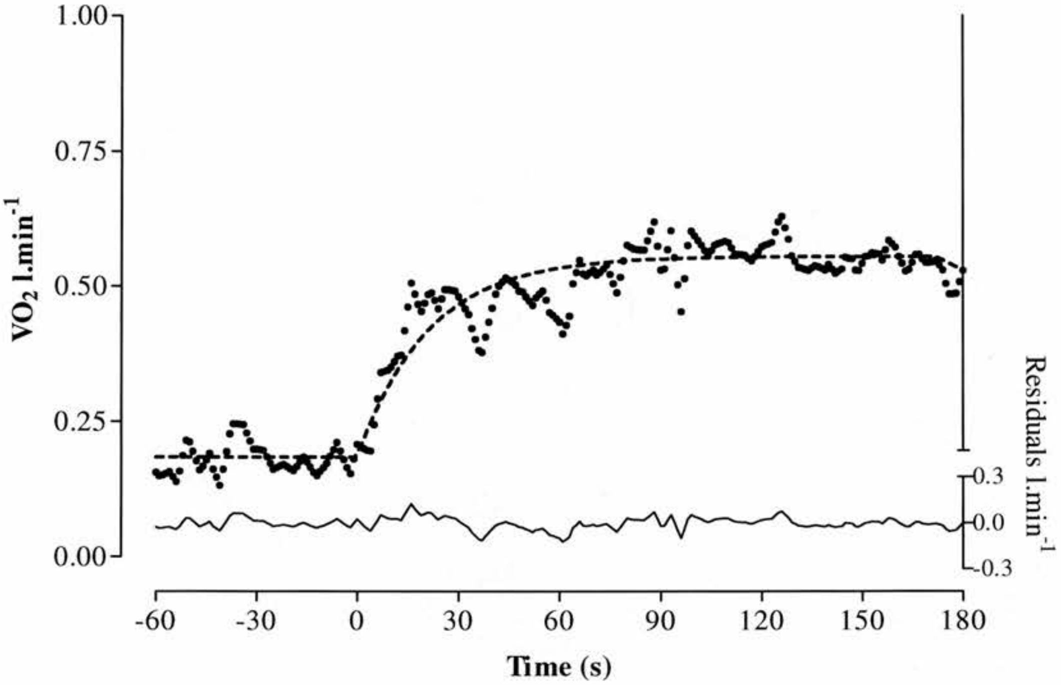


Figure 3b. Oxygen uptake response to walking for preliminary volunteer one. The dashed line represents the fit of the monoexponential model

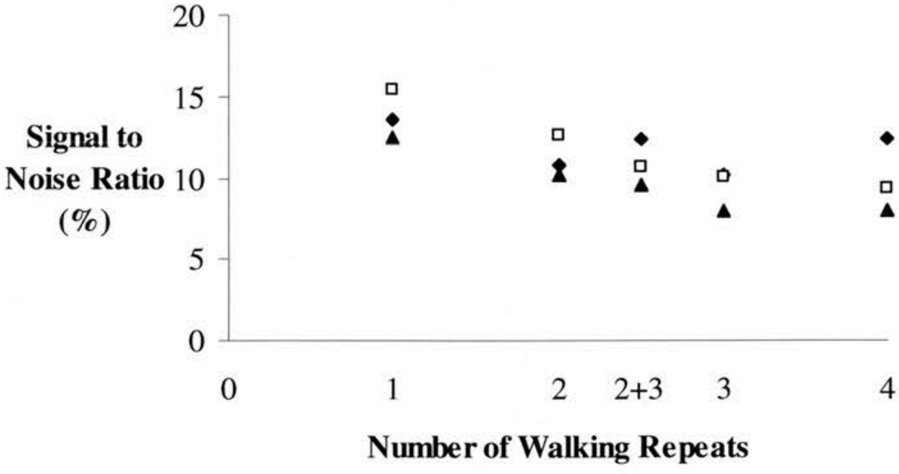
ii) Ensemble Averaging

The standard deviation of the residuals was determined to calculate the percentage signal to noise ratio (i.e. standard deviation of the residual values divided by the asymptotic (plateau) VO_2 value) thus indicating the degree of fit of the model. This along with R^2 values enabled an assessment of the optimum number of walking repeats to ensemble average.

Figure 3c presents the signal to noise ratio for each of the three preliminary volunteers on Visit One (A) and Visit Two (B). The signal to noise ratios are presented when walk 1 only on each visit was modelled; and the signal to noise ratio when walks 1 and 2 were ensemble averaged and then modelled; ensemble average of walks 1-3; ensemble average of walks 1-4; and ensemble average of walks 2 and 3. The number of walks ensemble averaged is shown on the x axis of Figure 3c ('Number of Walking Repeats Averaged'). A similar presentation approach for the R^2 values is shown in Figure 3d.

Signal to Noise Ratio (%)

A)



B)

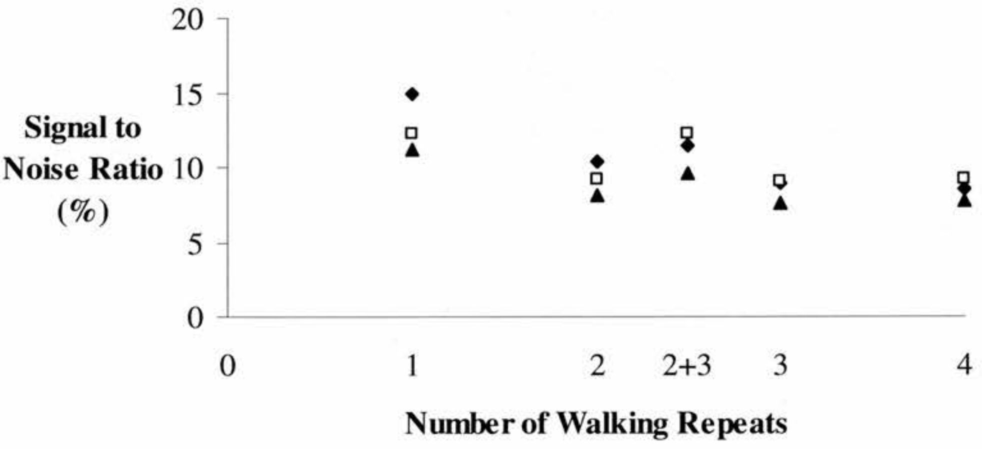
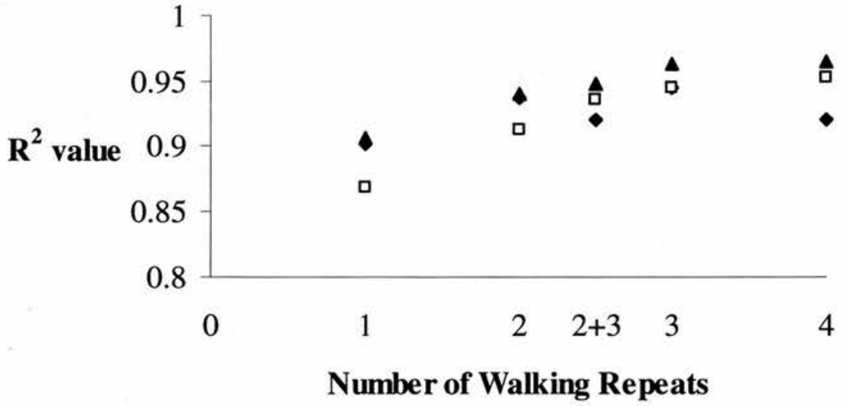


Figure 3c. Signal to noise ratios for preliminary volunteer one (diamonds), two (squares) and three (triangles) on Visit One (A) and Visit Two (B). The signal to noise ratios are presented for ensemble averaged data (i.e. walk 1 only; walks 1 and 2; walks 2 and 3 (i.e. 2+3 on x axis); walks 1-3; and walks 1-4)

R^2 values

A)



B)

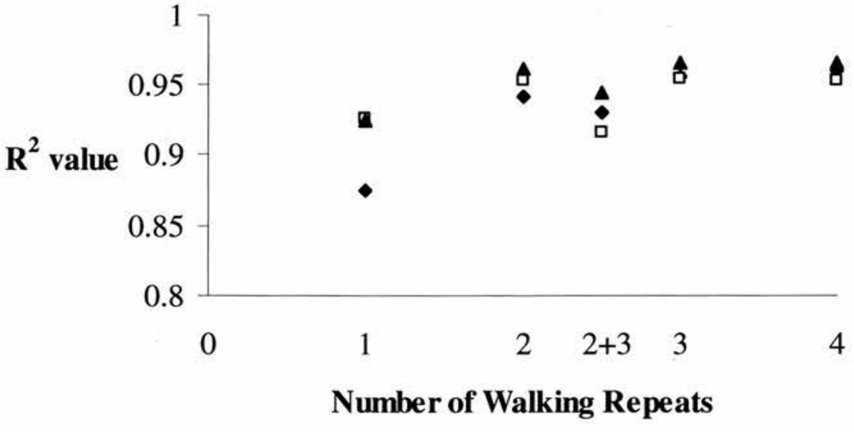


Figure 3d. R^2 values for preliminary volunteer one (diamonds), two (squares) and three (triangles) for Visit One (A) and Visit Two (B). The R^2 values are presented for ensemble averaged data (i.e. walk 1 only; walks 1 and 2; walks 2 and 3 (i.e. 2+3 on x axis); walks 1-3; and walks 1-4)

Summary of Preliminary Findings

- In order that the oxygen uptake response to standing was not detrimental to the on-transient of oxygen uptake, the decision was taken to begin from a standing start of one minute. One minute was sufficient for ventilation, gas exchange and heart rate to return to a steady baseline level. Two minutes of standing was considered too long by the preliminary volunteers.
- To ensure a bout of walking wasn't affected by a preceding bout, volunteers should be allowed seated rest for sufficient time between walking bouts until ventilation, gas exchange and heart rate had returned to pre-exercise levels.
- Coefficient of variation (COV %) was used to assess the variation in walking speed between laps. The median COV of individual lap walking speeds for the preliminary volunteers was 2.5% (maximum COV was 8.4%).
- The amplitude of the oxygen uptake response was sufficient to be modelled using conventional nonlinear monoexponential regression techniques.
- Three walks of three minutes were recommended with the oxygen uptake response to the ensemble averaged VO_2 response to the second and third walks modelled. In order to permit volunteer familiarisation with the study methodology it was decided to omit the oxygen uptake from the first walk from further analyses. To minimise the test duration while optimising the signal to noise ratio with ensemble averaging of walking repeats it was evident from the preliminary findings that averaging walks 2 and 3 was sufficient. No significant benefit was achieved when walk 4 was added to the modelling process. Due to the perturbation in oxygen uptake associated with

the standing process, it was decided to exclude the first 15 seconds of the 1 minute of baseline pre-walking standing data from the modelling process. This allowed the exponential model to project from a more stable and homogenous oxygen uptake baseline value.

Based on the preliminary findings a study methodology was suggested (detailed in pilot work methodology).This methodology was then applied to a group of healthy elderly volunteers (and further young volunteers) to investigate if they would respond in a similar manner to the three preliminary volunteers. The pilot work also enabled further familiarisation with the study protocol and modelling prior to the main study.

B) Pilot Study

Introduction

In a similar format to the preliminary study, the pilot study explored the practical, experimental and modelling considerations of the study methodology. As the pilot study was testing the measurement with older volunteers there were additional considerations.

Objectives of pilot study

Practical Considerations

i) The Metamax 3B system

The Metamax 3B system required the use of a face mask which fitted snugly over the volunteer's mouth and nose. With increasing age and loss of elastic tissue in the cheeks the mask may not fit so well. Also, while a face mask has advantages over a more conventional mouth piece when older individuals are considered, it may be viewed by some as claustrophobic, particularly if the walking tests require the system to be worn for some time. The first practical objective of the pilot study was to consider the suitability of the Metamax 3B system for the walking tests.

ii) Study Methodology

The second practical objective of the pilot study was ability of the volunteers to tolerate the study methodology (i.e. three walks of three minutes).

iii) Recovery between walking bouts

Inactivity and ageing may increase the amount of time needed for recovery between walking bouts. The third practical objective of the pilot study was to consider the time taken for ventilation, gas exchange and heart rate to return to pre-exercise levels.

Experimental Considerations

i) 'Constant-load' exercise

Similar to the preliminary study, the pilot work then assessed the experimental considerations. The first experimental objective was to assess the extent of variability in walking speed within each walking repeat.

ii) Steady state VO_2

The second experimental objective of the pilot study was the ability of the volunteers to achieve steady state oxygen uptake in three minutes. The time course of the increase in oxygen uptake at the onset of exercise has previously been shown to be slower in older individuals (Cunningham et al., 1993; Babcock et al., 1994i, Bell et al., 1999, Chilibeck et al., 1996i, Chilibeck et al., 1996ii, Scheuermann et al., 2002, DeLorey et al., 2004). The pilot work was therefore important to consider whether older individuals could attain steady state oxygen uptake conditions in three minutes similar to the young preliminary volunteers.

iii) Moderate Intensity Exercise

Particularly relevant when the older individuals were tested, was whether the walking exercise constituted moderate intensity exercise. When asked to walk at a comfortable pace it would be expected individuals would select a walking pace below their anaerobic threshold. Previous research in our Laboratory has investigated the $\%VO_2max$. individuals chose to walk at when asked to walk at a 'comfortable' speed (Fitzsimons et al., 2005). Healthy elderly volunteers (aged 78 years (SD 2.4), N=9) chose to walk at 56% of VO_2max. – i.e. an intensity that is less than the anaerobic threshold. Below the anaerobic threshold, the VO_2 kinetics reflect the onset of increased intracellular metabolism and the mechanisms of oxygen transfer. The VO_2 kinetics have been shown to follow a first order transfer function. Above the anaerobic threshold, the kinetics slow down with the work level (Sietsema et al., 1989) and their behaviour is complicated by the superimposition of a slow component (Whipp & Ward, 1990; Xu & Rhodes, 1999). The appearance of the slow component adds to the complexity of the VO_2 uptake profile and can make accurate calculation and interpretation of the O_2 deficit more difficult (Mettauer et al., 2000; Whipp & Ward, 1990; Xu & Rhodes, 1999). If the exercise remains below the anaerobic threshold the modelling process is therefore simplified and thought to be more accurate. The third experimental objective of the pilot study was to assess whether 'comfortable' self-paced walking constituted moderate intensity exercise in both young and older volunteers.

Modelling Considerations

i) Amplitude of the VO_2 response

Due to age related reductions in the functional capacity of the respiratory, cardiovascular and skeletal muscle systems, the absolute oxygen uptake in response to a given exercise instruction may be reduced (Fitzsimons et al., 2005). The first modelling objective of the pilot work was to identify if the amplitude of absolute oxygen uptake would be sufficient to be modeled.

ii) Ensemble Averaging

A lower amplitude of absolute oxygen uptake response may be associated with an increased signal to noise ratio. The second modeling objective of the pilot work was to investigate if a monoexponential model would fit the oxygen uptake data adequately, i.e. how good was the fit of the model. Would ensemble averaging of the second and third walks only be adequate?

Volunteers

Table 3d shows the characteristics of the pilot study volunteers. All volunteers were defined as 'healthy', were not in regular training and provided informed consent (page 53).

	Young	Healthy Elderly
Age (years)	22 (19 - 23)	78 (77 - 80)
Height (cm)	168 (162 – 177)	157 (153 – 164)
Mass (kg)	61 (54 – 65)	55 (47 - 59)

Table 3d. Characteristics of the five young healthy women and five healthy elderly women **pilot study** volunteers

Methodology

Volunteers were tested on two separate occasions. Individuals were asked to walk at a 'comfortable' pace walking around a 33.3m elliptical marked course for three minutes (see Appendix 2, page 226 for walking instructions used). Three minutes of seated pre-exercise oxygen uptake data were collected followed by one minute of standing and three minutes of walking followed by one minute of standing. This series was repeated two times (with seated rest periods of three minutes between each walk), on each of two separate occasions, with the second visit not more than two weeks after the first visit. Ventilation, gas exchange and heart rate were measured continuously. The time taken to complete each lap of the circuit was recorded.

Results

Practical Considerations

The pilot study volunteers all tolerated the Metamax 3B system well and completed the necessary study methodology without incident. Ventilation, gas exchange and heart rate returned to pre-exercise levels within three minutes of seated rest.

Experimental Considerations

i) 'Constant-load' exercise

Table 3e presents the coefficient of variation of the individual lap speeds for the young and healthy elderly pilot volunteers.

	Young		**Healthy Elderly**	
	Visit One	Visit Two	Visit One	Visit Two
Median	2.9	2.2	1.7	2.1
Range	0.9 - 4.6	1.0 - 4.1	1.2 - 3.5	0.8 - 3.7

Table 3e. Coefficient of variation of individual lap speeds (%) for pilot work volunteers

ii) Steady state VO_2

Table 3f presents the slope of the last 30s of walking (B value) for the young and healthy elderly pilot volunteers on walks 2 and 3 for each visit and also p values to assess whether the slope differed significantly from zero. The slope of oxygen uptake did not differ from zero in all volunteers hence steady state oxygen uptake was attained in three minutes.

		Walk 2 Mean VO_2 ($l.min^{-1}$)	B value ($l.min^{-1}.sec^{-1}$)	No. of data points	p value	Walk 3 Mean VO_2 ($l.min^{-1}$)	B value ($l.min^{-1}.sec^{-1}$)	No. of data points	p value
Young									
1	1								
	2	0.59	-0.002	13	0.32	0.59	0.002	13	0.45
2	1	0.60	-0.006	9	0.17	0.62	0.002	9	0.43
	2	0.83	0.000	8	0.86	0.74	0.004	7	0.26
3	1	0.63	0.002	13	0.42	0.60	0.000	12	0.74
	2	0.70	-0.001	11	0.54	0.64	-0.001	11	0.74
4	1	0.59	-0.001	9	0.56	0.58	-0.003	9	0.07
	2	0.60	0.000	8	0.97	0.55	-0.005	9	0.17
5	1	0.68	0.002	15	0.11	0.67	-0.003	14	0.33
	2	0.60	0.001	11	0.68	0.60	0.000	12	0.96
Healthy Elderly									
1	1	0.84	0.001	13	0.79	0.85	0.002	14	0.42
	2	0.93	0.001	15	0.60	0.93	0.001	15	0.78
2	1	0.58	0.000	12	0.81	0.48	-0.004	12	0.25
	2	0.41	-0.001	10	0.27	0.40	0.000	10	0.73
3	1	0.45	0.000	12	0.92	0.47	-0.006	10	0.04
	2	0.57	-0.003	12	0.13	0.54	-0.005	12	0.17
4	1	0.80	0.001	16	0.77	0.75	-0.003	15	0.06
	2	0.84	-0.001	16	0.45	0.81	-0.001	16	0.25
5	1	0.80	0.004	12	0.28	0.85	0.002	13	0.56
	2	0.88	-0.007	10	0.53	0.89	0.002	12	0.75

Table 3f. Mean VO_2 ($l.min^{-1}$), Slope (B value, $l.min^{-1}.sec^{-1}$), number of data points and significance (p value) of the final 30 seconds of oxygen uptake for young and healthy elderly volunteers on visits one and two

iii) Moderate Intensity Exercise

The mean Respiratory Exchange Ratio (RER) for the young group was 0.82 (SD 0.05) over the four walks (walks two and three on visit one and walks two and three on visit two). The mean RER for the healthy elderly group over the two visits was 0.79 (SD 0.04). Comfortable self-paced walking was of moderate intensity in both the young and older volunteers.

Modelling Considerations

i) Amplitude of the VO_2 response

The amplitude of absolute oxygen uptake response to comfortable self-paced walking was sufficient to be modeled in both the young and healthy elderly pilot study volunteers. Table 3g presents the parameters of the oxygen uptake response when fitted with a monoexponential nonlinear regression model for the young and healthy elderly pilot volunteers on visits one and two.

ii) Ensemble Averaging

The ensemble averaged oxygen uptake response to the second and third walks was adequately fitted with a monoexponential model. The goodness of fit of the model is presented in Table 3g (Sy.x; R^2; 95% Confidence Intervals (C.I.) for MRT).

		N	VO_2B ($l.min^{-1}$)	A1 ($l.min^{-1}$)	MRT (s)	Sy.x ($l.min^{-1}$)	R^2	95% C.I. for MRT
Young								
	Visit One	5	0.19	0.47	**18**	0.04	0.95	1.8
			0.04	0.09	**6**	0.01	0.01	0.3
	Visit Two	5	0.20	0.43	**25**	0.04	0.96	2.4
			0.02	0.09	**9**	0.01	0.01	1.0
Healthy Elderly								
	Visit One	5	0.21	0.50	**42**	0.05	0.92	4.5
			0.03	0.19	**15**	0.02	0.07	2.3
	Visit Two	5	0.20	0.54	**39**	0.05	0.95	3.5
			0.05	0.22	**10**	0.02	0.04	1.3

Table 3g. Kinetic variables of VO_2 (mean values (SD); N=5 young Visits One and Two; N=5 healthy elderly Visits One and Two) (VO_2B represents the pre-exercise VO_2 level; A1 is the amplitude of the VO_2 response; MRT the mean response time; Sy.x ($l.min^{-1}$) (the standard deviation of the residuals), R^2 and 95% Confidence Intervals quantify goodness of fit of the model)

Summary of pilot work

- Practically the Metamax 3B system and study methodology were well tolerated and three minutes of seated rest was sufficient for ventilation, gas exchange and heart rate to return to pre-exercise levels.

- Coefficient of variation (COV %) was used to assess the variation in walking speed between laps. The median COV of individual lap walking speeds for the young pilot volunteers was 2.6% (maximum COV was 4.6%) and for the healthy elderly pilot volunteers was 1.9% (maximum COV was 3.7%). On the basis of these and the preliminary study COV findings the decision was taken, (and in view of the findings of Bassey et al., 1976) to use a COV of ≤ 6% as a means of defining whether a walking repeat could be described as 'constant-load' exercise.

The ensemble averaged oxygen uptake response to the second and third walks was adequately described using a monoexponential model (GraphPad Prism). Prior to modelling, any breath greater than four standard deviations (caused by swallowing, coughing, sighing etc.) was removed (Rossiter et al., 1999). Due to the short exercise bout of 3 minutes, the decision was taken to analyse both Phases I and II of the oxygen uptake response to obtain a MRT, thereby maximizing the amount of oxygen uptake data included in the modelling processes. Additional rational for determination of a MRT was the observation by Whipp et al., 1982 that exercise begun from a background of light exercise (unloaded pedaling) resulted in a slower and smaller 'cardiodynamic' Phase I response. One minute of standing prior to the walking test may constitute light exercise in frail older patients, compromising the determination of Phase II onset.

The pilot study methodology was considered appropriate to attempt to answer the main research questions of the thesis. The practical, experimental and modelling considerations of the measurement of oxygen uptake kinetics at the onset of self-paced walking provided evidence as to the suitability of self-paced walking as an exercise mode to investigate MRT in healthy elderly people. Therefore it is now reasonable to try using self-paced walking to measure MRT in frail, elderly people.

CHAPTER 4: Are oxygen uptake kinetics at the onset of exercise, **intensity independent** within a range of 'moderate' exercise intensities?

Introduction

Volunteers

Methodology

Results

Discussion

Summary

Introduction

One concern with using self paced walking as a mode of exercise to examine oxygen uptake kinetics is that the intensity of the exercise may vary between tests, thus questioning the comparability of time constants obtained on different days. However it is generally believed that the time constant of oxygen uptake is invariant in the moderate intensity exercise domain (i.e. below the anaerobic threshold), but the evidence behind this assumption is inconsistent.

Five of eight studies reported in the literature provide evidence that the time constant of oxygen uptake is invariant with increasing exercise intensity. Barstow & Mole, 1991, Barstow et al., 1993 and Ozyener et al., 2001 provide evidence of an invariant time constant with increasing exercise intensity, and Whipp and Wasserman, 1972 and Casaburi et al., 1989 studies suggest oxygen uptake kinetics do not vary greatly within a moderate intensity exercise domain, i.e. exercise intensities not associated with sustained lactic acidosis. In contrast, three studies report increasing time constants with increasing exercise intensity (Carter et al., 2002; Paterson et al., 2003; Koppo et al., 2004).

The majority of the previous studies listed above have utilised % ventilatory threshold, % lactate threshold or the difference between these thresholds and VO_2max. as indicators of exercise intensity. It is therefore difficult to compare the studies and to make a judgement as to their relevance in relation to self-paced walking. Additionally, the relevance of assessing exercise intensity in terms of %

ventilatory threshold, % lactate threshold or the difference between these thresholds in relation to older people is questionable. This is due to the alteration of the anaerobic threshold when expressed as a percentage of VO_2max., with increasing age (Iredale and Nimmo, 1997). A more appropriate measure of exercise intensity when older individuals are considered may simply be exercise intensity expressed as a percentage of absolute VO_2max.

The contradictory nature of previous studies investigating exercise intensity and kinetics and the limited applicability to older people prompted further investigation of the effect of exercise intensity on oxygen uptake kinetics. Therefore, the aim of this study was to investigate the effect of exercise intensity expressed as a % of VO_2max., on oxygen uptake kinetics derived from treadmill walking. Due to the unsuitability of VO_2max. testing for frail, older individuals, younger volunteers were used in this study. This would examine what effect, if any, minor variations in walking speed (and therefore exercise intensity), from one test session to another would have on MRT.

Volunteers

Six healthy young female individuals (median age 22yrs (range 21-25yrs), Table 4a) volunteered to participate in this study. All volunteers were defined as 'healthy', were not in regular training and provided informed consent (page 53, Chapter 3 (Preliminary and Pilot)).

Volunteer	Age	Height (cm)	Weight (kg)
1	24	165	61
2	23	168	61
3	21	169	69
4	23	160	60
5	23	161	56
6	21	166	56
Median	23	166	61
Range	21 - 24	160 - 169	56 - 69

Table 4a. Study volunteer characteristics

Methodology

All volunteers attended a minimum of three visits.

Visit One – VO_2max. test

All volunteers undertook a VO_2max. treadmill test on Visit One to permit calculation of submaximal work rates (Figure 1, Appendix 4). Each VO_2max. treadmill test was medically supervised with blood pressure and E.C.G. monitored before, during and after each treadmill test. Ventilation and gas exchange were measured continuously throughout the test using a Metamax 3B ambulatory metabolic measurement system, (Cortex Biophysik). Ventilatory rate and fractional concentrations of oxygen and carbon dioxide were measured on a breath-by-breath basis, via a facemask. VO_2max. was deemed to have been achieved if the subject reached voluntary exhaustion, ≥90% of age predicted maximum heart rate and an RER of ≥1.1. VO_2max. was calculated as the average VO_2 of the final 30 seconds of the ramp protocol.

Visits Two and Three – Submaximal work rates

Previous research in our laboratory has investigated the %VO_2max. individuals choose to walk at in response to standard walking instructions commonly used in exercise guidelines (Fitzsimons et al., 2005). When asked to walk at a 'comfortable' pace, a group of young volunteers, (aged 20-23 years) chose to walk at 33% of VO_2max. In contrast, a group of healthy elderly volunteers (aged 78-83 years) chose to walk at 56% of VO_2max. with, more importantly, a range of 40-73% VO_2max. Based on this evidence the exercise intensities 50%, 65% and 80% VO_2max. were selected in an attempt to encompass the exercise intensity range elderly patients may choose to walk at when asked to walk at a comfortable speed. The treadmill work rate required for each volunteer for each of the three exercise intensities was determined from the relationship between work-rate and average %VO_2max. achieved during that VO_2max. stage (determined graphically). The appropriate treadmill slope was calculated from each work-rate given a treadmill speed throughout of 6.3km/h.

Laboratory Protocol used for Visits Two and Three

Volunteers performed rest to steady state exercise transitions on a motorised treadmill (Figure 4a). Gas exchange variables and blood pressure were monitored as previously stated. Heart rate was recorded continuously by telemetry (Polar A3). At the start of the second and third visits, each volunteer performed a rest-to-exercise transition corresponding to 65%VO_2max. for a duration of six minutes. This exercise bout was only to familiarise the volunteer with the rapid acceleration to steady state exercise (<1 second) and with the intensity of exercise required. Data obtained from this exercise bout was excluded from further analysis.

Following the familiarisation bout, volunteers performed randomly selected exercise bouts corresponding to three repeats of each exercise intensity over the second and third visits (four exercise bouts on visit 2 and five on visit 3). Each six minute exercise bout was following by at least twenty minutes of seated rest.

Figure 4a. A volunteer completing a moderate intensity bout wearing the Metamax 3B metabolic measurement system

Determination of oxygen uptake kinetics

Data obtained from nine exercise bouts (three repeats at each exercise intensity) were used in subsequent analysis. Details of the modelling methodology are given in Chapter 1 (Introduction), Pages 38-41 and Chapter 3 (Preliminary and Pilot), Page 74.

The presence of a linear trend in MRT values with increasing exercise intensity was considered using Repeated Measures (RM) ANOVA. The extent of the variation in MRT values across the three exercise intensities was considered using coefficient of variation (C.O.V.).

Results

Recorded values of VO_2 (expressed as a percentage of VO_2max.) were in good agreement to those intended (i.e. 50%, 65% and 80%). Each individual performed three walking repeats at each of three exercise intensities (nine exercise bouts). The median exercise intensities achieved are shown below (Figure 4b). Figure 4c illustrates the averaged oxygen uptake response of one individual (Volunteer 5, Table 4a) for each of the three exercise intensities.

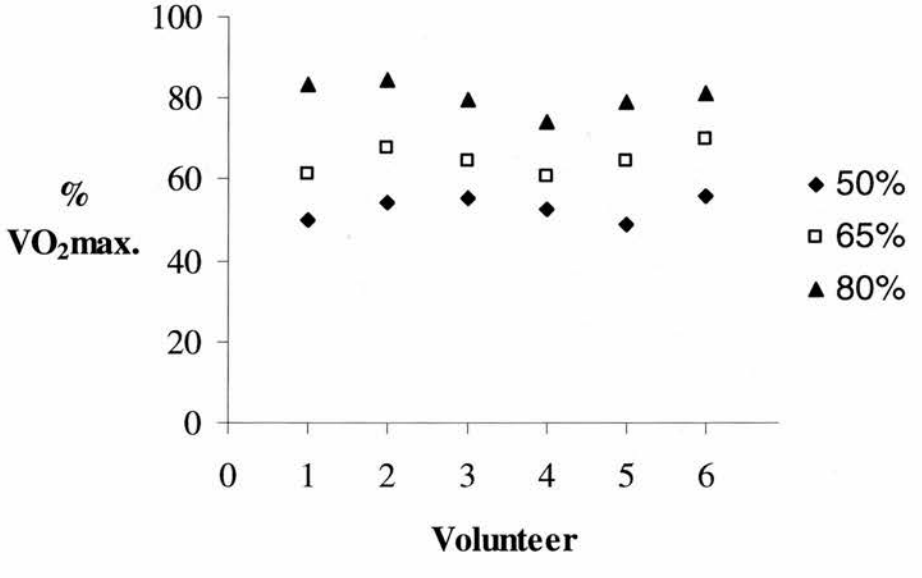


Figure 4b. %VO_2max. for each volunteer at each exercise intensity

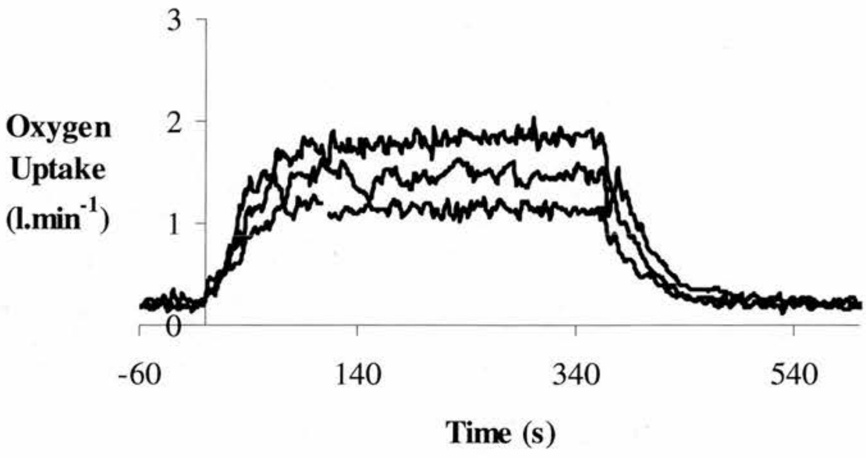


Figure 4c. Oxygen uptake response (second-by-second, average of three treadmill exercise bouts) corresponding to each exercise intensity for one individual (Volunteer 5) (top line represents 80% VO_2max., middle line represents 65% VO_2max. and bottom line represents 50% VO_2max.).

Oxygen uptake response was fitted with a monoexponential model to derive a time constant, MRT corresponding to each exercise intensity for each individual. A monoexponential model suitable for moderate intensity (i.e. below the lactate threshold) was used as there was no evidence of sustained lactic acidosis (Respiratory Exchange Ratios for the last 30s and the last 60s of each exercise bout are given in Table 1, Appendix 3, page 227). Additionally, steady state oxygen uptake conditions were achieved within the six minute exercise bout with no evidence of a slow component since VO_2 data at the end of exercise was no longer correlated with time (Mettauer et al. 2000), (Table 2, Appendix 3, page 228).

Volunteer	50%	65%	80%
1	37	38	Error
2	37	38	39
3	36	36	44
4	31	29	39
5	33	38	40
6	37	35	34
Median	**36**	**37**	**39**

Table 4b. MRT values (s) corresponding to each exercise intensity (50%, 65% and 80% VO_2max.)

There was no apparent significant linear trend in MRT values across the three exercise intensities (Table 4b). Repeated measures ANOVA statistically confirmed the lack of a linear trend (F (1, 4) = 0.20, p=0.68). The within subjects coefficient of variation was 9%.

Discussion

If VO_2 kinetics are to be considered as a suitable measure of an aspect of cardiorespiratory fitness with self-paced walking the mode of exercise, it is of considerable importance to consider the influence of exercise intensity. The pilot work presented in Chapter 3 (Pages 56 & 69) illustrates the consistency of walking speeds within a test session in both young and healthy elderly individuals when asked to complete a number of separate walks. This finding is supported by Cunningham et al., (1982). Although elderly individuals have been shown to walk consistently within a test session, it would be helpful to know if any minor variations in walking speed from one test session to another would impact on oxygen uptake kinetics. The aim of this study was to examine what effect, if any, minor variations in walking speed (and therefore in exercise intensity), from one test session to another would have on MRTs. This study investigated the influence of three exercise intensities (50%, 65% and 80% VO_2max.) on the MRT values in untrained, healthy young women during treadmill walking.

The MRT values for each individual in this study across the three exercise intensities were not dissimilar. RM ANOVA demonstrated no evidence of a significant linear trend across the three intensities ($p=0.68$). The COV was used to give a measure of the variation in MRT values for a given individual, which was 9%. The COV was similar that reported in other studies. Reybrouck et al. (2003) reported a COV of 8.4% for the oxygen deficit. Sietsema et al. (1994) reported COVs for MRTs in five "normal" subjects (four male and one female). The subjects cycled at three separate work rates on three to six different test days. The COV for the MRT determined for a work rate midway between the individual's lactic acidosis threshold and maximal work rate was 10+/-2%.

Summary

In this sample of young women of comparable age and fitness, variations in MRT between the three exercise intensities considered were not of physiological significance. Due to the unsuitability of VO_2max. testing for frail older individuals, younger volunteers were used to the consider the effect of exercise intensity (%VO_2max.) on MRT. The assumption is made these findings are applicable to frail older people. On the basis of these findings in young individuals, any unavoidable variations in exercise intensity between test sessions would be unlikely to mask intervention related effects on MRT values.

CHAPTER 5: Is the measurement of a time constant of oxygen uptake at the onset of 'comfortable' self-paced walking a **feasible** measure in healthy young and elderly volunteers and in frail patient groups?

Introduction

Feasibility, that is the relative ease with which a measure can be used, is an important factor when considering the applicability of a new measure to a particular population group. The feasibility of the measurement of oxygen uptake kinetics at the onset of self-paced walking was established in small groups of young and healthy elderly people (see Chapter 3). The purpose of this chapter was to explore feasibility further in young and healthy elderly volunteers and more importantly, investigate feasibility for those for whom the measure is intended – frail, elderly people. The feasibility of the measure was investigated in older people after a hip fracture or stroke to investigate if the criteria applied to the young and healthy volunteers in the pilot work chapter were suitable. As the feasibility of a measure is an extensive topic, it was assessed in this chapter in three categories (Figure 5a). The criteria in each category were satisfied before the next category was considered.

