Please cite the Published Version

THE INFLUENCE OF SEDENTARY BEHAVIOUR ON MUSCLE-TENDON PROPERTIES AND RESULTANT POSTURAL BALANCE IN OLDER ADULTS

JORGEN ANTONIN WULLEMS

A thesis submitted in partial fulfilment of the requirements of the Manchester Metropolitan University for the degree of Doctor of Philosophy

Department of Exercise and Sport Science

Manchester Metropolitan University

in collaboration with the Department of

Rehabilitation Sciences of the Katholieke

Universiteit Leuven

2018

Director of Studies

Dr. Gladys L. Onambélé-Pearson (Manchester Metropolitan University, United Kingdom)

ii

Co-supervisors

Prof. Sabine M.P. Verschueren (Katholieke Universiteit Leuven, Belgium)

Prof. Hans Degens (Manchester Metropolitan University, United Kingdom)

Dr. Christopher I. Morse (Manchester Metropolitan University, United Kingdom)

Funding

Acknowledgements

Abstract

In recent years, sedentary behaviour (SB) has been identified as a health risk, independent of physical activity (PA). With the population becoming increasingly sedentary, detailed analysis of its effects is required. It is proposed that in the elderly, arguably the most sedentary age group, SB might adversely affect musculoskeletal health hence leading to poorer physical functioning, less independence and higher risk of falling. Hence, this thesis aimed to study the associations between SB and muscle-tendon properties in older adults (aged ≥60 years). To do so, a machine learning algorithm was applied onto thigh-mounted accelerometry data. Algorithm performance was acceptable for a wide spectrum of physical activity intensities, and its concurrent validity was good. Then, a cross-sectional study on 105 older adults included a 7-day habitual activity monitoring week, and assessed gastrocnemius medialis (GM) muscle-tendon morphology, architecture, function, fatigue indices, mechanical and material properties, and postural balance. From the accelerometer data, both total amount and patterns of SB were extracted. Analysis of these outcomes ranged from simple comparison of general SB levels to compositional data analysis. Multiple linear regression models showed a few associations linking SB with detrimental outcomes with GM muscle properties (dimension, strength and force). Similarly, isotemporal substitution yielded a limited number of significant potential relative effects of SB behaviour alterations. GM tendon mechanical, material and morphological properties also showed associations. Interestingly, negative associations between SB and postural balance in this group of older adults were also identified. Overall, this thesis presents novel data from detailed analyses on SB and intrinsic muscle-tendon properties in older adults. Regardless of the somewhat limited associations between sleep and PA-independent SB outcomes and GM muscle-tendon properties in older adults, the negative relationship with a task associated with habitual physical independence (i.e. postural balance) warrants further investigation of SB in elderly.

Table of contents

List of tables

List of figures

Abbreviations

ACSA, anatomical cross-sectional area

AT, Achilles tendon

BMC, bone mineral content

BMI, body mass index

CSA, cross-sectional area

CV, coefficient of variation

DB, Douglas bag

DF, dorsiflexion

EE, energy expenditure

FITT, frequency, intensity, time and type

FRAT, falls risk assessment tool

GLM, general linear model

GM, gastrocnemius medialis

ICC, intraclass correlation coefficient

IMA, integrals of the moduli of the triaxial accelerometer

IQR, interquartile range

LIPA, light-intensity physical activity

MET, metabolic equivalent

MPF, median power frequency

MTU, muscle-tendon unit

MVC, maximum voluntary contraction

MVPA, moderate-to-vigorous physical activity

nMVC, net maximum voluntary contraction

PA, physical activity

PCSA, physiological cross-sectional area

PF, plantarflexion

RMS, root mean square

RVO_2, resting oxygen consumption

SB, sedentary behaviour

SD, standard deviation

sEMG, surface electromyography

SITT, sedentary behaviour frequency, interruptions, time and type

SMI, skeletal muscle index

sMVPA, sporadic moderate-to-vigorous physical activity

SVM, sum of vector magnitudes

TD, total displacement

TM, total movement

VA, voluntary activation

VO_2, oxygen consumption

WHO, World Health Organisation

YM, Young's modulus

Chapter 1. Introduction

Over the past years, time spent sitting has increased and still is increasing in modern societies. Sitting predominantly occurs at work, leisure or commuting. Although previous research showed that increased time spent sitting is negatively related to health (1,2), it was always assumed that sufficient levels of physical activity (PA) would counteract the adverse health effects. However, recent studies proved that, after controlling for PA, (prolonged) sitting has independent negative health effects (3–6).

Interestingly, the health effects of sitting have been described as early as the 17th century, but it was not until the 21st century that the study of sitting and its relations to health became more popular (7–9). In addition, instead of investigating sitting exclusively, researchers are focussing on all inactive behaviour, including lying or reclining. In other words, any sedentary behaviour (SB) during waking hours. Formally, SB is defined as any awake behaviour characterised by an energy expenditure ≤1.5 metabolic equivalents (METs) while in a seated or reclined posture (10). It is important to note that SB is distinct from PA, and thus does not necessarily reflect a lack of PA (10). This latter is related to meeting the lifestyle recommendations as outlined in PA guidelines. Most of these guidelines, however, lack recommendations specific to SB. The few official guidelines that include a brief statement on SB , are vague in that they simply recommend to limit time spent in prolonged SB bouts (11). Unfortunately, exact information on duration or frequency is missing and in fact, evidence for/against any impact of habitual mobility patterns on a number of physiological health markers is scarce.

To study SB, accurate assessment of SB is vital. According to the SITT formula (derived from the FITT formula to characterise PA and exercise), Sedentary behaviour frequency, number of Interruptions, Time (duration) and Type are valuable outcomes to be assessed (12). Generally, either subjective or objective methods can be used to study these variables. Although subjective methods are practical, easy to administer, inexpensive, useful in large-scale studies and do not alter behaviour (13–15), most have obvious caveats, like bias and the tendency to under-report SB (13,16,17). SB appears to be more difficult to recall than PA, because of its habitual nature (18,19). The combination of underestimation and low precision is likely to reduce the ability to accurately detect dose-response relationships between self-reported SB and health outcomes (15). Nevertheless, self-reports might give a detailed picture of how SB time is spent (20,21). Thus, subjective measures only allow

assessment of Type from the SITT formula. Unlike subjective methods, objective techniques (such as accelerometry) provide reliable and valid, ambulatory and long-term measures of both PA and SB, and it overcomes many of the above-mentioned limitations of self-reports (6,13,22–24). By providing outcomes, such as total SB time, sedentary bout time, sedentary pattern, and number and frequency of breaks in SB for instance, accelerometry allows assessment of all SITT formula variables, except for Type. However, modern technological advancements do allow objective assessment of individual's surroundings e.g. by using a body-worn time-lapse photography camera (25). Hence, objective methods (accelerometry in particular) are preferred in SB measurement. To optimise objective monitoring, a customised algorithm should be calibrated with respect to the population and activities/intensities under study (26), because variation in biomechanics and physiology can be substantially due to different movement patterns or metabolic demands.

Previous literature shows that SB increases with age, resulting in older adults (aged ≥60 years) being the most sedentary (Table 1.1) (20,27,28). Based on objective measures, older adults (aged ≥60 years) spend on average 8.5-9.6 hours/day sedentary (17,22,29), which equates to 65-80% of their waking day. Another accelerometer-based study showed that older adults spend approximately 80% of their awake time in SB which represents 8-12 hours/day (30). Other studies suggest that 67% of the older age population is sedentary for >8.5 hours/day (31), and approximately 47% of them are sedentary >80% of their waking hours (32). Although, the amount of SB reported seems to be wide ranging in the current literature, it is nevertheless clear that SB is highly prevalent in older adults. Detailed analyses show that most of their SB is spent at home and on their own (25). It is also notable that, older adults engage in approximately 16 types of SB daily, with TV viewing, reading, eating meals, computer use and transportation being the most common (33). According to the World Health Organisation (WHO), the number of older adults will increase from 11% to 22% by 2050, meaning there will be 2 billion people aged 60 years or older worldwide (34), with 20% aged ≥80 years (34). Given all the above, it is surprising that SB has only been studied limitedly in the elderly (4,21,35).

Despite the limited number of SB studies in older adults, evidence is growing on the health effects of SB in later life. However, a recent systematic review by Rezende et al. (30) suggests that to date evidence in older adults is inconclusive. Due to the limited quality of available studies, only scarce evidence exists for all the reported health outcomes associated with SB in elderly, except for the confirmed evidence on a previously established

dose-response relationship between SB and all-cause mortality (Figure 1.1) (30). Until now, the exact underlying mechanisms identifying the possible causal relationship between SB and adverse health outcomes remain uncertain and are therefore a research priority (5,8). Generally, most SB-related research has focused on cardiovascular and -metabolic outcomes, while other outcomes such as musculoskeletal health have received less attention.

During ageing musculoskeletal health deteriorates, this is not only marked by a loss of bone mass (osteopenia, osteoporosis), but also muscle mass, strength and function (termed sarcopenia), which in itself leads to an increased risk of falls and disability, a loss of independence, morbidity and increased mortality (36–40). Further, with ageing fatigability increases, which is an important measure of motor performance, as it is associated with a further decline in strength and power in a negative downwards spiral (41). Moreover, increased fatigue-induced variability of force or power is thought to interfere with daily activities, especially in the elderly (41). To date, the contribution of SB to sarcopenia and its determinants is still uncertain (5). However, SB in older adults, through muscle disuse, may accelerate sarcopenia (42). Since SB is also a driver for obesity (42), and adipose tissue is found to have a catabolic effect on muscle tissue (5), a combination of both sarcopenia and obesity, or sarcopenic obesity, results in an increased risk of disablement and frailty in older adults (43). In addition to muscular alterations, age-related tendon changes (i.e. increased tendon compliance) result in decreased postural balance, and as such is associated with mobility and independence loss in older adults due to the inherent fear linked to their higher falls risk (44). By continual under-loading of the tendon, SB is proposed to accelerate this tendon ageing process. Reports show that each year 28-35% of people aged 65 years or older experience a mild to severe (and even morbid) injurious fall, with the same being true in 32-42% of elderly aged >70 years (45). As a result of falling, older adults may exhibit both physical and psychological consequences (45). This makes falling in elderly not only a challenge for health, but also for social care resources. Indeed annual costs from fall-related injuries in the EU are estimated to be ≥£21.7 billion (≥€25 billion) and expected to exceed £39.1 billion (€45 billion) by the year 2050 (46).

Generally, days are composed of limited number of (in)activities which, apart from SB, involve sleep and PA. Although these phenomena cluster together, they are partly independent and it is becoming clear that so are their effects, including on musculoskeletal health (47). As discussed above, SB increases with ageing and has adverse effects on

muscle-tendon outcomes (5,27,28,42). Levels of sleep and PA, however, decrease with ageing and might have opposed associations with musculoskeletal health (47). Whilst, the positive associations of PA with human muscle-tendon properties are well-known, evidence for sleep is only limited. Nevertheless, sleep was identified as a risk factor for sarcopenia in older adults (48,49). Moreover, Piovezan et al. (50) have suggested that anabolic hormone cascades are inhibited, while catabolic pathways are enhanced in the skeletal muscle, due to age-related sleep problems. Given that sleep, SB and PA are partly co-dependent within a daily composition and (potentially) have independent effects on musculoskeletal health, it is important to consider all when studying the true associations between SB and muscle-tendon properties in elderly.

The combination of facts including western population ageing, elderly being the most sedentary age group, SB potentially accelerating the ageing-related decline in skeletal muscle-tendon properties and resultant postural balance (independent of sleep and PA), the scarcity of evidence of SB effects on musculoskeletal health and postural balance stability in elderly, highlights the timeliness of studying the direct impact of extent and/or pattern of engagement of this mobility behaviour in older adults (Figure 1.2).

Table 1.1. Sedentary behaviour across different age groups as assessed with accelerometry.

Matthews et al. (28)							
	Age groups						
	16 - 19	20 - 29	30 - 39	40 - 49	50 - 59	60 - 69	70 - 85
Male	7.9 (0.1)	7.3 (0.2)	7.2 (0.2)	7.6 (0.1)	7.9 (0.1)	8.8 (0.1)	9.5 (0.1)
Female	8.1 (0.1)	7.7 (0.1)	7.3 (0.1)	7.5 (0.1)	7.8 (0.1)	8.1 (0.1)	9.1 (0.1)

Martin et al. (27)			
	Age groups		
	20 - 39	40 - 59	60 - 69	≥70
Male	7.9 (0.1)	8.5 (0.1)	9.4 (0.2)	10.3 (0.1)
Female	7.9 (0.1)	8.3 (0.1)	8.7 (0.1)	9.8 (0.1)

Values represent mean (standard error (SE)) hours/day (adjusted for monitor-wearing time where appropriate).
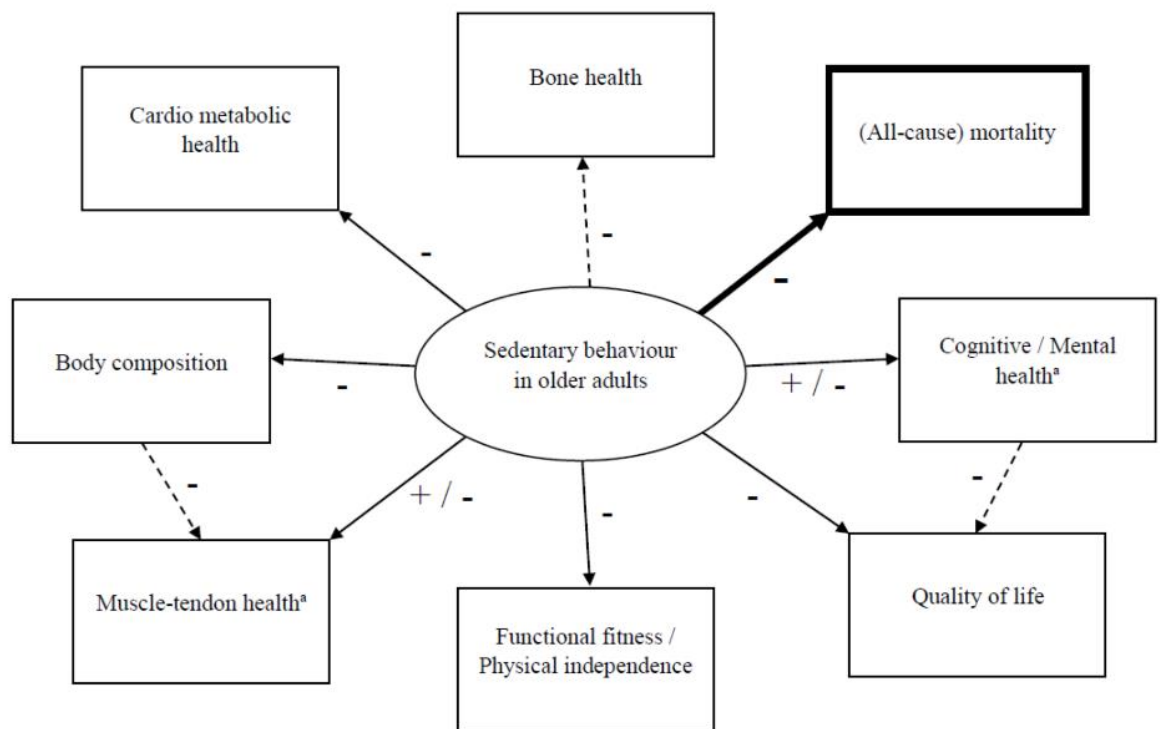
Figure 1.1. Overview of identified and suggested associations between sedentary behaviour and (health) outcomes in older adults as reported in literature.

+, positive association; -, negative association; Solid lines represent identified associations; Dashed lines represent suggested associations; Associations in bold are confirmed by a systematic review from Rezende et al. (30), [a]Outcome depends on the type of assessed sedentary behaviour (e.g. television viewing, computer use or reading).
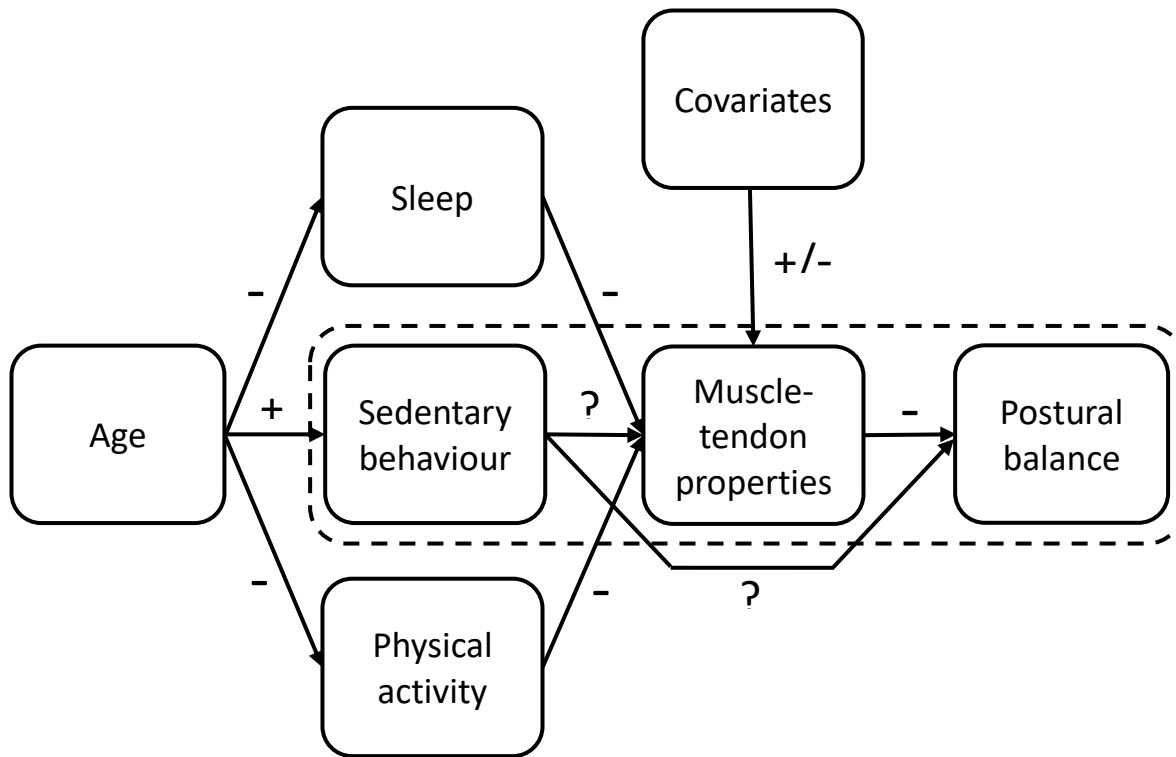
Figure 1.2. The association between age, muscle-tendon properties and postural balance, and the (mediating) role of sleep, sedentary behaviour, physical activity and other factors.

The dashed box and unknown associations (?) indicate the main foci of the thesis.

Thesis aim

The aim of the thesis is to understand how sedentary behaviour relates to musculoskeletal health and postural balance in older adults.

Thesis objectives

To realise the above aim, the thesis has the following objectives

- To develop an algorithm for assessment of SB and PA levels (i.e. habitual mobility patterns) in relatively healthy community-dwelling older adults (hereafter simply referred to as older adults) using thigh-mounted triaxial accelerometry;
- To monitor sleep, SB and PA levels in older adults for seven continuous days;
- To assess size, architecture, function and fatigability of the gastrocnemius medialis muscle in older adults and how this relates to habitual mobility patterns;
- To assess mechanical, material and morphological properties of the gastrocnemius medialis tendon in older adults and how this relates to habitual mobility patterns;

- To assess postural balance in older adults and how this relates to habitual mobility patterns.

Hypotheses

Related to the aim and objectives of this thesis, it is hypothesised that:

- A thigh-mounted triaxial accelerometer algorithm for the assessment of SB and PA levels in older adults is valid and robust;
- SB increases with ageing in older adults, while PA decreases;
- Size, architecture, function and fatigability of the gastrocnemius medialis muscle in older adults are negatively associated with SB (amount and pattern), irrespective of sleep and PA engagement;
- Mechanical, material and morphological properties of the gastrocnemius medialis tendon in older adults are negatively associated with SB (amount and pattern), irrespective of sleep and PA engagement;
- Postural balance in older adults is negatively associated with SB (amount and pattern), irrespective of sleep and PA engagement.

Thesis outline

Part I

The first part of the thesis concerns the development and (concurrent) validation of an accelerometer algorithm to classify activity intensities in an elderly sample population. The studies included in Part I were performed at both the Manchester Metropolitan University, UK and Katholieke Universiteit Leuven, Belgium, and the results are presented in the following chapters (Figure 1.3):

- *Chapter 2* describes the development and comparison of cut-off point and machine learning algorithms;
- *Chapter 3* describes the concurrent validity of the best performing algorithm from chapter one. It is compared against other activity monitors and their proprietary algorithms.

Part II

In part II, the independent associations of SB with different muscle-tendon properties and postural balance in older adults are investigated. The results come from a study performed at the Manchester Metropolitan University, UK, and are presented in the following chapters (Figure 1.3):

- *Chapter 4* describes the characteristics and the 7-day monitored sleep, SB and PA levels of the elderly studied in the next chapters;
- *Chapter 5* describes relationships of SB with size and architecture of the gastrocnemius medialis muscle. The chapter also includes sleep and PA data to compare the magnitude of modulation on these structural outcomes, where appropriate;
- *Chapter 6* describes relationships of SB with function and fatigability of the gastrocnemius medialis muscle. The chapter also includes sleep and PA data to compare the magnitude of modulation on these functional outcomes, where appropriate;
- *Chapter 7* describes relationships of SB with (i) mechanical, material and morphological properties of the gastrocnemius medialis tendon and (ii) postural balance. The chapter also includes sleep and PA data to compare the magnitude of modulation on the tendon and postural balance outcomes, where appropriate.

The thesis concludes with a chapter giving an overview of the main findings, limitations and considerations for future research.

Manchester
Metropolitan
University, UK

Katholieke
Universiteit
Leuven, Belgium

Chapter 2

N = 40

Chapter 3

N = 20

Chapter 4-7

N = 65

Part I

Part II
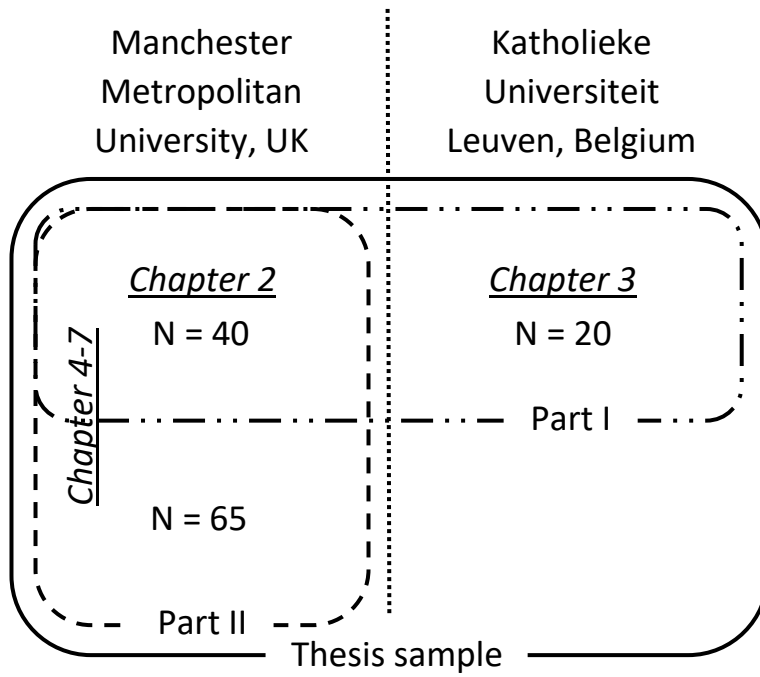
Thesis sample

Figure 1.3. Thesis structure and study samples.

Chapter 2. Performance of thigh-mounted triaxial accelerometer algorithms in objective quantification of sedentary behaviour and physical activity in older adults

Introduction

To evaluate the health effects of sedentary behaviour (SB) and physical activity (PA), including their role in healthy ageing, it is important to accurately and objectively monitor these aspects of habitual mobility or lack thereof (51). Motion-sensing technologies using accelerometers are typically used in mobility monitoring since they are pertained to be objective, and measurements can be carried out over a number of days (6,51–55). The concept of accelerometry to assess SB and PA is derived from Newton's Second Law, which gives the interaction between force, mass and acceleration by the formula: force = mass * acceleration (56). In the context of human movement, this formula can be expressed as: an activity characterised by moving a mass (i.e. body (segment)) at changing velocity over time (=acceleration). This acceleration results from forces generated by (and on) the muscles at the expense of energy (54). Several studies have shown positive linear relationships between energy expenditure (EE) and movement acceleration in people of different ages, while performing activities under standardised test conditions with the accelerometer close to the centre of mass (57–62). This allows EE to be estimated from acceleration signals and the classification of habitual daily activity as sedentary, light and moderate-to-vigorous, by using, until recently, cut-off point models. To illustrate this, when presenting the amount of movement acceleration as counts per minute, these models will classify an outcome of <100 as sedentary, 100-1951 as light and ≥1952 as moderate-to-vigorous (51).

However, with the preferred accelerometer mounting location shifting away from centre of mass sites such as the hip or waist (63–65), towards wrist-worn devices for the most part, the premise of a linear relationship between EE and movement acceleration and thus, the use of cut-off point models has become questionable. This commercially-led shift forces researchers to focus on posture detection only (i.e. the 'Sedentary Sphere' (66)) or to start looking into other, more sophisticated and complex, methods to analyse acceleration signals by e.g. machine learning (35,67,68). Machine learning is already used for activity recognition and has only recently been explored in PA research (35,68). By focusing on patterns and regularities, pattern recognition for example, can handle complex and non-linear data (51,69,70), potentially providing opportunities for SB and PA research (71).

Although some experts have advised to stop developing cut-off point algorithms and start using machine learning (72,73), to date the use of cut-off points remains preferred for intensity classification (24). One reason to continue using cut-off point models lies in the complex nature of machine learning, and the ease to understand and widespread adoption of cut-off points (26). Although proprietary cut-off points are not necessarily well understood either, the desire to compare results with previous cut-off point-based studies could be another reason. Notwithstanding, studies have already shown machine learning to outperform traditional cut-off point algorithms for activity recognition not only in healthy adults, but also in niche populations such as the young or the overweight/obese (51,71). However, validation of machine learning needs to be confirmed for all intended end-users/study populations, e.g. the elderly, prior to general adoption (54). Rosenberg et al. (74) recently showed high levels of accuracy and concurrent validity using Random Forest classifiers in older women.

The decision of researchers to choose a simpler, but less accurate method over a more challenging and accurate one for activity intensity classification, can be justified when using thigh-mounted triaxial accelerometry. Since the thigh is relatively close to the centre of mass, cut-off point models might still be valid in this situation, especially when adding posture detection to these models, which then enables distinguishing between sitting or lying down and standing for instance. Whilst the ActivPAL inclinometer is a good example of a valid thigh-mounted activity monitor (64,66), it uses black-boxed proprietary algorithms, thereby hampering progress in thigh-mounted accelerometer algorithm development. To date cut-off point models for thigh-mounted accelerometers are understudied, hence further investigation and detailed comparison with machine learning is needed.

All algorithms require value calibration and the eventual utility of an algorithm depends on the specific activities and intensities included in the calibration study (26). To ensure high accuracy of the algorithm in the general population, it is recommended to perform the calibration on a heterogeneous sample, matching the population of interest, and including a broad range of common activities ranging from sedentary to vigorous intensity (26,68,72,75). Algorithm performance is generally expressed in terms of overall accuracy and when it reaches ≥80% for example, an algorithm is deemed acceptable (35). However, even in possession of the overall (i.e. group) accuracy, algorithm performance on an individual (i.e. single end-user) level, remains unknown. Theoretically, performance can be

unacceptable in some individuals where algorithm robustness is lacking. If algorithm inaccuracy disproportionately affects some demographic groups over others, it may lead to misinterpretation of associations between either SB or PA and health. Thus, it is important to check robustness and benchmark end-user-specific performance of accelerometer algorithms developed on heterogeneous pooled-data sets prior to applying them to daily-life data. To date, evidence regarding this type of triangulation is sparse.

The main aim of the present chapter was to compare between traditional cut-off points and machine learning, for the provision of the best performing algorithm to classify SB and PA in a heterogeneous population of older adults using thigh-mounted triaxial accelerometry. It was hypothesised that machine learning outperforms cut-off point based algorithms through being robust for individual's physiological and non-physiological characteristics, more accurate and showing acceptable accuracies for all activity intensities. To test this hypothesis, this chapter (i) examines overall balanced accuracy and robustness of four heterogeneous pooled-data algorithms, (ii) compares participant-specific balanced accuracies between all four algorithms, and (iii) benchmarks both overall and participant-specific balanced accuracies of the algorithms.

Materials and methods

Participants

Forty healthy older adults (73.5 (6.3) years; 50% female) participated in this study (Table 2.1). Participants were excluded if they were: <60 years of age, terminally ill or receiving cancer treatment, diabetic, suffered from any central nervous system disease or condition, had a heart attack in the past 12 months or any currently unstable cardiovascular condition, had any pulmonary disease or condition that did not allow expired gas sampling, recently (within the past three months) injured or had surgery on either of their lower limbs, were not independently mobile or at least not able to complete a laboratory-based activity protocol without a (walking) aid, had been advised by their physician not to take on any physical activity or exercise, or were not competent to make an informed decision about study participation.

This study was approved by the local ethics committee of the Manchester Metropolitan University, UK. All participants gave written informed consent prior to their participation in this study.

Table 2.1. Study sample baseline characteristics.

Age (years)	73.5 (6.3)	
Sex	20 Female	20 Male
Body mass (kg)	72.2 (13.7)	
Body height (m)	1.67 (0.10)	
BMI (kg·m^{-2})	25.6 (4.3)	
Prandial state	20 Fasted*	20 Non-fasted*
RVO$_2$ (ml·kg^{-1}·min^{-1})	2.82 (1.00)	
Prosthetic lower limb joints	2 Yes	38 No
Cardiovascular medication	20 Yes	20 No
Physical fitness level$_{no\ cardiovascular\ meds}$	9 Less than good	11 Good or better
Preferred walking speed (km·h^{-1})$_{no\ prosthetic\ lower\ limb\ joints}$	3.7 (1.0)	
Falls risk	31 Low	9 Medium or high

Values represent arithmetic mean (SD) when normally distributed data, else median (IQR). SD, standard deviation; IQR, interquartile range; BMI, body mass index; RVO$_2$, resting oxygen consumption. *See details in the text below.

Baseline characteristics

From each participant, the following baseline characteristics were recorded: age, sex, body mass, body height, body mass index (BMI), prandial state, resting oxygen consumption (RVO$_2$), presence of prosthetic lower limb joints, use of heart rate controlling medication, physical fitness level, preferred walking speed and risk of falling (Table 2.1). Age (years), sex (female/male), prandial state (fasting/non-fasting), presence of prosthetic lower limb joints (yes/no) and use of cardiovascular (heart rate controlling) medication (yes/no) was determined through a health questionnaire on the day of testing. Body mass was assessed in kilograms using a digital body mass scale (seca GmbH & Co. KG., Hamburg, Germany) and body height was measured in centimetres using a stadiometer (Holtain Ltd., Crymych, UK). Both measures were determined up to the closest decimal with the participant barefoot and wearing light clothing only. The body mass index (BMI) was calculated by dividing body mass by squared body height (kg·m^{-2}). RVO$_2$ (ml·kg^{-1}·min^{-1}; STPD conditions: standard temperature and dry gas at standard barometric pressure) was assessed while sitting quietly on a chair for four minutes, together with resting heart rate (beats per minute). Both RVO$_2$ and resting heart rate were expressed as the arithmetic mean of the readings taken during the third and fourth minute of sitting. To increase the accuracy of RVO$_2$ baseline estimates, only data from fasted participants were used. Since resting heart rate served to estimate baseline physical fitness levels, participants who were on heart rate

controlling medication were not taken into account. Classification of the physical fitness levels was done using a standard resting heart rate table (76). Preferred walking speed ($km \cdot h^{-1}$) was based on the self-selected speed during treadmill walking in participants without prosthetic lower limb joints. Risk of falling (low/medium/high) was determined using the falls risk assessment tool (FRAT) (77).

Instrumentation

During the laboratory-based activity protocol participants were equipped with a number of instruments. First, two GENEActiv Original triaxial accelerometers (Activinsights Ltd., Kimbolton, UK) with range ±8 g (1 g = 9.81 $m \cdot s^{-2}$) and weighing 16 grams each, were fitted bilaterally on the anterior mid-thigh (at 50% of the distance between trochanter major and lateral femur epicondyle). Both accelerometers were mounted using Tegaderm™ transparent film dressing (3M Health Care, St. Paul, MN, USA) and set at a sample rate of 60 Hz. This frequency respects the Nyquist-Shannon sampling theorem, which states that the sample frequency should at least be twice the maximum frequency at which sampling is required. Since essentially all human body movement occurs below 20 Hz, the sampling rate should be ≥40 Hz (78,79). Orientation of the accelerometer axes during standing was: X = mediolateral, Y = vertical and Z = anteroposterior. The devices were used as calibrated by the manufacturer. GENEActiv was chosen as the brand of accelerometer, not only for this chapter but the whole thesis, because of its validity and reliability (80), technical features (e.g. triaxial), ease of access to raw data output, design for 24-hour wear (waterproof), ability to be worn in various body positions and unit costs compared to leading market competitors (£160). Next, participants wore a Polar T31 chest belt to monitor heart rate, which would then remain in place for the entirety of the test protocol (Polar Electro Oy, Kempele, Finland). To estimate energy expenditure during the activities (see below) we used indirect calorimetry. Expired gas samples were collected per activity via a standard mouthpiece and two-way T-shape non-rebreathing valve (2700 series) (Hans Rudolph Inc., Kansas City, MO, USA) into a Douglas Bag (DB) (Plysu Industrial Ltd., Milton Keynes, UK). Expired gas sample concentrations of oxygen and carbon dioxide inside the DB were determined using a Servomex 5200 gas analyser (Servomex Group Ltd., Crowborough, UK). The gas analyser was calibrated prior to each participant's testing session. The total volume of expired gas inside the DB was analysed using a calibrated dry gas meter (Harvard Apparatus Ltd., Edenbridge, UK).

Laboratory-based activity protocol

Participants were asked to perform ten laboratory-based activities of daily living which were assumed to be representative for older adults. Half of the participants (N=20, 50% female) were instructed to arrive in a 10-hour overnight fasted condition, allowing to drink water up to a maximum of 250 ml only, while the other half received no instructions. The protocol started with 20 minutes rest in a supine position. Then, the following ten standardised activities of daily living (four minutes each) were executed in the specified order: (i) lying supine on a treatment bed, (ii) sitting on a chair, (iii) standing upright, (iv) shuffling sideways, (v) free over-ground walking at self-selected speed, (vi) cycling on an ergometer at a preferred pace (Monark Exercise AB, Vansbro, Sweden), (vii) treadmill walking at 3.2 km·h^{-1}, (viii) treadmill walking at self-selected speed, (ix) treadmill walking at self-selected speed wearing a weighted vest (15% of body mass) and (x) brisk treadmill walking at a maximum speed of 6.5 km·h^{-1}. All treadmill walking was performed on a slat-belt treadmill (Woodway USA Inc., Waukesha, WI, USA). The first two minutes of each activity were used to reach a steady state in EE. During the second half of the activities, two one-minute expired gas samples were taken. To prevent any carry-over effects of fatigue, participants were seated between the activities until their heart rate returned to resting level. The total duration of the protocol was approximately 90 minutes. A standard digital video camera was time-synchronised and used to record the entire testing session, which served as a criterion measure and allowed direct observation of all activities post laboratory protocol completion.

Accelerometer data pre-processing & feature selection

Analysis of the triaxial accelerometer data required multiple steps. Firstly, raw acceleration signals per axis were filtered twice using a zero-phase fourth order low pass Butterworth filter: (i) a cut-off frequency of 20 Hz was applied to remove any noise and (ii) a cut-off frequency of 0.5 Hz was used to split the noise-filtered signal into static and dynamic acceleration signals, allowing determination of monitor orientation and movement (51,81). Secondly, two one-minute periods (identical to the gas sampling minutes) of both static and dynamic acceleration signals per axis were extracted per performed activity. Next, twenty time- and frequency domain based features per non-overlapping 10-s windows were determined per axis for each of the samples extracted from both the dynamic and static acceleration signals. These time- and frequency domain based features included: arithmetic mean, standard deviation (SD), minimum, maximum, median, interquartile range (IQR), skewness, kurtosis, root mean square, cross-correlation, roll, pitch, yaw, peak-

to-peak amplitude, peak intensity, zero-crossings, lag one autocorrelation, dominant frequency, amplitude of dominant frequency and entropy. Also, two resultant vectors were calculated over the three axes, one using arithmetic means and the other SDs. (Please see Liu et al. (82) for the applied formulas.) All data pre-processing was done using R 3.2.5 (83).

After data pre-processing, the 10s-window features were used to model four algorithms based on methods using either cut-off points or machine learning. Three algorithms including posture classification (based on the 10s-window arithmetic mean static acceleration of the Y-axis (static Y_{mean})) were derived from cut-off point analyses using dynamic acceleration data. The first algorithm used the sum of vector magnitudes (SVM) as an outcome,

$$SVM = \sum_{d=1}^{600} \sqrt{x_d{}^2 + y_d{}^2 + z_d{}^2}$$

where d represents the data-point number within the 10s-window. The second algorithm used summation of the time integrals of the moduli of the triaxial accelerometer signal (IMA), where

$$IMA = \int_{t=t_0}^{t_0+T} |x| \, dt + \int_{t=t_0}^{t_0+T} |y| \, dt + \int_{t=t_0}^{t_0+T} |z| \, dt$$

where T represents 10 seconds. The last cut-off point algorithm was adapted from our previous postural balance studies that focus on total movement (TM) using force plate balancing tasks (44), which is calculated as

$$TM = \sqrt{x_{SD}{}^2 + y_{SD}{}^2 + z_{SD}{}^2}$$

where SD represents the 10s-window standard deviation of the dynamic acceleration signal per axis. For the only machine learning algorithm we used Random Forest in this chapter, which is known for its high performance (68,84–86). Briefly, Random Forest is an ensemble method using the bootstrapping of multiple decision trees to predict an outcome. Prior to developing a Random Forest model, factor analyses were performed to select optimal features for the Random Forest classifier. Firstly, pairwise correlations between features were studied, removing either one of the factors when *r* >0.75, then feature selection was performed in R 3.2.5 (83) using the Boruta package (87). Eventually, 55 features were selected for the Random Forest model.

Activity intensity classification

To classify activity intensities, we used metabolic equivalent (MET) values. These values were calculated per participant for all the one-minute expired gas samples taken during the activity protocol. Due to individual differences, this was done by dividing the VO_2 (in $ml \cdot kg^{-1} \cdot min^{-1}$) during a one-minute activity sample by the participant's measured RVO_2. Thus,

$$MET_{1\ min\ act\ sample} = \frac{VO_{2-1\ min\ act\ sample}}{RVO_{2-participant}}$$

Intensity classification for each one-minute sample (6 x 10s-windows) was done by checking (i) the MET value and (ii) the participant's posture using the video recording. Practically, when the one-minute sample's MET value was ≤1.5, the laboratory-based activity was classified as either sedentary activity or standing, depending on the posture. Classifications of light-intensity PA (LIPA) and moderate-to-vigorous PA (MVPA) were based on the MET value only, meaning if >1.5 and <3 then an epoch was classified as LIPA, while epochs with MET values ≥3 were classified as moderate-to-vigorous PA (MVPA) (54). Intensity classification of the laboratory-based activities per this system represented the reference classification used for algorithm development and cross-validation.

Algorithm development and cross-validation

The initial step in cut-off point based algorithm development was to create a scatterplot in MS Office Excel 2016 (Microsoft Corp., Redmond, WA, USA) using the 10s-window data, with either SVM, IMA or TM values on the horizontal axis and MET values on the vertical axis. Next, trend line-analysis was performed and the line-of-best fit (i.e. showing the highest proportion of explained variance (R^2)) was chosen. The calculated cut-off points for SVM, IMA and TM represented MET values of 1.5 and 3, which allow classification of activity intensities per 10s-windows based on SVM, IMA and TM values, either or not combined with posture detection. Briefly, these cut-off point algorithms only use two steps in their classification structure: (i) comparing SVM, IMA or TM values with the calculated cut-off points and (ii) if necessary, posture detection (Table 2.2).

Random Forest model development on 10s-window features was performed in R 3.2.5 (83) using the randomForest package (88). The 10s-window reference classifications of the laboratory-based activities were used to train the Random Forest classifier (supervised machine learning) with the number of trees set to 100. This number was derived from out-of-bag error analyses (Figure 2.1).

For this chapter, pooled-data algorithms were developed using the leave-one-subject-out method. This means that the 10s-window data of N=39 (training sample; on average 1427 (8.6) data points for SB, 620 (7.4) for standing, 761 (19.9) for LIPA and 2937 (35.5) for MVPA) was used to develop the pooled-data algorithms, while the data of N=1 was used to cross-validate the algorithms. With N=40 this cross-validation procedure was repeated 40 times with another participant to be left out each iteration. Based on the performed 10s-window cross-validations, confusion matrices were created per participant per algorithm. Eventually, these matrices were used to determine balanced accuracy per intensity for each algorithm from two perspectives: (i) participant-specific and (ii) overall (all participants' confusion matrices summed).

$$Balanced\ accuracy\ (\%) = \frac{Sensitivity\ +\ Specificity}{2}$$

$$Sensitivity\ (\%) = \frac{True\ positives\ (N)}{True\ positives\ (N) + \ False\ negatives\ (N)} * 100$$

$$Specificity\ (\%) = \frac{True\ negatives\ (N)}{True\ negatives\ (N)\ + \ False\ positives\ (N)} * 100$$

where N represents the number of cases. Apart from the cross-validation, all algorithms were also tested on their own training samples to check for overfitting. Balanced accuracies of ≥80% were considered acceptable (35).

Table 2.2. Cut-off point algorithm classification scheme.

Rules		*Classification*
1	If MET value ≤1.5 and not upright, then:	Sedentary
2	Else: If MET value ≤1.5 and upright, then:	Standing
3	Else: If MET value >1.5 and <3, then:	LIPA
4	Else: MET value ≥3, then:	MVPA

MET, metabolic equivalent; LIPA, light-intensity physical activity; MVPA, moderate-to-vigorous physical activity.
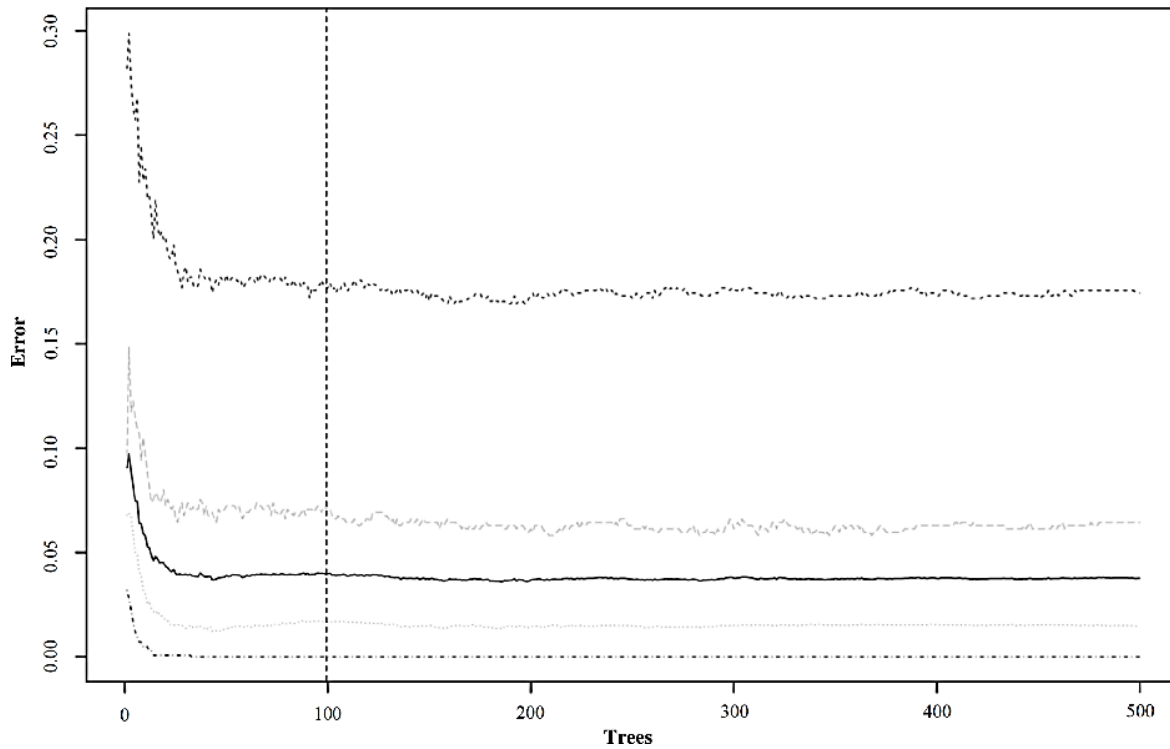
Figure 2.1. Out-of-bag error analyses for Random Forest modelling.

Statistical analyses

Prior to summarising or testing data, we checked its distribution for normality. Since we had a data sample of N=40, the Shapiro-Wilk test was used for this purpose. Baseline characteristics are presented as the arithmetic mean (SD) (or median (IQR)). To test robustness of the four pooled-data algorithms we assessed if continuous baseline characteristics were correlated with balanced accuracy values (either Pearson or Spearman correlation). Differences in balanced accuracy values between categories of categorical baseline characteristics were tested with the independent T-test (or Mann-Whitney U test). For the comparison between the four pooled-data algorithms the one-way ANOVA repeated-measures test (or the Friedman test) was performed. Balanced accuracy levels from these analyses are reported as arithmetic mean (95%-confidence interval (95%-CI) (or median (95%-CI)). In case multiple comparisons were necessary for hypothesis testing, either Bonferroni or Sidak correction was used to adjust P-values.

$$Adjusted\ P - value_{Bonferroni} = P_{value} * k$$

$$Adjusted\ P - value_{Sidak} = 1 - (1 - P_{value})^k$$

where k is the number of comparisons. For the current chapter, P-values were considered statistically significant when P <0.05.

20

With data variability, even within-subject under controlled conditions, and variance being one of the components for algorithm prediction errors, detailed data reliability checks were deemed highly important. Since 24 x 10s-windows bilateral accelerometer data and two one-minute expired gas samples were collected per laboratory-based activity, reliability of both main triaxial accelerometer (static Y_{mean}, SVM, IMA & TM) and oxygen consumption data was determined by calculating a coefficient of variation (CV) per activity per participant.

$$CV\ (\%) = \frac{SD_{activity/participant}}{Arithmetic\ mean_{activity/participant}} * 100$$

where SD represents standard deviation. To check for consistency across the activity protocol, all CVs were checked for correlation with MET values. If a correlation was found, data dispersion was determined (SD or IQR). Finally, depending on the distribution, either the arithmetic mean (95%-CI) or median (~95%-CI) was calculated over the moduli of all CVs per outcome variable to get sample-based reliability measures. In this chapter, a CV of <10% is considered acceptable.

All statistical analyses were executed using IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, NY, USA).

Results

Data reliability

Relationships with MET values were only found for the CVs of accelerometer outcomes SVM and static Y_{mean}, ρ -0.105 (P=0.046) and ρ -0.382 (P<0.001) respectively (Figure 2.2). IQRs for these variables were between 3.4% and 8.5% (SVM), and between 0.4% and 2.1% (static Y_{mean}). The sample-based CVs of static Y_{mean}, SVM, IMA and TM were 0.8% (0.7%, 1.0%), 5.5% (5.1%, 6.0%), 5.6% (5.2%, 6.2%) and 6.2% (5.7%, 7.0%) respectively. CVs of oxygen consumption data collected using the DB method also showed a negative relationship (ρ -0.495 (P<0.001)) with MET values. As shown by the IQR, VO_2 CVs were typically between 2.2% and 7.5%. The sample-based CV of the DB method was 4.4% (3.4%, 5.3%). For all variables, the CVs within the IQR were <10%.
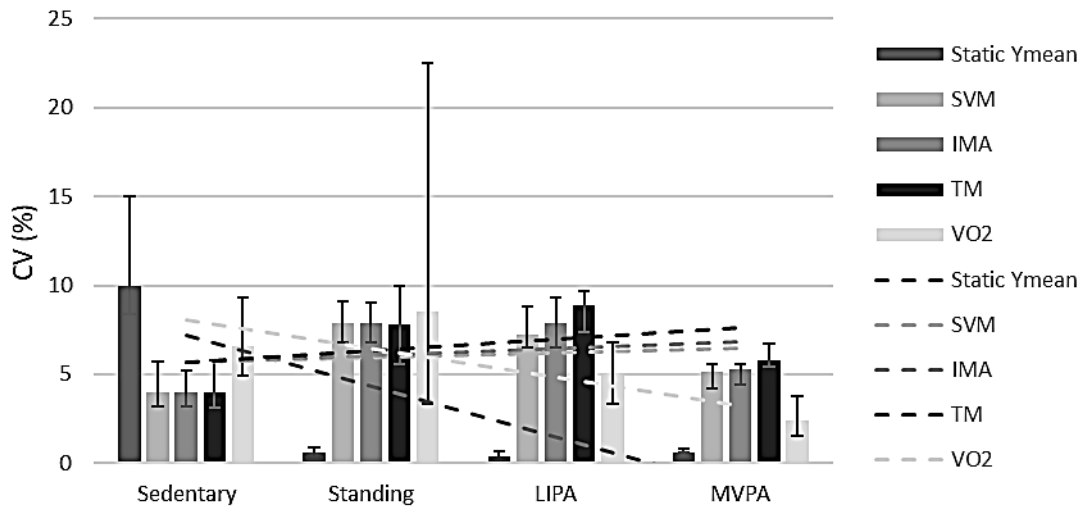
Figure 2.2. Reliability per intensity per outcome.

CV, coefficient of variation; LIPA, light-intensity physical activity; MVPA, moderate-to-vigorous physical activity; Static Y_{mean}, arithmetic mean static vertical acceleration; SVM, sum of vector magnitudes; IMA, integrals of the moduli of acceleration signals; TM, total movement; VO_2, oxygen consumption. Error bars represent 95%-confidence intervals. Dashed lines show correlations between coefficients of variation and intensities per outcome.

Overall balanced accuracy

The confusion matrix shows that all algorithms classified sedentary activity with overall balanced accuracies of ≥99.5% (Table 2.3). Sensitivity and specificity values were ≥99.2%.

Classification of standing was ≥95.5% accurate in all four models. Sensitivity was 92.5% in the cut-off point algorithms and 92.0% for Random Forest, while specificity was equal over the four algorithms (99.1%).

Most variation in overall balanced accuracies was found for LIPA, ranging from 74.3% (TM) to 80.6% (Random Forest). The confusion matrix revealed that the models' sensitivity was only 57.4%, 60.1%, 51.0% and 63.7%, for SVM, IMA, TM and Random Forest respectively. On the other hand, specificity values were ≥97.5% for all algorithms.

Finally, overall balanced accuracies of ≥93.3% were found for MVPA classification. Sensitivity was ≥97.3% in all models, while specificity varied from 88.8% (TM) to 92.9% (Random Forest).

The overall balanced accuracies per intensity per algorithm were comparable between the cross-validation and training sample, except for Random Forest (Table 2.3). Standing, LIPA and MVPA showed overall balanced accuracies of 100.0% on the training sample against 95.5%, 80.6% and 95.1% during cross-validation.

22

Table 2.3. Algorithm cross-validation confusion matrix.

Cross-validation								Individual results	Training sample
Method	Intensity	Reference				Sensitivity (%)	Specificity (%)	Balanced accuracy (%)	Acceptable level (%)	Balanced accuracy (%)
		Sedentary	Standing	LIPA	MVPA					
SVM	Sedentary	**1463**	0	12	0	99.9	99.7	99.8	100.0	99.8
	Standing	0	**588**	48	0	92.5	99.1	95.8	92.5	95.8
	LIPA	1	48	**448**	61	57.4	97.8	77.6	62.5	78.0
	MVPA	0	0	272	**2951**	98.0	90.6	94.3	100.0	94.4
IMA	Sedentary	**1463**	0	12	0	99.9	99.7	99.8	100.0	99.8
	Standing	0	**588**	48	0	92.5	99.1	95.8	92.5	95.8
	LIPA	1	48	**469**	66	60.1	97.8	78.9	65.0	79.2
	MVPA	0	0	251	**2946**	97.8	91.3	94.5	100.0	94.6
TM	Sedentary	**1454**	0	12	0	99.3	99.7	99.5	100.0	99.5
	Standing	0	**588**	48	0	92.5	99.1	95.8	92.5	95.8
	LIPA	10	47	**398**	67	51.0	97.6	74.3	57.5	74.5
	MVPA	0	1	322	**2945**	97.8	88.8	93.3	100.0	93.3
Random Forest	Sedentary	**1463**	0	34	0	99.9	99.2	99.6	100.0	100.0
	Standing	0	**585**	48	0	92.0	99.1	95.5	92.5	100.0
	LIPA	1	47	**497**	82	63.7	97.5	80.6	80.0	100.0
	MVPA	0	4	201	**2930**	97.3	92.9	95.1	100.0	100.0

SVM, sum of vector magnitudes; IMA, integrals of the moduli of acceleration signals; TM, total movement; LIPA, light-intensity physical activity; MVPA, moderate-to-vigorous physical activity. Bold values represent the number of correct classifications.

Robustness

Random Forest was the only algorithm not showing any changes or differences in balanced accuracies per intensity for all individual's baseline characteristics. The cut-off point algorithms did show changes for a single baseline characteristic each, namely body height. More specifically, balanced accuracies for standing were positively correlated with body height (all three algorithms ρ 0.392 (P=0.047)).

Algorithm comparison

Overall, differences in participant-specific balanced accuracies between algorithms were found for one intensity only (Figure 2.3). More specifically, participant-specific balanced accuracies for LIPA classification were different in three occasions, where SVM, IMA & Random Forest appeared superior over TM. The differences found were 4.1% (1.5%, 6.6%) (P=0.006), 6.3% (2.6%, 10.0%) (P<0.001) and -11.2% (-18.0%, -4.4%) (P=0.030) respectively.
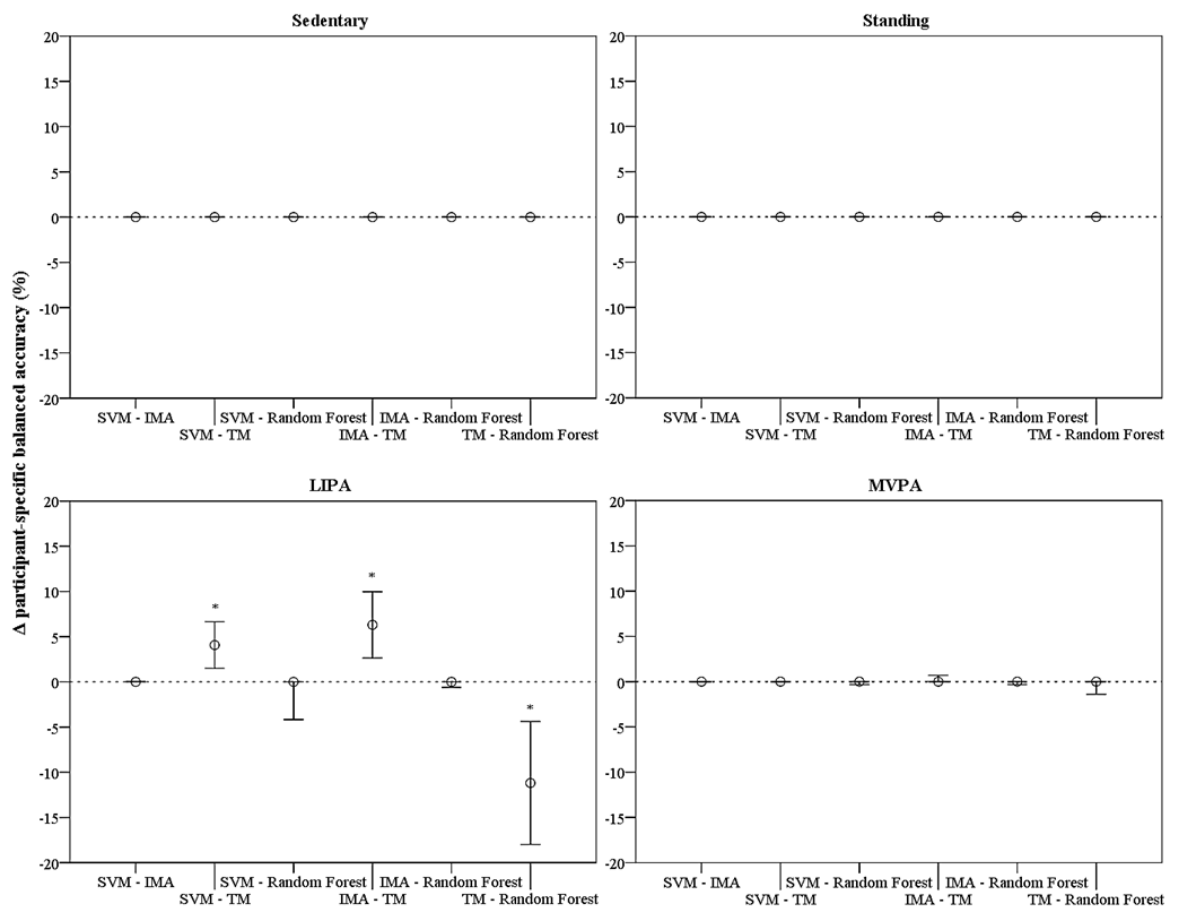
Figure 2.3. Pairwise comparisons between algorithms per intensity using participant-specific balanced accuracies.

SVM, sum of vector magnitudes; IMA, integrals of the moduli of acceleration signals; TM, total movement; LIPA, light-intensity physical activity; MVPA, moderate-to-vigorous physical activity; Error bars represent 95%-confidence intervals; Dashed line represents no difference; *P <0.05.

Algorithm benchmarking

Applying the critical 80%-threshold to the overall balanced accuracies of the pooled-data algorithms per intensity showed that all algorithms reached the threshold for sedentary activity, standing and MVPA classification (Table 2.3). However, only the Random Forest model also met the criterion for LIPA classification.

Benchmarking the participant-specific balanced accuracies per intensity for each algorithm revealed that all models had a perfect score (100.0%) for sedentary activity and MVPA (Table 2.3). The balanced accuracy for standing classification was acceptable for 92.5% of the participants in all algorithms. LIPA classification, however, showed acceptable balanced accuracies for only 62.5% (SVM), 65.0% (IMA) and 57.5% (TM) of the participants in the cut-off point algorithms, while this was 80.0% in Random Forest.

Discussion

The main aim of the current chapter was to compare between traditional cut-off points algorithms and a machine learning approach, to provide the best performing heterogeneous pooled-data algorithm to study SB and PA in older adults using thigh-mounted triaxial accelerometry. It is encouraging to note that all models showed acceptable overall balanced accuracies for classification of sedentary activity, standing and MVPA. As hypothesised however, Random Forest outperformed the cut-off point classifiers, being robust for all individual's physiological and non-physiological characteristics and the only algorithm with acceptable (≥80%) overall balanced accuracies over the whole range of activity intensities. In addition, participant-specific balanced accuracies of Random Forest were superior over TM when classifying LIPA.

The fact that Random Forest algorithm performance was better than cut-off point models of SB and PA intensity detection is likely owing to its ability to recognise patterns in non-linear and complex data by using a combination of multiple decision trees, each trained on a random set of features (26,51). To illustrate the difference with cut-off point algorithms, these models were developed using only two parameters from the triaxial accelerometer data, whereas modelling of the Random Forest algorithm used 55 parameters. Despite this, the differences in performance found between the cut-off point algorithms and Random Forest were only small. When comparing balanced accuracies between the cut-off point algorithms tested, an explanation for the results might come from the variability of the

parameters used to develop the algorithms. Since oxygen consumption data was used similarly for all models, this parameter did not result in any differences. Nevertheless, a negative relationship with MET values was identified, which indicates more variation for lower intensities, resulting in difficulties distinguishing between standing and LIPA for example. However, with an overall CV of 4.4% (3.4%, 5.3%), DB was generally regarded a reliable method in this chapter. The fact that all algorithms used the same parameter for posture detection, static Y_{mean} respectively, means that it can also be ruled out as a possible explanation for algorithm performance differences. With a CV of only 0.8% (0.7%, 1.0%) in this chapter, this parameter was considered highly reliable. Although a negative correlation between CVs and MET values was found, it did not affect posture detection much, since overall balanced accuracies were 97.1% for all models when classifying activities as either SB or non-SB. Based on balanced accuracies, TM is the lowest performing algorithm showing either similar or inferior balanced accuracy results per intensity when compared to the other cut-off-point algorithms. Although the CV of TM as a parameter is only 6.2% (5.7%, 7.0%), it is slightly higher than the CVs of SVM and IMA, 5.5% (5.1%, 6.0%) and 5.6% (5.2%, 6.2%) respectively. The use of a parameter representing dataset dispersion (the SD in TM), rather than a summation or integration of all data points may well be the explanation for comparatively sub-optimal performance. As reflected by their CVs, SVM and IMA are equally performing classifiers. Although not all parameter CVs showed consistency with increasing MET values, the CVs within the IQR of all parameters were of an acceptable level (<10%), which might have resulted in acceptable overall balanced accuracies (≥80%) for all intensities of the cut-off point algorithms, except LIPA. Generally, when looking at the overall balanced accuracies per cut-off point algorithm, a similar pattern is found. Sedentary activity and standing are the most accurately classified intensities, followed by MVPA and ultimately LIPA. The main issue with LIPA classification, for as well cut-off point algorithms as Random Forest, is the poor sensitivity (51.0% - 63.7%), which is predominantly caused by misclassification with MVPA. Since the MET value range for LIPA classification is relatively small compared to MVPA's, the LIPA/MVPA threshold is easily surpassed and therefore any amount of movement is more likely to be classified as MVPA instead of LIPA.

The positive relationships found between balanced accuracies and body height for standing classification in all three cut-off point algorithms during robustness analyses, may be due to another reason than body height. Although we standardised accelerometer mounting position by using 50% of the femur length, absolute measures show different positions,

which could affect accelerometer signals. Namely, the distance to the centre of rotation (hip and knee joint respectively) influences accelerometer measurements proportionally (89). For identical movements, the larger the distance to the centre of rotation (as in taller people), the greater the dynamic acceleration compared to that measured at positions closer to the centre of rotation (as in smaller people). This over-registration of dynamic acceleration could lead to false classification of activities with higher intensities instead. Looking at the confusion matrices, standing does show lower sensitivity values for the cut-off point algorithms, which results from misclassification with LIPA. Altogether, this implies that taller people would have lower balanced accuracies than smaller people, but frankly, we found positive correlations. Moreover, we only saw the robustness issues for standing and no other intensities. Therefore, it is plausible to assume that it was not body height to cause any changes in balanced accuracies of standing for the cut-off point algorithms. Further analysis showed that there were only three people with considerably lower balanced accuracies for standing (75% vs. ≥96.2%). Interestingly, they were amongst the smallest study participants (≤1.60 m). In addition, the confusion matrices showed that all the standing misclassifications happened in these three participants, while ten others of ≤1.60 m body height showed balanced accuracies like taller participants. Hence, when leaving the three out of the correlation analyses, no significant relationships between balanced accuracies of cut-off point algorithms for standing classification and body height were found anymore. When looking into more detail at the raw data, we noticed that the misclassifications in fact occurred during sideways shuffling, for which the three involved participants also happened to exhibit EE ≤1.5 MET. As a result of the latter, the reference classification for this activity was standing but the algorithms classified it as LIPA due to motion sensing. Thus, it was not the 'body height' parameter, which negatively affected the algorithm robustness results in these rare cases. Therefore, it is safe to say that all algorithms in this current study are robust, which is most probably the result of using a heterogeneous study sample.

Whilst it was encouraging to note that all algorithms showed acceptable overall balanced accuracies for classification of sedentary activity, standing and MVPA, Random Forest was the only model that also achieved the critical 80%-threshold for LIPA classification. Despite the generally good results, the disadvantage of an overall measure is that it can mask unacceptable algorithm performance on an individual basis. For that reason, it is also important to check the percentage of acceptable participant-specific balanced accuracies per intensity for each model. This revealed that, regardless of algorithm, individual

classification of sedentary activity and MVPA was always of an acceptable level, which allows categorisation of people based on the amount of SB and MVPA, such as active, inactive and active couch potato. Moreover, standing classification was acceptable for 92.5% of the participants in all algorithms. On the contrary, LIPA classification was acceptable in only ≤65.0% of the participants when using a cut-off point algorithm, while this number rose to 80.0% in case Random Forest was used. To summarise, these results show that the cut-off point algorithms presented in this chapter, can be used to detect SB, standing and MVPA in older adults confidently. Random Forest, however, is the only algorithm that can be used for LIPA classification too. This latter is exciting, because LIPA might play an important role in gaining health benefits by counteracting SB through PA in elderly (90). Moreover, performance of MVPA may have negative physiological effects, such as increased inflammation, and not necessarily elicit any greater physiological benefits over LIPA in the older adult population (91). Additionally, performing MVPA may have a high threshold, potentially affecting long-term adherence in elderly negatively (92).

Compared to recent research that, similarly to our present one, conducted laboratory-based testing to validate activity intensity identification algorithms including machine learning, our results are in fact a further improvement on these classifiers because we also focus on algorithm robustness and benchmark individual accuracies (35,67,93). Although comparing results between studies is complicated by differences in populations, monitor placement (mainly hip or wrist, against us thigh) that may influence classification (35), and outcome variables (e.g. Kappa statistic vs. balanced accuracy) (85), our overall finding is in agreement with Ellis et al. (51). They also showed improved free-living activity intensity classification with machine learning over traditional cut-off point models (without posture detection). However, it must be noted that their machine learning algorithm was developed using free-living accelerometer data only, while the traditional cut-off points were derived in the laboratory.

One could consider the development of algorithms under laboratory conditions as a limitation, given the fact that when laboratory-based, performance during real-life mobility monitoring is compromised (35,51). However, in the laboratory, conditions can be controlled and a whole range of activities and intensities can be studied allowing calibration, while simultaneously providing proof-of-concept such as thigh-mounted triaxial accelerometry in older adults (35,68). To improve the matching of performance from laboratory-based with free-living based accelerometer algorithms one may match the

amount of data collected on each behaviour with its prevalence in free-living and train the algorithms with bout lengths similar to true daily life behaviour (68). Although our use of steady-state data of activities with predefined length will improve algorithm accuracies (35), this may not be directly translated to data collected outside the laboratory, since steady-state is not necessarily reached in free-living conditions with activities being more sporadic (68). Also, Gyllensten and Bonomi (94) found that activities in free-living conditions exhibit a higher degree of overlapping characteristics in their acceleration features when compared with activities performed in the laboratory. Some free-living activities even show substantially different acceleration signals in comparison to when performed in the laboratory (35,68). Although we agree that true performance of our algorithms in real-life conditions cannot necessarily be derived from the balanced accuracies seen under laboratory settings and it will probably be lower in free-living, we do not expect the dramatic decrease (~13%–46%) reported elsewhere (35,51,68,93,94). There are several reasons supporting this expectation. Firstly, most of these studies are either not comparable to this chapter in terms of study population, modelling techniques/settings, extracted features, and accelerometer placement, or suffered from serious methodological issues such as using the same sample to both develop and validate algorithms (35,51,68,93,94). Secondly, we included few, but common basic activities for elderly persons in our protocol (33,95,96), and instructed participants to perform them as 'naturally as possible' i.e. using self-selected speed and/or intensity. Next, instead of activity classification, we used intensity classification (based on individual RVO_2 corrected MET values) in this chapter, which is a more generic system providing less options, and thus expected to be less prone to error when applied outside the laboratory (68). Finally, we used a heterogeneous sample, representing the true healthy community-dwelling older adult population, to develop the algorithms.

Another potential study limitation may be the fact that our models have been developed for application in a single thigh-mounted accelerometer, which does not allow perfect monitoring of PA, as perhaps wobbling of thigh mass or the lack of upper-body movement detection results in classification errors (54,71). Although it has been suggested that mounting multiple sensors could address the latter issue (54,71,97), study compliance may become compromised (93), something that is less of a problem with a single accelerometer (65,71). Moreover, thigh mounting can accurately distinguish between sitting and standing, which is not possible with traditional monitor placement at the hip or waist (31,63,64,98). This thigh placement is thus superior to detect upright stationary activities common in the

household, that tend to be more metabolically demanding than daily living activities that recruit only the upper body. Thigh mounting is also relatively close to the centre of mass, which is vital for good prediction of EE and monitoring of locomotion (54,60). Capturing locomotion is important in the elderly, because it provides information about potential for maintained/acquired physical independence (54). Generally, a combination between thigh-mounted accelerometry and machine learning is considered ideal, because the latter in fact makes sensor placement less relevant (71).

The major strength of our current approach is that its design and protocol are largely in accordance with the recommendations for accelerometry-based studies done by Welk et al. (75). To highlight these compelling elements, despite being modestly sized (~16.4 hrs of algorithm training data only), a study sample containing a large variety of physiological and non-physiological characteristics was used to develop four different accelerometer algorithms. The analyses were performed in more detail (such as focusing on robustness and benchmarking individual accuracies) than usually seen in the literature. The use of leave-one-subject-out cross-validation, ideal for smaller datasets, minimises the risk of overfitting with Random Forest machine learning and enhances the general applicability of the algorithms to new data (99). Additionally, by using a reliable method for measuring oxygen consumption (CV 4.4% (5.3%)) and correcting for individual metabolic baselines, coupled with direct observation, the reference intensity classification is highly accurate. Since both raw accelerometer data and videos were collected, post-study analyses will be possible such as algorithm tuning, epoch length optimisation or qualitative activity classification, but also comparisons with other monitors. Most importantly, this is the first study to conduct detailed analyses of heterogeneous pooled-data algorithms, ranging from simple cut-off point to complex machine learning, for the quantification of SB and PA in older adults using thigh-mounted triaxial accelerometry.

Future studies should focus on further analysis and development of the Random Forest algorithm to classify activities qualitatively. This will not only result in better prediction of EE (100), but also provide information not captured by intensity classification (51,68,72). Moreover, the Random Forest algorithm should be validated in a free-living set-up and compared to a similar algorithm developed on free-living data. Furthermore, comparisons with proprietary algorithms of commercially available activity monitors would be interesting, not least to allow direct comparison of data from different laboratories and hence the creation of large data sets. Overall, these suggestions would (i) improve

understanding of the associations between human activity and health that will inform future recommendations and guidelines for older adults to support healthy ageing (51,68,72) and (ii) help to improve current industry standards in activity monitoring in elderly.

Conclusions

Unlike the cut-off point algorithms, under laboratory conditions the Random Forest machine learning model showed acceptable algorithm performance throughout the whole range of activity intensities in older adults wearing a thigh-mounted triaxial accelerometer. Its performance of LIPA classification in particular, makes the algorithm highly relevant for this age group. The fact that this pattern recognition technique (i) does not require subgroup-specific calibrations and/or specific accelerometer body part positioning, (ii) is capable of recognising actual human activities and (iii) works independent of accelerometer brand/settings, signifies its potential large-scale applicability to distinguish SB and different levels/types of PA in older adults.

Chapter 3. Concurrent validity of activity monitors in older adults

Introduction

Both sedentary behaviour (SB) and physical activity (PA) are recognised as independent factors in healthy ageing (3,6,9). To study the dose-response relationships, monitors are preferred over questionnaires, since most limitations of subjective monitoring do not apply to objective methods (6,13,24). Objective monitoring is also useful for planning and evaluating interventions which can help to update recommendations in physical activity guidelines (6). For example, light-intensity PA (LIPA) is suggested to be important for counteracting the highly sedentary lifestyles of elderly (90). However, monitoring activity levels in older adults can be challenging.

Firstly, most activity monitor algorithms have been designed for and developed on younger and healthier populations, and as such, any established activity thresholds or cut-off points for activity intensities are unlikely to apply to other populations (6,101,102). This latter will compromise accuracy of movement behaviour monitoring. Generally speaking, ageing is associated with biomechanical, physiological and metabolic characteristics that influence perception of effort, and indeed, relative use of physiological reserves, to carry out activities of daily living (62,103). In other words, different age groups will be expected to exhibit different activity thresholds and hence cut-off points for metabolic demands at given activity intensities. Thus, in older adults, slower walking speeds, decreased fitness levels and even dependency on walking aids are factors that would tend to contribute to changes in metabolic demands (6,104). We would propose that whilst the goal standard for mobility behaviour monitoring would be to include each individual's physical and demographic characteristics thereby developing individualised algorithms, this is not very practical. An advance on current commercially available movement monitors would be to have these incorporate age-specific algorithms, as an acceptable compromise (6).

Although there is an increasing amount of literature on SB and PA effects on a number of health and quality of life outcomes in older persons (30,105), the data from the different laboratories tends to use diverse monitors and each of these will have been developed using different algorithms (24,68,98,106,107). In addition, it is unclear whether the anatomical site of monitor wear would impact on the apparatus's ability to accurately detect posture and activity intensity. To draw a good picture of the distinct effects of SB and PA in elderly, both the degree of monitor accuracy and agreement between monitors,

needs to be established. This will enable researchers and end-users alike, to pool all the information gathered from the numerous studies. In addition, where a monitor may diverse completely from the other units, this should also be highlighted so that spurious conclusions about cause-effects are avoided. Generally, an extensive comparison of activity monitors, as chosen for this chapter, has not been conducted in elderly yet. Moreover, evidence on their validity in older and slower moving people is limited (102).

Therefore, the purpose of the current chapter was to validate and compare six algorithms using four different activity monitors for the quantification of activity intensities in older adults. This was done by (i) determining participant-specific and overall balanced accuracies per algorithm, (ii) comparing participant-specific balanced accuracies between algorithms, and (iii) benchmarking participant-specific and overall balanced accuracies per algorithm. It was hypothesised that wearing an activity monitor on an anatomical site that would ease the distinction of standing from sitting/lying postures would increase the monitor's accuracy in detecting physical activity intensity. It was also hypothesised that an algorithm developed using data from older persons would outperform any other (proprietary) algorithms for each activity intensity when applied to an older adults study sample.

Materials and methods

Participants

Twenty older adults (70.0 (12.0) years; 50% female) participated in this study. Exclusion criteria were: <60 years of age, not able complete the laboratory-based activity protocol independently, any diagnosed neurological disease or condition, diabetic, terminally ill or currently receiving cancer treatment, myocardial infarction in the previous 12 months or any currently unstable cardiovascular condition, any pulmonary disease or condition that did not allow expired gas sampling, injuries or surgeries within the previous three months, previously advised by their physician not to undertake any physical activity/exercise, or not competent to make an informed decision about study participation.

This study was approved by the medical ethical board of University Hospital KU Leuven, Belgium. All participants provided written informed consent prior to study participation.

Baseline characteristics

The following baseline characteristics were determined for all participants: age (years), sex (female/male), body height (to the nearest 0.1 cm; barefoot), body mass (to the nearest 0.1 kg; barefoot and light clothing only) (Table 3.1). Additionally, the body mass index was calculated by dividing body mass by squared body height ($kg \cdot m^{-2}$). Resting oxygen consumption (RVO_2) ($ml \cdot kg^{-1} \cdot min^{-1}$; STPD conditions: standard temperature and dry gas at standard barometric pressure) was assessed per participant while sitting quietly on a chair for four minutes. At the same time resting heart rate was monitored (beats per minute), in order to estimate physical fitness levels according a standard heart rate table (76). This was not determined for participants who used heart rate controlling medication. Participants' self-selected walking speed on a treadmill was referred to as the preferred walking speed ($km \cdot h^{-1}$). Finally, a falls risk assessment tool classified risk of falling for each participant (low/medium/high) (77).

Table 3.1. Study sample characteristics.

Age (years)	70.0 (12.0)[¶]	
Sex	10 Female	10 Male
Body mass (kg)	73.4 (13.0)	
Body height (cm)	165.6 (8.1)	
BMI ($kg \cdot m^{-2}$)	26.7 (3.6)	
RVO_2 ($ml \cdot kg^{-1} \cdot min^{-1}$)	2.87 (0.52)	
Physical fitness level*	3 Less than good	11 Good or better
Preferred walking speed ($km \cdot h^{-1}$)	2.6 (2.0)[¶]	
Falls risk	19 Low	1 Medium or high

BMI, body mass index; RVO_2, resting oxygen consumption. *Only determined for participants not taking any heart rate controlling medication. [¶]Values represent either arithmetic mean (standard deviation) or median (interquartile range).

Instrumentation

Activity monitors

Four different activity monitors were simultaneously used for this study, respectively ActiGraph wGT3X-BT (ActiGraph, Ft. Pensacola, Florida, USA), ActivPAL[3c] VT (PAL Technologies, Glasgow, UK), GENEActiv Original (Activinsights Limited, Kimbolton, Cambridgeshire, UK) and DynaPort MM+ (McRoberts B.V., The Hague, The Netherlands). Each monitor was set to their default settings and worn as recommended by the manufacturer.

Thus, the ActiGraph wGT3X-BT (46 x 33 x 15 mm, 19 grams) sampled at 30 Hz (with the low-frequency extension filter applied) and was worn around the waist on the mid-axillary line of the right hip using an elastic band. The ActivPAL[3c] VT (35 x 53 x 7 mm, 15 grams) sampled at 20 Hz and was mounted on the right anterior mid-thigh (at 50% femur length; the latter being the distance between the trochanter major and the lateral femur epicondyle) using Tegaderm™ transparent film dressing (3M Health Care, St. Paul, MN, USA). The GENEActiv Original (43 x 40 x 13 mm, 16 grams) was worn on two locations each having its own sample frequency (non-dominant wrist using medical tape (100 Hz) and left anterior mid-thigh (at 50% femur length using Tegaderm™ transparent film dressing; 60 Hz)). Finally, the DynaPort MM+ (106.6 x 58 x 11.5 mm, 55 grams) was worn on the middle of the lower back using an elastic band and sampled at 100 Hz (Figure 3.1).

Figure 3.1. Study participant wearing all monitors.

Indirect calorimeter

A portable breath-by-breath metabolic system was used for indirect calorimetry (Oxycon Mobile JAEGER™/CareFusion, Hoechberg, Germany). The system comprised 2 units (sensor box and data exchange unit, each 126 x 96 x 41 mm) worn against the chest using a harness. In addition, a Polar T31 coded transmitter belt for heart rate monitoring (Polar Electro Oy, Kempele, Finland) and a face mask with a dead space of <30 mL (Hans Rudolph Inc, Kansas City, MO, USA) were used. A lightweight bi-directional 30 mL dead-space DVT volume sensor was connected to the facemask to which a Nafion sampling tube for exhaled air was connected. Due to its low weight (950 grams), the system caused minimal discomfort. Oxygen consumption (VO_2), carbon dioxide production (VCO_2), heart rate, respiratory rate and tidal volume were measured continuously for the duration of the laboratory protocol. All measured data (gas & flow signals and heart rate) were sent telemetrically to a calibration and receiver unit, itself connected to a laptop (IBM, Armonk, NY, USA) where it was processed using JLAB (Carefusion Germany 234 GmbH, Hoechberg, Germany). All data was backed up on an internal SD memory card inside the data exchange unit. The portable system was switched on at least 30 minutes prior to each participant's arrival at the laboratory, and a two-point gas calibration was completed using JLAB's automated procedure.

