University of Groningen

Adaptability of gait and balance across the adult lifespan

Vervoort, Danique

DOI:
[10.33612/diss.144620201](https://doi.org/10.33612/diss.144620201)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2020

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):
Vervoort, D. (2020). *Adaptability of gait and balance across the adult lifespan*. [Thesis fully internal (DIV), University of Groningen]. University of Groningen. <https://doi.org/10.33612/diss.144620201>

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

ADAPTABILITY OF GAIT AND BALANCE ACROSS THE ADULT LIFESPAN

Danique Vervoort

COLOPHON

This PhD-thesis was part of an international cooperation between the University of Groningen (Netherlands) and the University of Grenoble-Alpes (France).

The experiments described in chapter 2-5 were conducted at the Department for Human Movement Sciences, University Medical Center Groningen, the Netherlands.

PhD training was facilitated by the research institute School of Health Research (SHARE), part of the Graduate School of Medical Sciences Groningen.

The printing of this thesis was financially supported by:

- University of Groningen
- University Medical Center Groningen
- Research Institute School of Health Research (SHARE)
- Delsys Europe
- Stichting Beatrixoord Noord-Nederland

Paranimphs: Marika Leving
Natascha Assies

Cover and layout design: Ellen Beck
Printed by: Netzdruk

ISBN: 978-94-034-2796-6 (*verschijningsvorm: Eboek : PDF zonder DRM*)

ISBN: 978-94-034-2795-9 (*verschijningsvorm: Boek*)

© Copyright 2020, Danique Vervoort

All rights reserved. No part of this publication may be reproduced or transmitted in any form or by any means, electronic and mechanical, including photocopying, recording or any information storage or retrieval system, without written permission from the author.

university of
 groningen

Adaptability of gait and balance across the adult lifespan

PhD thesis

to obtain the degree of PhD at the
 University of Groningen
 on the authority of the
 Rector Magnificus Prof. C. Wijmenga
 and in accordance with
 the decision by the College of Deans.

This thesis will be defended in public on
 Monday 30 November 2020 at 14.30 hours

by

Danique Vervoort

born on 7 September 1993
 in Sint-Oedenrode

Supervisors

Dr. C.J.C. Lamothe

Prof. dr. T. Hortobagyi

Co-supervisors

Dr. N. Vuillerme

Dr. A.R. den Otter

Assessment Committee

Prof. dr. W. Zijlstra

Prof. dr. M. Pijnappels

Prof. dr. L.H.V. van der Woude

TABLE OF CONTENTS

CHAPTER 1	
General introduction	6
CHAPTER 2	
Multivariate analyses and classification of inertial sensor data to identify aging effects on the Timed-Up-and-Go test	14
CHAPTER 3	
Effects of aging and task prioritization on split-belt gait adaptation	34
CHAPTER 4	
Do gait and muscle activation patterns change at middle-age during split-belt adaptation?	52
CHAPTER 5	
Adaptive control of dynamic balance across the adult lifespan	72
CHAPTER 6	
General discussion	88
CHAPTER 7	
Appendices	98
· Summary	
· Samenvatting	
· Résumé	
· Dankwoord	
· About the author	
· Scientific output	
· Conference contributions	
· Research institute SHARE

CHAPTER 1

General Introduction

HISTORY OF HUMAN WALKING RESEARCH

Human walking has evolved over millions of years, starting from mammalian quadrupedal gait. The first human species that has been confirmed to occasionally walk upright, was the *Ardipithecus ramidus* about 4.4 million years ago. It then took several millions of years before a human species, the *Homo erectus*, became completely bipedal, which was about 1.89 million years ago [1]. The evolutionary origin of bipedal human gait is unclear but the most likely reason for the emergence of bipedal gait is the freeing of the upper extremities for tool use. Ever since humans are the only primates to walk this way. Therefore, it is no surprise that humans have been fascinated with upright walking as a form of locomotion for a long time. Historically, the first scientist to study human walking, also termed 'gait', was Giovanni Borelli. In 1680, his posthumous publication "De motu animalium" described the first theory on the biomechanics of walking [2]. Ever since the field of gait research has evolved. Some of the early milestones in gait research include the first description of the gait cycle in 1836 by the Weber brothers [3] and the first description of muscle activation during walking in 1927 by Scherb [4].

Gait has been previously defined as 'A method of locomotion involving the use of the two legs, alternately, to provide both support and propulsion, with at least one foot being in contact with the ground at all times' [5]. Human walking comprises distinct cycles of the lower limbs, which is described as 'the time interval between two successive occurrences of one of the repetitive events of walking, which starts at the instant at which one foot contacts the ground (heel-strike)' [5]. Within the gait cycle, only one foot is in contact with the ground for the largest part of the time, which places a high demand on dynamic balance control [6]. Control of dynamic balance is essential to remain upright while walking and prevent falls [7].

To fully understand gait, the contribution of the neuromuscular system to gait also needs to be assessed. The activation of muscles during different parts of the gait cycle drives the limbs to move from one position to the next in the gait cycle. All these muscles have distinct roles in movements, for example, the m. tibialis anterior mainly drives dorsiflexion of the foot during walking [8,9]. Although the individual muscles have distinct roles, muscles can also be activated simultaneously and generate specific movements. Simultaneously activated muscles are functional muscle groups. These functional muscle groups are controlled by a common activation pattern that allows the central nervous system to simplify neuromuscular control [10].

GAIT ADAPTABILITY

During walking, internal and external perturbations, such as sudden arm movements or walking on a slippery surface, pose challenges to the locomotor system. In order to respond to such challenges, adaptability of gait is necessary. Gait adaptation is defined as the capacity to adjust the gait pattern to environmental challenges or other task demands [11]. Adaptations have to be implemented in the gait pattern, and thus place a demand on the control of dynamic balance and the maintenance of forward progression [12]. When adaptability of gait is impaired, walking ability is more vulnerable to in- and external perturbations and the risk of falling increases [11]. This makes gait adaptability a prerequisite for retaining independent mobility.

Two main balance control mechanisms have been suggested to underlie gait adaptation, i.e., proactive and reactive control mechanisms [13]. Proactive control consists of adaptive responses before en-

countering a potential threat to balance control, and reactive control consists of adaptive responses to regain balance after a perturbation, for which a couple of steps are needed to recover [13]. With the use of these two control mechanisms, gait can be adapted not only to sudden perturbations but also to more continuous and sustained perturbations, such as walking on an unstable surface. In this thesis, gait adaptability refers to both the immediate adaptive responses and the continuous adaptation to a sustained perturbation. In Chapters 3-5, gait adaptability will be assessed with a split-belt treadmill, where gait is perturbed by imposing asymmetric belt speeds.

HEALTHY AGING

The human life expectancy has increased dramatically since the first species that walked bipedal and will continue to increase [14]. As a result of the increase in the proportion of the older population, 'healthy aging' has received substantial interest over the last century. Healthy aging is a focus point of the World Health Organization and is described as "the process of developing and maintaining the functional ability that enables wellbeing in older age" [15]. The main focus of healthy aging as proposed there is that older adults are able to do what they value throughout their lives. Since a clean bill of health is not a prerequisite for healthy aging, healthy aging is associated with age-related deterioration in sensory, neuromuscular and cognitive function [16–18]. This deterioration will eventually influence mobility, activities of daily living and quality of life [19].

CHANGES IN GAIT (ADAPTABILITY) AND BALANCE PERFORMANCE DUE TO HEALTHY AGING

The aging process modifies gait and balance performance. The walking pattern of older adults is characterized by slower gait speed, prolonged stance and double support times, shortened swing times, and shorter and wider steps [20,21]. These changes in the gait pattern of older adults likely affect the control of dynamic balance, leading to an increased risk of falls [11].

Combining walking with a concurrently performed cognitive task, i.e., dual-tasking, could magnify the detrimental effects of age on gait. When humans walk and perform a cognitive task such as talking, counting, or recalling past events, gait becomes modified because gait and certain cognitive functions partly rely on the same cortical resources [22]. Older adults either show a deteriorated performance on motor-cognitive dual-tasking [23] or choose to prioritize gait over the cognitive task [24,25], to safely move from one place to the next.

Healthy aging also modifies the activation of muscles during gait. Older adults show a distal-to-proximal shift in muscle activation [26], meaning that for instance, they depend less on activation of the m. soleus to push off, but increase activation of the hamstring muscles during the stance phase. Co-activation between agonist-antagonist muscle pairs is also increased in older adults [26]. This increased co-activation, combined with less separated bursts of activation between agonist-antagonist muscles [27], stiffens the limb during single support to increase stability during walking.

All these age-related effects on gait and balance are also likely to affect gait adaptability. Retaining the ability to adapt gait to sustained perturbations could be essential, especially for older adults, to maintain walking balance [28].

LIFESPAN APPROACH TO ASSESS AGE-RELATED CHANGES IN GAIT ADAPTABILITY

The effects of age on gait of older adults (65+) compared to young adults (18-30) have been documented in several studies. Surprisingly, the age group of middle-aged adults between 30 and 65 years old is often overlooked, while this age group represents the transitions in gait and balance from young to older adults. Understanding what precedes the changes at older age could be essential to increase our knowledge of age-related changes in gait and balance.

A reason why this age group could represent a period during which there are already age-related changes in normal gait is that the onset of aging on physiological processes already starts during mid-life. There are several changes in the sensorimotor system that start as early as the age of 30 years old. Reduction in muscle mass and muscle function starts after the second decade [29], and the rate of reductions further accelerates after the age of 50 by 1-2% per year [30]. This leads to a reduction in maximal voluntary leg force by 1-2% per year after age 50 [31,32]. Such early changes in physiological functioning could affect gait and balance performance as early as middle-age. Therefore, middle-aged adults could show the first signs of age-related changes in gait and balance.

The transitions in gait and balance with age could be shown by including data across the lifespan. A lifespan study has the advantage of showing data over the age continuum, allowing us to pinpoint the development of possible changes in gait adaptability. It has already been shown that gait speed and several other spatiotemporal parameters gradually decline with age while walking [21].

ASSESSMENT OF GAIT (ADAPTABILITY) AND BALANCE PERFORMANCE SMART DEVICES TO ASSESS GAIT AND BALANCE

With the current developments in technology, it is becoming feasible to also perform measurements without the use of a full laboratory set-up. One of these developments in measurement technology is the use of smart devices. Smart devices, such as inertial measurement units (IMU), are cheap, highly available and can be used independently of the location. Several studies have already shown that the use of IMU's can differentiate gait performance of healthy young and older adults [33,34].

Using smart devices allows for objective quantification and more detailed measurement of performances on clinical tests, such as the Timed-Up-and-Go (TUG). The TUG consists of tasks such as standing up, walking and turning, which are part of many activities during daily life. A combination of a smart device and the TUG could provide interesting and comprehensive in-depth information on gait and balance performance. This so-called instrumented TUG (iTUG) can classify a variety of pathologies versus healthy older adults [35–37]. Extending the use of the iTUG to assess healthy aging by distinguishing age groups of healthy adults would allow us to build a model that shows the effects of aging and can differentiate age groups based on gait and balance in clinical practice.

ADAPTATION OF GAIT AND BALANCE ON A SPLIT-BELT TREADMILL

In this thesis, gait adaptability and balance performance were assessed in the laboratory set-up by using the split-belt walking paradigm. With split-belt walking, one leg moves faster than the other leg due to belt speed differences. This initially causes asymmetric gait, which has to be adapted over time. The split-belt treadmill thus allows us to study the initial response to the belt speed perturbation, as well as locomotor adaptations to the sustained belt speed differences, while walking in a controlled

environment [38]. The split-belt walking paradigm has been popular in recent years [39–41] and has been used in studies from the early nineties [42] to study locomotion and locomotor adaptation in healthy individuals as well as in pathologies.