PRACTICAL

1. Did the volunteer tolerate the Metamax 3B system?
2. Could the volunteer complete three walks of three minutes?

EXPERIMENTAL

1. Was comfortable self-paced walking 'constant-load' exercise (COV$\leq$6%)?
2. Did the participants achieve a constant walking speed instantaneously?
3. Were steady-state VO_2 conditions achieved in three minutes?
4. Did comfortable self-paced walking constitute moderate intensity exercise?

MODELLING

1. Was the amplitude of the VO_2 response sufficient to be fitted with a monoexponential model?
2. How well did a monoexponential model fit the VO_2 data?
3. How long did it take to obtain a MRT value for a study visit?

Figure 5a. Flow diagram of the feasibility categories

The majority of these criteria have been discussed in the preliminary and pilot study chapter. It is not known however, if those findings would be replicated in frail older people. For example, the pilot study had previously shown the amplitude of the oxygen uptake response to comfortable self-paced walking was sufficient in young and healthy elderly volunteers. It was not known if this finding would also apply to frail, older men and women. The age related decline in lung function and skeletal muscle quality and quantity might be exacerbated in the patient groups. The ability of frailer individuals to generate a given amplitude of absolute oxygen uptake in response to exercise might therefore be reduced. As a result the oxygen signal to physiological noise ratio would increase and may result in data that cannot be characterised using nonlinear regression techniques.

Two additional criteria has been considered in this chapter – 1) the ability of participants to accelerate from a standing start to an invariant walking speed and 2) the time taken to derive the variables of interest.

1) The optimum methodology would be for volunteers to achieve and maintain a comfortable walking speed as soon as possible in order that any difference in oxygen uptake kinetics between individuals can be attributed to physiological differences and not the gradual acceleration of walking speed. As active, healthy individuals would be expected to achieve an invariant comfortable speed almost instantaneously this aspect of feasibility was not assessed in the pilot chapter. This assumption could not be applied to frail, patient groups.
2) The time taken to derive the parameters of gas exchange kinetics is an important aspect of the feasibility of this measure if it is to be used, for example in a large training study. Due to the likelihood of additional time being needed when the measure was applied to those for whom it was

intended, frail, older people, this aspect of feasibility was not considered in the pilot chapter.

Volunteers

Feasibility of the use of self-paced walking to examine oxygen uptake kinetics was investigated in four volunteer groups, a group of young, healthy men and women, a group of healthy elderly men and women, a group of women after a hip fracture and a group of men and women after a stroke (Table 5a).

			N	Age (years)	Height (cm)	Mass (kg)
1	**Young**		17	23 (20 - 29)	171 (161 - 195)	63 (54 - 101)
		Women	11	23 (20 - 29)	168 (161 - 173)	61 (54 - 75)
		Men	6	23 (20 - 26)	182 (178 - 195)	75 (69 - 101)
2	**Healthy Elderly**		8	80 (76 - 87)	169 (159 - 180)	71 (63 - 85)
		Women	4	79 (76 - 85)	167 (159 - 169)	67 (63 - 73)
		Men	4	81 (78 - 87)	174 (167.5 - 180)	74 (73 - 85)
3	**Hip Fracture**	Women	15	81 (72 - 91)	159 (149 - 170)	59 (43 - 75)
4	**Stroke**		66	74 (49 - 87)		70 (45 - 120)
		Women	30	74 (54 - 87)		65 (50 - 94)
		Men	36	72 (49 - 85)		75 (45 - 120)

Table 5a. Volunteer characteristics of Groups 1 - 4 (median (and range))

All volunteers in Groups 1 and 2 were defined as 'healthy', were not in regular training and provided informed consent (page 53).

Group 3 comprised 15 women after hip fracture (median time since fracture 7 months, range 2-13 months; Elderly Mobility Scale (Smith, 1994, Appendix 4, Figure 5) score 17 (median value); range (15 – 18)). The inclusion criteria were women aged 70 years and over with their first hip fracture in the preceding 18 months, ambulatory at discharge and not in institutional care. They were able to walk with or without aids, with or without supervision, but without assistance or prompting. The exclusion criteria were refusals, fractures due to primary and secondary bone malignancy, discharge from hospital specifically for terminal care and cognitive impairment defined as an Abbreviated Mental Test (Hodkinson, 1972) score of less than 7. Six hundred and thirty one females over 70 years were admitted to the Royal Infirmary, Edinburgh in the period from 1st September 2001 to 30th June 2003 with a hip fracture, from home/sheltered accommodation and discharged to home/sheltered accommodation/ Geriatric Orthopaedic Rehabilitation Unit (GORU) or died. Sixty two individuals met the selection criteria for this study and GP/consultant approval was obtained for 48 of them. Of the 48 individuals, 17 consented to participate in the study and 15 of them were tested on two occasions (Table 5a) (one individual was excluded due to geographical limitations and the other was no longer living independently following discharge from hospital).

Group 4 comprised 66 men and women who had suffered a stroke and completed inpatient rehabilitation. The individuals were part of a larger randomised exploratory trial (STARTER: STroke: A Randomised Trial of Exercise and Relaxation) delivering an exercise or relaxation intervention to stroke survivors. Men and women recruited for the study were required to understand the rational behind the trial, be ambulatory and have no absolute contraindications to exercise. The individuals were then randomized to 12 weeks of either a training or relaxation intervention. Further details on the STARTER trial are given in Appendix 5, Chief Scientist Office Final Report, 2005.

Methodology

Self-paced walking test

Groups 1, 2 and 3

Volunteers were asked to walk around an elliptical circuit (15.61m for young and healthy elderly volunteers and 13m for individuals after hip fracture; a change of location for the walking tests resulted in a slight amendment to the lap distance) for 3 minutes in response to a standard instruction (Appendix 2, page 226) asking them to walk at their 'comfortable' pace (Figure 5b). Each volunteer completed three walks with a rest of 3-4 minutes between each walk. For the duration of the walking test, Group 3 used their usual walking aid. Each individual stood for 1 minute before walking. Heart rate was measured by telemetry (Polar A3). Ventilation and gas exchange were measured continuously using a Metamax 3B ambulatory metabolic measurement system, (Cortex Biophysik).Ventilatory rate and fractional concentrations of oxygen and carbon dioxide were measured on a breath-by-breath basis, via a facemask. Three minutes of seated pre-exercise oxygen uptake data were collected followed by 1 minute of standing and three minutes of walking. This series was repeated twice (with rest periods in between each walk), on each of two separate occasions, with the second visit not more than two weeks after the first visit (Groups 1-3). The time taken to complete each lap of the circuit was recorded. Walking speed and the coefficient of variation of the individual lap speeds were calculated retrospectively.

Group 4

The stroke survivors were asked to complete the comfortable self-paced walking test (15.61m circuit) before, immediately after and four months following a 12 week physical training or relaxation intervention. The stroke survivors followed an identical methodology to Groups 1-3 given above although for these individuals the test sessions were pre intervention, post intervention and four months after the intervention. They were able to use their usual walking aid. On each occasion Group 4 attempted the walking tests at the end of a large battery of physical, functional and psychological assessments to investigate the response to a training/relaxation intervention (further details are given in Chapter 8).

Figure 5b. An individual from the hip fracture group (Group 3) completing the 'comfortable' self-paced walking test

Determination of oxygen uptake kinetics

Details of the modelling process are given in Chapter 1 (Introduction), Pages 38-43 and Chapter 3 (Preliminary and Pilot), Page 74.

Results

A. Practical

1. **Did the volunteer tolerate the Metamax 3B system?**

   With the exception of one Group 4 participant, who was unable to tolerate the face mask, all study participants tolerated the Metamax 3B system.

2. **Could the volunteer complete three walks of three minutes?**

   As shown in Table 5b, all study participants in Groups 1, 2 and 3 were capable of completing three walks each of three minutes (one of the women in Group 1 was unable to return for a second visit due to other commitments). In Group 4, (STARTER participants) on average 68% of individuals completed three walks of three minutes on a study visit (Visit One 68%, Visit Two 71% and Visit Three 65%, see also Table 5b). 33/66 (50%) of study participants in the stroke group completed three walks of three minutes on all three study visits.

	Number in Group	Number who completed 3 walks of 3 minutes	% of Group
Group 1			
Women			
Visit 1	11	11	100
Visit 2	10	10	100
Men			
Visit 1	6	6	100
Visit 2	6	6	100
Group 2			
Women			
Visit 1	4	4	100
Visit 2	4	4	100
Men			
Visit 1	4	4	100
Visit 2	4	4	100
Group 3			
Women			
Visit 1	15	15	100
Visit 2	15	15	100
Group 4			
Women			
Visit 1	30	17	57
Visit 2	30	20	67
Visit 3	30	16	53
Men			
Visit 1	36	28	78
Visit 2	36	27	75
Visit 3	36	27	75

Table 5b. Number of study volunteers in Groups 1-4 who completed 3 walks of 3 minutes

B. Experimental

1. Was comfortable self-paced walking 'constant-load' exercise?

The ability of the study participants to maintain an invariant walking speed for three minutes and therefore 'constant-load' exercise conditions was assessed by considering the extent of variation in walking speed from one lap to the next using the coefficient of variation (COV) of individual lap speeds, i.e. SD of individual laps/mean lap speed x 100. On the basis of preliminary and pilot studies COV findings the decision was taken, (and on the findings of Bassey et al., 1976) to use a COV of $\leq 6\%$ as a means of defining whether a walking repeat could be described as 'constant-load' exercise.

Table 5c gives median (and range) of COV of on the second and third walks for each of the four groups, along with the number of study participants with a COV$\leq 6\%$ in each group on both the second and third walks for each visit. The majority of study participants in Group 1 could maintain a constant walking speed. Surprisingly, a lower than expected number of Group 2 study volunteers (Healthy Elderly) maintained a constant walking speed (4/8 Visit 1; 3/8 Visit 2). Higher numbers of individuals with a constant speed were evident in Groups 3 (68% Visit 1; 73% Visit 2) and 4 (69% Visit 1; 62% Visit 2; 63% Visit 3) (see Table 5c for data for men and women). (The group median values presented in Table 5c are calculated as the median value of the COV for all individuals on both the second and third walk of each visit (the first walk for each individual was excluded)).

	Median COV of group (%)	Range of COV in group (%)	Proportion of gp with COV≤6% on 2nd & 3rd walks
Group 1			
Women			
Visit 1	3.2	1.7 – 7.6	8/11 (73%)
Visit 2	3.0	1.9 – 4.1	10/10 (100%)
Men			
Visit 1	3.8	1.9 – 12.0	5/6 (83%)
Visit 2	3.0	1.8 – 4.4	6/6 (100%)
Group 2			
Women			
Visit 1	5.2	3.8 – 11.2	1/4 (25%)
Visit 2	5.6	3.7 – 9.1	1/4 (25%)
Men			
Visit 1	3.9	1.9 – 20.9	3/4 (75%)
Visit 2	5.9	2.2 – 8.0	2/4 (50%)
Group 3			
Women			
Visit 1	4.2	0.3 – 14.2	10/15 (67%)
Visit 2	4.1	2.1 – 36.4	11/15 (73%)
Group 4			
Women			
Visit 1	4.6	1.8 – 10.1	14/30 (47%)
Visit 2	5.2	1.4 – 21.0	12/30 (40%)
Visit 3	5.2	1.6 – 17.0	9/30 (30%)
Men			
Visit 1	4.5	1.0 -13.2	17/36 (47%)
Visit 2	4.5	1.6 – 10.3	17/36 (47%)
Visit 3	4.9	1.5 – 10.6	18/36 (50%)

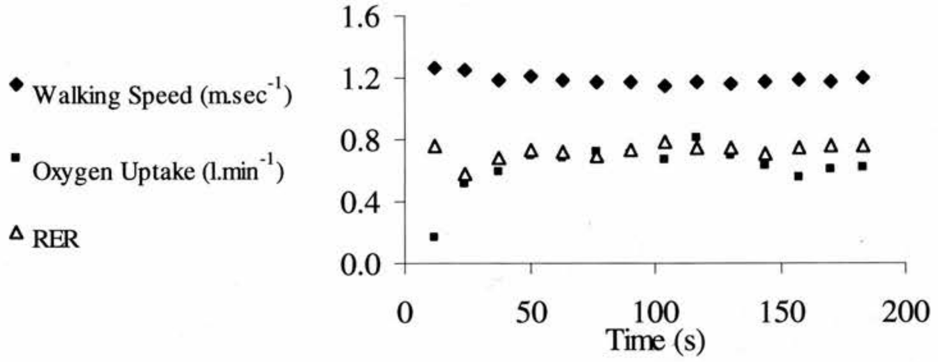
Table 5c. Coefficient of variation of individual lap speeds (COV %). COV data are presented only for those individuals who completed 3 walks of 3 minutes (see Table

5b). The proportion in each group with COV≤6% is given in relation to the initial group size.

2. Did the participants achieve a constant walking speed instantaneously?

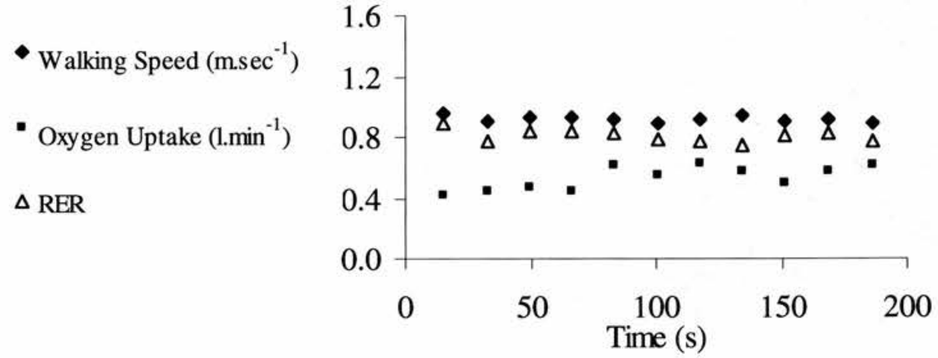
Figure 5c shows the oxygen uptake, walking speed and RER taken as an average over each lap for one walk for one volunteer from each of the four groups. The data are presented in this form to investigate whether a gradual increase in walking speed could explain the gradual increase in oxygen uptake at the onset of exercise. Information on the nature of the transfer from standing to walking is compromised by timing at the conclusion of each lap. But it is evident from Figure 5c that the comfortable walking speeds of the four individuals illustrated were rapidly achieved and maintained with VO_2 gradually achieving steady state.

A



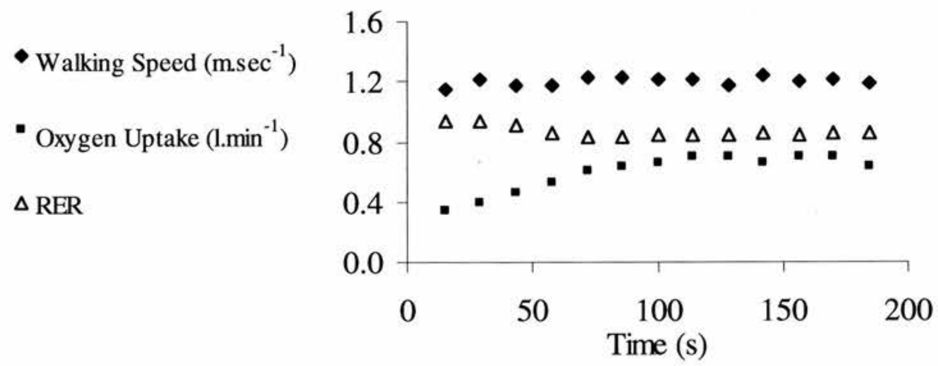
Walking Speed (m.sec-1)
Oxygen Uptake (l.min-1)
RER
1.6
1.2
0.8
0.4
0.0
0
50
100
150
200
Time (s)

B



Walking Speed (m.sec-1)
Oxygen Uptake (l.min-1)
RER
1.6
1.2
0.8
0.4
0.0
0
50
100
150
200
Time (s)

C



Walking Speed (m.sec-1)
Oxygen Uptake (l.min-1)
RER
1.6
1.2
0.8
0.4
0.0
0
50
100
150
200
Time (s)

D

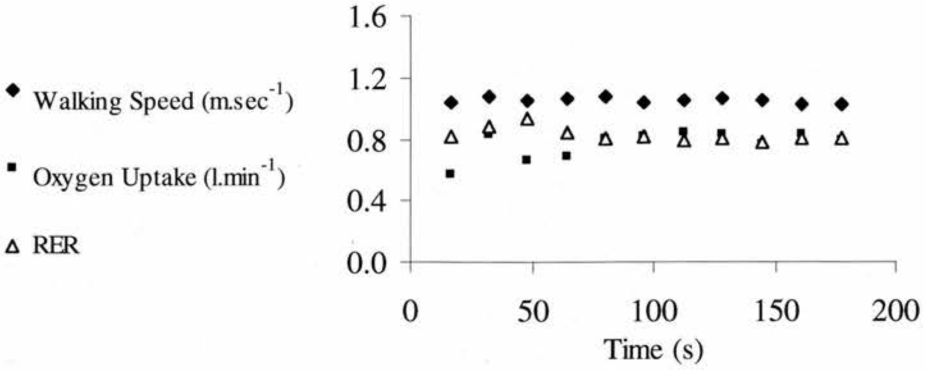


Figure 5c. Walking speed (filled diamonds)(m.sec^{-1}), Oxygen Uptake (filled squares) (VO_2) (l.min^{-1}) and Respiratory Exchange Ratio (unfilled triangles) (R.E.R.) (walk three, visit one) for one volunteer from Group One (A); Group Two (B); Group Three (C); and Group Four (D) (mean values for each lap)

Half lap time analysis

To further investigate the time taken to achieve a constant walking speed, half-lap times were collected from a sub-group of healthy young and elderly volunteers. Half-lap times were collected from five young volunteers (3 women, 2 men, Figure 5d) and 3 healthy elderly men (Figure 5e).

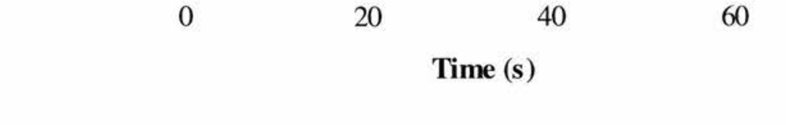


Figure 5d. Walking speed measured at the completion of 8 half laps for the young volunteers with the fastest (filled triangles), median (unfilled diamonds) and slowest (filled squares) walking speeds. (Data presented were collected on the third walk of visit two for each volunteer).

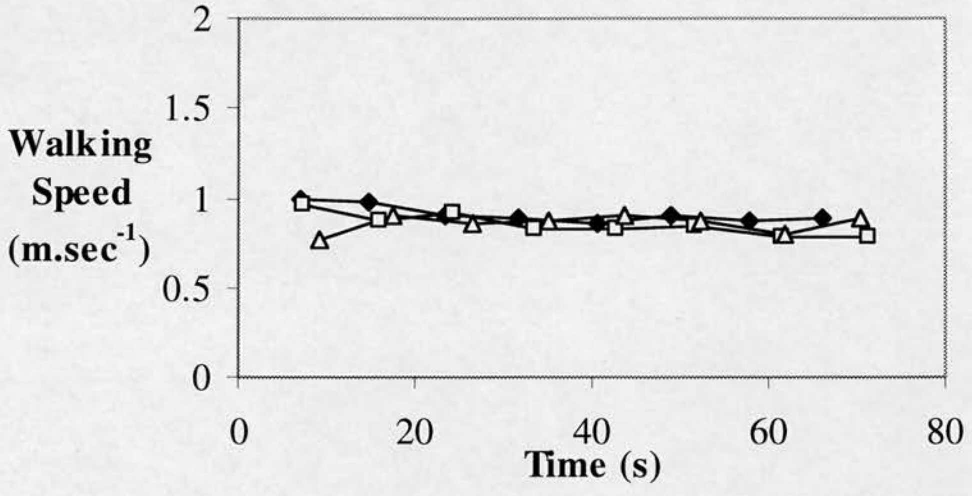


Figure 5e. Walking speed (m.sec^{-1}) measured at the completion of 8 half laps for three healthy elderly men. (Data presented were collected on the third walk of visit two for each volunteer)

Figures 5d and 5e counter the concern related to acceleration as they illustrate the ability of individuals to achieve and maintain a consistent walking speed. As evident in Figure 5c, the young volunteer with the fastest walking speed, the first time point (i.e. completion of first half lap) occurred after 4.1s, at which time point the individual had already achieved an invariant walking speed.

3. Were steady-state VO_2 conditions achieved in three minutes?

The slope (B value of linear regression) of the last 30s of oxygen uptake during the second and third walks was calculated as a means of investigating whether steady state oxygen uptake conditions had been achieved within the 3 minute exercise bout. Table 5d shows that the majority of individuals with COV≤6% could achieve steady state oxygen uptake conditions in three minutes.

		Mean VO_2 of last 30s ($l.min^{-1}$)	**B value ($l.min^{-1}.sec^{-1}$)**	**No. of data points**	**Mean p value**
Young	Visit				
Women	1	0.65 (0.10)	-0.002 (0.009)	10 (2)	0.34
	2	0.64 (0.13)	0.001 (0.007)	9 (3)	0.47
Men	1	0.91 (0.23)	0.001 (0.008)	11 (3)	0.61
	2	0.85 (0.23)	-0.000 (0.006)	11 (2)	0.51
Healthy Elderly					
Women	1	0.55 (0.01)	0.002 (0.003)	9 (0)	0.48
	2	0.56 (0.02)	-0.002 (0.001)	9 (0)	0.38
Men	1	0.68 (0.07)	-0.001 (0.002)	10 (2)	0.30
	2	0.77 (0.05)	-0.001 (0.002)	11 (1)	0.46
Hip Fracture	1	0.47 (0.17)	-0.003 (0.005)	12 (4)	0.44
	2	0.51 (0.15)	-0.002 (0.004)	12 (4)	0.38
Stroke					
Women	1	0.52 (0.15)	0.001 (0.004)	12 (2)	0.33
	2	0.51 (0.10)	-0.000 (0.004)	13 (2)	0.43
	3	0.51 (0.11)	-0.001 (0.002)	12 (2)	0.49
Men	1	0.73 (0.19)	-0.000 (0.004)	12 (2)	0.31
	2	0.69 (0.20)	-0.001 (0.006)	12 (2)	0.40
	3	0.73 (0.19)	-0.001 (0.004)	12 (2)	0.42

Table 5d. The mean VO_2 ($l.min^{-1}$), slope (B value, $l.min^{-1}.sec^{-1}$), number of data points and p value (p value <0.05 represents a significance deviation of B from zero)

of the last 30s of breath-by-breath oxygen uptake data. Values are presented as mean (SD).

4. Did comfortable self-paced walking constitute moderate intensity exercise?

The mean Respiratory Exchange Ratio (RER) value of the last 30s of walking exercise was calculated to assess if the exercise was below the anaerobic threshold and therefore of moderate intensity. As shown in the Table 5e when individuals were asked to walk comfortably they chose to walk below their anaerobic threshold as the RER is consistently <1.0.

		N	RER (COV≤6%)
Young			
Women	Visit 1	8	0.86 (0.07)
	Visit 2	10	0.85 (0.10)
Men	Visit 1	5	0.85 (0.05)
	Visit 2	6	0.89 (0.04)
Healthy Elderly			
Women	Visit 1	1	0.78
	Visit 2	1	0.84
Men	Visit 1	3	0.83 (0.03)
	Visit 2	2	0.86 (0.02)
Hip Fracture	Visit 1	10	0.76 (0.06)
	Visit 2	11	0.81 (0.05)
Stroke			
Women	Visit 1	14	0.83 (0.10)
	Visit 2	11	0.83 (0.09)
	Visit 3	8	0.89 (0.10)
Men	Visit 1	14	0.85 (0.08)
	Visit 2	15	0.84 (0.07)
	Visit 3	16	0.90 (0.08)

Table 5e. Mean (and SD) Respiratory Exchange Ratio (RER) for Groups 1-4 on Visits 1, 2 and 3 (Visit 3 Group 4 only). Group mean values were calculated from the

mean value from walks 2 and 3 for each individual. RER values are presented for those individuals with a COV≤ 6% (N=2 stroke women visits & N=6 stroke men visits were excluded as RER>1.0)

Modelling

1. **Was the amplitude of the VO_2 response sufficient to be fitted with a monoexponential model?**

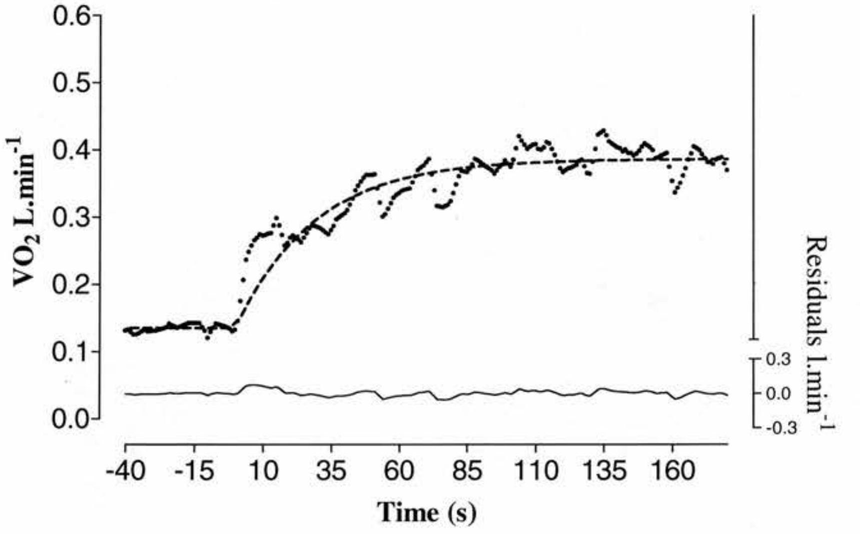
The numbers of test sessions from each group considered for modelling analyses are given in Table 5f.

	Nb of test sessions to be modelled	% of total group
Young women		
Visit One	8	73
Visit Two	10	100
Young men		
Visit One	5	83
Visit Two	4	67
Healthy Elderly women		
Visit One	1	25
Visit Two	1	25
Healthy Elderly men		
Visit One	3	75
Visit Two	2	50
Hip Fracture women		
Visit One	8	53
Visit Two	10	67
Stroke women		
Visit One	10	33
Visit Two	10	33
Visit Three	7	23
Stroke men		
Visit One	10	28
Visit Two	14	39
Visit Three	16	44

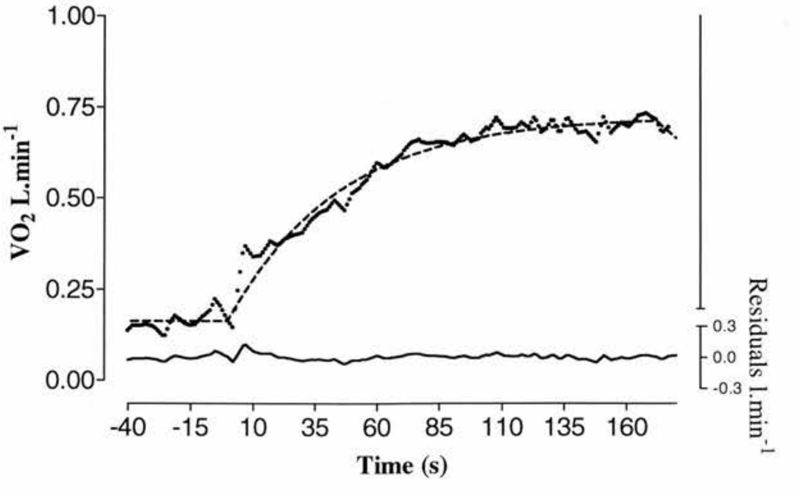
Table 5f. The number of study participants in each group (and expressed as a % of the number in each group initially) for whom a monoexponential model was applied to gas exchange data (those individuals who completed three walks of three minutes, COV≤6%, RER≤1.0, Steady State VO_2 conditions in the final 30 seconds of walking)

A monoexponential model was fitted to the oxygen uptake transient for those individuals who completed three walks, maintained a constant walking speed, achieved steady state VO_2 conditions in three minutes and RER was ≤ 1.0. The amplitude of the oxygen uptake response was sufficient to be fitted with a monoexponential model (Figure 5f).

A) Healthy Elderly



B) Hip Fracture



C) Stroke

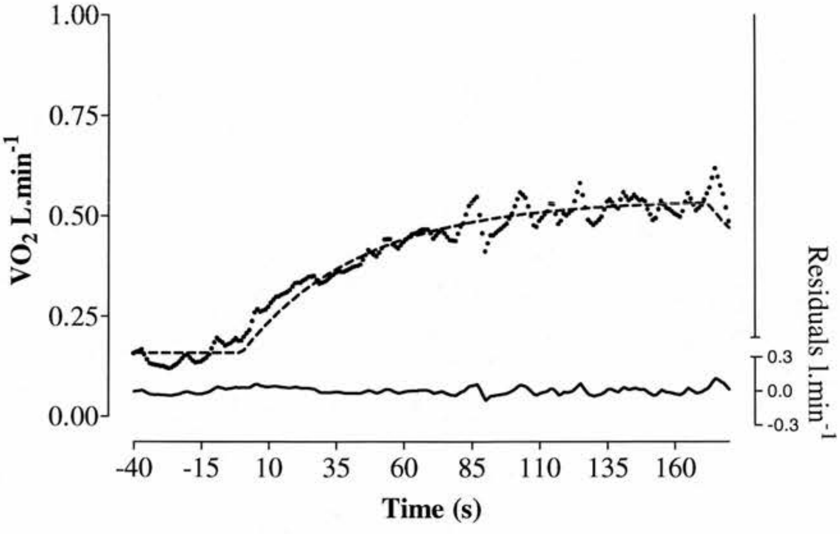


Figure 5f. Oxygen uptake response to walking for a healthy elderly participant (A); a hip fracture participant (B); and a stroke participant (C). The dashed line represents the fit of the monoexponential model.

Table 5g shows the mean kinetic parameters for each of the four groups. Values are presented for men and women separately. The ensemble averaged oxygen uptake response to the second and third walks was adequately fitted with a monoexponential model. The goodness of fit of the model is presented in Table 5g (Sy.x; R^2; 95% Confidence Intervals (C.I.) for MRT).

	Visit	VO_2B ($l.min^{-1}$)	A1 ($l.min^{-1}$)	MRT (s)	Sy.x ($l.min^{-1}$)	R^2	95% C.I.
Young women	1	0.20	0.47	**23**	0.05	0.93	2.6
	SD	0.07	0.04	7	0.01	0.02	1.0
	2	0.20	0.47	**22**	0.05	0.93	2.5
	SD	0.05	0.13	7	0.02	0.04	0.9
Young men	1	0.29	0.62	**16**	0.08	0.88	2.4
	SD	0.08	0.21	6	0.03	0.08	0.8
	2	0.28	0.66	**20**	0.07	0.90	2.5
	SD	0.09	0.22	6	0.01	0.05	0.7
Healthy elderly women	1	0.20	0.34	**38**	0.04	0.93	4.2
	2	0.19	0.37	**47**	0.03	0.95	4.5
Healthy elderly men	1	0.25	0.46	**36**	0.06	0.89	5.3
	SD	0.04	0.06	8	0.01	0.04	2.0
	2	0.29	0.51	**35**	0.06	0.90	4.7
	SD	0.03	0.02	2	0.01	0.04	1.3
Hip Fracture women	1	0.18	0.36	**52**	0.04	0.84	9.5
	SD	0.05	0.17	16	0.02	0.14	4.9
	2	0.18	0.36	**48**	0.05	0.80	10.5
	SD	0.03	0.15	8	0.02	0.15	5.3
Stroke women	1	0.14	0.33	**39**	0.04	0.88	6.0
	SD	0.03	0.10	11	0.01	0.06	2.3
	2	0.18	0.38	**54**	0.04	0.87	10.2
	SD	0.04	0.10	16	0.01	0.09	8.3
	3	0.17	0.39	**51**	0.04	0.89	7.9
	SD	0.03	0.07	13	0.02	0.08	4.4
Stroke men	1	0.27	0.48	**43**	0.06	0.89	6.9
	SD	0.07	0.17	20	0.03	0.06	4.7
	2	0.24	0.44	**42**	0.06	0.87	6.7
	SD	0.05	0.15	15	0.03	0.09	3.2
	3	0.28	0.47	**37**	0.06	0.91	5.2
	SD	0.14	0.15	15	0.02	0.04	3.1

Table 5g. Kinetic variables of VO_2 (mean and SD) on visit one and visit two (VO_2B represents baseline VO_2; A1 represents the amplitude of VO_2 response; MRT represents Mean Response Time; Sy.x, R^2 and 95% C.I. assess goodness of fit)

2. How well did a monoexponential model fit the VO_2 data?

The extent to which the oxygen uptake data from each individual could be described using the monoexponential model was explored using Sy.x and R^2 values and 95% confidence intervals for MRT. These values show the goodness of fit of the model was slightly lower in the patient groups but the fit was adequate in those test sessions modelled.

How many test sessions didn't provide a MRT?

Table 5h shows a break down of the number of study volunteers in each group who provided a MRT and rational for those volunteers who did not.

	Young		**Healthy Elderly**		**Hip Fracture**		**Stroke**		
	Visit 1	Visit 2	Visit 1	Visit 2	Visit 1	Visit 2	Visit 1	Visit 2	Visit 3
Consented volunteers	**17**	**16**	**8**	**8**	**15**	**15**	**66**	**66**	**66**
Completed three walks	17	16	8	8	15	15	45	47	43
COV≤6%	13	16	4	3	10	11	31	29	27
Steady state VO_2	13	14	4	3	8	10	22	27	26
RER≤1.0	13	14	4	3	8	10	20	24	23
Nb. of test sessions considered for modelling	13	14	4	3	8	10	20	24	23
Nb. of test sessions modelled adequately	**13**	**14**	**4**	**3**	**6**	**10**	**15**	**22**	**20**

Table 5h. Flow chart of number of volunteers in each group who provided a MRT and rational for those volunteers who did not

Of the 106 individuals who volunteered to participate in this study, 105 tolerated the Metamax 3B system. Of 277 study visits, on 214 visits individuals completed three walks of three minutes (77%). On 144 of those 214 visits, volunteers achieved and maintained an invariant walking speed and of those 144 steady pace visits, 119 achieved steady state oxygen uptake conditions within three minutes with a $RER \leq 1.0$. 119 study visits were therefore considered for modelling, with 107 visits (39% of 277) adequately described using a monoexponential model suitable for moderate intensity exercise (82% Group One; 44% Group Two; 53% Group Three; 29% Group Four).

3. How long did it take to obtain a MRT value for a study visit?

To consider the feasibility of this outcome measure within the context of, for example, a large training study, it is helpful to know the time scale involved in attaining a MRT value for each individual. Excluding the identification, recruitment and General Practitioner approval phase, each test session (calibration of Metamax 3B system; preparation of facility for walking test; explanation to volunteer; fitting of equipment; completion of walking test, book and wait for taxi with cup of tea and chat (10 minutes)) took 1 hour 55 minutes.

Analyses of test session data (downloading data from Metamax 3B system; analyses of COV of individual lap speeds; slope of VO_2 response; RER; preparation of VO_2 data for modelling (removal of errant breaths in VO_2 response; time-aligning to exercise onset; ensemble averaging of VO_2 from walks two and three); attempting to fit a nonlinear regression model to the VO_2 response) took 45 minutes per test session. It is therefore possible to suggest 2 hours 40 minutes be allocated to each test session in order to obtain a MRT value.

Further analysis of those individuals who didn't complete three walks

Approximately 1/3 of the stroke group could not complete three walks of three minutes. If oxygen uptake kinetics at the onset of self-paced walking were to be incorporated into further trials it is of interest to consider whether the analysis of one walking repeat rather than the ensemble average of two would significantly compromise the modelling parameters. Table 5i shows the number of volunteers in the stroke group who completed 0, 1, 2 or 3 walks on each of three visits.