Direct observation

A GoPro Hero3 video camera (GoPro Inc., San Mateo, CA, USA) was attached to the front of the participant's harness and used to record the entirety of the laboratory-based activity protocol. The recordings were stored on a microSD card and downloaded to a laptop after each session. This data allowed direct observation of all activities post laboratory protocol completion.

All instrumentation was time-synchronised with a laptop, used for initialising the activity monitors and analysing the collected data.

Laboratory-based activity protocol

All participants were instructed to refrain from physical exercises, stimulants or smoking at least four hours prior testing. The protocol was only executed once and consisted of 10 activities, which were performed in a random order, after a period of 20 minutes resting followed by sitting quietly on a chair: (i) sitting while watching TV, (ii) sweeping the floor, (iii) cycling on an ergometer (Technogym, Cesena, Italy), (iv) stairs negotiations (walking up

and down), (v) standing, (vi) walking with two shopping bags (2.5 kg each hand), (vii) walking on a treadmill at a self-selected speed (Forcelink, Culemborg, The Netherlands), (viii) sitting while doing desk work, (ix) doing the washing up and (x) lying on a bed. All activities were performed for four minutes, where the first two minutes were used to reach a steady-state and the last two minutes were for data recording. The only exception to this was walking the stairs, as participants walked two minutes before going up the stairs (one minute) and then walked two minutes again before going down (one minute). Hence, the total duration of this activity was six minutes (2+1+2+1) instead of four. For data quality purposes, all activities were extended by a second at least, to assure activity continuation throughout the whole data recording period. Participants were instructed to perform each activity as naturally as possible and at their preferred pace. To prevent any fatigue carry-over effects, participants were seated in-between activities and the next activity was not started until their heart rate returned to resting level as measured during initial quiet sitting on a chair. The total duration of the activity protocol was approximately 60 minutes.

Validation

All activity monitors were analysed using their own (proprietary) algorithms and software, and results were given per epoch, which varied for each monitor. The ActiGraph wGT3X-BT was analysed in 60s-epochs using the Freedson Adult VM3 algorithm as provided in the ActiLife-software, version 6.13.3 (ActiGraph, Ft. Pensacola, Florida, USA). Data collected with the ActivPAL3c VT was analysed in 15s-epochs using the ActivPAL3™-software, version 7.2.32 (PAL Technologies, Glasgow, UK). Two different algorithms were used for analysing the thigh-worn GENEActiv Original. One algorithm is known as 'Sedentary Sphere' (thigh-worn version) and analysed the data in 15s-epochs (98), while the other algorithm used Random Forest machine learning (100 trees) and 10s-epochs (Chapter 1). The wrist-worn GENEActiv Original, was also analysed in 15s-epochs, but using a wrist-worn version of the 'Sedentary Sphere' algorithm (66,106). Finally, the DynaPort MM+ was analysed in 60s-epochs using the company's online platform MyMcRoberts version 2.2.1 (McRoberts B.V., The Hague, The Netherlands).

Oxygen consumption data was measured by the Oxycon Mobile per 5s-epochs. To determine intensities of the activities performed during the protocol, VO_2 per 5s-epochs was divided by the participant's RVO_2. This resulted in metabolic equivalent (MET) values. RVO_2 was estimated by calculating the arithmetic mean over the 5s-epoch VO_2 collected during the last two minutes while sitting quietly on a chair. Since MET values were

calculated per 5s-epochs, this allowed average MET values to be calculated for all intervals as used in the activity monitors, respectively 10s, 15s and 60s-epochs. The average MET values were used to classify activity intensities per epoch by first checking the MET value and then (if necessary) the participant's posture (Table 3.2). The classifications resulting from this scheme served as the criterion measure and were compared to the activity monitor outputs. To allow direct comparison with the criterion measure, each epoch outcome per monitor was converted to these criterion measure classifications, if necessary (Table 3.3).

Participant-specific confusion matrices were created to determine balanced accuracies per activity intensity for each monitor. In addition, overall confusion matrices per monitor were created by summing the participant-specific matrices. The balanced accuracies were calculated as the arithmetic mean of the sensitivity and specificity results per activity intensity for each monitor.

$$Sensitivity\ (\%) = \frac{True\ positives\ (N)}{True\ positives\ (N) + False\ negatives\ (N)} * 100$$

$$Specificity\ (\%) = \frac{True\ negatives\ (N)}{True\ negatives\ (N)\ +\ False\ positives\ (N)} * 100$$

where N represents the number of cases. Balanced accuracies of ≥80% were considered of an acceptable level (35).

Table 3.2. Criterion measure classification scheme.

Rules	Intensity classification
1. If MET ≤1.5 and posture = sedentary, then	Sedentary
2. Else: If MET ≤1.5 and posture ≠ sedentary, then	Standing
3. Else: If MET >1.5 and <3, then	LIPA
4. Else: If MET ≥3, then	MVPA

MET, metabolic equivalent; LIPA, light-intensity physical activity; MVPA, moderate-to-vigorous physical activity.

Table 3.3 Monitor classification conversion scheme.

Rules	Classification
ActivPAL	
If epoch time predominantly = Sedentary, then	Sedentary
Else: If epoch time predominantly = Upright, then	Standing
Else: If epoch time predominantly = Stepping and MET <3, then	LIPA
Else: If epoch time predominantly = Stepping and MET ≥3, then	MVPA
ActiGraph	
If epoch time predominantly = Sitting or Lying, then	Sedentary
Else: If epoch time predominantly = Standing and VM = 0, then	Standing
Else: If epoch time predominantly = Standing and VM <2690, then	LIPA
Else: If epoch time predominantly = Standing and VM ≥2690, then	MVPA
DynaPort MM+	
If epoch class = Sitting or Lying, then	Sedentary
Else: If epoch class = Standing, then	Standing
Else: If epoch class = Shuffling or Walking and MET <3, then	LIPA
Else: If epoch class = Shuffling or Walking and MET ≥3, then	MVPA
GENEActiv Original – Thigh – Random Forest	
Classifications of this monitor are in line with the criterion measure	N/a
GENEActiv Original – Thigh & Wrist – Sedentary Sphere	
If epoch intensity/activity = Sleep, then	Sedentary
Else: If epoch intensity/activity = Sedentary or Light and posture = Sit/lie, then	Sedentary
Else: If epoch intensity/activity = Sedentary and posture = Standing, then	Standing
Else: If epoch intensity/activity = Light and posture = Standing, then	LIPA
Else: If epoch intensity/activity = Moderate or Vigorous, then	MVPA

MET, metabolic equivalent; LIPA, light-intensity physical activity; MVPA, moderate-to-vigorous physical activity; VM, Vector Magnitude.

Data reliability

Since MET values are a main part of the criterion measure classification scheme, it is important to check the reliability of this outcome for all epoch lengths used in the studied activity monitors, respectively 10, 15 and 60 seconds. To do this, for each epoch length a coefficient of variation (CV) per activity per participant was calculated as:

$$CV\ (\%) = \frac{SD_{activity/participant}}{Arithmetic\ mean_{activity/participant}} \times 100$$

where SD represents standard deviation. Depending on data normal distribution, either the arithmetic mean (SD) or median (interquartile range (IQR)) was calculated over the moduli

40

of all CVs per epoch length to obtain sample-based reliability measures. A CV <10% was considered acceptable. Additionally, CV consistency across the activity protocol was checked by examining the correlation between the CVs and accompanying MET values per epoch length. If a correlation was found, data dispersion was determined (SD or IQR).

Statistical analyses

All data was checked for normality by using the Shapiro-Wilk test. Baseline characteristics are presented as the arithmetic mean (SD) (or median (IQR)). Balanced accuracies are reported as arithmetic mean (95%-confidence interval (95%-CI) (or median (95%-CI)), except for those in the confusion matrices. To compare the balanced accuracies of the different monitors, a one-way ANOVA repeated-measures test (or the Friedman test for non-parametric data) was performed. Where multiple post-hoc comparisons were conducted, the Bonferroni correction was applied to adjust P-values.

$$Adjusted\ P - value_{Bonferroni} = (P_{value})k$$

where k is the number of comparisons. P-values were considered statistically significant when P <0.05.

All statistical analyses were executed using IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, NY, USA).

Results

Data reliability

MET CV values were negatively correlated with observed MET data for all epoch lengths, respectively ρ -0.448 (P<0.001) for 10s-epochs, ρ -0.482 (P<0.001) for 15s-epochs and ρ -0.236 (P=0.001) for 60s-epochs (Figure 3.1). The IQRs of these epoch lengths' CVs were between 7.9% - 19.8% (10s), 6.5% - 16.7% (15s) and 1.7% - 7.6% (60s). For 10s-epochs, the sample-based CV was 12.1% (11.2%, 13.2%), while it was 10.7% (9.1%, 12.0%) for 15s-epochs and 3.3% (2.7%, 4.2%) for 60s-epochs. Overall, only the 60s-epoch CVs were <10%.
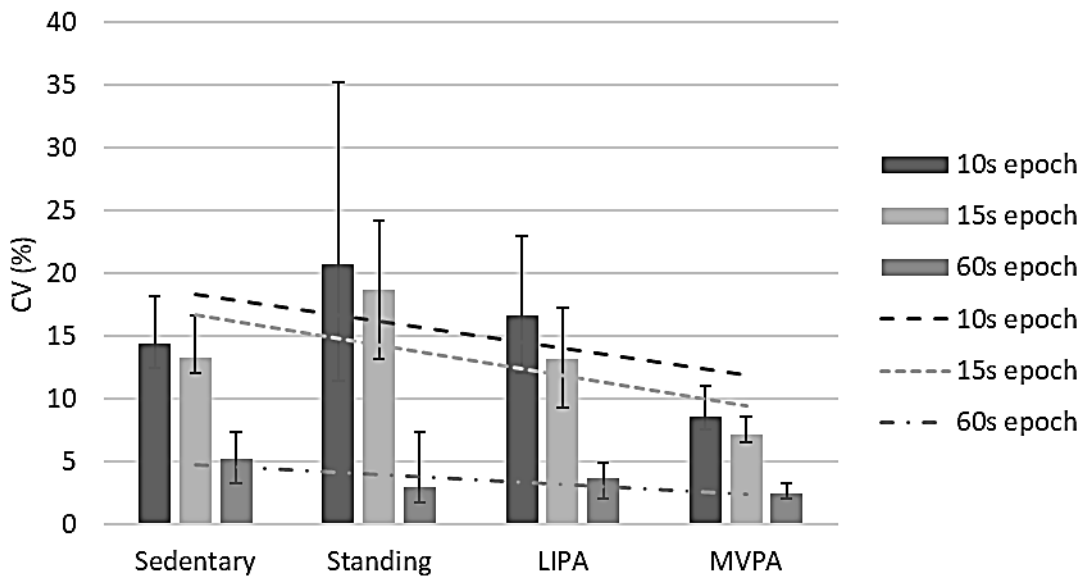
Figure 3.2. Metabolic equivalent value reliability per activity intensity per epoch length.

CV, coefficient of variation; LIPA, light-intensity physical activity; MVPA, moderate-to-vigorous physical activity. Error bars represent 95%-confidence intervals. Dashed lines show correlations between coefficients of variation and intensities per epoch length.

Overall monitor performance

The thigh-worn monitors (ActivPAL, Random Forest and Sedentary Sphere – Thigh) showed the best performance in classifying sedentary behaviour (all balanced accuracies ≥94.2%, with sensitivity ≥99.3% and specificity ≥88.5%) (Table 3.4). On the contrary, the other monitors' performances (ActiGraph, DynaPort MM+ and Sedentary Sphere – Wrist) ranged between 73.6% and 75.5%. Their sensitivity values ranged between 67.2% and 85.7%, while specificity was between 65.4% and 80.1%.

Balanced accuracies for standing classification varied from 42.4% (DynaPort MM+) to 90.1% (Sedentary Sphere – Thigh). The highest sensitivity was found for ActivPAL (94.0%) and the lowest for DynaPort MM+ (4.9%). Specificity was the highest for Random Forest (98.3%) and the lowest for DynaPort MM+ (79.8%).

ActiGraph showed the highest balanced accuracy for LIPA classification (69.7%), while DynaPort MM+ had the lowest (49.9%). Sensitivity values ranged from 0.0% (DynaPort MM+) to 66.7% (ActiGraph). Specificity was the highest for DynaPort MM+ (99.7%) and the lowest for ActiGraph (72.8%).

Finally, moderate-to-vigorous PA (MVPA) classification appeared to be between 68.8% (Sedentary Sphere – Wrist) and 85.4% (ActivPAL). Random Forest showed the highest

sensitivity (83.7%), while ActiGraph had the lowest (40.4%). Monitor specificity ranged between 85.4% (Random Forest) and 98.4% (ActiGraph).

Table 3.4 Algorithm cross-validation confusion matrix.

Monitor	Intensity	Reference				Sensitivity (%)	Specificity (%)	Balanced accuracy (%)	Acceptable level (%)
		Sedentary	Standing	LIPA	MVPA				
ActivPAL	Sedentary	**563**	0	53	0	99.3	95.4	97.4	100.0
	Standing	4	**156**	192	102	94.0	80.9	87.5	100.0
	LIPA	0	0	**17**	37	5.0	97.3	51.2	0.0
	MVPA	0	10	76	**519**	78.9	92.0	85.4	85.0
ActiGraph	Sedentary	**95**	11	21	22	68.3	80.0	74.2	52.6
	Standing	8	**16**	0	0	41.0	97.8	69.4	43.8
	LIPA	8	12	**50**	71	66.7	72.8	69.7	33.3
	MVPA	0	0	4	**63**	40.4	98.4	69.4	33.3
DynaPort MM+	Sedentary	**126**	37	27	35	85.7	65.4	75.5	40.0
	Standing	21	**2**	40	18	4.9	79.8	42.4	0.0
	LIPA	0	0	**0**	1	0.0	99.7	49.9	0.0
	MVPA	0	2	10	**114**	67.9	95.5	81.7	80.0
Random Forest	Sedentary	**842**	0	103	1	100.0	94.1	97.0	100.0
	Standing	0	**173**	37	4	70.3	98.3	84.3	85.0
	LIPA	0	45	**160**	159	31.7	90.3	61.0	5.0
	MVPA	0	28	205	**841**	83.7	85.4	84.5	95.0
Sedentary Sphere - Thigh	Sedentary	**566**	5	92	37	99.8	88.5	94.2	100.0
	Standing	0	**149**	97	53	89.8	90.4	90.1	100.0
	LIPA	1	12	**116**	215	34.3	83.6	59.0	0.0

		MVPA	0	0	33	**356**	53.9	96.9	75.4	40.0
Sedentary	Sphere - Wrist	Sedentary	**381**	17	111	104	67.2	80.1	73.6	40.0
		Standing	178	**131**	31	40	78.9	84.1	81.5	85.0
		LIPA	8	13	**78**	193	23.1	84.6	53.9	0.0
		MVPA	0	5	118	**324**	49.0	88.5	68.8	15.0

LIPA, light-intensity physical activity; MVPA, moderate-to-vigorous physical activity. Bold values represent the number of correct classifications.

Monitor comparison

Performance of sedentary classification was significantly different for ActivPAL and Random Forest when compared to all monitors, but not each other (Figure 3.2). Both showed higher participant-specific balanced accuracies. For classifying standing, Random Forest showed the most significant differences with other monitors, respectively ActivPAL (-3.5%, -7.4%, -0.9%, P=0.045) and DynaPort MM+ (-55.8%, -58.8%, -54.6%, P<0.001). Again, Random Forest also showed most differences with monitors for LIPA classification. Participant-specific balanced accuracies in this monitor were higher than in ActivPAL (-9.7%, -14.3%, -5.0%, P<0.001), DynaPort MM+ (-10.1%, -14.7%, -5.4%, P<0.001) and Sedentary Sphere – Wrist (8.4%, 2.5%, -12.0%, P<0.001). As for sedentary activity, MVPA classification favoured ActivPAL and Random Forest, which had similar performance and appeared significantly different to all monitors, except DynaPort MM+.
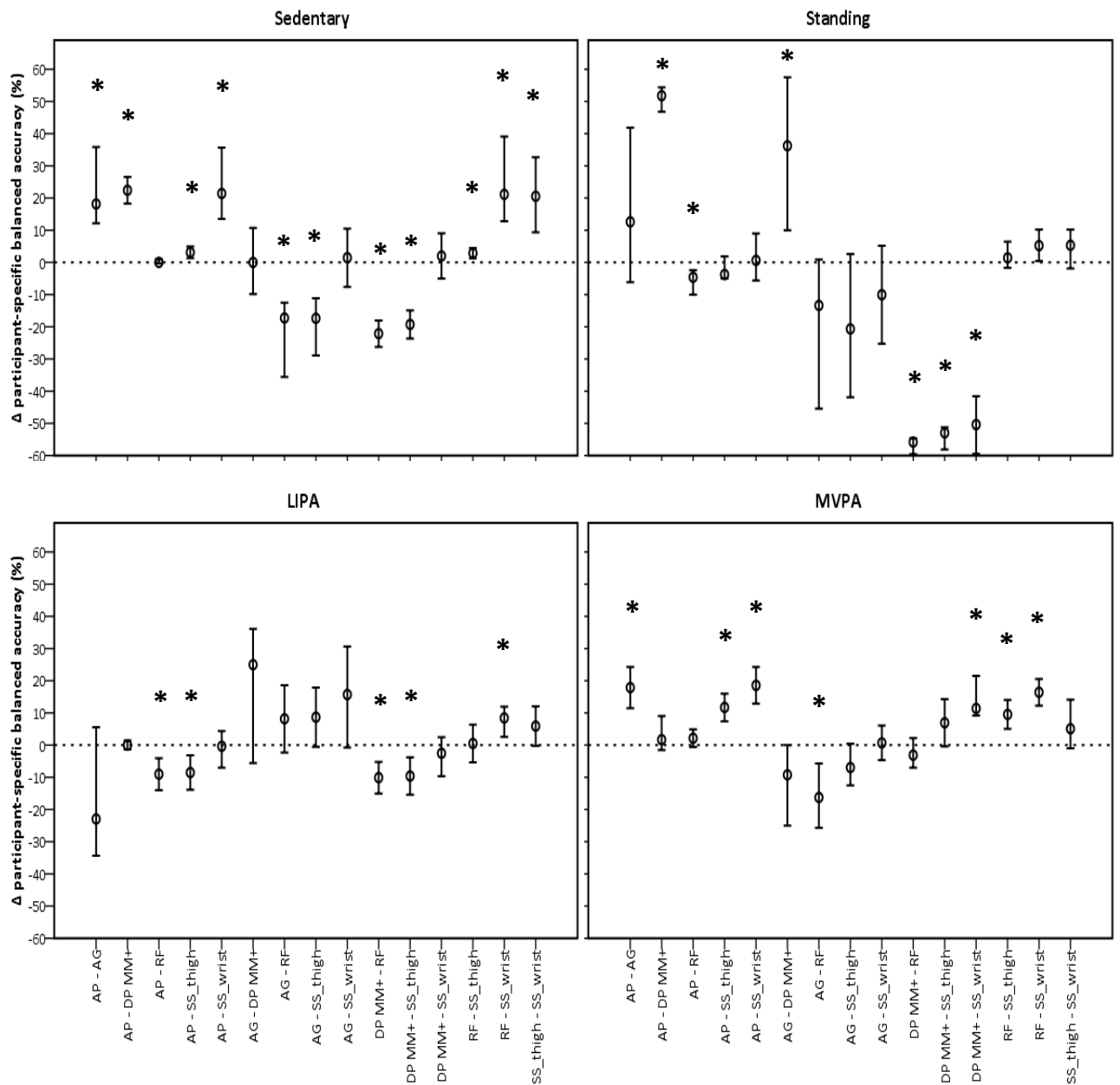
Figure 3.2 Pairwise comparisons between monitors per intensity using participant-specific balanced accuracies.

AP, ActivPAL; AG, ActiGraph; DP MM+, DynaPort MM+; RF, Random Forest; SS_thigh, Sedentary Sphere – Thigh; SS_wrist, Sedentary Sphere – Wrist; LIPA, light-intensity physical activity; MVPA, moderate-to-vigorous physical activity; Error bars represent 95%-confidence intervals; Dashed line represents no difference; *P <0.05.

Monitor benchmarking

Overall balanced accuracies for classification of sedentary activity were only of an acceptable level (≥80.0%) in the thigh-worn monitors (ActivPAL, Random Forest and Sedentary Sphere – Thigh) (Figure 3.3). Standing classification was acceptable in the same monitors, but also including Sedentary Sphere – Wrist. Interestingly, none of the monitors showed ≥80% overall balanced accuracy for classifying LIPA. Fortunately nevertheless,

ActivPAL, DynaPort MM+ and Random Forest reached the ≥80% overall balanced accuracy threshold for MVPA classification.

Checking the percentage of participants showing an acceptable level of participant-specific balanced accuracy, revealed that classification of sedentary activity was acceptable in all participants when using a thigh-worn monitor (Table 3.4). The other monitors showed a maximum of 52.6% only. Standing was classified acceptably in all participants when using ActivPAL or Sedentary Sphere – Thigh. In Random Forest and Sedentary Sphere – Wrist this number was 85.0%, while it appeared 43.8% and 0.0% in ActiGraph and DynaPort MM+ respectively. Acceptable levels of LIPA classification were the highest in ActiGraph (33.3%) followed by Random Forest (5.0%). All other monitors failed to reach an acceptable levels of LIPA classification. Acceptable MVPA classification varied significantly between the monitors. Random Forest tended to display the highest degree of MVPA classification balanced accuracy (95.0%), followed by ActivPAL (85.0%) and DynaPort MM+ (80.0%). The remaining monitors only had acceptable levels in ≤40.0% of the participants, respectively Sedentary Sphere – Thigh (40.0%), ActiGraph (33.3%) and Sedentary Sphere – Wrist (15.0%).
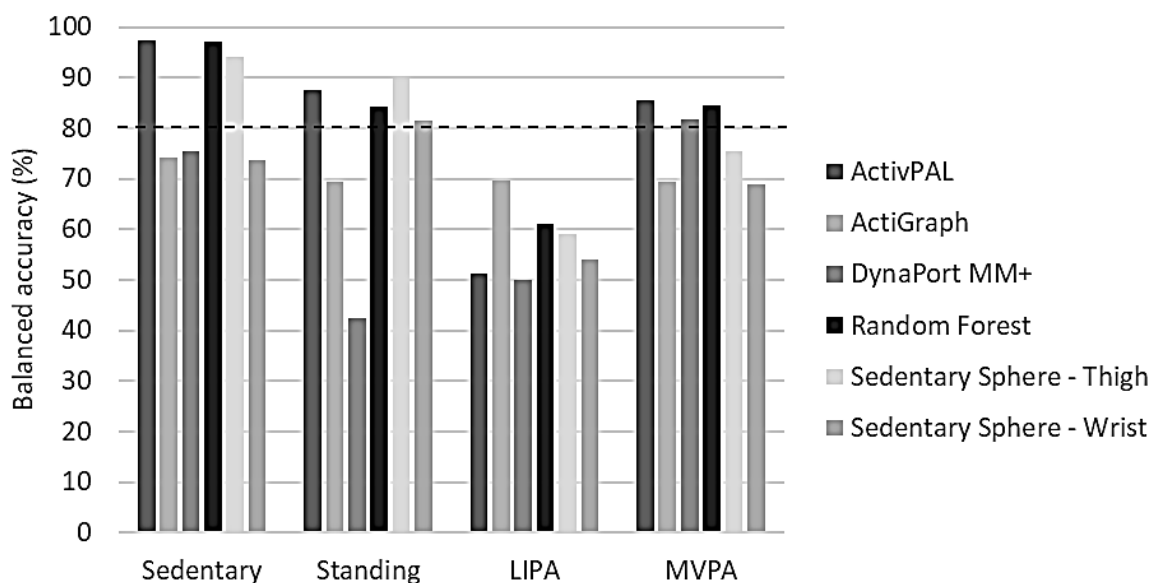
Figure 3.3. Benchmarking of overall balanced accuracies per activity intensity for each tested algorithm.

LIPA, light-intensity physical activity; MVPA, moderate-to-vigorous physical activity. Dashed line represents threshold for acceptable algorithm performance (80%).

Discussion

As hypothesised, algorithms specially developed using older persons and/or worn in anatomical positions that permitted the clear identification of posture, were the most accurate at classifying activity intensities in older adults. In particular, Random Forest appeared the best performing algorithm, in that at each activity intensity, it outperformed other algorithms/monitors. The fact that overall balanced accuracies were acceptable for sedentary, standing and MVPA classification is promising, just as their rate of acceptable individual results. Although most monitors showed good results for at least one activity intensity, ActivPAL is the only monitor with comparable performance to Random Forest. Again, thigh-worn monitors proved their value for the SB and standing classification. Another notable observation was that shorter epoch lengths proved more accurate than longer ones. Interestingly, none of the monitors showed acceptable outcomes for LIPA classification in our elderly participants. This would indicate the complexity of qualifying LIPA in this group and/or an inability for older individuals to carry an activity at that threshold. Given that LIPA is suggested to be important for counteracting SB especially within that age bracket (90), whilst minimising engagement in MVPA in order to maximise long-term compliance to adequate amounts of daily physical activity (92), the reason for the difficulties in reliably/accurately tracking LIPA using activity monitors in older adults warrants further study.

To check the potential cause for the low balanced accuracies for LIPA classification, the confusion matrix must be studied, which shows both sensitivity and specificity values per monitor for each activity intensity. Unlike specificity, sensitivity seems to be the issue. More specifically, three out of six monitors, including ActivPAL, DynaPort MM+ and Sedentary Sphere – Thigh, predominantly misclassify LIPA with standing. Random Forest and Sedentary Sphere – Wrist on the other hand, mainly misclassify LIPA with MVPA. ActiGraph is the sole monitor without such a LIPA classification issue. Under the assumption that activities were performed in a metabolic steady-state, with matching biomechanics, discrepancies between these two could lead to inaccuracies. Since we found a negative correlation between CVs of the METs and activity intensities, metabolic steady-state might not be the case for lower intensities, such as standing or LIPA. Also, it is known that activity monitoring in slower moving people, like elderly, is challenging (102). In normal ground walking for instance, older persons tend to utilise a larger number of small steps at a low pace to achieve motion (rather than quick and large, but less numerous steps) (108). This

might result in lower biomechanical values, not matching the higher metabolic demand. Indeed, the confusion matrix shows misclassification of LIPA with standing for example. The fact that ActiGraph is the only monitor to use a low-frequency extension filter, might explain why it does not have this classification issue. Basically, such a filter helps to pick up slow movements were other monitors (such as the three mentioned) do not sense it, which results in less misclassification. LIPA misclassification may have also occurred due to the incorporation of household activities in our activity protocol. An activity such as washing dishes, requires mainly upper limb action, hence monitors not attached to this anatomical site, will register less movement, while upper limb monitors might do the opposite. Interestingly, Random Forest is the only non-upper limb algorithm, which misclassifies LIPA with MVPA mostly. Presumably, this is caused by the fact it is using pattern recognition, which makes the monitor regard motion differently than just detecting the amount of movement. Finally, with the LIPA window being only small in terms of metabolic demands and yet similar in pattern to MVPA, it can be conceivable why misclassifications with MVPA could be made theoretically. Interestingly, a considerable amount of LIPA (≥15.7%), but MVPA in some cases too, was also misclassified as sedentary activity. A plausible explanation comes from the cycling activity that was performed. For this activity, the posture including thigh inclination near horizontal and hands holding the steer, potentially made classification difficult.

Apart from confusing cycling activity classification, measuring thigh inclination can also help to better distinguish between SB and standing (63,64). As seen in this chapter, the thigh-worn monitors performed better than the waist-worn (including lower back). Interestingly, also wrist-worn monitors seem to handle these classifications better. This is important information for deciding what monitor best to use if SB is a primary outcome measure. Another consideration is what epoch length to use. This chapter showed better performance with shorter epoch lengths, which is in line with previous research (109). However, the CVs of the MET values suggest otherwise. The smallest sample-based CV was found for 60s-epochs, while the largest were found for 10s-epochs. In fact, only the 60s-epochs CVs were acceptable for this steady-state data. Despite this, monitor performance was better with the smaller epoch lengths. Since activities were performed in the same fashion throughout the whole activity, it is suggested that better performance in epochs with higher CVs is not a direct result of smart or robust algorithms. Instead, because CVs were calculated over MET values, which were converted into intensities and eventually cross-validated, it rather proves robustness of the classification scheme.

50

The main reason for Random Forest to outperform the other monitors, may be through it use of pattern recognition instead of cut-off points for the classification of activity intensities. With most of the studied algorithms being proprietary, their exact mathematical iterations are unclear. However, it is safe to assume that they would largely rely on cut-off points. Studies have already shown that machine learning is more accurate than cut-off points in activity monitoring (51,71). Moreover, pattern recognition has been suggested as the future standard (24). Nevertheless, most current studies are still using cut-off point algorithms, potentially as these are more straight-forward to apply; even for the non-mathematically minded (24). Although machine learning algorithms make the requirement of specific anatomical attachment sites of an activity monitor less relevant (71), we propose that our application may be even more valuable given that it was developed using a model for thigh-mounted triaxial accelerometry. Our findings also lend further support to ActivPAL being considered as one of the gold standards and its widespread use as a criterion measure to validate other monitors (64,110).

Contextualising our findings in the light of the existing literature is challenging, not least, because of the scarcity of comparable 'mobility monitor' validation studies in older adults and the use of different outcomes measures. Nevertheless, comparisons with prior studies, which applied the monitors in the same fashion (none performed in older adults specifically, except for DynaPort MM+), show that the results of the ActivPAL monitor in this chapter were relatively comparable in the classification of SB (97.4% vs. lying horizontal 100.0% and sitting 91.0%), but worse for upright activities, such as standing and stepping (≤87.5% vs. 99.0%) (98,111). As for the ActiGraph, our results for sedentary activity were slightly better than the accuracy presented in a previous study (≤72.0% in theirs compared to 74.2% in ours), while accuracy of detecting upright activities was slightly better in the other study (74.0% vs. ≤69.7%) (98). However, Kerr et al. (68) showed worse mobility detection accuracy for all activities (≤43.0% vs. ≥69.4%), except sitting (84.0% vs. 74.2%). The accuracies of the DynaPort MM+ monitor as measured in this chapter, were lower than the results found by Hollewand et al. (107). They showed 79.6% for lying, 87.6% for sitting (both vs. 75.5%), 81.5% for standing (vs. 42.4%) and 91.7% for locomotion (vs. ≥49.9%). A study by Rowlands et al. (106) found accuracies of 74.0% and 91.0% for classifying SB and upright activities when using Sedentary Sphere – Wrist. The results in this chapter are similar for sedentary activity (73.6%), but worse for standing (81.5%), LIPA (53.9%) and MVPA (68.8%). When comparing the Sedentary Sphere – Thigh results from this chapter

with Edwardson et al. (98), it is clear that their findings are (slightly) better, respectively ≥99.8% vs. 94.2% for SB and ≥88.3% vs. ≥59.0% for upright activities.

To our knowledge, we are the first group to have validated this machine learning technique for thigh-worn accelerometry (Chapter 2). Comparing the present results against the data from Chapter 2, shows that the present findings are (slightly) worse for all intensities, respectively 99.6% vs. 97.0% for SB, 95.5% vs. 84.3% for standing, 80.6% vs. 61.0% for LIPA and 95.1% vs. 84.5% for MVPA. When focusing on Random Forest algorithms applied to accelerometer data collected from the hip or wrist, a lot of varying results have been published. For example, hip accuracies ranged from 75.0% - 94.0% for SB, from 64.0% - 89.0% for standing and from 73.0% - 97.0% for walking/running (51,68). Wrist classifiers showed 80.1% - 89.3% accuracy for sitting, 95.7% for standing and 91.7% - 93.7% for walking/running (51,112). Overall, our Random Forest result for sedentary activity is slightly better, whereas standing and MVPA are in line with the hip classifiers, but lower than the wrist algorithms. As mentioned above, the impact of the age discrepancy between ours and all these other studies cannot be underestimated.

The fact that this study was performed in a laboratory setting is a limitation because it does not show any information on how well the monitors will perform during free-living. However, the comparison made, provides useful information on how monitors will perform compared to each other, even in free-living when assuming their performance remains relatively the same. Although activities were performed in a standardised environment, we asked the participants to perform them as naturally as possible. One of the strengths of this chapter is that we concurrently compared a good selection of activity monitors used in research. Moreover, we used these as recommended by their developers/manufacturers, including the optimal body location and epoch length.

Overall, generalisation of findings is difficult because we only used a small study sample (N=20) of fit and healthy older adults. Nevertheless, this chapter presents highly valuable and important insights for activity monitoring in an understudied age group. Future research should validate and compare the studied monitors for quantifying free-living physical activity levels in the elderly. We would also recommend that device improvements be made in terms of ability to accurately detect LIPA, especially at least, in the elderly.

Conclusion

A thigh-worn triaxial GENEActiv with a Random Forest algorithm can be used best for accurate assessment of SB and PA in older adults. However, other monitors can be used, as they proved to be (partially) valid too. Generally, the decision of which monitor to use when, depends largely on the research question and setting.

Chapter 4. Descriptive analysis of the elderly cross-sectional study sample

Introduction

This chapter reports the descriptive statistics of the elderly cross-sectional study sample used to investigate several gastrocnemius medialis (GM) muscle-tendon properties, of which the findings are separately reported in the next three chapters. This muscle was chosen because it has been studied frequently regarding muscle architecture and size, and ultrasound scanning of it has been proven valid (113). Moreover, GM is also an important muscle for postural balance in older adults (44) and hence physical functioning. Last but not least it is an antigravity muscle, which shows fast impact of unloading (atrophy) as suggested in sedentary behaviour (SB).

Variables included in this analysis principally consist of anthropometric and accelerometer data. These data are important as they are the baseline characteristics of the cross-sectional study sample. Basically, the accelerometer data will be used to investigate potential associations with GM muscle-tendon properties, while anthropometric and other collected data will serve as covariates to adjust regression models, where appropriate. In addition to the descriptive analysis, this chapter also investigated both the further ageing effect on SB and physical activity (PA) levels, and the independence between SB and PA outcomes, which have been reported in literature previously and serve as important assumptions in this thesis (Chapter 1) (9,27,28,114).

Overall, the aim of this chapter was to check the representativeness of the study sample, which was done by comparing the study sample characteristics with existing evidence. It was hypothesised that (i) the cross-sectional study sample would be representative and (ii) SB and PA measures would show to be both affected by age and independent.

Materials and methods

A total sample of 106 healthy older adults participated in this study. They were initially recruited from an existing university database of former study participant, and later also in the local area via social meetings, posters and word-of-mouth. Participants were excluded if they were: aged <60 years, diabetic, had any issue affecting their mobility or ability to exert maximum force with the lower limb muscles/joints, had any recent (<3 months) injury

or surgery on their tested leg, not able to understand or follow up on study instructions, or not competent to make an informed decision about study participation.

This study was approved by the ethical review board of Manchester Metropolitan University, Crewe, UK. All participants provided written informed consent prior study participation.

Study visits

Participants visited the university on two separate occasions (≥7 days). On the first visit, participants completed questionnaires, were familiarised with the equipment to be used during the following visit and they were also fitted with an activity monitor. This visit lasted approximately one hour. On the second visit, proper testing took place, which included several tests such as a whole-body scan to measure body composition. In total, participants spent ~4 hours on the second laboratory visit (inclusive of a 30-45 mins breakfast ingestion break).

Questionnaires

All participants provided demographics and information about their previous and current PA and medical status via a general questionnaire. Additionally, information was collected about their smoking status and dietary intake. They also completed a falls risk assessment tool (FRAT), which served as a measure of frailty (77). This questionnaire consisted of five yes/no-questions about previous falls, medication usage, neurological problems, issues with balance and sit-to-stand ability. Based on their answers, participants were classified as having a low (≤1 yes), medium (2 yes) or high (≥3 yes) risk of falling.

Anthropometric data

All participants had their body height and mass taken on the first visit. Body height was measured barefoot and to the closest 0.1 cm using a wall-mounted stadiometer (Holtain Ltd., Crymych, UK). Body mass was measured wearing the least clothing as possible and to the nearest 0.1 kg using a digital body mass scale (seca GmbH & Co. KG., Hamburg, Germany). On the second visit, dual-energy X-ray absorptiometry (DEXA) (Hologic Discovery: Vertec Scientific Ltd, UK) was used to determine participants' body composition. Participants were instructed to arrive to the university campus after 10 hours overnight fasting. On the morning of testing they were only allowed to drink up to 250 mL of water. In addition, they were asked to void their bladder last thing prior to scanning and remove

all metal items on their body (if possible). All participants were laid in a supine position and underwent a ~7-minute whole body scan (effective dose 8.4 μSv), whilst wearing a hospital gown only. Using the built-in scan analysis software (Version 12.4; QDR for Windows, Hologic, Waltham, MA(115), USA), whole body analysis was performed to determine body compositional outcomes such as percentages of body fat mass, lean body mass and bone mineral content. Based on percent body fat mass, participants were classified, in terms of adiposity, as either normal or high (<40% or ≥40% in female, while <28% or ≥28% in male) (116). In addition, appendicular segmental masses were manually identified and assessed to be able to calculate the skeletal muscle index (SMI; appendicular lean mass per squared body height (kg·m^2)). This outcome was used for sarcopenia classification according to the suggested thresholds by Baumgartner et al. (115). Participants were deemed sarcopenic when SMI was <5.45 kg·m^2 for women and <7.26 kg·m^2 for men.

Accelerometer data

SB and PA levels were monitored for seven consecutive days using a triaxial accelerometer. The waterproof accelerometer that served as the activity monitor in this thesis, was the GENEActiv Original (43 x 40 x 13 mm, 16 grams) (Activinsights Limited, Kimbolton, Cambridgeshire, UK). It was mounted on the anterior mid-thigh (at 50% femur length using Tegaderm™ transparent film dressing (3M Health Care, St. Paul, MN, USA)) of the dominant leg (preferred for single-leg balance). The monitor was initialised to sample at 60 Hz. Participants were instructed to record their sleeping times on a provided log sheet, which allowed accurate analysis of daytime SB and PA. The accelerometer data was analysed with an in-house developed machine learning algorithm and software application (Chapter 2). This application provides a wide range of daily SB and PA outcomes, such as total time spent in different intensities, time spent in moderate-to-vigorous PA (MVPA) bouts of ≥10 continuous minutes, breaks in SB and distribution of SB bouts (Table 4.1). These outcomes were adopted from previous studies (16,117), which provide details on the calculations performed. The accelerometer data was only considered valid, if ≥5 days (of which ≥1 weekend day) were measured (90). This was the case in 105 out of 106 participants tested. Average values of all outcomes over the valid days were considered for further analyses.

In this thesis SB and PA outcomes were analysed on three different levels: (i) general SB levels combined with information on whether participants are physically active or not, (ii) compositional data analysis of total daily time spent in different behaviours (This type of analysis has been described in detail previously (118,119). Briefly, daily compositions are

transformed into isometric log-ratio coordinates, which are then unconstrained and allow the application of traditional multivariate statistics.), and (iii) daily SB pattern parameters combined with a variety of PA outcomes, such as percent standing, light-intensity PA (LIPA) or MVPA during PA bouts, or daily sporadic MVPA (sMVPA).

Table 4.1. Overview of accelerometer outcomes used in this thesis.

Accelerometer outcome[¶]	Description
Sleep (hrs)	Time spent sleeping
SB (hrs)	Time spent in SB
Standing (hrs)	Time spent standing
LIPA (hrs)	Time spent in LIPA
MVPA (hrs)	Time spent in MVPA
SB level (low/high)	Daily SB <8 or ≥8 hours
Breaks SB (n)	SB interruptions with ≥2 consecutive minutes upright activity
Short SB bouts (n)	SB bouts <30 minutes duration
Long SB bouts (n)	SB bouts ≥30 minutes duration
α	Scaling parameter sedentary bout length distribution
$X_{1/2}$ (mins)	Median SB bout duration
$W_{1/2}$ (%)	Fraction total sedentary time accumulated in bouts longer than median sedentary bout length
$W_{50\%}$ (mins)	Half of total SB is accumulated in SB bouts ≤ this duration
F (bouts·hrs^{-1})	Fragmentation index of SB bouts and total SB
Period (mins)	Mean period between SB bouts
PA bouts (n)	Bouts of ≥2 consecutive minutes upright activity
Total PA bouts time (mins)	Total PA bouts duration
SB during PA bout (%)	Percent of time spent in SB during PA bouts
Standing during PA bout (%)	Percent of time spent in standing during PA bouts
LIPA during PA bout (%)	Percent of time spent in LIPA during PA bouts
MVPA during PA bout (%)	Percent of time spent in MVPA during PA bouts
$MVPA_{\geq 10\ mins}$ (mins)	Total time spent in ≥10 consecutive minutes MVPA
sMVPA (mins)	Sporadic MVPA (total MVPA - $MVPA_{\geq 10\ mins}$)
Physically active (no/yes)	Weekly $MVPA_{\geq 10\ mins}$ <150 or ≥150 mins

SB, sedentary behaviour; PA, physical activity; LIPA, light-intensity physical activity; MVPA, moderate-to-vigorous physical activity; [¶]Daily measure, unless stated otherwise.

Statistical analyses

All data were checked for normality using either the Shapiro-Wilk or Kolmogorov-Smirnov tests. Normal distributed variables are presented as arithmetic mean (standard deviation (SD)), else as median (interquartile range (IQR)). To test the effect of age on SB and PA

measures, and the independence between SB and PA outcomes (excluding compositional data for the latter), either Pearson or Spearman correlation (non-parametric) was determined for continuous data. In case one of the variables was categorical, an independent T-test (or the non-parametric Mann-Whitney U test) was used. When both variables were categorical, either the Chi-square or Fisher's Exact test was conducted. To investigate co-dependencies between different behaviours of the compositional data, a variation matrix with log-ratio variances was created. Values close to zero, implied behaviours involved in the ratio to be highly proportional.

All statistical analyses were executed using IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, NY, USA). P-values <0.05 were considered statistically significant.

Results

Descriptive statistics

The mean (SD) age of the 105 participants tested, was 72.8 (6.0) years, while average anthropometrics showed body height of 166.3 (9.3) cm, body mass of 73.0 (13.4) kg and BMI of 25.9 (6.0) kg·m^{-2} (Table 4.2). Mean (SD) body composition consisted of 36.3 (7.9)% fat mass, 60.2 (7.5)% lean mass and 3.5 (0.7)% bone mineral content. About 45% of the subjects was deemed to be sarcopenic. Gender distribution in our predominantly white (99.0%) study sample was 53.3% female vs. 46.7% male. Although most people were classified with high adiposity (71.4%), frailty (15.2%) and history of major illness was low (16.3%). Our participants were on statins in 32.4% of the cases, while a current diagnosis of rheumatoid arthritis was only seen in 3.8% of the people. Only 2.9% of the participants smoked currently, while daily intake of ≥3 units alcohol was also low (4.9%). Regular intake of dairy and caffeine was 95.2% and 82.9% respectively. Finally, calcium/vitamin D supplements were used by 14.3% of the participants, while 22.1% recently performed resistance training.

Our participants spent 35.6% of their days sleeping, 39.4% in SB, 2.8% standing, 11.5% in LIPA and 10.7% in MVPA (Table 4.3). Overall, 81.9% spent ≥8 hours per day in SB, while only 10.5% was physically active. Combining these two outcomes, only 1.9% had both low SB levels and were physically active, while 16.2% had low SB but was not physically active, 8.6% had high SB and was physically active and 73.3% showed high SB levels combined with physical inactivity.

Table 4.2. Study sample characteristics.

Variable	Mean (SD) or ¶Median (IQR)	
Age (yrs.)	72.8 (6.0)	
Sex (female / male)	56	49
Ethnicity (white / black)	104	1
Body height (cm)	166.3 (9.3)	
Body mass (kg)	73.0 (13.4)	
BMI (kg·m^{-2})	25.9 (6.0)¶	
Body fat mass (%)	36.3 (7.9)	
Body lean mass (%)	60.2 (7.5)	
Body BMC (%)	3.5 (0.7)	
SMI (kg·m^{-2})	6.4 (1.8)¶	
Adiposity class (normal / high)	30	75
FRAT (low / medium-to-high)	89	16
History of major illness (no / yes)	87	17
Currently on statins (no / yes)	71	34
Currently smoking (no / yes)	102	3
Resistance training within previous 6 months (no / yes)	81	23
Regular consumption of dairy products (no / yes)	5	100
Caffeine intake (no / yes)	18	87
Current RA diagnosis (no / yes)	101	4
Daily alcohol intake ≥3 units (no / yes)	98	5
Calcium/vitamin D supplements intake (no / yes)	90	15

BMI, body mass index; BMC, bone mineral content; FRAT, falls risk assessment tool; RA, rheumatoid arthritis.

Table 4.3. Overview of the study sample's daily sedentary behaviour and physical activity levels.

Accelerometer outcome	Mean (SD) or ¶Median (IQR)	
Sleep (hrs)	8.4 (0.8)¶	
SB (hrs)	9.3 (1.5)	
Standing (hrs)	0.7 (0.3)	
LIPA (hrs)	2.9 (1.0)	
MVPA (hrs)	2.7 (1.0)	
SB level (low/high)	19	86
Breaks SB (n)	22.2 (3.5)	
Short SB bouts (n)	17.0 (3.8)	
Long SB bouts (n)	6.0 (1.2)	
α	1.45 (0.04)	
$X_{1/2}$ (mins)	8.8 (11.8)¶	

$W_{1/2}$ (%)	93.3 (11.2)[¶]	
$W_{50\%}$ (mins)	58.3 (22.9)[¶]	
F (bouts·hrs^{-1})	2.5 (0.7)[¶]	
Period (mins)	10.2 (2.9)[¶]	
PA bouts (n)	22.2 (3.5)	
Total PA bouts time (mins)	365.2 (95.9)	
SB during PA bout (%)	1.5 (0.7)[¶]	
Standing during PA bout (%)	11.8 (4.6)	
LIPA during PA bout (%)	44.2 (11.0)	
MVPA during PA bout (%)	42.5 (12.4)	
MVPA$_{\geq 10\ mins}$ (mins)	3.4 (10.6)[¶]	
sMVPA (mins)	153.5 (57.8)	
Physically active (no/yes)	94	11

SB, sedentary behaviour; PA, physical activity; LIPA, light-intensity physical activity; MVPA, moderate-to-vigorous physical activity; sMVPA, sporadic moderate-to-vigorous physical activity.

Further ageing and SB & PA

Most accelerometer outcomes did not show any significances with age, except for SB, LIPA, long SB bouts, total PA bouts time, LIPA during PA bout and MVPA during PA bout (Table 4.4). SB (0.230, p=0.018), long SB bouts (0.205, p=0.036) and MVPA during PA bout (0.276, p=0.004) were positively correlated with age, while LIPA (-0.370, p<0.001), total PA bouts time (-0.241, p=0.013) and LIPA during PA bout (-0.313, p=0.001) demonstrated negative correlations.

Table 4.4. Correlations between age and accelerometer outcomes.

Accelerometer outcome	Correlation coefficient	P-value
Sleep	0.091	0.354
SB	**0.230**	**0.018**
Standing	-0.145	0.141
LIPA	**-0.370**	**<0.001**
MVPA	0.009	0.924
SB level		0.273
Breaks SB	-0.026	0.793
Short SB bouts	-0.085	0.387
Long SB bouts	**0.205**	**0.036**
α	-0.134	0.175
$X_{1/2}$	-0.085	0.388
$W_{1/2}$	0.098	0.318

W$_{50\%}$	0.185	0.059
F	-0.113	0.250
Mean period between SB bouts	-0.186	0.058
PA bouts	-0.026	0.794
Total PA bouts time	**-0.241**	**0.013**
SB during PA bout	-0.063	0.526
Standing during PA bout	0.012	0.900
LIPA during PA bout	**-0.313**	**0.001**
MVPA during PA bout	**0.276**	**0.004**
MVPA$_{\geq 10\ mins}$	-0.164	0.095
sMVPA	0.043	0.666
Physically active		0.249

SB, sedentary behaviour; PA, physical activity; LIPA, light-intensity physical activity; MVPA, moderate-to-vigorous physical activity; sMVPA, sporadic MVPA, moderate-to-vigorous physical activity. Bold values represent significant outcomes.

Independency of SB & PA

General SB levels appeared independent of physical activity classification (Fisher's Exact test, p=1.000). Log-ratio variances from the compositional data analysis showed similar results, with only sleep and SB having a low log-ratio variance (0.0355) and thus showing co-dependency (Table 4.5). Generally, SB pattern parameters were independent from most PA pattern outcomes, such as SB during PA bout, standing during PA bout, LIPA during PA bout, MVPA during PA bout and MVPA$_{\geq 10\ mins}$ (Table 4.6).

Table 4.5. Log-ratio variances of compositional accelerometer data.

	Sleep	SB	Standing	LIPA	MVPA
Sleep	0.0000				
SB	0.0355	0.0000			
Standing	0.2912	0.3934	0.0000		
LIPA	0.1615	0.2661	0.2228	0.0000	
MVPA	0.2064	0.2667	0.3928	0.2982	0.0000

SB, sedentary behaviour; PA, physical activity; LIPA, light-intensity physical activity; MVPA, moderate-to-vigorous physical activity.

Table 4.6. SB-PA independencies for daily SB pattern parameters.

	PA bouts	Total PA bouts time	SB during PA bout	Standing during PA bout	LIPA during PA bout	MVPA during PA bout	MVPA$_{\geq 10}$ mins	sMVPA
Breaks SB	**1.000****	**0.275****	0.096	-0.155	**-0.192***	**0.223***	0.085	**0.323****
Short SB bouts	**0.947****	**0.450****	0.074	-0.125	-0.108	0.138	0.087	**0.389****
Long SB bouts	-0.124	**-0.691****	0.027	-0.026	-0.197	0.182	-0.039	**-0.341****
α	**0.325****	**0.486****	0.078	-0.103	0.102	-0.056	-0.106	**0.315****
X$_{1/2}$	**-0.489****	**-0.516****	0.098	0.017	0.079	-0.075	**-0.239***	**-0.404****
W$_{1/2}$	**0.219***	**0.256***	-0.125	-0.037	-0.078	0.070	**0.213***	**0.212***
W$_{50\%}$	**-0.527****	**-0.635****	0.087	-0.017	0.049	-0.059	**-0.237***	**-0.476****
F	**0.670****	**0.785****	-0.026	-0.066	-0.064	0.096	0.173	**0.622****
Mean period between SB bouts	**-0.329****	**0.747****	**-0.222***	0.140	0.173	-0.191	0.157	**0.306****

SB, sedentary behaviour; PA, physical activity; LIPA, light-intensity physical activity; MVPA, moderate-to-vigorous physical activity; sMVPA, sporadic moderate-to-vigorous physical activity. *P<0.05; **P<0.01.

Discussion

At the beginning of this chapter it was hypothesised that (i) the cross-sectional study sample would be representative and (ii) SB and PA measures would show to be both affected by age and independent. Generally, our data showed similar values to the general adult UK population in terms of anthropometrics (120) and gender distribution in elderly (121). Even including most participants aged 60-69 years, then aged 70-79 years and finally ≥80 years, is in accordance with the age groups' prevalence within the general population (121). Also, SB/PA levels and adherence to current UK PA guidelines are more or less in line with existing literature (17,27,28,92). Thus, the first hypothesis was confirmed.

The fact that both an increase in SB and decline in LIPA occurred with ageing, was in agreement with previous studies (27,122,123). A brief check of sex differences in outcomes such as total daily SB/PA, SB breaks and number of short/long SB bouts, showed similar outcomes with other reports too (17,22,27,32,124,125). Furthermore, the independencies found between SB and PA for the different levels of statistical analyses, were as expected. Therefore, the second hypothesis was also confirmed.

Conclusion

Overall, the cross-sectional study sample as described in this chapter, appears representative for the older UK population. SB and PA differed independently during further ageing, with SB increasing and PA decreasing respectively. This population is thus a good sample to study the effects of SB and PA separately and in combination on gastrocnemius medialis muscle-tendon properties in older adults within the next chapters.

Chapter 5. The association between sedentary behaviour and both resting skeletal muscle size and architecture in community-dwelling older adults

Introduction

Skeletal muscle ageing is a phenomenon characterised by a decrease in muscle mass (126) and strength (44,127–129), a decrease in agonist activation (130) and an increase in antagonist co-contraction (131). Generally, this results in a decreased functional capacity (132), and an increased disability and physical dependence of elderly (133–135). In addition, the increased morbidity, higher rate of hospitalisation and mortality after bone fractures due to falls in old age have been reported to be associated with lower muscle strength (136,137).

Apart from sarcopenia, an age-related drop in habitual physical activity (PA) levels are thought to, at least partially, explain some muscle ageing effects (130,138). Although evidence is limited and conflicting, sedentary behaviour (SB) is also suggested to be independently associated with muscle health (90). Multiple studies have reported a negative relationship between SB on one side and functional fitness and performance on the other (139–142). SB has also been identified mediating the association between obesity and falls in elderly (143). Especially the relation between SB and obesity is interesting, as it suggested that sarcopenia is catalysed by the amount of visceral and intramuscular fat tissue (5). Gianoudis et al. (5) examined the relation between sarcopenia and SB, and found that (i) higher overall daily sitting time resulted in a 33% increased risk of having sarcopenia and (ii) TV viewing time was inversely related to total body and leg lean mass. This latter finding was confirmed by another study, which suggested a direct relationship between (lower limb) adiposity in older men and SB (42). Counter-intuitively, they also found that increased and prolonged SB was associated with increased leg power and muscle quality (42). Although one study (42) quantified SB objectively, the other used subjective measures (5), which makes the validity of their study results questionable.

Besides muscle mass and fibre type composition, the power output, force generating capacity and maximal shortening velocity are also influenced by the architecture of the muscle (144–147). The muscle architecture is often described in terms of fascicle length (L_F), pennation angle (θ) and physiological cross-sectional area (PCSA), where the latter provides a more accurate measure of the contractile area than muscle anatomical cross-sectional area, especially for pennate muscles (as in this chapter) (148). PCSA is calculated

by dividing muscle volume (V_M) by L_F, and thus represents the number of parallel sarcomeres, which makes it directly proportional to maximum force production of the muscle (144,149). However, this is not the force at the tendon as not all force is transmitted according to the line of pull; to take that into account, the force has to be multiplied by the cosine of the angle of pennation, and preferably so during a maximal contraction (150). Clearly, skeletal V_M and architecture are highly significant for accurate understanding of muscle health. With ageing, not only V_M, but also L_F, θ and muscle PCSA are reduced (151), where the reduction in θ brings the muscle fascicles more in the line of pull and hence attenuates some of the loss of power and force in old age (147). Apart from ageing, other factors also have a significant impact on skeletal muscle, such as sex, body composition, genetic constitution and training status (152–156). Thus, it is important to consider some or at best all these factors when examining any effects on muscle size and architecture in a cross-sectional study of an aged population.

Overall, the literature has suggested several factors that contribute to muscle ageing, in which SB potentially might play a role. For example, as stated above, lower habitual daily activity levels might result in age-related muscle weakness (130). The same accounts for increased intramuscular fat infiltration, as seen in obesity. SB is proposed to cause muscle atrophy due to disuse, and to contribute to obesity due to a lack of movement (90). Furthermore, SB measures appeared independent of (most) PA outcomes (Chapter 3). Hence, SB might have adverse effects on skeletal muscle size and architecture, independent of factors such as age, sex, body composition and concurrent PA. To our knowledge, no study has yet comprehensively investigated the effect of SB on skeletal muscle size and architecture in a cross-sectional young-old to older-old population.

Therefore, the main aim of this chapter was to examine the independent association between SB and both resting skeletal muscle size and architecture in older adults. Different measures of SB were studied, respectively (i) SB level classification, (ii) total daily SB and (iii) daily SB patterns. It was hypothesised that muscle size and architecture are inferior in older adults with high vs. low SB, regardless of adherence to PA guidelines. Moreover, both total daily SB and daily SB patterns were hypothesised to be (detrimentally) associated with muscle size and architecture in the elderly.

Materials and methods

As described in Chapter 4 of this thesis, 105 healthy older adults participated in this cross-sectional study. As per the test protocol, participants came to the university for a second visit after the habitual daily activity monitoring week. During this visit, muscle size and architecture of the gastrocnemius medialis (GM) was assessed.

SB and PA outcomes

See chapter 4 for a detailed overview of the SB and PA outcomes used in this chapter.

Muscle size

For the assessment of the GM size, participants were placed in a prone position with their self-perceived dominant leg (preferred for single leg balance) extended and ankle fixed at a 90° angle (no plantar- (PF) or dorsiflexion (DF)). Real-time B-mode ultrasonography (Technos; Esaote S.p.A, Genoa, Italy) was used to assess GM muscle architecture. Firstly, the GM origin (0% GM length) and Achilles tendon insertion into the calcaneus were determined and marked by scanning these sites in a sagittal plane. The distance between these two sites represented the muscle-tendon unit length (L_{MTU}; cm). Next, the myotendinous junction was determined. Muscle length (L_M; cm) was defined as the distance between GM origin and the myotendinous junction (0-100% GM length). Knowing L_M allowed to position the ultrasound probe at 25, 50 and 75% GM length, which were marked on the skin using a water-soluble pen across the GM width. Thin strips (~2 mm) of micropore tape (Transpore, 3M, USA) were placed in axillary lines (~3.5 cm apart) along the GM length and across the three marked muscle sites (Figure 5.1). They served as echo-absorptive markers for the reconstruction of the muscle sites' anatomical cross-sectional area (ACSA). Water-soluble transmission gel (Aquasonic 100; Parker Laboratories Inc., Fairfield, NJ, USA) was placed over the ultrasound probe head to improve acoustic coupling during ultrasound scanning. Each section was then transversally scanned across the marked pathway from the medial to the lateral GM border, during which the ultrasound probe (7.5-MHz linear-array probe, 3.8 cm wide) was held perpendicular to the skin for the duration of the scanning procedure. While moving the probe steadily, minimal pressure was applied to avoid compression of muscle tissue. The ultrasound picture was recorded in real time onto a computer (25 frames per second) using capturing software (Adobe Premier Pro version 6), which allowed offline extraction of individual transverse frames. The shadows projected by the micropore tape and anatomical markers were used to reconstruct the

ACSAs at each of the three GM lengths of interest (25 (ACSA25), 50 (ACSA50) and 75% (ACSA75)) with photo editing software (Adobe Photoshop Elements, version 10) (Figure 5.2). The complete ACSAs were measured (cm^2) using digitising software (ImageJ 1.45; National Institutes of Health, Bethesda, MD, USA). Finally, muscle volume (V_M; cm^3) was calculated using the truncated cone method, which required the three measured ACSAs plus two assumed ACSAs at the GM origin (0%) and insertion (100%). For the latter two, a standard area of 0.5 cm^2 was used as previously done in our and other research groups. In total, the volumes of four different cones (0 - 25, 25 - 50, 50 - 75, and 75 - 100%) were calculated and summed for the muscle volume. The calculation of each cone volume was carried out using the following formula:

$$\text{Cone volume } (cm^3) = (h/3) * (ACSA_{base} + \sqrt{(ACSA_{base} * ACSA_{top})} + ACSA_{top})$$

where h = distance between the segments (cm), $ACSA_{base}$ = anatomical cross-sectional area (cm^2) of the cone base, and $ACSA_{top}$ = anatomical cross-sectional area (cm^2) of the cone top.
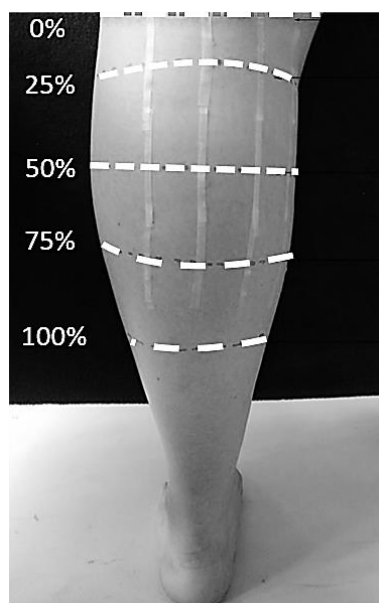
Figure 5.1. Example of a marked leg.

Figure 5.2. Anatomical cross-sectional area of the gastrocnemius medialis at 50% muscle length.

Muscle architecture

Architecture of the GM was measured with real-time B-mode ultrasonography while participants were seated in an isokinetic dynamometer (Cybex Norm; Cybex International, New York, NY, USA) with their hip at 85° angle, self-perceived dominant leg extended and foot secured to the footplate of the dynamometer at 90° angle (no PF or DF). Non-extending straps were used at the hip, distal thigh and chest to prevent extraneous movements. Resting measures of L_F and θ were obtained by placing the ultrasound probe perpendicular to the dermal surface in the mid-sagittal plane at 50% of the GM muscle length (Figure 5.3). Again, water-soluble transmission gel was placed over the ultrasound probe head to improve acoustic coupling during ultrasound scanning. The ultrasound picture was recorded in real time onto a computer using capturing software, from where individual images were extracted for post-testing analyses. L_F and θ were analysed on these images using digitising software. To do so, three fascicles had to be clearly visible in the area between the deep and superficial aponeuroses. L_F (cm) and θ (°) (defined as the angle between a fascicle's orientation and the tendon axis) were measured for all three fascicles, with the mean value recorded as the participant's data. In cases where a chosen fascicle extended beyond the scanning window, linear extrapolation was applied, but only if ≥60% of the fascicle was visible (151). These extrapolations have previously been shown to be valid (157).

With having the L_M, L_F and V_M measured, calculation of normalised fascicle length (L_{F-N}) and resting PCSA (cm^2) was performed. The first was done by dividing L_F (cm) by L_M (cm), while for the second V_M (cm^3) was taken over L_F (cm).
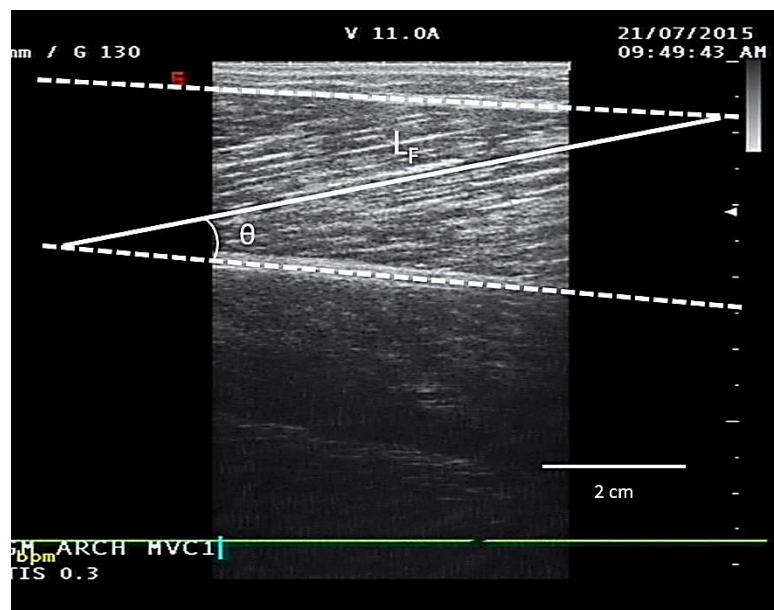
Figure 5.3. Muscle architecture at 50% gastrocnemius medialis muscle length.

L_F, fascicle length; θ, pennation angle. Upper dashed line represents superficial aponeurosis, bottom dashed line represents deep aponeurosis.

Reliability

Test-retest reliability for ultrasound scanning was investigated by intraclass correlation coefficients (ICCs) for absolute agreement using a two-way mixed model. Reliability values <0.5 were interpreted as poor, between 0.5 - 0.75 as moderate, between 0.75 - 0.9 as good and >0.9 as excellent (158). ICCs for the main muscle size properties measured in this chapter, were L_M = 0.941, ACSA25 = 0.824, ACSA50 = 0.910 and ACSA75 = 0.974. Main GM muscle architecture outcomes appeared to have ICCs of 0.700 for L_F and 0.645 for θ.

Statistical analyses

The outcome variables are displayed as mean (standard deviation (SD)) or median (interquartile range (IQR)) (Table 5.1). Prior to conducting any inferential statistical analysis, all outcome variables were checked for normality (either Kolmogorov-Smirnov or Shapiro-Wilk test). In case of non-normality, the variables were log-transformed and the distribution of the transformed data also checked. Since postural balance was performed in a subsample only, their representativeness of the whole study sample was assessed using an Independent samples T-test or Mann-Whitney U test. Potential covariates were

analysed per outcome variable by running a univariate General Linear Model (GLM). When a parameter appeared significant, it was treated as a covariate (Table 5.2). Since daily time spent in sleep, SB and physical activity (PA) is constrained to 24 hours, we used compositional data analysis for these accelerometer outcomes. This type of analysis has been described in detail previously (118,119). Briefly, daily compositions are transformed into isometric log-ratio coordinates, which are then unconstrained and allow the application of traditional multivariate statistics. In this chapter, both single and multiple linear regression analysis was used to study the associations with SB levels, proportional total daily SB and PA, and daily SB pattern parameters. The identified covariates were added to the regression models first, by using backward elimination, after which the predictor(s) of interest was/were entered. During backward elimination, parameters were retained if p-values were <0.20 (118). For all models, Durbin-Watson statistics (>1.0 and <3.0) were checked to identify any correlation between the predictor and covariates, and covariates with variance inflation factor ≥10.0 were removed from the regression model, one at the time. The same was done with individual cases showing Cook's distance ≥1.0. If significant associations were observed for the compositional data, isotemporal substitution was applied to the identified models including covariates, to calculate the relative effects (%) of re-allocating 10 minutes from one behaviour to the other, with respect to the study sample's mean outcomes. Ten minutes was chosen, not only because of its beneficial effects (for example when moderate-to-vigorous PA (MVPA) is performed) (159), but also because it is a realistic amount of time to replace in most elderly.

All statistical analyses were performed using IBM SPSS Statistics for Windows, version 24.0 (IBM Corp., Armonk, NY, USA) and p-values <0.05 were considered statistically significant.

Results

Descriptive statistics

Table 5.1 shows the study sample's descriptive statistics of the GM size and architecture.

Table 5.1. Study sample descriptive statistics of resting gastrocnemius medialis muscle size and architecture.

Resting GM variables	Mean (SD) or ¶median (IQR)
L_{MTU} (cm)	40.1 (3.5)
L_M (cm)	22.3 (3.2)
ACSA25 (cm^2)	11.6 (4.4)¶
ACSA50 (cm^2)	15.0 (5.3)¶
ACSA75 (cm^2)	8.8 (4.6)¶
V_M (cm^3)	185.5 (82.7)¶
L_F (cm)	7.4 (1.2)
L_{F-N}	0.34 (0.06)
θ (°)	15.2 (2.5)
PCSA (cm^2)	26.0 (10.0)¶

GM, gastrocnemius medialis; SD, standard deviation; IQR, interquartile range; L_{MTU}, muscle-tendon unit length; L_M, muscle length; ACSA, anatomical cross-sectional area; V_M, muscle volume; L_F, fascicle length; L_{F-N}, normalised fascicle length; θ, fascicle pennation angle; PCSA, physiological cross-sectional area.

Covariate analysis

The variables identified as covariates in this chapter, were: age, sex, body height, body mass, body mass index (BMI), skeletal muscle index (SMI), body fat mass, body lean mass, body bone mineral content (BMC), adiposity class, falls risk assessment tool (FRAT) score, menopause age, history of major illness, current resistance training, intake of dairy products, current rheumatoid arthritis diagnosis, calcium/vitamin D supplement usage, number of daily PA bouts, SB during PA bouts, standing during PA bouts, light-intensity PA (LIPA) during PA bouts and MVPA during PA bouts (Table 5.2).

Table 5.2. Correlation coefficients of covariate analysis.

	L_{MTU}	L_M	ACSA25[¶]	ACSA50[¶]	ACSA75[¶]	V_M[¶]	L_F	L_{F-N}	θ	PCSA[¶]
Age	-0.037	**-0.287**	**-0.230**	**-0.193**	-0.171	**-0.289**	-0.158	0.115	0.032	**-0.258**
Sex	**0.649**	**0.338**	0.167	**0.226**	**0.304**	**0.339**	0.144	-0.161	0.087	**0.338**
Ethnicity	-0.156	-0.115	-0.101	-0.078	-0.156	-0.140	-0.138	-0.046	-0.079	-0.085
Body height	**0.799**	**0.491**	**0.282**	**0.235**	**0.235**	**0.416**	**0.207**	**-0.220**	-0.035	**0.385**
Body mass	**0.508**	**0.347**	**0.500**	**0.580**	**0.487**	**0.593**	0.174	-0.142	**0.286**	**0.619**
BMI	0.032	0.055	**0.361**	**0.478**	**0.379**	**0.374**	0.035	-0.026	**0.347**	**0.433**
SMI	**0.489**	**0.347**	**0.431**	**0.490**	**0.482**	**0.543**	**0.193**	-0.116	**0.295**	**0.555**
Fat mass	**-0.458**	**-0.263**	0.085	0.137	0.021	-0.036	-0.089	0.127	0.129	-0.003
Lean mass	**0.450**	**0.257**	-0.081	-0.137	-0.020	0.035	0.086	-0.125	-0.117	0.002
BMC mass	**0.397**	**0.252**	-0.097	-0.101	-0.022	0.042	0.090	-0.116	**-0.225**	0.012
Adiposity class	0.062	-0.054	**0.304**	**0.409**	**0.282**	**0.270**	0.026	0.037	**0.289**	**0.310**
FRAT score	-0.158	**-0.195**	-0.125	-0.148	-0.178	**-0.219**	-0.156	0.005	0.035	-0.167
Menopause age	0.050	0.128	0.039	-0.232	**-0.280**	-0.075	0.058	-0.080	-0.141	-0.121
Major illness history	**0.232**	0.159	0.025	0.143	0.152	0.161	-0.039	-0.170	-0.004	**0.208**
Statins usage	0.123	0.009	-0.005	0.002	0.073	0.021	0.039	0.029	0.017	0.002
Smoking	**-0.199**	**-0.241**	-0.158	-0.072	-0.022	-0.179	-0.116	0.124	0.002	-0.150
Resistance training	-0.005	0.124	0.083	-0.030	-0.048	0.051	**0.213**	0.104	-0.181	-0.053
Dairy products	-0.041	0.039	0.040	-0.071	-0.076	-0.021	**-0.244**	**-0.273**	0.143	0.104
Caffeine intake	0.150	0.090	0.063	-0.008	0.030	0.059	0.099	0.016	-0.171	0.018
RA diagnosis	0.086	0.079	0.082	**0.195**	**0.219**	0.178	0.005	-0.058	0.084	**0.204**

Daily alcohol intake ≥3 units	0.188	0.155	0.024	0.100	0.161	0.150	0.056	-0.085	0.010	0.168
Calcium/vitamin D supplements	**-0.205**	-0.080	-0.079	-0.101	-0.090	-0.110	-0.010	0.048	-0.052	-0.128
PA bouts	0.129	0.140	0.040	0.112	0.104	0.137	**0.211**	0.072	-0.020	0.053
Total PA bouts time	-0.083	0.008	0.065	-0.090	-0.048	-0.021	0.170	0.167	-0.095	-0.119
SB during PA bout	-0.184	-0.097	-0.172	-0.127	**-0.200**	-0.180	-0.026	0.068	-0.094	**-0.206**
Standing during PA bout	-0.111	0.049	0.023	0.084	0.100	0.088	-0.041	-0.077	**0.267**	0.125
LIPA during PA bout	**-0.269**	-0.055	0.005	-0.006	-0.022	-0.029	0.007	0.053	-0.053	-0.033
MVPA during PA bout	**0.291**	0.036	-0.004	-0.019	-0.007	0.003	0.011	-0.022	-0.046	-0.006
MVPA$_{\geq 10\ mins}$	0.042	0.007	0.108	-0.031	0.067	0.033	-0.004	-0.020	-0.003	0.040
sMVPA	0.177	0.049	0.039	-0.047	-0.040	0.006	0.123	0.084	-0.088	-0.064
Physical activity status	0.052	-0.006	0.036	-0.032	0.095	0.016	-0.048	-0.037	0.001	0.045

L_{MTU}, muscle-tendon unit length; L_M, muscle length; ACSA, anatomical cross-sectional area; V_M, muscle volume; L_F, fascicle length; L_{F-N}, normalised fascicle length; θ, fascicle pennation angle; PCSA, physiological cross-sectional area; BMI, body mass index; BMC, bone mineral content; Skeletal muscle index; FRAT, falls risk assessment tool; RA, rheumatoid arthritis; PA, physical activity; SB, sedentary behaviour; LIPA, light-intensity physical activity; MVPA, moderate-to-vigorous physical activity; sMVPA, sporadic moderate-to-vigorous physical activity; ¶Log-transformed. Bold values represent significances at P<0.05 level.

No significant associations were identified between SB levels and both resting GM size and architecture in older adults, except for θ (β = 0.21, R^2_{adj} = 0.036) (Table 5.3). However, these associations disappeared when adjusting the regression models for covariates. The effect sizes of the models with covariates appeared 0.105 ≤ R^2_{adj} ≤ 0.834.

Table 5.3. Regression analysis results for sedentary behaviour levels.

	Without covariates				With covariates				
	B	95%-CI		β	R^2_{adj}	B	95%-CI		β	R^2_{adj}
L_{MTU}	0.35	-1.41	2.11	0.04	-0.008	0.20	-0.58	0.97	0.02	**0.834****
L_M	0.01	-1.60	1.62	0.00	-0.010	-0.07	-1.18	1.05	-0.01	**0.576****
ACSA25¶	0.05	-0.07	0.18	0.08	-0.003	-0.01	-0.12	0.10	-0.02	**0.297****
ACSA50¶	0.14	-0.01	0.29	0.18	0.023	0.04	-0.08	0.16	0.06	**0.411****
ACSA75¶	0.11	-0.06	0.28	0.13	0.006	0.03	-0.12	0.18	0.03	**0.283****
V_M¶	0.10	-0.07	0.27	0.11	0.004	0.04	-0.09	0.16	0.04	**0.551****
L_F	-0.25	-0.84	0.34	-0.08	-0.003	-0.06	-0.63	0.51	-0.02	**0.105****
L_{F-N}	-0.01	-0.04	0.02	-0.08	-0.003	0.00	-0.03	0.02	-0.02	**0.209****
θ	**1.36**	**0.15**	**2.58**	**0.21***	**0.036***	0.86	-0.29	2.01	0.13	**0.232****
PCSA¶	0.13	-0.01	0.27	0.18	0.023	0.06	-0.04	0.16	0.08	**0.540****

L_{MTU}, muscle-tendon unit length; L_M, muscle length; ACSA, anatomical cross-sectional area; V_M, muscle volume; L_F, fascicle length; L_{F-N}, normalised fascicle length; θ, fascicle pennation angle; PCSA, physiological cross-sectional area; 95%-CI, 95% confidence interval; ¶Log-transformed; *P<0.05; ** P<0.01.

Daily total SB and PA

Compositional data analysis showed significant associations between time spent in some behaviours relative to the others for a number of muscle size and architecture outcomes (Table 5.4). For example, MVPA was associated with L_{MTU} (β = 0.21, R^2_{adj} = 0.063), both sleep (β = -0.47) and SB (β = 0.60) (both R^2_{adj} = 0.038) with ACSA50, while sleep (β = -0.60) and SB (β = 0.71) (both R^2_{adj} = 0.085) were also associated with ACSA75, and both sleep (β = -0.43) and SB (β = 0.50) (both R^2_{adj} = 0.020) again with V_M. For GM muscle architecture, sleep (β = -0.45), SB (β = 0.58) and standing (β = 0.33) (all R^2_{adj} = 0.110) were associated with θ, while sleep (β = -0.41) and SB (β = 0.55) (both R^2_{adj} = 0.039) were associated with PCSA.

However, when adjusting the regression models for a variety of identified covariates, the above associations changed significantly. Muscle size showed associations between as well sleep (β=-0.49), SB (β=0.41) as LIPA (β=0.27) (all R^2_{adj} = 0.393) and ACSA75, while standing (β=0.17, R^2_{adj} = 0.578) was associated with V_M. Muscle architecture only showed

associations for LIPA with L_F (β=0.24, R^2_{adj} = 0.116) and L_{F-N} (β=0.21, R^2_{adj} = 0.224), and standing with both θ (β=0.31, R^2_{adj} = 0.296) and PCSA (β=0.21, R^2_{adj} = 0.573). Effect sizes for the models showing at least one significant association with time spent in a behaviour relative to the others, were $0.116 \leq R^2_{adj} \leq 0.578$. The adjusted R^2 values for the other models ranged from 0.318 through 0.831. Isotemporal substitution showed that the relative effects of re-allocating 10 minutes from one behaviour to another within the mean composition of the study sample's total daily SB and PA (sleep = 35.6%, SB = 39.4%, standing = 2.8%, LIPA = 11.5% and MVPA = 10.7%) for the models including behaviours significantly associated with muscle size and architecture and adjusted for covariates, varied from -0.041% through +0.033% (Table 5.5). These maximum changes were both seen in ACSA75, when substituting 10 min of standing with sleep and vice versa respectively.

Table 5.4 Regression analysis results for daily total sedentary behaviour and physical activity.