OBJECTIVES OF THIS THESIS

Most of the existing literature on the effects of age on gait (adaptability) only focusses on the effects of age later in life, i.e., in old age. It is essential to increase our knowledge of what precedes the changes in gait at older age. Therefore, this thesis aimed to shed light on the effects of age adaptability on gait and balance across the adult lifespan. Adaptability of gait adaptability and balance was assessed with two different tasks, the iTUG, and split-belt walking. By studying these two different tasks, this thesis will add more fundamental knowledge on the effects of age on gait adaptability, as well as a way to transfer this fundamental knowledge to differentiate age groups based on gait and balance in clinical practice.

To achieve the main objective of this thesis, the effects of age on adaptability of gait and balance across the adult lifespan, three sub-objectives were addressed. More specifically the sub-objectives were: 1) To gain insights into the effects of the natural, healthy aging process on gait and balance performance across the adult lifespan, with an emphasis on gait adaptation (cross-sectional design; Chapters 2-5); 2) To develop a model using gait and balance parameters of the iTUG that can discriminate different age groups, e.g., healthy young adults and older adults (Chapter 2); 3) To investigate possible underlying mechanisms of the age-related effects on gait adaptability (Chapters 3-4).

OUTLINE OF THIS THESIS

In **Chapter 2**, we examine which gait variables during the iTUG are associated with changes in performance across the adult lifespan. Subsequently, we determine how well these identified iTUG variables can distinguish two age groups across the lifespan. **Chapter 3** focusses on the adaptability of gait, and the effects of older age on adaptability and the prioritization of tasks. **Chapter 4** explains how muscle activation patterns during adaptation are affected at middle-age. These muscle activation patterns are also studied in relation to the adaptation of gait. **Chapter 5** describes how adaptive control of dynamic balance changes across the adult lifespan. Finally, the general discussion in **Chapter 6** provides a summary of the main results of the thesis and these results are discussed with a focus on the implications of this research.

REFERENCES

- Wayman E. Becoming human: the evolution of walking upright. In: Smithsonian. 2012.
- Borelli GA. *De motu animalium*. 1680.
- Weber W, Weber E. *Mechanik der menschlichen gewerkzeuge*. Göttingen: Dieterich; 1836.
- Abu-Faraj ZO, Harris GF, Smith PA, Hassani S. Human gait and clinical movement analysis. Wiley Encyclopedia of Electrical and Electronics Engineering. NY, USA: John Wiley & Sons, Inc.; 2015. pp. 1–34.
- Levine D, Richards J, Whittle M. Whittle's gait analysis. Elsevier Health Sciences UK; 2012.
- Hof AL, Gazendam MCJ, Sinke WE. The condition for dynamic stability. *J Biomech*. 2005;38: 1–8.
- Kuo DA, Donelan MJ. Dynamic principles of gait and their clinical implications. *Phys Ther*. 2010;90: 157–174.
- Dubo HI, Peat M, Winter DA, Quanbury AO, Hobson DA, Steinke T, et al. Electromyographic temporal analysis of gait: normal human locomotion. *Arch Phys Med Rehabil*. 1976;57: 415–420.
- Winter DA. Biomechanics and motor control of human movement. John Wiley & Sons; 2009.
- Ivanenko YP, Poppele RE, Lacquaniti F. Motor control programs and walking. *Neurosci*. 2006;12: 339–348.
- Woollacott M, Tang P-F. Balance control during walking in the older adult: research and its implications. *Phys Ther*. 1997;77: 646–660.
- Weerdesteyn V, Hollands KL, Hollands MA. Gait adaptability. *Handbook of clinical neurology*. Elsevier; 2018. pp. 135–146.
- Patla AE. Strategies for dynamic stability during adaptive human locomotion. *IEEE Eng Med Biol Mag*. 2003;22: 48–52.
- Kontis V, Bennett JE, Mathers CD, Li G, Foreman K, Ezzati M. Future life expectancy in 35 industrialised countries: projections with a Bayesian model ensemble. *Lancet*. 2017;389: 1323–1335.
- World Health Organization. What is Healthy Ageing? In: World Health Organization. 2018.
- Vandervoort AA. Aging of the human neuromuscular system. *Muscle Nerve Off J Am Assoc Electrodiagn Med*. 2002;25: 17–25.
- Stelmach GE, Hömberg V. Sensorimotor impairment in the elderly. Springer; 1993.
- Craik FIM, Salthouse TA. *The handbook of aging and cognition*. 3rd ed. Psychology Press; 2011.
- Iosa M, Fusco A, Morone G, Paolucci S. Development and decline of upright gait stability. *Front Aging Neurosci*. 2014;6.
- Winter DA. *The biomechanics and motor control of human gait: normal, elderly and pathological*. 2nd ed. University of Waterloo Press; 1991.
- Samson MM, Crowe A, De Vreede PL, Dessens JA, Dursma SA, Verhaar HJ. Differences in gait parameters at a preferred walking speed in healthy subjects due to age, height and body weight. *Aging Clin Exp Res*. 2001;13: 16–21.
- Holtzer R, Epstein N, Mahoney JR, Izzetoglu M, Blumen HM. Neuroimaging of mobility in aging: a targeted review. *Journals Gerontol Ser A Biol Sci Med Sci*. 2014;69: 1375–1388.
- Huxhold O, Li SC, Schmiedek F, Lindenberger U. Dual-tasking postural control: aging and the effects of cognitive demand in conjunction with focus of attention. *Brain Res Bull*. 2006;69: 294–305.
- Yogev-Seligmann G, Hausdorff JM, Giladi N. Do we always prioritize balance when walking? Towards an integrated model of task prioritization. *Mov Disord*. 2012;27: 765–770.
- Mersmann F, Bohm S, Bierbaum S, Dietrich R, Arampatzis A. Young and old adults prioritize dynamic stability control following gait perturbations when performing a concurrent cognitive task. *Gait Posture*. 2013;37: 373–377.
- Schmitz A, Silder A, Heiderscheid B, Mahoney J, Thelen DG. Differences in lower-extremity muscular activation during walking between healthy older and young adults. *J Electromyogr Kinesiol*. 2009;19: 1085–1091.
- Hortobágyi T, Solnik S, Gruber A, Rider P, Steinweg K, Helseth J, et al. Interaction between age and gait velocity in the amplitude and timing of antagonist muscle coactivation. *Gait Posture*. 2009;29: 558–564.
- McCrum C, Gerards MHG, Karamanidis K, Zijlstra W, Meijer K. A systematic review of gait perturbation paradigms for improving reactive stepping responses and falls risk among healthy older adults. *Eur Rev aging Phys Act*. 2017;14.
- Lexell J, Taylor CC, Sjöström M. What is the cause of the ageing atrophy? Total number, size and proportion of different fiber types studied in whole vastus lateralis muscle from 15- to 83-year-old men. *J Neurol Sci*. 1988;84: 275–294.
- Muscaritoli M, Lucia S, Molino A, Cederholm T, Fanelli FR. Muscle atrophy in aging and chronic diseases: is it sarcopenia or cachexia? *Intern Emerg Med*. 2013;8: 553–560.
- von Haehling S, Morley JE, Anker SD. An overview of sarcopenia: facts and numbers on prevalence and clinical impact. *J Cachexia Sarcopenia Muscle*. 2010;1: 129–133.
- Kennis E, Verschueren S, Van Roie E, Thomis M, Lefevre J, Delecluse C. Longitudinal impact of aging on muscle quality in middle-aged men. *Age (Omaha)*. 2014;36.
- Kosse NM, Vuillerme N, Hortobágyi T, Lamothe CJC. Multiple gait parameters derived from iPod accelerometry predict age-related gait changes. *Gait Posture*. 2016;46: 112–117.
- Kobsar D, Olson C, Paranjape R, Hadjistavropoulos T, Barden JM. Evaluation of age-related differences in the stride-to-stride fluctuations, regularity and symmetry of gait using a waist-mounted tri-axial accelerometer. *Gait Posture*. 2014;39: 553–557.
- Galan-Mercant A, Cuesta-Vargas AI. Differences in trunk accelerometry between frail and non-frail elderly persons in functional tasks. *BMC Res Notes*. 2014;7.
- Mirelman A, Weiss A, Buchman AS, Bennett DA, Giladi N, Hausdorff JM. Association between performance on Timed Up and Go subtasks and mild cognitive impairment: further insights into the links between cognitive and motor function. *J Am Geriatr Soc*. 2014;62: 673–678.

37. Rocchi L, Palmerini L, Weiss A, Herman T, Hausdorff JM. Balance testing with inertial sensors in patients with Parkinson's disease: assessment of motor subtypes. *IEEE Trans Neural Syst Rehabil Eng.* 2014;22: 1064–1071.
38. Reisman DS, Block HJ, Bastian AJ. Interlimb coordination during locomotion: what can be adapted and stored? *J Neurophysiol.* 2005;94: 2403–2415.
39. Sánchez N, Simha SN, Donelan JM, Finley JM. Taking advantage of external mechanical work to reduce metabolic cost: the mechanics and energetics of split-belt treadmill walking. *J Physiol.* 2019;597: 4053–4068.
40. Sato S, Choi JT. Increased intramuscular coherence is associated with temporal gait symmetry during split-belt locomotor adaptation. *J Neurophysiol.* 2019;122: 1097–1109.
41. Roper JA, Brinkerhoff SA, Harrison BR, Schmitt AC, Roemmich RT, Hass CJ. Persons with essential tremor can adapt to new walking patterns. *J Neurophysiol.* 2019;122: 1598–1605.
42. Dietz V, Zijlstra W, Duysens J. Human neuronal interlimb coordination during split-belt locomotion. *Exp brain Res.* 1994;101: 513–520.

CHAPTER 2

Multivariate analyses and classification of inertial sensor data to identify aging effects on the Timed-Up-and-Go test

PLoS One (2016). 11(6): e0155984.

Danique Vervoort¹, Nicolas Vuillerme^{2,3}, Nienke Kosse^{1,2}, Tibor Hortobágyi¹, Claudine JC Lamoth¹

¹ University of Groningen, University Medical Center Groningen, Center for Human Movement Sciences, Groningen, The Netherlands

² University Grenoble-Alpes, AGEIS, Grenoble, France

³ Institut Universitaire de France, Paris, France

ABSTRACT

Many tests can crudely quantify age-related mobility decrease but instrumented versions of mobility tests could increase their specificity and sensitivity. The Timed-Up-and-Go (TUG) test includes several elements that people use in daily life. The test has different transition phases: rise from a chair, walk, 180° turn, walk back, turn, and sit-down on a chair. For this reason, the TUG is an often-used test to evaluate in a standardized way possible decline in balance and walking ability due to age and or pathology. Using inertial sensors, qualitative information about the performance of the sub-phases can provide more specific information about a decline in balance and walking ability. The first aim of our study was to identify variables extracted from the instrumented Timed-Up-and-Go (iTUG) that most effectively distinguished performance differences across age (age 18–75). Second, we determined the discriminative ability of those identified variables to classify a younger (age 18–45) and older age group (age 46–75). From healthy adults ($n = 59$), trunk accelerations and angular velocities were recorded during iTUG performance. iTUG phases were detected with wavelet-analysis. Using a Partial Least Square (PLS) model, from the 72-iTUG variables calculated across phases, those that explained most of the covariance between variables and age were extracted. Subsequently, a PLS-discriminant analysis (DA) assessed classification power of the identified iTUG variables to discriminate the age groups. 27 variables, related to turning, walking and the stand-to-sit movement explained 71% of the variation in age. The PLS-DA with these 27 variables showed a sensitivity and specificity of 90% and 85%. Based on this model, the iTUG can accurately distinguish young and older adults. Such data can serve as a reference for pathological aging with respect to a widely used mobility test. Mobility tests like the TUG supplemented with smart technology could be used in clinical practice.