		Men	Women	Total
	Visit One			
	0	3	4	7
	1	3	8	11
	2	2	1	3
	3	28	17	45
Number of walks	**Visit Two**			
	0	4	8	12
	1	4	1	5
	2	1	1	2
	3	27	20	47
	Visit Three			
	0	7	8	15
	1	0	2	2
	2	2	4	6
	3	27	16	43

Table 5i. Number of individuals in the stroke group who completed 0, 1, 2 or 3 walks on Visits One, Two and Three

From this data it is evident that if walk one remained as a familiarisation walk and therefore excluded from modelling analyses and only the oxygen uptake response to walk 2 was modelled then 11 (3+2+6) more visits (out of a possible 198 (66 x 3 visits)) could be considered for modelling.

If the oxygen uptake data from walk 2 were analysed in an identical manner to the data from walks 2 & 3, then the same criteria should be applied to the test data. Firstly, walk one and walk two should have been of three minutes in duration. Of the 11 visits identified where the volunteers completed two walks, on 3 of those visits walk 2 was not three minutes in duration (i.e. walks 1 and 3 were three minutes in duration). Secondly, the slope of the last 30 seconds of oxygen uptake data from walk 2 should not differ significantly from zero and the RER should be ≤ 1. Six visits met these criteria and a monoexponential model was applied to the oxygen uptake data from walk 2 only (Table 5j).

		Slope						
Volunteer	Visit	B value (l.min^{-1}. sec^{-1})	p value	RER	MRT (s)	Sy.x (l.min^{-1})	R^2	95% C.I.
1	3	0.000	0.99	1.3				
2	3	-0.000	0.88	1.0	50	0.04	0.60	31.1 to 68.5
3	3	walk 2 only 157seconds						
4	1	walk 2 only 147 seconds						
5	2	-0.010	0.51	0.8	23	0.23	0.22	3.9 to 42.0
6	1	-0.001	0.80	1.0	model did not converge			
7	3	-0.014	0.04					
8	3	0.002	0.35	0.9	32	0.07	0.89	27.6 to 36.6
9	2	0.000	0.86	0.9	38	0.06	0.95	34.8 to 41.5
10	3	0.001	0.76	0.9	55	0.06	0.92	48.2 to 62.3
11	1	walk 1 only 118seconds						

Table 5j. Slope, RER and modelling variables (were appropriate) for the second walk only analyses

On one study visit (volunteer 6) the model did not converge on the data. Although MRT values were obtained for five individuals, they should be interpreted with care as the loss of the ensemble averaging process has compromised the goodness of fit of model to the data (e.g. Volunteer 5 R^2 value 0.22). Additionally the reasons why individuals did not complete three walks of three minutes are important. The principle reason volunteers stopped the walking test early was due pain or tiredness. Volunteers 8 and 9 reported back pain and hip pain respectively as reasons for wanted to stop the walking test. The impact of these reasons on the MRT is unclear. These findings suggest the feasibility of the measurement would not be significantly enhanced if two walks only were completed and walk 2 oxygen uptake data modelled.

Discussion

This chapter has considered if the measurement of oxygen uptake kinetics at the onset of self-paced walking is feasible in frail patient groups (after a hip fracture or stroke) and confirmed the findings of the pilot work chapter on the feasibility of the measurement in healthy young and elderly volunteers. By considering each aspect of feasibility (practical, experimental procedure and modelling considerations) it is possible to identify the main strengths and weaknesses of this measurement when applied to those individuals for whom the measure is intended - frail patient groups.

In practical terms, the Metamax 3B system was well tolerated. On the basis of the findings of the pilot study, 3 walks of 3 minutes were selected as the optimal study methodology. When the experimental procedure was considered (i.e. the ability to walk at constant speed within the moderate exercise domain and achieve steady state oxygen uptake conditions), the limiting criterion was the ability of an individual to walk at a constant speed. Encouragingly, when the modelling aspect of the feasibility was considered, nonlinear regression modelling techniques were applied to 119 study visits, with 107 visits adequately described using a monoexponential model suitable for moderate intensity exercise. Therefore 90% of study visits considered for modelling provided data of sufficient quality to be fit with a single monoexponential model. The 95% confidence intervals were 1-4 seconds in the young group; 4-7 seconds in the healthy elderly group; 3-22 seconds in the hip fracture group and 2-27 seconds in the stroke group. These confidence intervals are comparable to values reported in the literature (Rossiter et al., 1999 reported 95% C.I. of 2-5 seconds in a group of male healthy volunteers aged 21 to 59 years during rhythmic knee extension exercise; Chilibeck et al., 1996i reported 95% C.I. of 4 seconds in a group of young subjects (aged 26.3 +/- 2.5 years) and 10 seconds in a group of healthy older subjects (aged 66.7 +/- 6.7 years) during cycling exercise; Bell et al., 2001 reported 95% C.I. of 2-10 seconds during knee extension exercise in healthy, older men aged 77 +/- 7 years).

The principle limiting factors in the feasibility of this measurement are therefore the ability of individuals to complete the necessary study protocol (3 walks of 3 minutes) and the ability of individuals to achieve and maintain an invariant walking speed. The first limiting factor, the ability to complete the protocol, relates to levels of frailty. Analysing the oxygen uptake response of the second walk only did not significantly improve the number of test sessions from which a MRT could be obtained. This suggests that a walking test of any form would be difficult in the frailer study participants.

The second limiting factor, achievement and maintenance of an invariant walking pace, was more prevalent with increasing age but could not be attributed primarily to level of frailty. In an attempt to reduce or remove these limiting factors, the methodology could be improved by more extensive testing in frail patient groups to investigate the threshold of frailty/fitness/function at which the test becomes unfeasible. To encourage individuals to more readily achieve and maintain a constant walking pace, a larger walking circuit may help. The necessary use of a 15.61m circuit may provide some explanation as to why some individuals had difficulty maintaining a constant speed. More frequent measuring of walking speed would provide greater characterisation of walking speed, particularly in the first lap.

Attempting the walking tests at the end of a large battery of outcome measures as part of the STARTER trial may have compromised the number of individuals who felt able to complete the walking tests. In relation to other stroke survivors the participants in this study could be considered to be recovering well (median EMS stroke group = 20; median FIM stroke group 118). Although the hip fracture group had on average slower comfortable walking speeds than the stroke group (mean comfortable walking speed of the hip fracture group on Visit One was 0.57 $m.sec^{-1}$) and took longer to perform the sit to stand test (mean sit-to-stand on Visit One was 1.8 seconds), they all completed three walks of three minutes on both study visits. In contrast, the mean comfortable walking speed of the stroke group on Visit One was 0.7 $m.sec^{-1}$ and the average time taken to perform the sit to stand test on Visit One was 1.6 seconds. On average, 45/66 (68%) individuals in the stroke group completed the study protocol (45 individuals on Visit 1; 47 Visit 3; 43 Visit 3)). The length of the assessment set in the Starter trial may provide a rational for the inability of some volunteers in the stroke group to complete the walking tests.

The approach was taken to model the oxygen uptake response to the second walk only in the stroke group. It was anticipated this approach would increase the number of test sessions that could be considered for modelling as study visits where a volunteer managed two (instead of three) walks could be analysed. Unfortunately this was not the case, with only 5 extra MRT values obtained. If the measure was incorporated into a large battery of tests again then the number of study participants who could complete the methodology (3 walks of 3 minutes) may be enhanced if the walking test was either at the start of the assessment set of measurements or on a separate day to allow the volunteer to rest.

Summary

As the measure was acceptable to 'fitter' patients (for whom current measures are unsuitable) the feasibility threshold for oxygen uptake kinetics testing has been lowered. If the same study participants achieve the feasibility criteria on subsequent visits then oxygen uptake kinetics at the onset of self-paced walking is a feasible measure in frail patient groups. The application of the measure to frailer stroke patients is questionable.

CHAPTER 6: Is the measurement of a time constant of oxygen uptake at the onset of 'comfortable' self-paced walking a **valid** measure of an aspect of cardiorespiratory fitness?

Introduction

Volunteers

Methodology

Results

Discussion

Summary

Introduction

In preparing the introduction to this chapter the work of Safrit (1981) and Wood (1989) was drawn upon for definitions and explanations of the components of validity.

Oxygen uptake kinetics have never before been measured firstly with self-paced walking as the mode of exercise and secondly in very frail older people for whom standard exercise ergometry is unsuitable. The objective of this chapter was to consider the validity of oxygen uptake kinetics at the onset of self-paced walking as a valid measure of an aspect of cardiorespiratory fitness. Safrit, (1981, page 45) defined a valid test "as a measure that is sound in terms of the purpose of the test and meets satisfactory criteria for test construction". In this study, validity is therefore the extent to which MRT at the onset of self-paced walking measures the variable of interest, cardiorespiratory fitness.

Two aspects of validity must be considered: relevance and reliability (Safrit, 1981, page 46; Wood, 1989, page 24). Relevance is the "closeness of agreement between what the test measures and the function it is intended to measure" (Safrit, 1981). Reliability refers to the "precision and consistency of the measure", (Safrit, 1981). Reliability of a measure is therefore an important part of validity. (Reliability is considered separately in Chapter 7).

The objective of this chapter was to consider the **relevancy** aspect of validity of oxygen uptake kinetics measured at the onset of self-paced walking as a measure of an aspect of cardiorespiratory fitness. Figure 6a presents the classification of validity categories.

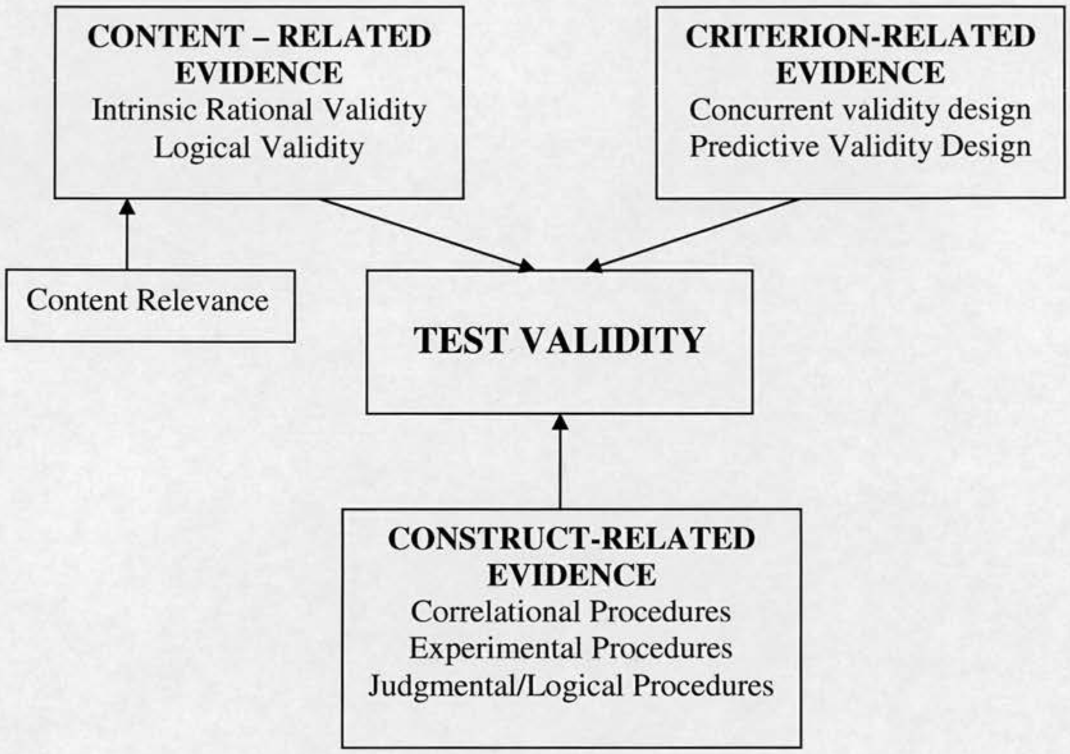


Figure 6a. Classification of test validity source (adapted from Wood, 1989, page 25; *Original Source*: Standards for Educational and Psychological Tests, American Psychological Association, 1985)

1. Content-Related Evidence of Validity

A measure can be said to possess content validity if it can be judged to provide a good representative sample of a defined population (Safrit, 1981, pages 46 & 47). To assess content validity it is necessary to define the population to which the test is being applied; precisely describe the sample of the population; and examine the degree to which the test items represent the population (Wood, 1989, page 26).

To examine the content validity of oxygen uptake kinetics measured at the onset of self-paced walking the test was applied to a sample of four distinct population groups – a healthy young group, healthy elderly group, a group of individuals after a hip fracture with a median age of 78 years and a group of individuals after a stroke with a median age of 72 years. A qualitative assessment of the similarities and differences between these groups would provide a judgement as to whether the MRT values demonstrated content validity and appeared clinically credible.

The rate of oxygen uptake at the onset of exercise (VO_2 kinetics), has previously been shown to be slower in older individuals (Babcock et al., 1994i, Bell et al., 1999, Chilibeck et al., 1996i, Chilibeck et al., 1996ii, DeLorey et al., 2004, Scheuermann et al., 2002) and to be accelerated in younger and older adults following training (Phillips et al., 1995, Babcock et al., 1994ii, Bell et al., 2001) (Phillips et al., 1995 (N=7, 23+/-1 year); Babcock et al., 1994ii (N=8, mean age 72 years); Bell et al., 2001 (N=5, 77+/-7 years)). These data indicate that individuals with lower levels of cardiorespiratory fitness would be expected to have higher MRTs. The MRT values of the young group might be expected to be the lowest as they should not be showing the effect of ageing on their cardiovascular and respiratory systems and might also be expected to have the highest levels of cardiorespiratory fitness. The healthy elderly group might be expected to have shown the effects of healthy ageing and have lower levels of cardiorespiratory fitness than the young volunteers, with correspondingly higher MRT values than the young volunteers. The hip fracture and stroke groups might be expected to have higher MRT values than both the young and healthy elderly groups, primarily due to ageing and lower levels of cardiorespiratory fitness caused by a combination of inactivity, ageing and disease.

2. Criterion-Related Evidence of Validity

Criterion-related validity is examined by a comparison of the measures from the new test with measures from other tests that are considered to directly measure the characteristic in question, in this case cardiorespiratory fitness (Safrit, 1981, page 55). This type of validity was assessed in two categories: A) Concurrent validity - the comparison of a MRT with a measure having established validity (VO_2max.), and B) Predictive validity - how well MRT could be predicted from performance in other outcome measures (Safrit, 1981, page 55).

A) Concurrent validity

In this study, oxygen uptake kinetics at the onset of self-paced walking could act as a substitute for another measure of cardiorespiratory fitness, for example, maximum oxygen uptake (VO_2max.). The test with established validity is known as the criterion test. Therefore concurrent validity is defined as "the degree to which a test correlates with a criterion test" (Safrit, 1981, pages 55 and 56). In order to demonstrate the concurrent aspect of criterion validity of MRT, a comparison was made with VO_2max. Due to the unsuitability of VO_2max. when frail patients are considered, this comparison only involved the young and healthy elderly volunteers.

It might be expected that those individuals with the highest levels of cardiorespiratory fitness, i.e. high VO_2max. values, would have the lowest MRT values. The time course of oxygen uptake (tau values) at the onset of exercise has previously been reported to be significantly correlated with VO_2max for both older (N=29, age 68.9 +/- 5.8 yr) and young (N=16, age 26.3 +/- 2.5yr) individuals (Chilibeck et al., 1996ii). This relationship seems plausible as a 'well adapted' cardiorespiratory system would be expected to perform well over a range of exercise intensities. An individual with a 'faster' adjustment of oxygen uptake at the beginning of exercise may also be expected to be capable of delivering and utilizing oxygen more efficiently at maximum levels of exercise. Therefore it would be expected that the higher an individual's VO_2max., the lower the MRT value for oxygen uptake at the onset of exercise.

B) Predictive validity

Predictive validity is of interest when a test user is interested in predicting how a study participant would perform in a "complex" test, in this case MRT, by assessing behaviour in a "simpler" test (Safrit, 1981, pages 57-58). If there is no relationship between the two variables then the outcome of the simpler test cannot be used to predict performance in the more complex test. Finding the means to explore predictive validity of a new measure of cardiorespiratory fitness in frail, older people is challenging due to the lack of comparable tests. One possibility is the Polar Fitness Test. This test is incorporated in Polar heart rate monitors and predicts VO_2max. on the basis of heart rate variability at rest.

Another possibility is to compare MRT with comfortable walking speed. The walking test used to examine oxygen uptake kinetics is a composite measure of an individual's cardiorespiratory fitness and also their flexibility, coordination, mobility, lower limb strength and power, and balance. Although walking speed is a composite measure, correlations between measures of aspects of cardiorespiratory fitness and walking speed have previously been made. For example, Kline et al., 1987 reported a correlation (*r* value) of 0.93 between an estimated measure of cardiorespiratory fitness (VO_2max.) from a 1-Mile Track Walk Test (Rockport Fitness Test) and actual VO_2max.

To characterise the functional ability of the hip fracture and stroke patients, they performed a functional test namely the sit to stand test and the score in the Elderly Mobility Scale was collected. Additionally as part of the STARTER trial, the stroke patients performed the 3-metre timed up and go test and the Functional Independence Measure (F.I.M.) score (further details on these outcome measures are given in the Methods Section of this chapter, page 130-132). These outcome measures were selected for comparison with MRT because, while they too are composite measures similar to walking speed, they provide some indirect insight into an individual's general physical ability and functional mobility. Individuals who score well on these function tasks might be expected to have higher levels of cardiorespiratory fitness.

3. Construct-Related Evidence of Validity

Construct validity was not assessed in relation to self-paced walking and oxygen uptake kinetics.

Volunteers

Four groups of volunteers participated in the study (Groups 1-4). Group 1 were young healthy men and women; Group 2 were healthy elderly men and women; Group 3 were elderly women after a hip fracture; and Group 4 were men and women recovering from a stroke (Table 6a). Data from the original pilot study were also included in the assessment of concurrent validity (Group 5, N=5 young women; N=5 healthy elderly women).

Group			**N**	**Age (yrs)**	**Height (cm)**	**Mass (kg)**
1	Young		16	23 (20-29)	171 (161-195)	63 (54-101)
		Women	10	24 (20-29)	169 (161-173)	61 (54-75)
		Men	6	23 (22-26)	182 (178-195)	76 (69-101)
2	Healthy Elderly		4	79 (78-87)	171 (168-176)	71 (64-75)
		Women	1	78	169	64
		Men	3	80 (78-87)	172 (168-176)	73 (70-75)
3	Hip Fracture	Women	12	78 (73-91)	169 (149-169)	64 (43-75)
4	Stroke		41	72 (49-86)		70 (45-120)
		Women	15	74 (60-86)		64 (50-79)
		Men	26	70 (49-85)		77 (45-120)
5	Pilot Young	Women	5	22 (18-23)	168 (164-177)	61 (54-65)
	Pilot Healthy Elderly	Women	5	78 (77-80)	157 (153-164)	55 (47-59)

Table 6a. Volunteer characteristics (Median and Range), (only individuals who provided at least one MRT value were included in studies of validity and therefore this table)

Methodology

Self-paced walking test

Detailed explanation of the methodology used for the self-paced walking tests for Groups 1-5 is given in Chapter Five (Feasibility) Methods Section, Pages 95-96.

Measurement of Maximum Oxygen Uptake (VO_2max.)

Maximum oxygen uptake (VO_2 max) was measured during a continuous progressive treadmill exercise test (Figure 6b). For the women in Group One, a VO_2max. ramp protocol was used (Figure 1, Appendix 4). For the men in Group One a similar ramp protocol was used but higher work rates were delivered (Figure 2, Appendix 4). In Treadmill Protocols 1 and 2, the work rate increased every 30s until the subject reached exhaustion. For Group Two a modified Naughton Protocol (Balady et al., 2000) was used for both the men and women (Figure 3, Appendix 4).

Each VO_2max. treadmill test was medically supervised with blood pressure and E.C.G. monitored before, during and after exercise. Ventilation and gas exchange were measured continuously throughout the test using a Metamax 3B ambulatory metabolic measurement system, (Cortex Biophysik). Ventilatory rate and fractional concentrations of oxygen and carbon dioxide were measured on a breath-by-breath basis, via a facemask (Figure 6b). VO_2max. was deemed to have been achieved if the volunteer reached voluntary exhaustion, $\geq$90% of age predicted maximum heart rate and an RER of $\geq$1.1 (Zhou et al., 2001). VO_2max. was calculated as the average VO_2 of the last 30 seconds of the protocol. The volunteers were also asked to rate their perception of exertion at the end of each work stage using the Borg scale (Borg, 1982) (Figure 4, Appendix 4).

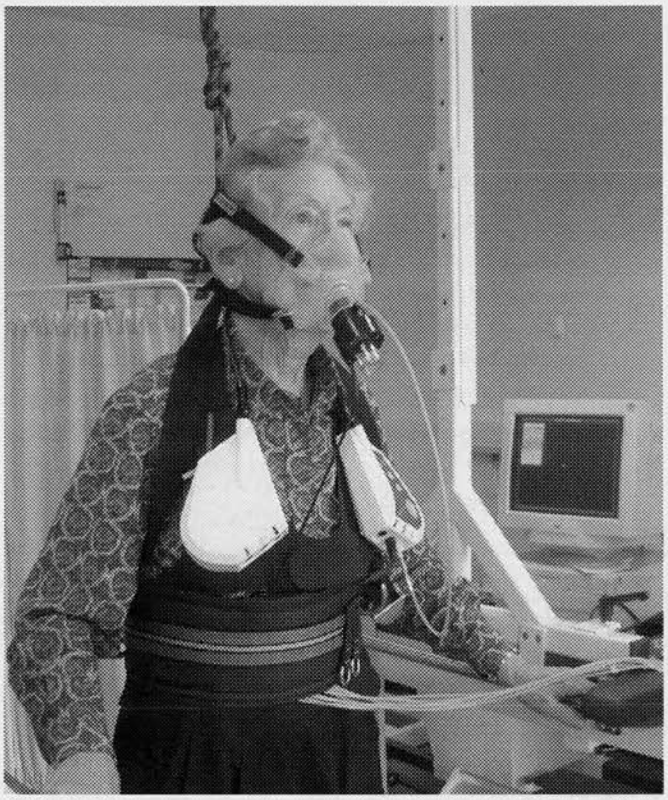


Figure 6b. Healthy elderly volunteer completing a modified Naughton treadmill testing protocol

<u>Polar Fitness Test</u>

The hip fracture group completed the Polar Fitness Test on their first study visit. Individuals were asked to sit quietly for 10 minutes while wearing a Polar Heart Rate Monitor and then the test was performed (VO_2max. value is predicted within 10-15 seconds based on resting R-R intervals).

<u>Walking Speed</u>

The average comfortable walking speed on each study visit was calculated from the average walking speed of the individual laps on the second and third walks.

Sit to stand

The sit to stand test, defined as the time taken to stand straight up from a chair without arms (Bohannon, 1995) was performed by the study participants in the hip fracture and stroke groups.

Elderly Mobility Scale (EMS)

The Elderly Mobility Scale, with a maximum score of 20, is based on an individual's ability to perform timed functional tasks of everyday living (Smith, 1994). An Elderly Mobility Scale score was obtained for the hip fracture group on their first test session. A score for the stroke group was obtained on each of their three study visits. (see Appendix 4, Figure 5 for Elderly Mobility Scale).

3 metre timed up and go

For the 3 metre timed up and go test, individuals are asked to stand up from a chair without using the chair arms, walk three metres away and return to the chair and sit down (Podsiadlo and Richardson, 1991). The entire task was timed for the study participants in the stroke group on each visit.

Functional Independence Measure (FIM)

The Functional Independence Measure is a widely accepted functional assessment measure, with an 18-item scale commonly used to assess progress during rehabilitation and level of disability (State University of New York Buffalo Guide, 1993).

The most endurance related aspects of the FIM scale are the locomotion items i.e. whether the individual can walk independently and safely or whether assistance is required and whether the individual can manage stairs. The Functional Independence

Measure was applied to the stroke group on each of their three study visits. (See Appendix 4, Figure 6 for FIM scale).

Results

1. Content-Related Evidence of Validity

To assess content validity and clinical credibility of MRT values at the onset of comfortable self-paced walking, a comparison was made between the MRT values obtained from young and healthy elderly volunteers (Groups 1 and 2) and hip fracture and stroke patients (Groups 3 and 4). Figure 6c illustrates the MRTs obtained from Groups 1-4 on Visit One.

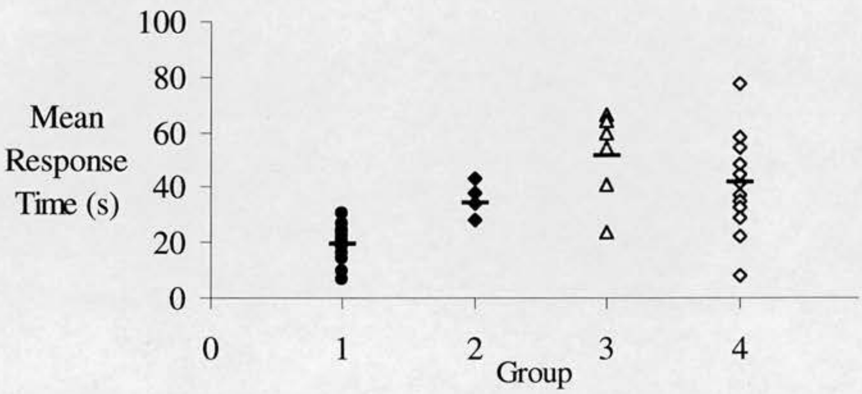


Figure 6c. MRT values from Visit One for volunteers in Group One (young, filled circles N=13), Group 2 (healthy elderly, filled diamonds N=4), Group 3 (hip fracture, unfilled triangles N=6) and Group 4 (stroke, unfilled diamonds N=15) (lines represent mean value)

2. **Criterion-Related Evidence of Validity**

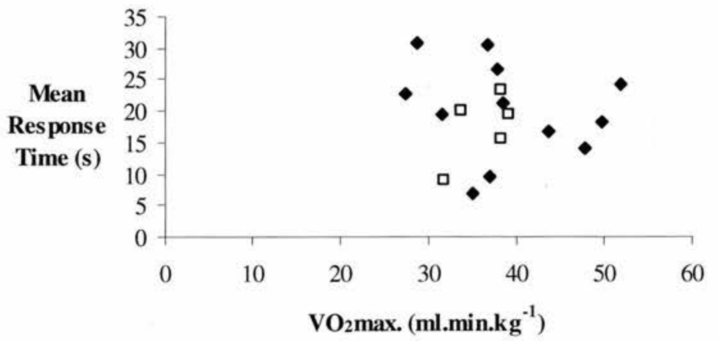
A) **Concurrent validity** - the comparison of the new measure of an aspect of cardiorespiratory fitness (MRT) with a measure having established validity of an aspect of cardiorespiratory fitness (VO_2max.)

There was no evidence of a significant negative correlation between VO_2max. and MRT (Table 6b and Figure 6d).

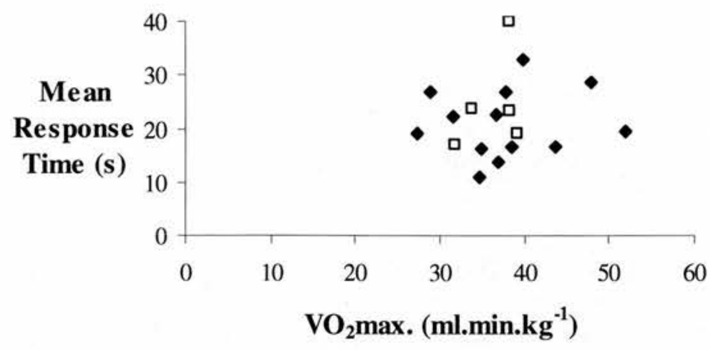
		N	**Rho value**	**p value**
Young	Visit One	17	-0.1	0.74
	Visit Two	18	0.2	0.53
Healthy Elderly	Visit One	6	-0.5	0.27
	Visit Two	6	0.4	0.47

Table 6b. Spearman's rho correlation coefficient of the relationship between MRT and VO_2max. and significance (p value)

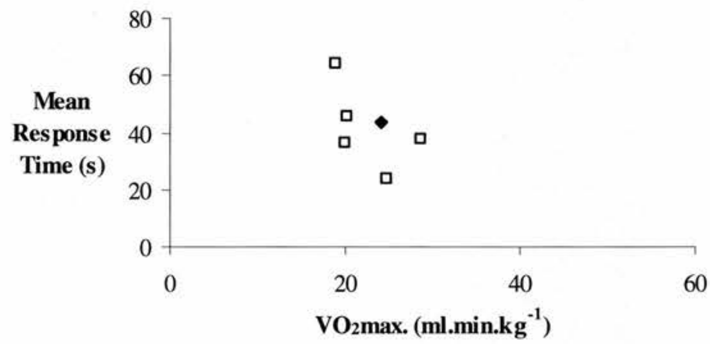
i – Young Visit One



ii – Young Visit Two



iii – Healthy Elderly Visit One



iv – Healthy Elderly Visit Two

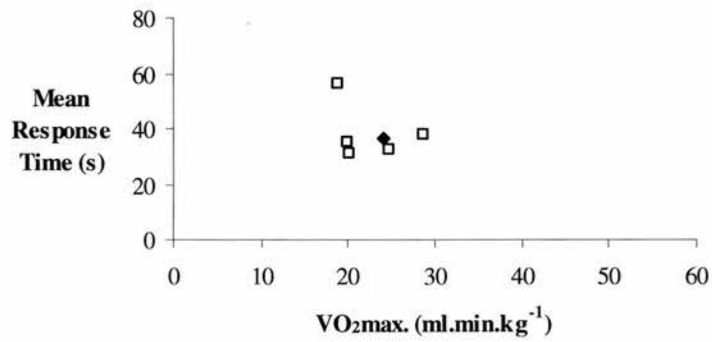


Figure 6d. Scatterplots of MRT values (s) and $VO_2max.$ ($ml.min.kg^{-1}$) for the young volunteers on Visit One (i) and Visit Two (ii) and the healthy elderly volunteers on Visit One (iii) and Visit Two (iv) (diamonds represent main study volunteers and squares represent pilot study volunteers in Graphs i-iv)

B) Predictive validity

i) MRT versus Polar Fitness Test

The Polar Fitness Test did not provide rational estimations of VO_2max. in the hip fracture group (either a value was not given at the conclusion of the test or a value was given that was obviously incorrect).

ii) MRT versus walking speed

Table 6b shows the relationship between each individual's 'comfortable' walking speed and MRT for Groups 1-4. A significant negative correlation between 'comfortable' walking speed and MRT was evident on the third visit in the stroke group only. Scatterplots of the relationship between MRT and walking speed for each of the four groups are given in Appendix 4, Figure 7.

		N	**Rho value**	**p value**
Young	Visit One	16	0.4	0.22
	Visit Two	13	0.3	0.21
Healthy Elderly	Visit One	4	0.8	0.2
	Visit Two	3	1.0	<0.01
Hip Fracture	Visit One	6	0.1	0.87
	Visit Two	10	-0.3	0.41
Stroke	Visit One	15	-0.2	0.49
	Visit Two	22	0.0	0.98
	Visit Three	23	**-0.5**	**0.04***

Table 6c. Spearman's rho correlation coefficient of the relationship between MRT and walking speed and significance (p value) (* correlation is significant at the 0.05 level (2-tailed))

iii) MRT versus Sit-to-Stand

There was no evidence of a significant positive relationship between MRT and sit to stand (Table 6d). Scatterplots of the relationship between MRT and 'sit-to-stand' are given in Appendix 4, Figure 8.

		N	Rho value	p value
Hip Fracture	Visit One	5	-0.1	0.87
	Visit Two	8	0.6	0.12
Stroke	Visit One	15	-0.2	0.53
	Visit Two	21	-0.1	0.70
	Visit Three	20	0.4	0.10

Table 6d. Spearman's rho correlation coefficient of the relationship between MRT and sit-to-stand and significance (p value) in the hip fracture and stroke groups

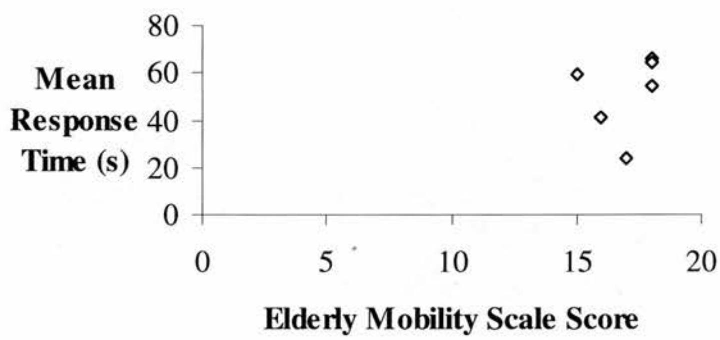
iv) MRT versus Elderly Mobility Scale Score

There was no evidence of a significant negative correlation between MRT and Elderly Mobility Scale Score in the hip fracture group (Table 6e, Figure 6e). (Spearman's correlation coefficient was not calculated for the stroke group as the Elderly Mobility Scale measurement had a negatively skewed distribution due to ceiling or near-ceiling effects).

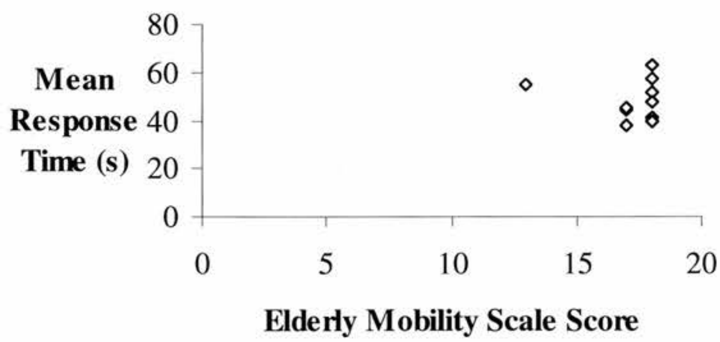
		N	Rho value	p value
Hip Fracture	Visit One	6	0.4	0.43
	Visit Two	10	-0.2	0.66
Stroke	Visit One	15	-	-
	Visit Two	22	-	-
	Visit Three	19	-	-

Table 6e. Spearman's rho correlation coefficient of the relationship between MRT and Elderly Mobility Scale (EMS) and significance (p value) in the hip fracture and stroke groups

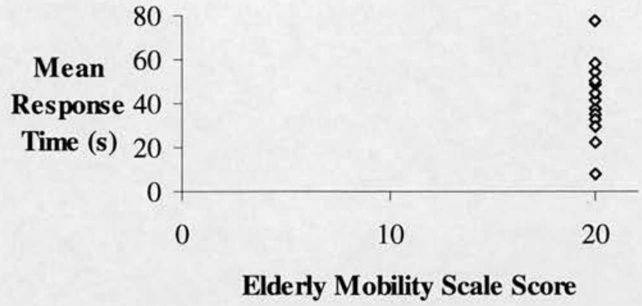
i - Hip Fracture Visit One



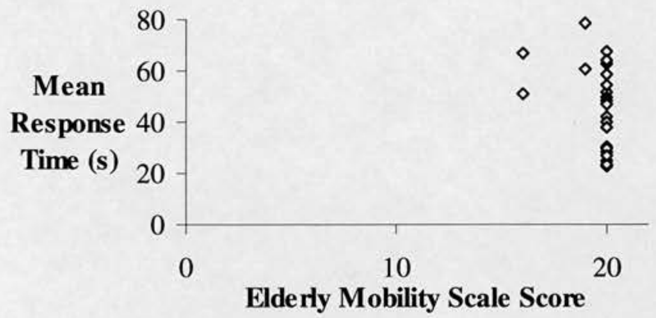
ii - Hip Fracture Visit Two



iii - Stroke Visit One



iv - Stroke Visit Two



v - Stroke Visit Three

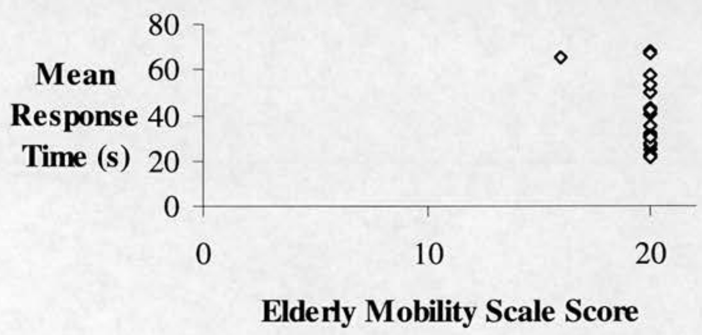


Figure 6e. Scatterplots of MRT values (s) and Elderly Mobility Scale Score for the Hip Fracture Group on Visit One (N=6) and Two (N=10) (Graphs i & ii) and the Stroke group on Visit One (N=15) (Graph iii), Visit Two (N=22) (Graph iv) and Visit Three (N=19 (one missing EMS score)) (Graph v)

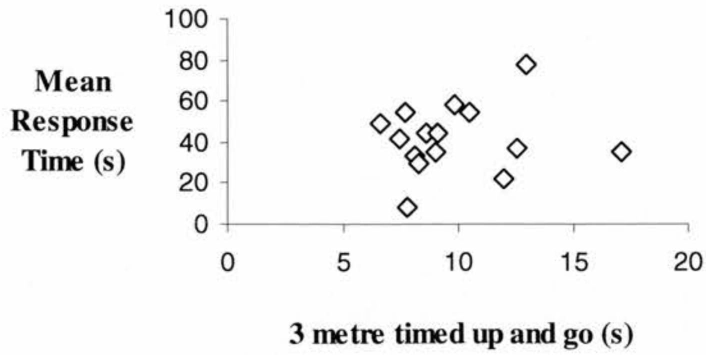
v) MRT versus 3-metre timed up and go

A significant positive correlation between MRT and 3-metre timed up and go was evident on Visit 3 only in the stroke group (rho = 0.5; p value = 0.01), Table 6f and Figure 6f.