		Without covariates			With covariates		
		B	β	R^2_{adj}	B	β	R^2_{adj}
L_{MTU}	Sleep	-1.22	-0.08		1.00	0.06	
	SB	1.70	0.16		-0.26	-0.02	
	Standing	-0.95	-0.12	**0.063***	-0.06	-0.01	**0.831****
	LIPA	-1.38	-0.13		-0.40	-0.04	
	MVPA	**1.85**	**0.21***		-0.29	-0.03	
L_M	Sleep	-1.43	-0.10		1.72	0.12	
	SB	0.97	0.10		-1.89	-0.20	
	Standing	0.17	0.02	-0.035	0.85	0.12	**0.585****
	LIPA	-0.08	-0.01		-0.34	-0.04	
	MVPA	0.37	0.05		-0.35	-0.04	
ACSA25[¶]	Sleep	-0.37	-0.32		-0.07	-0.06	
	SB	0.22	0.29		-0.08	-0.11	
	Standing	0.03	0.06	-0.009	0.04	0.07	**0.318****
	LIPA	0.07	0.09		0.11	0.15	
	MVPA	0.05	0.07		0.00	0.00	
ACSA50[¶]	Sleep	**-0.64**	**-0.47***		-0.35	-0.26	
	SB	**0.52**	**0.60***		0.20	0.22	
	Standing	0.07	0.11	0.038	0.07	0.10	**0.426****
	LIPA	0.05	0.05		0.16	0.18	
	MVPA	0.00	0.00		-0.07	-0.10	
ACSA75[¶]	Sleep	**-0.96**	**-0.60***	**0.085***	**-0.78**	**-0.49****	**0.393****

	SB	**0.73**	**0.71***		**0.41**	**0.41***	
	Standing	0.15	0.19		0.13	0.17	
	LIPA	0.06	0.06		**0.28**	**0.27****	
	MVPA	0.02	0.03		-0.04	-0.05	
V_M¶	Sleep	**-0.68**	**-0.43***		-0.17	-0.11	
	SB	**0.50**	**0.50***		0.02	0.02	
	Standing	0.09	0.11	0.020	**0.13**	**0.17***	**0.578****
	LIPA	0.05	0.05		0.08	0.08	
	MVPA	0.04	0.04		-0.06	-0.07	
L_F	Sleep	-1.00	-0.19		-1.13	-0.21	
	SB	0.22	0.06		0.36	0.10	
	Standing	-0.09	-0.03	-0.001	-0.19	-0.07	**0.116****
	LIPA	0.51	0.14		**0.83**	**0.24***	
	MVPA	0.37	0.13		0.11	0.04	
L_{F-N}	Sleep	-0.04	-0.15		-0.07	-0.27	
	SB	0.00	0.02		0.04	0.23	
	Standing	-0.01	-0.04	-0.003	-0.01	-0.11	**0.224****
	LIPA	0.03	0.16		**0.04**	**0.21***	
	MVPA	0.01	0.09		0.01	0.07	
θ	Sleep	**-5.16**	**-0.45***		-3.22	-0.28	
	SB	**4.24**	**0.58****		2.63	0.36	
	Standing	**1.84**	**0.33****	**0.110****	**1.70**	**0.31****	**0.296****
	LIPA	-0.67	-0.09		-0.32	-0.04	
	MVPA	-0.25	-0.04		-0.80	-0.13	
PCSA¶	Sleep	**-0.53**	**-0.41***		-0.20	-0.15	
	SB	**0.46**	**0.55***		0.15	0.18	
	Standing	0.10	0.15	0.039	**0.13**	**0.21****	**0.573****
	LIPA	-0.01	-0.02		0.02	0.02	
	MVPA	-0.02	-0.02		-0.10	-0.15	

L_{MTU}, muscle-tendon unit length; L_M, muscle length; ACSA, anatomical cross-sectional area; V_M, muscle volume; L_F, fascicle length; L_{F-N}, normalised fascicle length; θ, fascicle pennation angle; PCSA, physiological cross-sectional area; SB, sedentary behaviour; LIPA, light-intensity physical activity; MVPA, moderate-to-vigorous physical activity; ¶Log-transformed; *P<0.05; ** P<0.01.

Table 5.5. Relative effects (%) on muscle size and architecture of re-allocating proportional time spent in daily total sedentary behaviour and physical activity for regression models showing significant associations.

Outcome variable	+10 mins	-10 mins				
		Sleep	SB	Standing	LIPA	MVPA
ACSA75[¶]	Sleep	+0.000	-0.007	-0.041	-0.013	-0.009
	SB	+0.007	+0.000	+0.013	+0.002	+0.006
	Standing	+0.033	-0.010		-0.006	
	LIPA	+0.012	-0.002	+0.008	+0.000	+0.006
	MVPA	+0.009	-0.006		-0.006	
V_M[¶]	Sleep			-0.006		
	SB			-0.002		
	Standing	+0.005	+0.002	+0.000	+0.001	+0.003
	LIPA			-0.001		
	MVPA			-0.004		
L_F	Sleep				-0.007	
	SB				-0.002	
	Standing				-0.013	
	LIPA	+0.007	+0.002	+0.016	+0.000	+0.004
	MVPA				-0.004	
L_{F-N}	Sleep				-0.008	
	SB				+0.000	
	Standing				-0.014	
	LIPA	+0.008	+0.000	+0.016	+0.000	+0.003
	MVPA				-0.003	
θ	Sleep			-0.033		
	SB			+0.006		
	Standing	+0.026	-0.005	+0.000	+0.012	+0.016
	LIPA			-0.015		
	MVPA			-0.019		
PCSA[¶]	Sleep			-0.010		
	SB			+0.001		
	Standing	+0.008	-0.001	+0.000	+0.003	+0.007
	LIPA			-0.004		
	MVPA			-0.008		

ACSA, anatomical cross-sectional area; V_M, muscle volume; L_F, fascicle length; L_{F-N}, normalised fascicle length; θ, fascicle pennation angle; PCSA, physiological cross-sectional area; SB, sedentary behaviour; LIPA, light-intensity physical activity; MVPA, moderate-to-vigorous physical activity; [¶]Log-transformed.

Daily SB pattern parameters

Only few significant associations with muscle architecture outcomes were found for SB pattern parameters (Table 5.6). L_M was associated with $X_{1/2}$ (β = -0.20, R^2_{adj} = 0.030), while L_F was associated with Breaks SB and Short SB bouts, as $W_{50\%}$ and F were associated (β = 0.21, R^2_{adj} = 0.035; β = 0.21, R^2_{adj} = 0.036; β = -0.24, R^2_{adj} = 0.047 and β = 0.22, R^2_{adj} = 0.041 respectively).

As seen above, adding covariates to the regression models changed identified associations significantly. Only two outcomes showed significant associations, one for muscle size (L_M) and the other for muscle architecture (L_F). For L_M, an association was found with Breaks SB (β = 0.14, R^2_{adj} = 0.590), $W_{50\%}$ (β = -0.21, R^2_{adj} = 0.607) and F (β = 0.17, R^2_{adj} = 0.594), whereas VM was associated with $W_{50\%}$ (β = -0.16, R^2_{adj} = 0.564) and L_F was associated with Breaks SB (β = 0.25, R^2_{adj} = 0.164), Short SB bouts (β = 0.24, R^2_{adj} = 0.159), $W_{1/2}$ (β = -0.20, R^2_{adj} = 0.186) and F (β = 0.24, R^2_{adj} = 0.156). The adjusted R^2 values for the latter regression models including covariates, varied from 0.155 through 0.607. Effect sizes for the other regression models with covariates, were 0.208 ≤ R^2_{adj} ≤ 0.837.

Table 5.6. Regression analysis results for daily sedentary behaviour pattern parameters.

		Without covariates					With covariates				
		B	95%-CI		β	R^2_{adj}	B	95%-CI		β	R^2_{adj}
L_{MTU}	Breaks SB	0.13	-0.07	0.33	0.13	0.007	0.06	-0.02	0.15	0.06	**0.835****
	Short SB bouts	0.06	-0.12	0.24	0.06	-0.006	0.05	-0.02	0.13	0.06	**0.833****
	Long SB bouts	0.51	-0.04	1.05	0.18	0.023	0.05	-0.20	0.30	0.02	**0.833****
	α	-5.52	-22.15	11.12	-0.06	-0.005	0.51	-6.62	7.65	0.01	**0.833****
	$X_{1/2}$	-0.01	-0.02	0.00	-0.16	0.017	0.00	-0.01	0.00	0.00	**0.834****
	$W_{1/2}$	0.03	-0.07	0.12	0.05	-0.007	0.02	-0.02	0.06	0.04	**0.833****
	$W_{50\%}$	-0.02	-0.06	0.01	-0.11	0.004	-0.01	-0.02	0.01	-0.04	**0.832****
	F	-0.18	-1.27	0.91	-0.03	-0.009	0.27	-0.19	0.74	0.05	**0.832****
	Period	-0.20	-0.48	0.08	-0.14	0.010	-0.10	-0.22	0.02	-0.07	**0.837****
L_M	Breaks SB	0.13	-0.05	0.31	0.14	0.010	**0.13**	**0.01**	**0.25**	**0.14***	**0.590****
	Short SB bouts	0.10	-0.07	0.26	0.12	0.004	0.11	0.00	0.22	0.13	**0.587****
	Long SB bouts	0.14	-0.36	0.64	0.06	-0.007	0.01	-0.36	0.39	0.01	**0.576****
	α	2.94	-12.24	18.12	0.04	-0.008	8.05	-2.33	18.43	0.10	**0.584****
	$X_{1/2}$	**-0.01**	**-0.02**	**0.00**	**-0.20***	**0.030***	-0.00	-0.01	0.00	-0.07	**0.580****
	$W_{1/2}$	-0.01	-0.10	0.08	-0.03	-0.009	-0.03	-0.09	0.04	-0.06	**0.579****
	$W_{50\%}$	-0.03	-0.06	0.00	-0.17	0.019	**-0.04**	**-0.06**	**-0.01**	**-0.21****	**0.607****
	F	0.23	-0.76	1.22	0.05	-0.008	**0.84**	**0.16**	**1.53**	**0.17***	**0.594****
	Period	-0.03	-0.29	0.23	-0.02	-0.009	-0.00	-0.19	0.19	-0.00	**0.576****
ACSA25[¶]	Breaks SB	0.00	-0.01	0.02	0.04	-0.008	0.00	-0.01	0.01	0.02	**0.298****

	Short SB bouts	0.00	-0.01	0.01	0.03	-0.009	0.00	-0.01	0.01	0.06	**0.300****
	Long SB bouts	0.01	-0.03	0.05	0.03	-0.009	-0.02	-0.06	0.01	-0.12	**0.309****
	α	-0.13	-1.34	1.09	-0.02	-0.009	-0.24	-1.27	0.80	-0.04	**0.293****
	$X_{1/2}$	0.00	0.00	0.00	-0.04	-0.008	0.00	0.00	0.00	-0.02	**0.302****
	$W_{1/2}$	0.00	-0.01	0.00	-0.09	-0.002	0.00	-0.01	0.01	-0.01	**0.297****
	$W_{50\%}$	0.00	0.00	0.00	-0.06	-0.006	0.00	0.00	0.00	-0.09	**0.304****
	F	0.00	-0.08	0.08	0.00	-0.010	0.05	-0.02	0.12	0.12	**0.311****
	Period	0.00	-0.02	0.02	0.02	-0.009	0.01	0.00	0.03	0.14	**0.314****
	Breaks SB	0.01	-0.01	0.03	0.11	0.003	0.01	0.00	0.02	0.12	**0.425****
	Short SB bouts	0.00	-0.01	0.02	0.05	-0.007	0.01	0.00	0.02	0.12	**0.422****
	Long SB bouts	0.04	-0.01	0.08	0.16	0.016	0.00	-0.04	0.04	-0.01	**0.408****
	α	0.16	-1.26	1.57	0.02	-0.009	0.57	-0.58	1.72	0.08	**0.414****
ACSA50[¶]	$X_{1/2}$	0.00	0.00	0.00	-0.05	-0.007	0.00	0.00	0.00	-0.07	**0.406****
	$W_{1/2}$	-0.01	-0.01	0.00	-0.14	0.010	0.00	-0.01	0.00	-0.05	**0.411****
	$W_{50\%}$	0.00	0.00	0.00	-0.01	-0.010	0.00	0.00	0.00	-0.09	**0.415****
	F	-0.03	-0.12	0.06	-0.06	-0.006	0.05	-0.02	0.13	0.11	**0.419****
	Period	-0.02	-0.04	0.01	-0.14	0.010	0.00	-0.02	0.02	-0.01	**0.408****
	Breaks SB	0.01	-0.01	0.03	0.10	0.001	0.01	-0.01	0.02	0.08	**0.288****
	Short SB bouts	0.00	-0.01	0.02	0.05	-0.007	0.01	-0.01	0.02	0.07	**0.287****
ACSA75[¶]	Long SB bouts	0.04	-0.01	0.10	0.15	0.014	0.00	-0.05	0.05	0.01	**0.282****
	α	0.41	-1.23	2.05	0.05	-0.007	0.52	-0.87	1.92	0.06	**0.286****
	$X_{1/2}$	0.00	0.00	0.00	0.16	0.015	0.00	0.00	0.00	-0.09	**0.286****

	$W_{1/2}$	-0.01	-0.01	0.00	-0.11	0.002	0.00	-0.01	0.01	-0.03	**0.283****
	$W_{50\%}$	0.00	0.00	0.00	-0.02	-0.009	0.00	-0.01	0.00	-0.12	**0.296****
	F	-0.02	-0.13	0.08	-0.04	-0.008	0.05	-0.04	0.15	0.10	**0.291****
	Period	-0.01	-0.04	0.01	-0.10	0.001	0.01	-0.01	0.04	0.09	**0.289****
V_M¶	Breaks SB	0.01	-0.01	0.03	0.14	0.009	0.01	-0.00	0.03	0.12	**0.564****
	Short SB bouts	0.01	-0.01	0.03	0.09	-0.001	0.01	-0.00	0.02	0.12	**0.563****
	Long SB bouts	0.03	-0.02	0.09	0.12	0.005	-0.00	-0.04	0.04	-0.01	**0.549****
	α	0.31	-1.31	1.93	0.04	-0.008	0.60	-0.55	1.75	0.07	**0.554****
	$X_{1/2}$	0.00	0.00	0.00	-0.14	0.009	-0.00	-0.00	0.00	-0.09	**0.557****
	$W_{1/2}$	-0.01	-0.01	0.00	-0.11	0.003	-0.00	-0.01	0.00	-0.06	**0.553****
	$W_{50\%}$	0.00	-0.01	0.00	-0.10	0.000	**-0.00**	**-0.01**	**-0.00**	**-0.16***	**0.564****
	F	0.00	-0.11	0.10	-0.01	-0.010	0.08	-0.00	0.15	0.14	**0.565****
	Period	-0.01	-0.04	0.02	-0.08	-0.003	0.00	-0.02	0.02	0.01	**0.549****
L_F	Breaks SB	**0.07**	**0.01**	**0.14**	**0.21***	**0.035***	**0.09**	**0.02**	**0.15**	**0.25****	**0.164****
	Short SB bouts	**0.07**	**0.01**	**0.12**	**0.21***	**0.036***	**0.08**	**0.02**	**0.13**	**0.24****	**0.159****
	Long SB bouts	-0.06	-0.25	0.12	-0.07	-0.005	0.00	-0.18	0.18	0.00	**0.155****
	α	5.31	-0.17	10.79	0.19	0.025	3.94	-1.51	9.40	0.14	**0.167****
	$X_{1/2}$	0.00	-0.01	0.00	-0.08	-0.004	0.00	0.00	0.01	0.07	**0.174****
	$W_{1/2}$	0.00	-0.04	0.03	-0.02	-0.009	**-0.03**	**-0.07**	**0.00**	**-0.20***	**0.186****
	$W_{50\%}$	**-0.01**	**-0.03**	**0.00**	**-0.24***	**0.047***	-0.01	-0.02	0.00	-0.16	**0.172****
	F	**0.42**	**0.06**	**0.77**	**0.22***	**0.041***	**0.44**	**0.10**	**0.78**	**0.24***	**0.156****
	Period	0.03	-0.07	0.12	0.06	-0.006	0.04	-0.06	0.13	0.08	**0.160****

L_{F-N}	Breaks SB	0.00	0.00	0.00	0.07	-0.004	0.00	0.00	0.00	0.07	**0.214****
	Short SB bouts	0.00	0.00	0.00	0.10	-0.001	0.00	0.00	0.00	0.07	**0.213****
	Long SB bouts	0.00	-0.01	0.00	-0.11	0.003	0.00	-0.01	0.01	0.00	**0.208****
	α	0.18	-0.09	0.44	0.13	0.007	0.11	-0.12	0.35	0.08	**0.215****
	$X_{1/2}$	0.00	0.00	0.00	-0.01	-0.010	0.00	0.00	0.00	0.09	**0.218****
	$W_{1/2}$	0.00	0.00	0.00	0.02	-0.009	0.00	0.00	0.00	-0.03	**0.209****
	$W_{50\%}$	0.00	0.00	0.00	-0.07	-0.005	0.00	0.00	0.00	-0.07	**0.213****
	F	0.02	0.00	0.03	0.17	0.020	0.01	-0.01	0.02	0.09	**0.217****
	Period	0.00	0.00	0.01	0.08	-0.003	0.00	0.00	0.00	0.02	**0.209****
θ	Breaks SB	-0.01	-0.15	0.12	-0.02	-0.009	0.01	-0.11	0.14	0.02	**0.278****
	Short SB bouts	-0.04	-0.17	0.08	-0.07	-0.005	0.00	-0.11	0.11	0.00	**0.278****
	Long SB bouts	0.27	-0.11	0.66	0.14	0.010	0.13	-0.23	0.48	0.06	**0.281****
	α	-8.87	-20.51	2.76	-0.15	0.012	-7.42	-17.41	2.58	-0.12	**0.293****
	$X_{1/2}$	0.00	-0.01	0.01	0.07	-0.005	0.00	0.00	0.00	-0.05	**0.280****
	$W_{1/2}$	-0.03	-0.10	0.04	-0.08	-0.004	-0.01	-0.07	0.05	-0.01	**0.278****
	$W_{50\%}$	0.02	-0.01	0.04	0.13	0.008	0.02	0.00	0.04	0.15	**0.286****
	F	-0.55	-1.31	0.20	-0.14	0.010	-0.23	-0.93	0.47	-0.06	**0.281****
	Period	-0.13	-0.33	0.06	-0.13	0.008	-0.08	-0.26	0.10	-0.08	**0.284****
PCSA¶	Breaks SB	0.00	-0.01	0.02	0.05	-0.007	0.00	-0.01	0.02	0.05	**0.536****
	Short SB bouts	0.00	-0.01	0.01	0.00	-0.010	0.00	-0.01	0.01	0.05	**0.536****
	Long SB bouts	0.04	0.00	0.08	0.17	0.020	0.00	-0.03	0.03	-0.01	**0.534****
	α	-0.35	-1.69	1.00	-0.05	-0.007	-0.03	-1.01	0.95	0.00	**0.534****

$X_{1/2}$	0.00	0.00	0.00	0.19	0.028	0.00	0.00	0.00	-0.10	**0.538****
$W_{1/2}$	-0.01	-0.01	0.00	-0.13	0.007	0.00	-0.01	0.00	-0.04	**0.535****
$W_{50\%}$	0.00	0.00	0.00	0.01	-0.010	0.00	0.00	0.00	-0.03	**0.534****
F	-0.06	-0.14	0.03	-0.13	0.006	0.01	-0.05	0.08	0.03	**0.534****
Period	-0.02	-0.04	0.01	-0.13	0.008	0.00	-0.02	0.02	-0.01	**0.534****

L_{MTU}, muscle-tendon unit length; L_M, muscle length; ACSA, anatomical cross-sectional area; V_M, muscle volume; L_F, fascicle length; L_{F-N}, normalised fascicle length; θ, fascicle pennation angle; PCSA, physiological cross-sectional area; Breaks SB, sedentary behaviour interruptions with ≥2 consecutive minutes upright activity; Short SB bouts, sedentary behaviour bouts <30 minutes duration; Long SB bouts, sedentary behaviour bouts ≥30 minutes duration; α, scaling parameter sedentary bout length distribution; $X_{1/2}$, median SB bout duration; $W_{1/2}$, fraction total sedentary time accumulated in bouts longer than median sedentary bout length; $W_{50\%}$, half of total SB is accumulated in SB bouts ≤ this duration; F, fragmentation index of SB bouts and total SB; Period, mean period between SB bouts; 95%-CI, 95% confidence interval; ¶Log-transformed; *P<0.05; ** P<0.01.

Discussion

Although associations between measures of SB and skeletal muscle outcomes in older adults were identified with non-adjusted regression models, only few associations remained after correcting for covariates. More specifically, general SB was not associated with GM muscle size and architecture in this group of elderly. In addition, total daily time spent in SB relative to other daily behaviours, showed no associations with any resting skeletal muscle outcome, except for a positive instead of the hypothesised negative association with ACSA75, meaning that the ACSA at 75% GM length will increase with more SB. Looking into more detail we found, however, that L_M was positively associated with more breaks in SB, bouts of longer duration that make up 50% of total daily SB and higher ratio of SB bouts to total SB, whereas V_M is negatively associated with bouts of longer duration that make up 50% of total daily SB and L_F increased with a higher number of either SB breaks, SB bouts <30 minutes duration or ratio of SB bouts to total SB and decreased with a greater fraction of total sedentary time accumulated in bouts longer than the median sedentary bout length. Apart from SB, more proportional time spent sleeping was found to decrease ACSA at 75% GM length in elderly, while the opposite occurred with time spent in LIPA relative to other daily behaviours. Furthermore, increased time spent standing relative to other daily behaviours will increase not only GM volume in older adults, but also θ and PCSA. Finally, higher proportions of daily time spent in LIPA was suggested to increase L_F and L_{F-N}. Overall, these findings show that long bouts of SB with little interruptions have a negative impact on muscle, which can be counteracted by performing regular light physical activity.

The fact that no significant associations were observed for SB levels, might result from the classification used, which is very general and only requires daily total SB to distinguish between low and high SB (160). Since total SB can be similar between people, but patterns, and thus health associations, completely different, using overall volume measures is inconclusive (9). Moreover, with SB being part of a composition of daily activity behaviours, focusing on SB volume alone may lead to incorrect results (118). Therefore, we also used both compositional data analysis and studied SB pattern parameters to assess whether this would show any associations with resting muscle size and architecture.

Nevertheless, the observation of increased ACSA75 with more time spent in SB relative to other behaviours seems counter-intuitive. However, the negative association between SB and body mass in elderly (Chapter 1), imposing a larger load on the muscle may well explain

this finding. This is in agreement with previous literature, which proposed that increased fat mass induce extra loading on skeletal muscles of the lower limb (161), resulting in higher absolute muscle strength, possibly due to greater total body mass (162). This was systematically demonstrated by Tomlinson et al. (153) who found positive correlations (all $r \geq 0.39$) between measures of body composition (e.g. BMI, body mass and fat mass) and GM θ, V_M and PCSA. However, since extensive covariate analysis was performed prior regression model development in this chapter, the finding of increased ACSA75 with more time spent in SB relative to other behaviours cannot be explained by any of the studied covariates. Since both SB and ageing potentially result in skeletal muscle fat infiltration, this could also explain an increase in ACSA75. In this chapter muscle morphology was determined, but not composition. Thus, it is possible that the increase in ACSA is due to fat infiltration rather than muscle tissue growth. Unfortunately, we only assessed whole-body composition instead of lower limb too. Nevertheless, the results of time re-allocation for SB showed only very small relative effects on ACSA75, respectively $\leq 0.013\%$ increase when adding 10 minutes to daily total SB and $\leq 0.010\%$ decrease when losing 10 minutes of SB. Therefore, it can be questioned whether daily total SB will noticeably affect GM size, in this case ACSA75. The same applies to all the identified associations with other daily total behaviours, such as sleep, standing and LIPA. Their relative effects on a variety of muscle size and architecture outcomes for substituting 10 minutes from one behaviour to another, do not exceed 0.041%. Given that mechanical overload, as in resistance training, is important to achieve changes in muscle size and architecture (163), it seems plausible that the relative effects of habitual daily activities, which generally lack overloading, are at best very small only. Interestingly, most of the identified associations with compositional data analysis (75.0%) incorporate either standing or LIPA. However, it is important to note that both behaviours have shown issues with accurate classification previously (Chapter 2 & 3), which may affect results.

Apart from total daily SB, it is important to focus on daily SB patterns, as total amounts could be similar but with different patterns. Generally, our results did not show any effects of SB pattern parameters on GM muscle size and architecture, except for L_M, V_M and L_F. The first outcome appeared to increase with better daily SB patterns, in this case more SB breaks, shorter bout durations making up 50% of total SB and higher ratio of SB bouts to total SB. Similarly, V_M was found to increase when shortening the bout durations making up 50% of total SB. With regards to L_F, this outcome appeared to become longer with 'better' daily SB patterns, which is a likely and positive result to note. However, it is

important to stress that no associations were found for L_{F-N}, which suggests that the identified associations between daily SB pattern parameters and L_F should be interpreted with caution. This is particularly true because the average L_F in this chapter is higher than reported in previous studies which also examined GM muscle architecture in elderly (127,153,164,165). However, these studies did not assess L_F (or any other size and architecture outcomes) with the foot in a 90° angle and an extended leg, as we did.

Having good-to-excellent ICCs for most (4 out of 6) of the muscle outcomes tested in this chapter showed that the collected data was reliable. Although, the remaining two outcomes (L_F and θ) showed lower ICCs of 0.700 and 0.645 respectively, these values could still be interpreted as moderate reliability. Therefore, the data in this chapter was generally regarded as being of acceptable quality, which is a major strength.

Conclusion

Regardless of the few identified associations, considerable changes in resting GM size and architecture due to SB seem questionable in older adults. What the implication of relationships and exact associations with other GM outcomes will be, such as muscle force generating capacity, is yet not clear.

Chapter 6. The association of sedentary behaviour with skeletal muscle strength, specific force and function in older adults

Introduction

According to the World Health Organization (WHO), over the next decades the proportion of older adults in the worldwide population will nearly double (from 12% to 22%). With this group being highly sedentary (27,28), research into the physiological effects of sedentary behaviour (SB) is becoming more prevalent. Although SB is defined as any waking behaviour characterised by an energy expenditure ≤1.5 times the resting metabolic rate while in a sitting, reclining or lying posture (10), it could also be thought of as infrequent skeletal muscle contractile activity (166). This is important as the literature suggests that SB affects skeletal muscle independent of the level of physical activity (90).

As the increased longevity results in an ever-increasing proportion of the population at older age, muscle ageing becomes more and more an issue as it plays an important role in the maintenance of physical independence and hence quality-of-later life. Skeletal muscle ageing is associated with decreased agonist activation capacity, increased antagonist co-activation, decreased muscle mass, smaller pennation angle and fascicle length, and reduced muscle strength (127,130,151). These age-related changes in muscle properties, often summarised under the term sarcopenia, are arguably the most significant challenges in the elderly (136). Like SB, sarcopenia increases with ageing and affects anybody from the highly active to the highly sedentary (167,168). Sarcopenia is not only considered a major factor in the decline of muscle strength, but also function (38,168,169). This results in major functional limitations for activities of daily living, increased morbidity, reduced quality of life, and higher rates of hospitalisation and mortality after falling in older adults (36,40,116,137). Further age-related muscular changes, are: larger proportion of non-contractile material and lower muscle specific force (force per unit physiological cross-sectional area (PCSA)) (127,170), which are likely caused by increased intramuscular fat (116). Interestingly, it is suggested that due to a combination of some ageing-induced changes, such as lower maximal motor unit discharge rates, slower contractile properties and relatively greater reliance on oxidative metabolism, elderly actually have better muscle fatigue resistance than young people (171). Nevertheless, with a well-established link between low levels of physical activity (PA) and obesity, it is expected for SB to play a role in weakening of the muscles.

Although PA has previously been linked to muscle strength and force, with previous research showing PA to be a modulator of neural activation (172) and that reduced PA levels can account for decreased fibre-specific tension (173), SB has only received little scientific attention to date. Especially in the elderly, the proof of SB effects on musculoskeletal health is scarce and in some cases counterintuitive. Generally, evidence exists that SB is not only associated with lower lean and higher fat mass, an increased risk of sarcopenia and limited physical function, but also increased leg power and muscle quality (for a review, read Wullems et al. (90)). However, the authors presenting the latter finding warned to interpret their results with caution. Of the studies on SB in elderly, most focus on functional fitness, whereas the studies on musculoskeletal health have limitations. For example, Gianoudis et al. (5) used self-reported measures of SB and uncorrected muscle strength, while Chastin et al. (42) used muscle power and lower limb fat free mass to define muscle quality. Thus, neither of both studies determined specific muscle force (normalising fascicle force to PCSA), which allows direct comparison between individuals after correcting for confounding variables such as muscle architecture, tendon moment arm length or neural drive (127). Also, no studies have used compositional data analysis to investigate associations between SB and muscle properties yet. Therefore, the true association between SB and muscle properties in older adults is still unknown. Since physical disability is largely determined by the lower limbs (36) and calf muscle-tendon properties may explain the majority of variance in postural balance for example (44), investigation of the calf muscle-tendon complex is important in the oldest age group.

The aim of the present study was to examine the association of SB with gastrocnemius medialis (GM) muscle strength, force and function in elderly. Associations were determined for different SB outcomes, respective total daily SB level, proportional total daily SB, and daily SB pattern parameters. It was hypothesised that (i) intrinsic GM muscle strength, (ii) GM specific force, and (iii) GM function are inferior when exhibiting high SB levels, regardless of being sufficiently physically active or not. Additionally, both proportional total daily SB and daily SB pattern parameters were expected to be detrimentally associated with all studied GM muscle outcomes in older adults.

Materials and methods

As described in Chapter 4 of this thesis, a total of 105 healthy older adults participated in this cross-sectional study. Per protocol, participants came to the university twice, at the

first visit they were familiarised with the testing equipment and an activity monitor was provided, while on the second visit (after a week of physical behaviour monitoring) they underwent muscle strength and function tests.

SB and PA outcomes

See chapter 4 for a detailed overview of the SB and PA outcomes used in this chapter.

Muscle strength

Participants sat on the chair of an isokinetic dynamometer with their hip at 85° angle, self-perceived dominant leg (preferred leg for single leg balance) extended and foot secured to the footplate of the dynamometer and the lateral malleolus aligned with the axis of rotation. Non-extending straps were used at the hip, distal thigh and chest to prevent extraneous movements. After a series of five submaximal plantar- (PF) and dorsiflexion (DF) contractions that served as a warm-up (50 - 75% self-perceived maximum voluntary contraction (MVC) with 10% increments), the ankle range of motion (RoM) was assessed. The ankle angles included the neutral position (no PF or DF) and angles of 10° increments towards, and including, maximum PF and DF. In every angle participants performed two rapid isometric MVCs of 2 - 3 second duration, whilst verbal encouragement and biofeedback were provided by the experimenter during each effort. Per trial, a combination of PF and DF MVC was performed, with 30-60 seconds between the trials (Figure 6.1). In case >10% difference was observed for PF, extra MVCs (maximum four in total) were performed to obtain the true maximal torque values. The PF/DF combination with the highest PF value was used for data analyses. Performing the above test, allowed to determine torque-angle relationships per participant.

To calculate true PF torques, antagonist co-activation was determined using surface electromyography (sEMG). After appropriate skin preparation, two bipolar Ag-AgCl sEMG electrodes (Ambu A/S, Ballerup, Denmark) were placed 20 mm apart at the proximal third of the tibialis anterior (TA) muscle belly on the line between the caput fibulae and the medial malleolus, with a reference electrode positioned on the ankle (SENIAM). The sEMG signal was sampled at 2,000 Hz and filtered using high- and low-pass filters set at 10 and 500 Hz, respectively (plus notch filter at 50 Hz). The median root mean square (RMS) of the sEMG signal was calculated over 1 s around the peak torque during each rapid PF and DF MVC. Eventually, antagonist torque output during PF MVC was calculated by dividing TA sEMG RMS during PF MVC by TA sEMG RMS during DF MVC, and multiplying DF MVC torque

by this ratio. Multiplying the same ratio by 100 resulted in percentage TA co-activation. The sum of the antagonist torque and PF MVC torque represented the net PF MVC (nMVC; N·m).
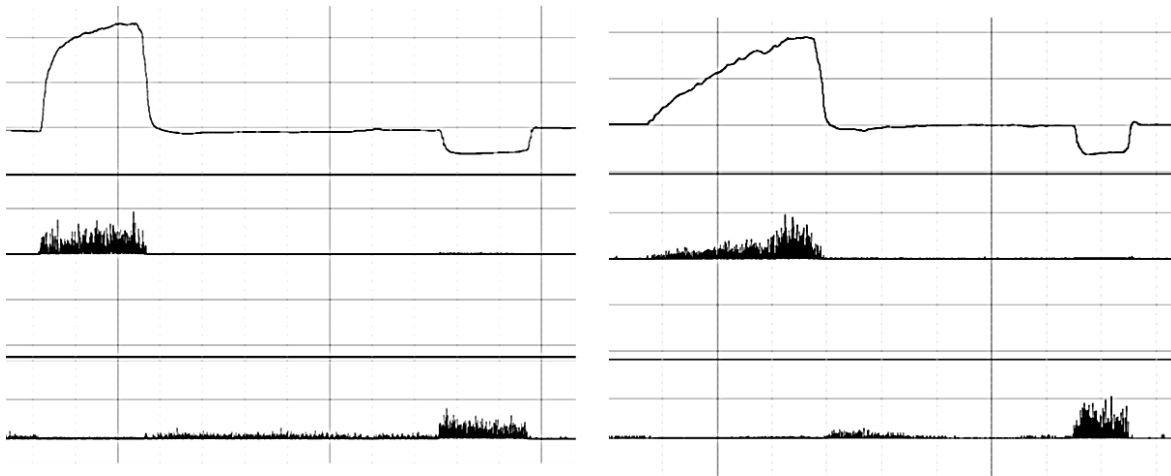
Figure 6.1. Rapid (left) and ramped (right) maximum voluntary contraction.

Top traces represent torque production during plantar- and dorsiflexion, middle traces represent gastrocnemius medialis muscle activation and bottom traces represent tibialis anterior activation.

Muscle volume and intrinsic strength

For the assessment of muscle volume, the set-up used was as described in Chapter 4 of this thesis. Briefly, B-mode ultrasonography (Technos; Esaote S.p.A, Genoa, Italy) was used to determine the anatomical cross-sectional area (ACSA) at three sites of the GM muscle (25, 50 and 75% GM length). Using these ACSAs muscle volume can be estimated using the truncated cone formula.

Intrinsic GM muscle strength (N·m·cm^{-3}) was calculated by dividing the PF net MVC by the GM muscle volume.

Muscle specific force

The setup for the measurement of GM architecture has also been described in Chapter 5, however, only partially. In short, B-mode ultrasonography was used to allow measurements of GM fascicle length (L_F) and pennation angle (θ) during PF isometric MVC. To do so, participants sat on the chair of the isokinetic dynamometer, as described above, and were instructed to perform a ramped PF isometric MVC over 5 seconds with their ankle in a neutral position (0°; no PF or DF). Each ramped PF MVC was followed by a rapid DF MVC, while verbal encouragement and biofeedback were provided by the experimenter during each effort (Figure 6.1). To obtain true values, a total of three MVC combinations

were performed, with 30 - 60 seconds between the trials. If >10% difference was observed between all values, extra ramped MVCs were executed (maximum five in total). The trial with the highest PF torque was used for data analysis. Probe placement, ultrasound recording, and extraction and analysis of individual images at PF isometric MVC was as described in Chapter 5. Synchronisation of the muscle strength data and ultrasound recording was performed using a square wave signal generator. Again, sEMG was used in these trials to allow the calculation of net PF MVC.

Next, Achilles tendon (AT) force (N) was calculated by dividing the net PF MVC by the tendon moment arm in the neutral ankle angle (0°) (m). The latter was assessed by taking an instant vertebral assessment in high definition (IVA-HD) scan of the ankle in two positions using single-energy X-ray absorptiometry (SXA), at respectively 10° PF and 10° DF (174). To keep the ankle in a fixed position, the foot was strapped to a tool that set the joint angle. A sagittal image of the ankle joint was taken twice (one per angle) with the lateral malleolus placed on the bed and within the imaging zone. Anatomical landmarks of the talus were used to overlap the two images and determine the ankle joint centre of rotation. Additionally, a straight line was used to identify the midline of the Achilles tendon on both images. Then, another straight line was drawn on both images from the centre of rotation perpendicular to the Achilles tendon midline, which represented the tendon moment arms for 10° PF and 10° DF (Figure 6.2). Adapted from the Reuleaux method (175), the tendon moment arm for the 0° angle was calculated as the average of the 10° PF and 10° DF tendon moment arms.

It was assumed that 20.3% of the AT force was generated by the GM (176). Calculation of the GM's contribution combined with the measured θ during the ramped PF MVC allowed determination of fascicle force (N). Fascicle force was calculated by dividing the GM muscle force by the cosine of θ. Finally, GM specific force (N·cm^{-2}) was calculated by dividing fascicle force by PCSA$_{MVC}$ (cm^2), where PCSA$_{MVC}$ is determined as the ratio of resting GM muscle volume over L_F during ramped PF isometric MVC.

QM Results:

	Post Hght (mm)	Mid Hght (mm)	Ant Hght (mm)	Mid Wedge	Mid Wedge
L4	18.0	16.0	18.0	1.00	0.89
Std Dev	1mm	1mm	1mm	.05	.05

Physician's Comment:

18 mm
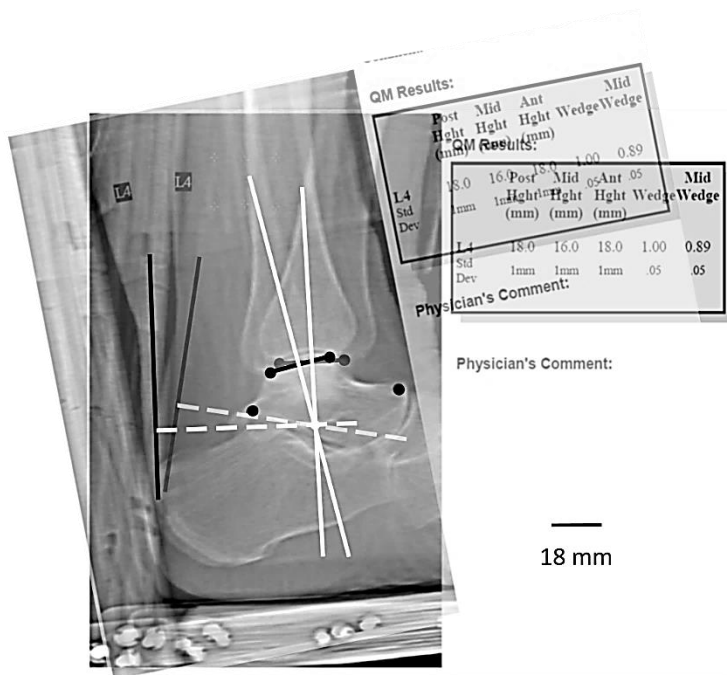
Figure 6.2. Example of the Achilles tendon moment arm analysis.

Dashed lines represent the Achilles tendon moment arms in both 10° plantar- and dorsiflexion.

Voluntary muscle activation

The level of voluntary activation (VA) was measured using supramaximal single twitch stimulation during a rapid PF MVC with the joint set at 0°. Electrical muscle stimulation was administered percutaneously to the PF muscle group via two 50 × 100 mm self-adhesive electrodes (American Imex, Irvine, CA, USA) placed distal to the popliteal crease (cathode) and the myotendinous junction of the soleus (anode). The amplitude of the stimulus was determined by administering twitches starting from 50 mA (with subsequent increments of 10 – 50 mA until no further increase in twitch torque was elicited), while the participant sat on the chair of the dynamometer in the same position as earlier, but in a relaxed state (Figure 6.3). The supramaximal stimulation (200 μs pulse width and 400 volts) singlet was applied during the plateau phase of a rapid PF isometric MVC, which was performed three times with 60 seconds between the trials (Figure 6.3). Singlets were chosen because several studies reported no differences when comparing single twitches, doublets, quadruplets and quintuplets and to minimise discomfort in older adults (177–179). The level of voluntary muscle activation was calculated for the highest of three PF MVCs, applying the interpolated twitch technique, which is given by 1 minus the ratio of the superimposed twitch torque over the resting twitch torque. Multiplying the result by 100 gives the percentage of voluntary agonist muscle activation.
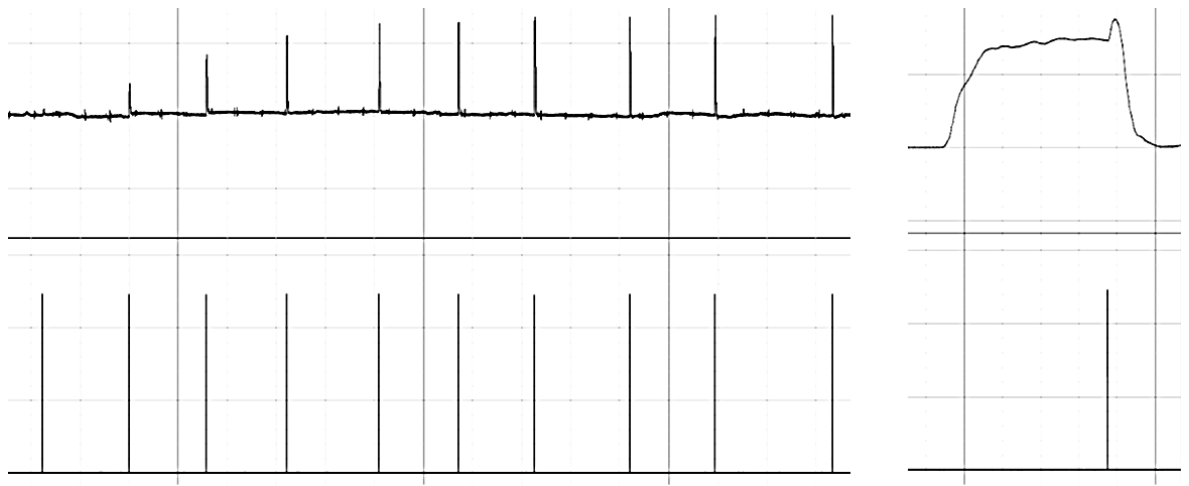
Figure 6.3. Twitch-response curve (left) and supramaximal stimulation applied during maximum voluntary contraction (right).

Top traces represent torque production, while bottom traces represent applied stimulations.

Muscle fatigue

Participants were asked to perform two muscle fatigue protocols, one isometric and the other isokinetic. For the first protocol, participants had to sustain a submaximal isometric PF contraction (at 75% MVC) for as long as possible, up to a maximum of 60 seconds with their ankle in a neutral position (0°), as described above (Figure 6.4). sEMG allowed to measure GM muscle recruitment during the first and last 5 seconds of the trial (or 8.33% of the trial duration if <60 seconds). The captured raw sEMG data of both bouts underwent Fast Fourier Transformation to determine their median power frequencies (MPF), which is a well-known and frequently used method for assessment of muscle fatigue using sEMG (180,181). Generally, muscle fatigue is featured by several outcomes such as an increase in EMG amplitude or a decrease in MPF. The outcomes taken from this trial, were: trial duration (s), relative change in MPF ((MPF_{END} - MPF_{START})/MPF_{START}) and rate of change in MPF (relative change in MPF normalised for trial duration). Data was only analysed from participants who managed to sustain at 75% MVC level for the whole trial duration. Finally, data from 44 participants was left to analyse.

After 5-10 minutes rest, a single PF isometric MVC was performed in the neutral angle, to check whether participants were recovered from the isometric fatigue protocol. When the torque output of the PF MVC was within 10% range of previous recorded MVCs for the same ankle angle, the participant was deemed recovered. For the isokinetic protocol, participants were instructed to perform continuous rapid PF and DF each at a speed of 149°·s^{-1} and 300°·s^{-1} respectively (Figure 6.4). These speeds were chosen because the first

appeared the optimal speed for triceps surae torque-velocity during PF in elderly (126), while the latter was a relatively easy speed to perform DF without fatiguing the TA quicker than the GM. Participants were asked to perform the trial for as long as possible, but allowed to stop in case of too much discomfort as a result of fatigue or when three consecutive PFs showed torque output <50% of the average torque over the first three PFs at the start of the trial. The same outcomes as in isometric fatigue were calculated over the first and last three PFs for a total of 101 participants. Average values per both series of three PFs were recorded as the start and end measurement of the isokinetic trial.
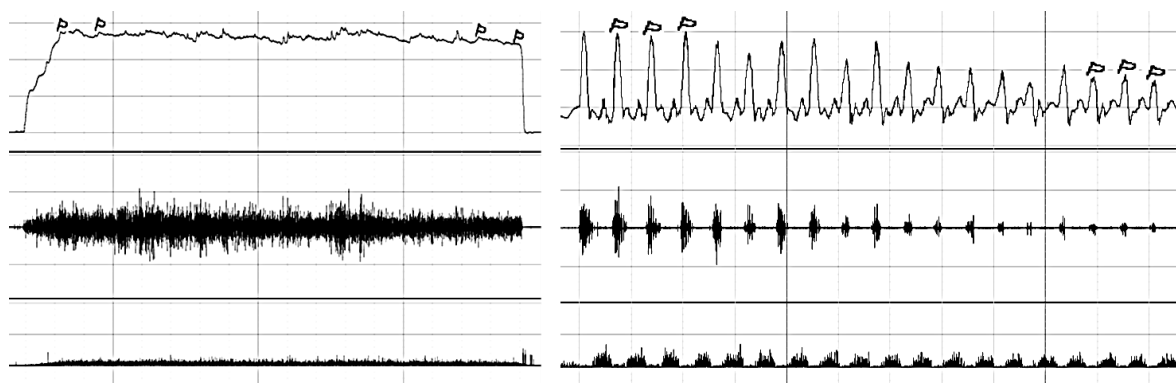
Figure 6.4. Isometric (left) and isokinetic (right) fatigue protocols.

Top traces represent torque production during plantar- and dorsiflexion, middle traces represent gastrocnemius medialis muscle activation and bottom traces represent tibialis anterior activation.

Reliability

Test-retest reliability was determined for the main outcomes under study in this chapter, using intraclass correlation coefficients (ICCs) for absolute agreement using a two-way mixed model. Reliability values <0.5 were interpreted as poor, between 0.5 - 0.75 as moderate, between 0.75 - 0.9 as good and >0.9 as excellent (158). L_{F-MVC} showed an ICC of 0.910, while θ_{MVC} was 0.878. The ICC for the measurement of tendon moment arm was 0.733, however for both PF torque values measured during the rapid and ramped MVCs in the neutral ankle angle the ICCs were 0.997 and 0.989 respectively. Determination of the peak angle and accompanying torque appeared reliable with ICCs of 0.940 and 0.993. Finally, repeated measurements for TA coactivation and GM activation capacity had ICCs of 0.925 and 0.891.

Statistical analyses

The outcome variables are displayed as mean (standard deviation (SD)) or median (interquartile range (IQR)) (Table 6.1). Prior conducting any inferential statistical analysis,

all outcome variables were checked for normality (either Kolmogorov-Smirnov or Shapiro-Wilk test). In case of non-normality, the variables were log-transformed and the distribution of the transformed data also checked. Potential covariates were analysed per outcome variable by running a univariate General Linear Model (GLM). When a parameter appeared significant, it was treated as a covariate (Table 6.2-3). Since daily time spent in sleep, SB and physical activity (PA) is constrained to 24 hours, we used compositional data analysis for these accelerometer outcomes. This type of analysis has been described in detail previously (118,119). Briefly, daily compositions are transformed into isometric log-ratio coordinates, which are then unconstrained and allow the application of traditional multivariate statistics. In this chapter, both single and multiple linear regression analysis was used to study the associations with SB levels, proportional total daily SB and PA, and daily SB pattern parameters. The identified covariates were added to the regression models first, by using backward elimination, after which the predictor(s) of interest was/were entered. During backward elimination, parameters were retained if p-values were <0.20 (118). For all models, Durbin-Watson statistics (>1.0 and <3.0) were checked to identify any correlation between the predictor and covariates, and covariates with variance inflation factor ≥10.0 were removed from the regression model, one at the time. The same was done with individual cases showing Cook's distance ≥1.0. If significant associations were observed for the compositional data, isotemporal substitution was applied to the identified models including covariates, to calculate the relative effects (%) of re-allocating 10 minutes from one behaviour to the other, with respect to the study sample's mean outcomes. Ten minutes was chosen, not only because of its beneficial effects (for example when moderate-to-vigorous PA (MVPA) is performed) (159), but also because it is a realistic amount of time to replace in most elderly.

All statistical analyses were performed using IBM SPSS Statistics for Windows, version 24.0 (IBM Corp., Armonk, NY, USA) and p-values <0.05 were considered statistically significant.

Results

Descriptive statistics

Table 6.1 shows the study sample's descriptive statistics of the GM muscle strength, force and function.

Table 6.1. Study sample descriptive statistics of gastrocnemius skeletal muscle strength, specific force and function.

Outcome variable	Mean (SD) or ¶median (IQR)
Ankle angle MVC_{Peak} (°)	-5.0 (8.0)[¶]
Net torque at angle MVC_{Peak} (N·m)	85.9 (32.1)
Intrinsic strength at angle MVC_{Peak} (N·m·cm^{-3})	0.43 (0.26)[¶]
Net torque at 0° angle (N·m)	78.3 (29.9)
Intrinsic strength at 0° angle (N·m·cm^{-3})	0.37 (0.23)[¶]
AT moment arm (mm)	55.4 (4.8)
L_{F-MVC} (cm)	4.9 (1.7)[¶]
θ_{MVC} (°)	22.0 (8.5)[¶]
$PCSA_{MVC}$ (cm^2)	39.7 (23.4)[¶]
AT force (N)	1314.8 (533.0)
Fascicle force (N)	287.7 (178.9)[¶]
Specific force (N)	6.78 (3.62)[¶]
TA co-activation (%)	9.1 (7.4)[¶]
GM activation capacity (%)	86.7 (14.5)[¶]
$Fatigue_{ISOM}$ duration (s)	60.0 (0.0)[¶]
$Fatigue_{ISOM}$ relative change RMS EMG (%)	-23.8 (36.0)[¶]
$Fatigue_{ISOM}$ rate of relative change RMS EMG (%·s^{-1})	-0.41 (0.61)[¶]
$Fatigue_{ISOM}$ relative change MPF (%)	-4.0 (82.8)[¶]
$Fatigue_{ISOM}$ rate of relative change MPF (%·s^{-1})	-0.07 (1.38)[¶]
$Fatigue_{ISOK}$ duration (s)	34.4 (17.1)[¶]
$Fatigue_{ISOK}$ relative change RMS EMG (%)	-51.6 (46.3)[¶]
$Fatigue_{ISOK}$ rate of relative change RMS EMG (%·s^{-1})	-1.46 (1.28)[¶]
$Fatigue_{ISOK}$ relative change MPF (%)	-1.1 (35.2)[¶]
$Fatigue_{ISOK}$ rate of relative change MPF (%·s^{-1})	-0.02 (1.05)[¶]

MVC, maximum voluntary contraction; AT, Achilles tendon; L_{F-MVC}, fascicle length during MVC; θ_{MVC}, fascicle pennation angle during MVC; $PCSA_{MVC}$, physiological cross-sectional area during MVC; TA, tibialis anterior; GM, gastrocnemius medialis; Isom, isometric condition; Isok, isokinetic condition; RMS, root mean square; EMG, electromyography; MPF, median power frequency; SD, standard deviation; IQR, interquartile range.

Covariate analysis

The variables identified as covariates in this chapter, were: sex, ethnicity, body height, body mass, body mass index (BMI), skeletal muscle index (SMI), body fat mass, body lean mass, body bone mineral content (BMC), adiposity class, falls risk assessment tool (FRAT) score, menopause age, current use of statins, smoking, calcium/vitamin D supplement usage, daily total PA bouts time, SB during PA bouts, standing during PA bouts, light-intensity PA

(LIPA) during PA bouts, MVPA during PA bouts, sporadic MVPA (sMVPA), and physical activity status (Table 6.2-3).

Table 6.2. Correlation coefficients of covariate analysis for gastrocnemius muscle strength, force and function.

	Angle MVC$_{Peak}$[¶]	Net torque MVC$_{Peak}$[¶]	Intrinsic strength MVC$_{Peak}$[¶]	Net torque 0° angle	Intrinsic strength 0° angle[¶]	AT moment arm	L$_{F-MVC}$[¶]	θ$_{MVC}$[¶]	PCSA$_{MVC}$[¶]	AT force	Fascicle force[¶]	Specific force[¶]	TA co-activation[¶]	GM AC[¶]
Age	0.095	-0.172	0.026	-0.153	0.041	0.182	-0.079	0.007	-0.172	-0.145	-0.141	0.001	-0.082	0.120
Sex	0.009	**0.455**	0.116	**0.482**	0.159	**0.410**	-0.069	**0.266**	**0.371**	**0.452**	**0.467**	0.191	-0.104	**0.269**
Ethnicity	0.081	-0.079	0.048	-0.060	0.070	0.002	**-0.265**	0.152	0.060	-0.035	0.003	-0.055	0.060	N/a
Body height	-0.006	**0.485**	0.076	**0.523**	0.125	**0.519**	0.041	0.081	**0.349**	**0.446**	**0.422**	0.160	-0.023	0.098
Body mass	**0.239**	0.175	**-0.339**	**0.229**	**-0.260**	**0.467**	0.013	**0.265**	**0.522**	0.238	0.246	**-0.220**	0.060	-0.024
BMI	**0.284**	-0.137	**-0.428**	-0.098	**-0.367**	0.181	-0.023	**0.235**	**0.348**	-0.043	-0.016	**-0.362**	0.069	-0.091
SMI	0.072	**0.363**	-0.124	**0.401**	-0.059	**0.356**	-0.085	**0.428**	**0.544**	**0.420**	**0.431**	-0.022	-0.060	0.160
Fat mass	**0.219**	**-0.490**	**-0.393**	**-0.490**	**-0.394**	-0.166	0.090	-0.141	-0.104	**-0.434**	**-0.411**	**-0.388**	0.175	**-0.267**
Lean mass	**-0.236**	**0.497**	**0.401**	**0.494**	**0.399**	0.160	-0.081	0.138	0.097	**0.434**	**0.409**	**0.392**	-0.185	**0.269**
BMC mass	0.042	**0.250**	0.173	**0.277**	**0.204**	0.183	-0.156	0.124	0.150	**0.296**	**0.299**	**0.209**	-0.007	0.156
Adiposity class	**0.341**	**-0.201**	**-0.393**	-0.164	**-0.334**	**0.200**	0.086	0.057	0.192	-0.128	-0.077	**-0.280**	0.080	-0.062
FRAT score	0.185	**-0.195**	-0.035	-0.154	0.014	0.099	-0.047	-0.081	-0.133	**-0.208**	**-0.233**	-0.147	-0.041	0.046
Menopause age	-0.022	0.062	0.125	0.055	0.115	-0.173	0.033	-0.015	-0.097	0.086	0.088	0.175	0.129	-0.079
Major illness history	-0.032	0.025	-0.061	0.057	-0.032	0.121	-0.026	0.051	0.157	0.053	0.082	-0.056	0.014	0.125
Statins usage	-0.032	0.185	0.132	0.167	0.124	0.056	0.008	0.042	0.036	0.108	0.108	0.093	-0.089	-0.031
Smoking	-0.153	-0.068	0.073	-0.114	0.012	**-0.247**	0.011	-0.011	-0.172	-0.044	-0.042	0.119	-0.156	N/a
Resistance training	-0.028	0.108	0.045	0.117	0.035	-0.064	0.061	-0.059	-0.006	0.105	0.075	0.096	0.061	0.021

Dairy products	0.061	0.122	0.152	0.129	0.154	-0.136	-0.144	0.081	0.085	0.117	0.092	0.026	-0.027	-0.078
Caffeine intake	0.018	0.072	0.026	0.069	0.003	-0.163	0.011	0.003	0.013	0.136	0.097	0.103	-0.158	-0.015
RA diagnosis	-0.028	-0.023	-0.129	-0.072	-0.173	0.035	0.042	0.014	0.127	-0.051	-0.049	-0.184	0.041	-0.043
Daily alcohol intake ≥3 units	-0.061	0.135	-0.012	0.118	-0.017	0.187	-0.084	0.072	0.191	0.055	0.055	-0.132	-0.070	0.074
Calcium/vitamin D supplements	0.018	**-0.219**	-0.124	**-0.212**	-0.123	0.015	0.024	-0.105	-0.122	**-0.241**	**-0.288**	**-0.224**	-0.066	0.001
PA bouts	-0.050	-0.026	-0.129	-0.060	-0.165	0.048	0.182	-0.038	-0.002	-0.020	-0.030	-0.034	-0.066	-0.036
Total PA bouts time	**-0.270**	0.101	0.140	0.068	0.108	-0.171	0.056	-0.024	-0.082	0.053	0.052	0.144	0.066	0.208
SB during PA bout	-0.109	0.012	0.127	0.002	0.099	**-0.267**	0.063	-0.154	**-0.197**	-0.002	-0.030	0.158	-0.116	-0.113
Standing during PA bout	-0.013	-0.148	-0.158	-0.141	-0.148	-0.057	-0.047	0.128	0.109	-0.152	-0.105	**-0.232**	0.103	0.241
LIPA during PA bout	0.080	-0.105	-0.068	-0.107	-0.090	-0.144	0.002	-0.079	-0.056	-0.044	-0.088	-0.049	0.067	-0.066
MVPA during PA bout	-0.060	0.148	0.113	0.147	0.130	0.163	0.013	0.030	0.020	0.096	0.119	0.122	-0.093	-0.030
MVPA≥10 mins	0.018	0.082	0.089	0.103	0.114	0.059	0.005	0.015	0.017	0.112	0.105	0.108	-0.129	-0.009
sMVPA	**-0.263**	0.191	0.178	0.161	0.166	-0.015	0.040	0.016	-0.025	0.115	0.145	**0.197**	0.009	0.188
Physical activity status	0.054	0.101	0.127	0.138	0.161	0.053	-0.060	0.066	0.051	0.136	0.149	0.128	-0.100	0.049

MVC, maximum voluntary contraction; AT, Achilles tendon; $L_{F\text{-}MVC}$, fascicle length during MVC; θ_{MVC}, fascicle pennation angle during MVC; $PCSA_{MVC}$, physiological cross-sectional area during MVC; TA, tibialis anterior; GM, gastrocnemius medialis; AC, activation capacity; BMI, body mass index; SMI, skeletal muscle index; BMC, bone mineral content; FRAT, falls risk assessment

tool; RA, rheumatoid arthritis; PA, physical activity; SB, sedentary behaviour; LIPA, light-intensity physical activity; MVPA, moderate-to-vigorous physical activity; sMVPA, sporadic moderate-to-vigorous physical activity; ¶Log-transformed. Bold values represent significances at P<0.05 level.

Table 6.3. Correlation coefficients of covariate analysis for gastrocnemius medialis fatigue indices.

	Fatigue$_{ISOM}$					Fatigue$_{ISOK}$				
	Duration[¶]	Relative change RMS EMG[¶]	Rate of change RMS EMG[¶]	Relative change MPF[¶]	Rate of change MPF[¶]	Duration[¶]	Relative change RMS EMG[¶]	Rate of change RMS EMG[¶]	Relative change MPF[¶]	Rate of change MPF[¶]
Age	-0.198	-0.177	-0.201	-0.073	0.030	-0.173	-0.042	-0.026	-0.044	-0.070
Sex	0.049	**-0.326**	-0.219	-0.008	-0.139	0.022	-0.145	0.029	-0.159	-0.130
Ethnicity	N/a	N/a	N/a	N/a	N/a	-0.178	0.072	0.022	0.137	**0.225**
Body height	0.042	-0.179	-0.114	0.194	0.001	-0.073	-0.003	0.085	-0.112	-0.107
Body mass	0.151	0.068	0.099	0.093	-0.115	-0.063	-0.060	0.031	-0.183	-0.121
BMI	0.159	0.216	0.208	-0.036	-0.152	-0.012	-0.051	-0.005	-0.139	-0.067
SMI	0.060	-0.160	-0.089	0.057	-0.080	0.041	**-0.203**	-0.012	-0.176	-0.111
Fat mass	0.159	**0.455**	**0.357**	-0.025	-0.041	-0.086	0.125	-0.008	0.020	0.033
Lean mass	-0.156	**-0.457**	**-0.357**	0.030	0.040	0.086	-0.123	0.017	-0.018	-0.030
BMC mass	-0.145	**-0.318**	-0.260	-0.038	0.029	0.067	-0.104	-0.089	-0.040	-0.070
Adiposity class	0.295	0.177	0.207	-0.049	-0.216	-0.176	0.084	0.023	-0.177	-0.176
FRAT score	-0.181	0.019	-0.027	0.004	-0.064	-0.057	-0.062	-0.087	-0.110	-0.115
Menopause age	**0.445**	0.115	0.263	-0.131	-0.351	0.177	-0.040	0.134	-0.016	-0.032
Major illness history	0.103	-0.062	-0.074	0.032	-0.015	0.153	0.066	0.181	0.079	0.025
Statins usage	-0.041	-0.007	0.031	0.000	-0.064	0.106	**-0.282**	-0.127	-0.174	-0.119
Smoking	0.032	0.052	0.034	-0.002	-0.041	-0.087	0.023	-0.033	0.097	0.098

Resistance training	0.092	-0.011	0.082	0.135	0.047	0.040	0.015	0.055	0.078	0.095
Dairy products	-0.032	0.140	0.108	0.016	0.045	-0.148	0.014	-0.007	0.122	0.119
Caffeine intake	-0.092	0.287	0.238	-0.141	-0.058	-0.121	-0.010	0.019	0.037	-0.089
RA diagnosis	0.046	0.223	0.189	0.122	0.008	-0.022	-0.067	-0.049	-0.110	-0.053
Daily alcohol intake ≥3 units	0.047	-0.151	-0.110	0.139	0.097	0.075	-0.098	-0.068	0.054	0.070
Calcium/vitamin D supplements	0.067	0.184	0.172	-0.051	0.006	0.004	-0.042	-0.069	0.011	-0.036
PA bouts	0.092	-0.039	-0.056	0.032	0.089	-0.048	-0.059	0.015	-0.021	-0.110
Total PA bouts time	-0.021	-0.180	-0.147	0.076	0.056	-0.024	0.053	0.005	0.034	0.011
SB during PA bout	0.107	0.091	0.089	-0.039	-0.047	0.079	-0.113	-0.060	-0.086	-0.084
Standing during PA bout	0.151	-0.018	-0.032	-0.075	-0.044	0.013	0.058	-0.052	0.063	0.068
LIPA during PA bout	-0.102	**0.351**	0.228	-0.144	0.004	-0.083	0.082	0.022	0.065	0.061
MVPA during PA bout	0.032	**-0.303**	-0.192	0.150	0.014	0.065	-0.090	0.003	-0.078	-0.076
MVPA$_{\geq 10\ mins}$	-0.145	**-0.339**	-0.293	0.143	0.050	0.088	-0.045	-0.034	-0.001	-0.007
sMVPA	0.054	**-0.327**	-0.224	0.156	0.034	0.040	-0.028	0.022	-0.078	-0.084
Physical activity status	-0.131	**-0.365**	**-0.307**	0.041	-0.036	0.129	-0.031	0.012	-0.072	-0.045

Isom, isometric condition; Isok, isokinetic condition; RMS, root mean square; EMG, electromyography; MPF, median power frequency; BMI, body mass index; SMI, skeletal muscle index; BMC, bone mineral content; FRAT, falls risk assessment tool; RA, rheumatoid arthritis; PA, physical activity; SB, sedentary behaviour; LIPA, light-intensity physical activity; MVPA, moderate-to-vigorous physical activity; sMVPA, sporadic moderate-to-vigorous physical activity; [¶]Log-transformed. Bold values represent significances at $P<0.05$ level.

SB levels

Both ankle angle MVC_{Peak} (β = 0.35, R^2_{adj} = 0.114) and intrinsic strength at MVC_{Peak} angle (β = -0.20, R^2_{adj} = 0.029) were significantly associated with SB levels, however, when adjusting for covariates only the positive association with ankle angle MVC_{Peak} (β = 0.28, R^2_{adj} = 0.176) remained (Table 6.4). Effect sizes for the covariate-adjusted models, were: -0.023 $\leq$ R^2_{adj} $\leq$ 0.355.

Table 6.4. Regression analysis results for sedentary behaviour levels.

Outcome variable	Without covariates					With covariates				
	B	95%-CI lower bound	95%-CI upper bound	β	R^2_{Adj}	B	95%-CI lower bound	95%-CI upper bound	β	R^2_{Adj}
Ankle angle MVC$_{Peak}$[¶]	**0.44**	**0.21**	**0.68**	**0.35****	**0.114****	**0.36**	**0.13**	**0.59**	**0.28****	**0.176****
Net torque at angle MVC$_{Peak}$	-7.17	-23.41	9.07	-0.09	-0.002	-2.80	-16.62	11.03	-0.03	**0.320****
Intrinsic strength at angle MVC$_{Peak}$[¶]	**-0.22**	**-0.43**	**0.00**	**-0.20***	**0.029***	-0.04	-0.24	0.16	-0.04	**0.220****
Net torque at 0° angle	-3.49	-18.63	11.66	-0.05	-0.008	2.44	-10.50	15.38	0.03	**0.355****
Intrinsic strength at 0° angle[¶]	-0.18	-0.39	0.04	-0.16	0.016	-0.02	-0.23	0.19	-0.02	**0.173****
AT moment arm	2.13	-0.28	4.53	0.17	0.082	1.66	-0.40	3.72	0.13	**0.350****
L$_{F-MVC}$[¶]	0.02	-0.12	0.15	0.02	-0.009	0.02	-0.11	0.16	0.03	**0.053***
θ$_{MVC}$[¶]	0.03	-0.10	0.16	0.05	-0.008	0.01	-0.10	0.13	0.02	**0.167****
PCSA$_{MVC}$[¶]	0.09	-0.10	0.28	0.09	-0.001	0.02	-0.15	0.18	0.02	**0.344****
AT force	-90.15	-360.17	179.86	-0.07	-0.005	-12.32	-254.34	229.69	-0.01	**0.290****
Fascicle force[¶]	-0.08	-0.31	0.15	-0.07	-0.005	-0.04	-0.25	0.17	-0.03	**0.285****
Specific force[¶]	-0.17	-0.37	0.02	-0.17	0.021	-0.07	-0.26	0.11	-0.07	**0.183****
TA co-activation[¶]	-0.04	-0.34	0.26	-0.02	-0.009					
GM activation capacity[¶]	-0.09	-0.30	0.12	-0.12	-0.004	-0.08	-0.28	0.12	-0.10	0.048
Fatigue$_{ISOM}$ duration[¶]	-0.02	-0.09	0.06	-0.08	-0.018	-0.02	-0.09	0.06	-0.08	-0.018
Fatigue$_{ISOM}$ relative change RMS EMG[¶]	0.00	-0.25	0.25	0.00	-0.024	-0.09	-0.31	0.14	-0.11	**0.234****
Fatigue$_{ISOM}$ rate of change RMS EMG[¶]	0.00	0.00	0.00	0.01	-0.024	0.00	-0.01	0.00	-0.07	**0.121***

Fatigue$_{ISOM}$ relative change MPF¶	-0.05	-0.80	0.71	-0.02	-0.023	-0.05	-0.80	0.71	-0.02	-0.023
Fatigue$_{ISOM}$ rate of change MPF¶	0.01	-0.01	0.02	0.14	-0.006	0.01	-0.01	0.02	0.14	-0.006
Fatigue$_{ISOK}$ duration¶	-0.09	-0.27	0.09	-0.10	-0.001	-0.09	-0.27	0.09	-0.10	-0.001
Fatigue$_{ISOK}$ relative change RMS EMG¶	-0.23	-0.65	0.19	-0.11	0.001	-0.18	-0.58	0.23	-0.08	**0.080***
Fatigue$_{ISOK}$ rate of change RMS EMG¶	0.00	-0.01	0.01	-0.06	-0.006	0.00	-0.01	0.01	-0.06	-0.006
Fatigue$_{ISOK}$ relative change MPF¶	-0.14	-0.31	0.03	-0.17	0.018	-0.14	-0.31	0.03	-0.17	0.018
Fatigue$_{ISOK}$ rate of change MPF¶	-0.01	-0.01	0.00	-0.16	0.016	-0.01	-0.01	0.00	-0.17	**0.061***

MVC, maximum voluntary contraction; AT, Achilles tendon; L$_{F-MVC}$, fascicle length during MVC; θ_{MVC}, fascicle pennation angle during MVC; PCSA$_{MVC}$, physiological cross-sectional area during MVC; TA, tibialis anterior; GM, gastrocnemius medialis; Isom, isometric condition; Isok, isokinetic condition; RMS, root mean square; EMG, electromyography; MPF, median power frequency; ¶Log-transformed; *P<0.05; **P<0.01.

Daily total SB and PA

Compositional data analysis showed that time spent in some of the studied behaviours relative to the others, were significantly associated with a few GM muscle strength, force and function outcomes (Table 6.5). For example, nMVC at peak angle was positively associated (β = 0.20, R^2_{adj} = 0.007) with proportional time spent in MVPA, however, this association disappeared when correcting the model for covariates. The same was true for θ_{MVC}, which was associated with sleep (β = -0.41), SB (β = 0.46) and standing (β = 0.24) (all R^2_{adj} = 0.048). After correcting for covariates, only the association with standing remained (β = 0.21, R^2_{adj} = 0.221). $PCSA_{MVC}$ was significantly associated with sleep (β = -0.38) and SB (β = 0.48) (both R^2_{adj} = 0.143). However, both associations were mitigated by adding covariates. Nevertheless, standing was found significantly associated now (β = 0.20, R^2_{adj} = 0.398). Next, AT force was initially not associated with any daily behaviour, but after adding covariates to the regression model it was positively associated with LIPA (β = 0.23, R^2_{adj} = 0.325). GM activation capacity was positively associated with standing, both before and after covariate adjustment (β = 0.34, R^2_{adj} = 0.082 vs. β = 0.35, R^2_{adj} = 0.180). Significant associations were also found for one outcome from the isometric fatigue protocol, relative change in RMS EMG respectively. This outcome was associated with MVPA (β = -0.38, R^2_{adj} = 0.148) prior to covariate adjustment, but the association disappeared after adding covariates. The isokinetic protocol did not show any associations at all. Overall, the effect sizes of the multiple regression models including significant associations, were 0.180 ≤ R^2_{adj} ≤ 0.398, while for the other models they ranged from -0.086 through 0.362.

Isotemporal substitution revealed that the relative effects (%-change from study sample means) of re-allocating 10 minutes from one behaviour to another within the mean composition of the study sample's total daily SB and PA (sleep = 35.6%, SB = 39.4%, standing = 2.8%, LIPA = 11.5% and MVPA = 10.7%) for the models including behaviours significantly associated with either muscle architecture, force or function and adjusted for covariates, varied from -0.030% through +0.036% (Table 6.6). These maximum changes were both seen for relative change in AT force, when substituting 10 min of LIPA with standing and vice versa respectively.

Table 6.5. Coefficients of multiple regression models based on compositional data analysis.

Outcome variable		Without covariates			With covariates		
		B	β	R^2_{Adj}	B	β	R^2_{Adj}
	Sleep	-0.14	-0.06	0.037	-0.04	-0.02	**0.115****

Ankle angle MVC$_{Peak}$[¶]	SB	0.43	0.29		0.24	0.16	
	Standing	-0.07	-0.07		-0.08	-0.07	
	LIPA	-0.01	-0.01		0.09	0.06	
	MVPA	-0.20	-0.17		-0.20	-0.16	
Net torque at angle MVC$_{Peak}$	Sleep	-37.64	-0.25	0.007	-24.93	-0.17	**0.318****
	SB	17.26	0.18		18.10	0.19	
	Standing	-2.63	-0.04		0.68	0.01	
	LIPA	6.57	0.07		15.52	0.16	
	MVPA	**15.85**	**0.20***		-10.01	-0.13	
Intrinsic strength at angle MVC$_{Peak}$[¶]	Sleep	0.41	0.21	0.014	0.15	0.08	**0.206****
	SB	-0.47	-0.37		-0.05	-0.04	
	Standing	-0.09	-0.09		-0.08	-0.09	
	LIPA	0.00	0.00		-0.03	-0.02	
	MVPA	0.15	0.14		0.00	0.00	
Net torque at 0° angle	Sleep	-31.43	-0.23	0.000	-17.26	-0.13	**0.362****
	SB	15.93	0.18		15.37	0.17	
	Standing	-3.14	-0.05		-0.16	0.00	
	LIPA	4.58	0.05		13.09	0.15	
	MVPA	13.51	0.18		-11.67	-0.16	
Intrinsic strength at 0° angle[¶]	Sleep	0.50	0.25	0.014	0.29	0.15	**0.161****
	SB	-0.50	-0.39		-0.15	-0.12	
	Standing	-0.09	-0.10		-0.08	-0.09	
	LIPA	-0.05	-0.04		-0.02	-0.01	
	MVPA	0.15	0.14		-0.05	-0.05	
AT moment arm	Sleep	-3.69	-0.17	0.039	0.65	0.03	**0.351****
	SB	5.02	0.35		2.12	0.15	
	Standing	-0.97	-0.09		-0.04	-0.00	
	LIPA	-1.10	-0.08		-1.06	-0.07	
	MVPA	0.75	0.06		-1.67	-0.14	
L$_{F-MVC}$[¶]	Sleep	-0.03	-0.02	-0.033	0.07	0.05	0.039
	SB	0.00	0.00		-0.05	-0.06	
	Standing	-0.05	-0.08		-0.08	-0.14	
	LIPA	0.05	0.07		0.04	0.05	
	MVPA	0.03	0.04		0.02	0.03	
θ$_{MVC}$[¶]	Sleep	**-0.48**	**-0.41***	0.048	-0.38	-0.33	**0.221****
	SB	**0.34**	**0.46***		0.26	0.35	
	Standing	**0.14**	**0.24***		**0.12**	**0.21***	
	LIPA	-0.04	-0.05		0.05	0.06	
	MVPA	0.04	0.06		-0.07	-0.11	

PCSA$_{MVC}$[¶]	Sleep	**-0.67**	**-0.38***	0.143	-0.37	-0.21	**0.398****
	SB	**0.54**	**0.48***		0.20	0.18	
	Standing	0.15	0.17		**0.17**	**0.20***	
	LIPA	-0.04	-0.04		0.12	0.10	
	MVPA	0.01	0.02		-0.13	-0.14	
AT force	Sleep	-655.76	-0.27	-0.002	-406.71	-0.17	**0.325****
	SB	362.96	0.23		324.63	0.21	
	Standing	-86.02	-0.07		-52.96	-0.04	
	LIPA	181.99	0.11		**370.21**	**0.23***	
	MVPA	194.68	0.15		-237.67	-0.18	
Fascicle force[¶]	Sleep	-0.51	-0.24	-0.005	-0.23	-0.11	**0.298****
	SB	0.27	0.20		0.15	0.11	
	Standing	-0.02	-0.02		0.01	0.01	
	LIPA	0.08	0.05		0.23	0.17	
	MVPA	0.19	0.17		-0.16	-0.15	
Specific force[¶]	Sleep	0.15	0.09	0.035	0.07	0.04	**0.182****
	SB	-0.28	-0.24		-0.06	-0.06	
	Standing	-0.17	-0.20		-0.15	-0.17	
	LIPA	0.12	0.10		0.15	0.13	
	MVPA	0.17	0.18		-0.01	-0.01	
TA co-activation[¶]	Sleep	0.02	0.01	-0.018			
	SB	-0.06	-0.04				
	Standing	0.17	0.13				
	LIPA	-0.01	-0.00				
	MVPA	-0.12	-0.08				
GM activation capacity[¶]	Sleep	0.15	0.11	0.082	0.20	0.14	**0.180***
	SB	-0.24	-0.27		-0.26	-0.30	
	Standing	**0.23**	**0.34***		**0.23**	**0.35***	
	LIPA	-0.12	-0.13		0.00	0.00	
	MVPA	0.04	0.05		-0.11	-0.15	
Fatigue$_{ISOM}$ duration[¶]	Sleep	-0.19	-0.24	-0.053	0.03	0.08	-0.086
	SB	0.15	0.30		-0.04	-0.15	
	Standing	0.06	0.17		0.01	0.07	
	LIPA	-0.04	-0.09		0.01	0.02	
	MVPA	0.00	0.00		-0.01	-0.04	
Fatigue$_{ISOM}$ relative change RMS EMG[¶]	Sleep	0.53	0.37	**0.148***	0.56	0.39	**0.244****
	SB	-0.32	-0.35		-0.45	-0.49	

110

	Standing	-0.17	-0.25		-0.18	-0.26	
	LIPA	0.17	0.18		0.12	0.13	
	MVPA	**-0.29**	**-0.38***		-0.15	-0.19	
Fatigue$_{ISOM}$ rate of change RMS EMG¶	Sleep	0.01	0.31		0.01	0.34	
	SB	0.00	-0.28		-0.01	-0.40	
	Standing	0.00	-0.21	0.041	0.00	-0.22	0.099
	LIPA	0.00	0.10		0.00	0.06	
	MVPA	0.00	-0.28		0.00	-0.12	
Fatigue$_{ISOM}$ relative change MPF¶	Sleep	-0.15	-0.03		-0.15	-0.03	
	SB	0.05	0.02		0.05	0.02	
	Standing	-0.11	-0.05	-0.061	-0.11	-0.05	-0.061
	LIPA	-0.05	-0.02		-0.05	-0.02	
	MVPA	0.45	0.19		0.45	0.19	
Fatigue$_{ISOM}$ rate of change MPF¶	Sleep	0.02	0.16		0.02	0.16	
	SB	-0.02	-0.22		-0.02	-0.22	
	Standing	-0.01	-0.08	-0.078	-0.01	-0.08	-0.078
	LIPA	0.00	0.04		0.00	0.04	
	MVPA	0.00	0.05		0.00	0.05	
Fatigue$_{ISOK}$ duration¶	Sleep	0.29	0.18		0.29	0.18	
	SB	-0.20	-0.19		-0.20	-0.19	
	Standing	0.06	0.07	-0.021	0.06	0.07	-0.021
	LIPA	-0.17	-0.16		-0.17	-0.16	
	MVPA	0.01	0.01		0.01	0.01	
Fatigue$_{ISOK}$ relative change RMS EMG¶	Sleep	-0.42	-0.11		-0.43	-0.11	
	SB	0.21	0.09		0.29	0.12	
	Standing	-0.03	-0.02	-0.029	0.03	0.02	0.047
	LIPA	0.30	0.12		0.07	0.03	
	MVPA	-0.05	-0.03		0.05	0.03	
Fatigue$_{ISOK}$ rate of change RMS EMG¶	Sleep	-0.01	-0.17		-0.01	-0.17	
	SB	0.01	0.14		0.01	0.14	
	Standing	0.00	0.14	-0.018	0.00	0.14	-0.018
	LIPA	0.00	0.02		0.00	0.02	
	MVPA	0.00	-0.02		0.00	-0.02	
Fatigue$_{ISOK}$ relative change MPF¶	Sleep	0.34	0.22		0.34	0.22	
	SB	-0.26	-0.27		-0.26	-0.27	
	Standing	-0.03	-0.04	-0.019	-0.03	-0.04	-0.019
	LIPA	0.02	0.02		0.02	0.02	
	MVPA	-0.07	-0.08		-0.07	-0.08	
	Sleep	0.01	0.22	-0.021	0.01	0.16	0.020

	SB	-0.01	-0.25		-0.01	-0.20
Fatigue$_{ISOK}$ rate of change MPF¶	Standing	0.00	-0.02		0.00	0.03
	LIPA	0.00	0.00		0.00	0.01
	MVPA	0.00	-0.09		0.00	-0.09

MVC, maximum voluntary contraction; AT, Achilles tendon; L_{F-MVC}, fascicle length during MVC; θ_{MVC}, fascicle pennation angle during MVC; $PCSA_{MVC}$, physiological cross-sectional area during MVC; TA, tibialis anterior; GM, gastrocnemius medialis; Isom, isometric condition; Isok, isokinetic condition; RMS, root mean square; EMG, electromyography; MPF, median power frequency; SB, sedentary behaviour; LIPA, light-intensity physical activity; MVPA, moderate-to-vigorous physical activity; ¶Log-transformed; *$P<0.05$; **$P<0.01$.