INTRODUCTION

There is a growing interest in identifying an array of measurements that can assess relevant processes associated with healthy aging (e.g., [1–5]). Such “biomarkers” can concurrently change with age but can also predict aging-related phenotypes or subsequent health outcomes including morbidity, mortality, quality of life and health span. Measurements of biomarkers should be easy to administer and still provide clinically meaningful information as surrogate endpoints in interventions specifically designed to extend health span. Beyond interventions, population studies should also benefit from valid, reliable, low-cost indices of healthy aging [3]. In general, biomarkers comprise key bodily functions, which are known to decline during aging. Biomarkers should thus target physical capability and cognitive, physiological, musculoskeletal, endocrine and immune functions. Within the domain of motor function in aging, thanks to its high construct and convergent validity, reliability, and standardization the Timed-Up-and-Go (TUG) test has recently been proposed [4] and recommended as a potentially useful biomarker of healthy aging [3]. The TUG is routinely used as a composite test to assess leg strength (sit-to-stand), gait, and balance (180° turn; sit-to-stand, stand-to-sit). Constituent elements of TUG represent activities of daily living linked to quality of life in healthy aging. Unsurprisingly, TUG has hence become a popular and informative mobility test that provides age-, gender-, and pathology-specific data on old adults’ balance and gait function [6,7]. Even though a stopwatch is sufficient to assess TUG performance [8], total time as a summary measure cannot characterize the execution quality of its sub-phases. Such an omission is unfortunate considering that the postures and the transitions between phases of TUG are frequently administered as individual tests for the quantification of dynamic balance, walking ability [9], the capacity to sequence tasks [10], and even to assess fall risks [11]. Miniaturization, low weight, inconspicuousness, validity, reliability, low cost, and versatility of automated algorithms to analyse a variety of motor tasks have made such devices the tool of choice for objective quantification of motor function with aging. Such sensor features make it possible to use wearable technology not only in a research setting but also in a clinical setting where individuals execute motor tasks in their natural environment [12,13].

Inertial measurement units (IMU's) with embedded 3D accelerometers and gyroscopes can quantify key phases of the instrumented TUG (iTUG) and provide in-depth information on functional performance [14–16]. Algorithms such as Hidden Markov Models [17], Dynamic Time Warping [18], and methods for dimensionality reduction can characterize temporal features of transition between phases of iTUG [19]. An automated detection of sub-phases of the iTUG can characterize movement in terms of smoothness, regularity, variability, maximal velocity, or range in angular velocity. Phases of iTUG are sensitive and can classify frail [20] versus healthy elderly [21,22] and identify those with fall risks [23], cognitive impairment [24], and assess stages or quantify movement impairments in Parkinson's disease [25–27].

The use of iTUG is complicated by the difficulty in selecting from the large number of variables those that are sensitive to individual differences in gait and balance performance. Frequently used variables include the mean, median, standard deviation and ranges of a signal characterizing sub-phases of the iTUG. In addition, measures related to variability (RMS), smoothness of performance (Jerk/slope), gait variability index (Phase variability Index, Harmonicity Ratio, Coefficient of Variation of stride times) have been suggested for quantifying performance during specific iTUG phases [10,14,19,23]. Most studies focused on distinguishing patients from healthy (older) adults. Moreover, the large number and variety of variables makes it difficult to determine the variables that could separate age groups

of healthy adults over the lifespan. Pattern recognition methods like Principal Component Analysis (PCA) are suitable to gain insights into data matrices and minimize redundancy. Palmerini et al. [19] applied PCA to search for a subset of variables relevant for three phases of the TUG, sit-to-stand, walking, and stand-to-sit. Of the initial 28 variables of healthy adults based on accelerometer signals embedded in a smartphone, a reduced set of twelve variables was extracted using PCA, but these analyses were not used to stratify participants by age and the device also operated without a gyroscope.

iTUG has previously been used for patient stratification. A linear discriminant analysis of iTUG data stratified nearly 80% of healthy and early-mild Parkinson's patients correctly, based on mediolateral (ML) and vertical Jerk during turning and anterior-posterior root mean square (RMS) during the sit-to-walk phase [25]. As compared with TUG duration measured with a stopwatch, a binary logistic regression analysis of a subset of three variables (jerk of the sit-to-stand, average step duration, standard deviation (STD) of the overall performance) was more accurate in classifying non-fallers and fallers [23]. A pattern-matching k-NN algorithm was also effective in distinguishing old adults with a low and high fall risk based on the RMS of the vertical acceleration during walking, the amplitude of the yaw signal during turning and the time to complete the test. Sit-to-stand and stand-to-sit related variables were not included in the classification [28].

Overall these studies show that a subset of parameters of the iTUG could classify certain types of patients. The current and sporadic evidence for using iTUG as a classification tool could be generalized and broadened by providing a normative database that characterizes a set of statistically selected variables for the postural and ambulatory elements of iTUG. Such data can then be used to assess the effects of natural aging and could serve as a basis for the identification of patients with mobility disability [10,19,23,25]. Therefore, the first aim of our study was to identify iTUG variables that are associated with changes in performances of the iTUG across the adult lifespan. Secondly, after identification of the most important iTUG variables, we assessed if these variables could accurately discriminate two age groups, one of age 18-45 and one of age 46-75 years. Because the onset of decline of muscle mass and muscle function starts around age 40-45 years, we chose a cut-off value of group division at age 45 [29-32]. We combined a wavelet analysis algorithm (to identify phases of iTUG) with a phase detection algorithm based on accelerometer and gyroscope data and applied statistical analyses to specify variables that could effectively classify healthy young versus old adults. To this aim, first, we used a Partial Least Square analysis (PLS), a method that combines dimensionality reduction and regression, to identify the variables of the iTUG that are sensitive to age. Second, we examined the classification power of the identified variables to stratify young and old adults, using a PLS-discriminant analysis.

METHODS

PARTICIPANTS

Fifty-nine healthy adults participated in the study (45 ± 18 years, range of age: 18 to 75, 46% male) and served as a basis for two age groups: 18-45 (28 ± 7 years; $n = 28$; 61% male; weight = 75.4 ± 7.6 kg; length = 178 ± 11.3 m) and 46-75 (62 ± 8 years; $n = 31$; 32% male; weight = 73.1 ± 13.3 kg; length = 169.5 ± 9.4 m). All subjects were healthy and active. Participants were asked to report the number of hours per week they engaged in physical activity during a typical week (e.g., tennis, dance, hiking, yoga). Participants in the younger group were on average 4.8 ± 2.0 hours active per week and participants in the older group 2.9 ± 2.2 hours per week.

Data of four participants (3 young; 1 old) was excluded from one of the two trials they performed because the data was not correctly recorded due to a corrupt memory card. The local Ethical Committee of the Center of Human Movement Sciences of the University Medical Center Groningen approved the research proposal. All participants signed a written informed consent before participating. The iTUG test was part of a larger study examining the effects of age on gait [31].

INSTRUMENTATION AND PROCEDURE

Trunk accelerations were measured during the TUG with an Inertial Measurement Unit (IMU; DynaPort® hybrid unit (56x61x15 mm, 54 g; McRoberts BV, The Hague, the Netherlands). The unit consists of a tri-axial accelerometer and gyroscope sensor (100 Hz sample frequency). Data was stored on an SD card for off-line analysis of the signals. The IMU was fixed with an elastic belt at the level of lumbar segment L3 over the participant's clothes. Participants performed the iTUG two times. The iTUG consisted of standing up from a chair without the use of the arms, walking 7 m, turning around a pion, walking 7 m back to the chair, and sitting down without the use of the arms. Participants were instructed to perform this task as fast as possible without running. Since the iTUG was performed in the context of a larger study the TUG trials were randomized with three other gait tests. All data analyses were performed off-line using Matlab software (version R2015b, The MathWorks Inc.).

PHASE DETECTING ALGORITHM

An algorithm was developed to detect five phases of the iTUG: 1) rising from a chair (sit-to-stand), 2) walking, 3) turning, 2) walking, 4) turning and 5) sitting down (stand-to-sit) [see also 16,22,23,33]. The two walking phases were pooled for gait analysis. Similar to the studies of Weiss et al. [22,23], identification of postural transitions during sit-to-stand and stand-to-sit was based on the pitch of the angular velocity signal and the anterior-posterior (AP) acceleration signal. Turns were identified from the yaw of the angular velocity signal [22,34]. We used a discrete wavelet approach to perform a time-frequency decomposition of the signals in order to identify the relevant signal peaks related to the start and end of phases of iTUG [33,35–37]. On the type of signals collected in the present study, a Daubechies (db) mother wavelet was appropriate [36,38,39].

STANDING-UP AND SITTING DOWN

The pitch signal was analysed with a db5 mother wavelet and its reconstruction was based on the level 4 approximation (4A). Thereafter, peaks (Fig. 1) in the reconstructed signal were detected using a peak detection algorithm 'findpeaks' of the signal toolbox of Matlab, which searches for local maxima in the signal. Fig. 1 presents the phases of standing-up and sitting-down. From 1a to 1b, the subject moves the trunk forward in preparation for rising from the chair. Subsequently, from 1b-1c the trunk is moved backward until standing upright. In the sitting down phase (3a-3c) the pattern is repeated.

Fig. 1. Representation of the Pitch signal for detecting standing-up and sitting down phases. Pitch signal or rotation around the mediolateral axis (dotted line) and reconstructed signal (solid line) using level 4 approximation of db5 wavelet. When the signal becomes negative (1a) the trunk moves forward until minimal angular velocity (1b). Subsequently when the participants stands-up the angular velocity also changes in direction. For sitting down the same pattern is visible (3a-3c).

Fig. 2. Representation of a yaw signal used for identifying the turn phases and of an AP acceleration signal for detecting steps during turns. The upper trace represents the yaw signal or rotation around the vertical axis (dotted line) and reconstructed signal (solid line) using a level 6 approximation of db5 wavelet. The turn is indicated by an increase/decrease in the yaw amplitude depending on the direction of the turn. The start of turning is when the zero line is crossed (2a; 2d) and the end of the turn when the zero line is again crossed (2c; 2f). The lower trace represents the AP acceleration signal (dotted line), reconstructed at level 3 with a db5 wavelet (solid line). Peaks indicate foot contact instances.

TURNING

To detect the turn at the end of the first walking trajectory and before sitting-down, a db5 mother wavelet was used on the yaw signals and the reconstruction was based on the level 6 approximation (Fig. 2). Depending on the direction of the turn a negative or positive peak appears. First, the minimum or maximum peak point in the wavelet is found (Fig. 2, upper trace: 2b; 2e). Thereafter, the first point where the yaw signal crossed the zero line is detected before and after the peak. This is done for both turns. To determine the number of steps used to turn, the trunk AP acceleration signal is reconstructed at approximate level 3 of db5 (Fig. 2, lower trace). The peaks in the acceleration signal represent a foot contact instance.