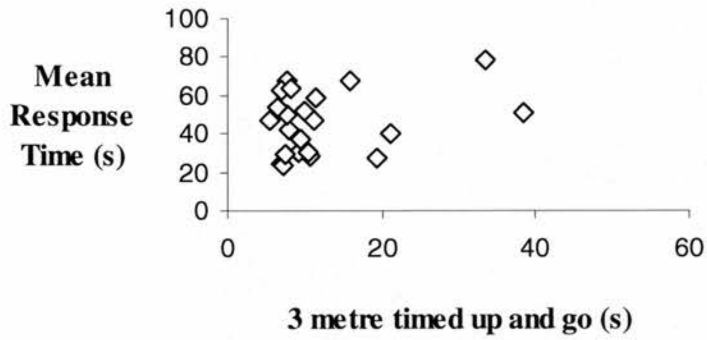
		N	Rho value	p value
Stroke Group	Visit One	15	0.1	0.65
	Visit Two	22	0.1	0.57
	Visit Three	20	**0.5**	**0.01***

Table 6f. Spearman's rho correlation coefficient of the relationship between MRT and 3-metre timed up and go and significance (p value) in the stroke group

i - Stroke Visit One



ii - Stroke Visit Two



iii - Stroke Visit Three

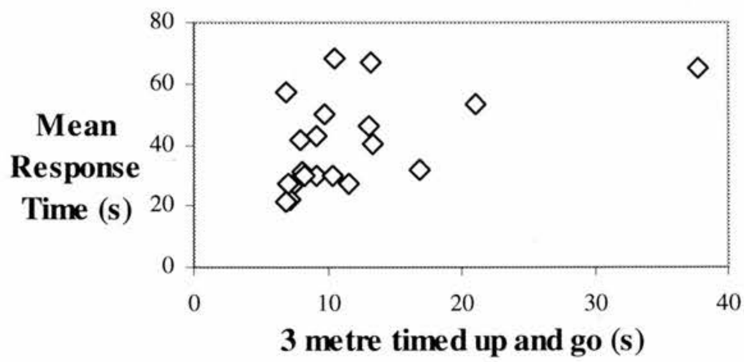


Figure 6f. Scatterplots of the relationship between MRT and 3 metre timed up and go for the Stroke group (Group 4) on Visit 1 (i), Visit 2 (ii) and Visit 3 (iii)

vi) MRT versus FIM score

There was no significant negative correlation between MRT and FIM score in the stroke group (Table 6g). Scatterplots of the relationship between MRT and FIM score are given in Appendix 4, Figure 9.

		N	Rho value	p value
Stroke	Visit One	15	0.5	0.06
	Visit Two	21	0.2	0.44
	Visit Three	20	-0.2	0.37

Table 6g. Spearman's rho correlation coefficient of the relationship between MRT and FIM score and significance (p value) in the stroke group

Discussion

The objective of this chapter was to consider the **relevancy** aspect of validity of oxygen uptake kinetics measured at the onset of self-paced walking as a measure of an aspect of cardiorespiratory fitness. Of the three types of validity identified, two have been investigated within the context of this measure – content related and criterion related validity.

1. Content-Related Evidence of Validity

Content validity was assessed by applying the measure (MRT measured at the onset of self-paced walking) to four groups of young men and women, healthy elderly men and women and frail patient groups. The expected relationship was that the individuals with lower levels of cardiorespiratory fitness and older individuals would show the highest MRT values. As illustrated in Figure 6c the young volunteers recorded the lowest MRT values with a mean value of 20 seconds on Visit One. This was followed by the healthy elderly group with a mean value of 37 seconds and then the stroke group with a mean value of 41 seconds and finally the hip fracture group with a mean value of 52 seconds. The MRT measured at the onset of self-paced walking was judged qualitatively to demonstrate content validity (McDowell, I. & Newell, C., 1996).

Criterion-Related Evidence of Validity

A) Concurrent validity

Concurrent validity of the MRT at the onset of self-paced walking was investigated by assessing the relationship between MRT and VO_2max. in young and healthy elderly volunteers. The expected relationship was the higher an individual's VO_2max. then the lower the MRT value (i.e. a negative correlation). This relationship was not evident and therefore concurrent validity of MRT at the onset of self-paced walking has not been demonstrated.

Although the link between VO_2max. and the time constant of the oxygen uptake kinetics has been investigated previously (Chilibeck et al., 1996ii) as well as in this study there is however, an underlying question as to the appropriateness of comparing VO_2max. and oxygen uptake kinetics. In relation to endurance training, it appears the rate and magnitude of improvements in VO_2max. and VO_2 kinetics with training appear to be dissociated (Babcock et al., 1994ii), suggesting the underlying physiological mechanisms associated with these aspects of cardiorespiratory fitness diverge. Therefore the lack of a correlation between VO_2 kinetics measured at the onset of self-paced walking and VO_2max. may be unsurprising. In addition, low/moderate intensity exercise and maximum intensity exercise are thought to elicit different cardiopulmonary responses i.e. maximum oxygen consumption is thought to be more heart rate dependent, while low/moderate submaximal exercise testing is thought to be more dependent on changes in pump function/stroke volume (Brunner-La Rocca et al. 1999). Brunner-La Rocca et al. (1999) found MRT was weakly to moderately correlated to peak VO_2 ($r=-0.49$, $p<0.001$) in 48 patients with mild to moderate chronic heart failure (mean age 55 (SD 10) years) (VO_2 kinetics were assessed during six minutes of treadmill walking at 1mph at 6% grade corresponding to approximately 0.5 W/kg body weight). They speculated that the higher the work load, the more heart rate dependent oxygen kinetics became. Therefore oxygen uptake kinetics at the onset of higher work loads might correlate better with maximum oxygen uptake. This finding is supported by Sietsema et al., 1989. The MRTs at the onset of higher workload cycling (100W and 150W) were significantly inversely correlated with peak VO_2 (N=10, aged 29 - 42 years). This might provide a rational for the lack of correlation between VO_2max. and MRT at the onset of comfortable self-paced walking as comfortable self-paced walking has previously been shown to be of low exercise intensity (33% VO_2max.) in young women and moderate exercise intensity (56% VO_2max.) in healthy elderly women (Fitzsimons et al., 2005).

A further means of assessing concurrent validity of oxygen uptake kinetics measured at the onset of self-paced walking might be a comparison with the 'gold-standard' measure of kinetics – oxygen uptake kinetics measured at the onset of square-wave exercise transitions on a cycle ergometer. There is however, a concern with this comparison in that some researchers have observed differences in oxygen uptake kinetics across different exercise modalities. Cerretelli et al., 1977 was the first study to compare VO_2 kinetics between exercise modes. They compared arm cranking to cycling and found the on-transient was significantly slower at the same VO_2 for arm cranking exercise compared to cycling. Carter et al., 2000 reported tau values were similar between running and cycling at a range of exercise intensities, contrasting with the findings of Hill et al., 2003 who reported significantly lower tau values at the onset of running compared to cycling exercise. Further research is required to uncover the effects of exercise mode on kinetics before a self-paced walking kinetics versus cycling/treadmill kinetics comparison is meaningful. A possible rationale for differences in kinetics between modes of exercise may be that the muscles used in day-to-day activities (such as walking) are likely to be relatively better trained than those used for other exercise modes. This explanation would be particularly important when older individuals are considered. This was the rational used by Chilibeck et al., 1996i to explain the significantly slower kinetics observed in at the onset of cycling compared to kinetics at the onset of treadmill walking or plantar flexion exercise in older (but not young) volunteers. This finding questions the validity of a comparison of oxygen uptake kinetics from the onset of self-paced walking with the measure of oxygen uptake kinetics at the onset of cycling exercise.

B) Predictive Validity

Predictive validity of the MRT measured at the onset of self-paced walking was assessed by exploring the relationship between the MRT value and the Polar Fitness Test as well as other measures of functional performance/mobility, i.e. walking speed, Sit-to-Stand time, Elderly Mobility Scale (EMS) Score, 3-metre timed up and go and the Functional Independence Measure (F.I.M.) score.

The Polar Fitness Test proved unsatisfactory in the hip fracture group and was therefore not applied to the stroke group. To my knowledge this is the first study to examine the use of the Polar Fitness Test in frail patients. Due to the inherent problem of utilizing any putative measurement of fitness in elderly people that relies upon heart rate, the Polar Fitness Test proved questionable, i.e., the test either did not provide a value of VO_2max., or gave a value which was obviously incorrect. The reasons are unknown but may have been due to previously undetected cardiac irregularities.

The MRT at the onset of self-paced walking was then compared with other measures of performance/mobility. A negative correlation with MRT was expected with walking speed, E.M.S score and F.I.M. score. A positive correlation was expected with sit-to-stand and 3-metre timed up and go. The presence or absence of these relationships was explored by investigating the rank correlation (Spearman's Rank Correlation) between MRT and each of the variables. Due to ceiling effects in both the hip fracture and stroke groups for the E.M.S. score the predictive validity of this measure in relation to MRT cannot be commented upon.

A significant correlation between MRT and comfortable walking speed was demonstrated once in the stroke group on Visit 3 (rho = -0.5; p=0.04). Similarly, a significant positive correlation between 3 metre timed up and go was evident in the stroke group on Visit 3 (rho = 0.5; p=0.01). Other significant correlations between MRT and comfortable walking speed, sit to stand, 3 metre timed up and go, or FIM score were not evident. Due to the small number of significant correlations between MRT and these functional and mobility measures, predictive validity of MRT has not been demonstrated.

Summary

A group comparison of MRT demonstrated content validity. Criterion-related concurrent validity and predictive validity of MRT were not demonstrated.

CHAPTER 7: Is the measurement of a time constant of oxygen uptake at the onset of 'comfortable' self-paced walking **reproducible**?

Introduction

Volunteers

Methodology

Results

Discussion

Summary

Introduction

If the MRT measured at the onset of self-paced walking is to be of use clinically then an estimate of the reliability of the measure is required. A reliable measure is essential in order for example, to assess the effectiveness of rehabilitation exercise training programmes. It is important to know if the effects of a training programme are 'real' or due to measurement error (Atkinson and Nevill, 1998). The size of measurement error associated with a particular measurement technique will impact on the statistical power of a study and sample size estimation for future experiments (Atkinson and Nevill, 1998).

Test reliability relates to how consistent a measure is over time (Atkinson and Nevill, 1998; Wood, 1989, page 24). It is realistic to assume some amount of error will be present with continuous measurements. Reliability could therefore be considered as the amount of measurement error that is acceptable for the measure to be of practical use.

Various types of reliability have been identified (Baumgarter, 1989, page 45).

1. **Relative Reliability**

   Relative reliability is the degree to which individuals maintain their position in a group when measures are made repeatedly (Baumgarter, 1989, page 46). A correlation coefficient is usually used to assess relative reliability (Atkinson and Nevill, 1998). The Pearson's correlation coefficient is commonly used to assess relative reliability, with the assumption if there is a high (>0.8) and statistically significant correlation then the equipment/measure is reliable (Atkinson and Nevill, 1998). A correlation coefficient based on rank position in a group (Spearman's) may however be more revealing when investigating relative reliability as it "has the added benefit of making no assumption on the shape of the data distribution and being less affected by outliers in the data" (Atkinson and Nevill, 1998).

2. **Absolute Reliability**

Absolute reliability is defined as "the amount of variability to be expected in a person's score if the person were tested again that day or several days later" (Baumgartner, 1989, page 46). Methods of assessing absolute reliability are the Standard Error of the Measurement (SEM) and Limits of Agreement method. Neither method is affected by the range of measurements (Atkinson and Nevill, 1998). They both provide an indication of the variability in repeated tests for specific individuals and are not dependent of an individual's rank position (Atkinson and Nevill, 1998). Absolute reliability measures such as SEM and Limits of Agreement are advantageous over measures of relative reliability as it is easier to extrapolate the results of absolute reliability studies to new individuals and compare reliability between different measurement tools (Atkinson and Nevill, 1995).

i. The SEM ($SEM=SD\sqrt{(1-ICC)}$ (SEM is the standard error of the measurement; SD is the sample standard deviation; ICC the intraclass correlation coefficient) is generally used as a summary statistic and is expressed in actual units of the measurement, which is useful since the smaller the SEM the more reliable the measurements (Atkinson and Nevill, 1995).The SEM is a measure of within-subject variation (Hopkins, 2000).

ii. Like SEM, the Limits of Agreement are a measure of within-subject variation (Hopkins 2000). The main difference between these statistics is that the Limits of Agreement assume there will be differences between repeated test measurements. By plotting the data with a line of equality, some insight can be gained into where all the points would lie if the measurements were the same on both test sessions (Bland and Altman, 1986). The Bland-Altman plot, (Bland & Altman, 1986) (the individual subject differences between the tests plotted against the respective individual means) gives an indication of systematic bias and random error by investigating the direction and size of the scatter around the zero line. The Bland and Altman plot will also provide some indication of whether the amount of random error increases as the size of the measured values increase (heteroscedasticity of the data) (Atkinson and Nevill, 1998). If the data do not show heteroscedasticity (i.e. correlation coefficient is near zero and the differences are normally distributed) then Limits of Agreement may be calculated (systematic bias +/- 1.96 x SD of test-retest differences).

3. Measurement error – systematic bias and random error

Systematic changes in a measure from one test session to the next can be due to effects such as learning, training, motivation or fatigue (Hopkins, 2000). Systematic bias might be introduced into the measurement of oxygen uptake kinetics if, for example, there was insufficient recovery time between tests. Random error could be introduced to a measurement due to, for example, biological variation (Atkinson and Nevill, 1998). Systematic bias (the average of the test-retest differences) and random error (random error component =1.96 x SD of test-retest differences) are both accounted for in the Limits of Agreement calculation.

The purpose of this study was to examine the reliability of oxygen uptake kinetics measured at the onset of self-paced walking using these various types of reliability. If the amount of variation is large from one visit to the next then the measurement may not be suitable for use with individual patients. It may however, still be suitable for use with a group. By studying the reproducibility of MRT at the onset of self-paced walking it would therefore be possible to obtain some indication of the value of MRT as an outcome measure within an individual and a group setting.

Volunteers

Reproducibility of MRT was studied in young (Group One) and healthy elderly (Group Two) men and women, and in women recovering from a hip fracture (Group Three, N=4 permitted a Visit One – Visit Two comparison) (Table 7a). Data obtained from pilot work were added to Groups One and Two respectively (i.e. an additional 5 young women and 5 healthy elderly women).

Group			N	Age (years)	Height (cm)	Mass (kg)
1	Young		18	23 (18-29)	171 (161-195)	64 (54-101)
		Women	13	22 (18-29)	170 (161-177)	61 (54-75)
		Men	5	23 (22-26)	182 (178-195)	76 (69-101)
Group 2	Healthy Elderly		8	78 (77-87)	163 (153-172)	57 (47-73)
		Women	6	78 (77-80)	160 (153-169)	55 (47-64)
		Men	2	83 (78-87)	170 (168-172)	71 (70-73)
Group 3	Hip Fracture	Women	4	82 (78-88)	159 (149-163)	54 (50-63)

Table 7a. Volunteer characteristics (those individuals who provided a Visit One – Visit Two comparison for MRT)

Methodology

Volunteers completed three 'comfortable' self-paced walks on each of two separate occasions, with the second visit not more than two weeks after the first visit. Detailed explanation of the methodology used is given in Chapter Five (Feasibility) Methods Section, Pages 95 and 96.

Results

Figure 7a shows the MRTs from the young, healthy elderly and hip fracture groups on Visit One and Visit Two.

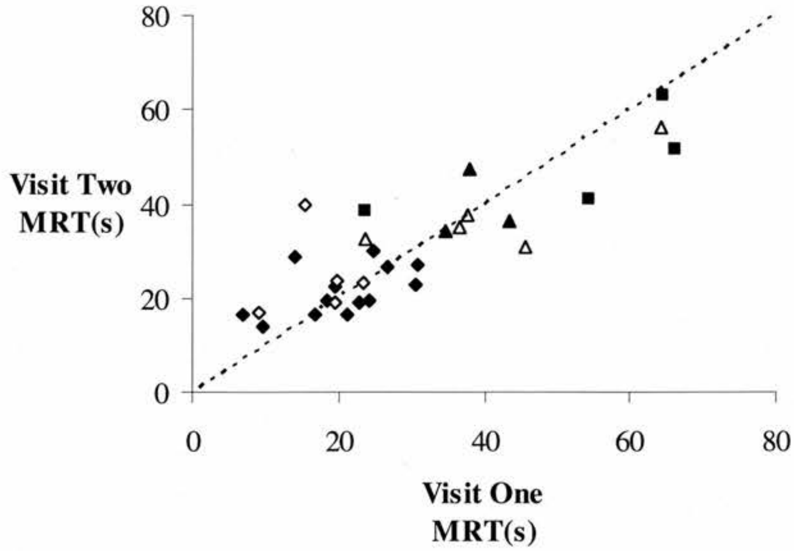


Figure 7a. MRT Visit One value plotted against MRT Visit Two value for Group One (diamonds), Group Two (triangles) and Group Three (squares), (unfilled symbols represent pilot work volunteers, the dashed line through the origin represents the line of equality)

Although MRT Visit One and MRT Visit Two values do not agree exactly the two measures are obviously related. The various aspects of reliability were then considered.

1. **Relative reliability**

To consider the relative reliability of the MRT in each of the three groups the rank listing for MRT was analysed (Table 7b).

A. Young group

Group One	MRT (s) Visit One	Rank	MRT (s) Visit Two	Rank
1	7	1	16	2
2	9	2	17	5
3	10	3	14	1
4	14	4	29	16
5	15	5	40	18
6	17	6	17	3
7	18	7	20	9
8	19.50	8	22	10
9	19.54	9	19	7
10	20	10	24	13
11	21	11	17	4
12	22.7	12	19	6
13	23.5	13	23	12
14	24	14	19	8
15	25	15	30	17
16	27	16	27	14
17	31	17	23	11
18	31	18	27	15

B. Healthy elderly group

Group Two	MRT (s) Visit One	Rank	MRT (s) Visit Two	Rank
1	24	1	32	2
2	35	2	34	3
3	37	3	35	4
4	37.7	4	38	6
5	38.0	5	47	7
6	44	6	37	5
7	46	7	31	1
8	64	8	56	8

C. Hip fracture group

Group Three	MRT (s) Visit One	Rank	MRT (s) Visit Two	Rank
2	24	1	38	1
1	54	2	41	2
4	64	3	63	4
3	66	4	52	3

Table 7b. Rank list for MRT on Visit One and Visit Two for A. Young group; B. Healthy elderly group and C. Hip fracture group

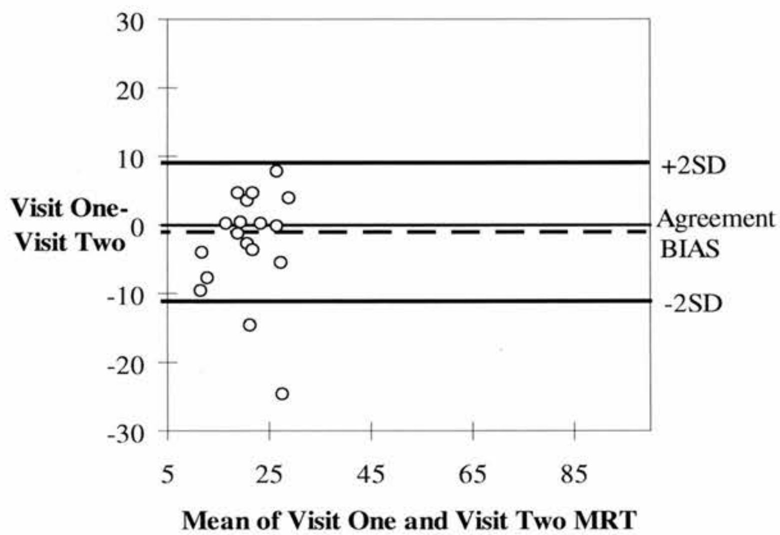
From the rankings of the sample of MRT values, a correlation coefficient (Spearman's correlation coefficient) was calculated. The Spearman's correlation coefficient for the young group gave an rho value of 0.5, with a p value of 0.06 (2-tailed). The Spearman's rho value for the healthy elderly group was 0.4 with a p value of 0.29 (2-tailed) and for the hip fracture group an rho value of 0.8 with a p value of 0.20 (2-tailed).

2. Absolute Reliability

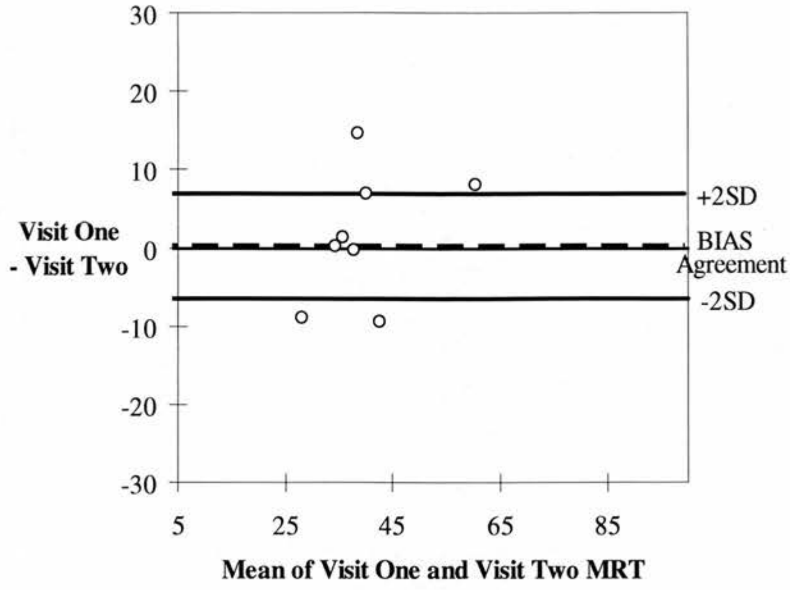
i. Standard Error of the Measurement (SEM)

To assess the absolute reliability for the MRT (the degree to which repeated measures vary for individuals), the Standard Error of the Measurement (SEM) was calculated. The SEM statistics can only be used if there is no heteroscedasticity present in the data, i.e. if the amount of absolute error is the same for individuals with high values as for individuals with low values. Examination of the direction and magnitude of the scatter of the MRT values using Bland-Altman plots (Figure 7b), showed no evidence of a systematic bias in the data. The data for each group do not show heteroscedasticity (it is difficult to assess in Group Three due to the small sample size). Homogeneity of variance between visit one and visit two for each of the three groups was non-significant, indicating no heteroscedasticity (young group Levene statistic 0.11, p value = 0.75 (based on the mean); healthy elderly group Levene statistic 0.23, p value = 0.64; hip fracture group Levene statistic 0.84, p value = 0.34).

(A)



(B)



(C)

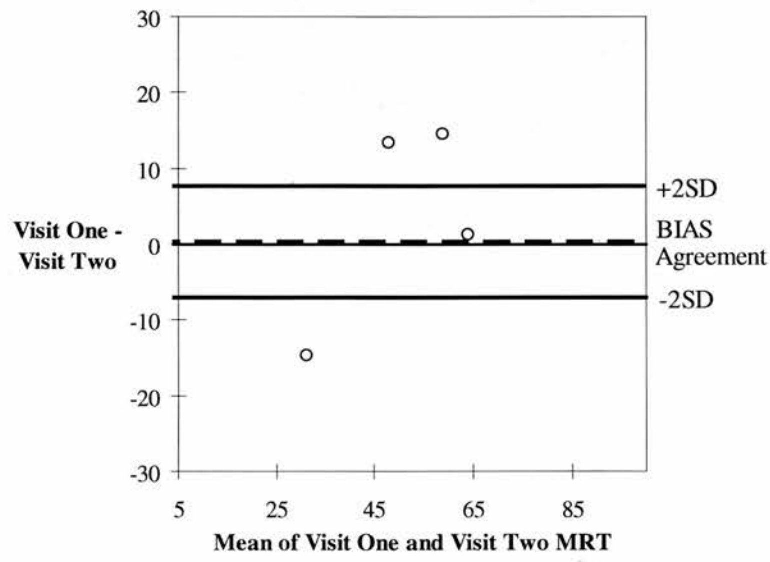


Figure 7b. Bland-Altman plots of the test-retest MRT values for Group One (A), Group Two (B) and Group Three (C)

SEM values for the young, healthy elderly and hip fracture volunteers are given in Table 7c.

	Young	Healthy elderly	Hip Fracture
SEM (s)	4.9	4.4	7.0

Table 7c. Standard Error of Measurement (SEM) for Visit One – Visit Two MRT values for Group One (young), Group Two (healthy elderly) and Group Three (hip fracture)

ii. Limits of Agreement

A more comprehensive indicator of absolute reliability i.e., Limits of Agreement was also calculated. Figure 7b (A-C, Bland-Altman plots) presents the test-retest data and shows the individual subject differences between the tests plotted against the respective individual means.

The limits of agreement, which represent the 95% likely range for the difference between a volunteer's MRT value on the two tests, were -18 to 13s for the young group, -15 to 18s for the healthy elderly group and -23 to 30s for the hip fracture group. Due to the small sample size associated with the Limits of Agreement calculation the results should be interpreted with caution. Altman, 1991 states a sample size of at least 50, but preferably larger, is desirable for a comparison study.

3. Measurement error

i. Systematic Bias

The grand mean for the young group was 21 seconds (i.e. the mean MRT value of Visits One and Two for the group). The systematic bias for the MRT from Visit One to Visit Two for the young group was -2.7 seconds (the Visit One MRT values were on average 2.7 seconds lower than the Visit Two MRT values). The systematic bias for the healthy elderly group was +1.6 seconds and the grand mean was 40 seconds. For the hip fracture group, the systematic bias was +3.7 seconds and the grand mean was 50 seconds. The systematic bias for each group is shown on the Bland and Altman plots as the dashed line (Figure 7b). The 95% confidence intervals of the bias included zero indicating the bias was not significant (-6.6 to 1.2 young group; -5.3 to 8.5 healthy elderly group; -17.9 to 25.3 hip fracture group).

ii. Random Error

The standard deviation of the differences in MRT between Visit One and Visit Two when multiplied by 1.96 is used to obtain a 95% random error component. The random error component for the young group was 15.3 seconds, for the healthy elderly group was 16.2 seconds and for the hip fracture group 26.6 seconds.

Discussion

The relative and absolute reliability of MRT measured at the onset of self-paced walking was considered in young and healthy elderly men and women and in women recovering from a hip fracture.

Relative reliability was assessed by ranking MRT within each group from Visit One and comparing with Visit Two. The Spearman's correlation coefficient for the young group gave an rho value of 0.5, with a p value of 0.06 (2-tailed). The Spearman's rho value for the healthy elderly group was 0.4 with a p value of 0.29 (2-tailed) and for the hip fracture group the rho value was 0.8 with a p value of 0.20 (2-tailed). For the test to have optimum clinical usefulness (i.e. identical MRT values on both test visits) then the correlation coefficient would have a value of one.

The standard error of the measurement (SEM) and Limits of Agreement methods were both used to assess the absolute reliability of the MRT. Both these statistics are unaffected by the range of measurements and therefore provide an indication of the variability in repeated tests for individuals, independent of group ranking positions (Atkinson and Nevill, 1998).

The SEM statistic is expressed in the units of measurement, therefore the smaller the SEM the more reliable the measurements (Atkinson and Nevill, 1998). The SEM for the young group was 4.9 seconds, for the healthy elderly group 4.4 seconds and for the hip fracture group 7.0 seconds. Koufaki et al., 2002i reported a SEM of 12.3

seconds in end-stage renal disease patients. The SEM is also of interest as it can only be used if the data do not show heteroscedasticity (i.e. the amount of absolute error is the same regardless of the value). Therefore it can be assumed that the SEM is the same for individuals in the group recording high MRT values as for the individuals in the group recording low MRT values.

Limits of Agreement represent the test-retest differences for 95% of a population. The Bland-Altman plots for each of the three groups did not show a systematic bias or significant heteroscedasticity of the data. The 95% Limits of Agreement were -18 to 13 seconds for the young group, -15 to 18 seconds for the healthy elderly group and -23 to 30 seconds for the hip fracture group. If, for example, a new study participant who had suffered a hip fracture completed the necessary methodology to obtain a MRT from self-paced walking on two separate occasions, it could be said (with an approximate 95% probability) that the difference in MRT between two tests would lie within the limits of agreement (-23 to 30 seconds). A comparison of the limits of agreement in this study with limits of agreement from other studies assessing reliability of oxygen uptake kinetics is helpful to consider if the limits of agreement are narrow enough for the test to be of practical clinical use. Kilding et al., (2001) reported Limits of Agreement for both tau and MRT values from nine young men (mean age 21 years) during cycling exercise. Volunteers performed three consecutive transitions of cycling at 30W for six minutes, followed by 6 minutes at a moderate intensity (80%VT) on two occasions. The 95% Limits of Agreement for tau were -13.4 to 12.8 seconds while for the MRT -6.7 to 8.1 seconds. The Limits of

Agreement in this study are wider for the healthy elderly and hip fracture groups than the values reported for young men by Kilding et al. This may be attributable to increased day to day variability often evident in (frail) older people.

Systematic bias and random error components were calculated for each group to assess measurement error. If there is a consistent bias then it is possible to adjust for this by subtracting the mean difference from the new measure (Bland and Altman, 1986). The systematic bias for the MRT from Visit One to Visit Two for the young group was -2.7 seconds. To express the bias within the context of the data, the grand mean (mean of Visit One and Visit Two) of MRT for the young group was 21 seconds and therefore the bias represents 13% of the grand mean. As systematic bias for the healthy elderly group was +1.6 seconds and the grand mean was 40 seconds, the bias represents 4% of the grand mean. For the hip fracture group, the systematic bias was +3.7 seconds and the grand mean was 50 seconds. The systematic bias represents 7% of the grand mean. Systematic changes can be as a result of volunteer motivation, fatigue or learning. It is unlikely any of these factors would have had a significant impact on oxygen uptake kinetics at the onset of self-paced walking as any small variations in exercise intensity (i.e. if an individual walks slightly faster or slower) would be expected to have a minor effect on MRT.

The random error component for the young group was 15.3 seconds, for the healthy elderly group was 16.2 seconds and for the hip fracture group was 26.6 seconds. The amount of random error was minimised by using a relatively straightforward testing protocol (3 walks of 3 minutes), thereby reducing any impact of protocol variation on the random error component. The greater the random error component, the more individuals would be required for a given hypothesised experimental change.

Summary

1. SEM of the measure in young (4.9s), healthy elderly (4.4s) and hip fracture (7.0s) compares favourably with comparable data in the literature (12.3s in end-stage renal disease patients, (Koufaki et al., 2002i).
2. There was no evidence of a significant systematic bias from Visit One to Visit Two in each of the three groups (therefore no effect of learning, familiarisation or motivation).
3. Limits of agreement for the hip fracture group were -23 to 30 seconds. For an intervention related improvement in MRT to be evident, it must fall out with these limits.

CHAPTER 8: Is the measurement of a time constant of oxygen uptake at the onset of 'comfortable' self-paced walking sensitive to a **physical training intervention** in frail individuals?

Introduction

There is a growing body of literature comparing VO_2 kinetics between trained and untrained men and women, and the effects of physical fitness training in both sedentary and well-trained healthy young individuals, and healthy elderly adults and patient groups. In 1976 Weltman and Katch compared the oxygen uptake responses of two groups of volunteers with differing levels of aerobic fitness (VO_2max.): they noted the group with higher VO_2max. (4.9 +/- 0.4 $l.min^{-1}$) had a "clear tendency to take up oxygen to steady state at a faster rate" than the group with lower VO_2max. (3.9 +/- 0.4 $l.min^{-1}$). In 1978, Hickson et al investigated the effects of endurance training on VO_2 kinetics. Seven men trained for 10 weeks (6 days/week, 40 minutes/session). This study measured VO_2 kinetics at 40%, 50%, 60% and 70% of pre-training VO_2max. and after training at the same absolute and relative work rates. Significantly faster VO_2 kinetics were reported after the training programme.

In the intervening period a body of literature has accumulated supporting the findings of Hickson and his co-workers in 1978 (e.g. Cerretelli et al., 1979; Hagberg et al., 1980; Casaburi et al., 1987; Womack et al., 1995 ; Phillips et al., 1995; Norris and Pederson, 1998). Cerretelli et al., 1979 demonstrated the effects of training on VO_2 kinetics were highly specific to the type of exercise being performed – in their case swimming versus running. Phillips et al., 1995 conducted one of the first studies to demonstrate how rapidly VO_2 kinetics respond to an endurance training programme. Following only 4 days of training in 7 untrained young men (cycling for 2 hours/day at 60% of pre-training VO_2max.) the time constant, MRT was reduced in the group from 38 seconds to 35 seconds (after 4 days) and then further to 28 seconds after 30 days of training (training was 5 out of every 6 days). As the majority of studies to date had used untrained volunteers, in 1998 Norris and Pederson examined the response of trained cyclists (VO_2max. ~4 $l.min^{-1}$) to an eight week training programme. Once again the mean tau value of the group was reduced from the pre-training value of 29 seconds to 24 seconds (4 weeks) and 22 seconds (8 weeks). These findings have been confirmed by the recent studies of Demarle et al., (2001) and Billat et al., (2002).

Oxygen uptake kinetics are known to slow with increasing age (Babcock et al., 1994i; Bell et al., 1999; Chilibeck et al, 1996ii), a finding which has also been described in Chapter 6 of this thesis (Validity). It is unclear whether the age related reduction in oxygen uptake kinetics is due directly to the physiological changes that occur with ageing or indirectly as a result of the reduced activity levels frequently observed in older people. A number of training studies have been performed in healthy older people in an attempt to examine this. In 1994 Babcock et al., (1994ii) examined the response to training in 8 sedentary healthy older men (aged 65-78 years). The men trained (40 minutes of cycling) thrice weekly for 6 months. The training programme resulted in a ~20% improvement in VO_2max. along with a significant reduction in tau values (mean tau value pre training 62 seconds and mean tau value post training 32 seconds). This represented a 49% reduction in tau values – considerably greater than that reported for comparable studies in young people and also reduced the tau values of the older sedentary men to values normally observed in healthy young people.

In support of the findings of Phillips et al., 1995 in healthy young volunteers, Fukuoka et al. (2002) showed the increased sensitivity of oxygen uptake kinetics to a period of training when compared to more usual measures of cardiorespiratory fitness, such as VO_2max. in middle aged subjects (~51 years, N=11). A significant reduction in the time constant, tau (46.9 seconds to 34.4 seconds) was evident 15 days into a 90 day combined endurance and resistance training programme. A significant increase in VO_2peak was only evident after 60 days of training.