Table 6.6. Relative effects (%) of isotemporal substitution on outcome variables.

Outcome variable	+10 mins	-10 mins				
		Sleep	SB	Standing	LIPA	MVPA
θ_{MVC}¶	Sleep			-0.016		
	SB			+0.005		
	Standing	+0.013	-0.004	+0.000	+0.002	+0.006
	LIPA			-0.002		
	MVPA			-0.007		
$PCSA_{MVC}$¶	Sleep			-0.015		
	SB			+0.001		
	Standing	+0.012	-0.001	+0.000	+0.001	+0.008
	LIPA			-0.001		
	MVPA			-0.009		
AT force	Sleep				-0.016	
	SB				-0.001	
	Standing				-0.030	
	LIPA	+0.015	+0.001	+0.036	+0.000	+0.019
	MVPA				-0.019	
GM activation capacity¶	Sleep			-0.001		
	SB			-0.011		
	Standing	+0.000	+0.009	+0.000	+0.005	+0.007
	LIPA			-0.006		
	MVPA			-0.008		

AT, Achilles tendon; θ_{MVC}, fascicle pennation angle during MVC; $PCSA_{MVC}$, physiological cross-sectional area during MVC; GM, gastrocnemius medialis; SB, sedentary behaviour; LIPA, light-intensity physical activity; MVPA, moderate-to-vigorous physical activity; ¶Log-transformed.

Daily SB pattern parameters

Ankle angle MVC$_{Peak}$ was significantly associated with a few SB pattern parameters, namely long SB bouts ($\beta = 0.26$, $R^2_{adj} = 0.056$), α ($\beta = -0.25$, $R^2_{adj} = 0.052$) and F ($\beta = -0.21$, $R^2_{adj} = $

112

0.034) (Table 6.7). However, all associations disappeared when adding covariates to the regression models. The opposite was found for nMVC and intrinsic strength at peak angle, nMVC at 0° angle and intrinsic strength at 0° angle, where no associations were observed initially, but did appear after adjusting for covariates. More specifically, $W_{1/2}$ was negatively associated with the first (β = -0.23, R^2_{adj} = 0.375) and third outcome (β = -0.24, R^2_{adj} = 0.412), whereas the second and fourth were associated with breaks in SB (β = -0.21, R^2_{adj} = 0.259 &. β = -0.25, R^2_{adj} = 0.235) and short SB bouts (β = -0.19, R^2_{adj} = 0.248 &. β = -0.22, R^2_{adj} = 0.221). Intrinsic strength at the neutral angle was also associated with $W_{50\%}$ (β = 0.24, R^2_{adj} = 0.214) and F (β = -0.21, R^2_{adj} = 0.213). For the AT moment arm long SB bouts and α were significantly associated in uncorrected models (β = 0.24, R^2_{adj} = 0.047 & β = -0.22, R^2_{adj} = 0.039), but not in corrected models. Period was negatively associated in both single and multiple linear regression models (β = -0.22, R^2_{adj} = 0.038 & β = -0.26, R^2_{adj} = 0.380). $W_{50\%}$ was only significantly associated (β = 0.30, R^2_{adj} = 0.410) after adjusting the model for covariates. $PCSA_{MVC}$ was negatively associated with $X_{1/2}$ (β = -0.20, R^2_{adj} = 0.370), but only in a covariate-adjusted model. Next, AT force, GM fascicle force and GM specific force were significantly associated with $W_{1/2}$. However, where associations were found for both models (β = -0.21, R^2_{adj} = 0.034 & β = -0.25, R^2_{adj} = 0.351) in AT force, as well GM fascicle as specific force only showed associations in covariate-adjusted models for $W_{1/2}$, respectively β = -0.20, R^2_{adj} = 0.326 & β = -0.23, R^2_{adj} = 0.241. Specific force was also found to be associated with α (β = 0.21, R^2_{adj} = 0.036), however this association disappeared when using corrected models. Finally, significant associations were also observed for GM activation capacity. More specifically, F was positively associated when using a single linear regression model (β = 0.32, R^2_{adj} = 0.083), while period was positively related in a multiple regression model (β = 0.27, R^2_{adj} = 0.113). Overall, the effect sizes of the multiple regression models including significant associations, were 0.113 $\leq R^2_{adj} \leq$ 0.412, while for the other models they ranged from -0.024 through 0.372.

Table 6.7. Regression analysis results for daily sedentary behaviour pattern parameters.

Outcome variable		Without covariates					With covariates				
		B	95%-CI lower bound	95%-CI upper bound	B	R^2_{Adj}	B	95%-CI lower bound	95%-CI upper bound	β	R^2_{Adj}
Ankle angle MVC$_{Peak}$[¶]	Breaks SB	-0.01	-0.03	0.02	-0.05	-0.007	0.00	-0.03	0.03	0.01	**0.149****
	Short SB bouts	-0.02	-0.04	0.01	-0.12	0.005	0.00	-0.03	0.02	-0.01	**0.149****
	Long SB bouts	**0.10**	**0.03**	**0.18**	**0.26****	**0.056****	0.03	-0.05	0.11	0.08	**0.154****
	α	**-2.96**	**-5.24**	**-0.68**	**-0.25***	**0.052***	-1.78	-4.04	0.48	-0.15	**0.169****
	$X_{1/2}$	0.00	0.00	0.00	0.11	0.003	0.00	0.00	0.00	0.02	**0.142****
	$W_{1/2}$	0.00	-0.01	0.01	-0.01	-0.010	0.01	-0.01	0.02	0.11	**0.160****
	$W_{50\%}$	0.00	0.00	0.01	0.15	0.013	0.00	-0.01	0.01	0.00	**0.149****
	F	**-0.16**	**-0.31**	**-0.01**	**-0.21***	**0.034***	-0.02	-0.19	0.15	-0.02	**0.149****
	Period	-0.03	-0.07	0.01	-0.17	0.019	0.01	-0.04	0.05	0.03	**0.150****
Net torque at angle MVC$_{Peak}$	Breaks SB	-0.25	-2.07	1.57	-0.03	-0.009	-0.91	-2.45	0.63	-0.10	**0.333****
	Short SB bouts	-0.13	-1.79	1.53	-0.02	-0.010	-0.68	-2.09	0.73	-0.08	**0.330****
	Long SB bouts	-0.55	-5.63	4.53	-0.02	-0.009	-0.36	-4.89	4.17	-0.01	**0.324****
	α	114.71	-37.67	267.09	0.15	0.012	113.51	-13.13	240.14	0.14	**0.340****
	$X_{1/2}$	-0.05	-0.16	0.05	-0.10	-0.001	0.00	-0.09	0.10	0.01	**0.321****
	$W_{1/2}$	-0.81	-1.70	0.08	-0.18	0.021	**-1.05**	**-1.78**	**-0.31**	**-0.23****	**0.375****
	$W_{50\%}$	-0.09	-0.42	0.25	-0.05	-0.007	0.17	-0.13	0.47	0.10	**0.333****
	F	-1.07	-11.12	8.97	-0.02	-0.009	-5.07	-13.92	3.79	-0.10	**0.333****

	Period	1.21	-1.39	3.82	0.09	-0.001	0.86	-1.40	3.12	0.06	**0.323****
Intrinsic strength at angle MVC$_{Peak}$¶	Breaks SB	-0.02	-0.04	0.01	-0.13	0.007	**-0.03**	**-0.05**	**-0.01**	**-0.21***	**0.259****
	Short SB bouts	-0.01	-0.03	0.02	-0.06	-0.006	**-0.02**	**-0.04**	**0.00**	**-0.19***	**0.248****
	Long SB bouts	-0.07	-0.13	0.00	-0.19	0.027	-0.01	-0.08	0.05	-0.04	**0.215****
	α	1.30	-0.75	3.35	0.12	0.006	0.11	-1.76	1.99	0.01	**0.219****
	X$_{1/2}$	0.00	0.00	0.00	0.00	-0.010	0.00	0.00	0.00	0.06	**0.213****
	W$_{1/2}$	0.00	-0.01	0.01	-0.04	-0.009	-0.01	-0.02	0.00	-0.12	**0.227****
	W$_{50\%}$	0.00	0.00	0.00	0.02	-0.010	0.00	0.00	0.01	0.21	**0.253****
	F	0.01	-0.12	0.15	0.02	-0.009	-0.13	-0.26	0.00	-0.19	**0.245****
	Period	0.03	0.00	0.06	0.17	0.019	0.00	-0.03	0.03	0.01	**0.219****
Net torque at 0° angle	Breaks SB	-0.52	-2.21	1.17	-0.06	-0.006	-1.29	-2.64	0.07	-0.15	**0.372****
	Short SB bouts	-0.43	-1.97	1.12	-0.05	-0.007	-1.00	-2.25	0.26	-0.13	**0.366****
	Long SB bouts	0.29	-4.44	5.01	0.01	-0.010	0.22	-3.95	4.39	0.01	**0.354****
	α	69.52	-73.08	212.13	0.10	-0.001	57.64	-62.22	177.50	0.08	**0.360****
	X$_{1/2}$	0.17	-0.07	0.42	0.14	0.011	0.01	-0.08	0.09	0.01	**0.349****
	W$_{1/2}$	-0.78	-1.61	0.04	-0.18	0.024	**-1.04**	**-1.71**	**-0.38**	**-0.24****	**0.412****
	W$_{50\%}$	-0.05	-0.36	0.27	-0.03	-0.009	0.21	-0.06	0.48	0.13	**0.365****
	F	-2.90	-12.23	6.42	-0.06	-0.006	-6.63	-14.60	1.35	-0.14	**0.367****
	Period	1.15	-1.27	3.58	0.09	-0.001	0.99	-1.07	3.04	0.08	**0.356****
Intrinsic strength at 0° angle¶	Breaks SB	-0.02	-0.04	0.00	-0.17	0.018	**-0.03**	**-0.05**	**-0.01**	**-0.25****	**0.235****
	Short SB bouts	-0.01	-0.03	0.01	-0.10	0.000	**-0.03**	**-0.05**	**0.00**	**-0.22***	**0.221****
	Long SB bouts	-0.06	-0.12	0.01	-0.16	0.016	-0.01	-0.08	0.06	-0.03	**0.174****

	α	0.83	-1.23	2.90	0.08	-0.004	-0.31	-2.25	1.62	-0.03	**0.174****
	$X_{1/2}$	0.00	0.00	0.00	0.02	-0.010	0.00	0.00	0.00	0.07	**0.169****
	$W_{1/2}$	0.00	-0.02	0.01	-0.06	-0.006	-0.01	-0.02	0.00	-0.13	**0.180****
	$W_{50\%}$	0.00	0.00	0.01	0.04	-0.008	**0.01**	**0.00**	**0.01**	**0.24***	**0.214****
	F	-0.01	-0.15	0.12	-0.02	-0.009	**-0.15**	**-0.27**	**-0.02**	**-0.21***	**0.213****
	Period	0.03	0.00	0.07	0.17	0.021	0.01	-0.02	0.04	0.05	**0.176****
	Breaks SB	0.07	-0.20	0.34	0.05	-0.007	-0.02	-0.25	0.21	-0.01	**0.340****
	Short SB bouts	-0.04	-0.29	0.20	-0.03	-0.008	-0.08	-0.29	0.13	-0.06	**0.343****
	Long SB bouts	**0.93**	**0.19**	**1.67**	**0.24***	**0.047***	0.62	-0.05	1.29	0.16	**0.361****
	α	**-25.91**	**-48.40**	**-3.42**	**-0.22***	**0.039***	-16.61	-35.26	2.05	-0.14	**0.360****
AT moment arm	$X_{1/2}$	0.00	0.00	0.00	-0.04	-0.008	0.01	-0.00	0.03	0.16	**0.358****
	$W_{1/2}$	0.10	-0.03	0.24	0.15	0.013	0.07	-0.05	0.19	0.10	**0.343****
	$W_{50\%}$	0.03	-0.02	0.08	0.13	0.007	**0.08**	**0.03**	**0.12**	**0.30****	**0.410****
	F	-0.97	-2.47	0.52	-0.13	0.006	-1.08	-2.43	0.27	-0.14	**0.356****
	Period	**-0.44**	**-0.82**	**-0.06**	**-0.22***	**0.038***	**-0.52**	**-0.84**	**-0.21**	**-0.26****	**0.380****
	Breaks SB	0.01	0.00	0.03	0.18	0.024	0.01	0.00	0.03	0.13	**0.069***
	Short SB bouts	0.01	0.00	0.02	0.16	0.016	0.01	-0.01	0.02	0.11	**0.064***
	Long SB bouts	0.00	-0.04	0.05	0.02	-0.009	0.00	-0.04	0.04	0.02	**0.052***
L_{F-MVC}[¶]	α	0.54	-0.74	1.81	0.08	-0.003	0.33	-0.92	1.58	0.05	**0.055***
	$X_{1/2}$	0.00	0.00	0.00	0.07	-0.005	0.00	0.00	0.00	0.06	**0.056***
	$W_{1/2}$	0.00	-0.01	0.00	-0.08	-0.004	0.00	-0.01	0.01	-0.06	**0.055***
	$W_{50\%}$	0.00	-0.01	0.00	-0.17	0.020	0.00	0.00	0.00	-0.10	**0.062***

	F	0.07	-0.01	0.15	0.16	0.016	0.05	-0.03	0.13	0.12	**0.066***
	Period	0.00	-0.02	0.02	-0.03	-0.009	0.00	-0.02	0.02	-0.03	**0.053***
θ_{MVC}¶	Breaks SB	0.00	-0.02	0.01	-0.04	-0.008	0.00	-0.02	0.01	-0.05	**0.169****
	Short SB bouts	0.00	-0.02	0.01	-0.05	-0.007	0.00	-0.01	0.01	-0.03	**0.168****
	Long SB bouts	0.01	-0.03	0.05	0.05	-0.008	-0.01	-0.04	0.03	-0.03	**0.168****
	α	-0.21	-1.42	1.00	-0.03	-0.009	-0.28	-1.38	0.81	-0.05	**0.169****
	$X_{1/2}$	0.00	0.00	0.00	-0.09	-0.001	0.00	0.00	0.00	-0.16	**0.190****
	$W_{1/2}$	0.00	-0.01	0.01	0.00	-0.010	0.00	0.00	0.01	0.06	**0.170****
	$W_{50\%}$	0.00	0.00	0.00	0.10	0.001	0.00	0.00	0.00	0.07	**0.172****
	F	-0.05	-0.12	0.03	-0.11	0.003	-0.02	-0.09	0.05	-0.05	**0.169****
	Period	0.00	-0.02	0.02	-0.03	-0.009	0.00	-0.01	0.02	0.04	**0.169****
$PCSA_{MVC}$¶	Breaks SB	0.00	-0.02	0.02	0.00	-0.010	0.00	-0.02	0.02	-0.02	**0.344****
	Short SB bouts	0.00	-0.02	0.01	-0.05	-0.008	0.00	-0.02	0.02	-0.01	**0.344****
	Long SB bouts	0.05	-0.01	0.10	0.15	0.013	0.00	-0.06	0.05	-0.01	**0.344****
	α	-0.41	-2.23	1.40	-0.04	-0.008	-0.07	-1.60	1.47	-0.01	**0.344****
	$X_{1/2}$	0.00	0.00	0.00	-0.17	0.020	**0.00**	**0.00**	**0.00**	**-0.20***	**0.370****
	$W_{1/2}$	0.00	-0.01	0.01	-0.06	-0.006	0.00	-0.01	0.01	0.01	**0.344****
	$W_{50\%}$	0.00	0.00	0.00	0.04	-0.009	0.00	0.00	0.00	-0.02	**0.345****
	F	-0.08	-0.20	0.04	-0.14	0.009	0.00	-0.11	0.10	0.00	**0.344****
	Period	-0.01	-0.04	0.02	-0.07	-0.005	0.01	-0.01	0.04	0.08	**0.350****
AT force	Breaks SB	-3.03	-33.27	27.21	-0.02	-0.009	-14.61	-40.19	10.96	-0.09	**0.299****
	Short SB bouts	-1.35	-28.91	26.21	-0.01	-0.010	-9.44	-33.10	14.21	-0.07	**0.294****

	Long SB bouts	-9.89	-94.24	74.45	-0.02	-0.009	-24.39	-100.75	51.98	-0.06	**0.293****
	α	2190.98	-329.27	4711.23	0.17	0.019	1874.97	-339.50	4089.43	0.14	**0.310****
	$X_{1/2}$	3.38	-0.89	7.66	0.16	0.014	-0.27	-1.80	1.26	-0.03	**0.291****
	$W_{1/2}$	**-15.86**	**-30.56**	**-1.17**	**-0.21***	**0.034***	**-18.85**	**-31.35**	**-6.34**	**-0.25****	**0.351****
	$W_{50\%}$	-1.05	-6.61	4.52	-0.04	-0.008	2.47	-2.56	7.49	0.09	**0.297****
	F	-45.42	-211.99	121.15	-0.05	-0.007	-91.87	-241.56	57.82	-0.11	**0.300****
	Period	14.64	-28.68	57.96	0.07	-0.005	14.64	-23.78	53.06	0.07	**0.294****
Fascicle force[¶]	Breaks SB	0.00	-0.03	0.02	-0.03	-0.009	-0.02	-0.04	0.01	-0.11	**0.298****
	Short SB bouts	0.00	-0.03	0.02	-0.02	-0.009	-0.01	-0.03	0.01	-0.09	**0.292****
	Long SB bouts	-0.01	-0.08	0.06	-0.02	-0.009	-0.03	-0.09	0.04	-0.07	**0.288****
	α	1.59	-0.59	3.76	0.14	0.010	1.34	-0.59	3.26	0.12	**0.298****
	$X_{1/2}$	0.00	0.00	0.00	-0.13	0.006	-0.00	-0.00	0.00	-0.08	**0.291****
	$W_{1/2}$	-0.01	-0.03	0.00	-0.19	0.027	**-0.01**	**-0.02**	**-0.00**	**-0.20***	**0.326****
	$W_{50\%}$	0.00	-0.01	0.00	-0.02	-0.009	0.00	-0.00	0.01	0.08	**0.291****
	F	-0.04	-0.19	0.10	-0.06	-0.006	-0.08	-0.21	0.05	-0.11	**0.296****
	Period	0.01	-0.03	0.05	0.06	-0.006	0.02	-0.01	0.05	0.10	**0.294****
Specific force[¶]	Breaks SB	0.00	-0.03	0.02	-0.03	-0.009	-0.02	-0.04	0.00	-0.14	**0.207****
	Short SB bouts	0.00	-0.02	0.02	0.02	-0.009	-0.01	-0.03	0.01	-0.10	**0.197****
	Long SB bouts	-0.05	-0.11	0.01	-0.18	0.021	-0.03	-0.09	0.03	-0.09	**0.196****
	α	**2.00**	**0.19**	**3.80**	**0.21***	**0.036***	1.28	-0.40	2.96	0.14	**0.206****
	$X_{1/2}$	0.00	0.00	0.00	0.02	-0.009	0.00	0.00	0.00	0.09	**0.190****
	$W_{1/2}$	-0.01	-0.02	0.00	-0.17	0.019	**-0.01**	**-0.02**	**0.00**	**-0.23****	**0.241****

	$W_{50\%}$	0.00	-0.01	0.00	-0.06	-0.006	0.00	0.00	0.01	0.10	**0.196****
	F	0.04	-0.08	0.16	0.06	-0.006	-0.06	-0.18	0.06	-0.10	**0.195****
	Period	0.02	-0.01	0.05	0.14	0.011	0.01	-0.02	0.04	0.08	**0.193****
TA co-activation[¶]	Breaks SB	-0.01	-0.04	0.02	-0.07	-0.006					
	Short SB bouts	-0.00	-0.04	0.03	-0.03	-0.009					
	Long SB bouts	-0.05	-0.14	0.04	-0.10	0.001					
	α	0.91	-1.90	3.72	0.06	-0.006					
	$X_{1/2}$	-0.00	-0.00	0.00	-0.11	0.002					
	$W_{1/2}$	0.01	-0.01	0.02	0.08	-0.003					
	$W_{50\%}$	0.00	-0.00	0.01	0.09	-0.002					
	F	-0.01	-0.19	0.18	-0.01	-0.010					
	Period	0.02	-0.03	0.06	0.06	-0.006					
GM activation capacity[¶]	Breaks SB	0.00	-0.03	0.02	-0.04	-0.017	-0.01	-0.03	0.01	-0.10	0.047
	Short SB bouts	0.00	-0.02	0.02	0.04	-0.017	0.00	-0.02	0.02	-0.02	0.038
	Long SB bouts	-0.05	-0.11	0.02	-0.20	0.020	-0.06	-0.12	0.01	-0.24	**0.095***
	α	1.80	-0.10	3.71	0.25	0.045	1.64	-0.22	3.51	0.23	**0.091***
	$X_{1/2}$	0.00	0.00	0.00	0.02	-0.018	0.00	0.00	0.00	0.06	0.041
	$W_{1/2}$	-0.01	-0.02	0.01	-0.13	0.000	-0.01	-0.02	0.00	-0.15	0.062
	$W_{50\%}$	0.00	-0.01	0.00	-0.06	-0.015	0.00	0.00	0.01	0.04	0.039
	F	**0.16**	**0.03**	**0.29**	**0.32***	**0.083***	0.13	-0.01	0.26	0.25	**0.114***
	Period	0.03	0.00	0.06	0.24	0.041	**0.03**	**0.00**	**0.06**	**0.27***	**0.113***
Fatigue$_{ISOM}$ duration[¶]	Breaks SB	0.00	-0.01	0.02	0.09	-0.015	0.00	-0.02	0.02	0.08	0.121

	Short SB bouts	0.00	-0.01	0.02	0.05	-0.021	0.00	-0.02	0.02	0.00	0.114
	Long SB bouts	0.01	-0.03	0.05	0.09	-0.015	-0.01	-0.03	0.01	-0.11	-0.012
	α	0.09	-1.20	1.37	0.02	-0.023	0.17	-1.60	1.94	0.04	0.116
	$X_{1/2}$	0.00	0.00	0.00	0.04	-0.022	0.00	0.00	0.00	0.03	-0.024
	$W_{1/2}$	0.00	-0.01	0.01	-0.09	-0.015	0.00	-0.01	0.00	-0.09	-0.017
	$W_{50\%}$	0.00	0.00	0.00	0.05	-0.022	0.00	0.00	0.00	-0.16	0.002
	F	0.04	-0.01	0.08	0.27	0.048	-0.02	-0.13	0.10	-0.06	0.118
	Period	0.00	-0.02	0.02	0.03	-0.023	0.00	-0.01	0.01	0.04	-0.022
Fatigue$_{ISOM}$ relative change RMS EMG[¶]	Breaks SB	0.00	-0.03	0.02	-0.04	-0.022	0.01	-0.02	0.03	0.08	**0.242****
	Short SB bouts	0.00	-0.03	0.02	-0.05	-0.022	0.01	-0.02	0.03	0.07	**0.239****
	Long SB bouts	0.01	-0.07	0.08	0.02	-0.023	-0.02	-0.09	0.05	-0.06	**0.223****
	α	-0.03	-2.39	2.33	0.00	-0.024	0.52	-1.58	2.63	0.07	**0.224****
	$X_{1/2}$	0.00	0.00	0.00	0.13	-0.007	0.00	0.00	0.00	0.04	**0.236****
	$W_{1/2}$	0.00	-0.02	0.01	-0.07	-0.018	0.00	-0.01	0.01	0.02	**0.235****
	$W_{50\%}$	0.00	0.00	0.01	0.10	-0.014	0.00	-0.01	0.00	-0.09	**0.227****
	F	-0.11	-0.28	0.05	-0.22	0.023	0.15	-0.04	0.34	0.30	**0.280****
	Period	-0.01	-0.05	0.03	-0.10	-0.014	0.00	-0.04	0.03	-0.02	**0.234****
Fatigue$_{ISOM}$ rate of change RMS EMG[¶]	Breaks SB	0.00	0.00	0.00	-0.06	-0.021	0.00	0.00	0.00	0.01	0.085
	Short SB bouts	0.00	0.00	0.00	-0.07	-0.019	0.00	0.00	0.00	0.01	0.085
	Long SB bouts	0.00	0.00	0.00	0.03	-0.023	0.00	0.00	0.00	-0.03	0.086
	α	0.00	-0.05	0.04	-0.03	-0.023	0.01	-0.03	0.05	0.04	0.086
	$X_{1/2}$	0.00	0.00	0.00	0.10	-0.014	0.00	0.00	0.00	0.04	0.086

	$W_{1/2}$	0.00	0.00	0.00	-0.05	-0.021	0.00	0.00	0.00	-0.02	0.085
	$W_{50\%}$	0.00	0.00	0.00	0.09	-0.015	0.00	0.00	0.00	-0.03	0.086
	F	0.00	-0.01	0.00	-0.24	0.037	0.00	0.00	0.00	-0.15	**0.126***
	Period	0.00	0.00	0.00	-0.03	-0.023	0.00	0.00	0.00	0.04	0.086
Fatigue$_{ISOM}$ relative change MPF¶	Breaks SB	0.01	-0.08	0.09	0.03	-0.023	0.01	-0.08	0.09	0.03	-0.023
	Short SB bouts	0.01	-0.07	0.09	0.04	-0.022	0.01	-0.07	0.09	0.04	-0.022
	Long SB bouts	-0.01	-0.24	0.23	-0.01	-0.024	-0.01	-0.24	0.23	-0.01	-0.024
	α	-1.94	-9.07	5.18	-0.08	-0.016	-1.94	-9.07	5.18	-0.08	-0.016
	$X_{1/2}$	0.00	0.00	0.00	-0.07	-0.019	0.00	0.00	0.00	-0.07	-0.019
	$W_{1/2}$	0.02	-0.02	0.06	0.15	0.000	0.02	-0.02	0.06	0.15	0.000
	$W_{50\%}$	0.00	-0.02	0.02	0.01	-0.024	0.00	-0.02	0.02	0.01	-0.024
	F	0.30	-0.21	0.80	0.18	0.010	0.30	-0.21	0.80	0.18	0.010
	Period	0.03	-0.09	0.16	0.09	-0.016	0.03	-0.09	0.16	0.09	-0.016
Fatigue$_{ISOM}$ rate of change MPF¶	Breaks SB	0.00	0.00	0.00	0.09	-0.016	0.00	0.00	0.00	0.09	-0.016
	Short SB bouts	0.00	0.00	0.00	0.12	-0.008	0.00	0.00	0.00	0.12	-0.008
	Long SB bouts	0.00	-0.01	0.01	-0.08	-0.017	0.00	-0.01	0.01	-0.08	-0.017
	α	-0.04	-0.29	0.21	-0.05	-0.022	-0.04	-0.29	0.21	-0.05	-0.022
	$X_{1/2}$	0.00	0.00	0.00	-0.07	-0.019	0.00	0.00	0.00	-0.07	-0.019
	$W_{1/2}$	0.00	0.00	0.00	0.15	-0.001	0.00	0.00	0.00	0.15	-0.001
	$W_{50\%}$	0.00	0.00	0.00	-0.10	-0.014	0.00	0.00	0.00	-0.10	-0.014
	F	0.00	-0.01	0.01	-0.10	-0.015	0.00	-0.01	0.01	-0.10	-0.015
	Period	0.00	0.00	0.00	0.00	-0.024	0.00	0.00	0.00	0.00	-0.024

	Breaks SB	-0.01	-0.03	0.02	-0.05	-0.008	-0.01	-0.03	0.02	-0.05	-0.008
	Short SB bouts	0.00	-0.02	0.01	-0.04	-0.008	0.00	-0.02	0.01	-0.04	-0.008
	Long SB bouts	0.00	-0.05	0.06	0.01	-0.010	0.00	-0.05	0.06	0.01	-0.010
	α	0.35	-1.37	2.07	0.04	-0.008	0.35	-1.37	2.07	0.04	-0.008
Fatigue$_{ISOK}$ duration[¶]	$X_{1/2}$	0.00	0.00	0.00	0.09	-0.002	0.00	0.00	0.00	0.09	-0.002
	$W_{1/2}$	0.00	-0.01	0.01	-0.05	-0.008	0.00	-0.01	0.01	-0.05	-0.008
	$W_{50\%}$	0.00	0.00	0.00	0.03	-0.009	0.00	0.00	0.00	0.03	-0.009
	F	-0.03	-0.15	0.08	-0.06	-0.007	-0.03	-0.15	0.08	-0.06	-0.007
	Period	0.01	-0.02	0.04	0.06	-0.006	0.01	-0.02	0.04	0.06	-0.006
	Breaks SB	-0.01	-0.06	0.03	-0.06	-0.007	-0.02	-0.06	0.03	-0.07	**0.078***
	Short SB bouts	-0.01	-0.05	0.04	-0.04	-0.009	-0.01	-0.06	0.03	-0.06	**0.077***
	Long SB bouts	-0.04	-0.17	0.09	-0.06	-0.006	-0.02	-0.15	0.11	-0.03	**0.073***
	α	-0.71	-4.71	3.29	-0.04	-0.009	-0.68	-4.52	3.16	-0.03	**0.074***
Fatigue$_{ISOK}$ relative change RMS EMG[¶]	$X_{1/2}$	0.00	0.00	0.00	0.01	-0.010	0.00	0.00	0.00	0.01	**0.073***
	$W_{1/2}$	0.01	-0.02	0.03	0.06	-0.007	0.00	-0.02	0.03	0.02	**0.073***
	$W_{50\%}$	0.00	-0.01	0.01	-0.02	-0.010	0.00	-0.01	0.01	-0.02	**0.073***
	F	0.00	-0.27	0.26	0.00	-0.010	-0.06	-0.31	0.20	-0.04	**0.075***
	Period	0.01	-0.06	0.08	0.02	-0.010	0.00	-0.07	0.07	0.00	**0.073***
	Breaks SB	0.00	0.00	0.00	0.02	-0.010	0.00	0.00	0.00	0.02	-0.010
Fatigue$_{ISOK}$ rate of change RMS EMG[¶]	Short SB bouts	0.00	0.00	0.00	0.03	-0.009	0.00	0.00	0.00	0.03	-0.009
	Long SB bouts	0.00	0.00	0.00	-0.04	-0.009	0.00	0.00	0.00	-0.04	-0.009
	α	0.00	-0.09	0.09	0.01	-0.010	0.00	-0.09	0.09	0.01	-0.010

	$X_{1/2}$	0.00	0.00	0.00	0.00	-0.010	0.00	0.00	0.00	0.00	-0.010
	$W_{1/2}$	0.00	0.00	0.00	0.03	-0.009	0.00	0.00	0.00	0.03	-0.009
	$W_{50\%}$	0.00	0.00	0.00	-0.01	-0.010	0.00	0.00	0.00	-0.01	-0.010
	F	0.00	-0.01	0.01	0.00	-0.010	0.00	-0.01	0.01	0.00	-0.010
	Period	0.00	0.00	0.00	-0.01	-0.010	0.00	0.00	0.00	-0.01	-0.010
Fatigue$_{ISOK}$ relative change MPF[¶]	Breaks SB	0.00	-0.02	0.02	-0.02	-0.010	0.00	-0.02	0.02	-0.02	-0.010
	Short SB bouts	0.00	-0.02	0.02	0.00	-0.010	0.00	-0.02	0.02	0.00	-0.010
	Long SB bouts	-0.02	-0.07	0.04	-0.07	-0.006	-0.02	-0.07	0.04	-0.07	-0.006
	α	-0.24	-1.84	1.35	-0.03	-0.009	-0.24	-1.84	1.35	-0.03	-0.009
	$X_{1/2}$	0.00	0.00	0.00	-0.01	-0.010	0.00	0.00	0.00	-0.01	-0.010
	$W_{1/2}$	0.00	-0.01	0.01	0.07	-0.005	0.00	-0.01	0.01	0.07	-0.005
	$W_{50\%}$	0.00	0.00	0.00	-0.04	-0.008	0.00	0.00	0.00	-0.04	-0.008
	F	0.03	-0.08	0.13	0.05	-0.008	0.03	-0.08	0.13	0.05	-0.008
	Period	0.01	-0.02	0.04	0.06	-0.006	0.01	-0.02	0.04	0.06	-0.006
Fatigue$_{ISOK}$ rate of change MPF[¶]	Breaks SB	0.00	0.00	0.00	-0.11	0.002	0.00	0.00	0.00	-0.06	0.035
	Short SB bouts	0.00	0.00	0.00	-0.09	-0.002	0.00	0.00	0.00	-0.05	0.033
	Long SB bouts	0.00	0.00	0.00	-0.05	-0.007	0.00	0.00	0.00	-0.05	0.034
	α	-0.01	-0.07	0.05	-0.02	-0.010	0.00	-0.06	0.06	0.01	0.031
	$X_{1/2}$	0.00	0.00	0.00	-0.02	-0.010	0.00	0.00	0.00	-0.02	0.031
	$W_{1/2}$	0.00	0.00	0.00	0.01	-0.010	0.00	0.00	0.00	-0.01	0.031
	$W_{50\%}$	0.00	0.00	0.00	0.03	-0.009	0.00	0.00	0.00	-0.04	0.032
	F	0.00	0.00	0.00	-0.02	-0.010	0.00	0.00	0.00	0.02	0.031

| | Period | 0.00 | 0.00 | 0.00 | 0.08 | -0.003 | 0.00 | 0.00 | 0.00 | 0.09 | 0.038 |

MVC, maximum voluntary contraction; AT, Achilles tendon; L_{F-MVC}, fascicle length during MVC; θ_{MVC}, fascicle pennation angle during MVC; $PCSA_{MVC}$, physiological cross-sectional area during MVC; TA, tibialis anterior; GM, gastrocnemius medialis; Isom, isometric condition; Isok, isokinetic condition; RMS, root mean square; EMG, electromyography; MPF, median power frequency; Breaks SB, sedentary behaviour interruptions with ≥2 consecutive minutes upright activity; Short SB bouts, sedentary behaviour bouts <30 minutes duration; Long SB bouts, sedentary behaviour bouts ≥30 minutes duration; α, scaling parameter sedentary bout length distribution; $X_{1/2}$, median SB bout duration; $W_{1/2}$, fraction total sedentary time accumulated in bouts longer than median sedentary bout length; $W_{50\%}$, half of total SB is accumulated in SB bouts ≤ this duration; F, fragmentation index of SB bouts and total SB; Period, mean period between SB bouts; [¶]Log-transformed; *P<0.05; ** P<0.01.

Discussion

The present study investigated associations of SB with GM muscle strength, specific force and function in older adults. It was hypothesised that (i) intrinsic GM muscle strength, (ii) GM specific force, and (iii) GM function are inferior in participants exhibiting high SB levels, regardless of being sufficiently active or not. Additionally, both proportional total daily SB and daily SB pattern parameters were expected to be detrimentally associated with all studied GM muscle outcomes in older adults. Our results partially support these hypotheses.

The fact that no differences were found between the SB level groups when correcting for covariates, might result from grouping our participants into broad categories (<8 or ≥8 hrs daily SB). This potentially attenuates any associations that we would see during linear regression analyses, due to large group variances. Nevertheless, an association with ankle angle of peak torque was identified, indicating that higher levels of SB are related to greater ankle angles (in other words more PF) indicating shorter muscle length. This is in agreement with literature, showing evidence that angle of peak torque shifts towards longer muscle lengths after training (182).

Compositional data analysis did not show any associations with GM strength, specific force or function for the proportion of total daily time spent in SB. On the contrary, three out of four identified associations involved time spent standing relative to the other daily behaviours, while one involved LIPA. The observed relationships all indicate improved outcomes when increasing the proportional time spent in these behaviours. Standing for example, was positively associated with θ_{MVC}, $PCSA_{MVC}$ and GM activation capacity. These findings are similar to the effects seen in response to training (183,184) and opposite to those resulting from disuse (185). Interestingly, no associations were found for any PA intensities, except between LIPA and AT force. Overall, it is important to stress that the results involving standing and LIPA should be interpreted with caution. This is mainly due to the issues with distinguishing between standing and LIPA, as seen in Chapter 2 & 3 of this thesis. As a result, associations are potentially over- or underestimated.

Apart from the fact that we applied single-twitch muscle stimulation, using the interpolation twitch technique to measure agonist activation capacity in human muscles (as in this chapter), can be quite challenging. Different authors have suggested a number of methodological and physiological considerations to be taken into account when applying the technique (186). Generally, the ability to maximally drive muscle is usually

overestimated and twitch interpolation is highly variable under constant circumstances (186). Hence, the results of this technique should be interpreted with caution. Nevertheless, test-retest reliability for the assessment of GM muscle activation capacity was good in this chapter (ICC = 0.891).

A number of associations was found for a variety of daily SB pattern parameters during multiple regression analysis. Interestingly, the relationships were mainly seen for GM strength and force outcomes. However, also the Achilles tendon moment arm appeared to decrease with 'better' daily SB pattern parameters. Although the tendon moment arm is determined by the anatomical constraints of the skeleton, a trend for smaller tendon moment arm lengths was observed in an exercise group compared to controls (163). This suggests that physical activity may affect the tendon moment arm, but how is unclear. The use of a new method to measure Achilles tendon moment arms in this chapter could have affected the results, however, analysis showed moderate reliability (ICC = 0.733), which indicates that the quality of the collected data is acceptable. Combining this with the excellent ICCs for PF torque values, means that the calculation of AT force was highly reliable.

The consensus is that decreased PA levels are one of the causing factors for the ageing-related decrease in muscle strength, force and function (138,187). In line with this, it was observed that an increase in the amount of SB spent in bouts longer than the median bout duration was associated with a decrease in net torque production. This was the case for both the peak torque angle and the neutral angle. As discussed in Chapter 5, the force a muscle can generate is proportional to the PCSA, yet no associations were observed for muscle size or architecture, except for the preferred SB bout length (β = -0.20, R^2_{adj} = 0.370). The lower force with increasing SB was also not explicable by changes in TA co-activation. However, an increase in the ability to activate the GM voluntarily was found with longer periods between separate SB bouts. Nevertheless, the fact that a result was found in only one out of nine SB pattern parameters, suggests that a true association between SB and net torque production is most probably lacking.

More associations were identified regarding intrinsic muscle strength. In general, these results all indicate an increase in intrinsic strength with increasing SB, opposite to what has previously been reported (127). However, with intrinsic strength being the ratio of net torque over muscle volume, the observed trends (less SB = higher volume) in muscle volume (chapter 5) might explain these findings. It must be noted that when correcting for

126

muscle volume, both contractile and non-contractile tissue is taken into account, and thus measures of intrinsic strength are not conclusive and can effect an overall decrease in muscle quality, e.g. due to fat infiltrations. Instead, specific force was calculated, which showed only one association. The identified parameter suggests that with an increased proportion of total daily SB spent in bouts longer than the median bout duration, force production decreases. Having not observed any associations between SB on one hand and muscle architecture during isometric MVC on the other, probably explains the consistency of identified associations from tendon force to fascicle force and eventually specific force. Overall, with the lack of associations for specific force, it can be concluded that SB is not associated with muscle force production.

In this chapter, no significant associations with any kind of SB outcome were found for TA co-activation and GM fatigue resistance, while only one was observed for both GM architecture during MVC and GM activation capacity. The fact that generally no association was found for muscle architecture is in line with the results seen in chapter 5. Although decreased activation capacity (130) and increased co-activation (188) was demonstrated during ageing, a recent review showed increased activation capacity but no change in co-activation in elderly after strength training (189). Combining this result with our findings, suggests that PA has an important role in neuromuscular function in older adults, as previously stated (187). The only association found for GM activation capacity and SB in this chapter, supports this as the relationship suggests that breaking sedentary behaviour with longer duration of non-SB activity increases GM activation capacity. Next, the absence of significant results regarding muscle fatigue resistance seems to be in line with literature. Compared to their younger counterparts, older adults have been identified with an age-related fatigue advantage under isometric conditions, regardless of PA levels (190). This is suggested to result from many changes in their neuromuscular system (171), such as a larger proportion of type I muscle fibres, which are more economical during isometric contractions (191,192) and might explain the absence of significant associations with either SB or PA. Finally, the remarkable lack of significant results for MVPA throughout the whole study overall, suggests that habitual levels of this PA intensity might be less important for the GM muscle properties studied in our elderly population under the given circumstances.

Although a total of 105 older adults were tested, some outcomes were examined in subpopulations for a variety of reasons. Interpretation of the results in these variables (i.e. GM activation capacity or muscle fatigue resistance) should therefore be done more

cautiously. Nonetheless, an important strength of this chapter is the high number of good-to-excellent ICCs (8 out of 9) indicating high reliability of the data used. As discussed above, the reliability for Achilles tendon moment arm measurements was moderate (ICC = 0.733), which means that this chapter's data holds more than acceptable quality.

Conclusion

Except for the consistent negative association of both GM strength and force with the proportion of daily total SB spent in bouts longer than or equal to the median SB bout duration, no other associations with SB outcomes were identified. The absence of any relationship with MVPA suggests that the detrimental effects of SB on GM force cannot be overcome by MVPA, but rather by reducing SB in older adults.

Chapter 7. The association of sedentary behaviour with gastrocnemius medialis tendon properties and postural balance in older adults

Introduction

Upright stability is an important factor for functional independence in the elderly, and is negatively associated with ageing (44). Previous studies have shown correlations between postural sway and plantar flexor characteristics in both young and old age groups, such as muscle volume and tendon stiffness (44,193,194). The muscle-tendon unit (MTU) consists of two components: (i) the muscle and (ii) the tendon. The muscle Is the contractile component where force is developed, while a tendon is used to transmit those forces from muscles to bones (188). A more compliant tendon would result in slower force development and may delay responses to impeding falls (188). The latter shows the important role tendons have within the MTU, which warrants their targeted study.

Although reports have shown that ageing does not only affect skeletal muscles, but also tendons, the effects identified are inconsistent (188). Nevertheless, the consensus is that elderly tendons are more compliant, which is mainly the result of tendon material changes (188,195). In addition, tendon cross-sectional area (CSA) increases with ageing, probably to compensate for changes in the mechanical properties in order to maintain appropriate tendon stiffness (195,196). Accumulation of scar tissue from previous injuries might also affect tendon CSA and compliance. The important functional implication of the stiffness reduction in elderly tendons is: a slower transmission of generated muscle forces. In other words, older people will be less effective at preventing falls, which can have serious impact on their lives (188). Fortunately, resistance training has been shown to effectively attenuate or even reverse the detrimental effect that ageing has on skeletal muscle and tendon (197,198). With regards to tendon adaptations, resistive loading can increase both stiffness and Young's modulus (YM) in elderly human tendons (199). However, conflicting evidence exist regarding the effects on tendon CSA (200). Nevertheless, it is believed that increased tendon stiffness after resistance training is due to changes in the material properties rather than hypertrophy of the tendon (188,196).

Where resistance training has beneficial effects, decreased PA levels are thought to be an important factor causing the age-related MTU changes (127,187,201). Since PA levels appeared to act independent of sedentary behaviour (SB) in older adults (Chapter 3), and a combination of the adverse effects of disuse on muscle-tendon properties (199) and the

positive relationship between age and SB (Introduction & Chapter 3), it would be highly interesting to examine the role of SB on tendon modulation in older adults. More specifically, investigating the associations between SB and both gastrocnemius medialis (GM) tendon properties and postural balance in older adults, have not yet been studied.

Hence, the main aim of this present chapter was to examine the associations of SB with GM tendon properties and postural balance in older adults. It was hypothesised that SB levels are detrimentally associated with GM tendon stiffness (through YM) and postural stability. However, a positive association was expected between SB levels and tendon CSA. Similar associations were also expected for total daily time spent in SB relative to other behaviours and daily SB pattern parameters.

Materials and methods

As described in Chapter 4 of this thesis, 105 healthy older adults participated in this cross-sectional study. Per protocol, participants came to the university twice: at the first visit they were familiarised with the testing equipment and an activity monitor was provided, while on the second visit (after a week of habitual daily activity monitoring) their GM tendon properties and postural balance were tested. In the participants that underwent postural stability assessment, this was performed before testing their tendon properties.

SB and PA outcomes

See chapter 4 for a detailed overview of the SB and PA outcomes used in this chapter.

Postural balance

To determine postural balance, a representative subgroup of 45 participants (without any disease or condition that could affect postural stability) were asked to stand barefoot and quietly (with hands hanging freely at either side) on a piezo-electric force platform (Kistler Instrument, Amherst, NY, USA) using their self-perceived dominant leg, while data was sampled at a frequency of 100 Hz. A total of six trials were performed (three times with eyes open and a visual focus point at eye level, about three meters in front of the participant; three times with eyes closed using blinding goggles) in a random order to minimise learning-effects. Participants were instructed to perform the single-leg stance (self-perceived dominant leg) for as longs as possible, up to 30 seconds maximum. To prevent any carry-over effect of fatigue, they sat down between two trials for at least two

minutes. For each trial, displacement of the centre-of-pressure was measured in both the anterior-posterior and mediolateral direction, which allowed calculation of total displacement (mm) using the following formula (44):

$$Total\ displacement = \sqrt{(RMS_{AP})^2 + (RMS_{ML})^2}$$

where RMS = root mean square, AP = anterior-posterior, and ML = mediolateral.

For each condition, the trial with the longest stance duration was analysed. To improve data quality, the first and last 5% of the selected trial data was discarded. Finally, three outcomes were determined per trial: duration (s), total displacement (mm) and sway frequency (total displacement normalised for trial duration (mm·s^{-1})).

Tendon size

Participants were placed in a prone position on a treatment bed, with the foot of their self-perceived dominant leg fixed in a neutral position (90° angle between foot and lower leg). While in this position, scanning of the Achilles tendon was performed using B-mode ultrasonography (Technos; Esaote S.p.A, Genoa, Italy). At first, the insertion of the tendon into the calcaneus was determined and marked. Next, the tendon was scanned longitudinally until the musculotendinous junction was identified. The position was then marked and thin strips (2 mm) of micropore tape (Transpore, 3M, USA) placed transversally across the tendon. The distance between the tendon insertion and musculotendinous junction was measured and represented the resting tendon length (cm; L_T). Positions 1, 2 and 3 cm above the tendon insertion were marked and scanned transversally, during which the ultrasound probe (7.5 MHz linear-array probe, 3.8 cm wide) was held perpendicular to the skin (Figure 7.1). Minimal pressure was maintained to avoid compression of tendon tissue. Water-soluble transmission gel (Aquasonic 100; Parker Laboratories Inc., Fairfield, NJ, USA) was placed over the ultrasound probe head to improve acoustic coupling. During the scanning, the real-time ultrasound image was recorded onto a PC with video capturing software (25 frames per second; Adobe premier pro version 6). This allowed offline extraction of individual transverse frames at the three identified sections of the tendon. The cross-sectional area (CSA) per section was measured (mm^2) using digitising software (ImageJ 1.45, National Institutes of Health, Bethesda, MD, USA). The three CSAs were averaged and then multiplied by 0.3 to calculate the GM tendon CSA for further data analysis. This value was based upon the assumption that the fraction of the GM tendon CSA was equivalent to the proportion of GM muscle CSA to the whole triceps surae (202,203).
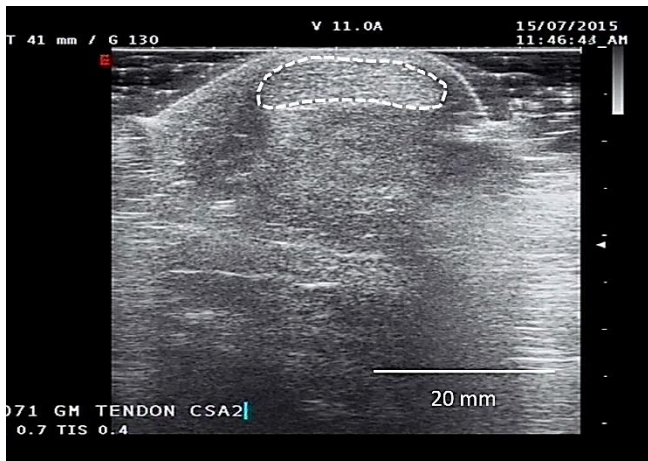
Figure 7.1. Analysis of Achilles tendon cross-sectional area at 2 cm above calcaneus insertion.

Tendon stiffness and Young's modulus

Participants sat on the chair of an isokinetic dynamometer (Cybex Norm; Cybex International, New York, NY, USA) with their hip in an 85° angle, self-perceived dominant leg extended and foot secured to the footplate of the dynamometer in an 0° angle (no plantar- (PF) or dorsiflexion (DF)) and the lateral malleolus aligned with the axis of rotation. Non-extending straps were used at the hip, distal thigh and chest to prevent extraneous movements. After a series of five submaximal PF and DF contractions that served as a warm-up (50 - 75% self-perceived maximum voluntary contraction (MVC)), participants performed a ramped isometric PF MVC over 5 seconds. Each ramped PF MVC was followed by a rapid isometric DF MVC (2 – 3 seconds), with verbal encouragement and biofeedback provided by the experimenter during each effort. These MVCs were performed in the 0° angle for both PF and DF, with 30-60 seconds between the trials. A total of three MVC combinations were performed, however, if >10% difference was observed between all values, extra ramped MVCs were executed (maximum five in total). The effort with the highest PF MVC value was used for data analyses. Tendon elongation during the ramped PF MVCs was assessed by B-mode ultrasonography, placing the probe over the micropore tape on the musculotendinous junction. Again, water-soluble transmission gel was placed over the ultrasound probe head to improve acoustic coupling. Real time recording of the ultrasound image was similar to that for the tendon CSAs. Synchronisation of the muscle strength data and ultrasound recording was performed using a square wave signal generator. This allowed the extraction of ultrasound images from 0 – 100% MVC, with 10% increments. The distance between the musculotendinous junction and the shadow cast from the echo-absorptive micropore was measured using digitising software. Corrections

132

were made for unwanted shift of the heel during the ramped isometric MVC, as identified in a previous study (204). Important for the analysis was that both the shadow and musculotendinous junction were clearly visible on the ultrasound images.

As described in Chapter 6, antagonist co-activation was determined using surface electromyography (sEMG) to allow calculation of true PF torques. In short, muscle activation of the tibialis anterior (TA) was determined by calculating the median root mean square (RMS) of the sEMG signal over 500 ms intervals around each 10% increment in ramped isometric PF MVC, while a period of 1 s around the peak torque during rapid isometric DF MVC was used. Antagonist torque output for each 10% increment of the ramped isometric PF MVC was calculated by dividing TA sEMG RMS during PF by TA sEMG RMS during DF, and multiplying the rapid isometric DF MVC torque by this ratio. This assumes a linear relation between DF torque and TA EMG (205). The sum of the antagonist torque and the ramped isometric PF MVC torque represented the net PF MVC (N·m).

Next, GM tendon force (N) at each 10% MVC interval was calculated by first dividing the net PF MVC by the tendon moment arm in the neutral ankle angle (0°) (mm; assessed with single energy X-ray absorptiometry, as detailed in Chapter 6), and then multiplying the result by 0.203. This latter value represents the assumption that 20.3% of the Achilles tendon force was generated by the GM (176).

To estimate GM tendon stiffness per participant, denoted as K (N·mm^{-1}), GM tendon force and corresponding elongation data was plotted and fitted with a second-order polynomial fixed through zero (average R^2 was 0.96 (0.05)). By calculating the polynomial's first derivative, the slope at each point of the force-elongation curve could be determined, which represented K. A total of three tendon stiffness outcomes were calculated: average K over the curve, maximum K and standardised K. For this latter, a force level of 74.3 N (as seen in our weakest participant) was used. From these results, Young's modulus (MPa) was calculated by multiplying K by the ratio of L$_T$ (mm) over tendon CSA (mm^2). Tendon stress and strain were calculated as the ratio of tendon force over tendon CSA (stress; MPa) and the ratio of tendon elongation over resting tendon length (strain; %).

Reliability

Test-retest reliability was determined for the main outcomes under study in this chapter, using the intraclass correlation coefficient (ICC) for absolute agreement using a two-way mixed model. Reliability values <0.5 were interpreted as poor, between 0.5 - 0.75 as

moderate, between 0.75 - 0.9 as good and >0.9 as excellent (158). L_T showed an ICC of 0.906, while for tendon CSA it was 0.970. Finally, both PF torque values and maximum tendon elongation measured during the ramped MVC in the neutral ankle angle had ICCs of 0.995 and 0.698 respectively.

Statistics

The outcome variables are displayed as mean (standard deviation (SD)) or median (interquartile range (IQR)) (Table 7.1). Prior to conducting any inferential statistical analysis, all outcome variables were checked for normality (either Kolmogorov-Smirnov or Shapiro-Wilk test). In case of non-normality, the variables were log-transformed and the distribution of the transformed data also checked. Since postural balance was performed in a subsample only, their representativeness of the whole study sample was assessed using an Independent samples T-test or Mann-Whitney U test. Potential covariates were analysed per outcome variable by running a univariate General Linear Model (GLM). When a parameter appeared significant, it was treated as a covariate (Table 7.2). Since daily time spent in sleep, SB and physical activity (PA) is constrained to 24 hours, we used compositional data analysis for these accelerometer outcomes. This type of analysis has been described in detail previously (118,119). Briefly, daily compositions are transformed into isometric log-ratio coordinates, which are then unconstrained and allow the application of traditional multivariate statistics. In this chapter, both single and multiple linear regression analysis was used to study the associations with SB levels, proportional total daily SB and PA, and daily SB pattern parameters. The identified covariates were added to the regression models first, by using backward elimination, after which the predictor(s) of interest was/were entered. During backward elimination, parameters were retained if p-values were <0.20 (118). For all models, Durbin-Watson statistics (>1.0 and <3.0) were checked to identify any correlation between the predictor and covariates, and covariates with variance inflation factor ≥10.0 were removed from the regression model, one at the time. The same was done with individual cases showing Cook's distance ≥1.0. If significant associations were observed for the compositional data, isotemporal substitution was applied to the identified models including covariates, to calculate the relative effects (%) of re-allocating 10 minutes from one behaviour to the other, with respect to the study sample's mean outcomes. Ten minutes was chosen, not only because of its beneficial effects (for example when moderate-to-vigorous PA (MVPA) is performed) (159), but also because it is a realistic amount of time to replace in most elderly.

All statistical analyses were performed using IBM SPSS Statistics for Windows, version 24.0 (IBM Corp., Armonk, NY, USA) and p-values <0.05 were considered statistically significant.

Results

Descriptive statistics

Table 7.1 shows the study sample's descriptive statistics of the GM tendon size, stiffness, YM and postural balance.

Table 7.1. Study sample descriptive statistics of GM tendon properties and postural balance.

Outcome variable		Mean (SD) or ¶median (IQR)
GM L_T (cm)		17.8 (2.4)
Maximal GM tendon elongation (mm)		13.6 (5.5)
GM tendon CSA (mm^2)		28.6 (8.2)¶
GM tendon force (N)		266.9 (108.2)
K	Average (N·mm^{-1})	19.4 (13.2)¶
	Maximum (N·mm^{-1})	28.3 (16.8)¶
	Standardised (N·mm^{-1})	23.2 (13.1)¶
YM	Average (MPa)	118.2 (74.5)¶
	Maximum (MPa)	163.8 (122.6)¶
	Standardised (MPa)	143.3 (87.1)¶
Maximal stress (MPa)		9.2 (5.3)¶
Maximal strain (%)		7.3 (5.3)¶
EO	Duration (s)	28.0 (24.0)¶
	TD (mm)	8.9 (11.5)¶
	Sway frequency (mm·s^{-1})	0.4 (2.5)¶
EC	Duration (s)	5.0 (4.0)¶
	TD (mm)	21.7 (14.0)¶
	Sway frequency (mm·s^{-1})	5.3 (7.2)¶

GM, gastrocnemius medialis; L_T, tendon length; CSA, cross-sectional area; *K*, stiffness; MVC, maximum voluntary contraction; YM, Young's modulus; EO, eyes open; TD, total displacement; EC, eyes closed; SD, standard deviation; IQR, interquartile range.

Covariate analysis

The variables identified as covariates in this chapter were: age, sex, ethnicity, body height, body mass, body mass index (BMI), skeletal mass index (SMI), body fat mass, body lean mass, body bone mineral content (BMC), adiposity class, falls risk assessment tool (FRAT) score, menopause age, history of major illness, smoking, calcium/vitamin D supplement

usage, total time spent in PA bouts, standing during PA bouts, light-intensity PA (LIPA) during PA bouts, moderate-to-vigorous PA (MVPA) during PA bouts, MVPA in bouts of ≥10 consecutive minutes and physical activity status (Table 7.2-3).

Table 7.2. Correlation coefficients of covariate analysis for tendon properties.

	GM L_T	Max Δ GM L_T	GM tendon CSA[¶]	GM tendon force	K_{Avg}[¶]	K_{Max}[¶]	K_{Std}[¶]	YM_{Avg}[¶]	YM_{Max}[¶]	YM_{Std}[¶]	Max stress[¶]	Max strain[¶]
Age	**0.323**	-0.158	0.101	-0.145	0.001	0.026	0.000	0.082	0.102	0.077	**-0.204**	**-0.241**
Sex	**0.489**	0.000	**0.529**	**0.452**	**0.303**	**0.391**	**0.425**	0.197	**0.298**	**0.326**	0.148	-0.115
Ethnicity	-0.073	-0.015	0.093	-0.035	0.016	0.019	-0.043	-0.049	-0.042	-0.103	-0.066	0.026
Body height	**0.504**	-0.046	**0.579**	**0.446**	**0.327**	**0.366**	**0.325**	0.192	**0.248**	**0.201**	0.054	-0.165
Body mass	**0.276**	0.057	**0.592**	**0.238**	0.023	0.186	0.186	-0.177	-0.002	-0.006	-0.124	0.006
BMI	-0.026	0.090	**0.279**	-0.043	-0.196	-0.031	-0.007	**-0.332**	-0.166	-0.142	-0.180	0.113
SMI	**0.249**	0.093	**0.582**	**0.420**	**0.225**	**0.302**	**0.321**	0.022	0.117	0.131	0.086	0.043
Fat mass	**-0.313**	0.032	**-0.268**	**-0.434**	**-0.427**	**-0.342**	**-0.322**	**-0.387**	**-0.316**	**-0.292**	**-0.263**	0.111
Lean mass	**0.310**	-0.037	**0.259**	**0.434**	**0.429**	**0.341**	**0.323**	**0.393**	**0.319**	**0.296**	**0.264**	-0.116
BMC mass	**0.240**	0.032	**0.283**	**0.296**	**0.279**	**0.241**	**0.219**	**0.206**	0.180	0.155	0.174	-0.028
Adiposity class	0.159	0.008	**0.204**	-0.128	-0.140	0.002	0.007	-0.177	-0.037	-0.032	**-0.207**	-0.039
FRAT score	0.029	-0.109	0.037	**-0.208**	-0.095	0.063	0.062	-0.088	0.066	0.064	**-0.208**	-0.153
Menopause age	-0.128	-0.094	0.085	0.086	0.161	**0.320**	0.243	0.030	0.170	0.108	0.022	-0.005
Major illness history	0.122	0.060	0.152	0.053	-0.028	0.050	0.094	-0.054	0.024	0.067	0.002	0.032
Statins usage	0.165	0.065	0.156	0.108	0.072	0.150	0.158	0.030	0.112	0.117	0.071	0.013
Smoking	0.030	-0.058	-0.086	-0.044	-0.028	-0.073	-0.029	0.030	-0.020	0.025	-0.066	-0.106
Resistance training	-0.169	0.054	0.026	0.105	0.055	-0.032	-0.015	0.001	-0.081	-0.064	0.079	0.088
Dairy products	-0.110	0.008	-0.032	0.117	0.161	0.101	0.093	0.130	0.078	0.068	0.157	0.036

Caffeine intake	0.097	-0.003	0.143	0.136	0.152	0.057	0.097	0.092	0.006	0.044	0.010	-0.034
RA diagnosis	0.019	-0.016	0.052	-0.051	0.128	0.168	0.091	0.052	0.100	0.021	-0.081	-0.016
Daily alcohol intake ≥3 units	0.070	0.000	0.135	0.055	-0.047	0.038	0.049	-0.085	0.001	0.011	-0.032	-0.022
Calcium/vitamin D supplements	-0.190	0.027	**-0.249**	**-0.241**	-0.174	-0.118	-0.107	-0.093	-0.047	-0.034	-0.076	0.027
PA bouts	0.002	-0.154	-0.096	-0.020	0.111	0.085	0.077	0.147	0.121	0.112	0.001	-0.117
Total PA bouts time	-0.131	0.095	-0.106	0.053	-0.062	-0.091	-0.082	-0.053	-0.084	-0.074	0.078	0.136
SB during PA bout	-0.138	0.019	-0.165	-0.002	0.020	-0.021	-0.008	0.057	0.015	0.027	0.095	0.017
Standing during PA bout	**-0.224**	0.118	-0.148	-0.152	**-0.293**	**-0.273**	**-0.211**	**-0.282**	**-0.270**	**-0.206**	-0.057	0.191
LIPA during PA bout	**-0.314**	0.147	**-0.269**	-0.044	-0.148	**-0.267**	**-0.262**	-0.131	**-0.254**	**-0.246**	0.045	**0.203**
MVPA during PA bout	**0.370**	-0.176	**0.303**	0.096	**0.241**	**0.341**	**0.312**	**0.220**	**0.326**	**0.294**	-0.023	**-0.254**
MVPA$_{\geq 10\ mins}$	0.052	-0.163	0.098	0.112	0.184	**0.321**	**0.371**	0.158	**0.300**	**0.345**	0.073	-0.161
sMVPA	0.189	-0.031	0.161	0.115	0.111	0.132	0.116	0.097	0.121	0.104	0.038	-0.058
Physical activity status	0.083	-0.106	0.115	0.136	0.140	**0.266**	**0.324**	0.113	**0.243**	**0.297**	0.116	-0.096

GM, gastrocnemius medialis; L_T, resting tendon length; CSA, cross-sectional area; K_{Avg}, average tendon stiffness; K_{Max}, maximum tendon stiffness; K_{Std}, standardised tendon stiffness; YM_{Avg}, average Young's modulus; YM_{Max}, maximum Young's modulus; YM_{Std}, standardised Young's modulus; EO_{TIME}, duration of eyes open condition; EO_{TD}, total displacement during eyes open condition; EO_{Hz}, postural sway frequency during eyes open condition; EC_{TIME}, duration of eyes closed condition; EC_{TD}, total displacement during eyes closed condition; EC_{Hz}, postural sway frequency during eyes closed condition; BMI, body mass index; SMI, skeletal muscle index; BMC, bone mineral content; FRAT, falls risk assessment tool; RA, rheumatoid arthritis; PA, physical activity; SB, sedentary behaviour; LIPA, light-intensity physical activity; MVPA, moderate-to-vigorous physical activity; sMVPA, sporadic moderate-to-vigorous physical activity; ¶log-transformed. Bold values represent significances at P<0.05 level.

Table 7.3. Correlation coefficients of covariate analysis for postural balance.

	EO$_{Time}$¶	EO$_{TD}$¶	EO$_{Hz}$¶	EC$_{Time}$¶	EC$_{TD}$¶	EC$_{Hz}$¶
Age	**-0.397**	0.138	**0.313**	**-0.308**	-0.092	0.192
Sex	-0.176	**0.388**	0.291	-0.038	**0.429**	0.253
Ethnicity	0.119	-0.142	-0.141	**0.323**	**-0.312**	**-0.414**
Body height	0.050	**0.298**	0.108	0.022	**0.369**	0.176
Body mass	-0.174	**0.485**	**0.336**	0.037	0.263	0.108
BMI	-0.235	**0.376**	**0.323**	0.026	0.062	0.012
SMI	-0.145	**0.440**	**0.296**	0.073	**0.329**	0.114
Fat mass	-0.046	-0.095	-0.015	0.015	**-0.346**	-0.192
Lean mass	0.056	0.081	0.003	-0.003	**0.337**	0.178
BMC mass	-0.066	0.205	0.137	-0.144	**0.332**	0.285
Adiposity class	-0.187	0.248	0.233	-0.038	0.089	0.076
FRAT score	**-0.430**	0.165	**0.347**	**-0.445**	-0.040	**0.326**
Menopause age	0.211	-0.205	-0.225	0.314	0.197	-0.160
Major illness history	-0.027	0.292	0.153	-0.084	**0.384**	0.266
Statins usage	-0.012	0.164	0.084	0.125	0.107	-0.042
Smoking	0.211	**-0.297**	-0.271	0.179	-0.079	-0.181
Resistance training	0.217	-0.223	-0.240	0.037	-0.258	-0.164
Dairy products	0.004	-0.039	-0.021	-0.125	0.154	0.178
Caffeine intake	0.148	-0.016	-0.100	-0.041	0.020	0.043
RA diagnosis	-0.054	-0.104	-0.014	0.057	-0.292	-0.197
Daily alcohol intake ≥3 units	0.011	0.105	0.042	0.109	0.053	-0.059
Calcium/vitamin D supplements	-0.059	0.068	0.069	-0.252	0.107	0.252
PA bouts	-0.020	0.037	0.030	-0.133	0.015	0.112
Total PA bouts time	**0.332**	0.019	-0.200	-0.013	0.102	0.063
SB during PA bout	0.011	-0.210	-0.105	0.168	-0.180	-0.224
Standing during PA bout	0.032	-0.058	-0.047	-0.010	0.128	0.074
LIPA during PA bout	**0.307**	-0.212	-0.292	0.027	-0.184	-0.116
MVPA during PA bout	-0.275	0.213	0.272	-0.030	0.129	0.090
MVPA$_{≥10 mins}$	0.107	0.149	0.002	0.168	**0.339**	0.046
sMVPA	0.048	0.110	0.021	-0.027	0.104	0.075
Physical activity status	0.081	0.145	0.017	0.149	**0.299**	0.039

GM, gastrocnemius medialis; L$_T$, resting tendon length; CSA, cross-sectional area; K_{Avg}, average tendon stiffness; K_{Max}, maximum tendon stiffness; K_{Std}, standardised tendon stiffness; YM$_{Avg}$, average Young's modulus; YM$_{Max}$, maximum Young's modulus; YM$_{Std}$, standardised Young's modulus; EO$_{TIME}$, duration of eyes

open condition; EO_{TD}, total displacement during eyes open condition; EO_{Hz}, postural sway frequency during eyes open condition; EC_{TIME}, duration of eyes closed condition; EC_{TD}, total displacement during eyes closed condition; EC_{Hz}, postural sway frequency during eyes closed condition; BMI, body mass index; SMI, skeletal muscle index; BMC, bone mineral content; FRAT, falls risk assessment tool; RA, rheumatoid arthritis; PA, physical activity; SB, sedentary behaviour; LIPA, light-intensity physical activity; MVPA, moderate-to-vigorous physical activity; sMVPA, sporadic moderate-to-vigorous physical activity; [¶]log-transformed. Bold values represent significances at P<0.05 level.

SB levels

No significant models, and thus associations between SB levels and GM tendon properties or postural balance were found without covariate-adjustment (Table 7.4 & Figure 7.2). Adding covariates to the models, however, did not result in any significant associations either, except for balance trial duration with eyes open (β = -0.26, R^2_{adj} = 0.293). The effect sizes of the other multiple linear regression models ranged from R^2_{adj} = 0.000 through 0.497.

Table 7.4. Single and multiple regression analysis results for SB levels.

Outcome variable		Without covariates					With covariates				
		B	95%-CI lower bound	95%-CI upper bound	β	R^2_{Adj}	B	95%-CI lower bound	95%-CI upper bound	β	R^2_{Adj}
GM L_T		3.38	-8.90	15.65	0.05	-0.007	0.41	-9.97	10.79	0.01	**0.372****
Max Δ GM L_T		-1.42	-4.30	1.46	-0.10	0.000	-1.42	-4.30	1.46	-0.10	0.000
GM tendon CSA[¶]		0.03	-0.08	0.14	0.05	-0.007	0.00	-0.09	0.08	-0.01	**0.497****
GM tendon force		-18.30	-73.11	36.51	-0.07	-0.005	-2.50	-51.63	46.63	-0.01	**0.290****
K	Average[¶]	-0.03	-0.27	0.20	-0.03	-0.010	0.08	-0.14	0.31	0.07	**0.186****
	Maximum[¶]	0.05	-0.21	0.31	0.04	-0.009	0.09	-0.16	0.33	0.07	**0.180****
	Standardised[¶]	0.05	-0.21	0.30	0.04	-0.009	0.08	-0.15	0.30	0.06	**0.223****
YM	Average[¶]	-0.04	-0.29	0.20	-0.04	-0.009	0.12	-0.12	0.35	0.10	**0.154****
	Maximum[¶]	0.04	-0.23	0.30	0.03	-0.010	0.13	-0.12	0.39	0.10	**0.113****
	Standardised[¶]	0.04	-0.22	0.30	0.03	-0.010	0.06	-0.18	0.30	0.04	**0.140****
Maximal stress[¶]		-0.11	-0.33	0.11	-0.10	-0.001	-0.01	-0.23	0.21	-0.01	**0.088****
Maximal strain[¶]		-0.13	-0.39	0.13	-0.10	0.000	-0.11	-0.36	0.15	-0.08	**0.045***
EO	Duration[¶]	-0.69	-1.43	0.05	-0.28	0.055	**-0.64**	**-1.29**	**-0.00**	**-0.26***	**0.293****
	TD[¶]	0.32	-0.24	0.88	0.17	0.007	0.24	-0.27	0.75	0.13	**0.270****[¶]
	Sway frequency[¶]	1.01	-0.17	2.19	0.25	0.043	0.89	-0.16	1.93	0.22	**0.260****
EC	Duration[¶]	0.09	-0.53	0.70	0.04	-0.021	0.09	-0.42	0.60	0.05	**0.288****
	TD[¶]	-0.07	-0.48	0.35	-0.05	-0.021	-0.03	-0.38	0.32	-0.02	**0.328****
	Sway frequency[¶]	-0.15	-0.94	0.63	-0.06	-0.020	-0.10	-0.79	0.59	-0.04	**0.215****

GM, gastrocnemius medialis; L$_T$, resting tendon length; CSA, cross-sectional area; K, tendon stiffness; YM, Young's modulus; EO, eyes open condition; TD, total displacement; EC, eyes closed condition; ¶log-transformed; *P<0.05; ** P<0.01.
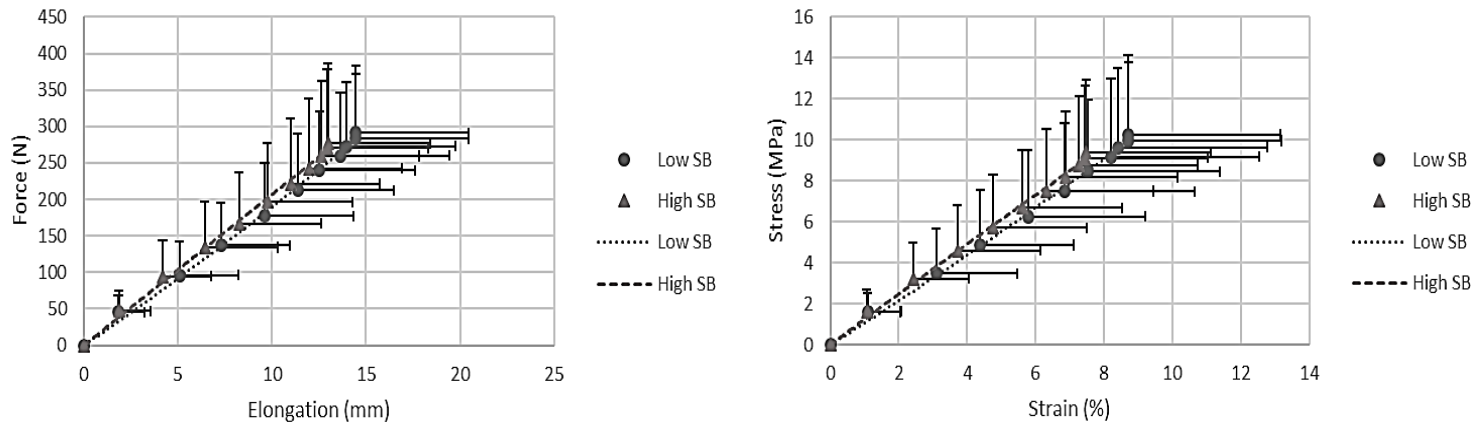
Figure 7.2. Comparison between low and high sedentary behaviour level groups for gastrocnemius medialis tendon stiffness (left) and Young's modulus (right).

GM, gastrocnemius medialis; SB, sedentary behaviour; Stress is the ratio of GM tendon force over resting GM tendon cross-sectional area; Strain is the ratio of GM tendon elongation over the GM tendon resting length. Error bars represent standard deviations.

Daily total SB and PA

Compositional data analysis showed several significant associations for a variety of outcomes (Table 7.5). More specifically, GM L_T was associated with both standing (β = -0.20) and MVPA (β = 0.25) when using an unadjusted model (R^2_{adj} = 0.132). However, in the covariate-adjusted model (R^2_{adj} = 0.377) all associations disappeared. The same happened in the models for GM tendon CSA, average *K*, maximum *K*, standardised *K*, average YM and maximum YM, where respectively MVPA (β = 0.22, R^2_{adj} = 0.080), standing (β = -0.24, R^2_{adj} = 0.046), MVPA (β = 0.24, R^2_{adj} = 0.099), MVPA (β = 0.21, R^2_{adj} = 0.068), standing (β = -0.23, R^2_{adj} = 0.034) and MVPA (β = 0.22, R^2_{adj} = 0.088) were associated at first, but not after developing new models including covariates (R^2_{adj} = 0.489, R^2_{adj} = 0.231, R^2_{adj} = 0.190, R^2_{adj} = 0.162, R^2_{adj} = 0.200 and R^2_{adj} = 0.144). The opposite was seen for GM tendon force, which was not associated at all, when using simple regression models but showed association with LIPA after adjusting (β = 0.23, R^2_{adj} = 0.325). Associations identified for postural balance with eyes open were stable across unadjusted and adjusted models for some activity intensities, but not for all. For example, trial duration was positively associated with sleep, but only in an adjusted model (β = 0.51, R^2_{adj} = 0.455), whereas SB was negatively associated in both models (β = -0.72, R^2_{adj} = 0.198 & β = -0.99, R^2_{adj} = 0.455). Total displacement was negatively associated with sleep (β = -0.71, R^2_{adj} = 0.104 & β = -0.55, R^2_{adj} = 0.293) but positively with SB (β = 0.88, R^2_{adj} = 0.104 & β = 0.62, R^2_{adj} = 0.293). Postural sway frequency was also associated with SB during eyes open condition in both models, respectively (β = 0.86, R^2_{adj} = 0.164 & β = 0.98, R^2_{adj} = 0.360). Nevertheless, sleep and MVPA were only associated in corrected models (β = -0.74 and β = 0.28, both R^2_{adj} = 0.360). Finally, total displacement during eyes closed condition was only associated with sleep (β = -0.85) and SB (β = 0.98) in uncorrected models (R^2_{adj} = 0.141). However, with the addition of covariates, another association appeared. Apart from sleep (β = -0.87) and SB (β = 1.13), standing (β = 0.28) was also associated with total displacement during the eyes closed condition in these models (R^2_{adj} = 0.484). Overall, the effect sizes of the multiple linear regression models including a significant association, were 0.293 ≤ R^2_{adj} ≤ 0.484. For the other corrected models (without an association), the effect sizes were: 0.009 ≤ R^2_{adj} ≤ 0.489.

Isotemporal substitution showed that the relative effects (%-change from study sample means) of re-allocating 10 minutes from one behaviour to another within the mean composition of the study sample's total daily SB and PA (sleep = 35.6%, SB = 39.4%, standing = 2.8%, LIPA = 11.5% and MVPA = 10.7%) for the models including behaviours significantly

associated with either GM tendon properties or postural balance and adjusted for covariates, varied from -0.709% through +0.562% (Table 7.6). These maximum changes were both seen for sway frequency during postural balance with eyes open, when substituting 10 min of sleep with standing and vice versa respectively.

Table 7.5. Coefficients of multiple regression models based on compositional data analysis.