Detection of the start and end of the walking phases was based on the previous phases and foot contact moments extracted from the AP acceleration signal (Fig. 3). The start of walk 1 was defined as the first peak after standing up (Fig. 1, 1c) and ended at the peak before the turn (Fig. 2, 2a). The second walk after turning started at the first peak after the turn (Fig. 2, 2c) and ended at the peak just before the turn for sitting-down (Fig. 2, 2d).

Fig. 3. Representation of an AP acceleration signal for detecting steps during walking. The signal represents the raw (dotted line) and reconstructed (solid line) anterior-posterior acceleration signal (Level 3 db5), used for defining step parameters. Arrows indicate heel strike.

VARIABLES CALCULATED FROM THE ITUG PHASES

We calculated the same variables for phases of iTUG that have been reported in the literature [10,14,19,22,23,25,28,40]. First, the duration of each phase was calculated. Second, we calculated the amplitude, range of the movement, variability, and smoothness of the movement for sit-to-stand, stand-to-sit, and for the two turns. Data for the two walking phases were combined. From foot contacts, step-related variables (e.g., stride time, number of steps) were calculated. From the ML and AP acceleration signals, we computed measures of stability and smoothness of gait. Altogether, we calculated 72 variables for the Partial Least Square (PLS) analysis (Table 1). Outcome measures were expressed in absolute values, being positive or negative signs according to the direction of the turn.

Table 1. Variables calculated for different phases of the iTUG.

Variables	iTUG components*	Description	Signal / M.U.
Time	Sit-to-stand; Stand-to-sit; Turns; Walking	Duration of each phase	Sec.
Mean	Sit-to-stand; Stand-to-sit; Turns; Walking	Average value over different identified phases of iTUG	Pitch deg./s Pitch deg./s Yaw deg./s AP acc. m/s ²
STD	Sit-to-stand; Stand-to-sit; Turns; Walking	Standard deviation calculated over identified phases of iTUG	Pitch deg./s Pitch deg./s Yaw deg./s AP acc. m/s ²
Range	Sit-to-stand; Stand-to-sit; Turns; Walking	Difference between maximum and minimum observation	Pitch deg./s Pitch deg./s Yaw deg./s AP acc. m/s ²
Max	Sit-to-stand; Stand-to-sit; Turns; Walking	Maximal value of the signal	Pitch deg./s Pitch deg./s Yaw deg./s AP acc. m/s ²
Median	Sit-to-stand; Stand-to-sit; Turns; Walking	Middle value of signal values	Pitch deg./s Pitch deg./s Yaw deg./s AP acc. m/s ²
RMS	Sit-to-stand; Stand-to-sit; Turns; Walking	Root Mean Square: $RMS = \sqrt{\frac{1}{N} \sum_{i=1}^N (x_i - \bar{x})^2}$ $x = \text{signal type}$	Pitch deg./s Pitch deg./s Yaw deg./s AP acc. m/s ²
Slope	Sit-to-stand; Stand-to-sit; Turns	Rate of change in angular velocity, direction and steepness	Yaw
N steps	Walking	Number of steps over the two walking tracts	n
Step time	Walking	Average time between right and left foot contact	AP acc. s.
CV step	Walking	Coefficient of Variation between steps $CV = \frac{\sqrt{\frac{1}{N} \sum_{i=1}^N (s_i - \bar{s})^2}}{\bar{s}} * 100$ $s = \text{step time} = \text{signal}, i = \text{step number}$	%
Phase deviation	Walking	$\varphi_i = (FCR_{t(i)} - FCL_{t(i)}) / (FCL_{t(i+1)} - FCL_{t(i)}) * 360^\circ$ $\varphi_i = \text{Point-estimate of relative phase as measure of timing between contralateral heel strikes. FCR = time instant right heel strikes. FCL = left heel strike}$ $\bar{\varphi}_{dev} = \frac{1}{N} \sum_{i=1}^N \varphi_i - 180$	AP acc. unit less
Phase variability	Walking	Average deviation from perfect symmetric gait Because the relative phase is a circular measure, circular statistics was applied to calculate the variance of the relative phase over strides.	unit less
Index of harmonicity	Walking	$IH = \frac{p_1}{\sum_{i=1}^{10} p_i}$ $p_i = \text{Power spectral density of fundament frequency}$ $\sum p_i = \text{the cumulative sum of power spectral densities of the 10 harmonics.}$ Higher IH indicates smoother gait pattern	AP - ML acc. unit less
Gait cycle Variability	Walking	$SD_i = \sqrt{\left(\frac{\sum_{j=1}^N (x_{ij} - Cycle_i)^2}{n - 1} \right)}$	AP - ML acc. unit less

		Point by point standard deviation for i^{th} sample, s_{ij} signal value for i^{th} sample j^{th} step cycle, i mean over cycle of i^{th} sample
		$PhVar = \sqrt{\frac{\sum_{i=1}^k STD_i^2}{k}}$
		Gait cycle var = average of individual point by point std values across all samples, k STD; standard deviation over i^{th} sample 1/step time
Frequency	Walking	AP - ML Acc. Hz/s

*As indicated in Fig. 1, sit-to-stand variables were calculated for phases 1b–1c, 1a–1c; for stand-to-sit from, 3a–3b; 3a–3c. Turn slope was calculated separately for phase 2a–2b; 2b–2c and 2d–2e; 2e–2f (see Fig. 2). AP = Anterior-Posterior; ML = Medio-Lateral; M.U. = Measurement Unit.

PLS ANALYSES

A Partial Least Squares (PLS) regression analysis was applied to determine the iTUG variables that were related to age (PLS-Toolbox 8.1 for Matlab, Eigenvector Research Inc.). PLS analysis combines PCA with regression analysis. Compared with step-wise regression or structural equation models, PLS methods can handle a larger set of independent variables with a lower number of observations. Moreover, multivariate PLS regression allows the modeling of multiple responses, while dealing with multicollinearity [41], which is often present in motion data, including walking. The general aim of the PLS analysis is to define a maximum covariance model and explain the relationship between the iTUG variables (X-matrix, predictors) and age (Y-matrix, responses). In other words, successive orthogonal factors are chosen that maximize the covariance between each X-score and the corresponding Y-score to find a model that best predicts age with a selected number of iTUG variables.

Two separate PLS analyses were performed consecutively. For the first PLS analysis, trial one was used as data input. With this data, a PLS model was built to determine the latent iTUG variables that most accurately predict age and also explains most of the covariance between iTUG variables and age. The second analysis consisted of a PLS-discriminant analysis (DA) to determine how accurately the iTUG variables identified by the first PLS analysis discriminate the two age groups.

The data were pre-processed by a z-transformation. For the first PLS analysis, the X-matrix consisted of the 72 iTUG variables and the Y-matrix of the 57 participants' age. By extracting the variables that contribute the most to the model, the number of variables is reduced to a smaller number of Latent Variables (LV). Any given LV explains a part of the total variance in the Y-matrix (age) by capturing the variance in the X-matrix (iTUG variables). The amount of variance of the iTUG variables explained by the models LV indicates the relevance of the variables in the prediction of age [41]. The number of LVs was determined by goodness of prediction (Q2).

$$Q2_k = 1 - \frac{PRESS_k}{RSS_{k-1}}$$

$$PRESS = \sum (y_{k-1,m} - \hat{y}_{k-1,-m})^2$$

where PRESS is the predictive sum of squares of the model containing k components and RSS is the residual sum of squares of the model [42]. The PRESS depends on the $y_{k-1,m}$ the residual of observation m when $k-1$ components are fitted in the model and $\hat{y}_{k-1,-m}$ the predicted y when the latest

observation of m is removed. When Q_2 reaches a plateau, before it decreases, this is considered the optimal number of latent variables.

To assess the PLS model, several outcomes were derived. First, the goodness of fit (R^2) of the model was determined. The R^2 explains how well the model fits the data and is calculated as follows:

$$R^2_k = 1 - \frac{RSS_k}{TSS}$$

The R^2 is defined by the residual sum of squares of the k th LV and the total sum of squares (TSS). Next, the weights of the PLS model were assessed. They illustrate the relationship between iTUG variables and the participant's age, with respect to the individual LV. The weights describe the importance of iTUG variables and age on the model for the individual LV. If they are near zero for all identified LVs than they add little to the model.

To identify which iTUG variables are of importance to the model the regression coefficients (RC) of the PLS matrix and the Variable Importance for Projection (VIP) are evaluated. Where the RC represents the influence each variable has in the prediction of the response (age), the VIP represents the values of each predictor (iTUG-variable) in fitting the PLS model for predictors as well as the responses. A large absolute coefficient for an iTUG variable (predictor) together with a VIP value > 0.8 indicates that a variable is a prime candidate in the model [41].

The VIP scores are calculated as follows:

$$VIP_j = \sqrt{p \sum_{k=1}^N [SS_k (w_{kj} / \|w_k\|^2)] / \sum_{k=1}^N (SS_k)}$$

with as SS_k the explained sum of squares of the k^{th} LV and N the number of LVs in the model. Hence the VIP_j weights w_{kj} quantify the contribution of each variable j according to the variance explained by each k^{th} LV. The selected variables were included in the second analysis, PLS-DA.

PLS-DA ANALYSIS

To determine the classification power of the iTUG variables identified in the first PLS analysis, a PLS-DA was performed on the dataset of the second iTUG trial. The iTUG variables selected from the first PLS analysis thus formed the X-matrix. For the discriminant analysis, the participants were separated into two age groups, one with age 18-45 and one group with an age of 46-75 years.

Based on the PLS-DA a Receiver Operating Characteristic (ROC) curve was constructed. This curve includes both the true positive rate (sensitivity) and false positive rate (specificity) of the model. Each point on the ROC-curve represents a sensitivity/specificity pair, which is related to a threshold that determines the optimal boundary between younger and older adults in the classification. The Area Under the Curve (AUC) is an indicator of the classification power of the model. It is the average value of sensitivity for all possible values of specificity. An AUC of 1 shows a perfect accuracy of the classification and an AUC of 0.5 is a pure guess of the result.

RESULTS

PHASE DETECTION OF THE ITUG

The PLS model contained three LVs, as the Q₂ had reached a plateau at LV3 before it decreased. The three LVs explained 30.5% of the co-variance between the iTUG variables (X-matrix), and 71% of the variance in age (respectively explaining 49.4%, 9.9% and 11.7% of the variance in age).

Fig. 4 shows the VIP scores and absolute RC for all the iTUG variables included in the analysis. The variables on the left side are negative RC representing lower values of all included parameters except for stand-to-sit median pitch and mean acceleration in the 3a-3b phase. These values were related to participants with higher age. In addition, positive RC, on the right side, indicates that higher values on these variables are related to higher age. As illustrated in Fig. 4, based on the criteria for selection of iTUG variables, (VIP score > 0.8 and RC > 0.04), 27 of the 72 iTUG variables were considered important to the PLS model. The 27 selected variables of the iTUG are related to different phases of the iTUG. Table 2 shows mean values, VIP scores, RC and the captured variance of each variable per LV.

Fig. 4. Variable Projection of Importance (VIP) scores and regression coefficient (RC) plot. The RC are giving as bars in absolute values. To the left and right of the vertical dotted line, respectively, the negative and positive RC are shown. The dotted black line represents the VIP scores (right y-axis). In order to be important to the model, the dots in the dotted line should be above the dashed line (VIP > 0.8, right Y-axis). The dark bars are the variables that entered the PLS-DA model. Note that due to the large number of variables included in the model, regression coefficients are relatively low.