While many patient populations are unlikely to perform maximum intensity exercise during activities of daily living, they are likely to perform transitions from rest/mild exercise to higher intensity exercise on a regular basis. An individual with slow VO_2 kinetics would be expected to have a larger oxygen deficit at the onset of exercise and a larger oxygen debt at the end of exercise. This results in more breathlessness, increased discomfort and a longer recovery period (Jones and Poole, 2005, page 390). Oxygen uptake kinetics and their sensitivity to interventions such as physical exercise training have become the subject of an increasing number of studies in clinical populations. Assessment of kinetics in patient populations can be challenging. Very low absolute work rates may have to be used due to reduced tolerance for physical activity (Jones and Poole, 2005, page 390). With very low absolute amplitudes of oxygen uptake the signal to noise ratio might be expected to be low and therefore confidence in the estimation of the modelling parameters will be reduced (Lamarra et al., 1987). The Phase I response can represent a larger proportion of the entire response to steady state (first suggested by Sietsema et al., 1989), (supporting the use of a MRT value instead of a tau value). Ideally a large number of rest to exercise transitions would be performed to adequately fit the oxygen uptake response and ensure confidence in the parameters. This can be difficult or impossible to achieve in many patient groups (Jones and Poole, 2005, page 390).

A number of disease conditions have been investigated and been shown to impact on an individual's oxygen uptake kinetics – for example in patients with prior myocardial infarction, chronic heart failure, COPD, peripheral arterial disease, Type II diabetes and end-stage renal disease (Koike et al, 1994; Sietsema et al 1994; Belardinelli et al., 1998; Otsuka et al 1997; Puente Maestu et al., 2003; Bauer et al., 1999; Regensteiner et al., 1998; Brandenburg et al., 1999; Koufaki et al 2002i,ii). Barstow et al. 1996 studied the effect of training 9 men with spinal cord injury (the volunteers were trained using electrical stimulation for 8 weeks (24 sessions each of 30 minutes). The MRT was significantly reduced from 154 seconds to 114 seconds. Puente Maestu et al., 2003 showed that training COPD patients (N=21 non-smoking men with severe, stable COPD, mean age 63 years) resulted in a significant reduction in tau from 84 seconds to 69 seconds (45 minute cycle ergometer training sessions, three times/week for six weeks). Similarly Otsuka et al. (1997) showed a significant reduction in tau values following training (from 64 seconds to 53 seconds) in patients with COPD (N=11, mean age 66 years, stable COPD; training three times per week for eight weeks). Participants in the Puente Maestu et al., (2003) and Otsuka et al. (1997) studies were required to perform an incremental exercise test on a cycle ergometer to the limit of tolerance as part of the trial. This suggests frailer COPD patients would have been excluded.

To date to the best of my knowledge, no studies investigating the response of oxygen uptake kinetics to physical fitness training after a stroke have been published. There is however a small but growing body of literature investigating the response of stroke patients to physical fitness training using other outcome measures. For example, Macko et al., (2005) investigated whether progressive treadmill aerobic training was more effective than conventional rehabilitation (stretching and low-intensity walking) to improve ambulatory function and cardiovascular fitness in patients with stroke (N=61; men and women >45 years of age with chronic (>6 months) hemiparetic gait after ischemic stroke). 25 patients completed the treadmill walking regimen and 20 patients the conventional rehabilitation (3 times per week for 6 months). Peak VO_2, 6 minute walk and Walking Impairment Questionnaire score were significantly improved in the treadmill training group with significant group-by-time interactions. Recent publications by Duncan et al., (2003) (and secondary analyses in Studenski et al., (2005)) and Pang et al., (2005) support the findings of Macko et al., (2005). Duncan et al., 2003 (and Studenski et al., 2005) reported significant improvements in balance, endurance, peak aerobic capacity and some aspects of quality of life following a targeted progressive physical fitness training intervention. The intervention group had significantly greater gains than a control group receiving usual care. Duncan et al., 2003 required potential volunteers to perform a cycle ergometer exercise stress test (the volunteer started pedalling at 60 rpm and 0 W, and workload was increased by 10 W each minute. Testing continued until "maximal effort" (90% maximal predicted heart rate) or a predefined end point was achieved) for inclusion in the exercise trial. Pang et al., 2005 investigated the effects of a community-based fitness and mobility exercise programme for older (aged 50 and over) adults. Significantly greater gains in cardiorespiratory fitness (VO_2max.), mobility and paretic leg strength were noted in the intervention group (N=32; progressive community based exercise programme) compared to the control group (N=31; seated upper extremity programme – no aerobic exercises, leg strengthening, or balance training were given) after thrice weekly classes for 19 weeks. While cardiorespiratory fitness was one of the principle outcomes of the study, the study design and applicability of the findings were compromised by the use of an inappropriate measure (VO_2max.) of cardiorespiratory fitness. In order to assess VO_2max. (and therefore inclusion in the trial), individuals had to pedal on a cycle ergometer at 60 revolutions per minute and to raise their heart rate to at least 60% of maximal heart rate. Once again, such methodologies may have excluded frailer stroke patients, arguably those who stand to benefit most from any improvements in their fitness.

Although the optimal training regimen for improving fitness after stroke remains to be established, it has been shown that stroke patients respond to exercise training. However the response of oxygen uptake kinetics to a training intervention in stroke patients is unknown. Additionally, by utilising VO_2peak and VO_2max. as outcome measures, previous studies may have excluded frailer stroke patients. The aim of this study was to investigate the sensitivity of oxygen uptake kinetics measured at the onset of self-paced walking to a progressive physical training intervention.

Volunteers

66 STARTER (STroke: A Randomised Trial of Exercise or Relaxation) study participants; 32 exercise group participants and 34 relaxation group participants.

	Exercise & Relaxation Groups	Exercise Group only	Relaxation Group only
N number	66	32	34
Mean age (SD)	71.9 (9.9)	72.0 (10.4)	71.7 (9.6)
Number of men	36	18	18

Table 8a. Stroke Patient Characteristics (Chief Scientist Office Final Report, Scottish Executive, CZB/4/46, Appendix Five)

Details of the identification of volunteers for the STARTER trial and the recruitment process are given in the Chief Scientist Office Final Report, Scottish Executive, CZB/4/46, Appendix Five, Figure 2.

Sample Size calculation

32 men and women were randomised to the training intervention. A sample size of N=28 was calculated for the assessment of effects of the training intervention given a predicted 20% difference in the MRT post intervention and a standard deviation of 17 seconds. A standard deviation of 17 seconds was reported for tau by Puente Maestu et al., (2001) in a group of COPD patients (N=35, mean age 64.4 years (SD 5)).

Methodology

Study participants were assessed at baseline, prior to the start of classes. Full details of the baseline assessments are given in the Chief Scientist Office Final Report, Scottish Executive, CZB/4/46, Appendix Five, Figure 2. At the end of the baseline assessment set, STARTER participants performed the self-paced walking tests. Detailed explanation of the methodology used for the self-paced walking tests is given in Chapter Five (Feasibility) Methods Section, Pages 95 and 96.

Study participants were randomised to either 12 weeks of exercise or relaxation classes. Classes took place three times a week (Monday, Wednesday and Friday). Further details of the randomisation process and the interventions, both exercise and relaxation delivered, are given in Appendix Five, Figure 2 (Chief Scientist Office Final Report, Scottish Executive, CZB/4/46).

Post-intervention assessments

Study participants were re-assessed at the end of the classes and also four months later. Volunteers performed the same tests as at baseline, including the self-paced walking tests. The follow-up assessments followed an identical format to the baseline assessments (Appendix Five, Figure 2 Chief Scientist Office Final Report, Scottish Executive, CZB/4/46).

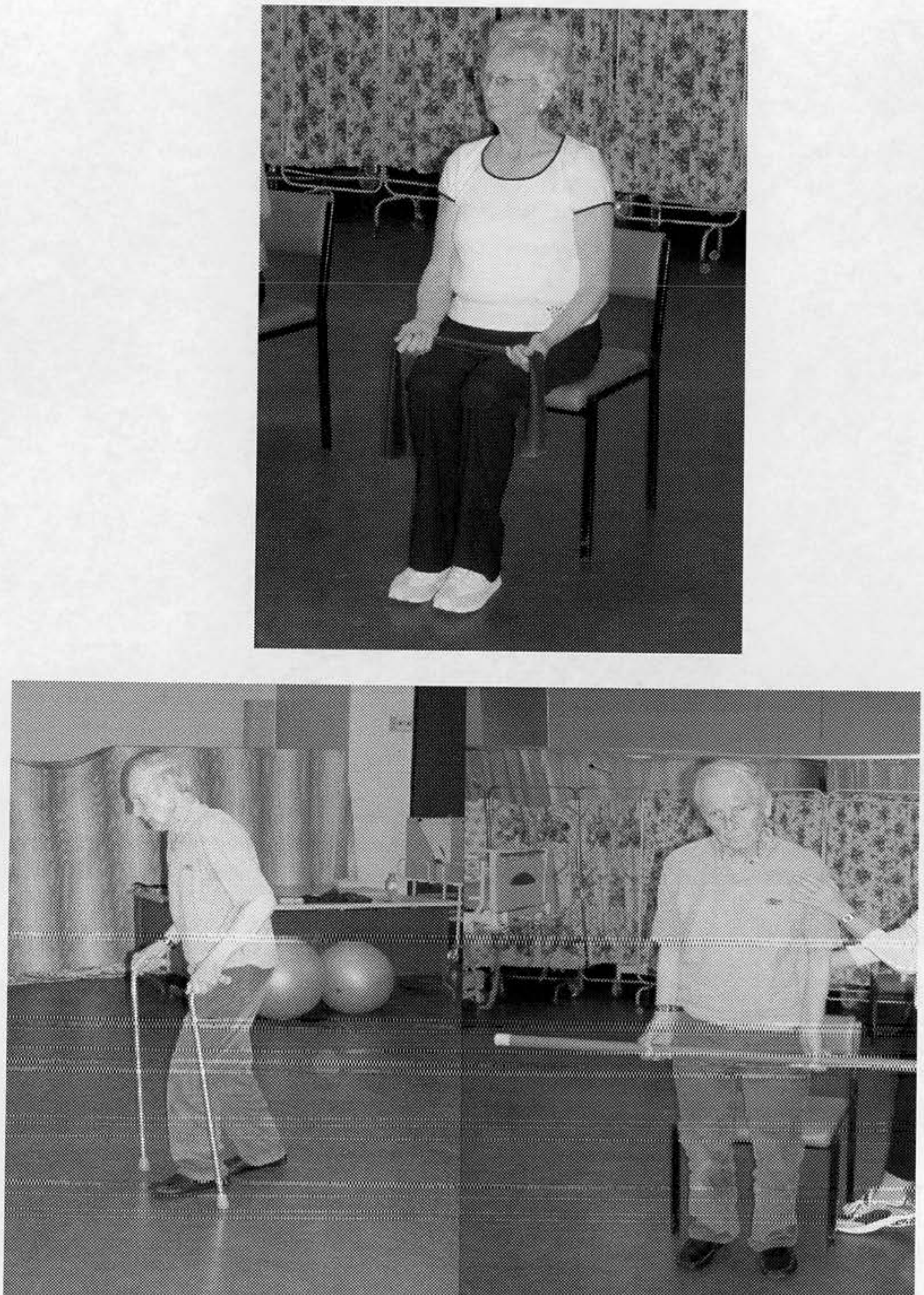


Figure 8a. Participants from the exercise group demonstrating some of exercises (top picture – therabands; bottom left – walking circuit; bottom right – bicep curls with pole)

Figure 8b. Relaxation class

Results

Training intervention

Of the thirty two individuals randomised to the exercise intervention, a MRT value was obtained for 7 individuals pre intervention (Visit One), an immediate post intervention MRT value was obtained for 11 individuals (Visit Two) and a four month post intervention follow-up (Visit Three) MRT was obtained for 9 individuals. A Visit One – Visit Two comparison of MRT was possible in only 4 individuals. A rational for the lower N numbers in each group is given in Chapter 5, Table 5h, Page 111 (Feasibility).

The MRTs for the training group are shown in Figure 8c for Visit One, Visit Two and Visit Three. The average MRT for the exercise group was 41.7 seconds (SD 21.1) on Visit One, 42.7 seconds (SD 15.0) on Visit Two and 42.6 seconds (SD 17.6) on Visit Three.

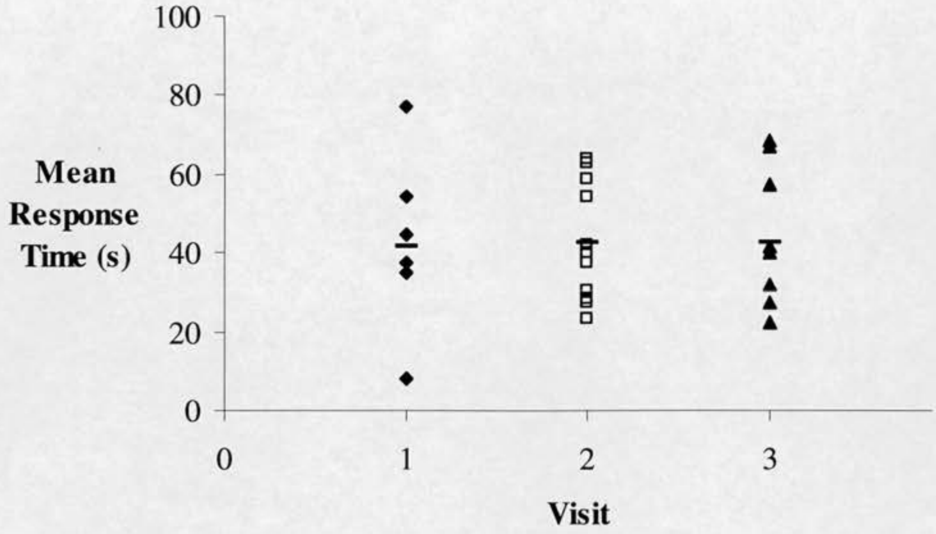


Figure 8c. Mean Response Times for the **training group** on Visits One (N=7), Two (N=11) and Three (N=9) (MRTs are shown for those who completed the necessary criteria for modelling, i.e. individuals who completed three walks, COV≤6%, RER≤1 and steady state VO_2 conditions).

Volunteer	Visit One	Visit Two	Visit Three
1	45	30	
2	35	23	22
3	37	29	
4	77	59	67
Mean	49	35	45
SD	20	16	32

Table 8b. Mean Response Times for those individuals in the **training group** who gave a Visit One-Visit Two comparison. (MRTs are shown for those who completed the necessary criteria for modelling, i.e. individuals who completed three walks, COV≤6%, RER≤1 and steady state VO_2 conditions).

Table 8b presents the MRT data for those individuals were the criteria permitted a Visit One – Visit Two comparison. In these individuals the MRT fell by, on average 13 seconds from 48.6 seconds on Visit 1 to 35.3 seconds on Visit 2, a reduction of ~27%.

Relaxation intervention

Of the thirty four individuals randomised to the relaxation intervention, a MRT value was obtained for 8 individuals pre intervention (Visit One), an immediate post intervention MRT value was obtained for 11 individuals (Visit Two) and a four month post intervention follow-up (Visit Three) MRT was obtained for 11 individuals. A Visit One – Visit Two comparison of MRT was possible in 4 individuals (Table 8c).

The MRTs for the participants of the relaxation group are shown in Figure 8d for Visit One, Visit Two and Visit Three. The average MRT for the relaxation group was 41.6 seconds (SD 12.6) on Visit One, 49.5 seconds (SD 17.0) on Visit Two and 38.9 seconds (SD 13.6) on Visit Three.

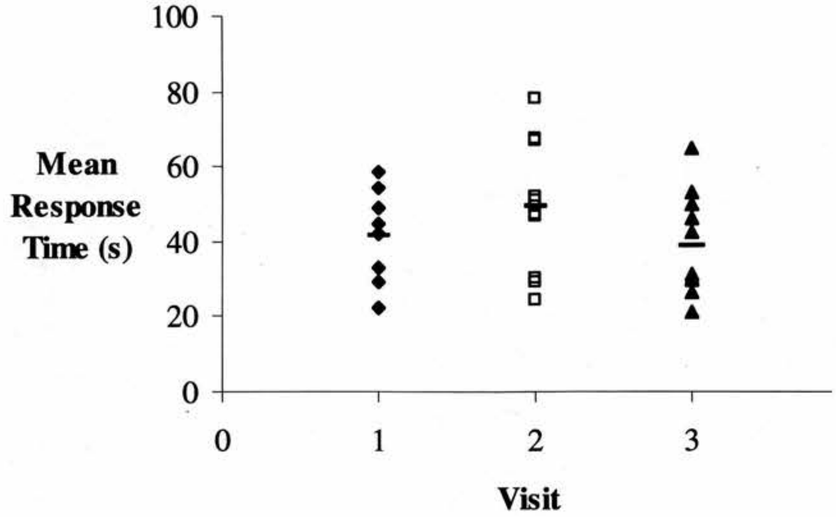


Figure 8d. Mean Response Times for the **relaxation group** on Visits One (N=8), Two (N=11) and Three (N=11) (MRTs are shown for those who completed the necessary criteria for modelling, i.e. individuals who completed three walks, COV≤6%, RER≤1 and steady state VO_2 conditions).

Volunteer	Visit One	Visit Two	Visit Three
1	22	52	
2	33	29	30
3	58	47	
4	42	50	
Mean	39	45	30
SD	15	10	

Table 8c. Mean Response Times for those individuals in the **relaxation group** who gave a Visit One-Visit Two comparison. (MRTs are shown for those who completed the necessary criteria for modelling, i.e. individuals who completed three walks, COV≤6%, RER≤1 and steady state VO_2 conditions).

RM ANOVA of a Visit One versus Visit Two comparison of both the relaxation and training group (within subject factor 'visit'; between subject factor 'group' (i.e. training or relaxation)) showed no significant difference between Visits One and Two ($F(1,6) = 0.71$, $p=0.43$) and no significant difference between groups ($F(1,6) = 0.001$, $p=0.98$). The interaction of the visit and group approached significance ($F(1, 6) = 4.2$, $p=0.09$. A significant interaction between visit and group would suggest the two groups had responded differently to the interventions. RM ANOVA of Visit One – Visit Three comparisons and Visit Two – Visit Three comparisons did not achieve significance within (Visit One vs Visit Three ($F(1,4) = 1.7$, $p=0.26$); Visit Two vs Visit Three ($F(1,3) = 2.0$, $p=0.25$)) or between subject factors (visit One vs Visit Three ($F(1,4) = 0.60$, $p=0.48$); Visit Two vs Visit Three ($F(1,3) = 0.06$, $p=0.82$)). Significant interactions between visit and group were not evident with either comparison (Visit One vs Visit Three (F (1,4) = 0.81, p=0.42); Visit Two vs Visit Three (F (1,3) = 0.10, p=0.78)).

In an attempt to increase the number of study participants who could achieve the feasibility criteria, the oxygen uptake response to the second walk only was modelled (the details of this analysis are given in Chapter 5 (Feasibility, Pages 113-116). Eleven additional study visits were considered for modelling. A MRT was obtained for five of those study visits (details of why six visits did not give a MRT are given in Table 5j, Page 115). Four of the five MRT values were from individuals who participated in the exercise group and one from the relaxation group. Addition of the five visits to the RM ANOVA of Visit One vs Visit Two did not alter the results of the previous RM ANOVA (Visit One vs Visit Two comparison (F (1,7) = 0.76, p =0.41); between groups comparison (F (1,7) = 0.04, p=0.84). The interaction of visit and group achieved borderline statistical significance (F (1,7) = 5.8, p=0.047). This suggests the training and relaxation groups may have responded in a different manner to the interventions. The within subject and between subject comparisons (with the addition of the second walk only data) of Visit One vs Visit Three and Visit Two vs Visit Three did not achieve statistical significance (Visit One vs Visit Three (F (1,4) = 1.7, 0.26); Visit Two vs Visit Three (F (1,4) = 0.002, 0.96). There was no evidence of a significant interaction between visit and group (Visit One vs Visit Three (F (1,4) = 0.81, p=0.42); Visit Two vs Visit Three (F (1,4) = 1.14, p=0.35)).

Discussion

The aim of this chapter was to investigate the sensitivity of oxygen uptake kinetics (MRT) measured at the onset of self-paced walking in men and women after a stroke to a physical training intervention. This was examined by randomising 66 men and women (mean age 72 years) recovering from a stroke to 12 weeks of either progressive exercise training or a 'control' intervention of relaxation classes. The response of oxygen uptake kinetics to endurance training programmes has previously been investigated in clinical populations (e.g. Barstow et al., 1996 and spinal cord injuries; Puente Maestu et al., 2003 and COPD patients; Otsuka et al., 1997 and COPD patients). This is the first study to examine the response of oxygen uptake kinetics to a progressive training intervention in men and women recovering from a stroke.

All four individuals who gave a Visit One – Visit Two comparison in MRTs showed a reduction in MRT. As shown in Table 8b, Volunteer One gave a reduction in MRT of 14s, Volunteer Two 12 seconds, Volunteer Three 9 seconds and Volunteer Four 19 seconds. Koufaki et al., 2002ii reported that following training in end-stage renal disease patients (12 weeks thrice weekly moderate intensity endurance training) the mean tau value of the group was 7 seconds lower (58.3 seconds pre training to 51.2 seconds post training).

When the Visit Two post training MRT values for the stroke group are considered in relation to the Limits of Agreement calculated for the hip fracture group (-23 to 30 seconds) then it is obvious none of the four individuals showed a decrease in MRT post training out with the Limits of Agreement of the measurement.

An important concern with the training results is the possibility of Type II error, i.e. the retention of the null hypothesis when it is false. In the presence of Type II error the conclusion drawn that the training did not produce a significant reduction in MRT would be reversed with a larger sample size. A sample size of N=28 was calculated to be required to assess the effects of a training intervention given a predicted 20% difference in MRT post intervention. 32 men and women were recruited to the training intervention. Poor tolerance of the study methodology in the frailer stroke patients compromised evaluation of the training intervention. A pre and post intervention comparison was possible in only 4 study participants. If a future physical training intervention study in men and women recovering from stroke sought a 30% reduction in MRT (~15 seconds) then N=37 study participants would be required for each group (intervention and control) based on a standard deviation of 20 seconds (Visit One SD obtained from those volunteers giving a V1-V2 comparison, Table 8c); power 90%; significance level 0.05. To counteract the low practical feasibility of the measure, it is recommended any future studies include additional volunteers or attempt to improve feasibility.

The relaxation intervention was chosen to act as a control, to duplicate the training effects of getting out and about and the benefits of being socially active. Of the 34 individuals randomised to the relaxation or 'control' group, a MRT was obtained from eight individuals on Visit One, eleven on Visit Two and eleven on Visit Three.

The average MRT for the relaxation group was 41.6 seconds on Visit 1, 49.5 seconds on Visit 2 and 38.9 seconds on Visit 3.

When the outcome measures of the volunteers were considered it was apparent only the 'fitter' volunteers gave a Visit One – Visit Two comparison. The stroke volunteers in both the training and relaxation groups who gave a Visit One – Visit Two comparison in MRT had a median walking speed of 0.8 $m.sec^{-1}$ (range 0.5 – 1.0 $m.sec^{-1}$); everyone had an EMS score of 20; median sit to stand was 0.8 seconds (range 0.6 – 1.7 seconds); median FIM score was 118.5 (range 112 – 124) and the median time taken to complete the 3 metre timed up and go test was 9.5 seconds (range 7.4 – 13.0 seconds). The stroke volunteers who did not give a Visit One – Visit Two comparison in MRT (for whatever reason) had a median walking speed of 0.6 $m.sec^{-1}$ (range 0.2 – 1.1 $m.sec^{-1}$); the median EMS score was 20 (range 15-20); the median time for the sit to stand test was 1.3 seconds (range 0.5 – 6.1 seconds); the median FIM score was 117 (range 95 – 126) and the median time taken for the 3 metre timed up and go test was 11.9 seconds (range 6.0 – 39.8 seconds) (median values are from the first visit only). It is apparent in the men and women who were at the lower end of the range of these functional measures a Visit One – Visit Two MRT comparison was not possible. Only the 'fitter' and more able study participants gave a Visit One – Visit Two MRT comparison. There were however study participants where a Visit One – Visit Two MRT comparison was not possible who were functionally comparable to the study participants who did. Further exploration of these men and women and a rationale for not completing the study methodology may increase the number of MRT values in future studies.

The effects of physical training on oxygen uptake kinetics are of interest because if kinetics are improved then exercise/physical activity tolerance will also be improved. It is however, unclear whether the faster VO_2 kinetics with training in older people are the result of enhancements in oxygen delivery, utilisation or both. Meredith et al., (1989) showed significant improvements (128%) in muscle mitochondrial capacity following 12 weeks of endurance training in older adults (N=10; mean age 65 years (+/- 2.9 years). In 1992 Coggan et al. showed significant improvements in capillary density and mitochondrial enzyme activity in the muscles of healthy older (aged 64 +/- 3 years) men and women in response to 9-12 months of endurance training. In 2001 Bell et al. attempted to identify the primary mechanism for the reduction in time course of oxygen uptake at the onset of exercise as a consequence of training in older individuals (i.e. delivery or utilisation (enhanced mitochondrial function)). Five older healthy men (aged 77+/-7 years) performed single leg endurance training (4 x 40 minutes sessions per week at 75-85VO_2max. for 8 weeks). Muscle capillarisation was examined and citrate synthase activity was used as a marker for mitochondrial density. Doppler ultrasonography was used to record leg blood flow kinetics. Bell et al. concluded that a training induced improvement in VO_2 kinetics from 92s to 48s in the trained leg could be attributed to intra-muscular adaptations and not to an improvement of oxygen delivery to muscle. They concluded this on the basis that the time constant for mean blood velocity was significantly faster than that of VO_2 both before and after training in both legs, and was not improved by training. Muscle capillarisation was not improved by training, while muscle citrate synthase activity was significantly increased in the trained leg. These findings agree with Puente Maestu et al., 2003 who found a training related reduction in VO_2 kinetics in COPD patients was significantly correlated with the change in muscle citrate synthase activity. The findings of Meredith et al., 1989; Coggan et al., 1992; Bell et al., 2001 and Puente Maestu et al., 2003 suggest that in this study the training related reduction in MRT observed in the 4 training group participants in this study might be attributable to adaptations in the muscle and therefore improved oxygen utilisation.

This suggestion is however, countered by the findings of Scheuermann et al. (2002) and Babcock et al (1994ii). Scheuermann et al., (2002) demonstrated that a bout of high intensity warm up exercise resulted in faster VO_2 kinetics in older (65 +/- 2 years) but not younger (26 +/- 1 year) volunteers. As heart rate was elevated prior to initiating a second exercise bout, the authors proposed that VO_2 kinetics in older individuals (in contrast to their younger counterparts) may be oxygen delivery limited. In addition Babcock et al., (1994ii) demonstrated a significant correlation between faster VO_2 kinetics and those of heart rate in older people (aged 72 years), again suggesting improved oxygen delivery may be, in part, responsible for the faster VO_2 kinetics observed after training. Although the investigation of heart rate kinetics was beyond the scope of this study, it is possible that a more rapid increase in heart rate and therefore oxygen delivery at the onset of exercise may be the mechanism responsible for the reduction in MRT values observed in the four study participants with a pre and post training intervention MRT comparison.

The men and women who participated in the Starter trial were on average, older than participants in previous studies (Table 8d) investigating the effect of exercise training on VO_2 kinetics in clinical patient populations (mean age of the stroke group in this study 72 years (SD 10); mean age of the eight study participants who gave a pre and post intervention comparison 66 years (SD 9).

	N	**Disease Condition**	**Age of study participants**
Otsuka et al., 1997	11	COPD	65.5 (SD 7.2)
Brandenburg et al., 1999	8	Type II diabetes	43 (SD 7)
Koufaki et al., 2002	18	End stage renal disease	54 (SD 17)
Puente Maestu et al., 2003	21	COPD	63 (10)

Table 8d. Age of study participants in previous clinical trials investigating the effects of exercise training on VO_2 kinetics.

Unlike the Starter trial, the methodology used in the other four training trials required the patients to perform an incremental exercise test to symptom limited maximum prior to participating in exercise classes. Men and women unable to perform such a test would have been excluded from the training trials. This suggests participants in the stroke group in this study were frailer than other oxygen uptake kinetics training trial participants.

This study has demonstrated that the assessment of VO_2 kinetics in a clinical sample of stroke patients is challenging and complex. The frailty of this study group was evident in the number of volunteers unable to complete the study methodology. ~1/3 of study participants in the stroke group were unable to complete three walks of three minutes, suggesting the measure may only be suitable for the less frail. The length of the trial assessment set may have compromised the walking tests.

Summary

Poor tolerance of the study methodology in the frailer stroke patients compromised evaluation of the training intervention. A before and after training comparison of MRT was possible in 4 stroke patients. A training related reduction in MRT (49s to 35s (mean values, N=4)) was shown.

CHAPTER 9: Conclusions and Future Work

The overall purpose of this thesis was to test whether oxygen uptake kinetics at the onset of self-paced walking might provide a measure of cardiorespiratory fitness suitable for use with frail patients.

Preliminary and pilot studies of self-paced walking and VO_2 kinetics (Chapter 3)

<u>Volunteers</u>

Healthy young and elderly

<u>Exercise mode</u>

Self-paced walking

<u>Conclusions</u>

The oxygen uptake response to self-paced walking achieved steady state conditions within three minutes and was of sufficient amplitude to be fitted with a monoexponential model to derive a time constant, MRT.

<u>Implications for Overall Purpose</u>

Subject to the exclusion of an effect of exercise intensity on MRT, comfortable self-paced walking was considered a suitable mode of exercise to investigate oxygen uptake kinetics in young and healthy elderly volunteers.

Exercise Intensity and VO_2 kinetics (Chapter 4)

<u>Volunteers</u>

Healthy young women

<u>Exercise Mode</u>

Treadmill walking

Conclusions

The lack of a significant linear trend in MRT values in the exercise range 50 – 80% VO_2max. provided further evidence of the suitability of self-paced walking as a mode of exercise. Any unavoidable variation in relative exercise intensity between tests would be unlikely to significantly impact on MRT.

Implications for Overall Purpose

On the basis of these, and the preliminary and pilot work findings, self-paced walking was considered a suitable exercise mode to investigate VO_2 kinetics in frail, patient groups.

The feasibility of MRT at the onset of self-paced walking (Chapter 5)

Volunteers

1. Healthy young men and women
2. Healthy elderly men and women
3. Women recovering from a hip fracture
4. Men and women recovering from a stroke

Exercise Mode

Self-paced walking

Conclusions

1. Oxygen uptake kinetics at the onset of self-paced walking proved feasible in young and healthy elderly men and women (37% of volunteers failed to achieve one or more feasibility criteria on Visit One (38% Visit Two)).

2. 47% of the hip fracture group failed to achieve one or more feasibility criteria on Visit One (33% Visit Two). The most limiting feasibility criterion was the inability to maintain a constant walking speed.

3. 70% of the stroke group failed to achieve one or more feasibility criteria on Visit One. The most limiting feasibility criteria were the inability to complete three walks of three minutes and the inability to maintain a constant walking speed.

Implications for Overall Purpose

If the same study participants achieve the feasibility criteria on subsequent visits then oxygen uptake kinetics at the onset of self-paced walking is a feasible measure in frail patient groups. The application of the measure to frailer stroke patients is questionable.

The validity of MRT at the onset of self-paced walking (Chapter 6)

Volunteers

- Content validity

1. Healthy young men and women
2. Healthy elderly men and women
3. Women recovering from a hip fracture
4. Men and women recovering from a stroke

- Criterion-related concurrent validity

1. Healthy young men and women
2. Healthy elderly men and women

- Criterion-related predictive validity

1. Healthy young men and women

2. Healthy elderly men and women

3. Women recovering from a hip fracture

4. Men and women recovering from a stroke

Exercise Mode

- Content validity

Self-paced walking

- Criterion-related concurrent validity

Treadmill walking

- Criterion-related predictive validity

Self-paced walking

Conclusions

- Content validity of MRT was demonstrated via a group comparison of MRT values.
- Criterion-related concurrent validity (MRT vs VO_2max.) was not demonstrated.
- Criterion-related predictive validity was not demonstrated.

Implications for Overall Purpose

An association between MRT at the onset of self-paced walking and other measures of cardiorespiratory fitness has not been demonstrated. The lack of significant correlations between MRT and VO_2max. and composite measures of functional ability may be unsurprising.

The reproducibility of MRT at the onset of self-paced walking (Chapter 7)

Volunteers

1. Healthy young men and women

2. Healthy elderly men and women

3. Women recovering from a hip fracture

Exercise Mode

Self-paced walking

Conclusions

The Standard Error of the Measurement (SEM) of the MRT was 4.9s in the young group, 4.4s in the healthy elderly group and 7.0s for the hip fracture group. Limits of agreement of MRT for the hip fracture group were -23 to 30s.There was no evidence of a significant systematic bias from Visit One to Visit Two. Relative reliability was not demonstrated.

Implications for Overall Purpose

The absolute measures of reliability provide an indication of the extent of test-retest variability of MRT measured at the onset of self-paced walking that could be expected in comparable volunteer groups. Intervention related changes to MRT at the onset of self-paced walking must fall out with these measures.

The sensitivity of MRT at the onset of self-paced walking to a physical training intervention (Chapter 8)

Volunteers

1. Men and women recovering from a stroke

Exercise mode

Self-paced walking

Conclusions

There was no significant difference between the pre and post intervention MRTs for both groups collectively. A reduction in MRT in the training group of 13.3 seconds was evident in those individuals who gave a comparison of pre and post training MRT values (N=4, 49s to 35s, ~27% reduction). Poor tolerance/feasibility of the study methodology in the frailer stroke patients compromised evaluation of the interventions.

Implications for Overall Purpose

The inability of study participants to achieve feasibility criteria on more than one visit compromised evaluation of the training and relaxation interventions.

Conclusions:

Oxygen uptake kinetics have been measured using a novel exercise mode i.e. self-paced walking. This presents an ethically reassuring means of measuring VO_2 kinetics as self-paced walking does not require an exercise intensity in excess of that used in every day life. As the measure was acceptable to 'fitter' patients (for whom current measures are unsuitable) the feasibility threshold for VO_2 kinetics testing has been lowered. However, the inability of frailer study participants to achieve feasibility criteria and inconclusive validity questions the applicability of this measure to those for whom it is intended – frail, older people. The association between MRT at the onset of self-paced walking in frail, older men and women and cardiorespiratory fitness remains a challenge.

BIBLIOGRAPHY

1. Altman DG. Practical statistics for medical research. Chapman and Hall, London. ISBN 0-412-27630-5. 1991.

2. Atkinson G and Nevill AM. Statistical methods for addressing measurement error (reliability) in variables relevant to sports medicine. Sports Medicine 26 (4), 217-238. 1998.

3. Babcock MA, Paterson DH, Cunningham DA and Dickinson JR. Exercise on-transient gas exchange kinetics are slowed as a function of age. Medicine and Science in Sports and Exercise 26 (4), 440-446. 1994i.

4. Babcock MA, Paterson DH and Cunningham DA. Effects of aerobic endurance training on gas exchange kinetics of older men. Medicine and Science in Sports and Exercise 26 (4), 447-454. 1994ii.

5. Balady GJ, Berra KA, Golding LA et al. ACSM's guidelines for exercise testing and prescription. 6th Edition, page 68. Lippincott, Williams and Wilkins. 2000.

6. Bangsbo J, Krustrup P, Gonzalez-Alonso J, Boushel R, Saltin B. Muscle oxygen kinetics at onset of intense dynamic exercise in humans. Am J Physiol Regulatory Integrative Comp Physiol. 279 (3), R899-R906. 2000.

7. Barstow TJ & Molé PA. Simulation of pulmonary O_2 uptake during exercise transients in humans. Journal of Applied Physiology, 63 (6), 2253-2261. 1987.

8. Barstow TJ & Mole PA. Linear and nonlinear characteristics of oxygen uptake kinetics during heavy exercise. Journal of Applied Physiology, 71 (6), 2099-2106. 1991.

9. Barstow TJ, Casaburi R & Wasserman K. O_2 uptake kinetics and the O_2 deficit as related to exercise intensity and blood lactate. Journal of Applied Physiology, 75 (2), 755-762. 1993.

10. Barstow TJ, Scremin AME, Mutton DL, Kunkel CF, Cagle TG, Whipp BJ. Changes in gas exchange kinetics with training in patients with spinal cord injury. Medicine and Science in Sport and Exercise, 28 (10), 1221-1228. 1996.