Outcome variable			Without covariates			With covariates		
			B	β	R^2_{Adj}	B	β	R^2_{Adj}
GM L_T		Sleep	2.02	0.02	**0.132****	4.93	0.04	**0.377****
		SB	7.30	0.10		1.47	0.02	
		Standing	**-11.12**	**-0.20***		-7.63	-0.14	
		LIPA	-12.99	-0.18		-3.66	-0.05	
		MVPA	**14.79**	**0.25***		4.89	0.08	
Max Δ GM L_T		Sleep	-4.38	-0.17	0.009	-4.38	-0.17	0.009
		SB	1.70	0.10		1.70	0.10	
		Standing	1.52	0.12		1.52	0.12	
		LIPA	2.20	0.13		2.20	0.13	
		MVPA	-1.16	-0.09		-1.16	-0.09	
GM tendon CSA[¶]		Sleep	-0.11	-0.11	**0.080***	0.10	0.11	**0.489****
		SB	0.14	0.22		-0.05	-0.08	
		Standing	-0.06	-0.13		-0.03	-0.07	
		LIPA	-0.09	-0.14		-0.02	-0.03	
		MVPA	**0.12**	**0.22***		0.00	0.00	
GM tendon force		Sleep	-133.12	-0.27	-0.002	-82.56	-0.17	**0.325****
		SB	73.68	0.23		65.90	0.21	
		Standing	-17.46	-0.07		-10.75	-0.04	
		LIPA	36.94	0.11		**75.15**	**0.23***	
		MVPA	39.52	0.15		-48.25	-0.18	
K	Average[¶]	Sleep	0.15	0.07	0.046	0.21	0.10	**0.231****
		SB	-0.05	-0.04		0.12	0.09	
		Standing	**-0.24**	**-0.24***		-0.19	-0.19	
		LIPA	-0.04	-0.03		-0.08	-0.06	
		MVPA	0.19	0.17		-0.03	-0.03	
	Maximum[¶]	Sleep	0.22	0.10	**0.099****	0.31	0.14	**0.190****
		SB	-0.05	-0.03		-0.01	0.00	
		Standing	-0.23	-0.20		-0.18	-0.16	
		LIPA	-0.23	-0.16		-0.20	-0.14	
		MVPA	**0.29**	**0.24***		0.08	0.06	

	Standardised¶	Sleep	0.25	0.11	**0.068***	0.33	0.15	**0.162***
		SB	-0.09	-0.06		-0.07	-0.05	
		Standing	-0.13	-0.12		-0.13	-0.12	
		LIPA	-0.29	-0.20		-0.11	-0.07	
		MVPA	**0.25**	**0.21***		0.01	0.01	
YM	Average¶	Sleep	0.30	0.14	0.034	0.11	0.05	**0.200***
		SB	-0.16	-0.12		0.22	0.16	
		Standing	**-0.24**	**-0.23***		-0.21	-0.20	
		LIPA	-0.05	-0.03		-0.04	-0.03	
		MVPA	0.17	0.15		-0.05	-0.05	
	Maximum¶	Sleep	0.37	0.16	**0.088***	0.32	0.14	**0.144***
		SB	-0.16	-0.11		-0.01	0.00	
		Standing	-0.22	-0.20		-0.21	-0.19	
		LIPA	-0.25	-0.16		-0.19	-0.13	
		MVPA	**0.27**	**0.22***		0.08	0.07	
	Standardised¶	Sleep	0.40	0.18	0.057	0.36	0.16	**0.106***
		SB	-0.20	-0.14		-0.06	-0.04	
		Standing	-0.13	-0.12		-0.12	-0.10	
		LIPA	-0.31	-0.21		-0.26	-0.17	
		MVPA	0.23	0.19		0.06	0.05	
	Maximal stress¶	Sleep	-0.19	-0.10	-0.031	-0.12	-0.06	**0.076***
		SB	0.02	0.02		0.16	0.13	
		Standing	0.02	0.02		0.04	0.05	
		LIPA	0.11	0.09		0.05	0.04	
		MVPA	0.03	0.03		-0.15	-0.14	
	Maximal strain¶	Sleep	-0.41	-0.18	**0.061***	-0.30	-0.13	**0.076***
		SB	0.11	0.08		0.09	0.06	
		Standing	0.21	0.19		0.22	0.20	
		LIPA	0.24	0.16		0.12	0.08	
		MVPA	-0.16	-0.13		-0.15	-0.12	
EO	Duration¶	Sleep	1.00	0.22	**0.198***	**2.28**	**0.51***	**0.455***
		SB	**-2.06**	**-0.72***		**-2.84**	**-0.99***	
		Standing	-0.14	-0.07		-0.07	-0.03	
		LIPA	0.84	0.29		0.26	0.09	
		MVPA	-0.23	-0.10		-0.48	-0.20	
	TD¶	Sleep	**-2.35**	**-0.71***	0.104	**-1.80**	**-0.55***	**0.293***
		SB	**1.88**	**0.88***		**1.30**	**0.62***	
		Standing	0.12	0.08		0.14	0.09	
		LIPA	0.06	0.03		0.43	0.20	

		MVPA	0.46	0.26		0.10	0.05	
	Sway frequency¶	Sleep	-3.36	-0.47	**0.164***	**-5.25**	**-0.74**	**0.360**
		SB	**3.93**	**0.86**		**4.48**	**0.98**	
		Standing	0.27	0.08		0.17	0.05	
		LIPA	-0.78	-0.17		0.17	0.04	
		MVPA	0.69	0.18		**1.05**	**0.28***	
EC	Duration¶	Sleep	-1.05	-0.30	-0.067	-0.31	-0.09	**0.244***
		SB	0.69	0.30		0.32	0.14	
		Standing	-0.09	-0.05		0.09	0.05	
		LIPA	0.35	0.15		-0.11	-0.05	
		MVPA	-0.01	-0.01		-0.12	-0.06	
	TD¶	Sleep	**-2.02**	**-0.85**	**0.141***	**-2.06**	**-0.87**	**0.484**
		SB	**1.50**	**0.98**		**1.72**	**1.13**	
		Standing	0.32	0.28		**0.32**	**0.28***	
		LIPA	0.05	0.03		0.28	0.18	
		MVPA	0.28	0.22		0.05	0.04	
	Sway frequency¶	Sleep	-0.96	-0.21	-0.044	-1.49	-0.33	**0.212***
		SB	0.81	0.27		1.20	0.41	
		Standing	0.41	0.18		0.19	0.09	
		LIPA	-0.30	-0.10		-0.09	-0.03	
		MVPA	0.29	0.12		0.44	0.18	

GM, gastrocnemius medialis; L_T, resting tendon length; CSA, cross-sectional area; K, tendon stiffness; YM, Young's modulus; EO, eyes open condition; TD, total displacement; EC, eyes closed condition; SB, sedentary behaviour; LIPA, light-intensity physical activity; MVPA, moderate-to-vigorous physical activity; ¶log-transformed; *P<0.05; ** P<0.01.

Table 7.6. Relative effects (%) of isotemporal substitution on outcome variables.

Outcome variable	+10 mins	-10 mins				
		Sleep	SB	Standing	LIPA	MVPA
GM tendon force	Sleep				-0.016	
	SB				-0.001	
	Standing				-0.030	
	LIPA	+0.015	+0.001	+0.036	+0.000	+0.019
	MVPA				-0.019	
EO Duration¶	Sleep	+0.000	+0.021	+0.058	+0.021	+0.024
	SB	-0.021	+0.000	-0.115	-0.025	-0.025
	Standing	-0.046	+0.091			
	LIPA	-0.020	+0.024			
	MVPA	-0.023	+0.023			
EO TD¶	Sleep	+0.000	-0.017	-0.095	-0.027	-0.025

146

	SB	+0.017	+0.000	+0.042	+0.009	+0.013
	Standing	+0.075	-0.034			
	LIPA	+0.026	-0.009			
	MVPA	+0.024	-0.013			
EO Sway frequency[¶]	Sleep	+0.000	-0.120	-0.709	-0.153	-0.184
	SB	+0.120	+0.000	+0.279	+0.110	+0.093
	Standing	+0.562	-0.220			+0.054
	LIPA	+0.147	-0.105			-0.034
	MVPA	+0.176	-0.089	-0.065	+0.034	+0.000
EC TD[¶]	Sleep	+0.000	-0.014	-0.082	-0.021	-0.020
	SB	+0.014	+0.000	+0.036	+0.010	+0.013
	Standing	+0.065	-0.028	+0.000	+0.004	+0.011
	LIPA	+0.020	-0.010	-0.005		
	MVPA	+0.019	-0.012	-0.013		

GM, gastrocnemius medialis; EO, eyes open condition; TD, total displacement; EC, eyes closed condition; SB, sedentary behaviour; LIPA, light-intensity physical activity; MVPA, moderate-to-vigorous physical activity; [¶]log-transformed. Bold values represent the relative change from the study sample's mean outcome for adjusted models including significant association(s) with any of the daily total behaviours.

Daily SB pattern parameters

Regression analysis showed several associations between daily SB pattern parameters and outcome variables (Table 7.7). For example, maximal tendon elongation was negatively associated with $W_{1/2}$ in the single linear regression model, (β = -0.22, R^2_{adj} = 0.041). However, the linear relationship disappeared completely when adding covariates. Although not associated in single regression models, GM tendon CSA was associated with Breaks SB when accounting for covariates (β = -0.15, R^2_{adj} = 0.518). The same was true for average *K* (β = -0.25, R^2_{adj} = 0.269), average YM (β = -0.29, R^2_{adj} = 0.256) and maximum YM (β = -0.23, R^2_{adj} = 0.216) with Period, and for total displacement during eyes closed postural balance with $X_{1/2}$ (β = -0.27, R^2_{adj} = 0.458). On the contrary, maximal strain and sway frequency during eyes open postural balance were associated with $W_{1/2}$ & Period (both maximal strain) and Long SB bouts (sway frequency) in an uncorrected model (β = -0.22, R^2_{adj} = 0.037 & β = 0.21, R^2_{adj} = 0.035 vs. β = 0.31, R^2_{adj} = 0.077), but this relationship disappeared after adding covariates. GM tendon force, maximal stress and trial duration during eyes open single-legged balance were the only outcomes showing models with consistent associations across single and multiple regression models. More specifically, GM tendon force was negatively associated with $W_{1/2}$ (β = -0.21, R^2_{adj} = 0.034 & β = -0.25, R^2_{adj} = 0.351) and so was maximal stress (β = -0.23, R^2_{adj} = 0.042 & β = -0.25, R^2_{adj} = 0.151), while

147

trial duration during eyes open postural balance was negatively associated with $X_{1/2}$ (β = -0.34, R^2_{adj} = 0.093 & β = -0.37, R^2_{adj} = 0.449) and Period (β = 0.34, R^2_{adj} = 0.094 & β = 0.29, R^2_{adj} = 0.331). Interestingly, the latter outcome was also associated with Long SB bouts in a single regression model (β = -0.36, R^2_{adj} = 0.108), but not after covariate-adjustment. Moreover, the opposite was seen for a negative association with $W_{50\%}$ in a multiple linear regression model (β = -0.26, R^2_{adj} = 0.312), but without showing a significant association in a single linear regression model. Overall, the effect sizes for the multiple linear regression models including significant associations of SB parameters, ranged from 0.151 through 0.518. The rest of the adjusted models had effect sizes of $0.067 \leq R^2_{adj} \leq 0.512$.

Table 7.7. Single and multiple regression analysis results for daily sedentary behaviour pattern parameters.

Outcome variable		Without covariates					With covariates				
		B	95%-CI lower bound	95%-CI upper bound	β	R^2_{Adj}	B	95%-CI lower bound	95%-CI upper bound	β	R^2_{Adj}
GM L_T	Breaks SB	0.02	-1.36	1.39	0.00	-0.010	-0.79	-1.92	0.33	-0.11	**0.392****
	Short SB bouts	-0.37	-1.62	0.88	-0.06	-0.006	-0.65	-1.68	0.37	-0.10	**0.390****
	Long SB bouts	3.62	-0.15	7.38	0.18	0.025	0.03	-3.39	3.45	0.00	**0.375****
	α	-84.58	-199.56	30.40	-0.14	0.011	-48.33	-147.59	50.93	-0.08	**0.385****
	$X_{1/2}$	0.01	-0.07	0.09	0.02	-0.009	0.05	-0.02	0.11	0.12	**0.388****
	$W_{1/2}$	0.38	-0.30	1.06	0.11	0.002	0.24	-0.33	0.80	0.07	**0.384****
	$W_{50\%}$	0.07	-0.18	0.33	0.06	-0.006	0.16	-0.06	0.38	0.12	**0.388****
	F	-4.12	-11.66	3.42	-0.11	0.002	-3.63	-10.14	2.87	-0.09	**0.383****
	Period	-1.75	-3.69	0.20	-0.17	0.021	-0.78	-2.47	0.92	-0.08	**0.380****
Max Δ GM L_T	Breaks SB	-0.24	-0.56	0.07	-0.15	0.013					
	Short SB bouts	-0.16	-0.45	0.14	-0.11	0.001					
	Long SB bouts	-0.46	-1.36	0.43	-0.10	0.001					
	α	20.37	-6.63	47.36	0.15	0.013					
	$X_{1/2}$	0.00	0.00	0.00	0.08	-0.004					
	$W_{1/2}$	**-0.18**	**-0.33**	**-0.02**	**-0.22***	**0.041***					
	$W_{50\%}$	0.01	-0.04	0.07	0.05	-0.008					
	F	-0.26	-2.04	1.52	-0.03	-0.010					

		Period	0.39	-0.06	0.85	0.17	0.020					
GM tendon CSA¶		Breaks SB	-0.01	-0.02	0.01	-0.10	0.000	**-0.01**	**-0.02**	**0.00**	-0.15*	**0.518****
		Short SB bouts	-0.01	-0.02	0.00	-0.15	0.012	-0.01	-0.02	0.00	-0.14	**0.512****
		Long SB bouts	0.03	0.00	0.07	0.19	0.025	0.00	-0.03	0.03	-0.01	**0.497****
		α	-0.55	-1.58	0.48	-0.10	0.001	-0.13	-0.90	0.65	-0.02	**0.497****
		$X_{1/2}$	0.00	0.00	0.00	-0.09	-0.002	0.00	0.00	0.00	-0.05	**0.499****
		$W_{1/2}$	0.00	-0.01	0.01	-0.01	-0.010	0.00	0.00	0.00	0.00	**0.497****
		$W_{50\%}$	0.00	0.00	0.00	0.06	-0.006	0.00	0.00	0.00	0.12	**0.507****
		F	-0.07	-0.13	0.00	-0.19	0.027	-0.04	-0.09	0.01	-0.12	**0.507****
		Period	-0.01	-0.02	0.01	-0.07	-0.004	0.01	-0.01	0.02	0.06	**0.500****
GM tendon force		Breaks SB	-0.61	-6.75	5.52	-0.02	-0.009	-2.97	-8.16	2.23	-0.09	**0.299****
		Short SB bouts	-0.27	-5.87	5.32	-0.01	-0.010	-1.92	-6.72	2.88	-0.07	**0.294****
		Long SB bouts	-2.01	-19.13	15.11	-0.02	-0.009	-4.95	-20.45	10.55	-0.06	**0.293****
		α	444.77	-66.84	956.38	0.17	0.019	380.62	-68.92	830.15	0.14	**0.310****
		$X_{1/2}$	0.69	-0.18	1.55	0.16	0.014	-0.05	-0.36	0.26	-0.03	**0.291****
		$W_{1/2}$	**-3.22**	**-6.20**	**-0.24**	**-0.21***	**0.034***	**-3.83**	**-6.36**	**-1.29**	**-0.25****	**0.351****
		$W_{50\%}$	-0.21	-1.34	0.92	-0.04	-0.008	0.50	-0.52	1.52	0.09	**0.297****
		F	-9.22	-43.03	24.59	-0.05	-0.007	-18.65	-49.04	11.74	-0.11	**0.300****
		Period	2.97	-5.82	11.77	0.07	-0.005	2.97	-4.83	10.77	0.07	**0.294****
K	Average¶	Breaks SB	0.01	-0.01	0.04	0.11	0.002	0.01	-0.02	0.03	0.04	**0.214****
		Short SB bouts	0.01	-0.01	0.03	0.09	-0.003	0.00	-0.02	0.02	0.01	**0.213****
		Long SB bouts	0.02	-0.06	0.09	0.04	-0.009	0.04	-0.03	0.11	0.11	**0.224****

	Parameter										
	α	0.23	-2.01	2.47	0.02	-0.010	-0.54	-2.63	1.54	-0.05	**0.215****
	$X_{1/2}$	0.00	0.00	0.00	-0.08	-0.004	0.00	0.00	0.00	-0.05	**0.215****
	$W_{1/2}$	0.00	-0.01	0.01	-0.02	-0.010	0.00	-0.02	0.01	-0.07	**0.217****
	$W_{50\%}$	0.00	-0.01	0.00	-0.06	-0.006	0.00	0.00	0.01	0.06	**0.216****
	F	0.00	-0.15	0.14	-0.01	-0.010	-0.09	-0.22	0.05	-0.12	**0.225****
	Period	-0.03	-0.06	0.01	-0.14	0.009	**-0.05**	**-0.08**	**-0.01**	**-0.25****	**0.269****
	Breaks SB	0.01	-0.02	0.04	0.08	-0.003	0.00	-0.02	0.03	0.01	**0.235****
	Short SB bouts	0.01	-0.02	0.03	0.04	-0.009	0.00	-0.02	0.02	-0.01	**0.235****
	Long SB bouts	0.04	-0.04	0.12	0.10	0.000	0.02	-0.05	0.09	0.05	**0.238****
	α	-1.30	-3.74	1.14	-0.11	0.001	-1.99	-4.17	0.18	-0.17	**0.249****
Maximum¶	$X_{1/2}$	0.00	0.00	0.00	-0.15	0.013	0.00	0.00	0.00	-0.14	**0.255****
	$W_{1/2}$	0.01	-0.01	0.02	0.08	-0.004	0.00	-0.01	0.02	0.04	**0.236****
	$W_{50\%}$	0.00	-0.01	0.00	-0.02	-0.010	0.00	0.00	0.01	0.06	**0.238****
	F	-0.05	-0.21	0.11	-0.06	-0.007	-0.11	-0.26	0.04	-0.14	**0.250****
	Period	-0.03	-0.07	0.01	-0.13	0.007	-0.04	-0.07	0.00	-0.18	**0.263****
	Breaks SB	0.01	-0.02	0.04	0.08	-0.005	-0.01	-0.03	0.02	-0.04	**0.266****
	Short SB bouts	0.00	-0.02	0.03	0.03	-0.010	-0.01	-0.03	0.02	-0.06	**0.268****
	Long SB bouts	0.04	-0.03	0.12	0.11	0.002	0.03	-0.04	0.10	0.08	**0.272****
Standardised¶	α	-0.85	-3.25	1.55	-0.07	-0.005	-1.24	-3.30	0.81	-0.11	**0.276****
	$X_{1/2}$	0.00	0.00	0.00	-0.11	0.001	0.00	0.00	0.00	-0.07	**0.269****
	$W_{1/2}$	0.00	-0.01	0.02	0.02	-0.010	0.00	-0.01	0.01	-0.02	**0.265****
	$W_{50\%}$	0.00	-0.01	0.00	-0.04	-0.009	0.00	0.00	0.01	0.08	**0.266****

		F	-0.05	-0.20	0.11	-0.06	-0.007	-0.10	-0.24	0.03	-0.13	**0.282****
		Period	-0.02	-0.06	0.02	-0.11	0.002	-0.03	-0.06	0.01	-0.14	**0.277****
YM	Average¶	Breaks SB	0.02	-0.01	0.05	0.15	0.011	0.01	-0.02	0.03	0.05	**0.179****
		Short SB bouts	0.02	-0.01	0.04	0.13	0.005	0.00	-0.02	0.02	0.01	**0.177****
		Long SB bouts	0.01	-0.07	0.08	0.02	-0.010	0.05	-0.03	0.12	0.12	**0.191****
		α	0.41	-1.91	2.73	0.04	-0.009	-0.72	-2.86	1.42	-0.06	**0.181****
		$X_{1/2}$	0.00	0.00	0.00	-0.05	-0.008	0.00	0.00	0.00	0.01	**0.177****
		$W_{1/2}$	0.00	-0.01	0.01	0.01	-0.010	0.00	-0.02	0.01	-0.05	**0.179****
		$W_{50\%}$	0.00	-0.01	0.00	-0.06	-0.007	0.00	0.00	0.01	0.09	**0.184****
		F	0.03	-0.12	0.18	0.04	-0.008	-0.09	-0.24	0.05	-0.13	**0.191****
		Period	-0.03	-0.07	0.01	-0.15	0.013	**-0.06**	**-0.09**	**-0.02**	**-0.29****	**0.256****
	Maximum¶	Breaks SB	0.02	-0.01	0.05	0.12	0.004	0.00	-0.03	0.03	0.02	**0.171****
		Short SB bouts	0.01	-0.02	0.04	0.08	-0.004	0.00	-0.03	0.02	-0.02	**0.171****
		Long SB bouts	0.03	-0.05	0.11	0.08	-0.004	0.05	-0.02	0.13	0.13	**0.182****
		α	-1.12	-3.58	1.35	-0.09	-0.002	-1.87	-4.15	0.40	-0.15	**0.187****
		$X_{1/2}$	0.00	0.00	0.00	-0.13	0.005	0.00	0.00	0.00	-0.10	**0.173****
		$W_{1/2}$	0.01	-0.01	0.02	0.10	0.001	0.00	-0.01	0.02	0.03	**0.172****
		$W_{50\%}$	0.00	-0.01	0.00	-0.02	-0.010	0.00	0.00	0.01	0.10	**0.173****
		F	-0.01	-0.17	0.15	-0.01	-0.010	-0.10	-0.26	0.05	-0.13	**0.181****
		Period	-0.03	-0.07	0.01	-0.15	0.011	**-0.05**	**-0.09**	**-0.01**	**-0.23***	**0.216****
	Standardised¶	Breaks SB	0.02	-0.01	0.04	0.11	0.002	0.00	-0.02	0.03	0.02	**0.183****
		Short SB bouts	0.01	-0.02	0.04	0.07	-0.006	0.00	-0.02	0.02	0.00	**0.183****

		Long SB bouts	0.04	-0.04	0.12	0.09	-0.002	0.03	-0.04	0.10	0.07	**0.188****
		α	-0.67	-3.12	1.78	-0.06	-0.007	-1.33	-3.62	0.95	-0.11	**0.191****
		$X_{1/2}$	0.00	0.00	0.00	-0.08	-0.004	0.00	0.00	0.00	-0.05	**0.185****
		$W_{1/2}$	0.00	-0.01	0.02	0.04	-0.009	0.00	-0.01	0.01	0.00	**0.183****
		$W_{50\%}$	0.00	-0.01	0.00	-0.04	-0.009	0.00	0.00	0.01	0.05	**0.186****
		F	-0.01	-0.17	0.15	-0.01	-0.010	-0.06	-0.20	0.09	-0.07	**0.188****
		Period	-0.03	-0.07	0.02	-0.13	0.006	**-0.05**	**-0.09**	**-0.01**	**-0.24***	**0.202****
Maximal stress[¶]		Breaks SB	0.00	-0.02	0.02	0.00	-0.011	-0.01	-0.03	0.02	-0.06	**0.092****
		Short SB bouts	0.00	-0.02	0.03	0.03	-0.009	-0.01	-0.03	0.02	-0.05	**0.090****
		Long SB bouts	-0.03	-0.10	0.04	-0.10	-0.001	-0.00	-0.07	0.06	-0.01	**0.088****
		α	1.75	-0.30	3.81	0.17	0.019	0.98	-1.05	3.01	0.10	**0.097****
		$X_{1/2}$	0.00	0.00	0.00	0.03	-0.010	0.00	-0.00	0.00	0.07	**0.094****
		$W_{1/2}$	**-0.01**	**-0.03**	**0.00**	**-0.23***	**0.042***	**-0.01**	**-0.03**	**-0.00**	**-0.25***	**0.151****
		$W_{50\%}$	0.00	-0.01	0.00	-0.05	-0.008	0.00	-0.00	0.01	0.12	**0.100****
		F	0.02	-0.11	0.16	0.04	-0.009	-0.05	-0.19	0.08	-0.08	**0.094****
		Period	0.01	-0.02	0.05	0.09	-0.003	-0.00	-0.04	0.03	-0.01	**0.088****
Maximal strain[¶]		Breaks SB	-0.02	-0.05	0.01	-0.12	0.003	-0.01	-0.04	0.02	-0.08	**0.073***
		Short SB bouts	-0.01	-0.03	0.02	-0.06	-0.007	-0.01	-0.03	0.02	-0.05	**0.069***
		Long SB bouts	-0.06	-0.14	0.02	-0.15	0.012	-0.03	-0.11	0.05	-0.08	**0.073***
		α	2.16	-0.25	4.58	0.18	0.022	1.97	-0.39	4.33	0.16	**0.099****
		$X_{1/2}$	0.00	0.00	0.00	0.08	-0.003	0.00	0.00	0.00	0.08	**0.079***
		$W_{1/2}$	**-0.02**	**-0.03**	**0.00**	**-0.22***	**0.037***	**-0.01**	**-0.03**	**0.00**	**-0.19**	**0.109****

153

		W50%	0.00	-0.01	0.01	0.01	-0.010	0.00	0.00	0.01	0.05	**0.069***
		F	0.02	-0.14	0.18	0.03	-0.010	0.01	-0.15	0.16	0.01	**0.067***
		Period	**0.04**	**0.00**	**0.08**	**0.21***	**0.035***	0.03	-0.01	0.07	0.15	**0.089****
EO	Duration[¶]	Breaks SB	-0.01	-0.09	0.08	-0.02	-0.023	-0.03	-0.10	0.05	-0.10	**0.313****
		Short SB bouts	0.02	-0.05	0.10	0.10	-0.014	-0.02	-0.09	0.05	-0.08	**0.308****
		Long SB bouts	**-0.28**	**-0.50**	**-0.06**	**-0.36***	**0.108***	-0.18	-0.39	0.02	-0.24	**0.325****
		α	3.75	-3.42	10.92	0.16	0.003	-1.18	-8.08	5.72	-0.05	**0.305****
		X1/2	**0.00**	**0.00**	**0.00**	**-0.34***	**0.093***	**-0.00**	**-0.00**	**-0.00**	**-0.37****	**0.449****
		W1/2	0.02	-0.03	0.06	0.12	-0.008	0.01	-0.03	0.05	0.07	**0.308****
		W50%	-0.01	-0.03	0.00	-0.24	0.038	**-0.01**	**-0.03**	**-0.00**	**-0.26***	**0.312****
		F	0.38	-0.08	0.84	0.25	0.040	0.30	-0.10	0.69	0.19	**0.308****
		Period	**0.14**	**0.02**	**0.25**	**0.34***	**0.094***	**0.12**	**0.02**	**0.22**	**0.29***	**0.331****
	TD[¶]	Breaks SB	0.01	-0.06	0.07	0.04	-0.022	-0.01	-0.07	0.04	-0.06	**0.257****
		Short SB bouts	-0.01	-0.06	0.05	-0.03	-0.022	-0.02	-0.07	0.04	-0.08	**0.259****
		Long SB bouts	0.11	-0.07	0.28	0.19	0.012	0.03	-0.13	0.20	0.06	**0.256****
		α	-0.79	-6.18	4.59	-0.05	-0.021	-0.26	-4.99	4.48	-0.01	**0.253****
		X1/2	0.00	0.00	0.00	0.04	-0.022	0.00	0.00	0.00	0.00	**0.253****
		W1/2	-0.01	-0.04	0.03	-0.05	-0.020	0.00	-0.03	0.02	-0.05	**0.255****
		W50%	0.00	-0.01	0.01	-0.02	-0.023	0.00	-0.01	0.01	-0.05	**0.256****
		F	-0.10	-0.45	0.25	-0.09	-0.015	-0.05	-0.39	0.29	-0.05	**0.255****
		Period	-0.02	-0.11	0.08	-0.05	-0.021	0.03	-0.05	0.11	0.10	**0.262****
	Sway frequency[¶]	Breaks SB	0.01	-0.12	0.15	0.03	-0.022	0.04	-0.08	0.16	0.09	**0.232****

	**	Short SB bouts	-0.03	-0.15	0.09	-0.08	-0.017	0.02	-0.09	0.13	0.04	**0.225****
		Long SB bouts	**0.39**	**0.03**	**0.75**	**0.31***	**0.077***	0.24	-0.10	0.58	0.19	**0.243****
		α	-4.55	-16.02	6.93	-0.12	-0.008	-0.17	-10.54	10.20	-0.00	**0.223****
		$X_{1/2}$	0.00	0.00	0.00	0.23	0.030	0.00	-0.00	0.00	0.22	**0.275****
		$W_{1/2}$	-0.02	-0.09	0.05	-0.10	-0.013	-0.01	-0.07	0.04	-0.07	**0.228****
		$W_{50\%}$	0.01	-0.01	0.04	0.15	-0.001	0.00	-0.02	0.03	0.04	**0.225****
		F	-0.48	-1.22	0.26	-0.20	0.017	-0.11	-0.81	0.59	-0.05	**0.225****
		Period	-0.15	-0.34	0.04	-0.24	0.034	-0.06	-0.24	0.13	-0.09	**0.231****
EC	Duration¶	Breaks SB	-0.03	-0.10	0.04	-0.13	-0.005	-0.03	-0.09	0.03	-0.13	**0.302****
		Short SB bouts	-0.02	-0.08	0.04	-0.10	-0.013	-0.03	-0.08	0.03	-0.13	**0.302****
		Long SB bouts	-0.03	-0.22	0.16	-0.04	-0.021	0.03	-0.13	0.20	0.05	**0.288****
		α	-0.50	-6.29	5.29	-0.03	-0.023	-0.93	-5.85	4.00	-0.05	**0.288****
		$X_{1/2}$	0.00	0.00	0.00	-0.01	-0.023	-0.00	-0.00	0.00	-0.02	**0.286****
		$W_{1/2}$	0.00	-0.03	0.04	0.03	-0.022	0.00	-0.03	0.03	0.00	**0.285****
		$W_{50\%}$	0.01	-0.01	0.02	0.16	0.002	0.01	-0.01	0.02	0.13	**0.301****
		F	-0.12	-0.50	0.25	-0.10	-0.013	-0.13	-0.45	0.19	-0.11	**0.298****
		Period	0.02	-0.08	0.11	0.05	-0.021	-0.00	-0.09	0.08	-0.01	**0.285****
	TD¶	Breaks SB	0.00	-0.04	0.05	0.02	-0.024	-0.02	-0.05	0.02	-0.12	**0.397****
		Short SB bouts	0.00	-0.05	0.04	-0.03	-0.023	-0.02	-0.05	0.02	-0.11	**0.395****
		Long SB bouts	0.06	-0.07	0.19	0.14	-0.003	0.02	-0.09	0.13	0.05	**0.384****
		α	-0.76	-4.68	3.15	-0.06	-0.020	-1.44	-4.57	1.69	-0.11	**0.391****
		$X_{1/2}$	0.00	0.00	0.00	-0.19	0.013	**0.00**	**0.00**	**0.00**	**-0.27***	**0.458****

	**	W$_{1/2}$	-0.01	-0.04	0.01	-0.18	0.010	-0.01	-0.03	0.00	-0.18	**0.416**
		W$_{50\%}$	0.00	-0.01	0.00	-0.15	-0.002	0.00	-0.01	0.01	0.02	**0.382**
		F	-0.07	-0.32	0.19	-0.08	-0.017	-0.13	-0.34	0.08	-0.16	**0.407**
		Period	0.01	-0.05	0.08	0.07	-0.019	0.02	-0.03	0.07	0.09	**0.392**
	Sway frequency¶	Breaks SB	0.03	-0.06	0.12	0.11	-0.011	0.02	-0.06	0.10	0.07	**0.218**
		Short SB bouts	0.02	-0.06	0.10	0.06	-0.019	0.01	-0.06	0.08	0.04	**0.215**
		Long SB bouts	0.09	-0.16	0.33	0.11	-0.011	0.06	-0.16	0.27	0.07	**0.219**
		α	-0.26	-7.70	7.18	-0.01	-0.023	-0.90	-7.50	5.69	-0.04	**0.215**
		X$_{1/2}$	0.00	0.00	0.00	-0.09	-0.015	-0.00	-0.00	0.00	-0.08	**0.221**
		W$_{1/2}$	-0.02	-0.06	0.03	-0.12	-0.009	-0.01	-0.05	0.03	-0.08	**0.220**
		W$_{50\%}$	-0.01	-0.03	0.01	-0.20	0.017	-0.00	-0.02	0.01	-0.09	**0.220**
		F	0.06	-0.43	0.54	0.04	-0.022	-0.02	-0.45	0.42	-0.01	**0.213**
		Period	0.00	-0.13	0.12	-0.01	-0.023	-0.00	-0.11	0.11	-0.00	**0.213**

GM, gastrocnemius medialis; L$_T$, resting tendon length; CSA, cross-sectional area; *K*, tendon stiffness; YM, Young's modulus; EO, eyes open condition; TD, total displacement; EC, eyes closed condition; Breaks SB, sedentary behaviour interruptions with ≥2 consecutive minutes upright activity; Short SB bouts, sedentary behaviour bouts <30 minutes duration; Long SB bouts, sedentary behaviour bouts ≥30 minutes duration; α, scaling parameter sedentary bout length distribution; X$_{1/2}$, median SB bout duration; W$_{1/2}$, fraction total sedentary time accumulated in bouts longer than median sedentary bout length; W$_{50\%}$, half of total SB is accumulated in SB bouts ≤ this duration; F, fragmentation index of SB bouts and total SB; Period, mean period between SB bouts; ¶log-transformed; *P<0.05; ** P<0.01.

Discussion

We hypothesised that SB is detrimentally associated with GM tendon properties and postural balance. Although we did not find any association for SB levels and proportional time spent in SB with GM tendon properties, negative association were observed for some postural balance outcomes. In addition, a variety of daily SB pattern parameters were also detrimentally associated with postural balance. Interestingly, some pattern outcomes were associated with GM tendon properties too, however, they showed rather counterintuitive associations at times, such as K, YM and maximal stress.

For human tendons, there are two mechanisms that account for stiffness adaptations: (i) changes in material properties (i.e. Young's modulus), and (ii) changes in tendon morphology (i.e. CSA) (196). Since changes in the CSA do not contribute much, if anything, to changes in stiffness, changes in material properties are the main adaptation to modulate tendon stiffness. As stated in the introduction of this chapter, the research on ageing-induced changes in tendon properties is inconclusive. Although the consensus is that tendon stiffness and Young's modulus decrease, and tendon CSA becomes larger, not all studies show these effects (155,195,196). In this chapter, no association was found between age and GM tendon properties, K and Young's Modulus, respectively. Tendon CSA was also not associated, however a positive correlation with tendon length was identified ($r = 0.323$, P<0.05), suggesting that longer resting GM tendon length is associated with older age. Theoretically, as for age-induced changes to muscle tissue, reduced activity levels in the elderly are also believed to be an important factor for the tendon property changes. This is based on the premise that the magnitude of loading seems key for the adaptive responses of human tendons (196,199). For example, previous studies have shown reductions in tendon stiffness and Young's modulus with simulated microgravity (during bed rest) (199), while opposed effects were seen after resistance training, even in elderly (195,200). Tendon CSA remained unchanged in both situations (196,199,200). Nevertheless, in this chapter, no correlations were seen during analysis of covariates, between resistance training and any of the tendon properties and the association with tendon length may be a type I error.

With the opposite effects of disuse during bed rest and resistance training from literature in mind, intuitively it makes sense that we did not find any associations for GM tendon stiffness, except with the mean period between SB bouts (average K). However, regardless whether SB is described as any waking behaviour with low energy expenditure performed

in a lying, seated or reclining position (10), or as a lack of muscular contractions (166), both are not similar to complete unloading. This means that, although SB can be found on the lower end of the physical activity continuum, it is still higher than bed rest and only when the reduction in activity falls below a certain threshold reductions in tendon stiffness occur (206). It is tempting to speculate that this most probably results from sufficient loading during breaks in SB. Yet, in this chapter a negative association between breaks in SB and tendon CSA (but also between period and all YM outcomes) was observed. Interestingly, looking at associations with PA intensities during PA bouts, LIPA is negatively and MVPA is positively associated. This suggests that LIPA is performed more than MVPA during SB breaks (Chapter 4). The fact that tendon CSA was associated with SB breaks only and not with other SB parameters warrants cautiousness when interpreting the results. In addition, with the model explaining ~52% of the variance, there are more predictors required to pinpoint the exact factors that determine tendon CSA. Although direct comparison of tendon mechanical properties with other studies is difficult, due to a variety of assumptions and methods used, comparison of morphological measures is more straightforward. Doing this, showed that the values of GM tendon CSA from this chapter are comparable to previous research (44).

As stated before, the primary role of tendons is to transmit muscle forces to the skeleton, thereby generating joint movement or stabilisation (196,199). For this reason, tendons play not only a significant role in locomotion, but also in maintaining postural balance (44,196). As a result of increased GM tendon compliance, the speed of force transmission is reduced and so is the ability for postural balance (44). Although only a few associations between SB parameters and tendon mechanical properties were observed within this study, a relatively large number of relationships were identified with postural balance. For example, trial duration during the eyes open condition appeared negatively associated with proportional time spent in SB, number of prolonged SB bouts and the median SB bout duration. In other words, the postural balance decreases with increasing SB. Proportional time spent in SB was also identified to increase total displacement whilst balancing on one leg with either the eyes open or closed. In addition, time spent standing relative to the other daily behaviours also increased total displacement when balancing with the eyes closed. Following from Chapter 2 & 3, all associations involving standing must be interpreted with caution. As a result of the negative association with trial duration and the positive one with total displacement, postural sway during eyes open postural balance also increases with more time spent in SB relative to the other daily behaviours. Interestingly, increasing the

158

median SB bout length was associated with less total displacement during eyes closed postural balance. However, we propose that this is due to the fact that trials in this condition were only very short in most participants (down to 1 second only). Thus, participants capable and willing to try correcting their position during these short trials had higher total displacement with only slightly longer duration (a trend was observed) than people who did not or could not. We suggest that it is rather the less sedentary than the more sedentary participant who would try to make postural balance corrections during an eyes closed trial. Although the above results seem intuitively correct, it is difficult to explain them with data from within this chapter. Having an overall lack of associations with either of the tendon mechanical properties, indicates that other factors might explain the discussed results. It has already been suggested that both muscle architecture and tendon properties are not responsible for functional deficit in elderly, but that it is likely caused by muscle size, intrinsic muscle properties and perhaps neural control instead (195).

Apart from tendon mechanical and morphological properties, we also tested associations of SB parameters with other outcomes, such as tendon force. Unlike SB level groups, which were not associated with any tendon outcome measure in this chapter, this variable was associated with the fraction of total daily SB spent in bouts longer than the median duration ($W_{1/2}$). It was indicated that while being engaged in shorter SB bouts, tendon force increases. Also, an increase in the time spent in LIPA relative to other behaviours, was positively associated with tendon force. Although the relative effects seem small (max. 0.036%), when substituting 10 minutes of LIPA for any other daily behaviour and vice versa. However, this was the case for all significant associations (max. 0.709%) identified during compositional data analysis in this chapter (Table 7.6). Moreover, LIPA classification was not shown valid for this study (Chapter 3) and thus, interpretation should rather be avoided. Since we only observed a few (debatable) associations with tendon properties, changes in force generating capacities are likely to mostly result from neuromuscular adaptations (188). As shown in the previous chapters, this statement is only partially confirmed.

Although a total of 105 older adults were tested, postural balance was examined in a subpopulation. Comparing characteristics and predictors of interest between the total sample and the subgroup, revealed no statistical differences. Hence, the subgroup within this chapter is deemed representative for the whole cross-sectional study sample and normal interpretation of results is allowed. A strong point of this chapter is the excellent

reliability of most (3 out of 4) outcomes measured. Only maximum tendon elongation showed a lower ICC of 0.698, which, however, still indicates moderate reliability. Overall, the data used within this chapter is thus of acceptable quality.

Conclusion

SB appears to have little effect on tendon properties, but does negatively affect balance. This suggests that the lower balance in SB is not due to increased tendon compliance, but rather to other factors, such as impaired neural control of balance.

Chapter 8. General discussion

Recap

The main aim of the current thesis was to investigate any sleep and physical activity (PA) independent association between sedentary behaviour (SB) (amount and/or pattern) and structure-mechanical properties of the gastrocnemius medialis (GM) muscle and tendon in older adults. To do so an algorithm for the assessment of SB and PA levels using thigh-mounted triaxial accelerometry was developed and applied to monitor habitual mobility patterns for seven continuous days. Following on from this, both GM muscle and tendon properties were assessed, more specifically: morphology, architecture, function, fatigability, mechanical and material properties. Finally, postural balance was examined as a functional outcome.

It was hypothesized that a thigh-mounted triaxial accelerometer algorithm for the assessment of SB and PA levels in older adults would be valid and robust. The results from Chapter 2 & 3 confirm this hypothesis by showing acceptable algorithm performance (validity and robustness) of an in-house developed model using Random Forest machine learning, throughout the spectrum of activity intensities in older adults wearing a thigh-mounted triaxial accelerometer. Comparison with concurrent activity monitors also showed high validity and suggested that a thigh-worn triaxial GENEActiv with a Random Forest algorithm can be used best for accurate assessment of SB and PA in older adults. Alternatively, we found that other monitors can also be used, depending on the research question and setting, as they proved to be (partially) valid too.

Next, it was hypothesised that when applying an objective method to quantify SB and PA levels, we would observe an increase in SB and a decrease in PA during further ageing in older adults. This latter was confirmed in our population. Chapter 4 thus showed that the study sample was representative for the population under study. Moreover, independence was found between several SB and PA outcomes for the different levels of statistical analyses applied within this thesis. This is an important finding as the initial premise for this research was that SB and PA co-exist but have independent health effects.

Part II of the thesis focused specifically on the associations between habitual daily activity outcomes (primarily SB, but also sleep and PA) and both GM muscle and tendon properties in elderly. For this part it was hypothesised that a detrimental association would exist between sleep and PA-independent SB (amount and pattern) and both structural and

functional GM muscle-tendon outcomes. The results of Chapter 5 & 6 identified a limited number of associations, linking SB with detrimental outcomes in GM muscle morphology, architecture, strength, force and function. However, since the models predicted relatively small effects, the hypothesis was only partially confirmed regarding GM muscle outcomes. Chapter 7 also showed a limited number of associations with GM tendon morphological, mechanical and material properties. Interestingly and as predicted, detrimental associations between SB and postural balance in older adults were identified. Hence, Chapter 7 further supported the initial hypothesis.

Studies' strengths and weaknesses

For the interpretation of the findings, it is important to discuss the strength and weaknesses of this thesis. To start on the latter, one of the main limitations of this thesis lies in its design. Part I of the thesis was only performed under laboratory conditions. Although this provided a controlled setting for the development and validation of the machine learning algorithm, it compromises its performance in free-living. The concurrent validation in Chapter 3 also showed that LIPA classification appeared to be poor, hence results involving this outcome should be interpreted very conservatively. By using a cross-sectional study design for Part II of the thesis, investigations were limited to associations only. Although this could be considered a limitation, the fact that there is a gap in literature regarding SB and GM muscle-tendon properties, it is a logical design to start exploring this area. Nevertheless, assumptions had to be made, for example when monitoring activity levels. It is possible that the accelerometer outcomes do not reflect true habitual behaviour, because people artificially altered their habitual physical activity behaviour due to a variety of reasons. These could include the mere fact of being conscious of being monitored (i.e. wearing the monitor) (207). However, by monitoring 7 days with a discrete accelerometer, which did not prevent participants from continuing their normal habitual activities, it is assumed that the effect is minimal. In addition, since data was averaged over one week, higher activity levels during the first days are expected to level out. Moreover, participants were monitored again when they reported their previous week might not be representative. This happened only twice and in both people, the data from the second monitoring week differed from the first, but was comparable to the rest of the study sample. With regards to sleeping times, log sheets were filled out by the participants, however, our accelerometer algorithm could account for any discrepancies between

reported times and accelerometer data. Furthermore, it is possible that weather/seasonal variation might have introduced noise into the data, resulting in fit and active people to stay inside and sit more than usually. In addition, it is unknown for how long the status quo habitual physical activity level has been reached and has impacted on the participant's physiology. This could be an issue, for example when people have recently changed their habitual activity levels. This change might not reflect their physiology as of yet, and thus, may add noise to the data. In terms of skeletal musculature for example, loading/unloading must be endured for a physiologically lengthy duration for an effect to have an impact on either signalling pathways and/or biomechanical response mechanisms. A case in point is that the typical muscle hypertrophy/atrophy interventions requires a minimum of 9 days for signalling and phenotypic responses (208–210). Another main limitation is the fact that this thesis was part of a larger cohort study. Within this study not only SB-associations with muscle-tendon properties were studied but also with cardio-metabolic outcomes. Hence, an accelerometer algorithm was developed to suit both research topics. Instead of focusing on all loading experienced during monitoring time, which is of high importance for studying muscle-tendon properties, the algorithm was customised to differentiate between active and inactive physical states. For example, when a person was upright for at least two consecutive minutes, this was defined as an activity bout. Whereas, one consecutive minute of SB was required for a sedentary bout. These definitions might affect pattern measures of both SB and PA, as short interruptions in SB or PA are neglected. Perhaps this is not a problem for cardio-metabolic outcomes, but it may result in missing potentially relevant data for investigating the true association between SB and muscle-tendon properties.

Studying an elderly population is both interesting and challenging, in a way that not only large between-subject variability exist amongst this age group, as evidenced from the large standard deviations and interquartile ranges within this thesis, but also within-subject variability (41). This latter can make interpretation of results complex. However, based upon our good-to-excellent test-retest reliability for most outcomes (15 out of 19), we assume this is not the case for our measurements. Regardless of the fact that 44.8% of our participants were sarcopenic (according to the skeletal mass index (SMI) thresholds from Baumgartner et al. (115)), generally, we included healthy community-dwelling older adults with relatively high activity levels only. This limits generalisation of our findings beyond this subgroup, as evidenced by the low R^2_{adj}-values for some our regression models (ranging between -0.086 and 0.837). Although, an attempt was initially made to recruit participants

from assisted-living facilities and care homes, these older adults were not forthcoming in their participation. Indeed, after placing adverts in three homes and visiting these two times (hence reaching a potential 60 participants), only less than ten residents came forward to be included in this body of research. As a result, the cross-sectional study sample can only reflect, with any degree of confidence, one end of the elderly age group. In other words, our sample lacks the frail older participants who are likely to be those that engage in SB the most. Thus, variance is missing, which complicates the development of regression models and might explain low R^2-values. Adding more factors is not expected to help in this case and will only decrease the observed power of the regression models. Since linear regression models were used for this thesis, it was assumed that the relationships between SB outcomes and both muscle-tendon properties and postural balance were linear. Obviously, in cases where this assumption is not true (however none of our existing data would suggest lack of linearity), linear regression models hold no value. Notwithstanding the above, research within the sedentarism area is explorative in nature, as such, all data is potentially useful and incrementally increases overall knowledge base. This additionally justifies the use of our cross-sectional study design, which does not allow examination of causal relationships, but was important for an initial investigation of our hypotheses. In fact, causal relationships, even in longitudinal study designs, are never straight forward to suggest.

With regards to the strengths of this thesis, it is undeniable that these lie in the advanced technology and analyses used to study the hypotheses. More specifically, the fact that machine learning was applied to determine habitual daily activity levels, and both compositional data analysis and SB pattern parameters were used, thereby providing greater details than simply including overall quantification of SB levels (although based on recommendations with medium to high confidence by Byrom et al. (117), only $W_{50\%}$ and daily total sedentary time should be used); this highlights the novelty of the current thesis. Next, the research was conducted on a reasonably sized study sample, providing good power for the identified significant associations. Moreover, the inclusion of a wide range of covariates in our analysis, comprising sex, body composition, comorbidities, concomitant medication and participation in resistance training, allowed improved interpretation of relationships. Finally, this thesis contains novel data regarding associations between sleep and PA-independent SB in older adults and a range of detailed GM muscle-tendon properties and postural balance.

Recommendations for future research

Based on the findings in this thesis, future research should focus on developing an accelerometer algorithm, which offers more representative daily muscle-tendon loading profiles in elderly. This can easily be achieved by not using minimum time thresholds for an activity to be counted, as doing so, possibly filters out relevant data. Also, developing an algorithm in a free-living setting will help to improve measurement accuracy. Moreover, focusing on actual activity types, rather than intensities, and classifying sleep as SB instead, might be more applicable for investigating the role of SB on skeletal muscle-tendon characteristics in elderly. Altogether, this may lead to improved understanding of potential associations. Future studies should also aim to include the two ends of the physical behaviour spectrum i.e. more sedentary elderly as well as master athletes, thereby increasing the variance in activity levels and allowing further reaching modelling. Furthermore, selecting a range of other relevant covariates to be added to the existing models, such as metabolic, genetic and hormonal factors, may also improve regression models. However, this requires a sufficiently large sample size not to decrease the power of the prediction models. More detailed information on metabolic balance might be useful as well. Finally, multiple periods of 7-day habitual activity monitoring should be performed, as this provides important information on possible changes in activity levels (e.g. due to seasonality) on a longitudinal scale. Doing this will help in better understanding of long term associations between SB and muscle-tendon properties in older adults.

On a more general note, it would also be very interesting to see what associations may be found in other populations, instead of healthy elderly, and whether they might be different. Next, as cross-sectional studies are currently dominating SB research, interventional studies should be performed to get closer to understanding the potential causal relationships, and ultimately, to determine dose-response effects of SB. This latter will allow the identification of preventative/counteractive mechanisms, and moreover, the development/update of current physical activity guidelines. Lastly, with SB being a multi-factorial phenomenon (211), which is deeply rooted in our system and society, research trying to unravel this complex behaviour and focusing on identifying strategies for successful long-term changes in SB, will be of high importance.

Conclusion

Generally, detrimental associations between sleep and PA-independent SB outcomes and GM muscle morphology, architecture, force production and neuromuscular function were few in this sample of relatively healthy older adults. The same was true for GM tendon morphological, mechanical and material properties. This may thus indicate a greater sensitivity of the musculotendinous parameters to high loading rather than periods of unloading. Key nonetheless, is the important observation that postural balance ability (and hence by extension, a maintenance of physical independence (212)) in elderly deteriorated with high levels of objectively quantified SB.

References

1.   Gardiner PA, Healy GN, Eakin EG, Clark BK, Dunstan DW, Shaw JE, et al. Associations between television viewing time and overall sitting time with the metabolic syndrome in older men and women: The Australian diabetes obesity and lifestyle study. J Am Geriatr Soc. 2011 May;59(5):788–96.

2.   Inoue S, Sugiyama T, Takamiya T, Oka K, Owen N, Shimomitsu T. Television Viewing Time is Associated with Overweight/Obesity Among Older Adults, Independent of Meeting Physical Activity and Health Guidelines. J Epidemiol. 2012;22(1):50–6.

3.   Rezende LFM de, Rodrigues Lopes M, Rey-López JP, Matsudo VKR, Luiz O do C. Sedentary Behavior and Health Outcomes: An Overview of Systematic Reviews. Lucia A, editor. PLoS One. 2014 Aug 21;9(8):e105620.

4.   Gennuso KP, Gangnon RE, Matthews CE, Thraen-Borowski KM, Colbert LH. Sedentary behavior, physical activity, and markers of health in older adults. Med Sci Sports Exerc. 2013 Aug;45(8):1493–500.

5.   Gianoudis J, Bailey CA, Daly RM. Associations between sedentary behaviour and body composition, muscle function and sarcopenia in community-dwelling older adults. Osteoporos Int. 2014 Feb;26(2):571–9.

6.   Gorman E, Hanson HM, Yang PH, Khan KM, Liu-Ambrose T, Ashe MC. Accelerometry analysis of physical activity and sedentary behavior in older adults: A systematic review and data analysis. Eur Rev Aging Phys Act. 2014 Jan;11(1):35–49.

7.   Franco G. Ramazzini and workers' health. Lancet. 1999 Sep 4;354(9181):858–61.

8.   Dunstan DW, Howard B, Healy GN, Owen N. Too much sitting - A health hazard. Diabetes Res Clin Pract. Elsevier Ireland Ltd; 2012 Sep;97(3):368–76.

9.   Owen N, Healy GN, Matthews CE, Dunstan DW. Too Much Sitting. Exerc Sport Sci Rev. 2010 Jul;38(3):105–13.

10.   Sedentary Behaviour Research Networ. Letter to the Editor: Standardized use of the terms "sedentary" and "sedentary behaviours". Appl Physiol Nutr Metab. 2012 Jun;37(3):540–2.

11.   Start Active - Stay Active. A report on physical activity from the four home countries' Chief Medical Officers. London, UK; 2011.

12. Tremblay MS, Colley RC, Saunders TJ, Healy GN, Owen N. Physiological and health implications of a sedentary lifestyle. Appl Physiol Nutr Metab. 2010 Dec;35(6):725–40.

13. Aguilar-Farías N, Brown WJ, Olds TS, (Geeske) Peeters GMEE. Validity of self-report methods for measuring sedentary behaviour in older adults. J Sci Med Sport. Sports Medicine Australia; 2015 Nov;18(6):662–6.

14. Celis-Morales CA, Perez-Bravo F, Ibañez L, Salas C, Bailey MES, Gill JMR. Objective vs. self-reported physical activity and sedentary time: effects of measurement method on relationships with risk biomarkers. PLoS One. 2012 Jan;7(5):e36345.

15. Chastin SFM, Culhane B, Dall PM. Comparison of self-reported measure of sitting time (IPAQ) with objective measurement (activPAL). Physiol Meas. 2014 Nov;35(11):2319–28.

16. Chastin SFM, Granat MH. Methods for objective measure, quantification and analysis of sedentary behaviour and inactivity. Gait Posture. 2010 Jan;31(1):82–6.

17. Harvey JA, Chastin SFM, Skelton DA. How sedentary are older people? A systematic review of the amount of sedentary behavior. J Aging Phys Act. 2015 Jul;23(3):471–87.

18. Bond DS, Thomas JG, Raynor HA, Moon J, Sieling J, Trautvetter J, et al. B-MOBILE - A smartphone-based intervention to reduce sedentary time in overweight/obese individuals: A within-subjects experimental trial. Edwards L, editor. PLoS One. 2014 Jun 25;9(6):e100821.

19. Hart TL, Swartz AM, Cashin SE, Strath SJ. How many days of monitoring predict physical activity and sedentary behaviour in older adults? Int J Behav Nutr Phys Act. 2011 Jan;8(1):62.

20. Rhodes RE, Mark RS, Temmel CP. Adult sedentary behavior: A systematic review. Am J Prev Med. Elsevier Inc.; 2012 Mar;42(3):e3-28.

21. Van Cauwenberg J, Van Holle V, De Bourdeaudhuij I, Owen N, Deforche B. Older adults' reporting of specific sedentary behaviors: validity and reliability. BMC Public Health. 2014 Jan;14(1):734.

22. Evenson K, Buchner D, Morland K. Objective Measurement of Physical Activity and

Sedentary Behavior Among US Adults Aged 60 Years or Older. Prev Chronic Dis. 2011;9(2):2–11.

23. Lohne-Seiler H, Hansen BH, Kolle E, Anderssen SA. Accelerometer-determined physical activity and self-reported health in a population of older adults (65–85 years): a cross-sectional study. BMC Public Health. BMC Public Health; 2014 Jan;14(1):284.

24. Pedišić Ž, Bauman A. Accelerometer-based measures in physical activity surveillance: current practices and issues. Br J Sports Med. 2015 Feb;49(4):219–23.

25. Leask CF, Harvey JA, Skelton DA, Chastin SF. Exploring the context of sedentary behaviour in older adults (what, where, why, when and with whom). Eur Rev Aging Phys Act. 2015 Dec 7;12(1):4.

26. Bassett DR, Rowlands A, Trost SG. Calibration and validation of wearable monitors. Med Sci Sports Exerc. 2012 Jan;44(SUPPL. 1):S32-8.

27. Martin KR, Koster A, Murphy RA, Van Domelen DR, Hung MY, Brychta RJ, et al. Changes in daily activity patterns with age in U.S. men and women: National health and nutrition examination survey 2003-04 and 2005-06. J Am Geriatr Soc. 2014 Jul;62(7):1263–71.

28. Matthews CE, Chen KY, Freedson PS, Buchowski MS, Beech BM, Pate RR, et al. Amount of time spent in sedentary behaviors in the United States, 2003-2004. Am J Epidemiol. 2008 Apr 1;167(7):875–81.

29. Evenson KR, Morland KB, Wen F, Scanlin K. Physical activity and sedentary behavior among adults 60 years and older: New York city residents compared with a national sample. J Aging Phys Act. 2014;22(4):499–507.

30. Rezende LFM de, Rey-López JP, Matsudo VKR, Luiz O do C. Sedentary behavior and health outcomes among older adults: a systematic review. BMC Public Health. 2014 Jan;14(1):333.

31. Stamatakis E, Davis M, Stathi A, Hamer M. Associations between multiple indicators of objectively-measured and self-reported sedentary behaviour and cardiometabolic risk in older adults. Prev Med (Baltim). 2012 Jan;54(1):82–7.

32. Davis MG, Fox KR, Hillsdon M, Sharp DJ, Coulson JC, Thompson JL. Objectively

measured physical activity in a diverse sample of older urban UK adults. Med Sci Sports Exerc. 2011 Apr;43(4):647–54.

33.   Lenz EK. Do Sedentary Behaviors Modify the Health Status of Older Adults? Int J Kinesiol Sport Sci J Kinesiol Sport Sci J Kinesiol Sport Sci. 2014 Feb 23;2(1):13–22.

34.   World Health Organization W. World Report on Ageing and Heath. Geneva, Switzerland; 2015.

35.   Sasaki JE, Hickey AM, Staudenmayer JW, John D, Kent JA, Freedson PS. Performance of activity classification algorithms in free-living older adults. Med Sci Sports Exerc. 2016 May;48(5):941–9.

36.   Brady AO, Straight CR, Evans EM. Body composition, muscle capacity, and physical function in older adults: An integrated conceptual model. J Aging Phys Act. 2014 Jul;22(3):441–52.

37.   Hamer M, Stamatakis E. Screen-Based Sedentary Behavior, Physical Activity, and Muscle Strength in the English Longitudinal Study of Ageing. PLoS One. 2013 Jan;8(6):e66222.

38.   Janssen I, Heymsfield SB, Ross R. Low relative skeletal muscle mass (sarcopenia) in older persons is associated with functional impairment and physical disability. J Am Geriatr Soc. 2002 May;50(5):889–96.

39.   Landi F, Cruz-Jentoft AJ, Liperoti R, Russo A, Giovannini S, Tosato M, et al. Sarcopenia and mortality risk in frail olderpersons aged 80 years and older: Results from iLSIRENTE study. Age Ageing. 2013 Mar;42(2):203–9.

40.   Landi F, Liperoti R, Russo A, Giovannini S, Tosato M, Capoluongo E, et al. Sarcopenia as a risk factor for falls in elderly individuals: Results from the ilSIRENTE study. Clin Nutr. Elsevier Ltd; 2012 Oct;31(5):652–8.

41.   Hunter SK, Pereira HM, Keenan KG. The aging neuromuscular system and motor performance. J Appl Physiol. 2016 Oct;121(4):982–95.

42.   Chastin SFM, Ferriolli E, Stephens NA, Fearon KCH, Greig C. Relationship between sedentary behaviour, physical activity, muscle quality and body composition in healthy older adults. Age Ageing. 2012 Jan;41(1):111–4.

43.   Stenholm S, Alley D, Bandinelli S, Griswold ME, Koskinen S, Rantanen T, et al. The

effect of obesity combined with low muscle strength on decline in mobility in older persons: results from the InCHIANTI Study. Int J Obes. 2009 Jun 21;33(6):635–44.

44. Onambele GL, Narici M V, Maganaris CN. Calf muscle-tendon properties and postural balance in old age. J Appl Physiol. 2006 Jun 19;100(6):2048–56.

45. Organization WH. Global Report on Falls Prevention in Older Age WHO Global Report on Falls Prevention in Older Age. 2007.

46. Turner S, Kisser R, Rogmans W. Falls among older adults in the EU-28: Key facts from the available statistics [Internet]. 2015 [cited 2017 Sep 29]. p. 1–5. Available from: https://eupha.org/repository/sections/ipsp/Factsheet_falls_in_older_adults_in_EU .pdf

47. Cepeda M, Koolhaas CM, van Rooij FJA, Tiemeier H, Guxens M, Franco OH, et al. Seasonality of physical activity, sedentary behavior, and sleep in a middle-aged and elderly population: The Rotterdam study. Maturitas. 2018 Apr;110:41–50.

48. Chien M-Y, Wang L-Y, Chen H-C. The Relationship of Sleep Duration with Obesity and Sarcopenia in Community-Dwelling Older Adults. Gerontology. 2015;61(5):399–406.

49. Hu X, Jiang J, Wang H, Zhang L, Dong B, Yang M. Association between sleep duration and sarcopenia among community-dwelling older adults. Medicine (Baltimore). 2017 Mar;96(10):e6268.

50. Piovezan RD, Abucham J, dos Santos RVT, Mello MT, Tufik S, Poyares D. The impact of sleep on age-related sarcopenia: Possible connections and clinical implications. Ageing Res Rev. 2015 Sep;23:210–20.

51. Ellis K, Kerr J, Godbole S, Staudenmayer J, Lanckriet G. Hip and wrist accelerometer algorithms for free-living behavior classification. Med Sci Sports Exerc. 2016 May;48(5):933–40.

52. Corder K, Ekelund U, Steele RM, Wareham NJ, Brage S. Assessment of physical activity in youth. J Appl Physiol. 2008 Sep;105(3):977–87.

53. Trost SG. State of the Art Reviews: Measurement of Physical Activity in Children and Adolescents. Am J Lifestyle Med. 2007 Aug 1;1(4):299–314.

54. Sasaki JE, Da Silva KS, Da Costa BGG, John D. Measurement of Physical Activity Using Accelerometers. In: Computer-Assisted and Web-Based Innovations in Psychology,

Special Education, and Health. Elsevier; 2016. p. 33–60.

55. Chen KY, Janz KF, Zhu W, Brychta RJ. Redefining the roles of sensors in objective physical activity monitoring. Med Sci Sports Exerc. 2012 Jan;44(SUPPL. 1):S13-23.

56. Chen KY, Bassett DR. The technology of accelerometry-based activity monitors: Current and future. Med Sci Sports Exerc. 2005 Nov;37(11 SUPPL.):S490-500.

57. Freedson PS, Melanson E, Sirard J. Calibration of the Computer Science and Applications, Inc. accelerometer. Med Sci Sports Exerc. 1998 May;30(5):777–81.

58. Copeland JL, Esliger DW. Accelerometer assessment of physical activity in active, healthy older adults. J Aging Phys Act. 2009 Jan;17(1):17–30.

59. Evenson KR, Catellier DJ, Gill K, Ondrak KS, McMurray RG. Calibration of two objective measures of physical activity for children. J Sports Sci. 2008 Dec;26(14):1557–65.

60. Freedson P, Pober D, Janz KF. Calibration of accelerometer output for children. Med Sci Sports Exerc. 2005 Nov;37(11 SUPPL.):S512–22.

61. Mattocks C, Leary S, Ness A, Deere K, Saunders J, Tilling K, et al. Calibration of an accelerometer during free-living activities in children. Int J Pediatr Obes. 2007;2(4):218–26.

62. Miller NE, Strath SJ, Swartz AM, Cashin SE. Estimating absolute and relative physical activity intensity across age via accelerometry in adults. J Aging Phys Act. 2010 Apr;18(2):158–70.

63. Kozey-Keadle S, Libertine A, Lyden K, Staudenmayer J, Freedson PS. Validation of wearable monitors for assessing sedentary behavior. Med Sci Sports Exerc. 2011 Aug;43(8):1561–7.

64. Aguilar-Farías N, Brown WJ, Peeters GMEEG. ActiGraph GT3X+ cut-points for identifying sedentary behaviour in older adults in free-living environments. J Sci Med Sport. Sports Medicine Australia; 2014 May;17(3):293–9.

65. Troiano RP, McClain JJ, Brychta RJ, Chen KY. Evolution of accelerometer methods for physical activity research. Br J Sports Med. 2014 Jul;48(13):1019–23.

66. Rowlands A V., Olds TS, Hillsdon M, Pulsford R, Hurst TL, Eston RG, et al. Assessing sedentary behavior with the geneactiv: Introducing the sedentary sphere. Med Sci

Sports Exerc. 2014 Jun;46(6):1235–47.

67.   Ellis K, Kerr J, Godbole S, Lanckriet G, Wing D, Marshall S. A random forest classifier for the prediction of energy expenditure and type of physical activity from wrist and hip accelerometers. Physiol Meas. 2014 Nov;35(11):2191–203.

68.   Kerr J, Patterson RE, Ellis K, Godbole S, Johnson E, Lanckriet G, et al. Objective assessment of physical activity: Classifiers for public health. Med Sci Sports Exerc. 2016 May;48(5):951–7.

69.   Preece SJ, Goulermas JY, Kenney LPJ, Howard D, Meijer K, Crompton R. Activity identification using body-mounted sensors—a review of classification techniques. Physiol Meas. 2009 Apr;30(4):R1–33.

70.   Yang CC, Hsu YL. A review of accelerometry-based wearable motion detectors for physical activity monitoring. Sensors. 2010;10(8):7772–88.

71.   Trost SG, Zheng Y, Wong W-K. Machine learning for activity recognition: hip versus wrist data. Physiol Meas. 2014 Nov;35(11):2183–9.

72.   Freedson P, Bowles HR, Troiano R, Haskell W. Assessment of physical activity using wearable monitors: Recommendations for monitor calibration and use in the field. Med Sci Sports Exerc. 2012 Jan;44(SUPPL. 1):S1-4.

73.   Heil DP, Brage S, Rothney MP. Modeling physical activity outcomes from wearable monitors. Med Sci Sports Exerc. 2012 Jan;44(SUPPL. 1):S50-60.

74.   Rosenberg D, Godbole S, Ellis K, DI C, Lacroix A, Natarajan L, et al. Classifiers for Accelerometer-Measured Behaviors in Older Women. Med Sci Sports Exerc. 2017 Mar;49(3):610–6.

75.   Welk GJ, McClain J, Ainsworth BE. Protocols for evaluating equivalency of accelerometry-based activity monitors. Med Sci Sports Exerc. 2012 Jan;44(SUPPL. 1):S39-49.

76.   Sport TE. Resting Heart Rate Table [Internet]. Vol. 2015, Unknown. 2015 [cited 2016 Sep 21]. Available from: http://www.topendsports.com/testing/heart-rate-resting-chart.htm

77.   PROFESSIONAL M. Assessment of falls risk in older people (Side 1) (Falls Risk Assessment Tool-FRAT) [Internet]. Qeen Mary College London. 2004 [cited 2014 Dec

17]. p. 1–2. Available from: http://www.1000livesplus.wales.nhs.uk/sitesplus/documents/1011/FRATtool.pdf

78. Bouten CVC, Koekkoek KTM, Verduin M, Kodde R, Janssen JD. A triaxial accelerometer and portable data processing unit for the assessment of daily physical activity. IEEE Trans Biomed Eng. 1997 Mar;44(3):136–47.

79. Karantonis DM, Narayanan MR, Mathie M, Lovell NH, Celler BG. Implementation of a real-time human movement classifier using a triaxial accelerometer for ambulatory monitoring. IEEE Trans Inf Technol Biomed. 2006 Jan;10(1):156–67.

80. Esliger DW, Rowlands A V., Hurst TL, Catt M, Murray P, Eston RG. Validation of the GENEA accelerometer. Med Sci Sports Exerc. 2011 Jun;43(6):1085–93.

81. Bayat A, Pomplun M, Tran DA. A study on human activity recognition using accelerometer data from smartphones. Procedia Comput Sci. 2014;34(C):450–7.

82. Liu S, Gao RX, Freedson PS. Computational methods for estimating energy expenditure in human physical activities. Med Sci Sports Exerc. 2012 Nov;44(11):2138–46.

83. R Development CT. R: A language and environment for statistical computing. Vol. 2.2.0. Vienna, Austria: R Foundation for Statistical Computing; 2005.

84. Bedogni L, Di Felice M, Bononi L. By train or by car? Detecting the user's motion type through smartphone sensors data. In: IFIP Wireless Days. IEEE; 2012. p. 1–6.

85. Attal F, Mohammed S, Dedabrishvili M, Chamroukhi F, Oukhellou L, Amirat Y. Physical Human Activity Recognition Using Wearable Sensors. Sensors. 2015 Dec 11;15(12):31314–38.

86. Ellis K, Godbole S, Marshall S, Lanckriet G, Staudenmayer J, Kerr J. Identifying Active Travel Behaviors in Challenging Environments Using GPS, Accelerometers, and Machine Learning Algorithms. Front Public Heal. 2014 Apr 22;2.

87. Kursa MB, Rudnicki WR. Feature Selection with the Boruta Package. J Stat Softw. 2010;36(11):1–13.

88. Liaw a, Wiener M. Classification and Regression by randomForest. R news. 2002;2(December):18–22.

89. Bernmark E, Wiktorin C. A triaxial accelerometer for measuring arm movements.
174

Appl Ergon. 2002 Nov;33(6):541–7.

90.   Wullems JA, Verschueren SMP, Degens H, Morse CI, Onambélé GL. A review of the assessment and prevalence of sedentarism in older adults, its physiology/health impact and non-exercise mobility counter-measures. Biogerontology. 2016 Jun 14;17(3):547–65.

91.   Onambélé-Pearson GL, Breen L, Stewart CE. Influence of exercise intensity in older persons with unchanged habitual nutritional intake: Skeletal muscle and endocrine adaptations. Age (Omaha). 2010 Jun;32(2):139–53.

92.   Jefferis BJ, Sartini C, Lee I-M, Choi M, Amuzu A, Gutierrez C, et al. Adherence to physical activity guidelines in older adults, using objectively measured physical activity in a population-based study. BMC Public Health. 2014 Dec 19;14(1):382.

93.   Bastian T, Maire A, Dugas J, Ataya A, Villars C, Gris F, et al. Automatic identification of physical activity types and sedentary behaviors from triaxial accelerometer: laboratory-based calibrations are not enough. J Appl Physiol. 2015 Mar 15;118(6):716–22.

94.   Gyllensten IC, Bonomi AG. Identifying types of physical activity with a single accelerometer: Evaluating laboratory-trained algorithms in daily life. IEEE Trans Biomed Eng. 2011 Sep;58(9):2656–63.

95.   Lord S, Chastin SFM, McInnes L, Little L, Briggs P, Rochester L. Exploring patterns of daily physical and sedentary behaviour in community-dwelling older adults. Age Ageing. 2011 Mar 1;40(2):205–10.

96.   Szanton SL, Walker RK, Roberts L, Thorpe RJ, Wolff J, Agree E, et al. Older adults' favorite activities are resoundingly active: Findings from the NHATS study. Geriatr Nurs (Minneap). 2015;36(2):131–5.

97.   Gao L, Bourke AK, Nelson J. Evaluation of accelerometer based multi-sensor versus single-sensor activity recognition systems. Med Eng Phys. 2014 Jun;36(6):779–85.

98.   Edwardson CL, Rowlands A V., Bunnewell S, Sanders J, Esliger DW, Gorely T, et al. Accuracy of posture allocation algorithms for thigh- and waist-worn accelerometers. Med Sci Sports Exerc. 2016 Jun;48(6):1085–90.

99.   Mannini A, Intille SS, Rosenberger M, Sabatini AM, Haskell W. Activity Recognition In

Youth Using a Single Accelerometer Placed at the Wrist or Ankle. Med Sci Sport Exerc. 2017 Nov;49(4):801–12.

100. Ruch N, Joss F, Jimmy G, Melzer K, Hanggi J, Mader U. Neural network versus activity-specific prediction equations for energy expenditure estimation in children. J Appl Physiol. 2013 Nov 1;115(9):1229–36.

101. van Remoortel H, Raste Y, Louvaris Z, Giavedoni S, Burtin C, Langer D, et al. Validity of six activity monitors in chronic obstructive pulmonary disease: A comparison with indirect calorimetry. PLoS One. 2012;7(6):1–11.

102. Van Remoortel H, Giavedoni S, Raste Y, Burtin C, Louvaris Z, Gimeno-Santos E, et al. Validity of activity monitors in health and chronic disease: a systematic review. Int J Behav Nutr Phys Act. 2012;9(1):84.

103. Byrne NM. Metabolic equivalent: one size does not fit all. J Appl Physiol. 2005 Sep 1;99(3):1112–9.

104. Clarke CL, Taylor J, Crighton LJ, Goodbrand JA, McMurdo MET, Witham MD. Validation of the AX3 triaxial accelerometer in older functionally impaired people. Aging Clin Exp Res. 2017 Jun 19;29(3):451–7.

105. McPhee JS, French DP, Jackson D, Nazroo J, Pendleton N, Degens H. Physical activity in older age: perspectives for healthy ageing and frailty. Biogerontology. 2016 Jun 2;17(3):567–80.

106. Rowlands A V, Yates T, Olds TS, Davies M, Khunti K, Edwardson CL. Sedentary Sphere: Wrist-Worn Accelerometer-Brand Independent Posture Classification. Med Sci Sports Exerc. 2016 Apr;48(4):748–54.

107. Hollewand AM, Spijkerman AG, Bilo HJG, Kleefstra N, Kamsma Y, van Hateren KJJ. Validity of an Accelerometer-Based Activity Monitor System for Measuring Physical Activity in Frail Older Adults. J Aging Phys Act. 2016 Oct;24(4):555–8.

108. Laufer Y. Effect of age on characteristics of forward and backward gait at preferred and accelerated walking speed. J Gerontol A Biol Sci Med Sci. 2005 May;60(5):627–32.

109. Gabriel K, McClain JJ, Schmid KK, Storti KL, High RR, Underwood DA, et al. Issues in accelerometer methodology: the role of epoch length on estimates of physical

activity and relationships with health outcomes in overweight, post-menopausal women. Int J Behav Nutr Phys Act. 2010;7(1):53.

110. Lyden K, Kozey Keadle SL, Staudenmayer JW, Freedson PS. Validity of Two Wearable Monitors to Estimate Breaks from Sedentary Time. Med Sci Sport Exerc. 2012 Nov;44(11):2243–52.

111. Steeves JA, Bowles HR, McClain JJ, Dodd KW, Brychta RJ, Wang J, et al. Ability of thigh-worn actigraph and activpal monitors to classify posture and motion. Med Sci Sports Exerc. 2015 May;47(5):952–9.

112. Pavey TG, Gilson ND, Gomersall SR, Clark B, Trost SG. Field evaluation of a random forest activity classifier for wrist-worn accelerometer data. J Sci Med Sport. 2017 Jan;20(1):75–80.

113. Kwah LK, Pinto RZ, Diong J, Herbert RD. Reliability and validity of ultrasound measurements of muscle fascicle length and pennation in humans: a systematic review. J Appl Physiol. 2013 Mar 15;114(6):761–9.

114. Katzmarzyk PT. Physical Activity, Sedentary Behavior, and Health: Paradigm Paralysis or Paradigm Shift? Diabetes. 2010 Nov 1;59(11):2717–25.

115. Baumgartner RN, Koehler KM, Gallagher D, Romero L, Heymsfield SB, Ross RR, et al. Epidemiology of sarcopenia among the elderly in New Mexico. Am J Epidemiol. 1998 Apr 15;147(8):755–63.

116. Erskine RM, Tomlinson DJ, Morse CI, Winwood K, Hampson P, Lord JM, et al. The individual and combined effects of obesity- and ageing-induced systemic inflammation on human skeletal muscle properties. Int J Obes. 2017 Jan 29;41(1):102–11.

117. Byrom B, Stratton G, Mc Carthy M, Muehlhausen W. Objective measurement of sedentary behaviour using accelerometers. Int J Obes. 2016 Nov 1;40(11):1809–12.

118. Chastin SFM, Palarea-Albaladejo J, Dontje ML, Skelton DA. Combined Effects of Time Spent in Physical Activity, Sedentary Behaviors and Sleep on Obesity and Cardio-Metabolic Health Markers: A Novel Compositional Data Analysis Approach. Devaney J, editor. PLoS One. 2015 Oct 13;10(10):e0139984.

119. Dumuid D, Stanford TE, Martin-Fernández J-A, Pedišić Ž, Maher CA, Lewis LK, et al.

Compositional data analysis for physical activity, sedentary time and sleep research. Stat Methods Med Res. 2017 May 30;096228021771083.

120. Sperrin M, Marshall AD, Higgins V, Renehan AG, Buchan IE. Body mass index relates weight to height differently in women and older adults: serial cross-sectional surveys in England (1992–2011). J Public Health (Bangkok). 2016 Sep;38(3):607–13.

121. Unknown. Overview of the UK population: July 2017. 2017.

122. Harvey JA, Chastin SFM, Skelton DA. Prevalence of sedentary behavior in older adults: A systematic review. Int J Environ Res Public Health. 2013 Dec;10(12):6645–61.

123. Jefferis BJ, Sartini C, Ash S, Lennon LT, Wannamethee SG, Lee IM, et al. Trajectories of objectively measured physical activity in free-living older men. Vol. 47, Medicine and Science in Sports and Exercise. 2015. 343-349 p.

124. Shiroma EJ, Freedson PS, Trost SG, Lee I-M. Patterns of Accelerometer-Assessed Sedentary Behavior in Older Women. JAMA. 2013 Dec 18;310(23):2562.

125. Jefferis BJ, Sartini C, Shiroma E, Whincup PH, Wannamethee SG, Lee I-M. Duration and breaks in sedentary behaviour: accelerometer data from 1566 community-dwelling older men (British Regional Heart Study). Br J Sports Med. 2015 Dec;49(24):1591–4.

126. Thom JM, Morse CI, Birch KM, Narici M V. Triceps surae muscle power, volume, and quality in older versus younger healthy men. J Gerontol A Biol Sci Med Sci. 2005 Sep;60(9):1111–7.

127. Morse CI, Thom JM, Reeves ND, Birch KM, Narici M V. In vivo physiological cross-sectional area and specific force are reduced in the gastrocnemius of elderly men. J Appl Physiol. 2005 Sep 1;99(3):1050–5.

128. Onambele GNL, Bruce SA, Woledge RC. Oestrogen status in relation to the early training responses in human thumb adductor muscles. Acta Physiol (Oxf). 2006 Sep;188(1):41–52.

129. Maden-Wilkinson TM, McPhee JS, Rittweger J, Jones DA, Degens H. Thigh muscle volume in relation to age, sex and femur volume. Age (Omaha). 2014 Feb 11;36(1):383–93.

178

130. Morse CI, Thom JM, Davis MG, Fox KR, Birch KM, Narici M V. Reduced plantarflexor specific torque in the elderly is associated with a lower activation capacity. Eur J Appl Physiol. 2004 Jun 1;92(1–2):219–26.

131. Klein CS, Rice CL, Marsh GD. Normalized force, activation, and coactivation in the arm muscles of young and old men. J Appl Physiol. 2001 Sep;91(3):1341–9.

132. Maden-Wilkinson TM, McPhee JS, Jones DA, Degens H. Age-Related Loss of Muscle Mass, Strength, and Power and Their Association With Mobility in Recreationally-Active Older Adults in the United Kingdom. J Aging Phys Act. 2015 Jul;23(3):352–60.

133. Papa E V, Dong X, Hassan M. Skeletal Muscle Function Deficits in the Elderly: Current Perspectives on Resistance Training. J Nat Sci. 2017 Jan;3(1).

134. Schaap LA, Koster A, Visser M. Adiposity, muscle mass, and muscle strength in relation to functional decline in older persons. Epidemiol Rev. 2013;35:51–65.

135. Visser M, Goodpaster BH, Kritchevsky SB, Newman AB, Nevitt M, Rubin SM, et al. Muscle mass, muscle strength, and muscle fat infiltration as predictors of incident mobility limitations in well-functioning older persons. J Gerontol A Biol Sci Med Sci. 2005 Mar;60(3):324–33.

136. Frontera WR, Reid KF, Phillips EM, Krivickas LS, Hughes VA, Roubenoff R, et al. Muscle fiber size and function in elderly humans: a longitudinal study. J Appl Physiol. 2008 Aug 1;105(2):637–42.

137. Rantanen T, Sakari-Rantala R, Heikkinen E. Muscle strength before and mortality after a bone fracture in older people. Scand J Med Sci Sports. 2002 Oct;12(5):296–300.

138. Degens H, Alway SE. Control of Muscle Size During Disuse, Disease, and Aging. Int J Sports Med. 2006 Feb;27(2):94–9.

139. Santos DA, Silva AM, Baptista F, Santos R, Vale S, Mota J, et al. Sedentary behavior and physical activity are independently related to functional fitness in older adults. Exp Gerontol. Elsevier Inc.; 2012 Dec;47(12):908–12.

140. Cawthon PM, Blackwell TL, Cauley JA, Ensrud KE, Dam TT, Harrison SL, et al. Objective assessment of activity, energy expenditure, and functional limitations in older men: The osteoporotic fractures in men study. Journals Gerontol - Ser A Biol Sci Med Sci.

2013 Dec;68(12 A):1518–24.

141. Dunlop DD, Song J, Arntson EK, Semanik PA, Lee J, Chang RW, et al. Sedentary Time in US Older Adults Associated With Disability in Activities of Daily Living Independent of Physical Activity. J Phys Act Health. 2015 Jan;12(1):93–101.

142. Dogra S, Stathokostas L. Sedentary behavior and physical activity are independent predictors of successful aging in middle-aged and older adults. J Aging Res. 2012 Jan;2012:190654.