SIT-TO-STAND PHASE

For the sit-to-stand phase, 3 of the 23 variables were included. Two of these variables summarize the angular velocity of the movement (pitch signal), in terms of its range and slope. The median of the AP acceleration was also included. Older participants had a larger range, steeper slope and overall a higher acceleration, indicating a movement with a faster change and larger angular movement during standing up and a higher acceleration on average during this period.

WALKING PHASE

Of the variables related to walking, 6 out of the 14 variables were included in the model: the RMS, gait cycle variability in both the AP and ML directions, the STD step time and the ML acceleration frequency, implying that younger adults had a more variable body sway and more variability between gait cycles and step-times. The variables related to the smoothness and regularity of the gait pattern, the mean step time and number of steps, were not included in the model.

TURN PHASES

For turn-to-walk 4 out of 6 variables were relevant to the PLS model: the slope of the turn phases, the time, and number of steps. During turning while walking, older adults took more time and steps to complete the turn, while the turn of young adults had a steeper slope while turning. A similar number of variables of the turn-to-sit was included, both the slopes and the amplitude and RMS of the angular velocity. During this movement, young adults had more body sway and a larger magnitude of angular velocity. Similarly to the turn-to-walk, young adults had a steeper slope while turning.

Table 2. VIP (Variable Importance for Projection) and Variance captured by the 3 LV in the PLS model. Only variables with a VIP score higher than 0.8 are included. The means of the variables in the first dataset are also shown. Note that due to the large number of variables included in the model, regression coefficients (RC) are relatively low in this type of PLS models.

Phase	Variable	RC	VIP Scores	Variance Captured			Young		Old	
				LV1	LV2	LV3	Mean	STD	Mean	STD
Sit-to-stand	Range pitch (B-C)	0.04	1.49	40.2	33.6	0.3	157.0		191.4	
	Slope pitch (B-C)	0.05	1.33	21.8	2.5	1.8	5	34.45	6	51.04
	Median AP (A-C)	0.07	1.46	27.2	15.2	0.1	2.58	1.00	2.94	0.98
Walk	RMS AP	-0.17	4.83	7.0	46.2	0.2	0.47	0.13	0.53	0.13
	RMS ML	-0.12	3.46	11.2	27.9	0.1	0.39	0.14	0.28	0.07
	Gait cycle variability ML	-0.12	3.17	8.4	26.5	0.1	0.20	0.04	0.17	0.04
	Gait cycle variability AP	-0.11	1.42	0.1	18.2	2.3	0.19	0.04	0.17	0.05
	STD step time	-0.07	0.81	4.9	0.2	3.9	0.20	0.05	0.19	0.04
	STD step time	-0.07	0.81	4.9	0.2	3.9	0.08	0.03	0.07	0.03
	Gait frequency ML	-0.07	0.90	4.4	1.0	1.2	4.64	2.19	4.06	1.40
Turn-to-walk	Time	0.16	3.79	7.9	15.0	0.5	2.00	0.47	2.55	0.68
	N steps	0.10	2.18	11.7	4.7	0.1	4.44	1.15	5.33	1.27
	Slope (A-B)	0.04	1.04	10.8	0.5	1.8	2.00	2.07	1.27	1.69
	Slope (B-C)	-0.08	1.18	4.7	4.5	1.7	1.69	1.13	1.17	0.92
Turn-to-sit	RMS	-0.09	1.68	2.5	21.2	1.4	108.0			
							2	20.94	98.97	20.19
	Amplitude	-0.13	2.30	1.5	16.3	0.3	183.2		171.6	
	Slope (D-E)	-0.09	1.34	0.7	20.6	0.1	0	23.33	0	26.25
	Slope (E-F)	-0.08	1.11	3.7	2.4	0.3	3.29	1.87	2.80	1.32
Stand-to-sit	Time (A-C)	-0.06	1.07	8.4	0.6	0.01	3.15	1.18	2.74	1.32
	Median pitch (A-C)	-0.08	1.42	20.9	13.0	7.0	1.38	0.29	1.24	0.35
	Median pitch (A-B)	-0.07	1.43	18.7	1.3	1.6	17.03	8.81	19.39	9.71
							12.45	12.06	14.09	9.71
									101.6	
	Max pitch (A-C)	0.13	1.72	8.1	13.4	25.6	87.95	40.36	2	35.92
	Mean pitch (A-C)	0.13	2.88	25.1	3.0	1.2	11.61	7.43	18.20	8.80
	Slope pitch (A-B)	0.04	1.64	25.2	0.8	0.2	1.53	0.76	2.09	1.05
							141.2		154.8	
	Range pitch (A-B)	0.08	0.86	13.5	32.0	12.1	0	34.13	8	37.82
	STD pitch (A-C)	0.09	0.96	10.5	18.1	21.9	37.91	11.35	41.72	11.27
	Mean AP (A-C)	-0.07	1.38	0.6	42.9	0.5	0.41	0.14	0.36	0.11
	STD AP (A-C)	0.11	1.75	23.0	27.6	5.4	0.22	0.05	0.25	0.06

STAND-TO-SIT PHASE

Ten out of the total 23 stand-to-sit variables were included in the model. In this phase, in contrast to the other iTUG phases, time was also included. Seven of these 10 variables summarize the angular velocity of the movement (pitch signal). These variables are the mean, median, STD and maximum of the angular velocity during the whole stand-to-sit movement and the median, range, and slope of the angular velocity during the first part of the stand-to-sit. The two remaining variables summarize the AP acceleration in terms of the mean and standard deviation of the total stand-to-sit.

Older adults had a faster movement and exhibited on average a higher angular velocity (mean/median) during the stand-to-sit. Their movements also showed a faster change and larger maximum angular velocity and in total a larger range of angular velocity. This was similar to the movement during the sit-to-stand.

During sitting down, young adults had a higher acceleration pattern with a smaller deviation from the mean. With the exception of these results and the higher acceleration of older adults during the sit-to-stand, no variables of the AP acceleration were included in the model of the sit-to-stand and stand-to-sit.

CLASSIFICATION POWER TO DISCRIMINATE AGE GROUPS

The PLS-DA analysis included the 27 variables identified by the PLS analysis. The model included two latent variables, as for two LVs, the Q2 showed the first peak before it decreased. 30.6% of the variance in iTUG measures explained 56% of the variance in age groups for these two LVs. The LVs explained respectively 44.1% and 11.5% of the variance in age. The goodness of prediction was 0.38. The analysis had a good accuracy of the classification as indicated by the area under the curve (AUC = 94.7%). Fig. 5A shows the ROC curve at the optimal cut-off point, 0.52. The sensitivity and specificity were 90% and 85%, respectively (Fig. 5B). These results indicate that 10% or 3 of 26 of the young adults were classified as old and 15% or 5 of 31 of the older adults were classified as young.

Fig. 5. Sensitivity and specificity plots. To determine the optimal cut-off point, sensitivity and specificity are plotted against the threshold (A), the optimal cut-off point is present at 0.52. The sensitivity is plotted against 1 - specificity for all cut-off values of the PLS-DA model in the ROC curve (B).

DISCUSSION

The present study addressed two main objectives: 1) which variables of the iTUG are most sensitive to distinguish age effects, and 2) what is the classification power of a model based on the variables detected by the first objective. These two objectives were addressed using a multivariate analysis, namely the Partial Least Squares (PLS) analysis. We identified 27 variables of iTUG that predicted age. The subsequent PLS-DA analysis using the 27 identified iTUG variables classified young and old adults with a power of 0.95 and sensitivity and specificity of 90% and 85%. We discuss these results with a perspective on how technology can enrich a widely used clinical test for the purpose of stratifying age groups and patients with high sensitivity and specificity.

ITUG PHASE DETECTION

In the present study, both an accelerometer and a gyroscope provided data for analyzing the phases of the iTUG in healthy young and older adults. For the phase detection an algorithm that combined a wavelet analysis with a peak detection algorithm was applied, to identify each of the five phases, i.e., sit-to-stand, walk, turn-to-walk, turn-to-sit, and stand-to-sit.

Conventionally, TUG performance is scored by a single outcome: total time of execution [8]. In our study, only the time it took to complete the turning phase during the walking period and the duration of the stand-to-sit discriminated older from younger adults. A possible explanation for this result could be that in the current study, we compared healthy participants at different ages ranging from 18 to 75 years of age. Young and older adults completed the iTUG in 14 and 15 s. This could imply that iTUG time has lower sensitivity to differentiate mobility between young and healthy aging old adults. For older adults, similar values are reported in other studies (range: 14.3-16.1 s [25]), whereas no reference values for young adults are available.

EXTRACTED ITUG VARIABLES

A combination of the 27 of 72 selected variables consistently identified age-related differences in iTUG performance. For the sit-to-stand and stand-to-sit phases, the variables that revealed differences between young versus old adults were mainly related to the angular velocity (pitch) signal and hardly any differences were detected in the AP accelerations. This is similar to results when comparing healthy older adults to MCI or PD patients [24,27]. The largest absolute number of variables included in the model were the 10 variables of the stand-to-sit phase. In contrast, only 3 variables of the sit-to-stand phase were included. Presumably, this contrast is related to the lack of reliability of this phase [25]. The data showed that in certain variables there were large differences between the sit-to-stand and stand-to-sit between age groups (Table 2). For example, older adults revealed a larger angular velocity pattern during these two phases and more variability in the angular velocity, an observation perhaps related to the use of greater motor variability during the sit-to-stand to compensate for strength deficits [43]. In another study, older adults have also been shown to be more variable during the sit-to-stand test than young adults [39]. However, this study reported a lower angular velocity during trunk flexion for older adults, while our results show the opposite. A possible explanation for this difference could be that contrary to our study with healthy older adults, the older adults were living in a residential care facility.

Almost all of the selected variables of the turn-to-walk and turn-to-sit were included in the final model. The slope of both turns, indicating fastness and smoothness of turns, was an important discriminating variable and was higher for young adults. For the turn during walking also the larger number of steps during the turn and the longer duration of turning added to the differentiation between the two age groups. For the turn before sitting down, the RMS and amplitude of the yaw signal added to the distinction between the age groups. These outcomes are in line with previous studies that have used the iTUG to distinguish healthy elderly from MCI [24] or PD patients [27] and elderly with an IADL disability [22]. This indicates that the variables during the turning phases of the iTUG not only distinguish age effects but also pathologies. The variables related to turns might be even more important in the case of pathology considering asymmetric gait in pathologies like stroke, Parkinson's disease, and fallers. Then the direction of the turn will provide additional information and turns should be made in both directions. In our study participants could choose in which direction they made the turn.

Variables of the walking phase in the iTUG that have been reported as being sensitive to discriminate gait of healthy (older) adults from that of patient groups were step regularity, number of steps, duration, IH and Jerk [23,24,27]. We found other parameters of walking to be important to the model, namely RMS (ML and AP), gait cycle variability (ML and AP), frequency (ML) and the STD of step time. The higher gait cycle variability, ML frequency, and STD of step time in young compared to older adults is different from results of previous studies reporting higher step variability in gait of frail elderly and of elderly with fall risk [31,44,45]. Our data suggest that adults categorized into a broad age bracket of 18 to 45 years tend to walk with features that resemble a dynamic gait that is somewhat erratic and variable, which is in line with earlier recent findings in this age group. Measures related to smoothness and symmetry of the gait pattern were not included in the model, presumably due to a too low number of steps when walking 7/14 meters. Even when we combined the two walking phases the average number of steps of young and older adults was 17. For smoothness and predictability measures of gait (depending on the type of measure), at least 50 steps are required [46].