11. Bassey EJ, Fentem PH, MacDonald IC & Scriven PA. Self-paced walking as a method for exercise testing in elderly and young men. Clinical Science and Molecular Medicine 51 (6), 609-612. 1976.

12. Bauer TA, Regensteiner JG, Brass EP, Hiatt WR. Oxygen uptake kinetics during exercise are slowed in patients with peripheral arterial disease. Journal of Applied Physiology, 87 (2), 809-816. 1999.

13. Baumgarter TA. Norm-referenced measurement: reliability. In: Safrit, MJ & Wood TM, editors. Measurement concepts in physical education and exercise science. 45-72. Champaign (IL): Human Kinetics. ISBN 0-87322-223-7. 1989.

14. Behnke BJ, Kindig CA, Musch TI, Koga S, Poole DC. Dynamics of microvascular oxygen pressure across the rest-exercise transition in rat skeletal muscle. Respiration Physiology, 126 (1), 53-63. 2001.

15. Behnke BJ, Barstow TJ, Poole DC. Relationship between VO_2 responses at the mouth and across exercising muscles. In 'Oxygen uptake kinetics in sport, exercise and medicine'. Editors Jones, A. M. and Poole, D. C. page 142. Routledge, U.K. 2005.

16. Belardinelli R, Zhang YY, Wasserman K, Purcaro A, Agostoni PG. A four-minute submaximal constant work rate exercise test to assess cardiovascular functional class in chronic heart failure. The American Journal of Cardiology, 81 (10), 1210-1214. 1998.

17. Bell C, Paterson DH, Kowalchuk JM & Cunningham DA. Oxygen uptake kinetics of older humans are slowed with age but are unaffected by hyperoxia. Experimental Physiology, 84 (4), 747-759. 1999.

18. Bell C, Paterson DH, Kowalchuk JM et al. Determinants of oxygen uptake kinetics in older humans following single-limb endurance exercise training. Experimental Physiology, 86 (5), 659-665. 2001.

19. Billat VL, Mille-Hamard L, Demarle A & Koralsztein JP. Effect of training in humans on off- and on-transient oxygen uptake kinetics after severe exhausting intensity runs. European Journal of Applied Physiology, 87 (6), 496-505. 2002.

20. Bland, M. An introduction to medical statistics. 3rd Edition, page 311. Oxford University Press. 2000.

21. Bland JM & Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. The Lancet, 8476 (Feb 8), 307-310. 1986.

22. Bohannon RW. Sit-to-stand test for measuring performance of lower extremity muscles. Perceptual and Motor Skills, 80 (1), 163-166. 1995.

23. Borg GAV. Psychophysical bases of perceived exertion. Medicine and Science in Sport and Exercise, 14 (5), 377-381. 1982.

24. Brandenburg SL, Reusch JEB, Bauer TA, Jeffers BW, Hiatt WR, Regensteiner JG. Effects of exercise training on oxygen uptake responses in women with type 2 diabetes. Diabetes Care, 22 (10), 1640-1646. 1999.

25. Brunner-La Rocca HP, Weilenmann D, Follatth F et al. Oxygen uptake kinetics during low level exercise in patients with heart failure: relation to neurohormones, peak oxygen consumption, and clinical findings. Heart, 81 (2), 121-127. 1999.

26. Carter H, Jones AM, Barstow TJ, Burnley M, Williams CA, Doust JH. Oxygen uptake kinetics in treadmill running and cycle ergometry: a comparison. Journal of Applied Physiology, 89 (3), 899-907. 2000.

27. Carter H, Pringle JSM, Jones AM, Doust JH. Oxygen uptake kinetics during treadmill running across exercise intensity domains. European Journal of Applied Physiology, 86 (4), 347-354. 2002.

28. Casaburi R, Storer TW, Ben Dov I, Wasserman K. Effect of endurance training on possible determinants of VO_2 during heavy exercise. Journal of Applied Physiology, 62 (1), 199-207. 1987.

29. Casaburi R, Barstow TJ, Robinson T, Wasserman K. Influence of work rate on ventilatory and gas-exchange kinetics. Journal of Applied Physiology, 67 (2), 547-555. 1989.

30. Cerretelli P, Shindell D, Pendergast DP, Di Prampero PE, Rennie DW. Oxygen uptake transients at the onset and offset of arm and leg work. Respiration Physiology 30 (1-2), 81-97. 1977.

31. Cerretelli P, Pendergast D, Paganelli WC, Rennie DW. Effects of specific muscle training on VO_2 on-response and early blood lactate. Journal of Applied Physiology, 47 (4), 761-769. 1979.

32. Chilibeck PD, Paterson DH, Smith WDF, Cunningham DA. Cardiorespiratory kinetics during exercises of different muscle groups and mass in old and young. Journal of Applied Physiology, 81 (3), 1388-1394. 1996i.

33. Chilibeck PD, Paterson DH, Petrella RJ, Cunningham DA. The influence of age and cardiorespiratory fitness on kinetics of oxygen uptake. Canadian Journal of Applied Physiology, 21 (3), 185-196. 1996ii.

34. Chief Scientist Office Final Report, Scottish Executive, CZB/4/46. A randomised exploratory trial of physical fitness training after stroke. 2005.

35. Coggan AR, Spina RJ, King DS, Rogers MA, Brown M, Nemeth PM, Holloszy JO. Skeletal muscle adaptations to endurance training in 60- to 70-yr-old men and women. Journal of Applied Physiology 72 (5), 1780-86. 1992.

36. Cunningham DA, Rechnitzer PA, Pearce ME, Donner AP. Determinants of self-selected walking pace across ages 19 to 66. Journal of Gerontology, 37 (5), 560-564. 1982.

37. Cunningham DA, Himann JE, Paterson DH, Dickinson JR. Gas exchange dynamics with sinusoidal work in young and elderly women. Respiration Physiology 91 (1), 43-56. 1993.

38. DeLorey DS, Kowalchuk JM, Paterson DH. Relationship between pulmonary O_2 uptake kinetics and muscle deoxygenation during moderate-intensity exercise. Journal of Applied Physiology, 95 (1), 113-120. 2003.

39. DeLorey DS, Kowalchuk JM and Paterson DH. Effect of age on $O\text{-}_2$ uptake kinetics and the adaptation of muscle deoxygenation at the onset of moderate-intensity cycling exercise. Journal of Applied Physiology, 97 (1), 165-172. 2004.

40. Demarle AP, Slawinski JJ, Laffite LP, Bocquet VG, Koralsztein JP, Billat VL. Decrease of oxygen deficit is a potential factor in increasing time to exhaustion after specific endurance training. Journal of Applied Physiology, 90 (3), 947-953. 2001.

41. Duncan P, Studenski S, Richards L et al. Randomised clinical trial of therapeutic exercise in subacute stroke. Stroke, 34 (9), 2173-2180. 2003.

42. Fitzsimons CF, Greig CA, Saunders DH, Lewis SH, Shenkin SD, Lavery C, Young A. Responses to walking-speed instructions: implications for health promotion for older adults. Journal of Aging and Physical Activity, 13 (2), 172-183. 2005.

43. Fukuoka Y, Grassi B, Conti M, Guiducci D, Sutti M, Marconi C, Cerretelli P. Early effects of exercise training on VO_2 on- and off-kinetics in 50-

year-old subjects. Pflugers Arch European Journal of Physiology, 443 (5-6), 690-697. 2002.

44. GraphPad Prism. http://www.graphpad.com/prism/Prism.htm

45. Grassi B, Poole DC, Richardson RS, Knight DR, Erickson BK, Wagner PD. Muscle O_2 uptake kinetics in humans: implications for metabolic control. Journal of Applied Physiology, 80 (3), 988-998. 1996.

46. Grassi B, Pogliaghi S, Rampichini S, Quaresima V, Ferrari M, Marconi C, Cerretelli P. Muscle oxygenation and pulmonary gas exchange kinetics during cycling exercise on-transitions in humans. Journal of Applied Physiology, 95 (1), 149-158. 2003.

47. Greig CA, Young A, Skelton DA, Pippet E, Butler FMM, Mahmud SM. Exercise studies with elderly volunteers. Age and Ageing, 23 (3), 185-189. 1994.

48. Greig CA. Editorial - The trainability of elderly people. Age and Ageing, 31 (4), 223-224. 2002.

49. Hagberg JM, Hickson RC, Ehsani AA, Holloszy JO. Faster adjustment to and recovery from submaximal exercise in the trained state. Journal of Applied Physiology, 48 (2), 218-224. 1980.

50. Hickson RC, Bomze HA, Hollozy JO. Faster adjustment of O_2 uptake to the energy requirement of exercise in the trained state. Journal of Applied Physiology, 44 (6), 877-881. 1978.

51. Hill DW, Halcomb JN, Stevens EC. Oxygen uptake kinetics during severe intensity running and cycling. European Journal of Applied Physiology, 89 (6), 612-618. 2003.

52. Hodkinson HM. Evaluation of a mental test score for assessment of mental impairment in the elderly. Age and Ageing, 1 (4), 233-238. 1972.

53. Hopkins WG. Measures of reliability in sports medicine and science. Sports Medicine, 30 (1), 1-15. 2000.

54. Iredale KF and Nimmo MA. The effect of aging on the lactate threshold in untrained men. Journal of Aging and Physical Activity, 5 (1), 39-49. 1997.

55. Jones AM & Poole DC. Oxygen uptake kinetics in sport, exercise and medicine. Pages 4, 13-14, 20, 390. Routledge, U.K. 2005.

56. Kilding A, Fysh M, Winter E, Challis N. Test-retest reproducibility of measures of oxygen uptake kinetics. 6th annual congress of the European College of Sport Science. 2001.

57. Kline GM, Porcari JP, Hintermeister R et al. Estimation of VO_2max. from a one-mile track walk, gender, age, and body weight. Medicine and Science in Sports and Exercise, 19 (3), 253-259. 1987.

58. Koga S, Shiojiri T, Kondo N. Measuring VO_2 kinetics. The practicalities. In 'Oxygen uptake kinetics in sport, exercise and medicine'. Editors Jones AM and Poole DC. Page 53. Routledge, U.K. 2005.

59. Koike A, Hiroe M, Adachi H et al. Oxygen uptake kinetics are determined by cardiac function at onset of exercise rather than peak exercise in patients with prior myocardial infarction. Circulation, 90 (5), 2324-2332. 1994.

60. Koppo K, Bouckaert J, Jones AM. Effects of training status and exercise intensity on phase II VO_2 kinetics. Medicine & Science in Sports & Exercise, 36 (2), 225-232. 2004.

61. Koufaki P, Naish PF, Mercer TM. Assessing the efficacy of exercise training in patients with chronic disease. Medicine and Science in Sports and Exercise, 34 (8), 1234-1241. 2002i.

62. Koufaki P, Mercer TH, Naish PF. Effects of exercise training on aerobic and functional capacity of end-stage renal disease patients. Clinical Physiology and Functional Imaging, 22 (2), 115-125. 2002ii.

63. Krogh A and Lindhard J. The regulation of respiration and circulation during the initial stages of muscular work. Journal of Physiology, 47, (1 & 2), 112-136. 1913.

64. Lamarra N, Whipp BJ, Ward SA, Wasserman K. Effect of interbreath fluctuations on characterizing exercise gas exchange kinetics. Journal of Applied Physiology, 62 (5), 2003-2012. 1987.

65. Linnarsson D. Dynamics of pulmonary gas exchange and heart rate changes at start and end of exercise. Acta Physiologica Scandinavica Suppl. 415, 1-68. 1974.

66. Macko RF, Ivey FM, Forrester LW et al. Treadmill exercise rehabilitation improves ambulatory function and cardiovascular fitness in patients with chronic stroke. A randomised controlled trial. Stroke, 36 (10), 2206-2211. 2005.

67. Mahler M. First-order kinetics of muscle oxygen consumption, and an equivalent proportionality between QO_2 and phosphorylcreatine level. Implications for the control of respiration. J. Gen. Physiol., 86 (1), 135-165. 1985.

68. McDowell I and Newell C. The quality of a measurement: validity and reliability. In: Measuring health. A guide to rating scales and questionnaires. 2[nd] Ed. 29-37. Oxford University Press. Oxford. 1996.

69. Meredith CN, Frontera WR, Fisher EC, Hughes VA, Herland JC, Edwards J, Evans WJ. Peripheral effects of endurance training in young and old subjects. Journal of Applied Physiology, 66 (6), 2844-2849. 1989.

70. Mettauer B, Zhao QM, Epailly E et al. VO_2 kinetics reveal a central limitation at the onset of subthreshold exercise in heart transplant recipients. Journal of Applied Physiology, 88 (4), 1228-1238. 2000.

71. Norris SR and Petersen SR. Effects of endurance training on transient oxygen uptake responses in cyclists. Journal of Sports Sciences, 16 (8), 733-738. 1998.

72. Otsuka T, Kurihara N, Fujii T, Fujimoto S, Yoshikawa J. Effect of exercise training and detraining on gas exchange kinetics in patients with chronic obstructive pulmonary disease. Clinical Physiology, 17 (3), 287-297. 1997.

73. Ozyener F, Rossiter HB, Ward SA, Whipp BJ. Influence of exercise intensity on the on- and off-transient kinetics of pulmonary oxygen uptake in humans. Journal of Physiology, 533 (3), 891-902. 2001.

74. Pang MYC, Eng JJ, Dawson AS, McKay HA, Harris JE. A community-based fitness and mobility exercise program for older adults with chronic stroke: A randomised, controlled trial. J Am Geriatr Soc., 53 (10), 1667-1674. 2005.

75. Paterson ND, Paterson DH and Kowalchuk JM. VO_2 kinetics are progressively slowed in regions of upper moderate-and heavy-intensity exercise domains. Medicine and Science in Sports and Exercise, 35 (5). Suppl. 1, S336. 2003.

76. Phillips SM, Green HJ, MacDonald MJ and Hughson RL. Progressive effect of endurance training on VO_2 kinetics at the onset of submaximal exercise. Journal of Applied Physiology, 79 (6), 1914-1920. 1995.

77. Piiper J, Di Prampero PE, Cerretelli P. Oxygen debt and high-energy phosphates in gastrocnemius muscle of the dog. American Journal of Physiology, 215 (3), 523-531. 1968.

78. Podsiadlo D and Richardson S. The timed 'Up and Go': a test of basic functional mobility for frail elderly persons. Journal of American Geriatrics Society, 39 (2), 142-148. 1991.

79. Puente-Maestu L, Sanz ML, Sanz P, Nunez An, Gonzalez F, Whipp BJ. Reproducibility of the parameters of the on-transient cardiopulmonary responses during moderate exercise in patients with chronic obstructive pulmonary disease. European Journal of Applied Physiology, 85 (5), 434-441. 2001.

80. Puente-Maestu L, Tena T, Trascasa C, Perez-Parra J, Godoy R, Garcia MJ, Stringer WW. Training improves muscle oxidative capacity and oxygenation recovery kinetics in patients with chronic obstructive pulmonary disease. European Journal of Applied Physiology, 88 (6), 580-587. 2003.

81. Regensteiner JG, Bauer TA, Reusch JEB et al. Abnormal oxygen uptake kinetic responses in women with type II diabetes mellitus. Journal of Applied Physiology, 85 (1), 310-317. 1998.

82. Reybrouck T. Gas exchange kinetics in patients with cardiovascular disease. Chest, 118 (2), 285-286. 2000.

83. Reybrouck T, Defoor J, Bijnens B, Mertens L, Gewillig M. Influence of work rate on the determinants of oxygen deficit during short-term submaximal exercise: implications for clinical research. Clinical Physiology and Functional Imaging, 23 (1), 42-49. 2003.

84. Rossiter HB, Ward SA, Doyle VL, Howe FA, Griffiths JR, Whipp BJ. Inferences from pulmonary O_2 uptake with respect to intramuscular [phosphocreatine] kinetics during moderate exercise in humans. Journal of Physiology, 518 (3), 921-932. 1999.

85. Rossiter HB, Howe FA, Ward SA, Kowalchuk JM, Griffiths JR, Whipp BJ. Intersample fluctuations in phosphocreatine concentration determined by 31P-magnetic resonance spectroscopy and parameter estimation of metabolic responses to exercise in humans. Journal of Physiology, 528 (2), 359-369. 2000.

86. Safrit MJ. Evaluation in physical education. 2nd Edition. Pages 45-70. Prentice-Hall, Inc. New York. ISBN 0-13-292250-9. 1981.

87. Scheuermann BW, Bell C, Paterson DH, Barstow TJ and Kowalchuk JM. Oxygen uptake kinetics for moderate exercise are speeded in older humans by prior heavy exercise. Journal of Applied Physiology, 92 (2), 609-616. 2002.

88. Sietsema KE, Cooper DM, Perloff, JK et al. Dynamics of oxygen-uptake during exercise in adults with cyanotic congenital heart-disease. Circulation, 73 (6), 1137-1144. 1986.

89. Sietsema KE, Daly JA, Wasserman K. Early dynamics of O_{-2} uptake and heart rate as affected by exercise work rate. Journal of Applied Physiology, 67 (6), 2535-2541. 1989.

90. Sietsema KE, Ben-Dov I, Zhang YY, Sullivan C, Wasserman K. Dynamics of oxygen uptake for submaximal exercise and recovery in patients with chronic heart failure. Chest, 105 (6), 1693-1700. 1994.

91. Smith, R. Validation and reliability of the elderly mobility scale. Physiotherapy, 80 (11), 744-747. 1994.

92. State University of New York, Buffalo. Guide for use of uniform data set for medical rehabilitation (Adult FIM). NY 14214. Version 4.0. 1993.

93. Studenski S, Duncan PW, Perera S, Reker D, Min Lai S, Richards L. Daily functioning and quality of life in a randomised controlled trial of therapeutic exercise for subacute stroke survivors. Stroke, 36 (8), 1764-1770. 2005.

94. U.S. Department of Health and Human Services. Physical activity and health: A report of the Surgeon General. Atlanta, GA. U.S. Department of Health and Human Services, Centres for Disease Control and Prevention, National Centre for Chronic Disease Prevention and Health Promotion, 32-33. 1996.

95. Ward SA. Determinants and limitation of pulmonary gas exchange during exercise. In 'Physiological determinants of exercise tolerance in humans'. Editors Whipp BJ & Sargeant AJ. Pages 117-119. Portland Press, London. ISBN 1 85578 026 7. 1999.

96. Wasserman K, Hansen JE, Sue DY, Casaburi R, Whipp BJ. Principles of exercise testing and interpretation. 3rd Edition. Pages 10-61. Lippincott, Williams and Wilkins. ISBN 0-683-30646-4. 1999.

97. Weltman A and Katch V. Min-by-min respiratory exchange and oxygen uptake kinetics during steady-state exercise in subjects of high and low max VO_2. Research Quarterly, 47 (3), 490-498. 1976.

98. Whipp BJ. Rate constant for kinetics of oxygen uptake during light exercise. Journal of Applied Physiology, 30 (2), 261-263. 1971.

99. Whipp BJ, Wasserman K. Oxygen uptake kinetics for various intensities of constant-load work. Journal of Applied Physiology, 33 (3), 351-356. 1972.

100. Whipp BJ, Ward SA, Lamarra N, Davis JA, Wasserman K. Parameters of ventilatory and gas exchange dynamics during exercise. Journal of Applied Physiology, 52 (6), 1506-1513. 1982.

101. Whipp BJ, Ward SA. Physiological determinants of pulmonary gas-exchange kinetics during exercise. Medicine and Science in Sports and Exercise, 22 (1), 62-71. 1990.

102. Womack CJ, Davis SE, Blumer JL, Barrett E, Weltman AL, Gaesser GA. Slow component of O_2 uptake during heavy exercise: adaptation to endurance training. Journal of Applied Physiology, 79 (3), 838-845. 1995.

103. Wood TM. The changing nature of norm-referenced validity. Pages 23-44. In: 'Measurement concepts in physical education and exercise science'. Editors Safrit MJ and Wood TM. Champaign (IL): Human Kinetics. 1989.

104. Xu F, Rhodes EC. Oxygen uptake kinetics during exercise. Sports Medicine, 27 (5), 313-327. 1999.

105. Zhou B, Conlee RK, Jensen R, Fellingham GW, George JD, Fisher AG. Stroke volume does not plateau during graded exercise in elite male distance runners. Medicine and Science in Sports and Exercise, 33 (11), 1849-1854. 2001.

APPENDICES

APPENDICES

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Kings College London (2005) *J Physiol* **565P** C36
Communications

The effect of exercise intensity on oxygen uptake kinetics in healthy young women

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Fitzsimons, C F; Carnwath, A ; McLellan, S ; Young, A ; Greig, C A;

1. Geriatric Medicine, School of Clinical Sciences and Community Health, University of Edinburgh, Edinburgh, United Kingdom. 2. University Department of Anaesthetics, Critical Care & Pain Medicine, School of Clinical Sciences and Community Health, University of Edinburgh, Edinburgh, United Kingdom.

The study of oxygen uptake kinetics (tau values) using self-paced walking as the mode of exercise may provide a convenient indirect measure of aerobic fitness. However, one concern is the effect of inadvertent differences in exercise intensity between tests upon derived tau values. Previous studies report conflicting results. The aim of this study was to examine the effect of exercise intensity on tau values derived from treadmill walking. Six untrained healthy young (median age 22.5 years (21-24 years)) women underwent VO_2max treadmill testing (visit 1) to permit calculation of sub-maximal work-rates of 50%, 65% and 80% VO_2max. A familiarization bout (6 min at 65% VO_2max) was

	50%	65%	80%
1	36.4	35.9	28.8
2	39.3	35.9	37.7
3	35.8	36.0	43.7
4	31.5	33.1	37.7
5	30.6	29.8	28.5
6	36.9	33.7	32.1
Median	36.0	34.8	34.9

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Table 1. Tau values (s) corresponding to each exercise intensity (50% 65% and 80% VO_2max)

	50%	65%	80%
1	36.4	35.9	28.8
2	39.3	35.9	37.7
3	35.8	36.0	43.7
4	31.5	33.1	37.7
5	30.6	29.8	28.5
6	36.9	33.7	32.1
Median	36.0	34.8	34.9

[download high resolution image]

Table 1. Tau values (s) corresponding to each exercise intensity (50% 65% and 80% VO_2max)

performed at the start of the 2nd and 3rd visits and excluded from further analysis. Subjects then performed 9 bouts of exercise (3 bouts of each intensity) over the 2nd and 3rd visits. Each 6 min exercise bout was followed by ≥20 min of seated rest. Breath-by-breath data (with spurious breaths removed) were interpolated on a second-by-second basis and time aligned to exercise onset. Ensemble averaged datasets were fitted with a monoexponential model to derive a tau value for each intensity. Repeated measures ANOVA showed no significant linear trend ($F_{(1,5)} = 0.24$, $p=0.883$). The within subjects coefficient of variation was 11.3% (Table 1). In this sample of young women of comparable age and fitness, variations in tau between these exercise intensities were not physiological significant. On the basis of these findings in young individuals, any unavoidable variations in exercise intensity between tests would be unlikely to mask intervention related effects on tau values.

The support of the Royal Society of Edinburgh/ Lloyds TSB and the University of Edinburgh is gratefully acknowledged.

was added to the primary monoexponential component, after a calculated time delay (TD_2). **Results**: Before training, the TD_1 of Δ[deoxyHb] kinetic was 6.5 ± 4.1 s for <VT and 6.5 ± 3.4 s for >VT (ns) (both significantly different from 0). The τ was significantly higher for <VT (26.5 ± 13.1 s) compared to >VT (15.9 ± 6.7 s). The amplitude of the Δ[deoxyHb] response was a function of exercise intensity, reaching, at steady state (~60-90 s), 43 ± 19% and 61 ± 25% of the ischemic value (used as a "physiological calibration") for <VT and >VT respectively. For >VT trials, a slow component issued after 131.8 ± 71 s (TD_2), that led to an amplitude of 69 ± 27% of ischemia, at 6 min. Training induced a significant increase in VT and VO_{2peak} (16 ± 11 and 17 ± 6% of pretraining value, respectively). Following training, at both exercise intensities, TD_1 was significantly increased (12.8 ± 2.9 and 9.3 ± 2.6 s for <VT and >VT respectively), while τ was significantly reduced (10.2 ± 6.3 and 10.5 ± 1.9 s for <VT and >VT respectively). No changes were induced by training in the amplitude of the primary component, in TD_2 or in the amplitude of the slow component, for >VT trials. **Conclusions**: As the on-transition starts, muscle oxygenation remains constant for a period (TD_1), which indicates a tight coupling between O_2 availability and O_2 needs. After training, at both exercise intensities, while TD_1 increases, τ decreases, the overall result being a faster muscle VO_2 kinetics. We suggest that changes in TD_1 reflect an increased ability to match O_2 delivery to a given O_2 demand, during the initial phase of metabolic transitions. The smaller τ of deoxygenation kinetics probably results from enhanced speed of energy transforming processes within the muscle, following aerobic training.

Oxygen Uptake Kinetics in Very Elderly Hip Fracture Survivors Measured at the Onset of Comfortable Self-Paced Walking

Claire F. Fitzsimons, A. Hamish R. W. Simpson, Archie Young, Carolyn A. Greig, Locomotor Sciences, Dept. Clinical Sciences and Community Health, University of Edinburgh, Scotland, U.K.

An acceptable measure of aerobic fitness is required for research to improve rehabilitation of frail, elderly patients. An inverse relationship between oxygen uptake kinetics and aerobic fitness has previously been demonstrated[1]. Oxygen uptake kinetics may therefore be a suitable index of aerobic fitness. Moreover, we have shown that self-paced walking is a suitable mode of exercise for studying oxygen uptake kinetics in frail, elderly women[2]. We now report oxygen uptake kinetics measured at the onset of comfortable self-paced walking in young and healthy elderly women and frail, hip fracture survivors. **Methodology.** VO_2 kinetics and walking speed were measured during 3 min of comfortable self-paced walking around an elliptical circuit in 5 young women (median age 22 years, range 19-23 years), 5 healthy elderly women (median age 78 years, range 77-80 years) and 15 elderly women who had suffered a hip fracture (median age 81 years, range 72-91 years, median time since fracture 7 months, range 2-13 months). Hip fracture survivors were required to be ambulatory and not in institutional care. Each individual completed three walks on 2 separate occasions. The first walk of each visit acted as familiarisation and was excluded from further analysis. The oxygen uptake response at the onset of the 2nd and 3rd walks was ensemble averaged, time aligned and fitted with a monoexponential model (with Phase 1 (T0-T19 excluded)) to derive a time constant (tau). One hip fracture survivor did not provide data that could be adequately fitted with a monoexponential model on either visit. **Results.** Repeated measures ANOVA demonstrated a significant, among groups difference in tau values ($p < .01$) (Figure 1). The young women's tau values were lower than those of the healthy elderly women ($p < .01$) and those of the hip fracture survivors ($p < .01$). The tau values of the hip fracture survivors tended to be higher than those of the healthy elderly women but this was not statistically significant ($p = .15$). **Conclusion.** Oxygen uptake kinetics can be measured at the onset of comfortable, self-paced walking, even in frail, elderly hip fracture survivors. We aim to test the validity of this measure as an index of aerobic fitness in frail elderly patients.

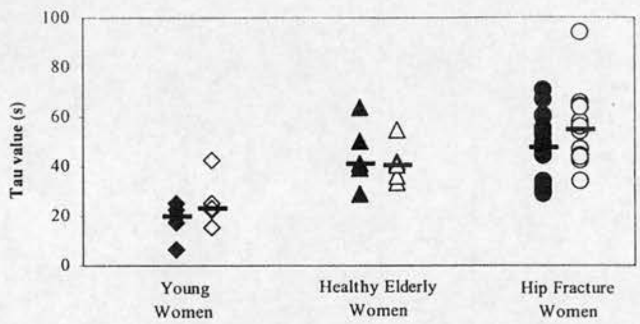

Figure 1. Tau value(s) of oxygen uptake at the onset of comfortable self-paced walking in young (N = 5), healthy elderly (N = 5) and hip fracture survivors (N = 14), (unfilled symbols represent Visit 2, lines represent median values).

Motor Learning in the Rehabilitation of Stroke Patients: Short Term or for Life? A Follow-Up 1 and 4 Years Poststroke

Birgitta Langhammer, Oslo University College, Oslo, Norway, Johan K Stanghelle, Sunnaas Sykehus

Objective. The purpose of this follow-up 1and 4 years poststroke was to study if the initial physiotherapy approach had had any long-term effects on mortality, motor function, postural control, activities of daily living, life quality, follow-up from community services and living conditions. **Design.** A randomised controlled trial of first time ever stroke patients, stratified according to gender and hemiplegic site. Group 1 (n = 33) and group 2 (n = 28) had initially physiotherapy according to Motor Relearning Programme and Bobath, respectively. **Main Outcome Measures.** The Motor Assessment Scale, the Sødring Motor Evaluation Scale (SMES), the Barthel ADL-index, the Nottingham Health Profile and Bergs Balance Scale was used. Following parameters were also registered: incidence of new strokes, other diseases, use of assistive devices, the patient's accommodation and use of services from the community. **Results**. The mortality rates were similar in the two groups. In both groups, the motor function, postural control and ADL were rapidly decreasing, leaving many of the patients dependent and with a high risk of falling. Life quality increased compared to the acute stage, but was still low in comparison with healthy persons. Most patients in both groups lived at home but were dependent on help from relatives and community services. Physiotherapy as follow-up service was not regular, neither common at 1 year poststroke but increasingly so at 4 years poststroke. The initial physiotherapy approach did not seem to have a major influence on the patients' possibility to cope in the long-term perspective. **Conclusion**. This follow-up at 1 and 4 years poststroke showed no major influence of 2 different physiotherapy regimens initially on the long-term function. The study confirmed a rapid deterioration of ADL and motor and an increased dependence on relatives to cope function in the poststroke patients. The study reveals a gap between the intense treatment in the acute phase while the patients have little or no follow up of physiotherapy treatment or any other kind of rehabilitation later.

In conclusion, the performance of the on-water vertical jump correlates poorly with the explosive ability of the lower body as that was assessed by the dry-land vertical jump. Furthermore, the ability to move the body vertically on-water differs significantly among players, depending on their position and on the level of competitiveness.

P10N-05

Is self-paced walking suitable for studies of oxygen uptake kinetics in frail elderly women?

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University of Edinburgh, United Kingdom

Keywords: elderly, self-paced walking, oxygen uptake

Current methodologies to examine oxygen uptake (VO2) kinetics involve cycle or treadmill ergometry, usually within a laboratory setting. However, this approach is problematic when one considers frail elderly people. This study has examined the use of self-paced walking as the mode of exercise. The purpose of this study is to determine whether comfortable self-paced walking can be described as 'constant load' exercise, and if so, to examine whether existing modelling techniques adequately describe the on-transient VO2 (phase 1 and 2) response to this form of exercise.
VO2 kinetics and walking speed were measured during three minutes of comfortable self-paced walking around an elliptical circuit in five young women (median age 22 years, range 19-23 years), five healthy elderly women (median age 78 years, range 77-80 years) and eleven elderly women who had suffered a hip fracture (median age 81 years, range 72-91 years, median time since fracture 5 months, range 2-13 months). The individual breath-by-breath responses for three repetitions were interpolated on a second-by-second basis and ensemble averaged to provide a single data set.
Comfortable self-paced walking could be described as 'constant load' exercise (coefficient of variation of individual lap speeds, young 2.7% (median), 0.9-4.6% (range), healthy elderly 1.9%, 0.8-3.7%, hip fracture 4.3%, 0.3-36.4%). The oxygen uptake data were adequately described using a non-linear monoexponential model (Sy.x values (standard deviation of residuals) young 0.0372 l.min-1 (mean value), healthy elderly 0.050 l.min-1, hip fracture 0.042 l.min-1; R2 values young 0.96 (mean value), healthy elderly 0.92, hip fracture 0.88).
This approach may provide the basis to examine oxygen uptake kinetics in individuals not capable of more traditional ergometry techniques.

P10N-06

A kinematic study of the pumping movement in Olympic sailboard

Rao Guillaume, Berton Eric, Favier Daniel, Gouard Philippe
LABM, France

Keywords: 3D analysis, sailboard, pumping movement

A better knowledge of the pumping movement in Olympic sailboard with consideration of kinematic and mechanical parameters will provide the basic guidelines for training elite athletes in order to gain an optimal pattern of the movement. The purpose of the present study is to identify the characteristics of a specific type of pumping movement (low rear wind velocity and high amplitude of oscillation) in olympic sailboard using a 3D motion analysis system (DLT computation). The pumping movement in sailboard has been investigated through a collaborative research work between Aerodynamics and Biomechanics of Motion Laboratory (LABM) and the French Sailing Federation (FFV).
The data reported in the present paper concern a specific experiment performed on May 2002 in the High Level Training Center of Marseille (France) and which has been based on video recording and kinematic data analysis of the sail mast movement. The video system consisted in three synchronized digital cameras located around a specific nautical track and recording multiple passing of one elite sailboarder. The whole space measurement (intersection of camera fields) was 15m x 10m in size. Passive markers were distributed all along the saill surface and the mast of the sailboard.
In particular, results have also provided the clear identification of different phases of traction and slide during a complete pumping movement cycle. Finally this study provides a visualisation software which gives to the coaches and athlete kinematic data on the sail and video information while the athletes pass through the nautical track. The present software version allows coach and athletes to quantify pumping mechanisms in order to identify the influence of the technical changes on the resulting movement produced by the athlete.

P10N-07

Comparison between two resistance training regimes: superslow vs. traditional training

Alberti Giampiero, Pizzini Giuliano, Gadina Guido, La Torre Antonio
University of Milano, Italy

Keywords: resistance strength training, superslow, strength gain

Various resistance training strategies are commonly used in order to improve strength in those athletes involved in sports that require muscular power. In Italy, many track and field coaches utilise a resistance training regime consisting in 10 RM per 10 series. However, some coaches are used to experiment different resistance training regimes in order to avoid training monotony especially in more experienced athletes. One of the most "original" alternatives is a strategy similar to the superslow-method in which the execution of the repetition is performed slowly. Thus, the aim of this study was to verify the effect on muscular strength of these two resistance training regimes.
Twelve male subjects with more than 5 years of resistance training were involved in the study. They were randomly assigned to two groups: superslow-method group (SG) and traditional-method group (TG). The superslow-resistance training method consisted of 6 consecutive series of 6 repetitions starting with 70% of 1 RM, decreasing the load of 20% in series 2 and 3, and decreasing of 10% in the following 3 series. The traditional method consisted of 10 series of 10 RM with 3 min of recovery between series. The subjects trained 3 times a week for 8 weeks. Before and after the training period a 1RM tests on different muscular groups were taken. Due to the low number of subjects a non parametric statistic was used (X2 test).
Five subjects for each group completed the study. Both groups significantly improved strength of all the muscular groups (from 5.9% to 23.5% in TG, and from 7.3% to 15.7% in SG). No differences were found between the two groups in strength gain.

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Studies of Human Performance in Older People: Health Questionnaire

Name:

Address:

Date of Birth:

Telephone no.:

If the answer is YES to any of the following questions, please give some details including dates where possible.

Have you any history of heart trouble?
(such as heart attack, angina, valve disease, palpitations, pains in chest, dizzy spells)

Have you any history of problems with blood vessels?
(such as thrombosis, embolus, claudication, aneurysm, dizzy spells, stroke, blood clots)

Have you any history of chest problems?
(bronchitis, asthma or wheezy chest)

Have you ever smoked?
(if YES please state whether you are a current or ex-smoker and how much)

Do you suffer from diabetes?
(if YES please state if insulin dependent)

Have you any history of major illness now or in the last 20 years?
(such as rheumatoid arthritis, blood disorders, cancer)

Have you any history of emotional or psychiatric problems?

Do you suffer from osteoarthritis?
(if YES please state joints affected and indicate mild, moderate or severe and any medication regularly taken)

Have you broken or fractured any bones? If so, when?

Do you have any problems with your bones?
(osteoporosis, loss of height)

Have you any history of back problems? If so, when did they start and do they still affect you in any way?

Have you had any surgery on your joints? If so, when?

Do you suffer from high blood pressure?

Have you had any acute illness in the last six months?
(such as influenza, recurrent sore-throat, bronchitis)

Please state any medication, prescribed or over the counter, regularly taken for any condition

Name of medication | How often medication is taken

Have you been in hospital in the last 5 years? If so, why and for how long?