143. Mitchell RJ, Lord SR, Harvey LA, Close JCT. Obesity and falls in older people: Mediating effects of disease, sedentary behavior, mood, pain and medication use. Arch Gerontol Geriatr. Elsevier Ireland Ltd; 2015;60(1):52–8.

144. Lieber RL, Fridén J. Functional and clinical significance of skeletal muscle architecture. Muscle Nerve. 2000 Nov;23(11):1647–66.

145. Lieber RL, Fridén J. Clinical significance of skeletal muscle architecture. Clin Orthop Relat Res. 2001 Feb;(383):140–51.

146. Ward SR, Eng CM, Smallwood LH, Lieber RL. Are Current Measurements of Lower Extremity Muscle Architecture Accurate? Clin Orthop Relat Res. 2009 Apr 30;467(4):1074–82.

147. Degens H, Erskine RM, Morse CI. Disproportionate changes in skeletal muscle strength and size with resistance training and ageing. J Musculoskelet Neuronal Interact. 2009;9(3):123–9.

148. Alexander RM, Vernon A. The dimensions of knee and ankle muscles and the forces they exert. J Hum Mov Stud. 1975;1:115–23.

149. Maganaris CN, Baltzopoulos V, Ball D, Sargeant AJ. In vivo specific tension of human skeletal muscle. J Appl Physiol. 2001 Mar;90(3):865–72.

150. Erskine RM, Jones DA, Maganaris CN, Degens H. In vivo specific tension of the human quadriceps femoris muscle. Eur J Appl Physiol. 2009 Aug;106(6):827–38.

151. Morse CI, Thom JM, Birch KM, Narici M V. Changes in triceps surae muscle architecture with sarcopenia. Acta Physiol Scand. 2005 Mar;183(3):291–8.

152. Wu R, Delahunt E, Ditroilo M, Lowery M, De Vito G. Effects of age and sex on neuromuscular-mechanical determinants of muscle strength. Age (Omaha). 2016

Jun 17;38(3):57.

153.   Tomlinson DJ, Erskine RM, Winwood K, Morse CI, Onambélé GL. The impact of obesity on skeletal muscle architecture in untrained young vs. old women. J Anat. 2014 Oct 14;225(6):675–84.

154.   Reeves ND, Narici M V, Maganaris CN. Effect of resistance training on skeletal muscle-specific force in elderly humans. J Appl Physiol. 2004 Mar;96(3):885–92.

155.   Stenroth L, Cronin NJ, Peltonen J, Korhonen MT, Sipilä S, Finni T. Triceps surae muscle-tendon properties in older endurance- and sprint-trained athletes. J Appl Physiol. 2016 Jan 1;120(1):63–9.

156.   Degens H, Korhonen MT. Factors contributing to the variability in muscle ageing. Maturitas. 2012 Nov;73(3):197–201.

157.   Reeves ND, Narici M V. Behavior of human muscle fascicles during shortening and lengthening contractions in vivo. J Appl Physiol. 2003 Sep;95(3):1090–6.

158.   Koo TK, Li MY. A Guideline of Selecting and Reporting Intraclass Correlation Coefficients for Reliability Research. J Chiropr Med. 2016 Jun;15(2):155–63.

159.   Hamer M, Stamatakis E, Steptoe A. Effects of substituting sedentary time with physical activity on metabolic risk. Med Sci Sports Exerc. 2014 Oct;46(10):1946–50.

160.   Ekelund U, Steene-Johannessen J, Brown WJ, Fagerland MW, Owen N, Powell KE, et al. Does physical activity attenuate, or even eliminate, the detrimental association of sitting time with mortality? A harmonised meta-analysis of data from more than 1 million men and women. Lancet. 2016 Sep;388(10051):1302–10.

161.   Lafortuna CL, Tresoldi D, Rizzo G. Influence of body adiposity on structural characteristics of skeletal muscle in men and women. Clin Physiol Funct Imaging. 2014 Jan;34(1):47–55.

162.   Maffiuletti NA, Jubeau M, Munzinger U, Bizzini M, Agosti F, De Col A, et al. Differences in quadriceps muscle strength and fatigue between lean and obese subjects. Eur J Appl Physiol. 2007 Sep 3;101(1):51–9.

163.   Reeves ND, Narici M V., Maganaris CN. In vivo human muscle structure and function: adaptations to resistance training in old age. Exp Physiol. 2004 Nov;89(6):675–89.

164.   Kuyumcu ME, Halil M, Kara Ö, Çuni B, Çağlayan G, Güven S, et al. Ultrasonographic

evaluation of the calf muscle mass and architecture in elderly patients with and without sarcopenia. Arch Gerontol Geriatr. 2016 Jul;65:218–24.

165.   Narici M V., Maganaris CN, Reeves ND, Capodaglio P. Effect of aging on human muscle architecture. J Appl Physiol. 2003 Dec;95(6):2229–34.

166.   Hamilton MT. The role of skeletal muscle contractile duration throughout the whole day: reducing sedentary time and promoting universal physical activity in all people. J Physiol. 2017 Jul 26;

167.   Pearson SJ, Young A, Macaluso A, Devito G, Nimmo MA, Cobbold M, et al. Muscle function in elite master weightlifters. Med Sci Sports Exerc. 2002 Jul;34(7):1199–206.

168.   Doherty TJ. Invited Review: Aging and sarcopenia. J Appl Physiol. 2003 Oct;95(4):1717–27.

169.   Newman AB, Haggerty CL, Goodpaster B, Harris T, Kritchevsky S, Nevitt M, et al. Strength and muscle quality in a well-functioning cohort of older adults: the Health, Aging and Body Composition Study. J Am Geriatr Soc. 2003 Mar;51(3):323–30.

170.   Kent-Braun JA, Ng A V, Young K. Skeletal muscle contractile and noncontractile components in young and older women and men. J Appl Physiol. 2000 Feb;88(2):662–8.

171.   Kent-Braun JA. Skeletal Muscle Fatigue in Old Age. Exerc Sport Sci Rev. 2009 Jan;37(1):3–9.

172.   Duchateau J, Enoka RM. Neural adaptations with chronic activity patterns in able-bodied humans. Am J Phys Med Rehabil. 2002 Nov;81(11 Suppl):S17-27.

173.   Trappe S, Gallagher P, Harber M, Carrithers J, Fluckey J, Trappe T. Single Muscle Fibre Contractile Properties in Young and Old Men and Women. J Physiol. 2003 Oct;552(1):47–58.

174.   Erskine RM, Morse CI, Day SH, Williams AG, Onambele-Pearson GL. The human patellar tendon moment arm assessed in vivo using dual-energy X-ray absorptiometry. J Biomech. 2014 Apr;47(6):1294–8.

175.   Maganaris CN, Baltzopoulos V, Sargeant AJ. In vivo measurement-based estimations of the human Achilles tendon moment arm. Eur J Appl Physiol. 2000 Nov 14;83(4–5):363–9.

176. Fukunaga T, Roy RR, Shellock FG, Hodgson JA, Edgerton VR. Specific tension of human plantar flexors and dorsiflexors. J Appl Physiol. 1996 Jan;80(1):158–65.

177. Herbert RD, Gandevia SC. Twitch interpolation in human muscles: mechanisms and implications for measurement of voluntary activation. J Neurophysiol. 1999 Nov;82(5):2271–83.

178. Allen GM, McKenzie DK, Gandevia SC. Twitch interpolation of the elbow flexor muscles at high forces. Muscle Nerve. 1998 Mar;21(3):318–28.

179. Scaglioni G, Martin A. Assessment of plantar flexors activation capacity: nerve versus muscle stimulation by single versus double pulse. Eur J Appl Physiol. 2009 Jul 7;106(4):563–72.

180. Allison GT, Fujiwara T. The relationship between EMG median frequency and low frequency band amplitude changes at different levels of muscle capacity. Clin Biomech (Bristol, Avon). 2002 Jul;17(6):464–9.

181. Cifrek M, Medved V, Tonković S, Ostojić S. Surface EMG based muscle fatigue evaluation in biomechanics. Clin Biomech. 2009 May;24(4):327–40.

182. Alegre LM, Ferri-Morales A, Rodriguez-Casares R, Aguado X. Effects of isometric training on the knee extensor moment–angle relationship and vastus lateralis muscle architecture. Eur J Appl Physiol. 2014 Nov 7;114(11):2437–46.

183. Erskine RM, Jones DA, Williams AG, Stewart CE, Degens H. Inter-individual variability in the adaptation of human muscle specific tension to progressive resistance training. Eur J Appl Physiol. 2010 Dec 12;110(6):1117–25.

184. McMahon GE, Morse CI, Burden A, Winwood K, Onambélé GL. Impact of Range of Motion During Ecologically Valid Resistance Training Protocols on Muscle Size, Subcutaneous Fat, and Strength. J Strength Cond Res. 2014 Jan;28(1):245–55.

185. Suetta C. Plasticity and function of human skeletal muscle in relation to disuse and rehabilitation: Influence of ageing and surgery. Dan Med J. 2017 Aug;64(8).

186. Horstman AM, Enoka RM, Girard O, Babault N, Herzog W, Racinais S, et al. Comments on Point:Counterpoint: The interpolated twitch does/does not provide a valid measure of the voluntary activation of muscle. J Appl Physiol. 2009 Jul 1;107(1):359–66.

187. Rosenberg IH. Sarcopenia: origins and clinical relevance. J Nutr. 1997;127(5 Suppl):990S–991S.

188. Narici M V., Maffulli N, Maganaris CN. Ageing of human muscles and tendons. Disabil Rehabil. Informa UK Ltd UK; 2008 Jan 7;30(20–22):1548–54.

189. Arnold P, Bautmans I. The influence of strength training on muscle activation in elderly persons: A systematic review and meta-analysis. Exp Gerontol. 2014 Oct;58:58–68.

190. Avin KG, Frey Law LA. Age-Related Differences in Muscle Fatigue Vary by Contraction Type: A Meta-analysis. Phys Ther. 2011 Aug 1;91(8):1153–65.

191. Stienen GJ, Kiers JL, Bottinelli R, Reggiani C. Myofibrillar ATPase activity in skinned human skeletal muscle fibres: fibre type and temperature dependence. J Physiol. 1996 Jun 1;493 (Pt 2:299–307.

192. Barnouin Y, McPhee JS, Butler-Browne G, Bosutti A, De Vito G, Jones DA, et al. Coupling between skeletal muscle fiber size and capillarization is maintained during healthy aging. J Cachexia Sarcopenia Muscle. 2017 Aug;8(4):647–59.

193. Kouzaki M, Shinohara M. Steadiness in plantar flexor muscles and its relation to postural sway in young and elderly adults. Muscle Nerve. 2010 Apr 30;42(1):78–87.

194. Kouzaki M, Masani K. Postural sway during quiet standing is related to physiological tremor and muscle volume in young and elderly adults. Gait Posture. 2012 Jan;35(1):11–7.

195. Stenroth L, Peltonen J, Cronin NJ, Sipila S, Finni T. Age-related differences in Achilles tendon properties and triceps surae muscle architecture in vivo. J Appl Physiol. 2012 Nov 15;113(10):1537–44.

196. Bohm S, Mersmann F, Arampatzis A. Human tendon adaptation in response to mechanical loading: a systematic review and meta-analysis of exercise intervention studies on healthy adults. Sport Med - Open. 2015 Dec 27;1(1):7.

197. Reeves ND, Narici MV, Maganaris CN. Musculoskeletal adaptations to resistance training in old age. Man Ther. 2006 Aug;11(3):192–6.

198. Onambele-Pearson GL, Pearson SJ. The magnitude and character of resistance-training-induced increase in tendon stiffness at old age is gender specific. Age

(Omaha). 2012 Apr 20;34(2):427–38.

199.   Reeves ND. Adaptation of the tendon to mechanical usage. J Musculoskelet Neuronal Interact. 2006;6(2):174–80.

200.   Svensson RB, Heinemeier KM, Couppé C, Kjaer M, Magnusson SP. Effect of aging and exercise on the tendon. J Appl Physiol. 2016 Dec 1;121(6):1237–46.

201.   Marini M, Sarchielli E, Brogi L, Lazzeri R, Salerno R, Sgambati E, et al. Role of adapted physical activity to prevent the adverse effects of the sarcopenia. A pilot study. Ital J Anat Embryol. 113(4):217–25.

202.   Fukunaga T, Roy RR, Shellock FG, Hodgson JA, Day MK, Lee PL, et al. Physiological cross-sectional area of human leg muscles based on magnetic resonance imaging. J Orthop Res. 1992 Nov;10(6):926–34.

203.   Wickiewicz TL, Roy RR, Powell PL, Edgerton VR. Muscle architecture of the human lower limb. Clin Orthop Relat Res. 1983 Oct;(179):275–83.

204.   Maganaris CN, Paul JP. Tensile properties of the in vivo human gastrocnemius tendon. J Biomech. 2002 Dec;35(12):1639–46.

205.   Maganaris CN, Baltzopoulos V, Sargeant AJ. Differences in human antagonistic ankle dorsiflexor coactivation between legs; can they explain the moment deficit in the weaker plantarflexor leg? Exp Physiol. 1998 Nov;83(6):843–55.

206.   Tremblay MS, Colley RC, Saunders TJ, Healy GN, Owen N. Physiological and health implications of a sedentary lifestyle. Appl Physiol Nutr Metab. 2010 Dec;35(6):725–40.

207.   Davis RE, Loprinzi PD. Examination of Accelerometer Reactivity Among a Population Sample of Children, Adolescents, and Adults. J Phys Act Heal. 2016 Dec;13(12):1325–32.

208.   Miles MP, Clarkson PM, Bean M, Ambach K, Mulroy J, Vincent K. Muscle function at the wrist following 9 d of immobilization and suspension. Med Sci Sports Exerc. 1994 May;26(5):615–23.

209.   Seynnes OR, de Boer M, Narici M V. Early skeletal muscle hypertrophy and architectural changes in response to high-intensity resistance training. J Appl Physiol. 2007 Jan;102(1):368–73.

210. Bostock EL, Morse CI, Winwood K, McEwan IM, Onambélé-Pearson GL. Omega-3 fatty acids and vitamin D in immobilisation: Part A- Modulation of appendicular mass content, composition and structure. J Nutr Health Aging. 2017 Jan 10;21(1):51–8.

211. Miles MP, Clarkson PM, Bean M, Ambach K, Mulroy J, Vincent K. Muscle function at the wrist following 9 d of immobilization and suspension. Med Sci Sports Exerc. 1994 May 15;26(5):615–23.

212. Prata MG, Scheicher ME. Correlation between balance and the level of functional independence among elderly people. Sao Paulo Med J. 2012;130(2):97–101.

Appendix I

Published paper(s):

CrossMark

REVIEW ARTICLE

A review of the assessment and prevalence of sedentarism in older adults, its physiology/health impact and non-exercise mobility counter-measures

Jorgen A. Wullems · Sabine M. P. Verschueren · Hans Degens · Christopher I. Morse · Gladys L. Onambélé

Abstract This literature review focuses on aspects of sedentary behaviour (SB) in elderly. Since it has been identified as a distinct health risk, independent of physical activity, SB is a significant issue. This is particularly true for an ageing population as evidence shows that older adults (aged ≥65 years) are the most sedentary age group (on average 8.5–9.6 h daily sitting time). Accurate SB assessment is important for understanding this habitual behaviour and its impact. However, SB measurement is challenging, regardless of the method used. Although negative associations of SB in elderly have been reported for several health outcomes, evidence is inconclusive, apart from the evidence on the adverse SB effect on the all-cause mortality rate. Generally, strategies have been proposed to counteract SB, of which breaking prolonged sedentary bouts with at least light-intensity physical activity seems to be the most promising. Overall, further research in elderly is required to increase the evidence and to either support or refute the current findings. Moreover, further research will help to develop informed SB guidelines for an optimal strategy to counteract SB and its health effects in older adults.

Keywords Ageing physiology · Musculoskeletal · Older adults · Physical activity · Sedentary behaviour

J. A. Wullems · C. I. Morse · G. L. Onambélé (✉)
Department of Exercise and Sport Science, Institute for Performance Research, Manchester Metropolitan University, Crewe Green Road, Crewe CW1 5DU, UK
e-mail: g.pearson@mmu.ac.uk

S. M. P. Verschueren
Musculoskeletal Rehabilitation Research Group, Department of Rehabilitation Sciences, KU Leuven, Louvain, Belgium

H. Degens
School of Healthcare Science, Manchester Metropolitan University, Manchester, UK

H. Degens
Lithuanian Sports University, Kaunas, Lithuania

Introduction

Contrary to general perceptions, sedentary behaviour (SB) does not necessarily reflect a lack of physical activity (PA) (Sedentary Behaviour Research Network 2012). Instead, SB is defined as any waking behaviour characterized by an energy expenditure ≤1.5 metabolic equivalent of task (MET) while in a seated or reclined posture (Sedentary Behaviour Research Network 2012). Currently, time spent sitting is increasing in modern societies, presumably linked to activities related to work, leisure or commuting. Previous research has shown that higher sitting time is related to poorer health (Gardiner et al. 2011c; Inoue et al. 2012). Recent health improvement strategies have focused on increasing PA (Kikuchi et al. 2014). While

🙄 Springer

PA contributes to healthy ageing and plays a key role in the prevention of non-communicable diseases and disability, including cardiovascular disease, cancer, metabolic syndrome, mental disorders, musculoskeletal diseases and even all-cause mortality (de Rezende et al. 2014a; Gorman et al. 2014; Gennuso et al. 2015), studies that controlled for PA intensity provide evidence that also (prolonged) SB is an independent determinant of health (Gennuso et al. 2013; Gorman et al. 2014; de Rezende et al. 2014b; Gianoudis et al. 2015). This has led to the proposal of a novel stratagem for reducing health risks through not only increasing PA, but also decreasing SB (Hamilton et al. 2008; Owen et al. 2011).

Recently, the study of SB and its relation to health has become more popular (de Rezende et al. 2014a), but at present most underlying mechanisms by which SB has deleterious health effects remain unknown (Gianoudis et al. 2015). Moreover, existing studies have generally focused on different outcome measures and presented divergent conclusions, making the formulation of a cohesive understanding of the interaction between SB and health, as yet, impossible (de Rezende et al. 2014b). Although SB research shows that older adults (aged ≥65 years) are the most sedentary, this age group has only been studied limitedly (Gennuso et al. 2013; Van Cauwenberg et al. 2014b). This makes it difficult to allow policy recommendations giving detailed information on how to reduce SB in older adults (Harvey et al. 2013). With an ageing population, the increased SB is challenging for both health and social care resources, and better understanding of the relationship between SB and health in the elderly requires more and better-targeted research (de Rezende et al. 2014a). To aid in developing targeted research programmes it is important to identify and summarize current findings of SB in older adults.

Hence, the aim of this review was to describe multiple aspects of SB in older adults, from its assessment, prevalence, physiology, health impact, through to any known potential counteracting strategies.

The strategy used to meet the aims of this literature review was based on a search in four different electronic databases (PubMed, CINAHL, The Cochrane Library and Sedentary Behaviour Research Database) combining the following key words: "sedentary behaviour", "older adults", and "health". Where possible, the following search limits were used: English language and age group 65+. This search

(performed on 02 December 2015) identified 825 peer-reviewed articles. All were screened for potential inclusion based first on the title and abstract, and if not excluded, the full-texts were checked for eligibility. Generally, eligible articles focused on SB (or a proxy measure, but not physical inactivity) as a main independent or dependent variable in healthy, community-dwelling older adults (aged ≥60 years) only. In addition to the electronic databases search, reference lists of the eligible articles (n = 41) were hand-searched to identify any missed papers (n = 7) (Fig. 1). Table 1 shows an overview of the 48 included papers, which are fundamental to this review.

Assessment of sedentary behaviour

Similar to characterising PA and exercise by the FITT formula, describing the Frequency, Intensity, Time (duration) and Type of activity, SB is suggested to be characterised by the SITT formula, which describes Sedentary behaviour frequency, number of Interruptions, Time (duration) and Type (Tremblay et al. 2010). These variables provide valuable information on SB and should therefore be assessed in any study dealing with SB. Since the need to quantify SB emerged, efforts have been undertaken to develop suitable measurement techniques. Overall, these can be classified as either subjective or objective, and both have different outcome measures. According to previous research (Pate et al. 2008; Chastin and Granat 2010; Pedišić and Bauman 2015), studies on SB initially relied on self-reported methods, such as questionnaires and/or logs. Subjective methods are practical, easy to administer, inexpensive, useful in large-scale studies and do not alter behaviour (Celis-Morales et al. 2012; Chastin et al. 2014a; Aguilar-Farías et al. 2015). They will provide SB outcomes in terms of total sitting time, total screen time or TV time. If surrogate or proxy SB measures (e.g. TV viewing or total screen time) are used as an indicator of total SB, conclusions can however only be drawn limited to the used measures, because the association with total objective SB seems rather weak, even if the proxy measure is objective (Pate et al. 2008; Visser and Koster 2013; Chastin et al. 2014a). Although the number of SB questionnaires for older adults increases and quality improves in terms of acceptable reliability measures, validity of self-reported total sedentary time
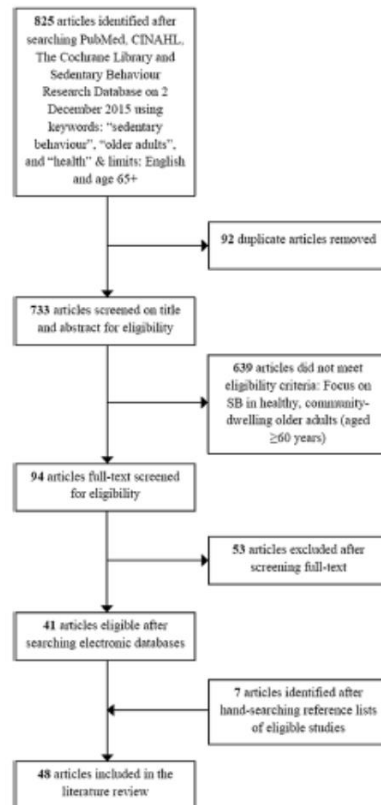
Fig. 1 Literature search flow diagram

against accelerometer-derived SB is not strong yet (Gardiner et al. 2011a; Hekler et al. 2012; Visser and Koster 2013; Van Cauwenberg et al. 2014b; Aguilar-Farías et al. 2015). A major flaw is that most studies validate questionnaires against sensors unable to capture SB accurately due to the inability of measuring postural orientation, e.g. thigh inclination (Chastin et al. 2014a). Generally, most subjective measures have obvious caveats, like bias and the tendency to under-report SB (Chastin and Granat 2010; Harvey

et al. 2015; Aguilar-Farías et al. 2015). SB appears to be more difficult to recall than PA, because of its habitual nature (Hart et al. 2011; Bond et al. 2014). Especially for older adults it is a challenge to accurately estimate sitting-time (van Uffelen et al. 2011). The combination of underestimation and low precision is likely to reduce the ability to accurately detect dose–response relationships between self-reported SB and health outcomes (Chastin et al. 2014a). Nevertheless, so-called past or previous day recall questionnaires have been reported as promising since they are easy-to-administer, compare favourably with other sedentary time questionnaires, criterion validity is high, and systematic errors low (Clark et al. 2013; Matthews et al. 2013). Self-reports might give a detailed picture of how, where and why SB time is spent, which could be essential for developing interventions and public policy (Rhodes et al. 2012; Matthews et al. 2013; Kozey Keadle et al. 2014; Van Cauwenberg et al. 2014b; Busschaert et al. 2015). Thus, subjective methods can provide useful information and should not be ignored in SB assessment, but they should not be used as sole means to assess SB, and the development of accurate self-report tools to measure (specific) SB in elderly is still required (Van Cauwenberg et al. 2014b; Gennuso et al. 2015).

Although many objective techniques are available to capture PA, there are only few to measure SB, in particular accelerometers (Tremblay et al. 2010). Accelerometry is preferred by most studies since it provides reliable and valid measures of both PA and SB, and it overcomes many of the above-mentioned limitations of self-reports (Evenson et al. 2012; Gorman et al. 2014; Lohne-Seiler et al. 2014; Aguilar-Farías et al. 2014; Pedišić and Bauman 2015). However, it is important to mention that different accelerometers use distinct methods to measure SB. One quantifies SB by a lack of movement, and the other by postural allocation. The first type only uses estimates of energy expenditure in combination with cut-off points to define SB. However this results in misclassification as standing is difficult to distinguish from sitting when performed below the sedentary cut-off point (Stamatakis et al. 2012; Aguilar-Farías et al. 2014). Devices measuring postural allocation are more accurate in assessing SB and therefore not only recommended but also used as reference standard (Kozey-Keadle et al. 2011; Aguilar-Farías et al. 2014). When compared to self-reports,

189

Table 1 Overview of the 48 included studies after literature search

Data presented in paragraph(s)	Author(s)	Study population	Subjective or objective SB tool	General finding(s)
Original studies				
Assessment of SB	Van Cauwenberg et al. (2014b)	n = 508	Both	Validity for older adults' self-reported total sitting time against accelerometer-derived sedentary time was not strong, but comparable to previous studies
	Aguilar-Farías et al. (2014)	n = 37	Objective	The results suggest that cut-points are dependent on unit of analyses (i.e. epoch length and axes); cut-points for a given epoch length and axis cannot simply be extrapolated to other epoch lengths
	Hekler et al. (2012)	n = 870	Both	CHAMPS items effectively measured high-light, total activity, and MVPA in seniors, but further refinement is needed for sedentary and low-light activity
	van Uffelen et al. (2011)	n = 55	Subjective	The accuracy of older adults' self-reported sitting time is questionable given the challenges they have in answering sitting-time questions
	Gardiner et al. (2011a)	n = 48	Both	The summary measure of total sedentary time has good repeatability and modest validity and is sufficiently responsive to change suggesting that it is suitable for use in interventions with older adults
Prevalence and types of SB	Shiroma et al. (2013)	n = 7247	Objective	Older women spent about two-thirds of waking time in SB, most of which occurred in bouts lasting less than 30 min
	Arnardottir et al. (2013)	n = 579	Objective	Sedentary time is high in Icelandic older adults who have high life-expectancy and live north of 60° northern latitude, while PA declines with increasing age and body mass index. Women spend more time in low-light PA, but less in MVPA than men
	Evenson et al. (2014)	n = 760	Objective	The New York sample spent a longer proportion of time in SB and light activities, but more time in MVPA than the country sample. Urbanicity may explain these differences
	Evenson et al. (2012)	n = 2630	Objective	MVPA estimates vary among adults aged 60 or older, depending on the cut point chosen, and most of their time is spent in SBs
	Lord et al. (2011)	n = 56	Objective	Walking, sedentary and transitory behaviours are distinct from each other, and together explain daily function
	Jefferis et al. (2015a)	n = 1419	Objective	Among older adults, the steep decline in total PA occurred due to reductions in MVPA whilst light PA is relatively spared and sedentary time and long sedentary bouts increase
Health impact of SB—Musculoskeletal health & functional fitness	Mitchell et al. (2015)	n = 5681	Subjective	SB was identified as mediator for the association between obesity and falls in community living older people
	Gianoudis et al. (2015)	n = 162	Subjective	Higher levels of SB in older adults were associated with reduced muscle mass and an increased risk of sarcopenia in community-dwelling older adults, independent of PA
	Dunlop et al. (2015)	n = 2286	Objective	These U.S. national data show a strong relationship between greater time spent in SB and the presence of ADL disability, independent of time spent in moderate or vigorous activity

190

Table 1 continued

Data presented in paragraph(s)	Author(s)	Study population	Subjective or objective SB tool	General finding(s)
	Santos et al. (2012)	n = 312	Objective	Elderly who spend more time in PA or less time in SBs exhibit improved functional fitness and other confounders
	Chastin et al. (2012)	n = 30	Objective	The pattern of SB accumulation varies between older adults and is associated with muscle quality and adiposity
	Cawthon et al. (2013)	n = 1983	Objective	Older men with lower total energy expenditure, lower moderate activity, or greater sedentary time were more likely to develop a functional limitation
Health impact of SB—Cardio metabolic health & mortality	Ensrud et al. (2014)	n = 2918	Objective	In older men exceeding current guidelines on PA, greater time spent in SB is associated with increased mortality risk
	Chase et al. (2014)	n = 54	Objective	SB is associated with an adverse metabolic effect on low-density lipoprotein in seniors, even those who meet guideline recommendations for an active 'fit' adult
	Gennuso et al. (2013)	n = 1914	Objective	The results suggest that sufficient MVPA did not ameliorate the negative associations between SB and cardio metabolic risk factors or functional limitations in the current sample
	Inoue et al. (2012)	n = 1806	Subjective	Spending less time watching TV, a predominant SB, was associated with lower risk of being overweight or obese, independent of meeting PA guidelines
	Stamatakis et al. (2012)	n = 2765	Both	SB is associated with cardio metabolic risk factors, but the associations are more consistent when it is measured by self-report that includes TV viewing
	Gardiner et al. (2011c)	n = 1958	Subjective	High levels of SB were associated with greater prevalence of the metabolic syndrome
	Bankoski et al. (2011)	n = 1367	Objective	The proportion of sedentary time was strongly related to metabolic risk, independent of PA
	Gao et al. (2007)	n = 455	Subjective	A high prevalence of the metabolic syndrome in a representative sample of Caribbean-origin Hispanic elders was associated with prolonged television viewing, independent of PA and energy intake
	León-Muñoz et al. (2013)	n = 2635	Subjective	Compared with consistently sedentary older adults, consistently non-sedentary individuals showed reduced all-cause mortality. Individuals who changed sitting time experienced an intermediate reduction in mortality
	Pavey et al. (2015)	n = 6656	Subjective	Prolonged sitting-time was positively associated with all-cause mortality. Women who reported sitting for more than 8 h/day and did not meet PA guidelines had an increased risk of dying within the next 9 years
	Gómez-Cabello et al. (2012)	n = 3136	Subjective	Sitting time increases the risk of overweight-obesity and overfat in women and the risk of central obesity in men, independently of walking time
Health impact of SB—Other (health) outcomes & quality of life	Withall et al. (2014)	n = 228	Objective	Steps, MVPA and lower limb function were independently and moderately positively associated with perceived physical well-being but relationships with mental well-being variables were weak. No significant associations between SBs and well-being were observed

191

Table 1 continued

Data presented in paragraph(s)	Author(s)	Study population	Subjective or objective SB tool	General finding(s)
	Balboa-Castillo et al. (2011)	n = 1097	Subjective	Greater leisure-time PA and less leisure-time SB were independently associated with better long-term health-related QoL in older adults
	Vance et al. (2008)	n = 158	Subjective	Partial support was found for PA to improve and SB to worsen cognitive health
	Verghese et al. (2003)	n = 469	Subjective	Participation in certain seated leisure activities (like reading or playing board games) is associated with a reduced risk of dementia, even after adjustment for base-line cognitive status and after the exclusion of subjects with possible preclinical dementia
Strategies to counteract the health effects of SB	Meneguci et al. (2015)	n = 3296	Subjective	Socio-demographic, clinical, and health behaviour factors are associated with high sitting time in older adults from South-eastern Brazil
	Sardinha et al. (2015)	n = 215	Objective	Breaking-up sedentary time is associated with better physical function in older adults; and, it may have an important place in future guidelines on preserving older adults' physical function to support ADL
	Gardner et al. (2014)	n = 120	Both	N/a
	Chastin et al. (2014b)	n = 11	Subjective	Older adults consider self-efficacy, functional limitations, ageist stereotyping, locus of control, and pain as determinants of their SB
	van der Berg et al. (2014)	n = 565	Objective	Some demographic, socioeconomic, and biomedical determinants in midlife were associated with considerably more sedentary time per day in old age
	Van Cauwenberg et al. (2014a)	n = 50,986	Subjective	There is a cross-sectional link between older adults' television viewing time and social composition of their neighbourhood, formal participation, access to alternative activities, and safety from crime
	Fitzsimons et al. (2013)	n = 24	Both	A consultation approach may help individuals reduce time spent in SBs
	Davis et al. (2014)	n = 217	Objective	Promoting regular breaks in sedentary time might be useful in maintaining or increasing lower extremity function and later life independence
	Kikuchi et al. (2013)	n = 1665	Subjective	Particular socio-demographic and behavioural characteristics related to TV time among Japanese older adults have been identified, but they differ by gender
	Gardiner et al. (2011b)	n = 59	Objective	Sedentary time in older adults can be reduced following a brief intervention based on goal setting and behavioural self-monitoring
	Nicklas et al. (2014)	n = 48	Objective	Self-monitoring of spontaneous PA and SB enhanced successful maintenance of lost weight
	Uffelen et al. (2012)	n = 6116	Subjective	It is suggested that older women with a high health risk profile and social risk profile may particularly benefit from interventions to promote both reducing sitting time and increasing PA or at least light activities
	Dogra and Stathokostas (2014)	n = 14,560	Subjective	Several specific correlates of extended sitting time were identified; these findings have implications for public health strategies targeting older adults

192

Table 1 continued

Data presented in paragraph(s)	Author(s)	Study population	Subjective or objective SB tool	General finding(s)
Reviews				
Prevalence and types of SB	Harvey et al. (2013)	n = 372,550	Both	Whether measurements are subjective or objective, the majority of older adults are sedentary
	Harvey et al. (2015)	n = 349,698	Both	Time spent sedentary ranges from 5.3 to 9.4 h per waking day in older adults
Health impact of SB—Overall	de Rezende et al. (2014a)	n = 335,503	Both	The data supports the relationship between SB and mortality in older adults

SB sedentary behaviour, *CHAMPS* community healthy activities model program for seniors, *MVPA* moderate-to-vigorous physical activity, *PA* physical activity, *ADL* activities of daily living, *TV* television, *QoL* quality of life, *Na* not applicable

accelerometers are expensive (≥£190 per unit), there is potential bias due to a Hawthorne effect (behaviour change in response to the awareness of being observed) and data-analysis is labour-intensive (Visser and Koster 2013; Pedišić and Bauman 2015), at least until an analysis template has been created. However, accelerometry enables more robust, objective, ambulatory and long-term recording of acceleration signals (Chastin and Granat 2010; Tremblay et al. 2010), and provides outcomes, such as total SB time, sedentary bout time, sedentary pattern, and number and frequency of breaks in SB. Nonetheless, accelerometry only addresses the energetic ontology of the definition of SB and there is no consensus on a standardised method for accelerometer data processing and analysis (e.g. non-validated cut-points or epoch lengths) (Gorman et al. 2014; Pedišić and Bauman 2015). Assumptions are still required to quantify accelerometry-based PA and SB in older adults, resulting in a potential danger of misinterpretation (Evenson et al. 2012; Kowalski et al. 2012; Gorman et al. 2014; Kozey Keadle et al. 2014). With modern technological advances, accelerometer use is assumed to be more straightforward and easy to implement. Furthermore, the possibilities of objective SB monitoring will continue to increase and provide an ever more-detailed and accurate objective picture of SB in elderly.

The main reason for preferring accelerometry in SB measurement is that it provides an objective assessment of SB and may thereby help to understand how SB is related to healthy ageing (Visser and Koster 2013; Van Cauwenberg et al. 2014b). Nevertheless, accelerometers should not substitute but supplement questionnaires (Pedišić and Bauman 2015). Self-reports are still needed to assess engagement in specific SBs and provide more detailed (qualitative) information that cannot be obtained with accelerometers (Rhodes et al. 2012; Lohne-Seiler et al. 2014; Van Cauwenberg et al. 2014b). Generally, it is suggested that SB associations are complex to interpret because they depend on the type of SB studied and the measurement method used (Table 2) (Stamatakis et al. 2012; de Rezende et al. 2014b). For example, Lenz (2014) noted that in older adults TV viewing had more associations with cardio metabolic outcomes than reports of total SB, while Celis-Morales et al. (2012) concluded that, due to underestimation, self-reports might miss some significant trends that will be found when objective assessments are used.

When capturing SB in older adults, different parameters have to be taken into account, depending on the method applied, i.e. mounting position, data filtering and algorithm, and type of device and/or questionnaire used. Additionally, potential confounders like age, gender, health status or socioeconomic status have to be considered. Another important consideration to accurately estimate SB is the number of complete data acquisition days needed. Compared with PA, more monitoring days are needed to reliably estimate SB because it is less predictable on a daily basis (Hart et al. 2011). In older adults, 5 monitoring days are required to provide a reliable (ICC = 0.80) SB estimate when using an objective method, while only 3 days are necessary to monitor PA with the same level of reliability (Hart et al. 2011). Increasing the number of monitoring days to either 7, 11 or 21, will improve the reliability of SB monitoring resulting in ICCs of 0.85, 0.90 and 0.95 respectively (Hart et al. 2011). Since studies are divergent on whether there is a difference in SB between week and weekend days in older adults, it is advised to include both when using a

Table 2 Brief overview of the complex SB associations with cardio metabolic outcomes

SB associations	Adults (18–73 years)		Older adults (≥60 years)													
	Celis-Morales et al. (2012) (n = 317)		Gennuso et al. (2013) (n = 1914)	Lenz (2014) (n = 70)						Gao et al. (2007) (n = 455)	Gardiner et al. (2011c) (n = 1958)		Stamatakis et al. (2012) (n = 2765)			
	Obj.	Subj.	Obj.	Subj.						Subj.	Subj.		Obj.	Subj.		
Cardio metabolic risk factors	Acc.	Total SB	Acc.	TV	Reading	Eating	Computer	Transport	Total SB	TV	TV	Total SB	Acc.	TV	Non-TV leisure sitting	Total SB
Glucose/GI	+	+	+		+						+					
Insulin	+	+														
HOMA_IR/diabetes	+	+												+	+	+
HbA1C																
TC/CR	+	+								+						
HDL	+	+		+						+		+		+		+
LDL	+	+							+							
TG	+	+		+								+				
SBP	+	+		+						+		+				
DBP	+	+		+						+		+				
Weight			+						+							
BMI/overweight/Obesity	+	+	+							+				+		+
WC/WHR/AO	+	+	+	+					+	+		+	+	+		+
Body fat	+	+	+	+		+										
CRP			+													

SB sedentary behaviour, *Obj.* objective method, *Subj.* subjective method, *Acc.* accelerometer, *TV* television viewing, *GI* glucose intolerance, $HOMA_{IR}$ homeostasis model assessment-estimated insulin resistance, *TC* total cholesterol, *CR* cholesterol ratio, *HDL* high-density lipoprotein, *LDL* low-density lipoprotein, *TG* triglycerides, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *BMI* body mass index, *WC* waist circumference, *WHR* waist-to-hip ratio, *AO* abdominal obesity, *CRP* C-reactive protein, *HbA1C* glycated haemoglobin, + significant association

<7-day monitoring protocol (Hart et al. 2011; Davis et al. 2011; Visser and Koster 2013). Compared to objective methods, self-reports show larger day-to-day differences and therefore they require more monitoring days (preferably ≥7) to reliably predict SB (Hart et al. 2011).

Generally, SB assessment in older adults is challenging, regardless of the method applied or outcome measures used. A combination of both objective (using postural allocation) and self-reported methods used in a 7-day monitoring protocol is currently suggested to be optimal for assessing SB in older adults.

Prevalence and types of sedentary behaviour

Daily function in older adults is mainly subdivided in walking, postural transitions and SB (Lord et al. 2011), with several studies reporting that most of their time is spent in SBs (Healy et al. 2008; Davis et al. 2011; Evenson et al. 2012; Shiroma et al. 2013; Jefferis et al. 2015b). Previous literature shows that SB increases with age, resulting in older adults (aged ≥60 years) being the most sedentary (Matthews et al. 2008; Rhodes et al. 2012; Martin et al. 2014) and old-older adults being more sedentary than young-older adults (Table 3) (Evenson et al. 2012; Martin et al. 2014; Harvey et al. 2015). Interestingly, after retirement (from ~65 years of age) the amount of SB transiently reduces, while the percentage of ambulatory activity increases (Godfrey et al. 2014). Not only the amount of SB and long sedentary bouts increase with ageing in older adults, but also the decline in total daily PA accelerates (Table 3) (Davis et al. 2011; Harvey et al. 2013; Buchman et al. 2014; Martin et al. 2014;

Jefferis et al. 2015a). This latter decline is characterized by: (1) lower PA volume, (2) less higher-intensity PA, and (3) lower frequency of getting out and about (Davis et al. 2011). This results in old-older adults (aged ≥85 years) performing only one third of the activity performed by young-older adults (aged 70–74.9 years) at peak activity times (Davis et al. 2011).

According to national surveys, adults are on average sedentary for 8 h of the waking day, and this figure rises to >10 h in older adults (Matthews et al. 2008; Davis et al. 2011; Lenz 2014). However, two systematic reviews describe that self-reported SB in older adults (aged ≥60 years) is on average 5.3 h/day only (Harvey et al. 2015), with ~60 % reporting sitting >4 h/day during waking hours (Harvey et al. 2013). When using objective measurements, older adults (aged ≥60 years) spend on average 8.5–9.6 h/day sedentary (Evenson et al. 2012, 2014; Harvey et al. 2015), which equals 65–80 % of their waking day. Other accelerometer-based studies showed that older adults spend approximately 75–80 % of their awake time in SB which represents 8–12 h/day (Arnardottir et al. 2013; de Rezende et al. 2014a). Other studies suggest that 67 % of the older age population is sedentary for >8.5 h/day (Stamatakis et al. 2012), and that about half (47 %) of them are sedentary >80 % of their waking hours (Davis et al. 2011). In general, older adult men spend more time in SB (~75 % of the day) than older adult women (~66 % of the day), but in both the total time of SB is primarily the result of accumulation of many relatively short SB bouts of less than 30 min (Davis et al. 2011; Evenson et al. 2012; Shiroma et al. 2013; Harvey et al. 2015; Jefferis et al. 2015b).

Table 3 Comparison of accelerometer-derived SB across different age groups

Matthews et al. (2008)

	Age groups						
	16–19	20–29	30–39	40–49	50–59	60–69	70–85
Male	7.9	7.3	7.2	7.6	7.9	8.8	9.5
Female	8.1	7.7	7.3	7.5	7.8	8.1	9.1

Martin et al. (2014)

	Age groups			
	20–39	40–59	60–69	≥70
Male	7.9	8.5	9.4	10.3
Female	7.9	8.3	8.7	9.8

Values represent mean hours/day adjusted for monitor-wearing time

SB sedentary behaviour

For a better and more detailed understanding of SB, it is important to assess typical SBs. Previous research has shown that older adults engage in approximately 16 types of SB daily, with TV viewing, reading, eating meals, computer use and transportation being the most common (Lenz 2014). Generally, TV viewing and computer use are the main SB measures, followed by the overall assessment of time-spent sitting (van Uffelen et al. 2011; Rhodes et al. 2012; Visser and Koster 2013). Time spent TV viewing combined with computer use is termed screen time (Harvey et al. 2013). About 53 % of the older adults report daily screen time >4 h, and ~94 % >2 h (Harvey et al. 2013). When splitting screen time, older adults watch on average 3.3 h TV, with more than half of the age group (54 %) sitting in front of the TV for 3 h, while about one third watches TV >3.6 h and 15 % >4 h daily (Harvey et al. 2013). Around 65 % of older adults use computers, but <10 % use it more than 1.6 h daily (Harvey et al. 2013). A more general outcome, like leisure sitting time (excluding TV time), is reported by older adults to be on average 3.3 h daily, and reported by ~54 % to be >3 h (Patel et al. 2010; Harvey et al. 2015). Total sitting time >3 h is reported in older adults by 78 %, with ~59 % reporting sitting >4 h, ~27 % reporting >6 h and 5 % reporting >10 h daily (Harvey et al. 2013).

Although the amount of SB varies in the current literature depending on the assessment method used (range 5.3–12 h/day), it is nevertheless clear that SB is highly prevalent in older adults. PA appears to be lower and of less intensity, making light-intensity PA (LIPA) the most common type of PA within the oldest age groups (Table 3). This suggests that LIPA is the most feasible PA in elderly, which is of interest to counteract SB, as will be discussed later.

Sedentary physiology

Research into the physiology and health impacts of SB has recently increased and represents an exciting new field of study, which is distinct but complementary to exercise physiology, namely sedentary physiology (Tremblay et al. 2010; Sedentary Behaviour Research Network 2012; Dunstan et al. 2012a). Associations between SB and several outcomes have been reported. However, the mechanisms underlying the association between SB and adverse health effects remain

uncertain and are therefore a research priority (Dunstan et al. 2012a; Gianoudis et al. 2015). To date, physiological mechanisms for four different outcomes have been proposed regardless of age, namely:

- *Cardio metabolic* It has been proposed that reduced energy expenditure and muscle contractions not only lead to reduced insulin sensitivity and an increase in pro-inflammatory cytokines (Tremblay et al. 2010; Yates et al. 2012), but also decreased lipoprotein lipase (LPL) activity and muscle glucose transporter (GLUT) protein content (Tremblay et al. 2010; Gianoudis et al. 2015);
- *Vascular* Studies have shown that shear rate, FMD and brachial artery diameter decrease, while endothelial cell damage and blood pressure increase with increasing SB (Demiot et al. 2007; Hamburg et al. 2007; Thosar et al. 2015);
- *Muscle–tendon* It is proposed that continual underloading due to SB, negatively affects muscle–tendon properties, since muscle–tendon disuse causes changes (e.g. muscle atrophy and increased tendon compliance). Aside from that, SB is thought to be a determinant driver for obesity (Chastin et al. 2012). Generally, it is proposed that an increase in visceral and intermuscular fat stimulates the release of pro-inflammatory cytokines and decrease of anti-inflammatory markers from adipose tissue, having a catabolic effect on muscle tissue by impairing muscle protein synthesis (Gianoudis et al. 2015). This will affect muscle performance, however that does not only arise from muscular but also neural factors (Tomlinson et al. 2014);
- *Skeletal* SB is thought to change the balance between bone resorption and deposition, mainly by a rapid increase in bone resorption (marked by increased deoxypyridinoline, urinary calcium and type I collagen cross-linked N-telopeptides) without concomitant changes in bone formation, resulting in reduced bone mineral content and increased risk of osteoporosis (Kim et al. 2003; Tremblay et al. 2010).

Health impact of sedentary behaviour

Despite a high prevalence, SB in older adults has so far received limited scientific attention (Gennuso et al.
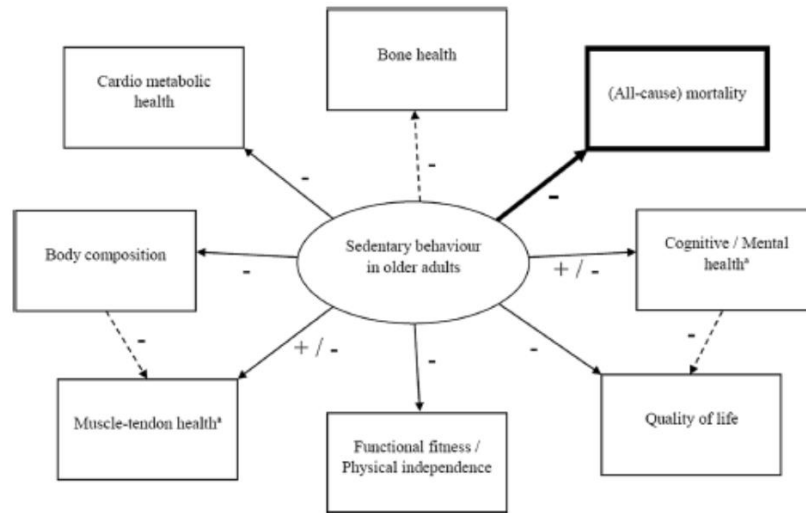
Fig. 2 Overview of identified and suggested associations between SB and (health) outcomes in older adults as reported in literature + positive association; − negative association; *solid lines* represent identified associations; *dashed lines* represent suggested associations; Associations in *bold* are confirmed by a systematic review from de Rezende et al. (2014a). [a]Outcome depends on the type of assessed SB (e.g. TV viewing, computer use or reading)

2013; Van Cauwenberg et al. 2014b). A general overview of reported (health) outcomes, independently associated with SB in healthy, community-dwelling older adults, is provided below (Fig. 2).

Musculoskeletal health & functional fitness

Although proof of SB effects on musculoskeletal health is limited in elderly, some interesting findings have been reported. Evidence shows for example, that associations between screen-based SB and muscle strength, independently of PA, are context-specific where TV viewing is associated with lower muscle strength while opposite effects are observed for computer use (Hamer and Stamatakis 2013). This might result from lower energy expenditure and unhealthier eating behaviours during TV watching, but also a potential confounding effect of education level on computer use (Visser and Koster 2013; Lenz 2014). Further, a study examining the relation between sarcopenia and SB, showed that higher volumes of TV viewing time were related to lower total body and leg lean mass after adjusting for fat mass, which was positively associated with the duration of watching TV (Gianoudis et al. 2015). Another study confirmed this latter finding by suggesting that SB is directly related to (lower limb) adiposity in older men, but increased and prolonged SB was also, unexpectedly, associated with increased leg power and muscle quality in these men (Chastin et al. 2012). Possible explanations for this latter finding were, e.g. carrying more body fat may provide a training stimulus or results reflect adiposity developing in previously strong men who have recently become sedentary. However, according to Chastin et al. (2012), their results should be interpreted with caution since the study sample was not necessarily representative of elderly in general. Other research shows that higher levels of SB in older adults are associated with an increased risk of sarcopenia and limited physical function, independent of PA or other potential confounding factors (Gennuso et al. 2013; Gianoudis et al. 2015). These findings are

🖄 Springer

197

confirmed by other studies showing that even after adjusting for PA and other confounders, objectively measured SB is negatively associated with functional fitness and the ability to perform activities of daily living (Santos et al. 2012; Cawthon et al. 2013; Dunlop et al. 2015). According to Marques et al. (2014), SB is only a predictor for the risk of losing physical independence when not controlling for PA intensities. However, this finding might result from misclassification of participants due to using accelerometer data of less than five monitoring days and a self-reported measure of physical function. Santos et al. (2012) found that PA was positively related to functional fitness, independent of SB, and therefore they concluded that both SB reduction and PA increase in older adults might preserve functional fitness and performance in terms of daily functioning tasks and independent living. Especially obese people could benefit from this since SB has been identified as a mediator for the association between obesity and falls in elderly (Mitchell et al. 2015). A study on successful ageing, which represents the physical, psychosocial, and social success with which adults age, showed that SB is associated with lower odds of successful ageing (Dogra and Stathokostas 2012). Although a dose-dependent relationship exists between SB and each of the three successful ageing components, the strongest association was found between SB and functional limitations (physical component) (Dogra and Stathokostas 2012). Functional dependence in old age is more likely to develop in older adults who are not physically active, or who were not so during their middle age (Dogra and Stathokostas 2012; Marques et al. 2014).

Skeletal measures are limited to a single report, showing that independent of time spent engaging in PA, SB is negatively associated with femur bone mineral density in older women only (Chastin et al. 2014c).

Cardio metabolic health & mortality

Regarding risk factors for cardio metabolic diseases, TV viewing and self-reported SB are positively associated with (i) dyslipidaemia characterised by increased triglycerides and lower high-density lipoprotein (HDL), (ii) obesity, (iii) hypertension and (iv) glucose intolerance (in women only) (Gao et al. 2007; Gardiner et al. 2011c; Inoue et al. 2012; Lenz 2014). These findings are in agreement with another study suggesting that self-reported SB (TV viewing in particular) and, to a lesser extent, objectively measured SB in older adults are negatively associated with two cardio metabolic risk proxies, independently of PA: (1) cholesterol index and (2) diabetes prevalence (Stamatakis et al. 2012). Gennuso et al. (2013) also reported that associations between accelerometer-derived SB and various health outcomes in older adults were not modified by PA, however they only found independent associations with body mass (index), waist circumference, C-reactive protein and plasma glucose, but not with blood pressure, cholesterol markers and triglycerides (Gennuso et al. 2013). Nevertheless, Chase et al. (2014) showed that objectively measured SB was associated with an adverse metabolic effect on low-density lipoprotein (LDL) levels in physically active elderly. Overall, most studies suggest that watching TV and/or engaging in large amounts of total SB is negatively associated with the (cardio metabolic) health of older adults (Bankoski et al. 2011; Gardiner et al. 2011c; Gómez-Cabello et al. 2012; Lenz 2014). Moreover, SB also negatively affects mortality independently of PA, either or not caused by cardio metabolic disorders (Dogra and Stathokostas 2012; Stamatakis et al. 2012; Martínez-Gómez et al. 2013; León-Muñoz et al. 2013; Ensrud et al. 2014; Pavey et al. 2015).

Other (health) outcomes & quality of life (QoL)

Although Withall et al. (2014) did not find an association between SB and subjective well-being of older adults, evidence shows that in the elderly, less leisure-time SB is independently associated with better long-term health-related QoL and cognitive performance (Balboa-Castillo et al. 2011; Steinberg et al. 2015). The number of sitting hours were inversely related with the scale scores of physical functioning, physical role, bodily pain, vitality, social functioning and mental health (Balboa-Castillo et al. 2011). Obesity, diabetes and hypertension are possible mediating mechanisms for these associations between SB and well-being (Balboa-Castillo et al. 2011). As stated earlier in this review, leisure-time SB types are differently associated with health markers in older adults (Kesse-Guyot et al. 2012; Kikuchi et al. 2014). For example, higher passive SB (e.g. TV viewing) is associated with a higher likelihood of being

198

Biogerontology (2016) 17:547–565

overweight, adverse health behaviours (like poor diet) and greater psychological distress, while mentally-active sedentary time (i.e. reading or computer use) is not associated with health-related attributes and may involve (i) beneficial processes which prevent for the deleterious impact of sitting in older adults, (ii) provide mental stimulation improving cognitive performance capacities and (iii) improve social interaction and QoL (Verghese et al. 2003; Vance et al. 2008; Kesse-Guyot et al. 2012; Visser and Koster 2013; Kikuchi et al. 2014). Overall across age groups, most sedentary activities are suggested to decrease communication with family, reduce the social network and increase the risk of depression, anxiety and stress, which would explain the poorer QoL associated with SB (Balboa-Castillo et al. 2011).

In spite of the limited number of SB studies in older adults, evidence is growing on the (in general) adverse health effects of SB. A recent systematic review by de Rezende et al. (2014a), accounting for the quality of SB studies in older adults (assessed with the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) tool), suggests, however, that to date evidence is inconclusive. Due to the limited quality of available studies, only scarce evidence exists for all the reported health outcomes associated with SB in elderly, except for the evidence on a previously established dose–response relationship between SB and all-cause mortality, which was confirmed (Fig. 2) (de Rezende et al. 2014a). Moreover, the evidence on musculoskeletal health and functional fitness in relation to SB in elderly, has not been graded by de Rezende et al. (2014a). Overall, the present evidence of independent associations between SB and health outcomes in older adults should be carefully interpreted, and further research, to either support or refute the current findings, is needed to draw firm conclusions which will lead to informed SB-minimisation strategies and guidelines for older adults (de Rezende et al. 2014a).

Strategies to counteract the health effects of sedentary behaviour

Regardless of the inconclusive evidence on all of the possible negative health effects of SB in older adults, multiple studies have already proposed strategies to counteract the health impact of SB. These strategies can be classified as either interventional or preventative.

Generally, research shows that especially prolonged sedentary bouts instead of frequent sedentary bouts, have negative health effects, and therefore sitting duration should be focused on more than on frequency (Bond et al. 2014; Chastin et al. 2014c). To date, several studies on different age groups (including older adults) have already shown that breaking prolonged sedentary bouts can be effective, particularly in decreasing the cardio metabolic disease risk (Healy et al. 2008; Bankoski et al. 2011; Bond et al. 2014; Gianoudis et al. 2015; Bailey and Locke 2015), while results on musculoskeletal health and function appear to be equivocal (Gianoudis et al. 2015). Nevertheless, both Sardinha et al. (2015) and Davis et al. (2014) found an association between breaks in SB and better physical function in older adults. Although all these findings make breaking prolonged SB a very promising intervention, it has not been studied as such in elderly yet and, only few studies have been conducted to promote adoption of this approach overall (Bond et al. 2014). In general, it is not necessary to decrease SB dramatically before any health effect can be achieved. This was shown by Pronk et al. (2012), who noted that only 16 % decrease in SB already generated health benefits in employees with sedentary jobs. Other non-elderly studies reported improved cardio metabolic factors in participants breaking every 20–30 min of sitting with just ~2 min of PA (Dunstan et al. 2012b; Peddie et al. 2013; Bailey and Locke 2015). These results are highly stimulating in counteracting SB, since it is a habitual lifestyle and therefore difficult to change (Hart et al. 2011; Bond et al. 2014).

It appears that the intensity of the SB interruption is an important factor regarding its health effect (Chastin et al. 2012; Bailey and Locke 2015). Bailey and Locke (2015) showed that interrupting sitting with standing alone is not sufficient and that at least LIPA (e.g. light-intense walking) is required. A possible explanation is that minor increases in contractile activity (which are associated and easily achieved with LIPA) can dramatically increase muscle GLUT-1 & 4 content and glucose tolerance in sedentary individuals (Tremblay et al. 2010; Latouche et al. 2013; Sardinha et al. 2015). This is ideal, since LIPA is not only inversely related with SB, but also a feasible approach for older adults to increase total PA and ameliorate the

deleterious health effects of SB (Hamilton et al. 2008; Healy et al. 2011). However, it needs to be determined if there might be any adverse consequences of shifting SB into LIPA, especially in case of older adults who may be more prone to lower-body musculoskeletal problems (Tremblay et al. 2010). Changing SB to moderate-to-vigorous PA (MVPA) (e.g. brisk walking, walking stairs or exercising) would potentially lead to spontaneous compensatory behaviour resulting in a less fragmented and possibly, higher total SB in turn, and is therefore not preferred (Chastin et al. 2012). Epidemiologic evidence suggests that having a positive balance between LIPA and SB is desirable due to the inverse linearity of LIPA with a number of cardio metabolic biomarkers (Hamilton et al. 2008). It is known that physiological responses and adaptations may differ within and between physiological systems (Tremblay et al. 2010). For sedentary people it is suggested that LIPA might only have beneficial effects on the cardiovascular and metabolic systems, but not on the musculoskeletal system possibly due to a lack of overload, which is normally required for improvement of this particular system. Results from a preliminary study support this and suggest that vigorous PA during breaks is associated with higher muscle quality in older adults (Chastin et al. 2012). However, new evidence from a small study in young males (mildly active only i.e. not involved in any type of exercise program and not having undergone a systematic resistance training program within 1 year prior onset of the intervention) indicates that also mild walking can improve muscle strength (Maeo et al. 2015). Nevertheless, small changes from SB to LIPA can already lead to a decrease in risk for chronic diseases and mortality (Tremblay et al. 2010). Moreover, these small changes also increase physical functioning which reduces the risk of falls, allowing older adults to live independently and enhance the quality of later life (Sardinha et al. 2015). These advantages are not necessarily associated with MVPA and do also not require prolonged periods of PA (Sardinha et al. 2015). However, regular MVPA is still important in the prevention and treatment of chronic diseases, even in older adults (Dunstan et al. 2012a). Therefore, both PA and SB should be part of general guidelines, but more studies are needed to create informed guidelines for SB in the elderly (de Rezende et al. 2014a). In addition to breaking prolonged SB and reducing total SB, studies have also reported that specific, primarily

passive SB (e.g. TV watching) should be targeted, since this type of SB is also related to other adverse health behaviours, like poor diet (Visser and Koster 2013). Overall, no definitive recommendations regarding the maximum total SB, number and duration of breaks, and optimal interventional strategy to stimulate breaking prolonged SB exists currently, as it requires more research (Dunstan et al. 2012a).

Regardless of this, as well as motivational interviewing (which was successful in stimulating PA in elderly (Letourneau and Goodman 2014), as the emerging use of technology might be promising tools to stimulate and alert breaks in SB. A recent example of the latter method is a study by Bond et al. (2014) who successfully used smartphone and activity monitor applications that provide personal feedback and prompt frequent short sitting breaks based on real-time data. However, their study was performed on a middle-aged population, so it is unclear whether this will also be effective in older adults, but expectations are high. Although interventions might be successful in the short-term, future research is necessary to examine also the long-term post-intervention effects on the amount and pattern of SB and PA. In order to design successful intervention programs it is important to know what reasons (apart from health or age) older adults might have that make them (more) sedentary or stay inside, such as social, economic and environmental factors (Uffelen et al. 2012; Kikuchi et al. 2013; Van Cauwenberg et al. 2014a; Dogra and Stathokostas 2014; Meneguci et al. 2015). A preliminary study by Chastin et al. (2014b) reported some specific factors, considered as determinants of SB by older adults themselves, like self-efficacy, functional limitations, ageist stereotyping, locus of control (the extent to which people believe they have personal control over events and outcomes in their lives), and pain. Considering these factors when designing SB-reducing interventions, might presumably lead to tailored strategies with high efficacy (Chastin et al. 2014b). Other characteristics of successful intervention programs to reduce SB in older adults might include personalised goal setting and feedback as part of behavioural self-monitoring using a consultation approach (Gardiner et al. 2011b; Fitzsimons et al. 2013). Something like this was already proven successful in preventing weight regain in elderly (Nicklas et al. 2014). Or maybe even some form of reinforcement or habit formation like in a newly 'On

Your Feet to Earn Your Seat' randomized controlled trial (Gardner et al. 2014).

Instead of interventions, it might also be useful to see whether large amounts of (prolonged) SB can be prevented in elderly. Therefore, it is important to gain knowledge about the risk factors of SB. Previous research has shown that demographic, socioeconomic and biomedical variables in midlife (e.g. not being married, primary education, living in a duplex or living in an apartment (vs. villa), being obese, and having a heart disease) were associated with a higher prevalence of SB in older age, and thus might be useful to predict which people will be highly sedentary as an older adult (van der Berg et al. 2014). This will potentially lead to prevention programs, targeted at those people identified, and might reduce SB prevalence in older adults.

Although all the suggestions for both intervention and prevention strategies may have potential, most of them are based on preliminary data only and thus need further investigation to increase evidence and generalizability.

Conclusion

Based on this review, it can be concluded that older adults are the most sedentary age group, with an accelerometer-derived average daily sitting time of 8.5–9.6 h, representing 65–80 % of their waking time. Although the literature reports negative associations of SB in elderly with outcomes such as less favourable cardio metabolic health, musculoskeletal health, body composition, physical functioning, mental health and QoL, evidence so far is inconclusive apart from the evidence on the adverse effect of SB on the all-cause mortality rate. Prevention of prolonged SB by frequent breaks, while doing at least LIPA, is a promising strategy to counteract adverse health effects. Even though it has not been studied as an intervention in older adults yet, it is expected to be effective on this age group too. This is not only because LIPA appears to be the most common type of PA within the oldest age groups, but also due to the availability of advanced technology. Overall, more studies in elderly are required to increase the evidence level and develop informed SB guidelines including an optimal strategy to counteract SB and its health effects. Nevertheless, the current evidence allows advising and encouraging

elderly to limit their SB, as described in the latest physical activity guidelines.

References

Aguilar-Farías N, Brown WJ, Peeters GMEEG (2014) ActiGraph GT3X+ cut-points for identifying sedentary behaviour in older adults in free-living environments. J Sci Med Sport 17:293–299. doi:10.1016/j.jsams.2013.07.002

Aguilar-Farías N, Brown WJ, Olds TS, Geeske Peeters GMEE (2015) Validity of self-report methods for measuring sedentary behaviour in older adults. J Sci Med Sport 18:662–666. doi:10.1016/j.jsams.2014.08.004

Arnardottir NY, Koster A, Van Domelen DR et al (2013) Objective measurements of daily physical activity patterns and sedentary behaviour in older adults: age, gene/environment susceptibility-Reykjavik study. Age Ageing 42:222–229. doi:10.1093/ageing/afs160

Bailey DP, Locke CD (2015) Breaking up prolonged sitting with light-intensity walking improves postprandial glycemia, but breaking up sitting with standing does not. J Sci Med Sport 18:294–298. doi:10.1016/j.jsams.2014.03.008

Balboa-Castillo T, León-Muñoz LM, Graciani A et al (2011) Longitudinal association of physical activity and sedentary behavior during leisure time with health-related quality of life in community-dwelling older adults. Health Qual Life Outcomes 9:47. doi:10.1186/1477-7525-9-47

Bankoski A, Harris TB, McClain JJ et al (2011) Sedentary activity associated with metabolic syndrome independent of physical activity. Diabetes Care 34:497–503. doi:10.2337/dc10-0987

Bond DS, Thomas JG, Raynor H et al (2014) B-MOBILE—a smartphone-based intervention to reduce sedentary time in overweight/obese individuals: a within-subjects experimental trial. PLoS One 9:e100821. doi:10.1371/journal.pone.0100821

Buchman AS, Wilson RS, Yu L et al (2014) Total daily activity declines more rapidly with increasing age in older adults. Arch Gerontol Geriatr 58:74–79. doi:10.1016/j.archger.2013.08.001

Busschaert C, De Bourdeaudhuij I, Van Holle V et al (2015) Reliability and validity of three questionnaires measuring context-specific sedentary behaviour and associated correlates in adolescents, adults and older adults. Int J Behav Nutr Phys Act 12:117. doi:10.1186/s12966-015-0277-2

Cawthon PM, Blackwell TL, Cauley J et al (2013) Objective assessment of activity, energy expenditure, and functional limitations in older men: the osteoporotic fractures in men study. J Gerontol A Biol Sci Med Sci 68:1518–1524. doi:10.1093/gerona/glt054

Springer

Celis-Morales CA, Perez-Bravo F, Ibañez L et al (2012) Objective vs. self-reported physical activity and sedentary time: effects of measurement method on relationships with risk biomarkers. PLoS One 7:e36345. doi:10.1371/journal.pone.0036345

Chase JM, Lockhart CK, Madden KM (2014) Accelerometer-based measures of sedentary behavior and cardio-metabolic risk in active older adults. Clin Investig Med 37:108–116

Chastin SFM, Granat MH (2010) Methods for objective measure, quantification and analysis of sedentary behaviour and inactivity. Gait Posture 31:82–86. doi:10.1016/j.gaitpost.2009.09.002

Chastin SFM, Ferriolli E, Stephens NA et al (2012) Relationship between sedentary behaviour, physical activity, muscle quality and body composition in healthy older adults. Age Ageing 41:111–114. doi:10.1093/ageing/afr075

Chastin SFM, Culhane B, Dall PM (2014a) Comparison of self-reported measure of sitting time (IPAQ) with objective measurement (activPAL). Physiol Meas 35:2319–2328. doi:10.1088/0967-3334/35/11/2319

Chastin SFM, Fitzpatrick N, Andrews M, DiCroce N (2014b) Determinants of sedentary behavior, motivation, barriers and strategies to reduce sitting time in older women: a qualitative investigation. Int J Environ Res Public Health 11:773–791. doi:10.3390/ijerph110100773

Chastin SFM, Mandrichenko O, Helbostadt JL, Skelton DA (2014c) Associations between objectively-measured sedentary behaviour and physical activity with bone mineral density in adults and older adults, the NHANES study. Bone 64:254–262. doi:10.1016/j.bone.2014.04.009

Clark BK, Winkler E, Healy GN et al (2013) Adults' past-day recall of sedentary time: reliability, validity, and responsiveness. Med Sci Sports Exerc 45:1198–1207. doi:10.1249/MSS.0b013e3182837f57

Davis MG, Fox KR, Hillsdon M et al (2011) Objectively measured physical activity in a diverse sample of older urban UK adults. Med Sci Sports Exerc 43:647–654. doi:10.1249/MSS.0b013e3181f36196

Davis MG, Fox KR, Stathi A et al (2014) Objectively measured sedentary time and its association with physical function in older adults. J Aging Phys Act 22:474–481. doi:10.1123/japa.2013-0042

de Rezende LFM, Rey-López JP, Matsudo VKR, do Carmo Luiz O (2014a) Sedentary behavior and health outcomes among older adults: a systematic review. BMC Public Health 14:333. doi:10.1186/1471-2458-14-333

de Rezende LFM, Rodrigues Lopes M, Rey-López JP et al (2014b) Sedentary behavior and health outcomes: an overview of systematic reviews. PLoS One 9:e105620. doi:10.1371/journal.pone.0105620

Demiot C, Dignat-George F, Fortrat J-O et al (2007) WISE 2005: chronic bed rest impairs microcirculatory endothelium in women. Am J Physiol Heart Circ Physiol 293:H3159–H3164. doi:10.1152/ajpheart.00591.2007

Dogra S, Stathokostas L (2012) Sedentary behavior and physical activity are independent predictors of successful aging in middle-aged and older adults. J Aging Res 2012:190654. doi:10.1155/2012/190654

Dogra S, Stathokostas L (2014) Correlates of extended sitting time in older adults: an exploratory cross-sectional analysis of the

Canadian Community Health Survey Healthy Aging Cycle. Int J Public Health 59:983–991. doi:10.1007/s00038-014-0540-3

Dunlop DD, Song J, Arnston EK et al (2015) Sedentary time in US older adults associated with disability in activities of daily living independent of physical activity. J Phys Act Health 12:93–101. doi:10.1123/jpah.2013-0311

Dunstan DW, Howard B, Healy GN, Owen N (2012a) Too much sitting—a health hazard. Diabetes Res Clin Pract 97:368–376. doi:10.1016/j.diabres.2012.05.020

Dunstan DW, Kingwell BA, Larsen R et al (2012b) Breaking up prolonged sitting reduces postprandial glucose and insulin responses. Diabetes Care 35:976–983. doi:10.2337/dc11-1931

Ensrud KE, Blackwell TL, Cauley JA et al (2014) Objective measures of activity level and mortality in older men. J Am Geriatr Soc 62:2079–2087. doi:10.1111/jgs.13101

Evenson KR, Buchner DM, Morland KB (2012) Objective measurement of physical activity and sedentary behavior among US adults aged 60 Years or older. Prev Chronic Dis 9:2–11

Evenson KR, Morland KB, Wen F, Scanlin K (2014) Physical activity and sedentary behavior among adults 60 years and older: New York City residents compared with a national sample. J Aging Phys Act 22:499–507. doi:10.1123/japa.2012-0345

Fitzsimons CF, Kirk A, Baker G et al (2013) Using an individualised consultation and activPAL™ feedback to reduce sedentary time in older Scottish adults: results of a feasibility and pilot study. Prev Med (Baltim) 57:718–720. doi:10.1016/j.ypmed.2013.07.017

Gao X, Nelson ME, Tucker KL (2007) Television viewing is associated with prevalence of metabolic syndrome in Hispanic elders. Diabetes Care 30:694–700. doi:10.2337/dc06-1835

Gardiner PA, Clark BK, Healy GN et al (2011a) Measuring older adults' sedentary time: reliability, validity, and responsiveness. Med Sci Sports Exerc 43:2127–2133. doi:10.1249/MSS.0b013e31821b94f7

Gardiner PA, Eakin EG, Healy GN, Owen N (2011b) Feasibility of reducing older adults' sedentary time. Am J Prev Med 41:174–177. doi:10.1016/j.amepre.2011.03.020

Gardiner PA, Healy GN, Eakin EG et al (2011c) Associations between television viewing time and overall sitting time with the metabolic syndrome in older men and women: the Australian diabetes, obesity and lifestyle study. J Am Geriatr Soc 59:788–796. doi:10.1111/j.1532-5415.2011.03390.x

Gardner B, Thuné-Boyle I, Iliffe S et al (2014) "On Your Feet to Earn Your Seat", a habit-based intervention to reduce sedentary behaviour in older adults: study protocol for a randomized controlled trial. Trials 15:368. doi:10.1186/1745-6215-15-368

Gennuso KP, Gangnon RE, Matthews CE et al (2013) Sedentary behavior, physical activity, and markers of health in older adults. Med Sci Sports Exerc 45:1493–1500. doi:10.1249/MSS.0b013e318288a1e5

Gennuso KP, Matthews CE, Colbert LH (2015) Reliability and validity of 2 self-report measures to assess sedentary behavior in older adults. J Phys Act Health 12:727–732. doi:10.1123/jpah.2013-0546

Gianoudis J, Bailey CA, Daly RM (2015) Associations between sedentary behaviour and body composition, muscle function and sarcopenia in community-dwelling older adults. Osteoporos Int 26:571–579. doi:10.1007/s00198-014-2895-y

Godfrey A, Lord S, Galna B et al (2014) The association between retirement and age on physical activity in older adults. Age Ageing 43:386–393. doi:10.1093/ageing/aft168

Gómez-Cabello A, Pedrero-Chamizo R, Olivares PR et al (2012) Sitting time increases the overweight and obesity risk independently of walking time in elderly people from Spain. Maturitas 73:337–343. doi:10.1016/j.maturitas.2012.09.001

Gorman E, Hanson HM, Yang PH et al (2014) Accelerometry analysis of physical activity and sedentary behavior in older adults: a systematic review and data analysis. Eur Rev Aging Phys Act 11:35–49. doi:10.1007/s11556-013-0132-x

Hamburg NM, McMackin CJ, Huang AL et al (2007) Physical inactivity rapidly induces insulin resistance and microvascular dysfunction in healthy volunteers. Arterioscler Thromb Vasc Biol 27:2650–2656. doi:10.1161/ATVBAHA.107.153288

Hamer M, Stamatakis E (2013) Screen-based sedentary behavior, physical activity, and muscle strength in the English longitudinal study of ageing. PLoS One 8:e66222. doi:10.1371/journal.pone.0066222

Hamilton MT, Healy GN, Dunstan DW et al (2008) Too little exercise and too much sitting: inactivity physiology and the need for new recommendations on sedentary behavior. Curr Cardiovasc Risk Rep 2:292–298. doi:10.1007/s12170-008-0054-8

Hart TL, Swartz AM, Cashin SE, Strath SJ (2011) How many days of monitoring predict physical activity and sedentary behaviour in older adults? Int J Behav Nutr Phys Act 8:62. doi:10.1186/1479-5868-8-62

Harvey JA, Chastin SFM, Skelton DA (2013) Prevalence of sedentary behavior in older adults: a systematic review. Int J Environ Res Public Health 10:6645–6661. doi:10.3390/ijerph10126645

Harvey JA, Chastin SFM, Skelton DA (2015) How sedentary are older people? A systematic review of the amount of sedentary behavior. J Aging Phys Act 23:471–487. doi:10.1123/japa.2014-0164

Healy GN, Dunstan DW, Salmon J et al (2008) Breaks in sedentary time: beneficial associations with metabolic risk. Diabetes Care 31:661–666. doi:10.2337/dc07-2046

Healy GN, Matthews CE, Dunstan DW et al (2011) Sedentary time and cardio-metabolic biomarkers in US adults: NHANES 2003-06. Eur Heart J 32:590–597. doi:10.1093/eurheartj/ehq451

Hekler EB, Buman MP, Haskell WL et al (2012) Reliability and validity of CHAMPS self-reported sedentary- to- vigorous intensity physical activity in older adults. J Phys Act Health 9:225–236

Inoue S, Sugiyama T, Takamiya T et al (2012) Television viewing time is associated with overweight/obesity among older adults, independent of meeting physical activity and health guidelines. J Epidemiol 22:50–56. doi:10.2188/jea.JE20110054

Jefferis BJ, Sartini C, Ash S et al (2015a) Trajectories of objectively measured physical activity in free-living older men. Med Sci Sports Exerc 47:343

Jefferis BJ, Sartini C, Shiroma E et al (2015b) Duration and breaks in sedentary behaviour: accelerometer data from 1566 community-dwelling older men (British Regional Heart Study). Br J Sports Med 49:1591–1594. doi:10.1136/bjsports-2014-093514

Kesse-Guyot E, Charreire H, Andreeva VA et al (2012) Cross-sectional and longitudinal associations of different sedentary behaviors with cognitive performance in older adults. PLoS One 7:e47831. doi:10.1371/journal.pone.0047831

Kikuchi H, Inoue S, Sugiyama T et al (2013) Correlates of prolonged television viewing time in older Japanese men and women. BMC Public Health 13:213. doi:10.1186/1471-2458-13-213

Kikuchi H, Inoue S, Sugiyama T et al (2014) Distinct associations of different sedentary behaviors with health-related attributes among older adults. Prev Med (Baltim) 67:335–339. doi:10.1016/j.ypmed.2014.08.011

Kim H, Iwasaki K, Miyake T et al (2003) Changes in bone turnover markers during 14-day 6 degrees head-down bed rest. J Bone Miner Metab 21:311–315. doi:10.1007/s00774-003-0426-6

Kowalski K, Rhodes R, Naylor P-J et al (2012) Direct and indirect measurement of physical activity in older adults: a systematic review of the literature. Int J Behav Nutr Phys Act 9:148. doi:10.1186/1479-5868-9-148

Kozey Keadle S, Lyden K, Hickey A et al (2014) Validation of a previous day recall for measuring the location and purpose of active and sedentary behaviors compared to direct observation. Int J Behav Nutr Phys Act 11:12. doi:10.1186/1479-5868-11-12

Kozey-Keadle S, Libertine A, Lyden K et al (2011) Validation of wearable monitors for assessing sedentary behavior. Med Sci Sports Exerc 43:1561–1567. doi:10.1249/MSS.0b013e31820ce174

Latouche C, Jowett JBM, Carey AL et al (2013) Effects of breaking up prolonged sitting on skeletal muscle gene expression. J Appl Physiol 114:453–460. doi:10.1152/japplphysiol.00978.2012

Lenz EK (2014) Do sedentary behaviors modify the health status of older adults? Int J Kinesiol Sport Sci J Kinesiol Sport Sci J Kinesiol Sport Sci 2:13–22. doi:10.7575/aiac.ijkss.v.2n.1p.13

León-Muñoz LM, Martínez-Gómez D, Balboa-Castillo T et al (2013) Continued sedentariness, change in sitting time, and mortality in older adults. Med Sci Sports Exerc 45:1501–1507. doi:10.1249/MSS.0b013e3182897e87

Letourneau K, Goodman JH (2014) A patient-centered approach to addressing physical activity in older adults: motivational interviewing. J Gerontol Nurs 40:26–33. doi:10.3928/00989134-20140819-01

Lohne-Seiler H, Hansen BH, Kolle E, Anderssen SA (2014) Accelerometer-determined physical activity and self-reported health in a population of older adults (65–85 years): a cross-sectional study. BMC Public Health 14:284. doi:10.1186/1471-2458-14-284

Lord S, Chastin SFM, McInnes L et al (2011) Exploring patterns of daily physical and sedentary behaviour in community-dwelling older adults. Age Ageing 40:205–210. doi:10.1093/ageing/afq166

Maeo S, Yamamoto M, Kanehisa H (2015) Muscular adaptations to short-term low-frequency downhill walking training. Int J Sports Med 36:150–156

Marques EA, Baptista F, Santos DA et al (2014) Risk for losing physical independence in older adults: the role of sedentary time, light, and moderate to vigorous physical activity. Maturitas 79:91–95. doi:10.1016/j.maturitas.2014.06.012

Martin KR, Koster A, Murphy RA et al (2014) Changes in daily activity patterns with age in U.S. men and women: National Health and Nutrition Examination Survey 2003–04 and 2005–06. J Am Geriatr Soc 62:1263–1271. doi:10.1111/jgs.12893

Martínez-Gómez D, Guallar-Castillón P, León-Muñoz LM et al (2013) Combined impact of traditional and non-traditional health behaviors on mortality: a national prospective cohort study in Spanish older adults. BMC Med 11:47. doi:10.1186/1741-7015-11-47

Matthews CE, Chen KY, Freedson PS et al (2008) Amount of time spent in sedentary behaviors in the United States, 2003–2004. Am J Epidemiol 167:875–881. doi:10.1093/aje/kwm390

Matthews CE, Keadle SK, Sampson J et al (2013) Validation of a previous-day recall measure of active and sedentary behaviors. Med Sci Sports Exerc 45:1629–1638. doi:10.1249/MSS.0b013e3182897690

Meneguci J, Sasaki JE, da Silva Santos Á et al (2015) Socio-demographic, clinical and health behavior correlates of sitting time in older adults. BMC Public Health 15:65. doi:10.1186/s12889-015-1426-x

Mitchell RJ, Lord SR, Harvey LA, Close JCT (2015) Obesity and falls in older people: mediating effects of disease, sedentary behavior, mood, pain and medication use. Arch Gerontol Geriatr 60:52–58. doi:10.1016/j.archger.2014.09.006

Nicklas BJ, Gaukstern JE, Beavers KM et al (2014) Self-monitoring of spontaneous physical activity and sedentary behavior to prevent weight regain in older adults. Obesity (Silver Spring) 22:1406–1412. doi:10.1002/oby.20732

Owen N, Sugiyama T, Eakin EE et al (2011) Adults' sedentary behavior determinants and interventions. Am J Prev Med 41:189–196. doi:10.1016/j.amepre.2011.05.013

Pate RR, Neill JRO, Lobelo F (2008) The evolving definition of "'Sedentary.'" 29208:173–178

Patel AV, Bernstein L, Deka A et al (2010) Leisure time spent sitting in relation to total mortality in a prospective cohort of US adults. Am J Epidemiol 172:419–429. doi:10.1093/aje/kwq155

Pavey TG, Peeters GG, Brown WJ (2015) Sitting-time and 9-year all-cause mortality in older women. Br J Sports Med 49:95–99. doi:10.1136/bjsports-2012-091676

Peddie MC, Bone JL, Rehrer NJ et al (2013) Breaking prolonged sitting reduces postprandial glycemia in healthy, normal-weight adults: a randomized crossover trial. Am J Clin Nutr 98:358–366. doi:10.3945/ajcn.112.051763

Pedišić Ž, Bauman A (2015) Accelerometer-based measures in physical activity surveillance: current practices and issues. Br J Sports Med 49:219–223. doi:10.1136/bjsports-2013-093407

Pronk NP, Katz AS, Lowry M, Payfer JR (2012) Reducing occupational sitting time and improving worker health: the take-a-stand project, 2011. Prev Chronic Dis 9:1–9

Rhodes RE, Mark RS, Temmel CP (2012) Adult sedentary behavior: a systematic review. Am J Prev Med 42:e3–e28. doi:10.1016/j.amepre.2011.10.020

Santos DA, Silva AM, Baptista F et al (2012) Sedentary behavior and physical activity are independently related to

functional fitness in older adults. Exp Gerontol 47:908–912. doi:10.1016/j.exger.2012.07.011

Sardinha LB, Santos DA, Silva AM et al (2015) Breaking-up sedentary time is associated with physical function in older adults. J Gerontol A Biol Sci Med Sci 70:119–124. doi:10.1093/gerona/glu193

Sedentary Behaviour Research Network (2012) Letter to the editor: standardized use of the terms "sedentary" and "sedentary behaviours". Appl Physiol Nutr Metab 37:540–542. doi:10.1139/h2012-024

Shiroma EJ, Freedson PS, Trost SG, Lee I-M (2013) Patterns of accelerometer-assessed sedentary behavior in older women. JAMA 310:2562–2563. doi:10.1001/jama.2013.278896

Stamatakis E, Davis M, Stathi A, Hamer M (2012) Associations between multiple indicators of objectively-measured and self-reported sedentary behaviour and cardiometabolic risk in older adults. Prev Med (Baltim) 54:82–87. doi:10.1016/j.ypmed.2011.10.009

Steinberg SI, Sammel MD, Harel BT et al (2015) Exercise, sedentary pastimes, and cognitive performance in healthy older adults. Am J Alzheimers Dis Other Demen 30:290–298. doi:10.1177/1533317514545615

Thosar SS, Bielko SL, Mather KJ et al (2015) Effect of prolonged sitting and breaks in sitting time on endothelial function. Med Sci Sports Exerc 47:843–849. doi:10.1249/MSS.0000000000000479

Tomlinson DJ, Erskine RM, Morse CI et al (2014) Combined effects of body composition and ageing on joint torque, muscle activation and co-contraction in sedentary women. Age (Dordr) 36:9652. doi:10.1007/s11357-014-9652-1

Tremblay MS, Colley RC, Saunders TJ et al (2010) Physiological and health implications of a sedentary lifestyle. Appl Physiol Nutr Metab 35:725–740. doi:10.1139/H10-079

Uffelen V, Jannique GZ, Gellecum V, Yolanda R (2012) Which older women could benefit from interventions to decrease sitting time and increase physical activity? Jannique GZ van Uffelen, PhD *† Kristiann C Heesch, PhD § Yolanda R van Gellecum * Nicola W Burton, PhD * Wendy J Brown, PhD * * The Universit

Van Cauwenberg J, De Donder L, Clarys P et al (2014a) Relationships of individual, social, and physical environmental factors with older adults' television viewing time. J Aging Phys Act 22:508–517. doi:10.1123/japa.2013-0015

Van Cauwenberg J, Van Holle V, De Bourdeaudhuij I et al (2014b) Older adults' reporting of specific sedentary behaviors: validity and reliability. BMC Public Health 14:734. doi:10.1186/1471-2458-14-734

van der Berg JD, Bosma H, Caserotti P et al (2014) Midlife determinants associated with sedentary behavior in old age. Med Sci Sports Exerc 46:1359–1365. doi:10.1249/MSS.0000000000000246

van Uffelen JGZ, Heesch KC, Hill RL, Brown WJ (2011) A qualitative study of older adults' responses to sitting-time questions: do we get the information we want? BMC Public Health 11:458. doi:10.1186/1471-2458-11-458

Vance DE, Webb NM, Marceaux JC et al (2008) Mental Stimulation, Neural Plasticity, and Aging. J Neurosci Nurs 40:241–249. doi:10.1097/01376517-200808000-00008

Verghese J, Lipton RB, Katz MJ et al (2003) Leisure activities and the risk of dementia in the elderly. N Engl J Med 348:2508–2516. doi:10.1056/NEJMoa022252

Visser M, Koster A (2013) Development of a questionnaire to assess sedentary time in older persons—a comparative study using accelerometry. BMC Geriatr 13:80. doi:10.1186/1471-2318-13-80

Withall J, Stathi A, Davis M et al (2014) Objective indicators of physical activity and sedentary time and associations with subjective well-being in adults aged 70 and over. Int J

Environ Res Public Health 11:643–656. doi:10.3390/ijerph110100643

Yates T, Khunti K, Wilmot EG et al (2012) Self-reported sitting time and markers of inflammation, insulin resistance, and adiposity. Am J Prev Med 42:1–7. doi:10.1016/j.amepre.2011.09.022

Accepted paper(s):

RESEARCH ARTICLE

Performance of thigh-mounted triaxial accelerometer algorithms in objective quantification of sedentary behaviour and physical activity in older adults

Jorgen A. Wullems[1,2]*, Sabine M. P. Verschueren[2], Hans Degens[3,4], Christopher I. Morse[1], Gladys L. Onambélé[1]

1 Health, Exercise and Active Living Research Centre, Department of Exercise and Sport Science, Manchester Metropolitan University, Crewe, United Kingdom, 2 Musculoskeletal rehabilitation research group, Department of Rehabilitation Sciences, KU Leuven, Belgium, 3 School of Healthcare Science, Manchester Metropolitan University, Manchester, United Kingdom, 4 Lithuanian Sports University, Kaunas, Lithuania

* jorgen.a.wullems@stu.mmu.ac.uk

Abstract

Accurate monitoring of sedentary behaviour and physical activity is key to investigate their exact role in healthy ageing. To date, accelerometers using cut-off point models are most preferred for this, however, machine learning seems a highly promising future alternative. Hence, the current study compared between cut-off point and machine learning algorithms, for optimal quantification of sedentary behaviour and physical activity intensities in the elderly. Thus, in a heterogeneous sample of forty participants (aged ≥ 60 years, 50% female) energy expenditure during laboratory-based activities (ranging from sedentary behaviour through to moderate-to-vigorous physical activity) was estimated by indirect calorimetry, whilst wearing triaxial thigh-mounted accelerometers. Three cut-off point algorithms and a Random Forest machine learning model were developed and cross-validated using the collected data. Detailed analyses were performed to check algorithm robustness, and examine and benchmark both overall and participant-specific balanced accuracies. This revealed that the four models can at least be used to confidently monitor sedentary behaviour and moderate-to-vigorous physical activity. Nevertheless, the machine learning algorithm outperformed the cut-off point models by being robust for all individual's physiological and non-physiological characteristics and showing more performance of an acceptable level over the whole range of physical activity intensities. Therefore, we propose that Random Forest machine learning may be optimal for objective assessment of sedentary behaviour and physical activity in older adults using thigh-mounted triaxial accelerometry.