In summary, the combination of 27 iTUG variables was sensitive to age. In particular variables characterizing gait and the turns were included in the model and these variables were mostly higher in young compared to older adults. In addition, the stand-to-sit phase seemed to differentiate the age groups more accurately than the sit-to-stand. A possible explanation for the larger inclusion of walking-related variables is the fact that gait is a cyclic movement contrary to the discrete transition movement of standing up or sitting down. During walking, older adults may have a more limited set of effective motor solutions compared to young adults, thereby reducing the (goal equivalent) variability [47]. In contrast, during a discrete movement as sitting to standing or vice versa, older adults show more variability [43]. Overall these results underscore the importance of separately assessing the different sub-phases of the iTUG.

CLASSIFICATION

We deliberately included adults with a wide range of ages to assess changes in iTUG performance over the lifespan of healthy adults. In spite of using non-distinct groups, our misclassification rate was only 14%. This result is comparable with the model that was previously developed to distinguish fallers from non-fallers (12%) [23]. Our misclassification rate is lower than a previous model that distinguished two distinct groups, namely healthy older adults from PD patients (22.5%) [25]. This implies that the classification of the current model is similar and possibly better at distinguishing different

groups. This could be due to the fact that in the current model 27 variables are included, while the other two models only included three variables. The choice of only a limited number of variables by Palmerini et al. [25], was based on the statistical model they used, which will lead to overfitting with a small sample size and a large number of parameters. For this reason, we decided to apply a PLS method, because this method is effective in handling relatively small sample sizes with a large number of variables with multi-collinearity [41,48]. Although the current classification values were good, the model could still be improved. A possible way to improve the classification power (sensitivity/specificity) of the model is to increase the number of age groups with an equal distribution of ages over all groups and/or also increase the number of participants in order to obtain a reference model and/or include more trials in the model to increase the reliability of the individual parameters.

A practical implication of the current model is that the iTUG can be used to successfully distinguish a group of individuals into unique sub-groups (e.g. healthy adults vs. frail adults). A recent trend is to use smart devices, like an iPod or smartphone, as sensors. These devices include embedded accelerometers and gyroscopes. Several studies suggest that these smart devices are reliable to characterize key features of iTUG and gait [40,49,50]. This development of the use of smartphones in combination with the development and assessment of models to classify patients, age groups and task effects could have an impact on clinical practice. Smart devices are easy to use, inexpensive, and their use is becoming widespread. Wireless links to an external computer would allow clinicians or researchers to analyze the data without retrieval of the device itself. Also, apps can be programmed for research or clinical practice and the data could then be combined and validated against other data derived from clinical tests [49].

CONCLUSION

The current analysis shows that iTUG variables can accurately distinguish healthy young and older adults. A combination of 27 variables, from primarily the turns, walking, and stand-to-sit phase, was effective to identify iTUG performance in relation to age. The data revealed that young versus older adults executed the TUG with faster and smoother turns and more variable gait cycles and trunk sway during gait. Older adults compared to young adults had a larger angular velocity pattern during the transitions, stand-to-sit, and sit-to-stand. Future research should implement the current iTUG analyses for the classification of old adults aging normally and those aging with pathologies. Combined with smart technology, the model could then be used to stratify patients with high sensitivity and specificity in clinical practice.

REFERENCES

- Cooper R, Kuh D, Cooper C, Gale CR, Lawlor DA, Matthews F, et al. Objective measures of physical capability and subsequent health: a systematic review. *Age Ageing*. 2011;40: 14–23.
- Gershon RC, Wagster M V, Hendrie HC, Fox NA, Cook KF, Nowinski CJ. NIH toolbox for assessment of neurological and behavioral function. *Neurology*. 2013;80: S2–6.
- Lara J, Cooper R, Nissan J, Ginty AT, Khaw KT, Deary IJ, et al. A proposed panel of biomarkers of healthy ageing. *BMC Med*. 2015;13: 222.
- Lara J, Godfrey A, Evans E, Heaven B, Brown LJ, Barron E, et al. Towards measurement of the Healthy Ageing Phenotype in lifestyle-based intervention studies. *Maturitas*. 2013;76: 189–199.
- Reuben DB, Magasi S, McCreath HE, Bohannon RW, Wang Y-C, Bubela DJ, et al. Motor assessment using the NIH Toolbox. *Neurology*. 2013;80: S65–75.
- Botolfson P, Helbostad JL, Moe-Nielsen R, Wall JC. Reliability and concurrent validity of the Expanded Timed Up-and-Go test in older people with impaired mobility. *Physiother Res Int*. 2008;13: 94–106.
- Podsiadlo DA, Richardson S. The timed “Up & Go”: a test of basic functional mobility for frail elderly persons. *J Am Geriatr Soc*. 1991;39: 142–148.
- Mathias S, Nayak US, Isaacs B. Balance in elderly patients: the “get-up and go” test. *Arch Phys Med Rehabil*. 1986;67: 387–389.
- Sheehan KJ, Greene BR, Cunningham C, Crosby L, Kenny RA. Early identification of declining balance in higher functioning older adults, an inertial sensor based method. *Gait Posture*. 2014;39: 1034–1039.
- Zampieri C, Salarian A, Carlson-Kuhta P, Aminian K, Nutt JG, Horak FB. The instrumented timed up and go test: potential outcome measure for disease modifying therapies in Parkinson's disease. *J Neurol Neurosurg Psychiatry*. 2010;81: 171–176.
- Greene BR, O'Donovan A, Romero-Ortuno R, Cogan L, Scanail CN, Kenny RA. Quantitative falls risk assessment using the timed up and go test. *IEEE Trans Biomed Eng*. 2010;57: 2918–2926.
- Bonato P. Wearable Sensors and Systems. *IEEE Eng Med Biol Mag*. 2010;29: 25–36.
- 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;9: 21.
- Salarian A, Horak FB, Zampieri C, Carlson-Kuhta P, Nutt JG, Aminian K. iTUG, a sensitive and reliable measure of mobility. *IEEE Trans Neural Syst Rehabil Eng*. 2010;18: 303–310.
- Godfrey A, Lara J, Del Din S, Hickey A, Munro CA, Wiuff C, et al. iCap: instrumented assessment of physical capability. *Maturitas*. 2015;82: 116–122.
- Godfrey A, Lara J, Munro CA, Wiuff C, Chowdhury SA, Del Din S, et al. Instrumented assessment of test battery for physical capability using an accelerometer: a feasibility study. *Physiol Meas*. 2015;36: N71.
- Jallon P, Dupre B, Antonakios M. A graph based method for timed up & go test qualification using inertial sensors. 2011 IEEE International Conference on Acoustics, Speech and Signal Processing (ICASSP). 2011. pp. 689–692.
- Al-Jawad A, Adame MR, Romanovas M, Hobert M, Maetzel W, Traechter M, et al. Using multi-dimensional dynamic time warping for TUG test instrumentation with inertial sensors. *IEEE International Conference on Multisensor Fusion and Integration for Intelligent Systems (MFI)*. 2012. pp. 212–218.
- Palmerini L, Mellone S, Rocchi L, Chiari L. Dimensionality reduction for the quantitative evaluation of a smartphone-based Timed Up and Go test. 2011 International Conference of the IEEE Engineering in Medicine and Biology Society. 2011. pp. 7179–7182.
- Greene BR, Doherty EP, O'Halloran A, Kenny RA. Frailty status can be accurately assessed using inertial sensors and the TUG test. *Age Ageing*. 2014;43: 406–411.
- Galan-Mercant A, Cuesta-Vargas AI. Differences in trunk accelerometry between frail and non-frail elderly persons in functional tasks. *BMC Res Notes*. 2014;7: 100.
- Weiss A, Mirelman A, Buchman AS, Bennett DA, Hausdorff JM. Using a body-fixed sensor to identify subclinical gait difficulties in older adults with IADL disability: maximizing the output of the timed up and go. *PLoS One*. 2013;8.
- Weiss A, Herman T, Plotnik M, Brozgov M, Giladi N, Hausdorff JM. An instrumented timed up and go: the added value of an accelerometer for identifying fall risk in idiopathic fallers. *Physiol Meas*. 2011;32: 2003–2018.
- Mirelman A, Weiss A, Buchman AS, Bennett DA, Giladi N, Hausdorff JM. Association between performance on Timed Up and Go subtasks and mild cognitive impairment: further insights into the links between cognitive and motor function. *J Am Geriatr Soc*. 2014;62: 673–678.
- Palmerini L, Mellone S, Avanzolini G, Valzania F, Chiari L. Quantification of motor impairment in Parkinson's disease using an instrumented timed up and go test. *IEEE Trans Neural Syst Rehabil Eng*. 2013;21: 664–673.
- Rocchi L, Palmerini L, Weiss A, Herman T, Hausdorff JM. Balance testing with inertial sensors in patients with Parkinson's disease: assessment of motor subtypes. *IEEE Trans Neural Syst Rehabil Eng*. 2014;22: 1064–1071.
- Herman T, Weiss A, Brozgov M, Giladi N, Hausdorff JM. Identifying axial and cognitive correlates in patients with Parkinson's disease motor subtype using the instrumented Timed Up and Go. *Exp Brain Res*. 2014;232: 713–721.
- Zakaria NA, Kuwae Y, Tamura T, Minato K, Kanaya S. Quantitative analysis of fall risk using TUG test. *Comput Methods Biomech Biomed Engin*. 2015;18: 426–437.
- Moore AZ, Caturegli G, Metter EJ, Makrogiannis S, Resnick SM, Harris TB, et al. Difference in muscle quality over the adult life span and biological correlates in the Baltimore Longitudinal Study of Aging. *J Am Geriatr Soc*. 2014;62: 230–236.
- Vandervoort AA. Aging of the human neuromuscular system. *Muscle Nerve*. 2002;25: 17–25.
- Kosse NM, Vuillerme N, Hortobágyi T, Lamothe CJC. Multiple gait parameters derived from iPod accelerometry predict age-related gait changes. *Gait Posture*. 2016;46: 112–117.
- Danneskiold-Samsøe B, Bartels EM, Bülow PM, Lund H, Stockmarr A, Holm CC, et al. Isokinetic and isometric muscle strength in a healthy population with special reference to age and gender. *Acta Physiol*. 2009;197: 1–68.
- Bidargaddi N, Klingbeil L, Sarella A, Boyle J, Cheung V, Yelland C, et al. Wavelet based approach for posture transition estimation using a waist worn accelerometer. 2007 International Conference of the IEEE Engineering in Medicine and Biology Society. 2007. pp. 1884–1887.