Do you have any physical disabilities?
(such as visual or hearing problems)

Is there any other illness or condition that affects your general health or interferes with your mobility?

Approximately how tall are you?

Approximately how much do you weigh?

Your Doctor's Name:

Your Doctor's Address:

Thank you for completing this questionnaire

Appendix 2B. Exclusion criteria to define 'healthy' (i.e. 'disease-free') elderly subjects for exercise studies (Greig et al., 1994)

1. History of myocardial infarction within the previous 10 years
2. Cardiac illness: e.g. symptoms of aortic stenosis, acute pericarditis, acute myocarditis, aneurysm, severe angina, clinically significant valvular disease, uncontrolled dysrrhythmia, claudication, within the previous 10 years
3. Thrombophlebitis or pulmonary embolus within the previous 10 years
4. History of cerebrovascular disease
5. Acute febrile illness within the previous 6 months
6. Moderate or severe airflow obstruction
7. Metabolic disease (e.g. diabetes, thyroid disease), whether controlled or uncontrolled
8. Major systemic disease diagnosed or active within the previous 20 years (e.g. cancer, rheumatoid arthritis)
9. Significant emotional distress, psychotic illness or anything worse than mild anxiety or depression within the previous 10 years
10. Osteoarthritis, classified by inability to perform maximal contractions of upper and lower limbs without pain
11. Bone fracture sustained within the previous 2 years
12. 'Old person's fracture' after 40 years of age (wrist, hip, vertebral)
13. Non-arthroscopic joint surgery, ever, in the relevant limb part (i.e. hip, knee, ankle).

14. Any reason for a loss of mobility for greater than one week in the previous 6 months or greater than 2 weeks in the previous year
15. On daily medication (including daily simple analgesia); on oestrogen replacement therapy; on medication for hypertension, or with a diuretic for any other reason, even if not daily
16. Obese, i.e. a Quetelet index ($wt.ht^{-2}$) greater than 29.9
17. Resting systolic blood pressure > 200 mmHg, or resting diastolic blood pressure > 100 mmHg

CONSENT FORM

Re: The measurement of cardiorespiratory fitness during self-paced walking.

Name of investigators: Miss Claire Fitzsimons & Dr Carolyn Greig.

Address: Geriatric Medicine, The Chancellor's Building, University of Edinburgh, 49 Little France Crescent, Edinburgh.

Telephone: 0131 242 6909.

- I have read and understood the Subject Information Sheet and have had the opportunity to ask questions. ☐
- I agree for notice to be sent to my General Practitioner about my participation in this study. ☐
- I agree to the provision of any clinically significant information to my General Practitioner. ☐
- I understand that I am under no obligation to take part in this

study and have the right to withdraw from this study at any stage without having to give a reason. ☐

- I understand that this is non-therapeutic research from which I cannot expect to derive any benefit. ☐

- I agree to participate in this study. ☐

Name of volunteer subject:

Signature and date:

Signature of Investigator:

Date:

WALKING INSTRUCTIONS

We would like you to sit quietly for 2-3 minutes. You will then be asked to stand for one minute. You may take the arm of the person standing with you to steady yourself.

When you hear the instruction 'GO', you will begin walking at a COMFORTABLE PACE around the marked area. When you hear the instruction 'STOP', you will stand as still as possible for about 1 minute until you are asked to sit. The walks will be repeated 3 times.

Please remember that if you are feeling unwell or uncomfortable during the walking you may stop and my colleague or myself will come to you immediately.

Thank you.

	Last 30s of exercise				Last 60s of exercise		
		Exercise Bout				**Exercise Bout**		

Vol.	**Intensity ($\%VO_2max.$)**	**1**	**2**	**3**	**Intensity ($\%VO_2max.$)**	**1**	**2**	**3**
1	50	0.93	0.90	0.85	50	0.94	0.90	0.84
	65	0.92	0.93	0.82	65	0.93	0.93	0.88
	80	0.98	0.96	0.98	80	0.98	0.97	0.99
2	50	0.87	0.85	0.69	50	0.88	0.87	
	65	0.90	0.89	0.89	65	0.90	0.88	0.89
	80	0.98	0.98	1.01	80	0.98	0.96	1.01
3	50	0.93	0.97	0.93	50	0.93	0.97	0.94
	65	0.98	0.97	0.99	65	0.98	0.98	1.00
	80	0.95	1.03	0.99	80	0.94	1.02	0.99
4	50	0.89	error	0.85	50	0.89	error	0.88
	65	0.95	0.99	0.98	65	0.96	0.99	1.00
	80	1.03	1.03	1.01	80	1.06	1.03	1.01
5	50	1.02	0.99	0.97	50	1.00	1.00	0.96
	65	1.01	0.99	0.97	65	1.01	0.99	0.95
	80	1.05	1.06	1.07	80	1.06	1.07	1.06
6	50	0.84	0.92	0.89	50	0.84	0.90	0.90
	65	0.89	0.94	0.94	65	0.90	0.94	0.95
	80	0.96	0.95	1.02	80	0.96	0.94	1.02

Appendix 3A, Table 1. Respiratory exchange ratio (RER) of the last 30s (T330-T360) and last 60s (T300-T360) of each of three exercise bouts corresponding to each of the three exercise intensities (50, 65 and 80% $VO_2max.$)

Vol.	Inten.	Mean VO_2	B value	No. of data points	p value	Mean VO_2	B value	No. of data points	p value	Mean VO_2	B value	No. of data points	p value
1	50	1.1	0.006	11	0.14	1.2	0.003	12	0.67	1.3	0.003	13	0.72
	65	1.4	0.003	11	0.46	1.3	-0.009	12	0.30	1.6	0.011	12	0.17
	80	1.8	0.003	13	0.47	2.0	0.001	12	0.95	2.3	0.012	12	0.29
2	50	1.4	0.005	16	0.15	1.3	0.006	17	0.34	1.2	*-0.001*	20	*0.64*
	65	1.3	-0.008	14	0.12	1.6	-0.015	18	0.11	1.5	0.004	18	0.42
	80	1.9	0.014	19	0.02	1.8	-0.001	23	0.73	1.8	-0.001	22	0.82
3	50	1.3	0.000	13	0.94	1.2	-0.002	11	0.58	1.2	0.006	11	0.18
	65	1.5	0.006	15	0.23	1.5	0.000	15	0.96	1.3	0.001	11	0.87
	80	1.8	0.002	14	0.46	1.8	0.001	15	0.76	1.7	0.004	14	0.17
4	50	1.2	0.024	14	0.11		error on MM			1.0	-0.003	9	0.68
	65	1.4	0.003	15	0.79	1.5	0.003	16	0.76	1.4	-0.001	15	0.90
	80	1.7	0.003	19	0.74	1.6	0.004	16	0.54	1.5	0.004	15	0.29
5	50	1.1	0.004	13	0.23	1.1	0.002	13	0.45	1.2	-0.001	13	0.76
	65	1.5	-0.002	13	0.70	1.5	0.002	13	0.55	1.5	-0.011	15	0.51
	80	1.9	0.003	15	0.25	1.8	0.000	16	0.97	1.8	-0.004	15	0.50
6	50	1.3	0.003	13	0.56	1.2	0.002	16	0.55	1.2	0.005	15	0.25
	65	1.7	0.005	16	0.29	1.5	-0.007	17	0.50	1.4	-0.001	16	0.96
	80	2.1	-0.007	15	0.50	1.9	0.006	16	0.74	1.8	0.001	17	0.85

Appendix 3B, Table 2. Mean VO_2 ($l.min^{-1}$), slope of VO_2 (B value, $l.min^{-1}.sec^{-1}$), number of data points and p value of last 30 seconds of oxygen uptake data corresponding to each exercise intensity(p value <0.05 represents a significance deviation of B from zero)

Graded Exercise Test, WTCRF, University of Edinburgh

Protocol ______________ **Subject**____________________

Date ____________ **Age** __________

85% of HRmax. _____ **Age predicted HRmax.** ____

VO_2max. attempt number ______

Stage	Speed ($km.hr^{-1}$)	Grade (%)	Time (min)	RPE	BP	HR	ECG
Pre-Ex	-	-	-				
1	6.3	1	0 – 0.5				
2	6.3	2	0.5 - 1				
3	6.5	2	1 - 1.5				
4	6.5	3	1.5 - 2				
5	6.5	4	2 - 2.5				
6	6.5	5	2.5 - 3				
7	6.5	6	3 - 3.5				
8	6.5	7	3.5 - 4				
9	6.7	7	4 - 4.5				
10	6.7	8	4.5 - 5				
11	6.7	9	5 - 5.5				
12	6.7	10	5.5 - 6				
13	6.7	11	6 - 6.5				
14	6.7	12	6.5 - 7				
15	7	12	7 - 7.5				
16	7	13	7.5 - 8				
17	7	14	8 - 8.5				
18	7	15	8.5 - 9				
19	7	16	9 - 9.5				
20	7	17	9.5 - 10				
21	7	18	10 - 10.5				
22	7.2	18	10.5 - 11				
23	7.4	18	11 - 11.5				
24	7.4	19	11.5 - 12				
25	7.6	19	12 - 12.5				
26	7.8	19	12.5 - 13				
27	7.8	20	13 - 13.5				

Appendix Four Figure 1. VO_2max. treadmill protocol one (young, healthy women)

Graded Exercise Test sheet, WTCRF, University of Edinburgh

Protocol ____________ **Subject**_______________

Date __________ **Age** ________

85% of HRmax. _____ **Age predicted HRmax.** ____

VO_2max. attempt number ______

Stage	Speed ($km.hr^{-1}$)	Grade (%)	Time (min)	RPE	BP	HR	ECG
Pre-Ex	-	-	-				
1	9.0	0	0 - 3				
2	9.0	3	3 - 4				
3	9.0	5	4 - 5				
4	9.0	8	5 - 6				
5	9.0	10	6 - 7				
6	10	10	7 - 8				
7	10	13	8 - 9				
8	10	14	9 - 10				
9	11	14	10 - 11				
10	12	14	11 - 12				
11	13	14	12 - 13				
12	5	5	13 - 15				
13	2.1	0	15 - 17				

Appendix 4 Figure 2. VO_2max. treadmill protocol two (young, healthy men)

Modified Naughton Protocol, WTCRF, University of Edinburgh

Protocol ____________ **Subject** _________________
Date __________ **Age** ________

85% of HRmax. _____
Age predicted HRmax. ____

VO_2max. attempt number _____

Stage	Speed ($km.hr^{-1}$)	Grade (%)	Time (min)	RPE	BP	HR	ECG
Pre-Ex	-	-	-				
1	3.0	0	0 - 2				
2	3.0	4	2 - 5				
3	3.0	7	5 - 8				
4	3.0	11	8 - 11				
5	3.0	14	11 - 14				
6	3.0	16	14 - 17				
7	3.0	17	17 - 20				
8	1.5	0	20 - 35				

Appendix 4 Figure 3. VO_2max. treadmill protocol three (healthy elderly men and women)

6

7 - Very, very light

8

9 - Very light

10

11 - Fairly light

12

13 – Moderately hard

14

15 - Hard

16

17 - Very hard

18

19 - Very, very hard

20 - Exhaustion

Appendix 4 Figure 4. Borg Scale. Rating of perceived exertion (Borg, 1982)

EMS 1	Lying to sitting	Independent ☐1	Needs help of 1 person ☐2	Needs help of 2+ people ☐3	
EMS 2	Sitting to lying	Independent ☐1	Needs help of 1 person ☐2	Needs help of 2+ people ☐3	
EMS 3	Sit to stand	Independent in under 3 seconds ☐1	Independent in over 3 seconds ☐2	Needs help of 1 person (verbal of physical) ☐3	Needs help of 2+ people ☐4
EMS 4	Stand	Stands without support and able to reach ☐1	Stands without support but needs ☐2	Stands but needs support ☐3	Stands only with physical support ☐4
EMS 5	Gait	Independent (including use of sticks) ☐1	Independent with frame ☐2	Mobile with walking but erratic/ unsafe turning (needs occasional supervision) ☐3	Needs physical help to walk or constant supervision ☐4
EMS 6	Timed walk (6 metres)	Under 15 seconds ☐1	16-30 seconds ☐2	Over 30 seconds ☐3	Unable to cover 6 metres ☐4
EMS 7	Functional reach	Over 16 cm ☐1	8-16 cm ☐2	Under 8 cm or unable ☐3	

Appendix 4, Figure 5. Elderly Mobility Scale

The Functional Independence Measure

Feeding	**FIM 1**	
Grooming	**FIM 2**	
Bathing	**FIM 3**	
Dressing Upper Body	**FIM 4**	
Dressing Lower Body	**FIM 5**	
Toileting	**FIM 6**	
Bladder Management	**FIM 7**	
Bowel Management	**FIM 8**	
Bed, Chair, transfer	**FIM 9**	
Toilet transfer	**FIM 10**	
Bath or Shower transfer	**FIM 11**	
Locomotion Walk	**FIM 12**	
Stairs	**FIM 13**	
Comprehension Audio/Visual	**FIM 14**	
Expression Verbal, Non-Verbal	**FIM 15**	
Social Interaction	**FIM 16**	
Problem Solving	**FIM 17**	
Memory	**FIM 18**	
TOTAL		

Scoring

7 – Completely independent (timely & safely)

6 – Modified independence (extra time, concern for safety, uses equipment)

5 – Supervision (set-up / prompts)

4 – Minimal assistance (75%+)

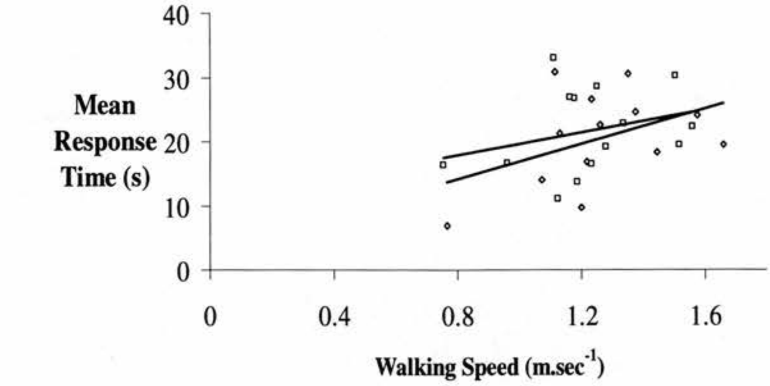
3 – Moderate assistance (50%+)

2 – Maximum assistance (25%+)

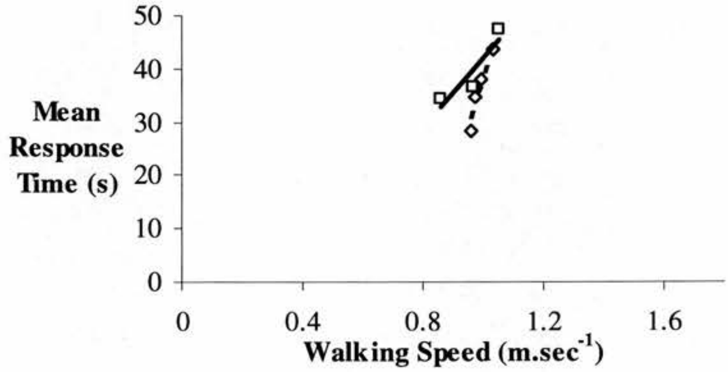
1 – Total assistance (< 25%+)

Appendix 4, Figure 6. The Functional Independence Measure (FIM)

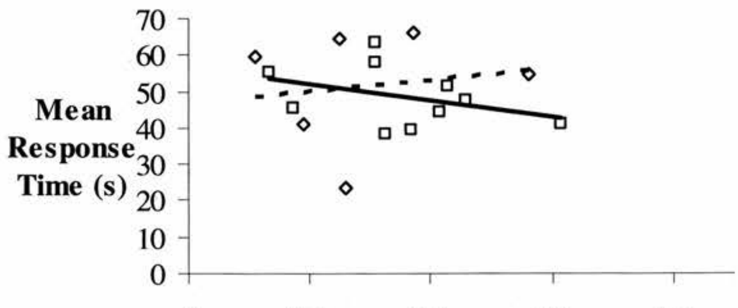
Graph One – Young Visits One and Two



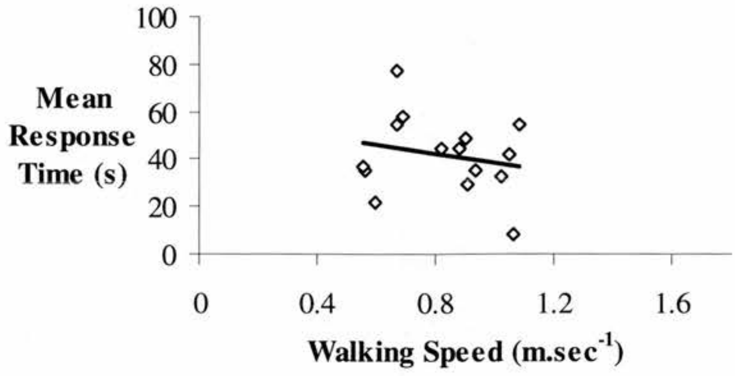
Graph Two - Healthy Elderly Visits One and Two



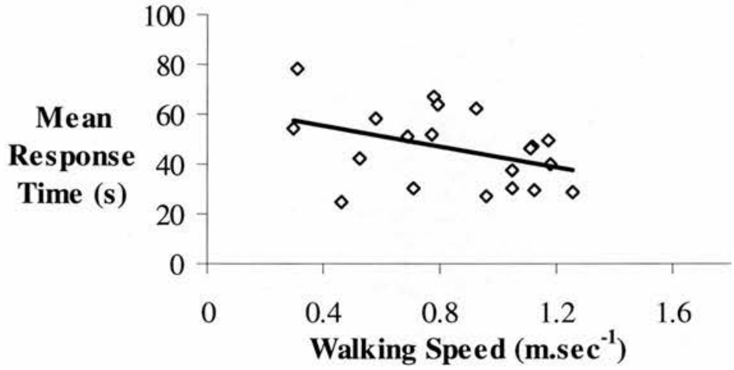
Graph Three – Hip Fracture Visits One and Two



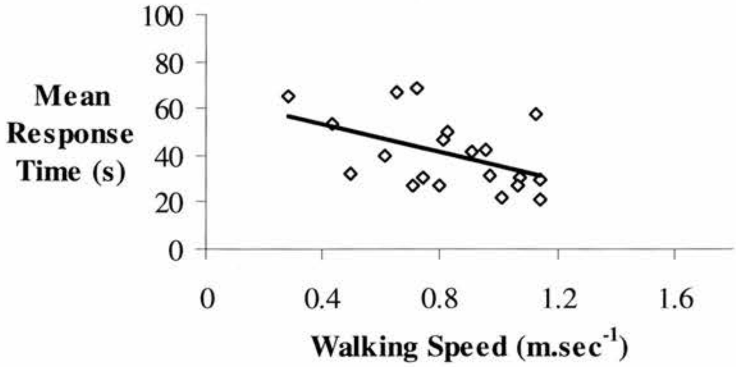
Graph Four - Stroke Visit One



Graph Five - Stroke Visit Two

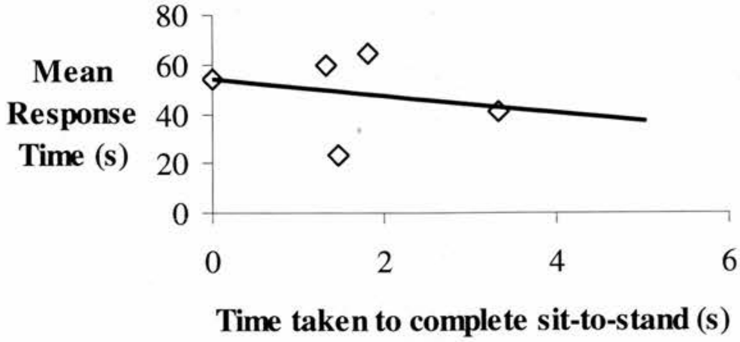


Graph Six - Stroke Visit Three

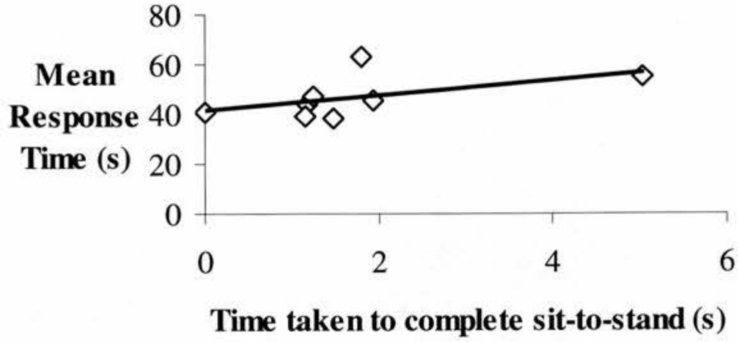


Appendix 4, Figure 7. Scatterplots of **MRT** values (s) and average **walking speed** (m.sec^{-1}) over the second and third walks on Visits 1 (diamonds) and 2 (squares) for Young (Graph 1), Healthy Elderly (Graph 2) and Hip Fracture (Graph 3), (dashed linear regression trend line represents Visit 1; solid line Visit 2). Graphs 4-6 present the Stroke group data from Visit 1, 2 and 3 respectively (solid line represents linear regression trend line)

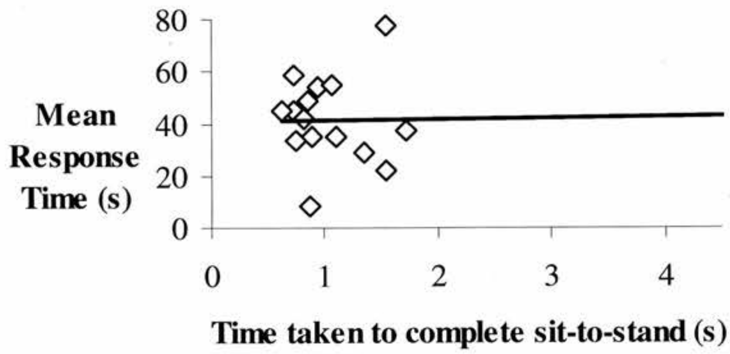
Graph One - Hip Fracture Visit One



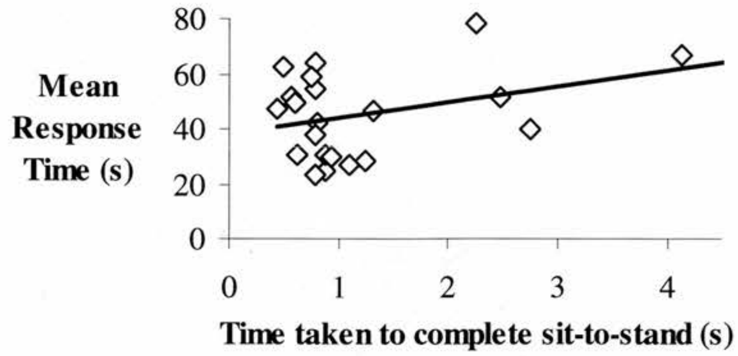
Graph Two - Hip Fracture Visit Two



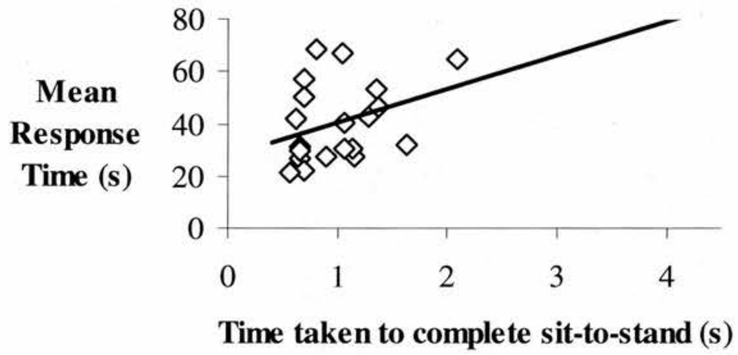
Graph Three - Stroke Visit One



Graph Four - Stroke Visit Two

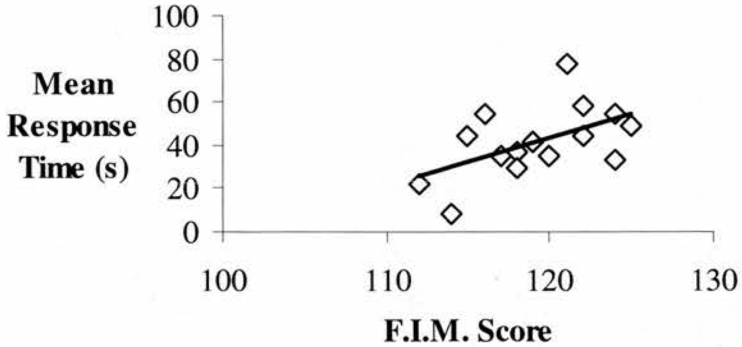


Graph Five - Stroke Visit Three

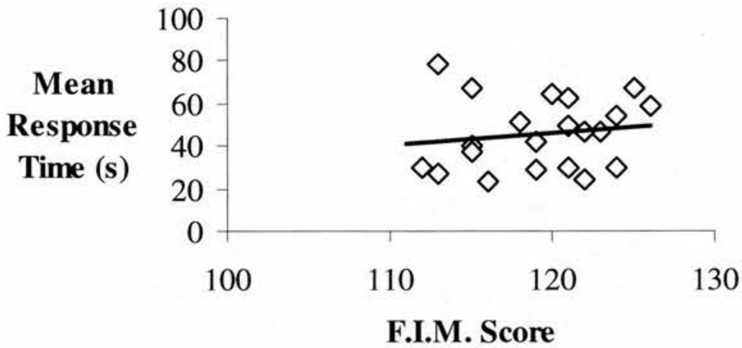


Appendix 4, Figure 8. Scatterplots showing the relationship between **MRT** (s) and time taken to perform **sit-to-stand** (s) for the Hip Fracture group on Visits One (Graph One) and Two (Graph Two) and the Stroke group on Visits One (Graph Three), Two (Graph Four) and Three (Graph Five)

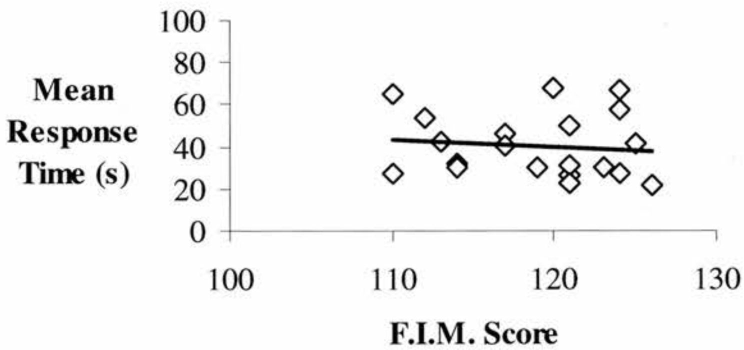
Graph One - Stroke Visit One



Graph Two - Stroke Visit Two



Graph Three - Stroke Visit Three



Appendix 4, Figure 9. Scatterplots showing the relationship between the **MRT** (s) and the **FIM** score for the stroke group on Visit One (Graph One), Visit Two (Graph Two) and Visit Three (Graph Three)

Names and roles of Investigators in the STARTER (Stroke: A Randomised Trial of Exercise and Relaxation) trial

STARTER was a Chief Scientist Office funded trial, with the University of Edinburgh as the Host Institution.

Gillian Mead (Principal Investigator and Grantholder), Senior Lecturer & Honorary Consultant, University of Edinburgh) – study design, including a contribution to the design of the relaxation and exercise interventions; recruitment; physician checks; supervision of study team at all stages of the trial; data analysis, dissemination and publication.

Carolyn Greig (Senior Research Fellow, University of Edinburgh and Co-Grantholder) – study design; collection of baseline and follow-up assessment data and assistance with collection of walking data; supervision of study team during earlier stages of trial; data dissemination and publication.

Susie Dinan (Senior Clinical Exercise Practioner and Co-grantholder) – Major role in design of exercise and relaxation interventions; quality assurance of delivery of the interventions; data dissemination and publication.

Archie Young (Professor of Geriatric Medicine & Honorary Consultant, University of Edinburgh and Co-grantholder) - study design; volunteer recruitment; physician checks; supervision of study team; data dissemination and publication.

David Saunders (Lecturer, University of Edinburgh and Co-grantholder) – Design and maintenance of trial database; assistance with design of exercise intervention; collection of baseline and follow-up assessment data (including data collection forms) and assistance with collection of walking data; data analysis, dissemination and publication.

Claire Fitzsimons (PhD Student, University of Edinburgh) - Planning and design of the self-paced walking tests and collection, calculation and analysis of baseline and follow-up assessment data for cardiorespiratory function and functional performance (i.e. 3 metre timed up and go, sit to stand, walking tests and calculation of walking speed and VO_2 kinetics criteria and MRT values); data dissemination and publication.

Susan Lewis (Research Fellow, University of Edinburgh) – Study design; data analysis, dissemination and publication.

Susan Quin (Research Assistant, University of Edinburgh) - Trial Co-ordinator

Irene Cunningham (Advanced Exercise Instructor, University of Edinburgh) – Delivery of exercise and relaxation interventions.

Caroline Rea (Research Assistant, University of Edinburgh) – Participant recruitment.

Gail Carin-Levy (Research Assistant) - Study design and data collection, data analysis, dissemination and publication of the qualitative responses to the STARTER trial.

Carol Downie (Occupational Therapist, Lothian University Hospitals Trust) – Consultant on design of the relaxation intervention.

Mark Smith (Physiotherapist, Lothian University Hospitals Trust) – Consultant on design of the exercise intervention.

Appendix 5, Figure 2

Appendix A

Chief Scientist Office Form 4

Final report form	**CSO reference number: CZB/4/46**

Please complete this form in 12 point font size

Project title: A Randomised Exploratory Trial of Physical Fitness Training after stroke Trial name: STARTER (STtroke: A Randomised Trial of Exercise or Relaxation)	
Start date: 1.10.02	Finish date: 23.02.05 (date of final outcome assessment)

Investigators (Grant holders):

GE Mead	S Dinan
CA Greig	A Young
DH Saunders	

Structure of final report:

1. Summary
2. Original aims
3. Methodology
4. Results
5. Discussion
6. Conclusions
7. Importance to NHS and possible implementation
8. Future research
9. Dissemination
10. Research workers
11. Financial statement
12. Executive summary (Focus on Research)

1. Summary

This exploratory trial randomised 66 ambulatory stroke patients (mean age 72 years) to a 12 week programme (three times a week) of either physical fitness training or relaxation (control intervention). Assessments were performed at baseline, immediately after the end of the interventions and four months after the end of the interventions.

The trial design was feasible, with high attendance rates at both the exercise and relaxation interventions and at the post-intervention assessments.

In the exercise group, there were significant improvements between baseline and the 1st post-intervention assessment in components of quality of life (role physical, general health, vitality, role emotional and mental health), anxiety component of the Hospital Anxiety and Depression Score (HADS), functional reach, extensor power of both legs, walking speed, walking economy, timed up-and-go and sit-to-stand time. At the 2nd post-intervention assessment, some improvement in extensor power of both legs, HADS-anxiety and sit-to-stand was still maintained.

In the relaxation group, there were significant improvements between baseline and the first post-intervention assessment in the mental health component of quality of life, extensor power of the unaffected leg and walking speed. At the 2nd post-intervention assessment, some improvement in all these measures was still maintained.

There were significantly greater gains between baseline and the 1st post-intervention assessment for the exercise group than the relaxation group for functional reach, role-physical, general health, walking economy and timed up-and-go.

A multicentre definitive trial is now required.

2. Original Aims

We had two aims. Firstly, we wished to test the feasibility of our trial design. Secondly, we wished to estimate the effect of physical fitness and relaxation on our outcome measures. We estimated that we could recruit 5 patients per month, i.e. a total of 90 patients.

3. Methodology

Identification of patients
Between October 2002 and July 2004, we visited the stroke wards at the Royal Infirmary (RIE), Liberton and Astley Ainslie Hospitals at least once a week, and identified independently ambulatory stroke patients. Stroke patients who had been admitted and discharged from the medical assessment ward were screened for

inclusion when reviewed in the RIE stroke clinic. Other eligibility criteria were a) absence of medical contraindications to fitness training [1] b) absence of significant dysphasia or confusion c) living in central or south Edinburgh, or in the suburbs south of Edinburgh and d) completed all their stroke rehabilitation.

We recorded the number of ambulatory patients assessed, the proportion fulfilling our other eligibility criteria, and the proportion of eligible patients agreeing to participate.

From August 2003, suitable patients who had been inpatients or who had attended the stroke clinic at the Western General Hospital were referred to the trial.

Baseline assessment

Eligible consenting patients attended the Human Performance Laboratory (old RIE, October 2002 to March 2003) or the Clinical Research Facility (New RIE, April 2003 onwards) shortly before the intervention. A physician checked that the patients still fulfilled the entry criteria and performed a limited neurological examination. One of three exercise physiologists assessed disability (Functional Independence Measure, FIM [2], Nottingham Extended ADL [3]), function (Rivermead mobility index (RMI) [4], functional reach [5], timed up-and-go [6] and sit-to-stand), elderly mobility score (EMS) [7], Functional ambulation category [8]), quality of life (SF-36v2 questionnaire) [9] and mood (HADS [10]).

The velocity of self-paced 'comfortable' walking was assessed during three bouts (separated by five minutes) of walking around a marked 17m circuit, completing sufficient laps to achieve a minimum of 3 minutes of walking [11]. During the walking, the patients wore a lightweight facemask connected to an ambulatory gas analysis system (Metamax 3B, Cortex MBH) to allow analysis of respiratory variables and calculation of walking economy i.e. oxygen cost per body mass per distance walked. Leg extensor explosive power (each leg) was measured using a Nottingham Power Rig [12].

Randomisation

Randomisation to either exercise or relaxation was done by the trial co-ordinator or Principal Investigator via a secure internet randomisation service (designed by Department of Clinical Neurosciences, University of Edinburgh), and stratified by gender, FIM score (cut-off of 120) and age (cut-off 70).

The interventions

Both interventions were delivered in the Old Function Hall at Liberton Hospital by an advanced exercise instructor on a Monday, Wednesday and Friday for 12 weeks. During the first week, the exercise instructor checked medication, blood pressure and resting pulse rate, and familiarised the patients with the techniques and equipment. At the start of all classes, the exercise instructor enquired whether the patients had fallen since the last class. Each class lasted one hour fifteen minutes (including either the exercise or relaxation intervention, and tea-and-chat after the interventions).

We asked patients to attend all 36 sessions, but for those who could not (e.g. due to intercurrent illness, pre-arranged holidays, social events or hospital appointments), there was an opportunity to attend a maximum of three 'catch up' sessions.

There were six separate and consecutive 'iterations' of groups of patients for each intervention. Each 'iteration' lasted 36 sessions (plus three 'catch-up' sessions).

The local taxi firm which we used initially was unreliable, so we arranged minibus transport (South Edinburgh Amenities Group) wherever practical. Some patients preferred to use public or private transport.

Physical fitness training (exercise)
The intervention was designed and quality assured by a clinical exercise practitioner with advice from a specialist stroke physiotherapist; and delivered by an advanced exercise instructor. It started with a 'warm-up', and ended with a 'warm-down'. The training included aerobic exercise which was progressive in nature i.e. increasing duration and intensity in specified, conservative (small) increments during the course of the programme. The aerobic training included walking, marching, cycle ergometry, ascending and descending purpose-built stairs, and simple, co-ordinated step patterns (or steps) to music. Progressive resistance training (strength and muscular endurance of upper and lower limbs, affected and unaffected sides) was also performed using progressively higher resistance elastic training devices (Therabands). Functional strengthening activities e.g. chair rises, squats, lunges and wall presses; and co-ordination and flexibility training were also integrated into the programme [13].

Relaxation (attention control) intervention
This intervention was devised in collaboration with a specialist occupational therapist, and delivered by the advanced exercise instructor. The relaxation intervention was seated and included deep breathing and progressive muscular relaxation. Techniques involving muscular contraction were not included so that unintentional fitness training was avoided.

Blinding
Patients could not be blinded to the type of intervention. We attempted to blind patients to the underlying hypothesis, by explaining that both interventions could have benefits. Patients were asked not to mention their allocated intervention when attending for the post-intervention outcome assessments. In order to assess the degree of unblinding, the physiologists guessed the intervention group.