207

Introduction

Ageing is associated with a decline in physical function and recent evidence not only suggests that this is largely attributable to increased sedentary behaviour (SB) in old age, but also states that breaking prolonged SB by carrying out physical activity (PA) of at least light-intensity may prove to be a promising counteraction strategy [1]. It is surprising that though most elderly exhibit high SB and low PA levels, leading to deleterious health outcomes, strategies to minimise poor lifestyle choices in this age group has only received relatively little scientific attention [1–3]. Ahead of this however, studies must first focus on improving the accuracy and validity of activity monitoring in older adults [4,5]. To evaluate the exact health effects of SB and PA, including their role in healthy ageing, it is important to accurately and objectively monitor these aspects of habitual mobility or lack thereof [6]. Motion-sensing technologies using accelerometers are typically used in mobility monitoring since they are assumed to be objective, and measurements can be carried out over a number of days [6–11].

The concept of accelerometry to assess SB and PA is derived from Newton's Second Law, which gives the interaction between force, mass and acceleration by the formula: force = mass * acceleration [12]. In the context of human movement, this formula can be expressed as: an activity is characterised by moving a mass (i.e. body (segment)) at changing velocity over time (= acceleration). This acceleration results from forces generated by (and on) the muscles at the expense of energy [10]. Several studies have shown positive linear relationships between energy expenditure (EE) and movement acceleration in people of different ages, while performing activities under standardised test conditions with the accelerometer close to the centre of mass [13–18]. This allows EE to be estimated from acceleration signals and the classification of habitual daily activity as sedentary, light and moderate-to-vigorous, by using, until recently, cut-off point models. To illustrate this, when presenting the amount of movement acceleration as counts per minute, these models will classify an outcome of <100 as sedentary, 100–1951 as light and $\geq$1952 as moderate-to-vigorous [6].

However, with the preferred accelerometer mounting location shifting away from centre of mass sites such as the hip or waist [19–21], towards wrist-worn devices for the most part, the premise of a linear relationship between EE and movement acceleration and thus, the use of cut-off point models has become questionable. This commercially-led shift forces researchers to focus on posture detection only (i.e. the 'Sedentary Sphere' [22]) or to start looking into other, more sophisticated and complex, methods to analyse acceleration signals by e.g. machine learning [2,23,24]. Machine learning is already used for activity recognition and has only recently been explored in PA research [2,24]. By focusing on patterns and regularities, pattern recognition for example, can handle complex and non-linear data [6,25,26], potentially providing opportunities for SB and PA research [27].

Although some experts have advised to stop developing cut-off point algorithms and start using machine learning [4,28], to date the use of cut-off points remains preferred for intensity classification [29]. One reason to continue using cut-off point models lies in the complex nature of machine learning, and the ease to understand and widespread adoption of cut-off points [30]. Although proprietary cut-off points are not necessarily well understood either, the desire to compare results with previous cut-off point-based studies could be another reason. Notwithstanding, studies have already shown machine learning to outperform traditional cut-off point algorithms for activity recognition not only in healthy adults, but also in niche populations such as the young or the overweight/obese [6,27]. However, validation of machine learning needs to be confirmed for all intended end-users/study populations, e.g. the elderly, prior to general adoption [10]. Rosenberg et al. [31] recently showed high levels of accuracy and concurrent validity using Random Forest classifiers in older women.

208

The decision of researchers to choose a simpler, but less accurate method over a more challenging and accurate one for activity intensity classification can possibly be justified when using thigh-mounted triaxial accelerometry. Since the thigh is relatively close to the centre of mass, cut-off point models might still be valid in this situation, especially when adding posture detection to these models, which then enables distinguishing between sedentary activity and standing for instance. Whilst the activPAL inclinometer is a good example of a valid thigh-mounted activity monitor [20,22], it uses black-boxed proprietary algorithms, thereby hampering progress in thigh-mounted accelerometer algorithm development. To date, cut-off point models for thigh-mounted accelerometers are understudied, hence further investigation and detailed comparison with machine learning is needed.

All algorithms require value calibration and the eventual utility of an algorithm depends on the specific activities and intensities included in the calibration study [30]. To ensure high accuracy of the algorithm in the general population, it is recommended to perform the calibration on a heterogeneous sample, matching the population of interest, and including a broad range of common activities ranging from sedentary to vigorous intensity [4,24,30,32]. Algorithm performance is generally expressed in terms of overall accuracy and when it reaches $\geq 80\%$ for example, an algorithm is deemed acceptable [2]. However, even in possession of the overall (i.e. group) accuracy, algorithm performance on an individual (i.e. single end-user) level, remains unknown. Theoretically, performance can be unacceptable in some individuals where algorithm robustness is lacking. If algorithm inaccuracy disproportionately affects some demographic groups over others, it may lead to misinterpretation of associations between either SB or PA and health. Thus, it is important to check robustness and benchmark end-user-specific performance of accelerometer algorithms developed on heterogeneous pooled-data sets prior to applying them to daily-life data. To date, evidence regarding this type of triangulation is sparse.

The main aim of the present study was to compare between traditional cut-off points and machine learning, for the provision of the best performing algorithm to classify SB and PA in a heterogeneous population of older adults using thigh-mounted triaxial accelerometry. It was hypothesised that machine learning outperforms cut-off point based algorithms through being robust for individual's physiological and non-physiological characteristics, more accurate and showing acceptable accuracies for all activity intensities. To test this hypothesis, this paper 1) examines overall balanced accuracy and robustness of four heterogeneous pooled-data algorithms, 2) compares participant-specific balanced accuracies between all four algorithms, and 3) benchmarks both overall and participant-specific balanced accuracies of the algorithms.

Materials and methods

Participants

Forty healthy older adults (73.5 (6.3) years; 50% female) participated in this study (Table 1). Participants were excluded if they were: <60 years of age, terminally ill or receiving cancer treatment, diabetic, suffered from any central nervous system disease or condition, had a heart attack in the past 12 months or any currently unstable cardiovascular condition, had any pulmonary disease or condition that did not allow expired gas sampling, recently (within the past three months) injured or had surgery on either of their lower limbs, were not independently mobile or at least not able to complete a laboratory-based activity protocol without a (walking) aid, had been advised by their physician not to take on any physical activity or exercise, or were not competent to make an informed decision about study participation.

209

Table 1. Study sample characteristics.

Age (years)	73.5 (6.3)	
Sex	20 Female	20 Male
Body mass (kg)	72.2 (13.7)	
Body height (m)	1.67 (0.10)	
BMI (kg·m^{-2})	25.6 (4.3)	
Prandial state	20 Fasting	20 Non-fasting
REE$_{fasting}$ (VO$_2$ ml·kg^{-1}·min^{-1})	2.82 (1.00)	
Prosthetic lower limb joints	2 Yes	38 No
Cardiovascular medication	20 Yes	20 No
Physical fitness level$_{no\ cardiovascular\ meds}$	9 Less than good	11 Good or better
Preferred walking speed (km·h^{-1})$_{no\ prosthetic\ lower\ limb\ joints}$	3.7 (1.0)	
Falls risk	32 Low	8 Medium or high

Values represent arithmetic mean (SD) when normally distributed data, else median (IQR).

SD, standard deviation; IQR, interquartile range; BMI, body mass index; REE, resting energy expenditure; VO$_2$, oxygen consumption.

https://doi.org/10.1371/journal.pone.0188215.t001

This study was approved by the local ethics committee of the Manchester Metropolitan University, UK. All participants gave written informed consent prior to their participation in this study.

Baseline characteristics

From each participant, the following baseline characteristics were recorded: age, sex, body mass, body height, body mass index (BMI), prandial state, resting energy expenditure (REE), presence of prosthetic lower limb joints, use of heart rate controlling medication, physical fitness level, preferred walking speed and risk of falling (Table 1). Age (years), sex (female/male), prandial state (fasting/non-fasting), presence of prosthetic lower limb joints (yes/no) and use of cardiovascular (heart rate controlling) medication (yes/no) was determined through a health questionnaire or orally on the day of testing. Body mass was assessed in kilograms using a digital body mass scale (Seca GmbH & Co. KG., Hamburg, Germany) and body height was measured in centimetres using a stadiometer (Holtain Ltd., Crymych, UK). Both measures were determined up to the closest decimal with the participant barefoot and wearing light clothing only. The body mass index (BMI) was calculated by dividing body mass by squared body height (kg·m^{-2}). REE was estimated by assessing oxygen consumption (VO$_2$) (ml·kg^{-1}·min^{-1}; STPD conditions: standard temperature and dry gas at standard barometric pressure) while sitting quietly on a chair for four minutes, together with resting heart rate (beats per minute). Both REE and resting heart rate were expressed as the arithmetic mean of the readings taken during the third and fourth minute of sitting. To increase the accuracy of REE baseline estimates, only data from fasted participants were used. Since resting heart rate served to estimate baseline physical fitness levels, participants who were on heart rate controlling medication were not taken into account. Classification of the physical fitness levels was done using a standard resting heart rate table [33]. Preferred walking speed (km·h^{-1}) was based on the self-selected speed during treadmill walking in participants without prosthetic lower limb joints. Risk of falling (low/medium/high) was determined using the falls risk assessment tool (FRAT) [34].

210

Instrumentation

During the laboratory-based activity protocol participants were equipped with different instruments. First, two GENEActiv Original triaxial accelerometers (Activinsights Ltd., Kimbolton, UK) with range ±8 g (1 g = 9.81 m·s⁻²) and weighing 16 grams each, were fitted bilaterally on the anterior mid-thigh (at 50% of the distance between trochanter major and lateral femur epicondyle). Both accelerometers were mounted using Tegaderm™ transparent film dressing (3M Health Care, St. Paul, MN, USA) and set at a sample rate of 60 Hz. This frequency respects the Nyquist-Shannon sampling theorem, which states that the sample frequency should at least be twice the maximum frequency at which sampling is required. Since essentially all human body movement occurs below 20 Hz, the sampling rate should be $\geq$40 Hz [35,36]. Orientation of the accelerometer axes during standing was: X = mediolateral, Y = vertical and Z = anteroposterior. The devices were used as calibrated by the manufacturer. Next, participants wore a Polar T31 chest belt to monitor heart rate, which would then remain in place for the entirety of the test protocol (Polar Electro Oy, Kempele, Finland). To estimate energy expenditure during the activities (see below) we used indirect calorimetry. Expired gas samples were collected per activity via a standard mouthpiece and two-way T-shape non-rebreathing valve (2700 series) (Hans Rudolph Inc., Kansas City, MO, USA) into a Douglas Bag (DB) (Plysu Industrial Ltd., Milton Keynes, UK). Expired gas sample concentrations of oxygen and carbon dioxide inside the DB were determined using a Servomex 5200 gas analyser (Servomex Group Ltd., Crowborough, UK). The gas analyser was calibrated prior to each participant's testing session. The total volume of expired gas inside the DB was analysed using a calibrated dry gas meter (Harvard Apparatus Ltd., Edenbridge, UK).

Laboratory-based activity protocol

Participants were asked to perform ten laboratory-based activities of daily living which were assumed to be representative for older adults. Half of the participants (N = 20, 50% female) were instructed to arrive in a fasting condition, allowing to drink water up to a maximum of 250 ml only, while the other half received no instructions. The protocol started with 20 minutes rest in a supine position. Then, the following ten standardised activities of daily living (four minutes each) were executed in the specified order: 1) lying supine on a treatment bed, 2) sitting on a chair, 3) standing upright, 4) shuffling sideways, 5) free over-ground walking at self-selected speed, 6) cycling on an ergometer at a preferred pace (Monark Exercise AB, Vansbro, Sweden), 7) treadmill walking at 3.2 km·h⁻¹, 8) treadmill walking at self-selected speed, 9) treadmill walking at self-selected speed wearing a weighted vest (15% of body mass) and 10) brisk treadmill walking at a maximum speed of 6.5 km·h⁻¹. All treadmill walking was performed on a slat-belt treadmill (Woodway USA Inc., Waukesha, WI, USA). The first two minutes of each activity were used to reach a steady state in EE. During the second half of the activities, two one-minute expired gas samples were taken. To prevent any carry-over effects of fatigue, participants were seated between the activities until their heart rate returned to resting level. The total duration of the protocol was approximately 90 minutes. A standard digital video camera was time-synchronised and used to record the entire testing session, which served as a criterion measure and allowed direct observation of all activities post laboratory protocol completion.

Accelerometer data pre-processing & feature selection

Analysis of the triaxial accelerometer data required multiple steps. Firstly, raw acceleration signals per axis were filtered twice using a zero-phase fourth order low pass Butterworth filter: 1) a cut-off frequency of 20 Hz was applied to remove any noise and 2) a cut-off frequency of

211

0.5 Hz was used to split the noise-filtered signal into static and dynamic acceleration signals, allowing determination of monitor orientation and movement [6,37]. Secondly, two one-minute periods (identical to the gas sampling minutes) of both static and dynamic acceleration signals per axis were extracted per performed activity. Next, twenty time- and frequency domain based features per non-overlapping 10-s windows were determined per axis for each of the samples extracted from both the dynamic and static acceleration signals. These time- and frequency domain based features included: arithmetic mean, standard deviation (SD), minimum, maximum, median, interquartile range (IQR), skewness, kurtosis, root mean square, cross-correlation, roll, pitch, yaw, peak-to-peak amplitude, peak intensity, zero-crossings, lag one autocorrelation, dominant frequency, amplitude of dominant frequency and entropy. Also, two resultant vectors were calculated over the three axes, one using arithmetic means and the other SDs. (Please see Liu et al. [38] for the applied formulas.) All data pre-processing was done using R 3.2.5 [39].

After data pre-processing, the 10-s window features were used to model four algorithms based on methods using either cut-off points or machine learning. Three algorithms including posture classification (based on the 10-s window arithmetic mean static acceleration of the Y-axis (static Y_{mean})) were derived from cut-off point analyses using dynamic acceleration data. The first algorithm used the sum of vector magnitudes (SVM) as an outcome,

$$SVM = \sum_{d=1}^{600} \sqrt{x_d^2 + y_d^2 + z_d^2}$$

where d represents the data-point number within the 10-s window. The second algorithm used summation of the time integrals of the moduli of the triaxial accelerometer signal (IMA), where

$$IMA = \int_{t=t_0}^{t_0+T} |x|dt + \int_{t=t_0}^{t_0+T} |y|dt + \int_{t=t_0}^{t_0+T} |z|dt$$

where T represents 10 seconds. The last cut-off point algorithm was adapted from our previous postural balance studies that focus on total movement (TM) using force plate balancing tasks [40], which is calculated as

$$TM = \sqrt{x_{SD}^2 + y_{SD}^2 + z_{SD}^2}$$

where SD represents the 10-s window standard deviation of the dynamic acceleration signal per axis. For the only machine learning algorithm we used Random Forest in this study, which is known for its high performance [24,41–43]. Briefly, Random Forest is an ensemble method using the bootstrapping of multiple decision trees to predict an outcome. Prior to developing a Random Forest model, analyses were performed to select optimal features for the Random Forest classifier. Firstly, pairwise correlations between features were studied, removing either one of the factors when $r > 0.75$, then feature selection was performed in R 3.2.5 [39] using the Boruta package [44]. Eventually, 55 features were selected for the Random Forest model.

Activity intensity classification

To classify activity intensities, we used metabolic equivalent (MET) values. These values were calculated per participant for all the one-minute expired gas samples taken during the activity protocol. Due to individual differences, this was done by dividing the VO_2 (in ml·kg^{-1}·min^{-1})

212

during a one-minute activity sample by the participant's calculated REE. Thus,

$$MET_{1\ min\ act\ sample} = \frac{VO_{2\_1\ min\ act\ sample}}{REE_{participant}}$$

Intensity classification for each one-minute sample (6 x 10-s windows) was done by checking 1) the MET value and 2) the participant's posture using the video recording. Practically, when the one-minute sample's MET value was ≤ 1.5, the laboratory-based activity was classified as either sedentary activity or standing, depending on the posture. Classification of light-intensity PA (LIPA) and moderate-to-vigorous PA (MVPA) was based on the MET value only, meaning if >1.5 and <3 then an epoch was classified as LIPA, while epochs with MET values ≥ 3 were classified as moderate-to-vigorous PA (MVPA) [10]. Intensity classification of the laboratory-based activities per this system represented the reference classification used for algorithm development and cross-validation.

Algorithm development and cross-validation

The initial step in cut-off point based algorithm development was to create a scatterplot in MS Office Excel 2016 (Microsoft Corp., Redmond, WA, USA) using the 10-s window data, with either SVM, IMA or TM values on the horizontal axis and MET values on the vertical axis. Next, trend line-analysis was performed and the line-of-best fit (i.e. showing the highest proportion of explained variance (R^2)) was chosen. The calculated cut-off points for SVM, IMA and TM represented MET values of 1.5 and 3, which allow classification of activity intensities per 10-s windows based on SVM, IMA and TM values, either or not combined with posture detection. Briefly, these cut-off point algorithms only use two steps in their classification structure: 1) comparing SVM, IMA or TM values with the calculated cut-off points and 2) if necessary, posture detection (Table 2).

Random Forest model development on 10-s window features was performed in R 3.2.5 [39] using the randomForest package [45]. The 10-s window reference classifications of the laboratory-based activities were used to train the Random Forest classifier (supervised machine learning) with the number of trees set to 100. This number was derived from out-of-bag error analyses (Fig 1).

For this study, pooled-data algorithms were developed using the leave-one-subject-out method. This means that the 10-s window data of N = 39 (training sample; on average 1427 (8.6) data points for SB, 620 (7.4) for standing, 761 (19.9) for LIPA and 2937 (35.5) for MVPA) was used to develop the pooled-data algorithms, while the data of N = 1 was used to cross-validate the algorithms. With N = 40 this cross-validation procedure was repeated 40 times with another participant to be left out each iteration. Based on the performed 10-s window cross-validations, confusion matrices were created per participant per algorithm. Eventually,

Table 2. Cut-off point algorithm classification scheme.

Rules		Classification
1	If MET value $\leq$ 1.5 and not upright, then:	Sedentary
2	Else: If MET value $\leq$ 1.5 and upright, then:	Standing
3	Else: If MET value >1.5 and <3, then:	LIPA
4	Else: MET value $\geq$ 3, then:	MVPA

MET, metabolic equivalent; LIPA, light-intensity physical activity; MVPA, moderate-to-vigorous physical activity.

https://doi.org/10.1371/journal.pone.0188215.t002

213
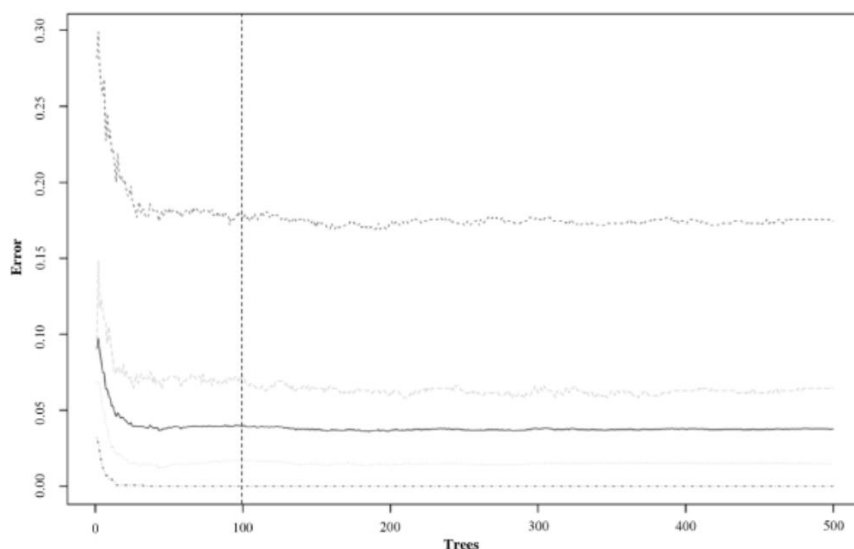
Fig 1. Out-of-bag error analyses for Random Forest modelling.

these matrices were used to determine balanced accuracy per intensity for each algorithm from two perspectives: 1) participant-specific and 2) overall (all participants' confusion matrices summed).

$$Balanced\ accuracy\ (\%) = \frac{Sensitivity + Specificity}{2}$$

$$Sensitivity\ (\%) = \frac{True\ positives\ (N)}{True\ positives\ (N) + False\ negatives\ (N)} * 100$$

$$Specificity\ (\%) = \frac{True\ negatives\ (N)}{True\ negatives\ (N) + False\ positives\ (N)} * 100$$

where N represents the number of cases. Apart from the cross-validation, all algorithms were also tested on their own training samples to check for overfitting. Balanced accuracies of $\geq 80\%$ were considered of an acceptable level [2].

Statistical analyses

Prior to summarising or testing data, we checked its distribution for normality. Since we had a data sample of N = 40, the Shapiro-Wilk test was used for this purpose. Baseline characteristics

214

are presented as the arithmetic mean (SD) (or median (IQR)). To test robustness of the four pooled-data algorithms we assessed if continuous baseline characteristics were correlated with balanced accuracy values (either Pearson or Spearman correlation). Differences in balanced accuracy values between categories of categorical baseline characteristics were tested with the independent T-test (or Mann-Whitney U test). For the comparison between the four pooled-data algorithms the one-way ANOVA repeated-measures test (or the Friedman test) was performed. Balanced accuracy levels from these analyses are reported as arithmetic mean (95%-confidence interval (95%-CI) (or median (~95%-CI)). In case multiple comparisons were necessary for hypothesis testing, either Bonferroni or Sidak correction was used to adjust P-values.

$$Adjusted\ P-value_{Bonferroni} = P_{value} * k$$

$$Adjusted\ P-value_{Sidak} = 1 - (1 - P_{value})^k$$

where k is the number of comparisons. For the current study, P-values were considered statistically significant when P <0.05.

With data variability, even within-subject under controlled conditions, and variance being one of the components for algorithm prediction errors, detailed data reliability checks were deemed highly important. Since 24×10-s windows bilateral accelerometer data and two one-minute expired gas samples were collected per laboratory-based activity, reliability of both main triaxial accelerometer (static Y_{mean}, SVM, IMA & TM) and oxygen consumption data was determined by calculating a coefficient of variation (CV) per activity per participant.

$$CV\ (\%) = \frac{SD_{activity/participant}}{Arithmetic\ mean_{activity/participant}} * 100$$

where SD represents standard deviation. To check for consistency across the activity protocol, all CVs were checked for correlation with MET values. If a correlation was found, data dispersion was determined (SD or IQR). Finally, depending on the distribution, either the arithmetic mean (95%-CI) or median (~95%-CI) was calculated over the moduli of all CVs per outcome variable to get sample-based reliability measures. In this study, a CV of <10% was considered acceptable.

All statistical analyses were executed using IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, NY, USA).

Results

Data reliability

Relationships with MET values were only found for the CVs of accelerometer outcomes SVM and static Y_{mean}, ρ -0.105 (P = 0.046) and ρ -0.382 (P<0.001) respectively. IQRs for these variables were between 3.4% and 8.5% (SVM), and between 0.4% and 2.1% (static Y_{mean}). The sample-based CVs of static Y_{mean}, SVM, IMA and TM were 0.8% (0.7%, 1.0%), 5.5% (5.1%, 6.0%), 5.6% (5.2%, 6.2%) and 6.2% (5.7%, 7.0%) respectively. CVs of oxygen consumption data collected using the DB method also showed a negative relationship (ρ -0.495 (P<0.001)) with MET values. As shown by the IQR, VO_2 CVs were typically between 2.2% and 7.5%. The sample-based CV of the DB method was 4.4% (3.4%, 5.3%). For all variables, the CVs within the IQR were <10%.

215

Table 3. Algorithm cross-validation confusion matrix.

Method	Intensity	Reference				Sensitivity (%)	Specificity (%)	Balanced accuracy (%)	Individual results Acceptable level (%)	Training sample Balanced accuracy (%)
		Sedentary	Standing	LIPA	MVPA					
SVM	Sedentary	1463	0	12	0	99.9	99.7	99.8	100.0	99.8
	Standing	0	588	48	0	92.5	99.1	95.8	92.5	95.8
	LIPA	1	48	448	61	57.4	97.8	77.6	62.5	78.0
	MVPA	0	0	272	2951	98.0	90.6	94.3	100.0	94.4
IMA	Sedentary	1463	0	12	0	99.9	99.7	99.8	100.0	99.8
	Standing	0	588	48	0	92.5	99.1	95.8	92.5	95.8
	LIPA	1	48	469	66	60.1	97.8	78.9	65.0	79.2
	MVPA	0	0	251	2946	97.8	91.3	94.5	100.0	94.6
TM	Sedentary	1454	0	12	0	99.3	99.7	99.5	100.0	99.5
	Standing	0	588	48	0	92.5	99.1	95.8	92.5	95.8
	LIPA	10	47	398	67	51.0	97.6	74.3	57.5	74.5
	MVPA	0	1	322	2945	97.8	88.8	93.3	100.0	93.3
Random Forest	Sedentary	1463	0	34	0	99.9	99.2	99.6	100.0	100.0
	Standing	0	585	48	0	92.0	99.1	95.5	92.5	100.0
	LIPA	1	47	497	82	63.7	97.5	80.6	80.0	100.0
	MVPA	0	4	201	2930	97.3	92.9	95.1	100.0	100.0

SVM, sum of vector magnitudes; IMA, integrals of the moduli of acceleration signals; TM, total movement; LIPA, light-intensity physical activity; MVPA, moderate-to-vigorous physical activity.

Overall balanced accuracy

The confusion matrix shows that all algorithms classified sedentary activity with overall balanced accuracies of ≥99.5% (Table 3). Sensitivity and specificity values were ≥99.2%.

Classification of standing was ≥95.5% accurate in all four models. Sensitivity was 92.5% in the cut-off point algorithms and 92.0% for Random Forest, while specificity was equal over the four algorithms (99.1%).

Most variation in overall balanced accuracies was found for LIPA, ranging from 74.3% (TM) to 80.6% (Random Forest). The confusion matrix revealed that the models' sensitivity was only 57.4%, 60.1%, 51.0% and 63.7%, for SVM, IMA, TM and Random Forest respectively. On the other hand, specificity values were ≥97.5% for all algorithms.

Finally, overall balanced accuracies of ≥93.3% were found for MVPA classification. Sensitivity was ≥97.3% in all models, while specificity varied from 88.8% (TM) to 92.9% (Random Forest).

The overall balanced accuracies per intensity per algorithm were comparable between the cross-validation and training sample, except for Random Forest (Table 3). Standing, LIPA and MVPA showed overall balanced accuracies of 100.0% on the training sample against 95.5%, 80.6% and 95.1% during cross-validation.

Robustness

Random Forest was the only algorithm not showing any changes or differences in balanced accuracies per intensity for all individual's baseline characteristics. The cut-off point algorithms did show changes for a single baseline characteristic each, namely body height. More

216

specifically, balanced accuracies for standing were positively correlated with body height (all three algorithms ρ 0.392 (P = 0.047)).

Algorithm comparison

Overall, differences in participant-specific balanced accuracies between algorithms were found for one intensity only (Fig 2). More specifically, participant-specific balanced accuracies for LIPA classification were different in three occasions, where SVM, IMA & Random Forest appeared superior over TM. The differences found were 4.1% (1.5%, 6.6%) (P = 0.006), 6.3% (2.6%, 10.0%) (P<0.001) and -11.2% (-18.0%, -4.4%) (P = 0.030) respectively.

Fig 2. Pairwise comparisons between algorithms per intensity using participant-specific balanced accuracies. SVM, sum of vector magnitudes; IMA, integrals of the moduli of acceleration signals; TM, total movement; LIPA, light-intensity physical activity; MVPA, moderate-to-vigorous physical activity; Error bars represent 95%-confidence intervals; Dashed line represents no difference; *P <0.05.

https://doi.org/10.1371/journal.pone.0188215.g002

217

Algorithm benchmarking

Applying the critical 80%-threshold to the overall balanced accuracies of the pooled-data algorithms per intensity showed that all algorithms reached the threshold for sedentary activity, standing and MVPA classification (Table 3). However, only the Random Forest model also met the criterion for LIPA classification.

Benchmarking the participant-specific balanced accuracies per intensity for each algorithm revealed that all models had a perfect score (100.0%) for sedentary activity and MVPA (Table 3). The balanced accuracy for standing classification was acceptable for 92.5% of the participants in all algorithms. LIPA classification, however, showed acceptable balanced accuracies for only 62.5% (SVM), 65.0% (IMA) and 57.5% (TM) of the participants in the cut-off point algorithms, while this was 80.0% in Random Forest.

Discussion

The main aim of the current paper was to compare between traditional cut-off points algorithms and a machine learning approach, to provide the best performing heterogeneous pooled-data algorithm to study SB and PA in older adults using thigh-mounted triaxial accelerometry. It is encouraging to note that all models showed acceptable overall balanced accuracies for classification of sedentary activity, standing and MVPA. As hypothesised however, Random Forest outperformed the cut-off point classifiers, being robust for all individual's physiological and non-physiological characteristics and the only algorithm with acceptable ($\geq$80%) overall balanced accuracies over the whole range of activity intensities. In addition, participant-specific balanced accuracies of Random Forest were superior over TM when classifying LIPA.

The fact that Random Forest algorithm performance was better than cut-off point models of SB and PA intensity detection is likely owing to its ability to recognise patterns in non-linear and complex data by using a combination of multiple decision trees, each trained on a random set of features [6,30]. To illustrate the difference with cut-off point algorithms, these models were developed using only two parameters from the triaxial accelerometer data, whereas modelling of the Random Forest algorithm used 55 parameters. Despite this, the differences in performance found between the cut-off point algorithms and Random Forest were rather small only. When comparing balanced accuracies between the cut-off point algorithms tested, an explanation for the results might come from the variability of the parameters used to develop the algorithms. Since oxygen consumption data was used similarly for all models, this parameter did not result in any differences. Nevertheless, with a CV of 4.4% (3.4%, 5.3%), DB proved to be a reliable method in the current study. The fact that all algorithms used the same parameter for posture detection, static Y_{mean} respectively, means that it can also be ruled out as a possible explanation for algorithm performance differences. With a CV of only 0.8% (0.7%, 1.0%) in this study, this parameter was considered highly reliable. Based on the balanced accuracies, TM is the lowest performing algorithm showing either similar or inferior balanced accuracy results per intensity when compared to the other cut-off-point algorithms. Although the CV of TM as a parameter is only 6.2% (5.7%, 7.0%), it is slightly higher than the CVs of SVM and IMA, 5.5% (5.1%, 6.0%) and 5.6% (5.2%, 6.2%) respectively. The use of a parameter representing dataset dispersion (the SD in TM), rather than a summation or integration of all data points may well be the explanation for comparatively poorer performance. As reflected by their CVs, SVM and IMA are equally performing classifiers. Although not all parameter CVs showed consistency with increasing MET values, the CVs within the IQR of all parameters were of an acceptable level (<10%), which might have resulted in acceptable overall balanced accuracies ($\geq$80%) for all intensities of the cut-off point algorithms, except LIPA. Generally,

218

when looking at the overall balanced accuracies per cut-off point algorithm, a similar pattern can be discovered. Sedentary activity and standing are the most accurately classified intensities, then MVPA and ultimately LIPA. The main issue with LIPA classification, for as well cut-off point algorithms as Random Forest, is the poor sensitivity (51.0%–63.7%), which is predominantly caused by misclassification with MVPA. Since the MET value range for LIPA classification is relatively small compared to MVPA's, the LIPA/MVPA threshold is easily surpassed and therefore any amount of movement is more likely to be classified as MVPA instead of LIPA.

The positive relationships found between balanced accuracies and body height for standing classification in all three cut-off point algorithms during robustness analyses, may be due to another reason than body height. Although we standardised accelerometer mounting position by using 50% of the femur length, absolute measures show different positions, which could affect accelerometer signals. Namely, the distance to the centre of rotation (hip and knee joint respectively) influences accelerometer measurements proportionally [46]. For identical movements, the larger the distance to the centre of rotation (as in taller people), the greater the dynamic acceleration compared to that measured at positions closer to the centre of rotation (as in smaller people). This over-registration of dynamic acceleration could lead to false classification of activities with higher intensities instead. Looking at the confusion matrices, standing does show lower sensitivity values for the cut-off point algorithms, which results from misclassification with LIPA. Altogether, this implies that taller people would have lower balanced accuracies than smaller people, but frankly, we found positive correlations. Moreover, we only saw the robustness issues for standing and no other intensities. Therefore, it is plausible to assume that it was not body height to cause any changes in balanced accuracies of standing for the cut-off point algorithms. Further analysis showed that there were only three people with considerably lower balanced accuracies for standing (75% vs. $\geq$96.2%). Interestingly, they were amongst the smallest study participants ($\leq$1.60 m). In addition, the confusion matrices showed that all the standing misclassifications happened in these three participants, while ten others of $\leq$1.60 m body height showed balanced accuracies like taller participants. Hence, when leaving the three out of the correlation analyses, no significant relationships between balanced accuracies of cut-off point algorithms for standing classification and body height were found anymore. When looking into more detail at the raw data, we noticed that the misclassifications in fact occurred during sideways shuffling, for which the three involved participants also happened to exhibit EE $\leq$1.5 MET. As a result of the latter, the reference classification for this activity was standing but the algorithms classified it as LIPA due to motion sensing. Thus, it was not the 'body height' parameter, which negatively affected the algorithm robustness results in these rare cases. Therefore, it is safe to say that all algorithms in this current study are robust, which is most probably the result of using a heterogeneous study sample.

Whilst it was encouraging to note that all algorithms showed acceptable overall balanced accuracies for classification of sedentary activity, standing and MVPA, Random Forest was the only model that also achieved the critical 80%-threshold for LIPA classification. Despite the generally good results, the disadvantage of an overall measure is that it can mask unacceptable algorithm performance on an individual basis. For that reason, it is also important to check the percentage of acceptable participant-specific balanced accuracy per intensity for each model. This revealed that individual classification of sedentary activity and MVPA was always of an acceptable level, which allows categorisation of people based on the amount of SB and MVPA, such as active, inactive and active couch potato. Moreover, standing classification was acceptable for 92.5% of the participants in all algorithms. On the contrary, LIPA classification was acceptable in only $\leq$65.0% of the participants when using a cut-off point algorithm, while this number rose to 80.0% in case Random Forest was used. To summarise, these results show

219

that the cut-off point algorithms presented in the current study, can be used to detect SB, standing and MVPA in older adults confidently. The Random Forest algorithm, however, can be used for the same outcomes, including LIPA classification too. This latter is exciting, because LIPA might play an important role in gaining health benefits by counteracting SB through PA in elderly [1]. Moreover, performance of MVPA may have negative physiological effects, such as increased inflammation, and not necessarily elicit any greater physiological benefits over LIPA in the older adult population [47]. Additionally, performing MVPA may have a high threshold as well as poor long-term adherence in elderly.

Compared to recent research that, similarly to our present one, conducted laboratory-based testing to validate activity intensity identification algorithms including machine learning, our results are in fact a further improvement on these classifiers because we also focus on algorithm robustness and benchmark individual accuracies [2,23,48]. Although comparing results between studies is complicated by differences in populations, monitor placement (mainly hip or wrist, against us thigh) that may influence classification [2], and outcome variables (e.g. Kappa statistic vs. balanced accuracy) [42], our overall finding is in agreement with Ellis et al. [6]. They also showed improved free-living activity intensity classification with machine learning over traditional cut-off point models (without posture detection). However, it must be noted that their machine learning algorithm was developed using free-living accelerometer data only, while the traditional cut-off points were derived in the laboratory.

One could consider the development of algorithms under laboratory conditions as a limitation, given the fact that when laboratory-based, performance during real-life mobility monitoring is compromised [2,6]. However, in the laboratory, conditions can be controlled and a whole range of activities and intensities can be studied allowing calibration, while simultaneously providing proof-of-concept such as thigh-mounted triaxial accelerometry in older adults [2,24]. To improve the matching of performance from laboratory-based with free-living based accelerometer algorithms one may match the amount of data collected on each behaviour with its prevalence in free-living and train the algorithms with bout lengths similar to true daily life behaviour [24]. Although our use of steady-state data of activities with predefined length will improve algorithm accuracies [2], this may not be directly translated to data collected outside the laboratory, since steady-state is not necessarily reached in free-living conditions with activities being more sporadic [24]. Also, Gyllensten and Bonomi [49] found that activities in free-living conditions exhibit a higher degree of overlapping characteristics in their acceleration features when compared with activities performed in the laboratory. Some free-living activities even show substantially different acceleration signals in comparison to when performed in the laboratory [2,24]. Although we agree that true performance of our algorithms in real-life conditions cannot necessarily be derived from the balanced accuracies seen under laboratory settings and it will probably be lower in free-living, we do not expect the dramatic decrease (~13%–46%) reported elsewhere [2,6,24,48,49]. There are several reasons supporting this expectation. Firstly, most of these studies are either not comparable to our study in terms of study population, modelling techniques/settings, extracted features, and accelerometer placement, or suffered from serious methodological issues such as using the same sample to both develop and validate algorithms [2,6,24,48,49]. Secondly, we included few, but common basic activities for elderly persons in our protocol [50–52], and instructed participants to perform them as 'naturally as possible' i.e. using self-selected speed and/or intensity. Next, instead of activity classification, we used intensity classification (based on individual REE corrected MET values) in our study, which is a more generic system providing less options, and thus expected to be less prone to error when applied outside the laboratory [24]. Finally, we used a heterogeneous sample, representing the true healthy older adult population, to develop the algorithms.

Another potential study limitation may be the fact that our models have been developed for application in a single thigh-mounted accelerometer, which does not allow perfect monitoring of PA, as perhaps wobbling of thigh mass or the lack of upper-body movement detection results in classification errors [10,27]. Although it has been suggested that mounting multiple sensors could address the latter issue [10,27,53], study compliance may become compromised [48], something that is less of a problem with a single accelerometer [21,27]. Moreover, thigh mounting can accurately distinguish between sitting and standing, which is not possible with traditional monitor placement at the hip or waist [19,20,54,55]. This placement is thus superior to detect upright stationary activities common in the household, that tend to be more metabolically demanding than activities that recruit only the upper body. Thigh mounting is also relatively close to the centre of mass, which is vital for good prediction of EE and monitoring of locomotion [10,16]. Capturing locomotion is important in elderly, because it provides information about physical independence [10]. Generally, a combination between thigh-mounted accelerometry and machine learning is considered ideal, because the latter in fact makes sensor placement less relevant [27].

The major strength of our current approach is that its design and protocol are largely in accordance with the recommendations for accelerometry-based studies done by Welk et al. [32]. To highlight these compelling elements, despite being modestly sized (~16.4 hrs of algorithm training data only), a study sample containing a large variety of physiological and non-physiological characteristics was used to develop four different accelerometer algorithms. The analyses were performed in more detail (such as focusing on robustness and benchmarking individual accuracies) than usually seen in the literature. The use of leave-one-subject-out cross-validation, ideal for smaller datasets, minimises the risk of overfitting with Random Forest machine learning and enhances the general applicability of the algorithms to new data [56]. Additionally, by using a reliable method for measuring oxygen consumption (CV 4.4% (5.3%)) and correcting for individual metabolic baselines, coupled with direct observation, the reference intensity classification is highly accurate. Since both raw accelerometer data and videos were collected, post-study analyses will be possible such as algorithm tuning, epoch length optimisation or activity classification, but also comparisons with other monitors. Most importantly, this is the first study to conduct detailed analyses of heterogeneous pooled-data algorithms, ranging from simple cut-off point to complex machine learning, for the quantification of SB and PA in older adults using thigh-mounted triaxial accelerometry.

Future studies should focus on further analysis and development of the Random Forest algorithm to classify activities qualitatively. This will not only result in better prediction of EE [57], but also provide information not captured by intensity classification [4,6,24]. Moreover, the Random Forest algorithm should be validated in a free-living set-up and compared to a similar algorithm developed on free-living data. Furthermore, comparisons with proprietary algorithms of commercially available activity monitors would be interesting, not least to allow direct comparison of data from different laboratories and hence the creation of large data sets. Overall, these suggestions would 1) improve understanding of the associations between human activity and health that will inform future recommendations and guidelines for older adults to support healthy ageing [4,6,24] and 2) help to improve current industry standards in activity monitoring in elderly.

Conclusions

Unlike the cut-off point algorithms, under laboratory conditions the Random Forest machine learning model showed acceptable algorithm performance throughout the whole range of activity intensities in older adults wearing a thigh-mounted triaxial accelerometer. Its performance

221

of LIPA classification in particular, makes the algorithm highly relevant for this age group. The fact that this pattern recognition technique 1) does not require subgroup-specific calibrations and/or specific accelerometer body part positioning, 2) is capable of recognising actual human activities and 3) works independent of accelerometer brand/settings, signifies its potential large-scale applicability to distinguish SB and different levels/types of PA in older adults.

Acknowledgments

Author Contributions

Conceptualization: Jorgen A. Wullems, Gladys L. Onambélé.

Funding acquisition: Sabine M. P. Verschueren, Hans Degens, Christopher I. Morse, Gladys L. Onambélé.

Supervision: Sabine M. P. Verschueren, Hans Degens, Christopher I. Morse, Gladys L. Onambélé.

Writing – review & editing: Jorgen A. Wullems, Sabine M. P. Verschueren, Hans Degens, Christopher I. Morse, Gladys L. Onambélé.

References

1. Wullems JA, Verschueren SMP, Degens H, Morse CI, Onambélé GL. A review of the assessment and prevalence of sedentarism in older adults, its physiology/health impact and non-exercise mobility counter-measures. Biogerontology. 2016 Jun 14; 17(3):547–65. https://doi.org/10.1007/s10522-016-9640-1 PMID: 26972899

2. Sasaki JE, Hickey AM, Staudenmayer JW, John D, Kent JA, Freedson PS. Performance of activity classification algorithms in free-living older adults. Med Sci Sports Exerc. 2016 May; 48(5):941–9. https://doi.org/10.1249/MSS.0000000000000844 PMID: 26673129

3. de Rezende LFM, Rey-López JP, Matsudo VKR, Luiz do C O. Sedentary behavior and health outcomes among older adults: a systematic review. BMC Public Health. 2014 Jan; 14(1):333.

4. Freedson P, Bowles HR, Troiano R, Haskell W. Assessment of physical activity using wearable monitors: Recommendations for monitor calibration and use in the field. Med Sci Sports Exerc. 2012 Jan; 44(SUPPL. 1):S1–4.

5. Patel S, Park H, Bonato P, Chan L, Rodgers M. A review of wearable sensors and systems with application in rehabilitation. J Neuroeng Rehabil. 2012 Apr 20; 9(1):21.

6. Ellis K, Kerr J, Godbole S, Staudenmayer J, Lanckriet G. Hip and wrist accelerometer algorithms for free-living behavior classification. Med Sci Sports Exerc. 2016 May; 48(5):933–40. https://doi.org/10.1249/MSS.0000000000000840 PMID: 26673126

7. Corder K, Ekelund U, Steele RM, Wareham NJ, Brage S. Assessment of physical activity in youth. J Appl Physiol. 2008 Sep; 105(3):977–87. https://doi.org/10.1152/japplphysiol.00094.2008 PMID: 18635884

8. Trost SG. State of the Art Reviews: Measurement of Physical Activity in Children and Adolescents. Am J Lifestyle Med. 2007 Aug 1; 1(4):299–314.

9. Gorman E, Hanson HM, Yang PH, Khan KM, Liu-Ambrose T, Ashe MC. Accelerometry analysis of physical activity and sedentary behavior in older adults: A systematic review and data analysis. Eur Rev Aging Phys Act. 2014 Jan; 11(1):35–49.

10. Sasaki JE, Da Silva KS, Da Costa BGG, John D. Measurement of Physical Activity Using Accelerometers. In: Computer-Assisted and Web-Based Innovations in Psychology, Special Education, and Health. Elsevier; 2016. p. 33–60.

11. Chen KY, Janz KF, Zhu W, Brychta RJ. Redefining the roles of sensors in objective physical activity monitoring. Med Sci Sports Exerc. 2012 Jan; 44(SUPPL. 1):S13–23.

12. Chen KY, Bassett DR. The technology of accelerometry-based activity monitors: Current and future. Med Sci Sports Exerc. 2005 Nov; 37(11 SUPPL.):S490–500. PMID: 16294112

222

13. Freedson PS, Melanson E, Sirard J. Calibration of the Computer Science and Applications, Inc. accelerometer. Med Sci Sports Exerc. 1998 May; 30(5):777–81. PMID: 9588623

14. Copeland JL, Esliger DW. Accelerometer assessment of physical activity in active, healthy older adults. J Aging Phys Act. 2009 Jan; 17(1):17–30. PMID: 19299836

15. Evenson KR, Catellier DJ, Gill K, Ondrak KS, McMurray RG. Calibration of two objective measures of physical activity for children. J Sports Sci. 2008 Dec; 26(14):1557–65. https://doi.org/10.1080/02640410802334196 PMID: 18949660

16. Freedson P, Pober D, Janz KF. Calibration of accelerometer output for children. Med Sci Sports Exerc. 2005 Nov; 37(11 SUPPL.):S512–22.

17. Mattocks C, Leary S, Ness A, Deere K, Saunders J, Tilling K, et al. Calibration of an accelerometer during free-living activities in children. Int J Pediatr Obes. 2007; 2(4):218–26. https://doi.org/10.1080/17477160701408809 PMID: 17852552

18. Miller NE, Strath SJ, Swartz AM, Cashin SE. Estimating absolute and relative physical activity intensity across age via accelerometry in adults. J Aging Phys Act. 2010 Apr; 18(2):158–70. PMID: 20440028

19. Kozey-Keadle S, Libertine A, Lyden K, Staudenmayer J, Freedson PS. Validation of wearable monitors for assessing sedentary behavior. Med Sci Sports Exerc. 2011 Aug; 43(8):1561–7. https://doi.org/10.1249/MSS.0b013e31820ce174 PMID: 21233777

20. Aguilar-Farías N, Brown WJ, Peeters GMEEG. ActiGraph GT3X+ cut-points for identifying sedentary behaviour in older adults in free-living environments. J Sci Med Sport. Sports Medicine Australia; 2014 May; 17(3):293–9.

21. Troiano RP, McClain JJ, Brychta RJ, Chen KY. Evolution of accelerometer methods for physical activity research. Br J Sports Med. 2014 Jul; 48(13):1019–23. https://doi.org/10.1136/bjsports-2014-093546 PMID: 24782483

22. Rowlands A V., Olds TS, Hillsdon M, Pulsford R, Hurst TL, Eston RG, et al. Assessing sedentary behavior with the geneactiv: Introducing the sedentary sphere. Med Sci Sports Exerc. 2014 Jun; 46(6):1235–47. PMID: 24263980

23. Ellis K, Kerr J, Godbole S, Lanckriet G, Wing D, Marshall S. A random forest classifier for the prediction of energy expenditure and type of physical activity from wrist and hip accelerometers. Physiol Meas. 2014 Nov; 35(11):2191–203. https://doi.org/10.1088/0967-3334/35/11/2191 PMID: 25340969

24. Kerr J, Patterson RE, Ellis K, Godbole S, Johnson E, Lanckriet G, et al. Objective assessment of physical activity: Classifiers for public health. Med Sci Sports Exerc. 2016 May; 48(5):951–7. PMID: 27089222

25. Preece SJ, Goulermas JY, Kenney LPJ, Howard D, Meijer K, Crompton R. Activity identification using body-mounted sensors—a review of classification techniques. Physiol Meas. 2009 Apr; 30(4):R1–33. https://doi.org/10.1088/0967-3334/30/4/R01 PMID: 19342767

26. Yang CC, Hsu YL. A review of accelerometry-based wearable motion detectors for physical activity monitoring. Sensors. 2010; 10(8):7772–88. https://doi.org/10.3390/s100807772 PMID: 22163626

27. Trost SG, Zheng Y, Wong W-K. Machine learning for activity recognition: hip versus wrist data. Physiol Meas. 2014 Nov; 35(11):2183–9. https://doi.org/10.1088/0967-3334/35/11/2183 PMID: 25340887

28. Heil DP, Brage S, Rothney MP. Modeling physical activity outcomes from wearable monitors. Med Sci Sports Exerc. 2012 Jan; 44(SUPPL 1):S50–60.

29. Pedišić Ž, Bauman A. Accelerometer-based measures in physical activity surveillance: current practices and issues. Br J Sports Med. 2015 Feb; 49(4):219–23. https://doi.org/10.1136/bjsports-2013-093407 PMID: 25370153

30. Bassett DR, Rowlands A, Trost SG. Calibration and validation of wearable monitors. Med Sci Sports Exerc. 2012 Jan; 44(SUPPL. 1):S32–8.

31. Rosenberg D, Godbole S, Ellis K, Di C, Lacroix A, Natarajan L, et al. Classifiers for Accelerometer-Measured Behaviors in Older Women. Med Sci Sports Exerc. 2017 Mar; 49(3):610–6. https://doi.org/10.1249/MSS.0000000000001121 PMID: 28222058

32. Welk GJ, McClain J, Ainsworth BE. Protocols for evaluating equivalency of accelerometry-based activity monitors. Med Sci Sports Exerc. 2012 Jan; 44(SUPPL. 1):S39–49.

33. Sport TE. Resting Heart Rate Table [Internet]. Vol. 2015, Unknown. 2015 [cited 2016 Sep 21]. http://www.topendsports.com/testing/heart-rate-resting-chart.htm

34. PROFESSIONAL M. Assessment of falls risk in older people (Side 1) (Falls Risk Assessment Tool-FRAT) [Internet]. Qeen Mary College London. 2004 [cited 2014 Dec 17]. p. 1–2. http://www.1000livesplus.wales.nhs.uk/sitesplus/documents/1011/FRATtool.pdf

35. Bouten CVC, Koekkoek KTM, Verduin M, Kodde R, Janssen JD. A triaxial accelerometer and portable data processing unit for the assessment of daily physical activity. IEEE Trans Biomed Eng. 1997 Mar; 44(3):136–47. https://doi.org/10.1109/10.554760 PMID: 9216127

223

36. Karantonis DM, Narayanan MR, Mathie M, Lovell NH, Celler BG. Implementation of a real-time human movement classifier using a triaxial accelerometer for ambulatory monitoring. IEEE Trans Inf Technol Biomed. 2006 Jan; 10(1):156–67. PMID: 16445260

37. Bayat A, Pomplun M, Tran DA. A study on human activity recognition using accelerometer data from smartphones. Procedia Comput Sci. 2014; 34(C):450–7.

38. Liu S, Gao RX, Freedson PS. Computational methods for estimating energy expenditure in human physical activities. Med Sci Sports Exerc. 2012 Nov; 44(11):2138–46. https://doi.org/10.1249/MSS. 0b013e31825e825a PMID: 22617402

39. R Development CT. R: A language and environment for statistical computing. Vol. 2.2.0. Vienna, Austria: R Foundation for Statistical Computing; 2005.

40. Onambele GL, Narici MV, Maganaris CN. Calf muscle-tendon properties and postural balance in old age. J Appl Physiol. 2006 Jun 19; 100(6):2048–56. https://doi.org/10.1152/japplphysiol.01442.2005 PMID: 16455811

41. Bedogni L, Di Felice M, Bononi L. By train or by car? Detecting the user's motion type through smartphone sensors data. In: IFIP Wireless Days. IEEE; 2012. p. 1–6.

42. Attal F, Mohammed S, Dedabrishvili M, Chamroukhi F, Oukhellou L, Amirat Y. Physical Human Activity Recognition Using Wearable Sensors. Sensors. 2015 Dec 11; 15(12):31314–38. https://doi.org/10. 3390/s151229858 PMID: 26690450

43. Ellis K, Godbole S, Marshall S, Lanckriet G, Staudenmayer J, Kerr J. Identifying Active Travel Behaviors in Challenging Environments Using GPS, Accelerometers, and Machine Learning Algorithms. Front Public Heal. 2014 Apr 22; 2.

44. Kursa MB, Rudnicki WR. Feature Selection with the Boruta Package. J Stat Softw. 2010; 36(11):1–13.

45. Liaw a, Wiener M. Classification and Regression by randomForest. R news. 2002; 2(December):18–22.

46. Bernmark E, Wiktorin C. A triaxial accelerometer for measuring arm movements. Appl Ergon. 2002 Nov; 33(6):541–7. PMID: 12507338

47. Onambélé-Pearson GL, Breen L, Stewart CE. Influence of exercise intensity in older persons with unchanged habitual nutritional intake: Skeletal muscle and endocrine adaptations. Age (Omaha). 2010 Jun; 32(2):139–53.

48. Bastian T, Maire A, Dugas J, Ataya A, Villars C, Gris J, et al. Automatic identification of physical activity types and sedentary behaviors from triaxial accelerometer: laboratory-based calibrations are not enough. J Appl Physiol. 2015 Mar 15; 118(6):716–22. https://doi.org/10.1152/japplphysiol.01189.2013 PMID: 25593289

49. Gyllensten IC, Bonomi AG. Identifying types of physical activity with a single accelerometer: Evaluating laboratory-trained algorithms in daily life. IEEE Trans Biomed Eng. 2011 Sep; 58(9):2656–63. https:// doi.org/10.1109/TBME.2011.2160723 PMID: 21712150

50. Lord S, Chastin SFM, McInnes L, Little L, Briggs P, Rochester L. Exploring patterns of daily physical and sedentary behaviour in community-dwelling older adults. Age Ageing. 2011 Mar 1; 40(2):205–10. https://doi.org/10.1093/ageing/afq166 PMID: 21239410

51. Lenz EK. Do Sedentary Behaviors Modify the Health Status of Older Adults? Int J Kinesiol Sport Sci J Kinesiol Sport Sci J Kinesiol Sport Sci. 2014 Feb 23; 2(1):13–22.

52. Szanton SL, Walker RK, Roberts L, Thorpe RJ, Wolff J, Agree E, et al. Older adults' favorite activities are resoundingly active: Findings from the NHATS study. Geriatr Nurs (Minneap). 2015; 36(2):131–5.

53. Gao L, Bourke AK, Nelson J. Evaluation of accelerometer based multi-sensor versus single-sensor activity recognition systems. Med Eng Phys. 2014 Jun; 36(6):779–85. https://doi.org/10.1016/j. medengphy.2014.02.012 PMID: 24636448

54. Stamatakis E, Davis M, Stathi A, Hamer M. Associations between multiple indicators of objectively-measured and self-reported sedentary behaviour and cardiometabolic risk in older adults. Prev Med (Baltim). 2012 Jan; 54(1):82–7.

55. Edwardson CL, Rowlands AV., Bunnewell S, Sanders J, Esliger DW, Gorely T, et al. Accuracy of posture allocation algorithms for thigh- and waist-worn accelerometers. Med Sci Sports Exerc. 2016 Jun; 48(6):1085–90. https://doi.org/10.1249/MSS.0000000000000865 PMID: 26741122

56. Mannini A, Intille SS, Rosenberger M, Sabatini AM, Haskell W. Activity Recognition In Youth Using a Single Accelerometer Placed at the Wrist or Ankle. Med Sci Sport Exerc. 2017 Nov; 49(4):801–12.

57. Ruch N, Joss F, Jimmy G, Melzer K, Hanggi J, Mader U. Neural network versus activity-specific prediction equations for energy expenditure estimation in children. J Appl Physiol. 2013 Nov 1; 115(9): 1229–36. https://doi.org/10.1152/japplphysiol.01443.2012 PMID: 23990244

224

Published book chapter(s):

Gladys Onambélé-Pearson, David Tomlinson, Declan Ryan & Jorgen Wullems. Chapter 20: Physical activity and the elderly/geriatric physiology. In: Nick Draper & Gareth Stratton, editors. Physical Activity: A multi-disciplinary introduction. 1st ed. Abingdon: Taylor and Francis Books/Routledge Publishing; 2018.

Chapter 20

Physical activity and the geriatric physiology

By Gladys Onambele-Pearson, Declan Ryan, David Tomlinson and Jorgen Wullems

Keywords: Diurnal Rhythm; Fall prevention; Limitations; Optimal protocol; Exercise Palatability;

1

I-Introduction

Based on the multitude of sources of information and recommendations pertaining to health recommendations for older persons, we would think that today's individuals (at least in the 1st world) aged 65 and over, are fully informed in the concept of, and engaged in the process of, maintaining physical and mental health in their later years. In broad terms, the current recommendations for physical activity tend to share the following principal attributes as summarised by the World Health Organisation or WHO (Organization, 2015):

1. They are neither gender, ethnic nor disease specific

2. A minimum of 150 minutes of moderate physical activity (MPA) or 75 minutes of vigorous physical activity (VPA) per week, inclusive of leisure time activities, housework, transportation and/or planned structured exercise.

3. Where physical activity involves an aerobic element, this should be carried out in a continuous bout of 10 minutes or more, as opposed to start and stop shorter bouts, for any health benefits to be imparted.

4. Postural balance exercises should be an integral part of the physical activities undertaken

5. Resistance training of large muscle groups, must be at least a twice weekly undertaking

6. Even in the presence of co-morbidities and frailty, physical activity to a person's capacity must be pursued

The degree to which the recommendations are fit for purpose, is somewhat under recent scrutiny, with poor health factors still appearing in many individuals who self-report as adhering to the recommendations.

II-The impact of exercise in the older person

The WHO proposes that the benefits to the individual who adheres to this lifestyle, include:

1. Decreased rates of all-cause mortality, coronary heart disease, high blood pressure, stroke, type 2 diabetes, colon cancer and breast cancer;

2. A higher level of cardiorespiratory and muscular fitness, healthier body mass and composition;

3. A 'biomarker profile' that modulates the prevention of cardiovascular disease, type 2 diabetes and the enhancement of bone health;

4. Higher levels of functional health, a lower risk of falling, and better cognitive function;

5. Reduced risk of moderate and severe functional limitations and role limitations.

There is no doubt to the general value of these recommendations in terms of the favourable health effects. It is however striking that no degree of individualisation is taken into account, given the known impact of socio-economic factors on the type and frequency of physical activity. Indeed it is recognised that in adolescents for instance, being female, of a lower social class, are key determinants of the variance in total physical activity undertaken (Raudsepp, 2006). Similarly, the physiological responses to exercises are also modulated by gender and/or decade of life. Thus, to advise on a physical activity programme in later life, influences on, and determinants of, activity levels need to be specifically considered. Indeed later life physical activity is a complex behaviour determined by many factors. Socio-economic status, social support from family and friends, and aspects of the geographical environment, are likely to influence physical activity participation (Farrell, Hollingsworth, Propper, & Shields, 2013), in not a dissimilar way to that seen in adolescents (Santos, Esculcas, & Mota, 2004). It would be expected that socio-economic status link to physical activity would include instrumental and

3

direct (transportation, logistics, payment of fees), motivational (encouragement), and/or observational (explicit modelling leading to improving intrinsic motivation) support.

This book chapter gathers information from the most up-to-date literature on the known impact (benefits & risks), and leads informed discussions on the palatability and adherence of older persons to popular physical activity regimes.

2.1. Structured exercise

As alluded to above, physical activity is a modifiable health behaviour. Whilst the importance of physical activity is extensively documented and well accepted by health professionals, how specific exercise affects known outcome measures in persons aged 65 and over is not necessarily clear. Physical activity is defined as any body movement produced by skeletal muscles that results in energy expenditure (Caspersen, Powell, & Christenson, 1985). Current recommendations for physical activity in the over 65's is 150 minutes of moderate activity or 75 minutes of vigorous activity (Bull & the Expert Working Group, 2010). The categorisation of physical activity is commonly intertwined with structured exercise as both terms have similar characteristics. Yet, exercise is a different concept as it is usually planned and time limited, and with the specific aim of increasing an aspect of physical fitness (Caspersen et al., 1985) (see figure 1.). Structured exercise can be categorised by intensity including: a) medium to vigorous exercise such as resistance or aerobic exercise, and b) low impact low intensity exercise such as yoga or seated exercise classes. Whilst the modality and intensity of exercise can differ, the focus of increasing/maintaining physical function in the elderly is the main aim in all protocols.

4

Figure 1. The links between structured modalities of training and physical fitness characteristics targeted in over 65's. (PRT = progressive resistance training; MVC = maximum voluntary contraction; ROM = range of motion)
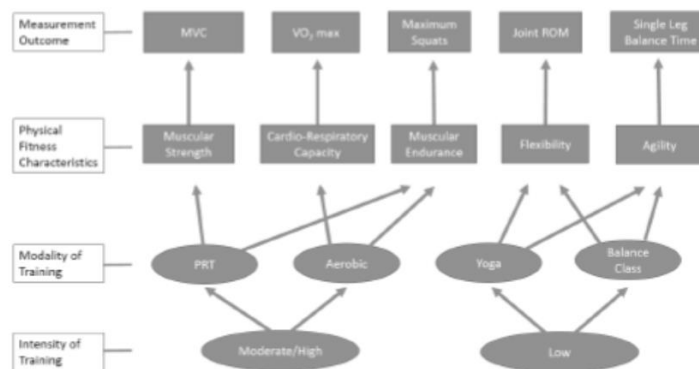
2.1.1. Resistance Exercise Training

The most beneficial intervention in view of increasing muscle structure and function and reducing age-related muscle weakness in the older person is resistance training. The effects of progressive resistance exercise (PRT) in the older person are well documented (Table 1). Interventional studies have shown significant gains in muscle strength (Taaffe, Pruitt, Pyka, Guido, & Marcus, 1996), muscle size (Harridge, Kryger, & Stensgaard, 1999), muscle activation capacity (Morse et al., 2005), specific force (Morse, Thom, Mian, Birch, & Narici, 2007), tendon stiffness (Onambele-Pearson & Pearson, 2012; Reeves, Narici, & Maganaris, 2003) and bone density (Nelson et al., 1994) following twice or thrice weekly sessions of PRT. The functional implications of these adaptations translates to increases in efficient sit-to-stand transitions (Fahlman, McNevin, Boardley, Morgan, & Topp, 2011), walking speed (Henwood & Taaffe, 2005), balance (Nelson et al., 1994; Onambele-Pearson, Breen, & Stewart, 2010a; Onambele et al., 2008) in a long list of other functional benefits. Improvements reported in

5

these functional tasks play a leading role in the maintenance of independent later life. Whilst the main adaptations of PRT centre on structural changes to skeletal muscle, there have been several studies demonstrating improvements in decreasing systemic inflammation biomarkers that are upregulated in ageing such as interlukin-6 (Onambele-Pearson et al., 2010a; Onambele-Pearson, Breen, & Stewart, 2010b; Prestes et al., 2009) and Tumour Necrosis factor α (Greiwe, Cheng, Rubin, Yarasheski, & Semenkovich, 2001). The inflamed endocrine milieu seen with increased age is in fact negatively associated with a variety of morbidities (e.g. cardiovascular disease), thus the impact of such co-morbidities is expanded upon later in this chapter.

It should nevertheless be noted that there are some risks associated with PRT in the older person, with the key aspect being the high intensity nature of the activity and the familiarity with the tasks for the individual. PRT places high stress levels on active muscles and joint structures, requires potentially uncomfortable physical positioning during repetitive loading, thus potentially increases the risk of injury (Kolber, Beekhuizen, Cheng, & Hellman, 2010).

6

230

Table 1. Adaptations associated with a variety of modalities of exercise in the elderly

Modality of Exercise	Intensity	Adaptations	Functional Tasks
Resistance exercise	Moderate to High	↑ Muscle Strength	↑ Gait Speed
		↑ Muscle Power	↑ Postural Balance
		↑ Muscle Size	↑ Sit to stand
		↑ Activation Capacity	↓ Risk of Falling
		↑ Tendon Stiffness	
		↓ Systemic Inflammatory Biomarkers	
Aerobic Exercise	Moderate to High	↑ Capillary Density	↑ Gait Speed
		↑ Mitochondrial Density	↑ Postural Balance
			↑ 6 minute walk time
		↑ Lipid Profile	
		↑ Blood Glucose Uptake	
		↓ Systemic Inflammatory Biomarkers	
		↑ Aerobic Power	
Dance	Low/Moderate/High	↑ Muscle Strength	↑ Gait Speed
		↑ Joint Range of Motion	↑ Flexibility
Yoga	Low	↑ Muscle Strength	↓ Risk of Falling
		↑ Joint Range of Motion	↑ Postural Balance
			↑ Flexibility
Balance Themed Exercise	Low	↑ Muscle Strength	↓ Risk of Falling
			↑ Postural Balance
Pilates/Core Based Exercise	Low	↑ Muscle Strength	↓ Risk of Falling
		↑ Joint Range of Motion	↑ Postural Balance
			↑ Flexibility

2.1.2. Aerobic Exercise Training

Aerobic/endurance training can be characterised by numerous activities that range from recreational walking to high intensity running. The stimulus placed on skeletal muscle here is different to that in resistance/strength based training, with repeated muscle contractions placing

a greater demand on the cardiovascular system. The benefits with this modality of training are the central and peripheral adaptations of the cardiovascular system, increasing the capacity to deliver oxygen (O_2) to working muscles during activity (Holloszy & Coyle, 1984) and improving the capability of skeletal muscles to generate energy via oxidative metabolism (Cadore, Pinto, Bottaro, & Izquierdo, 2014). These effects are achieved through structural increases in both mitochondrial and capillary density (Iversen et al., 2011) and a shift in fibre type towards oxidative slow twitch muscle fibres (Howald, Hoppeler, Claassen, Mathieu, & Straub, 1985).

There are two types of traditional aerobic exercise: (i) **continuous,** based on training at one uninterrupted level throughout the protocol or (ii) **interval,** based on training delivered in short high intensity bursts. Training intensity for over 65's tends to be set using varying methodologies. First, the subjective intensity assessment uses of a 10 point scale set at 5-6 with 0 classed as sitting and 10 being classed as an all-out effort for a minimum of 30 minutes, 5 days/week (Nelson et al., 2007a). Second, the more objective assessments either use heart rate, the participant's aerobic threshold or VO_2 max, or both in conjunction (Emerenziani et al., 2015). Whilst a traditional structured aerobic session is shown to increase an individual's functional capacity, unconventional dance based exercise classes have been shown to also increase cardiorespiratory endurance, strength/endurance, body agility, flexibility, body fat, and balance in elderly women (Hopkins, Murrah, Hoeger, & Rhodes, 1990; Serra et al., 2016; Wu, Tu, Hsu, & Tsao, 2016). This demonstrates that to reach the attainable goal of improving physical fitness, health and functional ability in over 65's, a variety of structured and semi-structured aerobic based training methods may be used.

Notably, an important factor to consider when choosing between training methodologies is whether the exercise meets the individual's physical, social and emotional requirements to make it a long-term lifestyle change. With moderate/vigorous intensity training

8

in particular, the over 65's tend to present poor exercise tolerance especially when they are frail, and with no previous history of structured exercise. In addition, blood pressure increases acutely during physical activity (Palatini, 1988). Therefore medical and training history should be taken into account when prescribing moderate/vigorous training intensity to this age group.

2.1.3. Low Intensity Low Impact Exercise

Previous research has shown the benefit of low impact structured exercise sessions such as yoga, tai chi, Pilates and balance themed classes on functional measures including flexibility (Geremia, Iskiewicz, Marschner, Lehnen, & Lehnen, 2015; Grabara & Szopa, 2015), lowering the risk of falling (Schmid, Van Puymbroeck, & Koceja, 2010), increasing postural balance (Taylor et al., 2012) and improving an individual's quality-of-life (Woodyard, 2011). It is possible that the intensity of the exercises being lower, means that they are more likely to be palatable to over 65's and especially to those who are either frail or have no previous history of structured physical exercise. Again in favour to such activities, is the fact the low intensity likely lowers any injury incidence owing to the avoidance of high levels of stress and strain on both the cardiovascular, musculoskeletal and endocrine systems, with in fact not clear benefit of higher exercise intensities in the older group (Onambele-Pearson et al., 2010a, 2010b).

2.2. Physical activity and its impact on a key physical functioning marker: falls

One in three adults in the UK over the age of 65 years fall at least once a year. In these individuals, injurious falls tend to result in loss of independence (Piirtola & Era, 2006), and are one of the leading causes of death from injury (Rubenstein, 2006). With over £2 billion currently spent every year by the NHS in relation to falls, and a predicted increase of 2 million in the number of people aged 65+ living in the UK by 2021, this will undoubtedly infer a hefty cost to the NHS.

The key modifiable risk factors associated with increased risk of falling include muscle weakness, balance and gait abnormalities (Granacher, Muehlbauer, & Gruber, 2012; Maki, Holliday, & Topper, 1994; Rubenstein & Josephson, 2002). Postural balance is an important prerequisite for independent and successful performance of daily living activities (Prata & Scheicher, 2012) including for instance, stairs negotiations and standing up from a chair (Granacher et al., 2012). With the obligatory aspect of ageing-related decrement in muscular performance and functional capacity, it is increasingly understood that lifestyle, and in particular habitual ambulation/physical activity, may modulate the rate and magnitude of these deleterious changes. For instance, a sedentary lifestyle (Participation in activities characterized by an energy expenditure ≤ 1.5 metabolic equivalents and a sitting or reclining posture (Owen, Healy, Matthews, & Dunstan, 2010)), has been shown to reduce the functional reserve capacity of older individuals or the excess above that needed for normal functioning. Such reserves are key, as they would normally allow for adaptations and responses to changes in the environment. Older adults aged >65+ years are the most sedentary in society with a sedentary time representing 65-80% of their waking day, with over 8.5 hours of that time spent sitting (Harvey, Chastin, & Skelton, 2015). Arguably, this lifestyle may contribute to elderly individuals being physically weaker, slower and having a reduced motor coordination in comparison to their younger counterparts (Enoka, 1994).