34. Soangra R, Lockhart TE, Van de Berge N. An approach for identifying gait events using wavelet denoising technique and single wireless IMU. *Proceedings of the Human Factors and Ergonomics Society Annual Meeting*. 2011. pp. 1990–1994.
35. Percival DB, Walden AT. *Wavelet methods for time series analysis*. Cambridge University Press; 2000.
36. Lockhart TE, Soangra R, Zhang J, Wu X. Wavelet based automated postural event detection and activity classification with single IMU (TEMPO). *Biomed Sci Instrum*. 2013;49: 224–33.
37. Najafi B, Aminian K, Paraschiv-Ionescu A, Loew F, Bula CJ, Robert P. Ambulatory system for human motion analysis using a kinematic sensor: monitoring of daily physical activity in the elderly. *IEEE Trans Biomed Eng*. 2003;50: 711–723.
38. Ayachi FS, Nguyen HP, Lavigne-Pelletier C, Goubault E, Boissy P, Duval C. Wavelet-based algorithm for auto-detection of daily living activities of older adults captured by multiple inertial measurement units (IMUs). *Physiol Meas*. 2016;37: 442–461.
39. Van Lummel RC, Ainsworth E, Lindemann U, Zijlstra W, Chiari L, Van Campen P, et al. Automated approach for quantifying the repeated sit-to-stand using one body fixed sensor in young and older adults. *Gait Posture*. 2013;38: 153–156.
40. Mellone S, Tacconi C, Chiari L. Validity of a Smartphone-based instrumented Timed Up and Go. *Gait Posture*. 2012;36: 163–165.
41. Eriksson L, Johansson E, Kettaneh-Wold N, Trygg J, Wikström C, Wold S. Multi-and megavariable data analysis. *Umetrics*; 2006.
42. Perez-Enciso M, Tenenhaus M. Prediction of clinical outcome with microarray data: a partial least squares discriminant analysis (PLS-DA) approach. *Hum Genet*. 2003;112: 581–592.
43. Greve C, Zijlstra W, Hortobágyi T, Bongers RM. Not all is lost: old adults retain flexibility in motor behaviour during sit-to-stand. *PLoS One*. 2013;8.
44. Hausdorff JM, Rios DA, Edelberg HK. Gait variability and fall risk in community-living older adults: a 1-year prospective study. *Arch Phys Med Rehabil*. 2001;82: 1050–1056.
45. Montero-Odasso M, Muir SW, Hall M, Doherty TJ, Kloseck M, Beauchet O, et al. Gait variability is associated with frailty in community-dwelling older adults. *Journals Gerontol Ser A*. 2011;66: 568–576.
46. König N, Singh NB, Von Beckerath J, Janke L, Taylor WR. Is gait variability reliable? An assessment of spatio-temporal parameters of gait variability during continuous overground walking. *Gait Posture*. 2014;39: 615–617.
47. Decker LM, Cignetti F, Potter JF, Studenski SA, Stergiou N. Use of motor abundance in young and older adults during dual-task treadmill walking. *PLoS One*. 2012;7.
48. Fernandez EA, Valtuille R, Willshaw P, Balzarini M. Partial least squares regression: a valuable method for modeling molecular behavior in hemodialysis. *Ann Biomed Eng*. 2008;36: 1305–1313.
49. Kosse NM, Caljouw S, Vervoort D, Vuillerme N, Lamoth CJC. Validity and reliability of gait and postural control analysis using the tri-axial accelerometer of the iPod touch. *Ann Biomed Eng*. 2015;43: 1935–1946.
50. Galán-Mercant A, Barón-López FJ, Labajos-Manzaneres MT, Cuesta-Vargas AI. Reliability and criterion-related validity with a smartphone used in timed-up-and-go test. *Biomed Eng Online*. 2014;13: 156.

SUPPORTING INFORMATION

Supporting information is available on the website of the publisher.

S1 Dataset. Contains all outcome parameters of the data of the first trial from which the first Partial Least Square Model was made.

S2 Dataset. File includes the extracted measures of the first PLS model which were used for the Partial Least Square Discriminant Analysis.

CHAPTER 3

Effects of aging and task prioritization on split-belt gait adaptation

Frontiers in Aging Neuroscience (2019) 11:10.

Daniqué Vervoort^{1,2}, Rob den Otter¹, Tom J.W. Buurke¹, Nicolas Vuillerme^{2,3}, Tibor Hortobágyi¹, Claudine JC Lamoth¹

¹University of Groningen, University Medical Center Groningen, Center for Human Movement Sciences, Groningen, The Netherlands

²University Grenoble-Alpes, AGEIS, Grenoble, France

³Institut Universitaire de France, Paris, France

ABSTRACT

BACKGROUND: Age-related changes in the sensorimotor system and cognition affect gait adaptation, especially when locomotion is combined with a cognitive task. Performing a dual-task can shift the focus of attention and thus require task prioritization, especially in older adults. To gain a better understanding of the age-related changes in the sensorimotor system, we examined how age and dual-tasking affect adaptive gait and task prioritization while walking on a split-belt treadmill.

METHODS: Young (21.5 ± 1.0 y, $n = 10$) and older adults (67.8 ± 5.8 y, $n = 12$) walked on a split-belt treadmill with a 2:1 belt speed ratio, with and without a cognitive Auditory Stroop task. Symmetry in step length, limb excursion, and double support time, and strategy variables swing time and swing speed were compared between the tied-belt baseline (BL), early (EA) and late split-belt adaptation (LA), and early tied-belt post-adaptation (EP).

RESULTS: Both age groups adapted to split-belt walking by re-establishing symmetry in step length and double support time. However, young and older adults differed on adaptation strategy. Older vs. young adults increased swing speed of the fast leg more during EA and LA (0.10-0.13 m/s), while young vs. older adults increased swing time of the fast leg more (2%). Dual-tasking affected limb excursion symmetry during EP. Cognitive task performance was 5-6% lower during EA compared to BL and LA in both age groups. Older vs. young adults had a lower cognitive task performance (max. 11% during EA).

CONCLUSION: Healthy older adults retain the ability to adapt to split-belt perturbations, but interestingly age affects adaptation strategy during split-belt walking. This age-related change in adaptation strategy possibly reflects a need to increase gait stability to prevent falling. The decline in cognitive task performance during early adaptation suggests task prioritization, especially in older adults. Thus, a challenging motor task, like split-belt adaptation, requires prioritization between the motor and cognitive task to prevent adverse outcomes. This suggests that task prioritization and adaptation strategy should be a focus in fall prevention interventions.

KEYWORDS: Split-belt walking, Adaptive Gait, Aging, Older adults, Dual-task, Task prioritization

INTRODUCTION

Humans adapt their gait to environmental challenges, which allows walking on uneven surfaces, avoiding obstacles, and maintaining balance when slipping or tripping. Advancing age modifies the locomotor system, which reduces the ability of older adults to adapt to environmental perturbations while walking [1,2]. The age-related changes include the distal-to-proximal shift in joint torques and powers [3] and an increase of co-activation of agonist and antagonist lower extremity muscles [4]. While the age-related changes increase joint stability, these changes may have negative effects, as the metabolic cost of walking increases ~20% with aging [5]. Not only are there quantitative adaptations, but age also modifies the strategies used to negotiate obstacle perturbations while walking. Older adults increase step length to avoid the obstacle, which increases the sense of stability by decreasing the forward momentum of the center of mass [6,7].

Much less is known however about whether and how older adults adapt their gait to asymmetrical gait perturbations that are ubiquitous in daily life. A good ability to react to such perturbations could be essential to maintain walking balance and prevent falls. Perturbation studies have shown that an increase in the ability to perform reactive responses is associated with a lower number of falls [8]. A split-belt treadmill allows us to study not only the reactive responses but also locomotor adaptations to a sustained perturbation during walking in a controlled environment [9]. By setting each belt to a different speed, both the immediate changes in step characteristics, i.e. early adaptation, and the time course of adaptation over several minutes until late adaptation can be determined.

Split-belt walking initially creates an asymmetry in step length and double support time. Young adults adapt their gait to re-establish symmetry in both step length and double support time [9]. During the entire adaptation phase, there is an asymmetry in limb excursion, i.e., stride length on the split-belt treadmill [10], due to the longer stride on the fast belt during split-belt walking [9]. When returning to tied-belt walking, the so-called early post-adaptation, participants show aftereffects, such as asymmetry in step length in the opposite direction from early adaptation [9]. An inability to re-establish symmetry in step length and double support time during split-belt adaptation and the absence of aftereffects are presumable markers of reduced gait adaptability [11,12]. The early detection of reduced gait adaptability can help in identifying older adults at risk for adverse reactions to perturbations and thus prevent falls.

Healthy older adults are capable of adapting to split-belt walking, but age affects adaptation strategy, especially during the early adaptation phase. Older adults are termed as “speed” adaptors, with a ± 0.15 m/s greater decrease in swing speed of the slow leg. In contrast, young adults are “timing” adaptors, indicated by a $\pm 5\%$ shorter swing time of the slow leg. To the best of our knowledge, the previously mentioned study is the only work that examined the effects of age on gait adaptation strategies [11].

Besides single-task gait adaptation, dual-task gait adaptation is of interest. Distraction-free gait is rare and dual-tasking is rather the norm than the exception in daily life. There is however no consensus concerning the effects of motor-cognitive dual-tasking on gait adaptation. Dual-tasking slowed the rate of adaptation on step length symmetry in the adaptation phase in young [13] and middle-aged adults [14]. Motor-cognitive dual-tasking also increased stance time on the fast belt and double support time on the slow belt in young adults [15], and another study reported that older adults exhibited a larger step time asymmetry [16].

The inconsistent results concerning motor-cognitive dual-tasking might be due to the types of cognitive tasks performed or the gait outcomes used, but could also be due to task prioritization. An integrated task prioritization model suggests that healthy adults perform and focus on the secondary cognitive task as long as the threat to postural control is low. A challenging environment or a demanding motor task can shift the focus of attention from the secondary cognitive task to the motor task in order to maintain gait [17].

While young adults can flexibly allocate attentional resources between two concurrent tasks [18], attentional capacity decreases with age, thus motor-cognitive dual-tasking becomes more challenging [19]. During dual-task split-belt walking, especially older adults may prioritize gait in order to adequately adapt to the perturbation of the split-belt. Indeed, after short perturbations, while performing a cognitive task, older adults prioritized dynamic stability, as shown by a sharp increase in the number of errors on the cognitive task [20]. While walking on elevated or narrow surfaces with a dual-task, older adults not only increased the number of errors on the cognitive task but also committed more missteps, suggesting that prioritization of the motor task in high-risk settings might fail for older adults [21].

The ability to adapt to the perturbation induced by the split-belt treadmill is essential to continue walking. However, this ability might be altered or affected by age, dual-tasking or task prioritization. Therefore, our aims were to determine: 1) The effect of split-belt adaptation and age on gait strategy and symmetry; 2) The effect of motor-cognitive dual-tasking on gait adaptation, and 3) Age-related differences in task prioritization during split-belt adaptation. We hypothesized that adaptations to split-belt walking occur independent of age, but young vs. older adults are “timing” and “speed” adaptors, respectively. We also expected that motor-cognitive dual-tasking would affect the ability to adapt to split-belt walking in the spatial or temporal gait outcomes. Furthermore, we hypothesized older vs. young adults will prioritize the motor adaptation task over the cognitive task in the most challenging early period of adaptation to split-belt walking.

MATERIAL AND METHODS

PARTICIPANTS

Healthy young (21.5 ± 1.0 years, 40% male, $n = 10$) and older adults (67.8 ± 5.8 years, 58% male, $n = 12$) who could walk without aids and follow verbal instructions were included in the study. Criteria for exclusion were orthopedic, neurological, and/or psychiatric disorders that might affect gait, and prior experience with split-belt walking. The Ethical Committee of the Center of Human Movement Sciences at the University Medical Center Groningen approved the study. All participants signed a written informed consent before the measurements.