Post-intervention assessments
Patients re-attended for an outcome assessment as soon as possible after the end of the interventions (1st post-intervention), and then four months later (2nd post-intervention).

Data checking and analysis
Data were collected on paper data collection sheets and then entered into an electronic database. All electronic data were checked to identify inconsistencies, obvious errors and missing fields. Additionally, a 10% random sample of entered

outcome data was checked by someone not involved with its entry. This revealed a 0.04% error rate for the initial data entry, hence, double entry of *all* data was deemed unnecessary.

Statistical Methods
The study design was intention to treat, so missing outcome data were replaced using the 'last observation carried forward' procedure. Very occasionally, if baseline data were missing, values were 'carried backwards' from the next assessment with valid data.

Normally distributed data were expressed as means and standard deviations. Otherwise, medians and inter-quartile ranges (IQR) were used. Many of the outcome variables had a skewed distribution. Usually the skew was negative due to ceiling or near-ceiling effects. Several different data transformations (positive skew - square root, logarithm and reciprocal; negative skew - reflection to reverse the order of the data followed by the same transformations) were compared for outcome variables which did not have a normal, or near-normal, distribution. The least extreme transformation that produced an acceptable distribution of the paired differences between baseline and the post-intervention assessments was selected.

Parametric tests were used for normally-distributed data and for satisfactorily transformed data (paired and independent samples t-tests). Alternatively, nonparametric methods were used (paired comparisons – Wilcoxon Signed Ranks test for symmetrical data distributions or the Sign test; independent samples – Mann-Whitney test).

A sensitivity analysis was conducted by applying all statistical procedures to both the original data and the data with missing values replaced. The two sets of analyses produced very similar results, only those for the full dataset are presented here.

4. Results

Feasibility of trial design

Recruitment
We assessed 301 ambulatory stroke patients, of whom 154 (51%) were ineligible (please see figure 1).

Of the 147 eligible patients, 67 (45%) refused. The remaining 80 patients consented, but between consent and baseline assessment, 14 (18%) changed their minds, 11 (14%) developed contraindications, and one (1%) died, leaving 54 (68%) patients who underwent baseline tests and were randomised. An additional 12 patients who had been referred from the Western General Hospital were eligible, consented and attended baseline assessments. Hence, 66 patients in total were randomised.

During the trial, the Principal Investigator was on maternity leave for 9 months. A research nurse was appointed to assist with recruitment but she was on sick leave for five months. Hence, recruitment was done mainly by the other investigators, none of whom had clinical responsibility for the patients on the stroke ward. These factors probably contributed to the short-fall in recruitment.

Characteristics of patients at baseline (table 1)

The mean age of patients was 72 years. As one of our entry criteria was 'independently ambulatory', the scores for mobility (RMI, Functional Ambulation category) and disability (FIM and Nottingham ADL) were high (table 2), and for some measures, (e.g. EMS) the maximum score was attained for a substantial number of patients (i.e. 'ceiling effect').

Randomisation

The secure internet-based randomisation service was quick and simple to use, and provided printed reports of treatment allocations when required. Thirty-two patients were allocated to exercise and 34 to relaxation.

Attendance at the classes

Although we stipulated a maximum of 36 sessions, some patients wished to attend the additional sessions and were allowed to do so.

For the 32 patients randomised to exercise, the median number of sessions attended was 36 (IQR 30 to 36.75).

For the 34 patients randomised to relaxation, the median number of sessions attended was 36 (IQR 30.5 to 37) (including two who withdrew before the classes started).

Attendance at post-intervention assessments

Sixty-four (97%) attended the 1st post-intervention assessment, and sixty-two (94%) attended the 2nd post-intervention assessment (one of the non-attenders withdrew from the trial before the start of the interventions and the others did not attend because of illness).

Feasibility of outcome measures

Outcome measures were performed at baseline, 1st post-intervention assessment and 2nd post-intervention assessment. Each assessment lasted around two hours. Of the total assessments (n=192), data were obtained for the over 90% of measurements at all three assessments (table 3). The reasons for non-completion of the individual tests included illness or limb pain (affecting, for example, the timed up-and-go), inadequate time, or because the physiologists decided that some of the assessments would have tired or upset patients.

Effectiveness of blinding

At the 1st post-intervention assessment, the physiologists guessed the allocated group for 56/63 patients. This guess was correct in 37/56 (66%) of patients. At the third assessment, a guess was made for 52/61 patients and was correct in 30/52 (58%). These data hint that there may have been a few instances of unblinding. When a guess was not made, this was because the outcome assessor had no idea of treatment allocation, and felt unable even to guess.

Falls

During the 3 month period of the interventions (but not during the classes), 8/32 patients in the exercise group reported 11 falls, and 4/34 patients in the relaxation group reported five falls (no significant difference between groups). Additionally, one patient allocated to relaxation fell at one of the outcome assessments.

Comparison of baseline and 1st post-intervention assessment, and between baseline and 2nd post-intervention assessment for the two groups (table 3)

In the exercise group, there were significant improvements between baseline and the 1st post-intervention assessment for components of the SF-36v2 (role physical, general health, vitality, role emotional and mental health), functional reach, the anxiety component of the HADS, extensor power of both legs, walking speed, walking economy, timed up-and-go and sit-to-stand. At the 2nd post-intervention assessment, some improvement in extensor power of both legs and sit-to-stand was still maintained.

In the relaxation group, there were significant improvements between baseline and the first post-intervention assessment in the mental health component of the SF-36v2, extensor power of the unaffected leg and walking speed. At the 2nd post-intervention assessment, some improvement in all of these measurements was still maintained.

Changes in the variables between baseline and post-intervention assessments: comparison of the change in groups (Table 4)

There were significantly greater gains between baseline and the 1st post-intervention assessment in the exercise group than the relaxation group for functional reach, role-physical, general health, walking economy and timed up-and -go.

Conclusions

All aspects of the study design were feasible. We achieved 73% of our recruitment target.

The exercise intervention improved some aspects of quality of life, mood, physical function and physical fitness. There were fewer benefits in the relaxation group. The majority of benefits in the exercise group were not maintained four months after the end of the intervention, suggesting that maintenance of benefits requires long-term participation in exercise.

It is very unlikely that the improvements reflect natural recovery after stroke because the median time between stroke and baseline assessment was 5 months (by which time almost all natural recovery would have occurred), and because some improvements were lost after the interventions had been completed.

The improvements in both groups were probably due to the effect of the interventions themselves, and due to the whole 'package' i.e. increased physical activity as a result of travelling to and from classes three times a week, a sociable journey in a minibus, sharing a group activity with other stroke survivors, and contact with an experienced exercise instructor with excellent interpersonal skills.

When we devised the trial, we elected not to use a 'usual care' group in addition to our 'attention control' group, as this would have added additional complexity and expense. Had we done this, we would have been able to start to tease out the extent to which the benefits might have been mediated by aspects of the whole 'package' other than exercise.

Importance to the NHS

This is the largest randomised trial comparing exercise training with relaxation for stroke patients, the first to use such an extensive battery of outcome assessments, and the first to investigate whether benefits are maintained long-term. Several community stroke physiotherapists have indicated that patients frequently ask whether there are suitable exercise classes in the community. Our data support the idea that exercise training, and to a lesser extent, relaxation, is beneficial after stroke.

We would like to develop training courses for exercise instructors in the leisure industry. This would include general training and education about stroke, plus specialised training in the delivery of exercise programmes to stroke patients. Classes in leisure centres would then be established and would be available to patients either as a service development or in the context of further trials.

Future research

The aims of this exploratory trial were to provide information on feasibility and effectiveness. Now that we have this information, we intend to seek funding for a multicentre Scottish study. One of the aims of this study would be to explore in more detail the effect of the interventions on disability as well as physical function and physical fitness. We have had expressions of interest from Dundee and Aberdeen stroke physicians. We will need to decide whether to include a 'usual care' group. This would increase the number of patients required, but would provide additional important information about the benefits of both interventions compared with usual care after stroke.

Further work is required to investigate the optimum way to facilitate the move from formal classes to lifelong participation in physical exercise.

Dissemination

We presented preliminary data on feasibility as a poster at the National Stroke Forum in April 2005. The poster was viewed by health professionals from all over Scotland and by Andy Kerr, Health Minister. Baseline and feasibility data were presented to a meeting of geriatricians and their multidisciplinary teams in Aberdeen in May 2005. We presented baseline data relating leg extensor power and physical function at the Spring Meeting of the Scottish British Geriatrics Society in Inverness, May 2005. After completing all the outcome assessments, a 'Personal View' was published in the BMJ describing the Principal Investigator's experience of attending the classes [14]. We plan to present the main results at national and international meetings. We will submit the main results to high impact journals, and will incorporate the results into the next issue of our Cochrane systematic review of fitness training after stroke [15].

Research workers

Gillian Mead (PI), Carolyn Greig, Irene Cunningham, Susie Dinan, Susan Lewis, Claire Fitzsimons, Dave Saunders, Susan Quin, Caroline Rea, Archie Young.

Carol Downie (occupational therapist) assisted in devising the relaxation intervention, and Mark Smith (physiotherapist) assisted in devising the exercise intervention.

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The assessments were carried out at the Clinical Research Facility, New Royal Infirmary from April 2003 onwards.

Word count: 2950

Financial statement

Attached

Executive summary

Attached (**word count 547**)

References

[1] Dinan S Physical Activity for vulnerable older adults In Physical Activity for Patietns: a exercise prescription. Eds A Young M Harries Royal College of Physicians of London 2001; p53-70

[2] State University of New York at Buffalo Guide for Use of Uniform Data Set for Medical Rehabilitation (Adult FIM) version 4.0 Buffalo NY

[3] Nouri FM Lincoln NB An extended activities of daily living scale for stroke patients Clinical Rehabilitation 1987;1:301-305

[4] Nouri FM Leadbitter D Assessment of motor function in stroke patients Physiotherapy 1979; 65:48-51

[5] Duncan PW Weiner DK Chandler J Studenski S Functional Reach: a new measure of balance Journal Gerontology 1990;45:M192-7

[6] Podsiadlo D Richardson S The timed 'Up and Go': a test of basic functional mobility for frail elderly persons Journal of American Geriatrics Society 1991;39:142-8

[7] Smith R Validation and Reliability of the Elderly Mobility Score Physiotherapy 1994;80:744-747

[8] Hesse S Bertelt C Schaffrin A Malezic M Mauritz KH Restoration of gait in non-ambulatory hemiparetic patients by treadmill training with partial body-weight support Archives of Physical Medicine and Rehabilitation 1994;75: 1087-93

[9] Ware JE Kosinski M Dewey JE How to score Version 2 of the SF-36 Health Survey. Lincoln, RI: QualityMetric Incorporated, 2000

[10] Zigmond AS Snaith RP The Hospital Anxiety and Depression Scale *Acta Psychiary Scan* 1983;67:361-370

[11] Fitzsimons CF, Greig CA, Saunders DH Lewis SH Shenkin SD Lavery C Young A Responses to walking-speed instructions: implications for health promotion in older adults Journal of Aging and Physical Activity 2005;13:172-83

[12] Greig CA Young A Skelton DA Pippet E Butler FMM Mahmud SM Exercise studies with elderly volunteers Age Ageing 1994;23:185-189

[13] Dinan S Skelton D Exercise for improving postural stability and reducing the risk of falls and injuries Ed K Malbut Leicester College 2000, p57058

[14] Mead G Exercise or Relaxation after stroke? BMJ 2005;330:1337

[15] Saunders D Greig C Young A Mead GE Physical fitness training for stroke patients (Cochrane review) In: *The Cochrane Library*, Issue 1, 2004. Chichester UK

Figure 1 Flow diagram indicating recruitment to STARTER

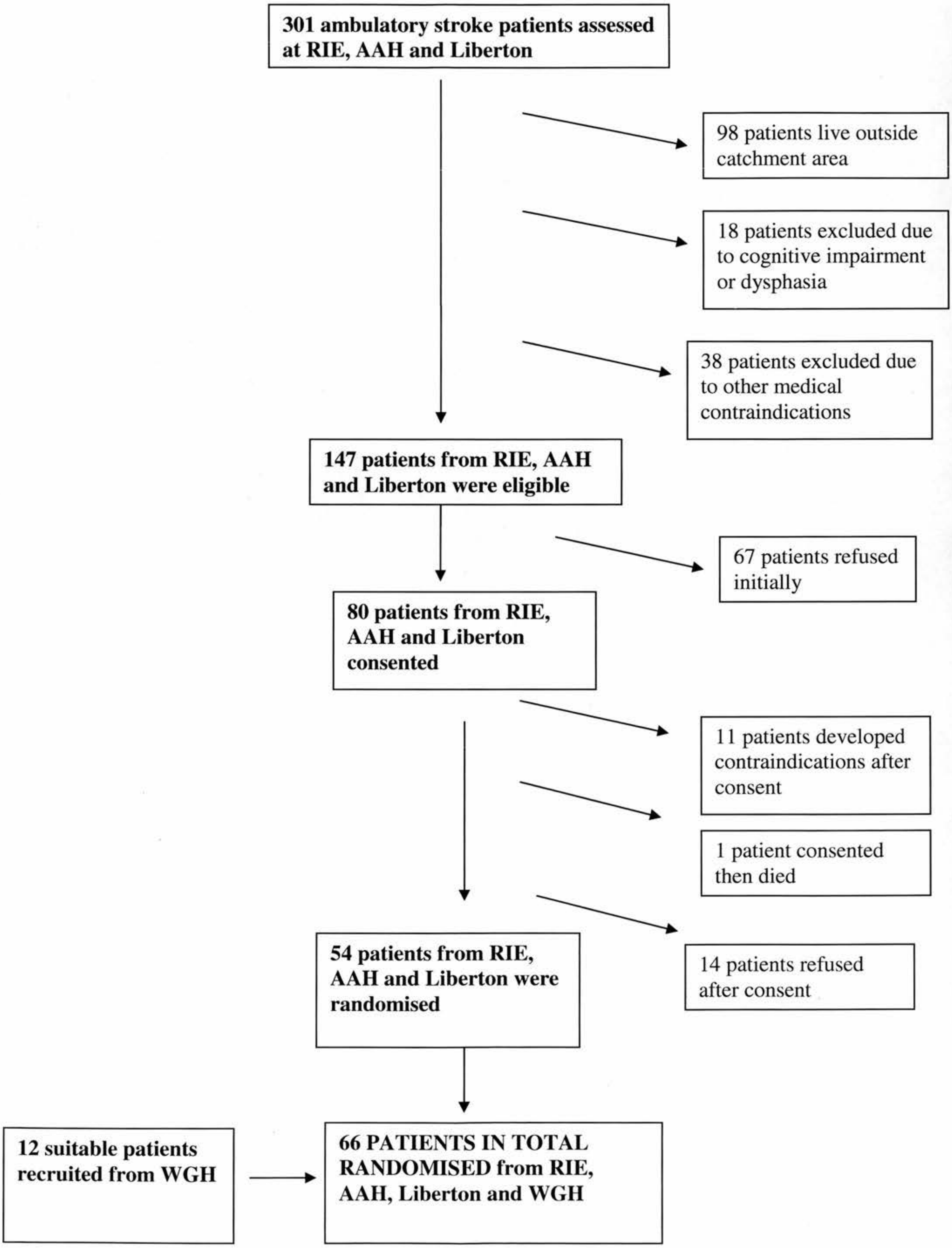

Table 1 Characteristics of patients at baseline.

	All patients (n=66)	**Exercise group (n=32)**	**Relaxation group (n=34)**
Age (mean (SD))	71.9 (9.9)	72.0 (10.4)	71.7 (9.6)
No (%) men	36 (55)	18 (56)	18 (53)
Required inpatient treatment for stroke	56 (85)	27 (84)	29 (85)
Length of in-patient stay (median (IQR))	17.5 (7-44) n=56	19 (7-39) n=27	16 (6.5-48.5) n=29
Outpatient treatment only	10 (15)	5 (16)	5 (15)
Type of stroke (OCSP):			
Total anterior circulation	2 (3)	1 (3)	1 (3)
Partial anterior circulation	32 (49)	16 (50)	16 (47)
Lacunar	19 (29)	10 (31)	9 (26)
Posterior circulation	12 (18)	4 (13)	8 (24)
uncertain	1 (1.5)	1 (3)	0
Ischaemic	60 (91)	28 (88)	32 (94)
Haemorrhagic	5 (8)	3 (9)	2 (6)
Unknown	1 (1.5)	1 (3)	0
Side of brain lesion:			
Right	27 (41)	12 (38)	15 (44)
Left	37 (56)	19 (59)	18 (53)
Bilateral	1 (1.5)	0	1 (3)
unknown	1 (1.5)	1 (3)	0
Time between stroke and baseline (median (IQR))	152 (74.5-281) n=65	171 (55-287) n=31	147.5 (78.8-235.5) n=34
Time between stroke and start of intervention (median (IQR))	175 (87-297) n=63	178 (86-307) n=31	161.5 (91.8-242.8) n=32
Smoking habit:			
Non-smoker	28 (42)	13 (41)	15 (44)
Ex-smoker	12 (18)	6 (19)	6 (18)
Smoker	25 (38)	13 (41)	12 (35)
Unknown	1 (1.5)	0	1 (3)
Drugs[ab]:			
Antiplatelet drugs	59 (91)	29 (94)	30 (88)
Antihypertensives	31 (48)	13 (42)	18 (53)
Statins	44 (68)	18 (58)	26 (77)
Anticoagulants	5 (8)	1 (3)	4 (12)
Other	60 (92)	29 (94)	31 (91)
Comorbid disease[ac]:			
Hypertension	31 (52)	12 (46)	19 (56)
Ischaemic heart disease	23 (38)	9 (35)	14 (41)
Cancer (prior or current)	6 (10)	4 (15)	2 (6)
Prior stroke	11 (18)	5 (19)	6 (18)
Prior TIA	4 (7)	2 (8)	2 (6)
Diabetes	3 (5)	2 (8)	1 (3)

Left ventricular failure	2 (3)	1 (4)	1 (3)
Other	36 (60)	19 (73)	17 (50)

Sitting systolic BP (mmHg) (mean (SD))	140.0 (18.1) n=63	140.6 (18.6) n=31	139.5 (17.9) n=32
Sitting diastolic BP (mmHg) (mean (SD))	73.2 (9.5) n=63	74.7 (10.0) n=31	71.7 (8.9) n=32
Standing systolic BP (mmHg) (mean (SD))	139.2 (19.8) n=63	139.5 (19.5) n=31	138.9 (20.4) n=32
Standing diastolic BP (mmHg) (mean (SD))	73.9 (9.8) n=61	76.0 (10.0) n=31	71.6 (9.3) n=30
Speech:			
Normal	45 (68)	21 (66)	24 (71)
Dysarthria	16 (24)	9 (28)	7 (21)
Expressive	4 (6)	1 (3)	3 (9)
Not recorded	1 (1.5)	1 (3)	0
Any arm weakness (score of <5 on MRC motor scale)	22 (33)	9 (28)	13 (38)
Any leg weakness (score of <5 on MRC motor scale)	15 (23)	7 (22)	8 (24)
Any inattention	4 (6)	2 (6)	2 (6)
Functional Ambulation Category			
Score of 4	7 (11)	3 (9)	4 (12)
Score of 5	59 (89)	29 (91)	30 (88)

Values are numbers (percentages) unless otherwise stated

[a] Multiple response variable - percentages do not add to 100

[b] For one subject (exercise group) there were no medications. Excluded from calculation of percentages.

[c] There were no comorbidities for six subjects (all exercise group). Excluded from calculation of percentages.

Table 2 Outcome variables at baseline for all subjects

Outcome variable at baseline	Number of subjects	Range	Mean (SD)	Median (IQ Range)	Floor effect n (%)	Ceiling effect n (%)
Functional Independence Measure (18-126)	66	95-126		117.5 (114–122)	0	2 (3.0)
Nottingham Extended ADL (0-22)	65	2-22		17 (12-19)	0	3 (4.6)
Rivermead Motor Assessment (1-15)	66	5-15		13 (11-14)	0	11 (16.7)
Functional Reach (cm)	64	0-38	26.1 (7.4)			
Elderly Mobility Score (0-20)	64	15-20		20 (20-20)	0	49 (76.6)
SF36 (0-100)						
Physical functioning	65	5-100	60.2 (25.1)		0	3 (4.6)
Role – physical	63	0-100		75(50-93.8)	1 (1.6)	10 (15.9)
Bodily pain	65	10-100		84 (56.5-100)	0	30 (46.2)
General health	65	10-100		67 (50-84.5)	0	1 (1.5)
Vitality	63	6.25-100	53.6 (20.6)		0	2 (3.2)
Social functioning	65	0-100		100 (62.5-100)	1 (1.5)	35 (53.8)
Role – emotional	63	0-100		91.7 (66.7-100)	1 (1.6)	27 (42.9)
Mental health	63	25-100		70 (55-85)	0	4 (6.3)
HADS anxiety (0-21)	65	0-17		6 (3-8.5)	6 (9.2)	0
HADS depression (0-21)	65	0-14		4 (2.5-6)	2 (3.1)	0
Leg extensor power (affected leg, W/kg)	64	0.074-2.58		0.92 (0.53-1.37)		
Leg extensor power (unaffected leg, W/kg)	61	0.33-2.93		1.05 (0.72-1.56)		
Comfortable walking speed (m/sec)	64	0.15-1.12	0.67 (0.24)			
Walking economy (VO_2 ml/kg/m)	62	0.042-0.38		0.12 (0.098-0.16)		
Timed up and go (seconds)	66	6-50.1		11.9 (8.3-17.2)		
Sit to stand (seconds)	65	0.5-6.1		1.34 (0.86-1.86		

Table 3. Comparison of baseline and post-intervention measurements after replacement of missing values

Variable	Exercise group (n=32)			Relaxation group (n=34)		
	Mean (SD)	Median (IQR)	p (no. pairs)*	Mean (SD)	Median (IQR)	p (no. pairs)*
Functional Independence Measure (18-126)						
Baseline		117.5 (114-121)			117.5 (112.8-122)	
1st post-intervention		118.5 (115-121.8)	0.60 (32)[b]		117.5 (114-122)	0.47 (34)[b]
2nd post-intervention		119.5 (113.3-122.8)	0.91 (32)[b]		115.5 (112-121)	0.73 (34)[b]
Nottingham Extended ADL (0-22)						
Baseline		17 (12.5-19)			17.5 (11.8-19)	
1st post-intervention		17 (13-19)	0.75 (32)[b]		16.5 (13-20)	0.31 (34)[b]
2nd post-intervention		17 (12.3-19)	0.62 (32)[b]		16.5 (12.8-19)	0.89 (34)[b]
Rivermead Motor Assessment (1-15)						
Baseline		13 (11.3-15)			13 (11-14)	
1st post-intervention		13 (12-15)	0.31 (32)[b]		13 (12-14)	0.59 (34)[b]
2nd post-intervention		13.5 (12-15)	0.085 (32)[b]		13 (11.8-14)	0.34 (34)[b]
Functional Reach (cm)						
Baseline		24.5 (20-31)			28 (23.8-32)	
1st post-intervention		28.5 (21-33.5)	0.043 (32)[b]		26.5 (22-31.3)	0.34 (34)[b]
2nd post-intervention		26.5 (21.3-33)	0.11 (32)[b]		27 (22.8-30.3)	0.21 (34)[b]
Elderly Mobility Score (0-20)						
Baseline		20 (19.3-20)			20 (19.8-20)	
1st post-intervention		20 (20-20)	0.51[d]		20 (19-20)	1.00[d]
2nd post-intervention		20 (19.3-20)	1.00[d]		20 (20-20)	1.00[d]

Table 3 (continued)

SF36 *(0-100):*						
Physical functioning						
Baseline	62.0 (24.7)			57.4 (26.1)		
1st post-intervention	63.1 (29.5)		0.65 (32)[c]	54.0 (22.7)		0.26 (34)[c]
2nd post-intervention	58.0 (28.8)		0.11 (32)[c]	55.7 (25.0)		0.62 (34)[c]
Role – physical						
Baseline		75.0 (51.6-93.8)			78.1 (48.4-93.8)	
1st post-intervention		90.6 (71.9-100)	0.003 (32)[d]		71.9 (50-93.8)	0.85 (34)[d]
2nd post-intervention		78.1 (62.5-100)	0.12 (32)[d]		62.5 (56.3-87.5)	0.33 (34)[d]
Bodily pain						
Baseline		92 (43-100)			79 (61-100)	
1st post-intervention		72 (24.5-100)	0.13 (32)[e]		72 (41-100)	0.21 (34)[e]
2nd post-intervention		61.5 (41.3-100)	0.14 (32)[e]		61 (41.8-100)	0.003 (34)[e]
General health						
Baseline		62 (47-77)			67 (52-88.3)	
1st post-intervention		72 (62-87)	0.007 (32)[b]		67 (45.8-85.5)	0.65 (34)[b]
2nd post-intervention		63.5 (45.5-77)	0.32 (32)[b]		67 (56.5-87.8)	0.72 (34)[b]
Vitality						
Baseline	53.0 (18.9)			53.3 (22.3)		
1st post-intervention	58.9 (18.3)		0.036 (32)[c]	57.7 (18.8)		0.20 (34)[c]
2nd post-intervention	55.3 (19.3)		0.50 (32)[c]	52.0 (23.2)		0.66 (34)[c]
Social functioning						
Baseline		100 (53.1-100)			100 (62.5-100)	
1st post-intervention		100 (75-100)	0.24 (32)[e]		93.8 (62.5-100)	0.90 (34)[e]
2nd post-intervention		100 (87.5-100)	0.018 (32)[e]		100 (62.5-100)	0.50 (34)[e]
Role – emotional						
Baseline		87.5 (75-100)			95.8 (56.2-100)	
1st post-intervention		100 (85.4-100)	0.033 (32)[e]		100 (64.6-100)	0.64 (34)[e]
2nd post-intervention		100 (77.1-100)	0.12 (32)[e]		95.8 (50-100)	0.90 (34)[e]
Mental health						
Baseline		70 (55-83.8)			70 (50-85)	
1st post-intervention		80 (65-90)	0.005 (32)[b]		80 (60-90)	0.013 (34)[b]
2nd post-intervention		75 (61.3-90)	0.20 (32)[b]		80 (58.8-90)	0.022 (34)[b]

Table 3 (continued)

HADS anxiety (0-21)								
Baseline			7 (5-9.8)				5.5 (1.8-8)	
1st post-intervention			5.5 (2-8)	0.020 (32)[a]			4.5 (1-7)	0.52 (34)[a]
2nd post-intervention			4 (1.25-9.5)	0.053 (32)[a]			5 (1-6.5)	0.89 (34)[a]
HADS depression (0-21)								
Baseline			4 (1.3-6)				4.5 (3-6)	
1st post-intervention			4 (1-7.8)	0.48 (32)[a]			4 (2-6)	0.77 (34)[a]
2nd post-intervention			4.5 (1-7)	0.42 (32)[a]			4 (2-7)	0.50 (34)[a]
Leg extensor power (affected leg, W/kg)	**n$**							
Baseline	31	1.01 (0.57)				1.01 (0.57)		
1st post-intervention	31	1.19 (0.64)		<0.001 (31)[c]		1.12 (0.58)		0.069 (34)[c]
2nd post-intervention	31	1.18 (0.59)		0.002 (31)[c]		1.15 (0.59)		0.011 (34)[c]
Leg extensor power (unaffected leg, W/kg)	**n$**							
Baseline	30	1.26 (0.72)				1.12 (0.50)		
1st post-intervention	30	1.39 (0.70)		0.042 (30)[c]		1.26 (0.63)		0.016 (34)[c]
2nd post-intervention	30	1.45 (0.74)		0.002 (30)[c]		1.27 (0.54)		0.001 (34)[c]

'Comfortable' walking speed (m/sec)					**n$**			
Baseline		0.66 (0.24)			33	0.67 (0.23)		
1st post-intervention		0.73 (0.24)		<0.001 (32)[c]	33	0.74 (0.27)		0.001 (33)[c]
2nd post-intervention		0.70 (0.26)		0.059 (32)[c]	33	0.74 (0.27)		<0.001 (33)[c]
Walking economy (VO_2 ml/kg/m)					**n$**			
Baseline			0.128 (0.099-0.170)		33		0.111 (0.097-0.137)	
1st post-intervention			0.126 (0.092-0.148)	0.047 (32)[b]	33		0.115 (0.094-0.142)	0.27 (33)[b]
2nd post-intervention			0.127 (0.086-0.158)	0.34 (32)[b]	33		0.113 (0.093-0.132)	0.92 (33)[b]
Timed up & go (seconds)								
Baseline			12.3 (8.5-17.0)				11.3 (8.2-17.7)	
1st post-intervention			11.4 (8.0-15.6)	0.013 (31)[f]			11.5 (8.5-15.9)	0.25 (31)[f]
2nd post-intervention			12.2 (8.0-18.1)	0.40 (32)[f]			10.9 (9.0-17.3)	0.66 (34)[f]

Sit to stand (seconds)						

Baseline		1.49 (0.87-1.77)			1.25 (0.80-1.99)	
1st post-intervention		0.95 (0.78-1.24)	<0.001 (32)[b]		0.97 (0.81-1.62)	0.079 (34)[b]
2nd post-intervention		1.11 (0.82-1.57)	0.030 (32)[b]		1.22 (0.75-1.46)	0.32 (34)[b]

Footnotes for table 3

* For comparison of 1st & 2nd follow-up with baseline
$ One subject had no LEP data for either leg at any stage. One subject had no LEP data for the unaffected leg at any stage. One subject had no walking data at any stage.
[a] Wilcoxon signed ranks tests on untransformed data
[b] Paired t-tests on transformed data: LEP – square root
walking economy – logarithm
sit-to-stand - reciprocal
FIM, Nottingham, Rivermead, functional reach, Mental Health (SF36), General Health (SF36) – square root of reflected data
[c] Paired t-tests on untransformed data
[d] Sign test on untransformed data
[e] Wilcoxon signed ranks test on transformed data (square root of reflected data)
[f] Paired t-tests on reciprocal transformed data - (extreme outliers (ID 37 & 51) excluded from 1st post-intervention data for significance tests to enable satisfactory transformation prior to statistical analysis)

'Affected and unaffected leg' refers to the leg affected by the stroke.

Table 4. Change in variables between baseline and post-intervention assessment after replacement of missing values

Outcome variable at baseline	Exercise group (n=32)		Relaxation group (n=34)		p value comparing change in groups
	Mean (SD) change	Median (IQR) change	Mean (SD) change	Median (IQR) change	
Functional Independence Measure (18-126)					
1st post-intervention		0 (-2 to 2)		1 (-1 to 3)	0.45[a]
2nd post-intervention		0 (-1 to 3)		-1 (-2.25 to 2.25)	0.52[a]
Nottingham Extended ADL (0-22)					
1st post-intervention		0 (-1 to 1)		0 (-1 to 2)	0.38[a]
2nd post-intervention		0.5 (-1 to 2)		0.5 (-2 to 2)	0.81[a]
Rivermead Motor Assessment (1-15)					
1st post-intervention		0 (0 to 1)		0 (-1 to 1)	0.51[a]
2nd post-intervention		0 (0 to 1)		0 (-0.25 to 1)	0.56[a]
Functional Reach					
1st post-intervention		2 (-1.75 to 7.25)		0 (-4.25 to 2)	0.031[b]
2nd post-intervention		2.5 (-3 to 6)		0 (-6.13 to 3)	0.039[b]
Elderly Mobility Score (0-20)					
1st post-intervention		0 (0 to 0)		0 (0 to 0)	-
2nd post-intervention		0 (0 to 0)		0 (0 to 0)	-

Table 4 (continued)

SF36 (0-100):					
Physical functioning					
1st post-intervention	1.09 (13.4)		-3.38 (17.3)		0.25[c]
2nd post-intervention	-4.02 (13.8)		-1.62 (18.8)		0.56[c]
Role – physical					
1st post-intervention		6.25 (0 to 23.4)		0 (-12.5 to 7.81)	0.008[a]
2nd post-intervention		6.25 (-6.25 to 25)		0 (-18.8 to 6.25)	0.08[a]
Bodily pain					
1st post-intervention		0 (-15 to 0)		0 (-16 to 3.25)	0.71[a]
2nd post-intervention		0 (-24 to 6.75)		-9 (-27.8 to 0)	0.34[a]
General health					
1st post-intervention		6.25 (0 to 25)		0 (-10 to 11.3)	0.036[b]
2nd post-intervention		-2.75 (-11.5 to 10)		0 (-8.5 to 10)	0.39[b]
Vitality					
1st post-intervention	5.86 (15.1)		4.41 (19.5)		0.74[c]
2nd post-intervention	2.28 (18.9)		-1.29 (16.6)		0.42[c]
Social functioning					
1st post-intervention		0 (0 to 25)		0 (-12.5 to 12.5)	0.26[a]
2nd post-intervention		0 (0 to 34.4)		0 (0 to 25)	0.25[a]
Role – emotional					
1st post-intervention		0 (0 to 16.7)		0 (-4.17 to 8.33)	0.27[a]
2nd post-intervention		0 (0 to 22.9)		0 (-18.8 to 10.4)	0.17[a]
Mental health					
1st post-intervention		5 (-3.75 to 15)		5 (-5 to 20)	0.63[b]
2nd post-intervention		0 (-5 to 15.9)		7.5 (-5 to 16.3)	0.51[b]
HADS anxiety (0-21)					
1st post-intervention		0 (-4 to 1)		0 (-2 to 1)	0.36[a]

2nd post-intervention			-0.5 (-4 to 1)		0 (-2 to 2.25)	0.24[a]
HADS depression (0-21)						
1st post-intervention			0 (-1 to 2)		0 (-1.25 to 1.25)	0.37[a]
2nd post-intervention			0 (-2 to 2)		0 (-1 to 2)	0.78[a]

Table 4 (continued)

Leg extensor power (affected leg, W/kg)	n$					
1st post-intervention	31	0.19 (0.26)		0.11 (0.34)		0.32[c]
2nd post-intervention	31	0.18 (0.30)		0.15 (0.32)		0.71[c]
Leg extensor power (unaffected leg, W/kg)	n$					
1st post-intervention	30	0.13 (0.32)		0.14 (0.31)		0.91[c]
2nd post-intervention	30	0.19 (0.31)		0.15 (0.25)		0.59[c]

'Comfortable' walking speed (m/sec)			n$			
1st post-intervention	0.069 (0.093)		33	0.072 (0.12)		0.91[c]
2nd post-intervention	0.036 (0.11)		33	0.073 (0.10)		0.16[c]
Walking economy (VO_2 ml/kg/m)			n$			
1st post-intervention		-0.0019 (-0.023 to 0.004)	33		0.0022 (-0.011 to 0.02)	0.029[b]
2nd post-intervention		-0.0054 (-0.027 to 0.016)	33		-0.0016 (-0.018 to 0.013)	0.47[b]
Timed up & go (seconds)						
1st post-intervention		-0.53 (-1.80 to 0.12)			0.38 (-0.32 to 1.47)	0.006[d]
2nd post-intervention		0.23 (-1.83 to 1.07)			0.13 (-0.62 to 1.91)	0.34[b]
Sit to stand (seconds)						
1st post-intervention		-0.15 (-0.51 to 0)			-0.19 (-0.59 to 0.075)	0.40[b]
2nd post-intervention		-0.11 (-0.5 to 0.02)			-0.03 (-0.46 to 0.12)	0.27[b]

$ One subject had no LEP data for either leg at any stage. One subject had no LEP data for the unaffected leg at any stage. One subject had no walking data at any stage.

[a] Mann-Whitney U test on untransformed data

[b] T-test on transformed data: LEP – square root
walking economy – logarithm
sit-to-stand - reciprocal
FIM, Nottingham, Rivermead, functional reach, Mental Health (SF36), General Health (SF36) – square root of reflected data

[c] T-test on untransformed data

[d] T-test on transformed data - (extreme outliers (ID 37 & 51) excluded from 1st post-intervention data for significance tests to enable satisfactory transformation prior to statistical analysis)

Appendix E

BTRC Final Report Assessment Form

Agenda number	
Please circle appropriate response	
Does the report answer the project's questions?	Yes No
Has the proposed methodology been followed?	Yes No
Does the study represent value for money?	Yes No
Does the report contain appropriate proposals for dissemination?	Yes No
Please circle appropriate score	
Excellent Good Satisfactory	Unsatisfactory
Further comments (these may be passed on to the grantholders)	
Member's name	