On the other side of the lifestyle spectrum, we have physical activity and/or exercise. Participation in regular physical activity (PA) elicits a number of favourable responses that are understood to contribute to healthy ageing. Studies show that training counteracts ageing-related postural impairments (Perrin, Gauchard, Perrot, & Jeandel, 1999) by acting on the motor response or on balance sensors (Gauchard, Gangloff, Jeandel, & Perrin, 2003; Howe, Rochester, Neil, Skelton, & Ballinger, 2011). Researchers report that a progressive heavy-resistance training program combined with explosive types of exercises leads to great gains not

only in maximal isometric and dynamic strength but also in explosive force production characteristics of the leg extensor muscles in both middle-aged and elderly men and women (Hakkinen et al., 1998). The strength gains are accompanied by considerable increases in the voluntary neural activation of the agonist muscles in both middle-aged and elderly subjects of both genders, with significant reductions taking place in the antagonist co-activation of the maximal extension action in both older person groups. Such adaptations are key for adequate/steady postural balance maintenance. In parallel, through a systemic review and meta-analysis (Thibaud et al., 2012), it is evident that physical activity in individuals over 60 years acts as a protecting factor against falls. Physically active older people are less at risk of falling (OR of 0.75 [95% CI of 0.64, 0.88] than those who are physically inactive or sedentary (OR of 1.41 [95% CI of 1.10, 1.82]).

2.3.Physical activity and its impact on a key psychological marker: Cognitive function

Cognitive function is an essential component of daily living and makes a significant contribution to quality of life (Williams & Kemper, 2010). Human ageing can lead to cognitive decline (Brehmer, Kalpouzos, Wenger, & Lovden, 2014), often termed Dementia, and affecting an estimated 36 million people, with Alzheimer's disease being the most common form (Larson, Yaffe, & Langa, 2013). Polypharmacy being an issue with the older person, non-pharmacological interventions that could help individuals maintain their cognitive capacity in older age and reduce levels of morbidity are therefore highly desirable.

There is growing evidence that exercise could protect against ageing-related dementia (Boots et al., 2015; Liu-Ambrose & Donaldson, 2009) as it has been associated with improved cognitive performance especially in tasks involving executive control (Komulainen et al., 2010; Prakash et al., 2011), which are the processes involved in selecting, scheduling and coordinating perception, memory and action (Pontifex, Hillman, Fernhall, Thompson, &

11

Valentini, 2009). Table 2, summarises further research in this area. Similarly, research suggests that higher cardiorespiratory fitness in middle-aged adults correlates with a lower risk of dementia later in life (Defina et al., 2013). In support of this theorem, studies in mice demonstrate that chronic exercise can reduce the risk of Alzheimer' Disease, delaying its onset and progression (Cho et al., 2015; Garcia-Mesa et al., 2011; Liu, Zhao, Zhang, & Shi, 2013). Interestingly, a community-based research study links cardiorespiratory fitness response with cognitive gains rather than the exercise dose (i.e., duration) itself (Vidoni et al., 2015).

Several theories have been proposed to explain the mechanisms underlying the exercise-cognition relationship. These include, but are not limited to, reduced levels of homocysteine (Chang, Tsai, Huang, Wang, & Chu, 2014; Garcia, Haron, Pulman, Hua, & Freedman, 2004), increased event-related brain potentials (Kamijo, Nishihira, Higashiura, & Kuroiwa, 2007; Szucs & Soltesz, 2010), the transient hypofrontality theory (Del Giorno, Hall, O'Leary, Bixby, & Miller, 2010; Dietrich, 2006) and increased cerebral blood flow (A. D. Brown et al., 2010; Querido & Sheel, 2007). Whilst it is beyond the scope of this book chapter to examine these in detail, the roles of brain-derived neurotrophic factor (BDNF) which is linked with neurogenesis in the brain thus plays an important role in brain plasticity, and insulin-like growth factor 1 (IGF-1) which is linked to protein synthesis stimulation, are arguably key. Exercise is associated with increased BDNF levels (Griffin et al., 2011; Komulainen et al., 2010). This is significant because low levels of BDNF have been linked to Alzheimer's disease. Importantly also, exercise increases IGF-1 concentrations (Chang et al., 2014; Sonntag, Ramsey, & Carter, 2005). This is potentially relevant since lower IGF-1 concentrations correlate with ageing-related cognitive decline (Al-Delaimy, von Muhlen, & Barrett-Connor, 2009; Voss, Nagamatsu, Liu-Ambrose, & Kramer, 2011).

Aerobic exercise and resistance training represent distinct forms of exercise with different physiological and metabolic demands (Pontifex et al., 2009). If interventions to

236

improve cognitive function are to be recommended, it is essential to understand how these exercise modalities affect cognition. It is also important to consider the effect of ageing on the responsiveness of the cognitive function system (Defina et al., 2013).

In recent studies of older persons, cognitive function was positively correlated with fitness (VO_{2max}) in older women aged 50-90 years (A. D. Brown et al., 2010). Similarly, higher fitness levels in older adults are correlated with improved Stroop test performance (Prakash et al., 2011), whereby during an executive function enabling task, irrelevant information or interference is inhibited so that an appropriate response can be selected (Etnier & Chang, 2009). In fact, meta-analytic reviews conclude a positive effect of aerobic exercise on cognition.

Table 2: Summary of studies investigating the effects on cognition of chronic resistance training

Date	Study	Sample Population	Intervention Period	Cognitive Test	Cognitive Test Oucome
1997	Tsutsumi et al.	Senior adults (M_{age} = 68 y)	12 weeks	Various Tests of Executive Function	No improvement
2006	Lachman et al.	Senior adults	3 and 6 months	WAIS Backward Digit Span	Improvement
2007	Cassilhas et al.	Senior men (65-75 y)	6 months	Various Tests of Working Memory	Improvement
2008	Liu-Ambrose et al.	Senior adults (over 70 y)	6 months	Stroop Test and Trail Making Test	Improvement
2010	Kimura et al.	Senior adults (over 65 y)	12 weeks	Task-switching Test	No improvement

A meta-analysis previously concluded that combinations of aerobic exercise and resistance training positively affected cognitive performance in older adults more than aerobic exercise alone (Colcombe & Kramer, 2003). However, studies that directly compare aerobic exercise and resistance training and their effect on cognition are in fact scarce. A study compared the effects of different exercise modalities on cognition among older persons aged

13

62-95 during a six-month intervention (A. K. Brown, Liu-Ambrose, Tate, & Lord, 2009). Participants were randomly assigned to either a group-exercise programme including twice-weekly resistance training and balance components, a twice-weekly flexibility and relaxation group or a control group. Participants were assessed for several aspects of cognition including fluid intelligence, with the Stroop test used to assess executive function. Executive function did not improve in any of the 3 groups. Fluid intelligence results increased significantly in the resistance training group only. Therefore the authors concluded that resistance training and balance exercises could reduce age-related cognitive decline in senior adults. However given that no aerobic training was in fact included, this leaves the door open for further research to confirm the contribution of aerobic exercise to cognitive function maintenance in older persons.

III-Evaluation of the impact of the exercise context

Low levels of physical activity and socio-economic status in middle-aged and older adults are associated with poor musculoskeletal, metabolic, cardiovascular and psychological health and this ultimately leads to loss of independent living and quality of life in old age. Interventions designed to increase physical activity levels and promote social interaction, particularly those with either a peer-mentor/lifestyle coaches, or an outdoors community-spirited emphasis such as walking groups, should lead to improved health status, owing to longer lasting uptake.

3.1.Indoor vs outdoor exercise prescription

A common reason for older person to start exercising is to increase their physiologic reserves and hence reduce the risk of falling. To achieve this, 50 hours of cumulative exercise is needed (Sherrington et al., 2008). In other words, long-term exercise participation is important for the older person, but unfortunately not a common habit in this segment of the

14

238

population (Organization, 2007). Although evidence on the (causal nature of the) relationship between the physical setting of exercise and health benefits in older person is limited (Kerr, Sallis, et al., 2012), there are some clear differences between both settings which may affect the impact and long-term adherence of the exercise behaviour.

Unlike outdoor exercise, an indoor environment allows older person to exercise in a clean and safe setting all year-round, independent of the weather or season (Hug, Hartig, Hansmann, Seeland, & Hornung, 2009). Additionally, these settings are most often equipped for both resistance and endurance training (Hug et al., 2009). Hence, indoor facilities are likely to be the optimal setting for optimal training in all including the older person. However, indoor exercise also presents a few disadvantages. Firstly, older adults often have vitamin D deficiency which is related to chronic conditions such as cardiovascular disease and bone health (Lauretani, Maggio, Valenti, Dall'Aglio, & Ceda, 2010). Therefore, it is suggested that by going outdoor, older adults may experience physical and mental benefits (e.g. reduced depression) and an improved sense of well-being from a combination of exercise and vitamin D (Matthew P. Buman & King, 2010; Frumkin, 2001; Kerr, Sallis, et al., 2012; Nelson et al., 2007b; St Leger, 2003; Thompson Coon et al., 2011). The fact that exercising outdoors occurs at a higher intensity but with a lower perceived exertion makes it different from indoor exercising, which may influence the beneficial effect of exercise ultimately (Ceci & Hassmén, 1991; Teas, 2007). In addition, long-term adherence of exercising indoors is a well-recognised issue (Thompson Coon et al., 2011). Studies have shown that outdoor exercise can have long-term health benefits in older adults (Jacobs et al., 2008; Kono, Kai, Sakato, & Rubenstein, 2004), since engaging in it is an important factor for behavioural maintenance (Hekler et al., 2013; Maas, van Dillen, Verheij, & Groenewegen, 2009). It is suggested that outdoor exercisers may enjoy the exercise more, and perform it for longer and/or more frequently (Maas et al., 2009). For example, previous research shows that over a period of time outdoor exercisers

15

239

accumulate significantly more minutes of intense exercise than indoor exercisers (Takano, Nakamura, & Watanabe, 2002). The presence of social interaction may play a key role in enjoyment and adherence to exercise (Gladwell, Brown, Wood, Sandercock, & Barton, 2013; Hug et al., 2009; Maas et al., 2009; Takano et al., 2002; Teas, 2007). In fact, research suggests that socialising opportunities appear to be more persuasive for persons to engage in exercise sessions than actual health benefits (Schasberger et al., 2009).

Despite the beneficial effects of outdoor exercise for older person, it may also adversely affect health through exposure to pollutants and a challenging neighbourhood design in a built-outdoor environment (Kerr, Marshall, et al., 2012). The latter may prevent older persons with impaired physical function and fear of falling from engaging in exercising outdoors (Michael, Green, & Farquhar, 2006; Murayama, Yoshie, Sugawara, Wakui, & Arami, 2012; Rantakokko et al., 2009). Therefore, these sub-populations would probably benefit with initially engaging in indoor exercise, e.g. to improve lower-extremity physical function and self-confidence, before going outdoors (Kerr, Sallis, et al., 2012). In that case, indoor settings are a viable temporary alternative to outdoors. Moreover, exercising in an appealing and supportive indoor environment may have better psychological effect and adherence than exercising in a busy, and hence perceived as threatening, urban environment (Thompson Coon et al., 2011). Hence, should the benefits of outdoor exercise be conclusively shown to outweigh those of indoor activities, it will become crucial for communities to provide both safe and attractive outdoor exercise locations for older person (Murayama et al., 2012; Takano et al., 2002). Even further, we would also argue that natural green, rather than built-outdoor environments might be the preferable option, since current evidence suggests that nature-based exercise provides greater physiological and psychological health benefits in adults (Bowler, Buyung-Ali, Knight, & Pullin, 2010; Gladwell et al., 2013; Pretty, Griffin, Sellens, & Pretty, 2003; Thompson Coon et al., 2011). However, it must be noted that subgroups of the population, and in particular the

older person, might have different responsiveness to exercising in green spaces (Richardson & Mitchell, 2010). Future research should therefore specifically investigate any age-sensitivity to/preference for, outdoors green environment-based physical activities.

Whilst the duration of participation prior to measureable psycho-physical effects is unclear, based on available literature, outdoor exercise might be preferred for older person (figure 2), even if outdoor pursuits may not necessarily be accessible/appealing to all (Thompson Coon et al., 2011). Nevertheless, as the older person tends to struggle to achieve optimal levels of activity for a number of intrinsic and extrinsic reasons, any exercise participation is encouraged as it will likely induce health benefits regardless of the physical setting for the exercises (Nelson et al., 2007b).

Figure 2. A balance representing the overall findings of indoor vs. outdoor exercise in elderly
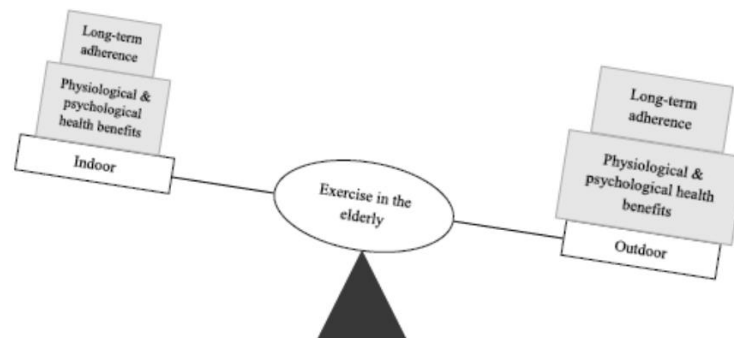
3.2.Energy Balance

Energy cannot be created or destroyed, it can only be transformed. Within human physiology, the equation: Energy Stores = Energy Intake (EI) – Energy Expenditure (EE) is commonly used. When EI = EE then body mass is likely to be maintained. EE is comprised of

17

Resting Metabolic Rate (RMR) (60-70% contribution), thermic (8-13% contribution), brown adipose tissue (2-3% contribution) and physical activity (15-30% contribution) (Wilson & Morley, 2003). The RMR of young males (18-33 years) is 1785.6 ± 43.2 kcal·day^{-1} and decreases approximately 3.50% per decade of ageing (69-89 years: 1497.6 ± 28.8 kcal·day^{-1}) (Fukagawa, Bandini, & Young, 1990). This is mainly due to reductions in fat-free mass (FFM) (explaining 82.8% and 45.3% of the variance in young adults and older adult's RMR, respectively (Bosy-Westphal et al., 2003)). With this decline in RMR, there is a subsequent decline in EI, known as physiological anorexia. Declined RMR can be attenuated with engagement in exercise, and is unlikely to be due to the preservation of dietary intake. Indeed, the difference in dietary intake between pre and post-menopausal runners is found to be similar to that of pre and post-menopausal sedentary women (Van Pelt et al., 1997).

With exercise for weight loss, most interventions do not meet the expected weight loss as over half of the groups compensate for the increased EE with increased EI (King, Hopkins, Caudwell, Stubbs, & Blundell, 2008; Thomas et al., 2012). When body mass is broken down into its components, partaking in exercise only (60 mins @ 75% of maximum oxygen utilisation, 5 times a week for 12 weeks) results in a lower reduction in fat mass compared to partaking in a dietary calories control regime or dieting (500 kcal·day^{-1} reduction) plus exercise (Solomon et al., 2008). More importantly, dieting plus exercise does improve cardio-metabolic variables that are associated with cardiovascular disease, by a greater amount compared to dieting or exercise alone. Improving health biomarkers in older adults is more important than weight loss *per se* because increasing BMI is not associated with an increased hazard risk (HR) of three-year follow up mortality (BMI > 35.0 kg·m^{-2} relative to 'healthy' BMI). On the other hand, being underweight (< 18.5 kg·m^{-2} BMI relative to a 'healthy' BMI population). The underweight older person may simply be the phenotypic expression of another underlying comorbidity since nearly 50% of this age group reported that weight loss had been

18

unintentional (Locher et al., 2007). In view of the above, it therefore appears that exercise and diet for weight loss should not be the focus in older adults, rather exercise and diet for improved health and physical functioning.

3.3.Physical status associated limitations to exercise

3.3.1. Frailty as a limitation to exercise

Currently, there is no consensus on the definition of frailty, though it is acknowledged that it incorporates the degradation of several physiological parameters, increased risk of falling, feelings of vulnerability, and is highly prevalent in older adults (Fried et al., 2001; Viña, Salvador-Pascual, Tarazona-Santabalbina, Rodriguez-Mañas, & Gomez-Cabrera, 2016). Engagement in physical activity, specifically walking and stair climbing, accounts for 30.0% and 20.0% of non-syncopal falls in older adults (Nevitt, Cummings, & Hudes, 1991). Therefore, consideration for the participant's physical limitations is needed prior to a physical activity intervention. Moderate-vigorous physical activity (MVPA, $3.0 - \geq 6.0 \times$ RMR) is the recommended aerobic intensity for health improvements. In NHANES cohort older adults (50+ years), an hour a day increase in older adult's MVPA was associated with a 0.045 point (95% CI 0.028, 0.063) reduction in the 46-item frailty index score (possible score range $0 - 1$) (Blodgett, Theou, Kirkland, Andreou, & Rockwood, 2015). However, attaining and maintaining this intensity of physical activity is difficult for older adults. Therefore, a focus towards functional and light intensity physical activity (LIPA, $1.50 - 3.00$ x RMR) would seem more appropriate. For example, 3 months thrice weekly, 'posture transition' training (sitting to standing, prone to supine) led to improvements in a physical performance test. These test comprised of placing a book on an overhead shelf, putting on a coat, picking up a penny from the floor, walking 50.0 feet, turning 360°, ascending stairs, raising from a chair, and Romberg

19

test (M. Brown et al., 2000) which, are all essential movements for daily function. The relationship between LIPA and physical and psychological health is also documented in epidemiology, predicting that the 30 minute substitution of sitting for LIPA can lead to similar improvements compared to MVPA (physical: b 0.46 95%CI 0.37,0.54, b 0.37 95%CI 0.28, 0.46, psychosocial: b 0.24 95%CI 0.12,0.36, b -0.02 95%CI -0.13, 0.10, respectively) (Matthew P Buman et al., 2010).

3.3.2. Cardiovascular Disease and cancer as limitations to exercise

Cardiovascular disease (CVD) mortality, after cancer, is most prevalent in older adults, increasing nearly two-fold per decade of life after the age of 55 (figure 3). Those who already suffer with CVD may be hesitant to participate in physical activity however, the rate of cardiovascular events during supervised exercise is reported to range from 1/50000 – 1/20000 patient hours of exercise (Franklin, Bonzheim, Gordon, & Timmis, 1998) with evidence to suggest participation will in fact reduce total and cardiac mortality by 27.0% (95%CI -2.00, 40.0) and 31.0% (95%CI -6.00, 49.0), respectively (Jolliffe et al., 2001).

The maintenance of physical activity is essential following a cardiac event in older adults as patients who attend more than 24 rehabilitation sessions were 19.0% relatively less likely to die within 5 years after a cardiac event compared to those with 24 sessions or fewer (Suaya, Stason, Ades, Normand, & Shepard, 2009).

244

Figure 3. The number of CVD and Cancer deaths in the United Kingdom for 2014 throughout older age. Adapted from [16].
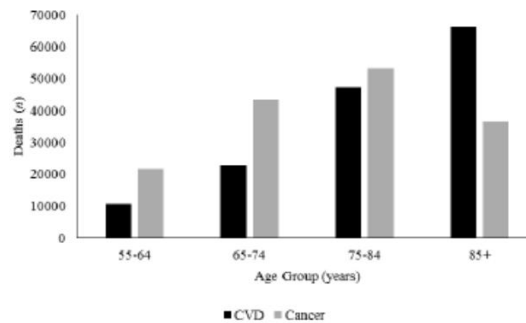
Along with CVD, cancer is one of the greatest causes of mortality in the UK (Townsend, Bhatnagar, Wilkins, Wickramasinghe, & Rayner, 2015). Cancer comes in many forms and therefore it is not possible to recommend the same levels of exercise for everyone. For example, those with immunity cancers should avoid the use of public fitness facilities due to the increased contraction risk of bacterial and viral infections through bodily fluid contact. Cancer and its' treatment inflicts psychological distress (e.g. feelings of fatigue, anxiety, depression) and has been the focus of physical activity research. A systematic review by Luctkar-Flude, Groll, Tranmer, and Woodend (2007) found that older adults have reduced feelings of fatigue and improved quality of life when exercise is taken up either during or following cancer treatment. Overall, research into the effects of physical activity on older cancer survivors is limited and requires further investigation (Daum, Cochrane, Fitzgerald, Johnson, & Buford, 2016). For now, the general consensus appears to be similar to that of healthy older adults, interventions should have a focus on functional and quality of life improvement.

21

3.4.Should the diurnal rhythm be a consideration for exercise in the older person?

Skeletal muscle is a highly plastic tissue that readily adapts to changes during and following a loading state (Campos et al., 2002). Increased load imposed on the skeletal muscle elicits adaptations that result in changes in the contractile characteristics of the muscle, ultimately leading to muscle hypertrophy (Hulmi et al., 2009). More specifically, when skeletal muscle is subjected to an overload stimulus, the resultant micro-injuries in the myofibers and extracellular matrix (Hulmi et al., 2009), leads to a chain of myogenic events (Housh, Housh, Johnson, & Chu, 1992). These events culminate in the enlargement of the diameter of individual fibres, thus resulting in an increase in muscle cross sectional area (CSA) and fascicle length, ultimately causing muscle hypertrophy (Seynnes, de Boer, & Narici, 2007).

Research into the different intensities, volume and load used in resistance training allow conclusions to be drawn on what may yield the best results when hypertrophy is the main emphasis for this of training. Researchers examined bodybuilders using a programme involving moderate load (65-75% 1RM), high volume (6-8reps) with short rest periods (1-2minute). Results showed that this produces a greater testosterone response than a high load (> 85% 1RM), low volume with long rest periods (3 minutes) (Kraemer et al., 1991; Kraemer et al., 1990). This type of training has also been shown to illicit the greatest increase in Growth Hormone (GH) response (Kanaley, Weltman, Pieper, Weltman, & Hartman, 2001; Kraemer et al., 1991; Kraemer et al., 1990) which inevitably increases Insulin Growth factor-1 (IGF-1) secretion allowing for greater protein synthesis (Borst et al., 2001). In addition, GH has mainly anabolic properties which spike after various forms of exercise (Crewther, Keogh, Cronin, & Cook, 2006). Resistance training promotes the increase of GH isoforms allowing for sustained action on target tissues (Ahtiainen, Pakarinen, Alen, Kraemer, & Hakkinen, 2003), as well as enhanced interaction with muscle cell receptors which facilitate exercise recovery and the

22

hypertrophic response (Crewther et al., 2006). The increase in GH is thought to be associated with a concurrent increase in IGF-1, thereby enabling further myogenic promotion (Velloso, 2008). Hormones such as Testosterone, Cortisol, GH and IGF-1 have been extensively examined as to their role in the muscles hypertrophic response to resistance training (Fry, 2004; Kraemer & Ratamess, 2005; Schoenfeld, 2013).

Research is pointing to an optimal timing for maximal exercise-induced gains. The premise is that testosterone has considerable anabolic effects, binding with androgen receptors and interacting with DNA, subsequently causing an increase in cell size (Kraemer & Ratamess, 2005). It can also have indirect effects on protein accretion through the release of GH (Kraemer et al., 1991), as well as promoting satellite cell replication and activation, at least in the first 20 weeks of use (for a review read (Kadi, 2008)). Data previously identified significant correlations between training-induced increase in Testosterone and muscle cross-sectional area (Ahtiainen et al., 2003). Interestingly, data also highlights diurnal variation in testosterone, with a peak between 7-9AM (Diver, Imtiaz, Ahmad, Vora, & Fraser, 2003). On the other hand, as cortisol increases protein metabolism, it could be suggested that the reduction of circulating cortisol levels would allow for a greater hypertrophic response, when the timing for exercise is optimised (Burley, Whittingham-Dowd, Allen, Grosset, & Onambele-Pearson, 2016). Cortisol levels peak during the early hours just before awakening with levels progressively decreasing throughout the day, reaching its lowest level between 5-7PM (Kanaley et al., 2001). Whilst exercise results in a decrease in Cortisol and greater reductions appear to be prevalent in the morning (Burley et al., 2016; Pledge, Grosset, & Onambele-Pearson, 2011; Sedliak, Finni, Peltonen, & Hakkinen, 2008), interestingly in terms of 'muscle growth promoting' endocrine milieu, the testosterone:cortisol ratio is at its peak in the evening. In view of the above, and in view also of the fact that androgen level naturally decrease with age (Kaufman & Vermeulen, 2005), some research now associates the diurnal fluctuations in these hormones, to an

23

optimisation of training routines, and hence tentatively point to training in the evening as the most favourable endocrine environment (Burley et al., 2016; Teo, Newton, & McGuigan, 2011).

IV- Summary & practical applications

In summary, the primary aim of increasing physical activity in someone aged over 65 is to improve their health, fitness and quality of life, whilst managing ageing-related co-morbidities and limitations to exercise. To ensure this criterion is achieved, the selection of activities should take a multi-faceted approach through the integration of numerous structured exercise methods. Whilst it is accepted that the gold standard for increasing muscle size and resultant strength is through PRT, both aerobic and balance focused training should be incorporated into a structured exercise program alongside PRT, not least for holistic health benefits. However, to ensure adherence and compliance to a structured exercise program, the focus should be individualised and programed to fit the specific needs and lifestyle of the individual, taking into account their physical status, group versus lone exercise preferences, including inclination or otherwise for activities in green outdoor spaces. The necessity to conduct conventional structured exercise is less of an issue in over 65's given that leisure-based dance classes are shown to increase both functional fitness and numerous physiological outcome measures.

Suggested further reading

A key aspect of physical exertion that has not been discussed in this book chapter to any extent is the engagement in sedentary behaviours. Indeed, it is increasingly becoming evident

24

248

that engagement in sedentary behaviours has distinct health effects, regardless of any

concurrent participation in physical activity the rest of the time. This effect is significant, not

least since sedentary behaviours tend to take up a greater proportion of modern daily living.

The publications below are readily available and provide up-to-date overviews of this

relatively new research area.

- Gladys Onambele-Pearson, Emma Bostock, Christopher Morse, Keith Winwood, Islay McEwan, Claire Stewart, 2015. Chapter: Sedentarism and the endo-metabolic system. In Sedentary Lifestyle: Predictive Factors, Health Risks and Physiological Implications. (Ed) Ahmad Alkhatib. Nova Science Publishers, New York [book in press]
- Gladys Onambele-Pearson, Jodi Ventre & Jon Adam Brown, 2017. Reducing sedentary behaviour among older people. Chapter 7.2. In The Palgrave Handbook of Ageing and Physical Activity Promotion. (Eds) Samuel Nyman. Palgrave Macmillan UK.
- Jorgen A. Wullems, Sabine M.P. Verschueren, Hans Degens, Christopher I. Morse, Gladys L. Onambélé, 2016. A review of the prevalence of sedentarism in older adults, its physiology/health impact and non-exercise mobility counter-measures. BSRA Special issue of the journal Biogerontology. 17(3):547-65. doi: 10.1007/s10522-016-9640-1
- Ryan D, Stebbings G and Onambele GL, 2015. The emergence of sedentary behaviour physiology and its effects on the cardiometabolic profile with ageing. [Age (Dordr). 2015 Oct;37(5):89. doi: 10.1007/s11357-015-9832-7. Epub 2015 Aug 28]

KEY ARGUMENTS

- The adherence and **palatability** of exercise is an important factor to consider when choosing the correct modality for older individuals.
- The dropout rate from **structured exercise** programs following 6 months has shown to be as high as 50% (Hong, Hughes, & Prohaska, 2008; Picorelli et al., 2014) in this age group.
- When comparing the compliance to, and palatability of, PRT vs. aerobic/endurance training, PRT is reported to be more **retentive** in elderly participants (Hong et al., 2008).
- It is suggested that the **lower impact forces** on joints during PRT compared to aerobic training and hence relatively lower discomfort, especially in participants who had osteoarthritis, may explain this retention (Picorelli et al., 2014).
- Further research should focus on understanding the **key to exercise adherence** in elderly individuals to ensure structured exercise continues for long-term sustainable success
- It is clear that a **holistic approach** (i.e. understanding the individual's physical, social and emotional reasoning for taking up or dropping out) is required in any exercise prescription in the elderly.

25

249

References

Ahtiainen, J. P., Pakarinen, A., Alen, M., Kraemer, W. J., & Hakkinen, K. (2003). Muscle hypertrophy, hormonal adaptations and strength development during strength training in strength-trained and untrained men. *European journal of applied physiology, 89*(6), 555-563. doi: 10.1007/s00421-003-0833-3

Al-Delaimy, W. K., von Muhlen, D., & Barrett-Connor, E. (2009). Insulinlike growth factor-1, insulinlike growth factor binding protein-1, and cognitive function in older men and women. *Journal of the American Geriatrics Society, 57*(8), 1441-1446. doi: 10.1111/j.1532-5415.2009.02343.x

Blodgett, J., Theou, O., Kirkland, S., Andreou, P., & Rockwood, K. (2015). The association between sedentary behaviour, moderate–vigorous physical activity and frailty in NHANES cohorts. *Maturitas, 80*(2), 187-191.

Boots, E. A., Schultz, S. A., Oh, J. M., Larson, J., Edwards, D., Cook, D., . . . Okonkwo, O. C. (2015). Cardiorespuratory fitness is associated with brain structure, cognition, and mood in a middle-aged cohort at risk for Alzheimer's disease. *Brain Imaging Behav, 9*(3), 639-649. doi: 10.1007/s11682-014-9325-9

Borst, S. E., De Hoyos, D. V., Garzarella, L., Vincent, K., Pollock, B. H., Lowenthal, D. T., & Pollock, M. L. (2001). Effects of resistance training on insulin-like growth factor-I and IGF binding proteins. *Medicine and science in sports and exercise, 33*(4), 648-653.

Bosy-Westphal, A., Eichhorn, C., Kutzner, D., Illner, K., Heller, M., & Müller, M. J. (2003). The age-related decline in resting energy expenditure in humans is due to the loss of fat-free mass and to alterations in its metabolically active components. *The Journal of nutrition, 133*(7), 2356-2362.

Bowler, D. E., Buyung-Ali, L. M., Knight, T. M., & Pullin, A. S. (2010). A systematic review of evidence for the added benefits to health of exposure to natural environments. *BMC Public Health, 10*, 456. doi: 10.1186/1471-2458-10-456

Brehmer, Y., Kalpouzos, G., Wenger, E., & Lovden, M. (2014). Plasticity of brain and cognition in older adults. *Psychol Res, 78*(6), 790-802. doi: 10.1007/s00426-014-0587-z

Brown, A. D., McMorris, C. A., Longman, R. S., Leigh, R., Hill, M. D., Friedenreich, C. M., & Poulin, M. J. (2010). Effects of cardiorespiratory fitness and cerebral blood flow on cognitive outcomes in older women. *Neurobiology of aging, 31*(12), 2047-2057. doi: 10.1016/j.neurobiolaging.2008.11.002

Brown, A. K., Liu-Ambrose, T., Tate, R., & Lord, S. R. (2009). The effect of group-based exercise on cognitive performance and mood in seniors residing in intermediate care and self-care retirement facilities: a randomised controlled trial. *British journal of sports medicine, 43*(8), 608-614. doi: 10.1136/bjsm.2008.049882

Brown, M., Sinacore, D. R., Ehsani, A. A., Binder, E. F., Holloszy, J. O., & Kohrt, W. M. (2000). Low-intensity exercise as a modifier of physical frailty in older adults. *Archives of physical medicine and rehabilitation, 81*(7), 960-965.

Bull, F. C., & the Expert Working Group. (2010). *Physical Activity Guidelines in the U.K.: Review and Recommendations*. Loughborough University.

Buman, M. P., Hekler, E. B., Haskell, W. L., Pruitt, L., Conway, T. L., Cain, K. L., . . . King, A. C. (2010). Objective light-intensity physical activity associations with rated health in older adults. *American journal of epidemiology, 172*(10), 1155-1165.

Buman, M. P., & King, A. C. (2010). Exercise as a Treatment to Enhance Sleep. *American Journal of Lifestyle Medicine, 4*, 500-514. doi: 10.1177/1559827610375532

Burley, S. D., Whittingham-Dowd, J., Allen, J., Grosset, J. F., & Onambele-Pearson, G. L. (2016). The Differential Hormonal Milieu of Morning versus Evening May Have an Impact on Muscle Hypertrophic Potential. *PLoS One, 11*(9), e0161500. doi: 10.1371/journal.pone.0161500

Cadore, E. L., Pinto, R. S., Bottaro, M., & Izquierdo, M. (2014). Strength and endurance training prescription in healthy and frail elderly. *Aging Dis, 5*(3), 183-195. doi: 10.14336/AD.2014.0500183

Campos, G. E., Luecke, T. J., Wendeln, H. K., Toma, K., Hagerman, F. C., Murray, T. F., . . . Staron, R. S. (2002). Muscular adaptations in response to three different resistance-training regimens: specificity of repetition maximum training zones. *European journal of applied physiology, 88*(1-2), 50-60. doi: 10.1007/s00421-002-0681-6

Caspersen, C. J., Powell, K. E., & Christenson, G. M. (1985). Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. *Public Health Rep, 100*(2), 126-131.

Ceci, R., & Hassmén, P. (1991). Self-monitored exercise at three different RPE intensities in treadmill vs field running. *Medicine and science in sports and exercise, 23*, 732-738.

Chang, Y. K., Tsai, C. L., Huang, C. C., Wang, C. C., & Chu, I. H. (2014). Effects of acute resistance exercise on cognition in late middle-aged adults: general or specific cognitive improvement? *Journal of science and medicine in sport / Sports Medicine Australia, 17*(1), 51-55. doi: 10.1016/j.jsams.2013.02.007

26

Cho, J., Shin, M. K., Kim, D., Lee, I., Kim, S., & Kang, H. (2015). Treadmill Running Reverses Cognitive Declines due to Alzheimer Disease. *Medicine and science in sports and exercise, 47*(9), 1814-1824. doi: 10.1249/MSS.0000000000000612

Colcombe, S., & Kramer, A. F. (2003). Fitness effects on the cognitive function of older adults: a meta-analytic study. *Psychol Sci, 14*(2), 125-130. doi: 10.1111/1467-9280.t01-1-01430

Crewther, B., Keogh, J., Cronin, J., & Cook, C. (2006). Possible stimuli for strength and power adaptation: acute hormonal responses. *Sports medicine, 36*(3), 215-238.

Daum, C., Cochrane, S., Fitzgerald, J., Johnson, L., & Buford, T. (2016). Exercise Interventions for Preserving Physical Function Among Cancer Survivors in Middle to Late Life. *The Journal of frailty & aging, 5*(4), 214.

Defina, L. F., Willis, B. L., Radford, N. B., Gao, A., Leonard, D., Haskell, W. L., . . . Berry, J. D. (2013). The association between midlife cardiorespiratory fitness levels and later-life dementia: a cohort study. *Annals of internal medicine, 158*(3), 162-168. doi: 10.7326/0003-4819-158-3-201302050-00005

Del Giorno, J. M., Hall, E. E., O'Leary, K. C., Bixby, W. R., & Miller, P. C. (2010). Cognitive function during acute exercise: a test of the transient hypofrontality theory. *J Sport Exerc Psychol, 32*(3), 312-323.

Dietrich, A. (2006). Transient hypofrontality as a mechanism for the psychological effects of exercise. *Psychiatry Res, 145*(1), 79-83. doi: 10.1016/j.psychres.2005.07.033

Diver, M. J., Imtiaz, K. E., Ahmad, A. M., Vora, J. P., & Fraser, W. D. (2003). Diurnal rhythms of serum total, free and bioavailable testosterone and of SHBG in middle-aged men compared with those in young men. *Clin Endocrinol (Oxf), 58*(6), 710-717.

Emerenziani, G. P., Gallotta, M. C., Meucci, M., Di Luigi, L., Migliaccio, S., Donini, L. M., . . . Guidetti, L. (2015). Effects of Aerobic Exercise Based upon Heart Rate at Aerobic Threshold in Obese Elderly Subjects with Type 2 Diabetes. *Int J Endocrinol, 2015*, 695297. doi: 10.1155/2015/695297

Enoka, R. M. (1994). *Neuromechanical basis of kinesiology* (2nd ed. ed.): Human Kinetics.

Etnier, J. L., & Chang, Y. K. (2009). The effect of physical activity on executive function: a brief commentary on definitions, measurement issues, and the current state of the literature. *J Sport Exerc Psychol, 31*(4), 469-483.

Fahlman, M. M., McNevin, N., Boardley, D., Morgan, A., & Topp, R. (2011). Effects of resistance training on functional ability in elderly individuals. *Am J Health Promot, 25*(4), 237-243. doi: 10.4278/ajhp.081125-QUAN-292

Farrell, L., Hollingsworth, B., Propper, C., & Shields, M. A. (2013). The Socioeconomic Gradient in Physical Inactivity in England. Centre for Market and Public Organisation: University of Bristol

Franklin, B. A., Bonzheim, K., Gordon, S., & Timmis, G. C. (1998). Safety of medically supervised outpatient cardiac rehabilitation exercise therapy: a 16-year follow-up. *Chest, 114*(3), 902-906.

Fried, L. P., Tangen, C. M., Walston, J., Newman, A. B., Hirsch, C., Gottdiener, J., . . . Burke, G. (2001). Frailty in older adults evidence for a phenotype. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 56*(3), M146-M157.

Frumkin, H. (2001). Beyond toxicity: human health and the natural environment. *Am J Prev Med, 20*, 234-240.

Fry, A. C. (2004). The role of resistance exercise intensity on muscle fibre adaptations. *Sports medicine, 34*(10), 663-679.

Fukagawa, N. K., Bandini, L. G., & Young, J. B. (1990). Effect of age on body composition and resting metabolic rate. *American Journal of Physiology-Endocrinology And Metabolism, 259*(2), E233-E238.

Garcia-Mesa, Y., Lopez-Ramos, J. C., Gimenez-Llort, L., Revilla, S., Guerra, R., Gruart, A., . . . Sanfeliu, C. (2011). Physical exercise protects against Alzheimer's disease in 3xTg-AD mice. *J Alzheimers Dis, 24*(3), 421-454. doi: 10.3233/JAD-2011-101635

Garcia, A., Haron, Y., Pulman, K., Hua, L., & Freedman, M. (2004). Increases in homocysteine are related to worsening of stroop scores in healthy elderly persons: a prospective follow-up study. *J Gerontol A Biol Sci Med Sci, 59*(12), 1323-1327.

Gauchard, G. C., Gangloff, P., Jeandel, C., & Perrin, P. P. (2003). Influence of regular proprioceptive and bioenergetic physical activities on balance control in elderly women. *J Gerontol A Biol Sci Med Sci, 58*(9), M846-850.

Geremia, J. M., Iskiewicz, M. M., Marschner, R. A., Lehnen, T. E., & Lehnen, A. M. (2015). Effect of a physical training program using the Pilates method on flexibility in elderly subjects. *Age, 37*(6), 119. doi: 10.1007/s11357-015-9856-z

Gladwell, V. F., Brown, D. K., Wood, C., Sandercock, G. R., & Barton, J. L. (2013). The great outdoors: how a green exercise environment can benefit all. *Extreme physiology & medicine, 2*, 3. doi: 10.1186/2046-7648-2-3

Grabara, M., & Szopa, J. (2015). Effects of hatha yoga exercises on spine flexibility in women over 50 years old. *J Phys Ther Sci, 27*(2), 361-365. doi: 10.1589/jpts.27.361

Granacher, U., Muehlbauer, T., & Gruber, M. (2012). A qualitative review of balance and strength performance in healthy older adults: impact for testing and training. *Journal of Aging Research, 2012*, 708905. doi: 10.1155/2012/708905

Greiwe, J. S., Cheng, B., Rubin, D. C., Yarasheski, K. E., & Semenkovich, C. F. (2001). Resistance exercise decreases skeletal muscle tumor necrosis factor alpha in frail elderly humans. *FASEB journal : official publication of the Federation of American Societies for Experimental Biology, 15*(2), 475-482. doi: 10.1096/fj.00-0274com

Griffin, E. W., Mullally, S., Foley, C., Warmington, S. A., O'Mara, S. M., & Kelly, A. M. (2011). Aerobic exercise improves hippocampal function and increases BDNF in the serum of young adult males. *Physiol Behav, 104*(5), 934-941. doi: 10.1016/j.physbeh.2011.06.005

Hakkinen, K., Newton, R. U., Gordon, S. E., McCormick, M., Volek, J. S., Nindl, B. C., . . . Kraemer, W. J. (1998). Changes in muscle morphology, electromyographic activity, and force production characteristics during progressive strength training in young and older men. *J Gerontol A Biol Sci Med Sci, 53*(6), B415-423.

Harridge, S. D., Kryger, A., & Stensgaard, A. (1999). Knee extensor strength, activation, and size in very elderly people following strength training. *Muscle Nerve, 22*(7), 831-839.

Harvey, J. A., Chastin, S. F., & Skelton, D. A. (2015). How Sedentary are Older People? A Systematic Review of the Amount of Sedentary Behavior. *Journal of aging and physical activity, 23*(3), 471-487. doi: 10.1123/japa.2014-0164

Hekler, E. B., Buman, M. P., Poothakandiyil, N., Rivera, D. E., Dzierzewski, J. M., Morgan, A. A., . . . Giacobbi, P. R. (2013). Exploring behavioral markers of long-term physical activity maintenance: a case study of system identification modeling within a behavioral intervention. *Health education & behavior : the official publication of the Society for Public Health Education, 40*, 51S-62S. doi: 10.1177/1090198113496787

Henwood, T. R., & Taaffe, D. R. (2005). Improved physical performance in older adults undertaking a short-term programme of high-velocity resistance training. *Gerontology, 51*(2), 108-115. doi: 10.1159/000082195

Holloszy, J. O., & Coyle, E. F. (1984). Adaptations of skeletal muscle to endurance exercise and their metabolic consequences. *J Appl Physiol Respir Environ Exerc Physiol, 56*(4), 831-838.

Hong, S. Y., Hughes, S., & Prohaska, T. (2008). Factors affecting exercise attendance and completion in sedentary older adults: a meta-analytic approach. *J Phys Act Health, 5*(3), 385-397.

Hopkins, D. R., Murrah, B., Hoeger, W. W., & Rhodes, R. C. (1990). Effect of low-impact aerobic dance on the functional fitness of elderly women. *Gerontologist, 30*(2), 189-192.

Housh, D. J., Housh, T. J., Johnson, G. O., & Chu, W. K. (1992). Hypertrophic response to unilateral concentric isokinetic resistance training. *Journal of applied physiology, 73*(1), 65-70.

Howald, H., Hoppeler, H., Claassen, H., Mathieu, O., & Straub, R. (1985). Influences of endurance training on the ultrastructural composition of the different muscle fiber types in humans. *Pflugers Archiv : European journal of physiology, 403*(4), 369-376.

Howe, T. E., Rochester, L., Neil, F., Skelton, D. A., & Ballinger, C. (2011). Exercise for improving balance in older people. *Cochrane Database Syst Rev*(11), CD004963. doi: 10.1002/14651858.CD004963.pub3

Hug, S.-M., Hartig, T., Hansmann, R., Seeland, K., & Hornung, R. (2009). Restorative qualities of indoor and outdoor exercise settings as predictors of exercise frequency. *Health & place, 15*, 971-980. doi: 10.1016/j.healthplace.2009.03.002

Hulmi, J. J., Kovanen, V., Selanne, H., Kraemer, W. J., Hakkinen, K., & Mero, A. A. (2009). Acute and long-term effects of resistance exercise with or without protein ingestion on muscle hypertrophy and gene expression. *Amino Acids, 37*(2), 297-308. doi: 10.1007/s00726-008-0150-6

Iversen, N., Krustrup, P., Rasmussen, H. N., Rasmussen, U. F., Saltin, B., & Pilegaard, H. (2011). Mitochondrial biogenesis and angiogenesis in skeletal muscle of the elderly. *Experimental gerontology, 46*(8), 670-678. doi: 10.1016/j.exger.2011.03.004

Jacobs, J. M., Cohen, A., Hammerman-Rozenberg, R., Azoulay, D., Maaravi, Y., & Stessman, J. (2008). Going outdoors daily predicts long-term functional and health benefits among ambulatory older people. *J Aging Health, 20*, 259-272. doi: 10.1177/0898264308315427

Jolliffe, J., Rees, K., Taylor, R. R., Thompson, D. R., Oldridge, N., & Ebrahim, S. (2001). Exercise-based rehabilitation for coronary heart disease. *The Cochrane Library*.

Kadi, F. (2008). Cellular and molecular mechanisms responsible for the action of testosterone on human skeletal muscle. A basis for illegal performance enhancement. *Br J Pharmacol, 154*(3), 522-528. doi: 10.1038/bjp.2008.118

Kamijo, K., Nishihira, Y., Higashiura, T., & Kuroiwa, K. (2007). The interactive effect of exercise intensity and task difficulty on human cognitive processing. *Int J Psychophysiol, 65*(2), 114-121. doi: 10.1016/j.ijpsycho.2007.04.001

28

252

Kanaley, J. A., Weltman, J. Y., Pieper, K. S., Weltman, A., & Hartman, M. L. (2001). Cortisol and growth hormone responses to exercise at different times of day. *The Journal of clinical endocrinology and metabolism, 86*(6), 2881-2889. doi: 10.1210/jcem.86.6.7566

Kaufman, J. M., & Vermeulen, A. (2005). The decline of androgen levels in elderly men and its clinical and therapeutic implications. *Endocr Rev, 26*(6), 833-876. doi: 10.1210/er.2004-0013

Kerr, J., Marshall, S., Godbole, S., Neukam, S., Crist, K., Wasilenko, K., . . . Buchner, D. (2012). The relationship between outdoor activity and health in older adults using GPS. *International Journal of Environmental Research and Public Health, 9*, 4615-4625.

Kerr, J., Sallis, J. F., Saelens, B. E., Cain, K. L., Conway, T. L., Frank, L. D., & King, A. C. (2012). Outdoor physical activity and self rated health in older adults living in two regions of the U.S. *Int J Behav Nutr Phys Act, 9*, 89. doi: 10.1186/1479-5868-9-89

King, N. A., Hopkins, M., Caudwell, P., Stubbs, R., & Blundell, J. E. (2008). Individual variability following 12 weeks of supervised exercise: identification and characterization of compensation for exercise-induced weight loss. *International Journal of Obesity, 32*(1), 177-184.

Kolber, M. J., Beekhuizen, K. S., Cheng, M. S., & Hellman, M. A. (2010). Shoulder injuries attributed to resistance training: a brief review. *Journal of strength and conditioning research / National Strength & Conditioning Association, 24*(6), 1696-1704. doi: 10.1519/JSC.0b013e3181dc4330

Komulainen, P., Kivipelto, M., Lakka, T. A., Savonen, K., Hassinen, M., Kiviniemi, V., . . . Rauramaa, R. (2010). Exercise, fitness and cognition – A randomised controlled trial in older individuals: The DR's EXTRA study. *European Geriatric Medicine, 1*(5), 266–272.

Kono, A., Kai, I., Sakato, C., & Rubenstein, L. Z. (2004). Frequency of going outdoors: a predictor of functional and psychosocial change among ambulatory frail elders living at home. *J Gerontol A Biol Sci Med Sci, 59*, 275-280.

Kraemer, W. J., Gordon, S. E., Fleck, S. J., Marchitelli, L. J., Mello, R., Dziados, J. E., . . . Fry, A. C. (1991). Endogenous anabolic hormonal and growth factor responses to heavy resistance exercise in males and females. *International journal of sports medicine, 12*(2), 228-235. doi: 10.1055/s-2007-1024673

Kraemer, W. J., Marchitelli, L., Gordon, S. E., Harman, E., Dziados, J. E., Mello, R., . . . Fleck, S. J. (1990). Hormonal and growth factor responses to heavy resistance exercise protocols. *Journal of applied physiology, 69*(4), 1442-1450.

Kraemer, W. J., & Ratamess, N. A. (2005). Hormonal responses and adaptations to resistance exercise and training. *Sports medicine, 35*(4), 339-361.

Larson, E. B., Yaffe, K., & Langa, K. M. (2013). New insights into the dementia epidemic. *N Engl J Med, 369*(24), 2275-2277. doi: 10.1056/NEJMp1311405

Lauretani, F., Maggio, M., Valenti, G., Dall'Aglio, E., & Ceda, G. P. (2010). Vitamin D in older population: new roles for this 'classic actor'? *The aging male : the official journal of the International Society for the Study of the Aging Male, 13*, 215-232. doi: 10.3109/13685538.2010.487551

Liu-Ambrose, T., & Donaldson, M. G. (2009). Exercise and cognition in older adults: is there a role for resistance training programmes? *British journal of sports medicine, 43*(1), 25-27. doi: 10.1136/bjsm.2008.055616

Liu, H. L., Zhao, G., Zhang, H., & Shi, L. D. (2013). Long-term treadmill exercise inhibits the progression of Alzheimer's disease-like neuropathology in the hippocampus of APP/PS1 transgenic mice. *Behav Brain Res, 256*, 261-272. doi: 10.1016/j.bbr.2013.08.008

Locher, J. L., Roth, D. L., Ritchie, C. S., Cox, K., Sawyer, P., Bodner, E. V., & Allman, R. M. (2007). Body mass index, weight loss, and mortality in community-dwelling older adults. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 62*(12), 1389-1392.

Luctkar-Flude, M. F., Groll, D. L., Tranmer, J. E., & Woodend, K. (2007). Fatigue and physical activity in older adults with cancer: a systematic review of the literature. *Cancer nursing, 30*(5), E35-E45.

Maas, J., van Dillen, S. M. E., Verheij, R. A., & Groenewegen, P. P. (2009). Social contacts as a possible mechanism behind the relation between green space and health. *Health & place, 15*, 586-595. doi: 10.1016/j.healthplace.2008.09.006

Maki, B. E., Holliday, P. J., & Topper, A. K. (1994). A prospective study of postural balance and risk of falling in an ambulatory and independent elderly population. *Journal of gerontology, 49*(2), M72-84.

Michael, Y. L., Green, M. K., & Farquhar, S. A. (2006). Neighborhood design and active aging. *Health & place, 12*, 734-740. doi: 10.1016/j.healthplace.2005.08.002

Morse, C. I., Thom, J. M., Mian, O. S., Birch, K. M., & Narici, M. V. (2007). Gastrocnemius specific force is increased in elderly males following a 12-month physical training programme. *Eur J Appl Physiol, 100*(5), 563-570. doi: 10.1007/s00421-006-0246-1

Morse, C. I., Thom, J. M., Mian, O. S., Muirhead, A., Birch, K. M., & Narici, M. V. (2005). Muscle strength, volume and activation following 12-month resistance training in 70-year-old males. *European journal of applied physiology, 95*(2-3), 197-204. doi: 10.1007/s00421-005-1342-3

Murayama, H., Yoshie, S., Sugawara, I., Wakui, T., & Arami, R. (2012). Contextual effect of neighborhood environment on homebound elderly in a Japanese community. *Arch Gerontol Geriatr, 54*, 67-71. doi: 10.1016/j.archger.2011.03.016

Nelson, M. E., Fiatarone, M. A., Morganti, C. M., Trice, I., Greenberg, R. A., & Evans, W. J. (1994). Effects of high-intensity strength training on multiple risk factors for osteoporotic fractures. A randomized controlled trial. *JAMA, 272*(24), 1909-1914.

Nelson, M. E., Rejeski, W. J., Blair, S. N., Duncan, P. W., Judge, J. O., King, A. C., . . . Castaneda-Sceppa, C. (2007a). Physical activity and public health in older adults: recommendation from the American College of Sports Medicine and the American Heart Association. *Med Sci Sports Exerc, 39*(8), 1435-1445. doi: 10.1249/mss.0b013e3180616aa2

Nelson, M. E., Rejeski, W. J., Blair, S. N., Duncan, P. W., Judge, J. O., King, A. C., . . . Castaneda-Sceppa, C. (2007b). Physical Activity and Public Health in Older Adults: Recommendation from the American College of Sports Medicine and the American Heart Association. *Medicine and science in sports and exercise, 39*(8), 1435-1445. doi: DOI 10.1249/mss.0b013e3180616aa2

Nevitt, M. C., Cummings, S. R., & Hudes, E. S. (1991). Risk factors for injurious falls: a prospective study. *Journal of gerontology, 46*(5), M164-M170.

Onambele-Pearson, G. L., Breen, L., & Stewart, C. E. (2010a). Influence of exercise intensity in older persons with unchanged habitual nutritional intake: skeletal muscle and endocrine adaptations. *Age, 32*(2), 139-153. doi: 10.1007/s11357-010-9141-0

Onambele-Pearson, G. L., Breen, L., & Stewart, C. E. (2010b). Influences of carbohydrate plus amino acid supplementation on differing exercise intensity adaptations in older persons: skeletal muscle and endocrine responses. *Age, 32*(2), 125-138. doi: 10.1007/s11357-009-9129-9

Onambele-Pearson, G. L., & Pearson, S. J. (2012). The magnitude and character of resistance-training-induced increase in tendon stiffness at old age is gender specific. *Age, 34*(2), 427-438. doi: 10.1007/s11357-011-9248-y

Onambele, G. L., Maganaris, C. N., Mian, O. S., Tam, E., Rejc, E., McEwan, I. M., & Narici, M. V. (2008). Neuromuscular and balance responses to flywheel inertial versus weight training in older persons. *Journal of biomechanics, 41*(15), 3133-3138. doi: 10.1016/j.jbiomech.2008.09.004

Organization, W. H. (2007). *WHO global report on falls prevention in older age.*

Organization, W. H. (2015). global reference list of 100 core health indicators.

Owen, N., Healy, G. N., Matthews, C. E., & Dunstan, D. W. (2010). Too much sitting: the population health science of sedentary behavior. *Exercise and sport sciences reviews, 38*(3), 105-113. doi: 10.1097/JES.0b013e3181e373a2

Palatini, P. (1988). Blood pressure behaviour during physical activity. *Sports medicine, 5*(6), 353-374.

Perrin, P. P., Gauchard, G. C., Perrot, C., & Jeandel, C. (1999). Effects of physical and sporting activities on balance control in elderly people. *British journal of sports medicine, 33*(2), 121-126.

Picorelli, A. M., Pereira, D. S., Felicio, D. C., Dos Anjos, D. M., Pereira, D. A., Dias, R. C., . . . Pereira, L. S. (2014). Adherence of older women with strength training and aerobic exercise. *Clinical interventions in aging, 9*, 323-331. doi: 10.2147/CIA.S54644

Piirtola, M., & Era, P. (2006). Force platform measurements as predictors of falls among older people - a review. *Gerontology, 52*(1), 1-16. doi: 10.1159/000089820

Pledge, D., Grosset, J. F., & Onambele-Pearson, G. L. (2011). Is there a morning-to-evening difference in the acute IL-6 and cortisol responses to resistance exercise? *Cytokine, 55*(2), 318-323. doi: 10.1016/j.cyto.2011.05.005

Pontifex, M. B., Hillman, C. H., Fernhall, B., Thompson, K. M., & Valentini, T. A. (2009). The effect of acute aerobic and resistance exercise on working memory. *Medicine and science in sports and exercise, 41*(4), 927-934. doi: 10.1249/MSS.0b013e3181907d69

Prakash, R. S., Voss, M. W., Erickson, K. I., Lewis, J. M., Chaddock, L., Malkowski, E., . . . Kramer, A. F. (2011). Cardiorespiratory fitness and attentional control in the aging brain. *Front Hum Neurosci, 4*, 229. doi: 10.3389/fnhum.2010.00229

Prata, M. G., & Scheicher, M. E. (2012). Correlation between balance and the level of functional independence among elderly people. *Sao Paulo Med J, 130*(2), 97-101.

Prestes, J., Shiguemoto, G., Botero, J. P., Frollini, A., Dias, R., Leite, R., . . . Perez, S. (2009). Effects of resistance training on resistin, leptin, cytokines, and muscle force in elderly post-menopausal women. *J Sports Sci, 27*(14), 1607-1615. doi: 10.1080/02640410903352923

Pretty, J., Griffin, M., Sellens, M., & Pretty, C. (2003). Green Exercise: Complementary Roles of Nature, Exercise and Diet in Physical and Emotional Well-Being and Implications for Public Health Policy., *1.*

Querido, J. S., & Sheel, A. W. (2007). Regulation of cerebral blood flow during exercise. *Sports medicine, 37*(9), 765-782.

30

Rantakokko, M., Mänty, M., Iwarsson, S., Törmäkangas, T., Leinonen, R., Heikkinen, E., & Rantanen, T. (2009). Fear of moving outdoors and development of outdoor walking difficulty in older people. *Journal of the American Geriatrics Society, 57*, 634-640. doi: 10.1111/j.1532-5415.2009.02180.x

Raudsepp, L. (2006). The relationship between socio-economic status, parental support and adolescent physical activity. *Acta Pædiatrica, 95*, 93-98.

Reeves, N. D., Narici, M. V., & Maganaris, C. N. (2003). Strength training alters the viscoelastic properties of tendons in elderly humans. *Muscle Nerve, 28*(1), 74-81. doi: 10.1002/mus.10392

Richardson, E. A., & Mitchell, R. (2010). Gender differences in relationships between urban green space and health in the United Kingdom. *Social science & medicine (1982), 71*, 568-575. doi: 10.1016/j.socscimed.2010.04.015

Rubenstein, L. Z. (2006). Falls in older people: epidemiology, risk factors and strategies for prevention. *Age Ageing, 35 Suppl 2*, ii37-ii41. doi: 10.1093/ageing/afl084

Rubenstein, L. Z., & Josephson, K. R. (2002). The epidemiology of falls and syncope. *Clinics in geriatric medicine, 18*(2), 141-158.

Santos, M. P., Esculcas, C., & Mota, J. (2004). The relationship between socioeconomic status and adolescents' organized and nonorganized physical activities. *Ped Exerc Sci, 16*, 210-218.

Schasberger, M. G., Hussa, C. S., Polgar, M. F., McMonagle, J. A., Burke, S. J., & Gegaris, A. J. (2009). Promoting and developing a trail network across suburban, rural, and urban communities. *Am J Prev Med, 37*, S336-344. doi: 10.1016/j.amepre.2009.09.012

Schmid, A. A., Van Puymbroeck, M., & Koceja, D. M. (2010). Effect of a 12-week yoga intervention on fear of falling and balance in older adults: a pilot study. *Arch Phys Med Rehabil, 91*(4), 576-583. doi: 10.1016/j.apmr.2009.12.018

Schoenfeld, B. J. (2013). Postexercise hypertrophic adaptations: a reexamination of the hormone hypothesis and its applicability to resistance training program design. *Journal of strength and conditioning research / National Strength & Conditioning Association, 27*(6), 1720-1730. doi: 10.1519/JSC.0b013e31828ddd53

Sedliak, M., Finni, T., Peltonen, J., & Hakkinen, K. (2008). Effect of time-of-day-specific strength training on maximum strength and EMG activity of the leg extensors in men. *J Sports Sci, 26*(10), 1005-1014. doi: 10.1080/02640410801930150

Serra, M. M., Alonso, A. C., Peterson, M., Mochizuki, L., Greve, J. M., & Garcez-Leme, L. E. (2016). Balance and Muscle Strength in Elderly Women Who Dance Samba. *PLoS One, 11*(12), e0166105. doi: 10.1371/journal.pone.0166105

Seynnes, O. R., de Boer, M., & Narici, M. V. (2007). Early skeletal muscle hypertrophy and architectural changes in response to high-intensity resistance training. *Journal of applied physiology, 102*(1), 368-373. doi: 10.1152/japplphysiol.00789.2006

Sherrington, C., Whitney, J. C., Lord, S. R., Herbert, R. D., Cumming, R. G., & Close, J. C. T. (2008). Effective exercise for the prevention of falls: a systematic review and meta-analysis. *Journal of the American Geriatrics Society, 56*, 2234-2243. doi: 10.1111/j.1532-5415.2008.02014.x

Solomon, T. P., Sistrun, S. N., Krishnan, R. K., Del Aguila, L. F., Marchetti, C. M., O'Carroll, S. M., . . . Kirwan, J. P. (2008). Exercise and diet enhance fat oxidation and reduce insulin resistance in older obese adults. *Journal of applied physiology, 104*(5), 1313-1319.

Sonntag, W. E., Ramsey, M., & Carter, C. S. (2005). Growth hormone and insulin-like growth factor-1 (IGF-1) and their influence on cognitive aging. *Ageing research reviews, 4*(2), 195-212. doi: 10.1016/j.arr.2005.02.001

St Leger, L. (2003). Health and nature-new challenges for health promotion. *Health promotion international, 18*, 173-175.

Suaya, J. A., Stason, W. B., Ades, P. A., Normand, S.-L. T., & Shepard, D. S. (2009). Cardiac rehabilitation and survival in older coronary patients. *Journal of the American College of Cardiology, 54*(1), 25-33.

Szucs, D., & Soltesz, F. (2010). Stimulus and response conflict in the color-word Stroop task: a combined electro-myography and event-related potential study. *Brain Res, 1325*, 63-76. doi: 10.1016/j.brainres.2010.02.011

Taaffe, D. R., Pruitt, L., Pyka, G., Guido, D., & Marcus, R. (1996). Comparative effects of high- and low-intensity resistance training on thigh muscle strength, fiber area, and tissue composition in elderly women. *Clin Physiol, 16*(4), 381-392.

Takano, T., Nakamura, K., & Watanabe, M. (2002). Urban residential environments and senior citizens' longevity in megacity areas: the importance of walkable green spaces. *Journal of epidemiology and community health, 56*, 913-918.

Taylor, D., Hale, L., Schluter, P., Waters, D. L., Binns, E. E., McCracken, H., . . . Wolf, S. L. (2012). Effectiveness of tai chi as a community-based falls prevention intervention: a randomized controlled

31

trial. *Journal of the American Geriatrics Society, 60*(5), 841-848. doi: 10.1111/j.1532-5415.2012.03928.x

Teas, J., Hurley, T., Ghumare, S., & Ogoussan, K. (2007). Walking Outside Improves Mood for Healthy Postmenopausal Women. *Clinical Medicine Insights. Oncology, 1*, 35-43.

Teo, W., Newton, M. J., & McGuigan, M. R. (2011). Circadian rhythms in exercise performance: implications for hormonal and muscular adaptation. *J Sports Sci Med, 10*(4), 600-606.

Thibaud, M., Bloch, F., Tournoux-Facon, C., Brèque, C., Rigaud, A. S., Dugué, B., & Kemoun, G. (2012). Impact of physical activity and sedentary behaviour on fall risks in older people: a systematic review and meta-analysis of observational studies. *Eur Rev Aging Phys Act, 9*(1), 5-15. doi: 10.1007/s11556-011-0081-1

Thomas, D., Bouchard, C., Church, T., Slentz, C., Kraus, W., Redman, L., . . . Westerterp, K. (2012). Why do individuals not lose more weight from an exercise intervention at a defined dose? An energy balance analysis. *Obesity Reviews, 13*(10), 835-847.

Thompson Coon, J., Boddy, K., Stein, K., Whear, R., Barton, J., & Depledge, M. H. (2011). Does participating in physical activity in outdoor natural environments have a greater effect on physical and mental wellbeing than physical activity indoors? A systematic review. *Environmental science & technology, 45*, 1761-1772. doi: 10.1021/es102947t

Townsend, N., Bhatnagar, P., Wilkins, E., Wickramasinghe, K., & Rayner, M. (2015). Cardiovascular disease statistics 2015. In E. Dicks (Ed.). London.

Van Pelt, R. E., Jones, P. P., Davy, K. P., DeSouza, C. A., Tanaka, H., Davy, B. M., & Seals, D. R. (1997). Regular Exercise and the Age-Related Decline in Resting Metabolic Rate in Women 1. *The Journal of Clinical Endocrinology & Metabolism, 82*(10), 3208-3212.

Velloso, C. P. (2008). Regulation of muscle mass by growth hormone and IGF-I. *Br J Pharmacol, 154*(3), 557-568. doi: 10.1038/bjp.2008.153

Vidoni, E. D., Johnson, D. K., Morris, J. K., Van Sciver, A., Greer, C. S., Billinger, S. A., . . . Burns, J. M. (2015). Dose-Response of Aerobic Exercise on Cognition: A Community-Based, Pilot Randomized Controlled Trial. *PLoS One, 10*(7), e0131647. doi: 10.1371/journal.pone.0131647

Viña, J., Salvador-Pascual, A., Tarazona-Santabalbina, F. J., Rodriguez-Mañas, L., & Gomez-Cabrera, M. C. (2016). Exercise training as a drug to treat age associated frailty. *Free Radical Biology and Medicine, 98*, 159-164.

Voss, M. W., Nagamatsu, L. S., Liu-Ambrose, T., & Kramer, A. F. (2011). Exercise, brain, and cognition across the life span. *Journal of applied physiology, 111*(5), 1505-1513. doi: 10.1152/japplphysiol.00210.2011

Williams, K. N., & Kemper, S. (2010). Interventions to reduce cognitive decline in aging. *J Psychosoc Nurs Ment Health Serv, 48*(5), 42-51. doi: 10.3928/02793695-20100331-03

Wilson, M.-M. G., & Morley, J. E. (2003). Invited review: aging and energy balance. *Journal of applied physiology, 95*(4), 1728-1736.

Woodyard, C. (2011). Exploring the therapeutic effects of yoga and its ability to increase quality of life. *Int J Yoga, 4*(2), 49-54. doi: 10.4103/0973-6131.85485

Wu, H. Y., Tu, J. H., Hsu, C. H., & Tsao, T. H. (2016). Effects of Low-Impact Dance on Blood Biochemistry, Bone Mineral Density, the Joint Range of Motion of Lower Extremities, Knee Extension Torque, and Fall in Females. *Journal of aging and physical activity, 24*(1), 1-7. doi: 10.1123/japa.2014-0088

32

Appendix II

Conference presentation(s):

Healthy Ageing from Molecules to Organisms – 18-20 May 2015, Hinxton, UK.

A novel triaxial accelerometer data algorithm for quantifying physical activity and sedentary behaviour both in young and older adults.

Jorgen A. Wullems[1], Christopher I. Morse[1], Hans Degens[2], Sabine M.P. Verschueren[3], Gladys Onambélé-Pearson[1].

[1]Department of Exercise and Sport Science, Institute for Performance Research, Manchester Metropolitan University, Crewe, UK; [2]School of Healthcare Science, Manchester Metropolitan University, Manchester, UK; [3]Musculoskeletal rehabilitation research group, Department of Rehabilitation Sciences, KU Leuven, Leuven, Belgium.

Background: Accelerometry is a promising avenue to quantify accurately total daily activity, classified as physical activity (PA) and sedentary behaviour (SB). Both PA and SB independently have distinct health effects. Therefore, accurate measurement of PA and SB is key to designing individualised lifestyle recommendations. Although a non-age-specific algorithm would be ideal for this purpose, it is a challenge to develop a highly accurate one due to differences between age groups in energy expenditure levels per type of PA and SB.

Objective: To examine the feasibility of applying a novel, non-age-specific algorithm using both cut-off points and postural orientation, to monitor PA and SB objectively.

Methods: Triaxial accelerometer (thigh-mounted) and gas analysis data were collected from two participants (aged 23 and 73, respectively) during a set of laboratory-based standardised activities of daily living (e.g. lying down, sitting, standing and walking). In addition, 24-hour accelerometer data was collected for both participants. A novel algorithm that includes total movement (TM) calculation, TM cut-off points and postural orientation was applied to the laboratory-based accelerometer data to determine the accuracy in assessing activities when using either age-specific (young or old) or non-age-specific (pooled) cut-off points. The 24-hour samples were used to identify differences in PA and SB outcomes between the different cut-off points.

Results: The novel algorithm showed high accuracy and minimal between-subject differences when applied to the laboratory-based accelerometer data using either age-specific or non-age-specific cut-off points. Moreover, excellent absolute agreement per each participant existed between the 24-hour sample-based PA and SB outcomes using the different cut-off points.

Conclusions: Based on this preliminary study, a novel algorithm that includes non-age-specific cut-off points and postural orientation is a promising development towards objective computation of daily PA and SB levels. Ultimately, this algorithm would help quantify the effects of ageing on physiological function, independent of daily activity factors.

International Conference on Movement and Nutrition in Health and Disease, 12-14 June 2015, Regensburg, Germany.

Algorithm development for objectively monitoring physical activity and sedentary behaviour.

Authors: Jorgen A. Wullems[1], Christopher I. Morse[1], Hans Degens[2], Sabine M.P. Verschueren[3] and Gladys Onambélé-Pearson[1].

Authors' affiliations: [1]Department of Exercise and Sport Science, Institute for Performance Research, Manchester Metropolitan University, Crewe, UK.

[2]School of Healthcare Science, Manchester Metropolitan University, Manchester, UK.

[3]Musculoskeletal rehabilitation research group, Department of Rehabilitation Sciences, KU Leuven, Leuven, Belgium.

Key words: Physical activity, sedentary behaviour, accelerometer, algorithm.

Background: Total daily activity can be classified as either physical activity (PA) or sedentary behaviour (SB) [1]. Each is thought to have health effects, independent of the other [2]. To obtain insight into a person's long-term health prognosis, it is important to monitor daily behaviour accurately, accounting for both PA and SB. Accelerometry is a promising avenue to accurately quantify both PA and SB [3]. Nevertheless, this technique has its limitations in that there is no current consensus for a gold-standard device or method of data analysis [3].

Objectives: To develop an algorithm using both cut-off points and postural orientation to monitor PA and SB objectively.

Methods: Triaxial accelerometer data of a 73-year old woman was collected using a thigh-mounted device during a standardised gas analysis protocol of free-living activities in a laboratory setting and during 24 hours in free-living conditions. These data were used to develop an algorithm that calculates multiple accelerometer outcomes; activity counts (AC; generally accepted and most commonly used), sum of vector magnitudes (SVM; software-based outcome of the device) and total movement (TM; derived from the standard deviation values of the three accelerometer axes at discrete time points). All outcomes were used to create different algorithms according to the following steps: 1) The three

outcomes were correlated to energy expenditure (EE); 2) Cut-off points (SB vs. PA) for each outcome were defined using two different methods (receiver operating curve (ROC) vs. line-of-best-fit); 3) The impact of using postural orientation (thigh inclination) as a filter before or after the cut-off point analysis in the algorithm, was determined. As a result, twelve different algorithms were created. To determine the most accurate algorithm, all were applied to the laboratory-based data sample. The 24-hour data sample was used to present potential outcomes based on the optimal algorithm, including time in PA and SB, and number of SB breaks.

Results: TM correlated best with EE, whilst cut-off points were most accurately calculated with the line-of-best-fit. Using postural orientation as a filter before cut-off point analysis removes most of the noise and increases algorithm accuracy. When applying all twelve algorithms to the 24-hour data sample, the algorithm using TM, the cut-off points calculated with the line-of-best fit and using postural orientation as a filter before cut-off point analysis, proved optimal. Based on this algorithm, an overview of daily PA and SB pattern was calculated (Figure 1).
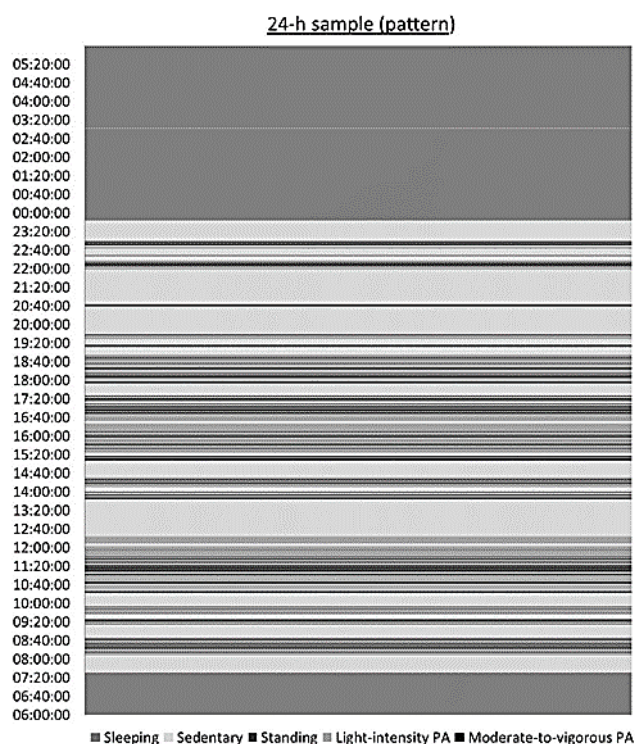

Figure 1. Bar chart representing 24-hour PA & SB pattern.

Conclusions: Cut-off points and postural orientation are important factors in objectively monitoring PA and SB, especially when added to an algorithm using TM, which results in high accuracy. This finding is important not only for investigating total daily activity in

humans, but also improved understanding of the exact health benefits of both PA and SB. Since this was a preliminary study, the algorithm should be further tested and defined.

References:

1. Lord S, Chastin SFM, McInnes L, Little L, Briggs P, Rochester L (2011). Exploring patterns of daily physical and sedentary behaviour in community-dwelling older adults. Age Ageing 40:205-210.

2. Gorman E, Hanson HM, Yang PH, Khan KM, Liu-Ambrose T, Ashe MC (2014). Accelerometry analysis of physical activity and sedentary behavior in older adults: a systematic review and data analysis. Eur Rev Aging Phys Act 11:35-49.

3. Pedišić Ž, Bauman A (2014). Accelerometer-based measures in physical activity surveillance: current practices and issues. British journal of sports medicine:bjsports-2013-093407.

WHAT IS A PHYSIOLOGICALLY RELEVANT OUTCOME MEASURE AND EPOCH LENGTH IN OBJECTIVELY QUANTIFYING SEDENTARISM?

Wullems Jorgen A.[1], Morse Christopher I.[1], Degens Hans[1,2], Verschueren Sabine M.P.[3], Onambélé-Pearson Gladys[1]

jorgen.a.wullems@stu.mmu.ac.uk, [1]Manchester Metropolitan University, UK; [2]Lithuanian Sports University, Lithuania; [3]University of Leuven, Belgium

<u>Relevance of the research.</u> Total daily activity can be classified in terms degree of sedentary behaviour (SB) or physical activity levels (PA). Both SB and low PA have distinct negative effects on health and it is therefore important to accurately monitor daily mobility behaviour to obtain insight into a person's long-term health prognosis (1,2). Although accelerometry is preferred in most studies, there is no current consensus for a gold-standard device, or method of data analysis (3). Indeed, use of inappropriate devices or data analysis has the potential danger of misinterpreting the true pattern of daily behaviour (2). Accurate measurement of SB and PA is key to designing individualised lifestyle recommendations (4). This is of importance in older adults (≥65 years of age) since they are the most sedentary and less physically active age group (5). We believe that using thigh-mounted triaxial accelerometry combined with an algorithm that includes a physiologically relevant outcome measure and epoch length can monitor objectively and accurately SB and PA. This objective approach will eventually help to understand how SB and PA are related to healthy ageing (6).

The <u>aim</u> of the research is to refine an algorithm to monitor objectively SB and PA in elderly, and the <u>objective</u> is to determine the physiologically relevant outcome measure and epoch length to be included.

<u>Research methods and organization.</u> Triaxial accelerometer data (thigh-mounted bilaterally; 60 Hz sampling rate) and expired gas were collected from six participants (algorithm-refining group: n=5, aged 67-82 years; 2 women; body mass index (BMI) 21.6-35.8 $kg \cdot m^{-2}$ & algorithm validation group: n=1, aged 72 years; female; BMI 23.8 $kg \cdot m^{-2}$) during a set of laboratory-based standardised activities of daily living (three minutes each) of different intensities; such as lying down, sitting, standing and walking. Expired gas was

collected during the final minute of each activity. These samples were used to estimate energy expenditure (EE) and calculate the metabolic equivalent (MET) of the simulated activities of daily living. The accelerometer data acquired during the same minute was analysed using 18 different combinations of epoch lengths (1, 5, 10, 15, 30 and 60 seconds) and outcome measures (activity counts (AC; summed acceleration signals divided by device resolution)), sum of vector magnitude (SVM) and total movement (TM)). The outcome of each combination was plotted against EE to 1) explore correlations, and 2) calculate algorithm cut-off points according to 1.5 and 3.0 MET thresholds. For these purposes, data from the algorithm-refining group was used only. Next, all 18 algorithms (using both thigh orientation and cut-off points) were applied to the accelerometer data from the algorithm validation group only. The applied algorithms classified each epoch as either, SB, standing, light-intensity PA (LIPA) or moderate-to-vigorous PA (MVPA). To investigate which algorithm (and thus outcome measure and epoch length) was most valid, agreement with the actual performed activity per epoch was determined.

Results and discussion. Correlations coefficients found for SVM and TM were >0.70 regardless of epoch length, whilst AC showed a correlation coefficient of 0.79 for the 1 second epoch length, but <0.56 for the others. Excellent agreement (100%) with the actual performed activity per epoch was shown when classifying SB, irrespective of outcome measure or epoch length. Standing was difficult to detect when using AC (highest agreement 7%, while 100% agreement was found for both SVM and TM regardless of epoch length, with the exception of using TM/30 seconds epoch (75%). High agreement was found for classifying PA, independent of epoch length (AC: 75-86%; SVM: 96-100%; TM: all 100%). When focusing on PA intensity, LIPA seems more difficult to correctly classify than MVPA, regardless of epoch length (AC: 0-34% vs. 85-100%; SVM: 37-75% vs. all epochs 100%; TM: 0-36% vs. all epochs 100%). Inferior results when using AC could be due to the lack of overall variation in outcome measure, resulting in overlapping activity type clusters. The fact that preliminary data were used might explain the under- and overestimation of LIPA and MVPA respectively.

Conclusions. The preliminary results of this study suggest that the optimal epoch length for determining sedentarism is dependent on the eventual outcome measure.

References:

1.   Lord S, Chastin SFM, McInnes L, Little L, Briggs P, Rochester L (2011). Exploring patterns of daily physical and sedentary behaviour in community-dwelling older adults. Age Ageing, 40 (2), 205-210.

2.   Gorman E, Hanson HM, Yang PH, Khan KM, Liu-Ambrose T, Ashe MC (2014). Accelerometry analysis of physical activity and sedentary behavior in older adults: a systematic review and data analysis. Eur Rev Aging Phys Act, 11, 35-49.

3.   Pedišić Ž, Bauman A (2015). Accelerometer-based measures in physical activity surveillance: current practices and issues. Br J Sports Med, 49 (4), 219-223.

4.   Rezende LF, Rey-López JP, Matsudo VK, do Luiz O (2014). Sedentary behavior and health outcomes among older adults: a systematic review. BMC Public Health, 14, 333.

5.   Gennuso KP, Gangnon RE, Matthews CE, Thraen-Borowski KM, Colbert LH (2013). Sedentary behavior, physical activity, and markers of health in older adults. Med Sci Sports Exerc, 45 (8), 1493-1500.

6.   Visser M, Koster A (2013). Development of a questionnaire to assess sedentary time in older persons--a comparative study using accelerometry. BMC Geriatr, 13, 80.

The association of sedentary behaviour with muscle-tendon properties in older adults

Jorgen Wullems (MMU, UK & KU Leuven, Belgium)

Supervisory team:
Dr Gladys Pearson (MMU, UK)
Prof Sabine Verschueren (KU Leuven, Belgium)
Dr Christopher Morse (MMU, UK)
Prof Hans Degens (MMU, UK)

Manchester Metropolitan University

MOVE-AGE Annual conference 2017

KU LEUVEN