INSTRUMENTATION AND PROCEDURE

Participants walked on an M-Gait treadmill (Motekforce Link, Amsterdam, The Netherlands), with two belts that can be controlled separately. With the embedded force plates in the treadmill, ground reaction forces were sampled at 1000 Hz. Infrared emitting diodes were placed on the feet (5th metatarsal head) and ankle (lateral malleolus) and recorded at 100 Hz (Optotrak, Northern Digital, Ontario, Canada).

Participants walked on the split-belt treadmill, starting with 3 min of tied-belt walking at both 1.0 m/s and 0.5 m/s (baseline), then split-belt walking with one belt moving at 1.0 m/s and the other belt at 0.5 m/s for 6 min (adaptation) and finally with tied-belts at 0.5 m/s for 6 min (post-adaptation; Fig. 1).

In the first condition (single-task), participants walked on the split-belt treadmill for a total of 18 min without a cognitive task. In the second condition (dual-task), participants walked while performing a cognitive task. This task order was chosen in order to minimize the learning effect of re-exposure to split-belt walking, which could potentially affect single-task adaptation and task prioritization during the second condition. Even though we cannot exclude that there were effects of motor learning in the second condition, due to the first condition, earlier studies have revealed that participants still show adaptation during re-exposure to the split-belt [14,22], allowing us to test our hypothesis on task prioritization.

Between the two conditions, participants could rest for 2 min or longer if needed. The fast belt was randomly assigned to the left or right leg. In the dual-task condition, the fast belt was assigned to the other side as in the single-task condition, in order to minimize the learning effect of re-exposure to the split-belt.

The cognitive task was the Auditory Stroop test. The Auditory Stroop test consists of the words “high” and “low” in a high or low pitch. Participants were instructed to call out the pitch of the word they heard, ignoring the actual word presented [15]. Participants had to be able to hear the words of the Auditory Stroop test. The test was performed in a control condition while sitting and during the dual-task condition at the last minute of the slow baseline (BL) until the first minute of adaptation (EA); the last minute of adaptation (LA) until the first minute of post-adaptation (EP); and the last minute of post-adaptation (LP; Fig. 1). No instructions on task prioritization were given. Verbal responses were recorded to determine the number of correct responses.

Fig. 1. Split-belt paradigm. Healthy young and older adults walked on a split-belt treadmill programmed to speed up one of the belts from 0.5 m/s to 1.0 m/s under single and dual-task conditions. The single-task condition was always performed before the dual-task condition. Note that the fast and slow belts were randomly assigned per participant to the left or right leg for single-task walking. If the fast belt was assigned to the left belt in the single-task, then in the dual-task condition the right belt was the fast belt. The dual-task was performed during five phases: the late slow baseline (BL), early adaptation (EA), late adaptation (LA), early post-adaptation (EP) and the late post-adaptation (LP). Abbreviations: DT = dual-task.

DATA ANALYSIS

Data were analyzed off-line with custom made Matlab codes (R2015b, The MathWorks Inc.). Vertical ground reaction forces were filtered with a second-order low-pass Butterworth filter (15 Hz cut-off). Data from the Optotrak markers were filtered with a second-order high-pass Butterworth filter (0.5 Hz cut-off).

Heel-strike and toe-off were determined at the moment the vertical forces crossed the threshold of 50 N. The foot contact moments were then used to calculate the outcome variables for the first and last five strides of the BL, EA, LA, and EP phases, allowing the following three comparisons: EA vs. BL (effect of the perturbation), LA vs. EA (adaptive change), EP vs. BL (aftereffects). For both spatial variables, limb excursion and step length, the foot contact moments were resampled to match the Optotrak sample frequency.

Symmetry variables were calculated for spatial variables step length (SL) and limb excursion (LE) and the temporal variable double support time (DS). SL was calculated as the anterior-posterior distance between the ankle markers of both legs at heel-strike of the leading leg [9]. With x as the position of the lateral malleolus marker (latmal) at the i^{th} sample.

$$SL_{fast}(i) = x_{latmal_{fast}}[t_{heelstrike\ fast}(i)] - x_{latmal_{slow}}[t_{heelstrike\ fast}(i)]$$

LE was defined as the distance travelled by the ankle marker in the anterior-posterior direction from heel-strike to toe-off of one limb [10].

$$LE(i) = x_{latmal}[t_{heelstrike}(i)] - x_{latmal}[t_{toeoff}(i)]$$

DS was defined as the time (t) both feet were in contact with the ground [9].

$$DS_{fast}(i) = t_{toeoff\ slow}(i) - t_{heelstrike\ fast}(i)$$

Symmetry in SL (SLS), LE (LES), and DS (DSS) was calculated as follows [13]:

$$Symmetry(i) = \frac{Fast(i) - Slow(i)}{Fast(i) + Slow(i)}$$

To reduce the SL asymmetry induced by the split-belt perturbation, the fast leg needs to be placed further forward than the slow leg. This can be achieved by using two strategies: 1) increasing the time spent in swing, or 2) increasing swing speed. Therefore, the strategy variables percentage swing time (SwT) and swing speed (SwS) were calculated as [11]:

$$SwT_{fast/slow}(i) = \frac{t_{heelstrike(i)} - t_{toeoff(i)}}{t_{heelstrike(i+1)} - t_{heelstrike(i)}} \times 100$$

$$SwS_{fast/slow}(i) = \frac{LE(i)}{t_{heelstrike(i)} - t_{toeoff(i)}}$$

For all gait variables, the dual-task cost (DTC) was determined from the single and dual-task condition values, with DTC values above zero indicating a larger value in the single-task condition and values below zero indicating that there was an effect of the dual-task [18].

$$DTC = \frac{(single\ task - dual\ task)}{single\ task} * 100$$

Cognitive task performance (CTP) was calculated with the following formula, with n as the number of stimuli. A value of one indicates perfect performance.

$$CTP = \frac{n_{correct}}{n_{total}}$$

STATISTICAL ANALYSIS

To examine the effect of split-belt walking and if young and older adults differ on split-belt adaptation (aim 1), a repeated measures ANOVA was conducted with within factor Phase (BL-EA-LA-EP) and between factor Group (young vs. older adults) during single-task split-belt walking for the dependent gait variables. When a main effect of phase was found, a post hoc dependent samples t-test with Holm-Bonferroni correction was applied to the following phase comparisons: EA vs. BL (effect of the perturbation), LA vs. EA (adaptive change), EP vs. BL (aftereffects). For significant interaction effects, the difference between age groups was tested with an independent samples t-test for each phase separately.

To address the second aim, the differences between single and dual-task split-belt walking were assessed using planned comparison t-tests to determine if DTC was different from zero for each of the four phases (BL-EA-LA-EP).

For the third aim, the differences in prioritization during dual-task split-belt adaptation between young and older adults, adaptation effects were first tested with a repeated measures ANOVA for the dual-task condition with within factor Phase (BL-EA-LA-EP) and between factor Group (young vs. older adults) for all gait variables. Post hoc testing was done similarly as for the first aim. The cognitive task performance was tested with a similar repeated measures ANOVA with the CTP as dependent variable. Differences between the age groups during the control task (sitting) were tested with an independent samples t-test to test if there were differences between the age groups during the single task. Statistical analysis was performed using SPSS (24.0, IBM Corp. Armonk, NY, USA). Level of significance was set at $p < 0.05$.

RESULTS

SINGLE-TASK SPLIT-BELT ADAPTATION AND DIFFERENCES BETWEEN YOUNG AND OLDER ADULTS

For the single-task split-belt condition, a significant main effect of phase was found for the symmetry variables, step length symmetry (SLS; $F_{(2,3,47)} = 28.3$; $p < 0.001$), limb excursion symmetry (LES; $F_{(1,8,35)} = 130.8$; $p < 0.001$) and double support symmetry (DSS; $F_{(2,1,42)} = 46.0$; $p < 0.001$), as well as for the strategy variables, swing time of the fast (SwT_{fast} ; $F_{(3,60)} = 122.6$; $p < 0.001$) and slow leg (SwT_{slow} ; $F_{(2,3,46)} = 23.0$; $p < 0.001$) and swing speed of the fast (SwS_{fast} ; $F_{(3,60)} = 102.5$; $p < 0.001$) and slow leg (SwS_{slow} ; $F_{(2,2,44)} = 64.1$; $p < 0.001$). Post-hoc testing revealed that for the symmetry variables SLS and DSS, an asymmetry occurred in early adaptation (EA) due to the perturbation of the changing belt speeds, while symmetry was re-established in late adaptation (LA). The early post-adaptation phase (EP) showed aftereffects of SLS and DSS asymmetry in the opposite direction from early adaptation. During the entire adaptation phase, both early and late adaptation, there is an asymmetry in LES due to the longer stride on the fast belt (see Fig. 2). For the strategy variables, an increase was seen in swing time of the fast leg

and swing speed for both legs during early adaptation, while there was a decrease in swing time of the slow leg. While swing time of the fast leg and swing speed of the slow leg slightly decreased until late adaptation, swing speed of the fast leg continued to increase (see Fig. 3). Table 1 presents the direction of the changes of the gait variables over the phases and the corresponding post hoc statistics.

Fig. 2. Adaptation plots of the symmetry variables for young and older adults during the single-task split-belt condition. The adaptation plot shows the development of the mean and standard deviation of the symmetry variables over the split-belt condition, starting with the 90 steps of the slow baseline, then 230 steps of the adaptation phase and then the post-adaptation phase with 180 steps. The symmetry values for step length (A-B), limb excursion (G-H) and double support time (M-N) and the separate values for the fast and slow leg (step length (C-F), limb excursion (I-L) and double support time (O-R)) are shown for young (left) and older adults (right).

Fig. 3. Adaptation plots of the strategy variables for young and older adults during the single-task split-belt condition. The adaptation plot shows the development of the mean and standard deviation of the strategy variables swing time (A-B) and swing speed (C-D) over the split-belt condition. The adaptation plot starts with the 90 steps of the slow baseline, then 230 steps of the adaptation phase and then the post-adaptation phase with 180 steps. Values of the fast leg are shown in black, values of the slow leg are shown in grey.

Table 1. Post hoc tests for the main effect of phase in the single-task split-belt condition.

Variable	Post hoc tests for the main effect of phase								
	EA - BL			LA - EA			EP - BL		
	Diff	t ₍₂₁₎	p	Diff	t ₍₂₁₎	p	Diff	t ₍₂₁₎	p
SLS	-0.04 ± 0.09	-1.90	0.07	0.10 ± 0.07	6.04	<0.001	0.13 ± 0.09	6.72	<0.001
LES	0.19 ± 0.07	13.45	<0.001	0.06 ± 0.05	5.62	<0.001	0.08 ± 0.06	6.02	<0.001
DSS	0.15 ± 0.10	6.73	<0.001	-0.12 ± 0.11	-5.27	<0.001	-0.09 ± 0.08	-5.43	<0.001
SWT _{fast} (%)	9.34 ± 3.59	12.19	<0.001	-2.14 ± 2.46	-4.09	0.001	-0.09 ± 2.58	-0.16	0.87
SWT _{slow} (%)	-3.53 ± 3.33	-4.96	<0.001	2.30 ± 2.26	4.76	<0.001	2.21 ± 3.94	2.62	0.016
SwS _{fast} (m/s)	0.32 ± 0.14	11.19	<0.001	0.06 ± 0.12	2.45	0.023	0.12 ± 0.10	5.39	<0.001
SwS _{slow} (m/s)	0.32 ± 0.18	8.12	<0.001	-0.17 ± 0.14	-5.50	<0.001	-0.01 ± 0.10	-0.68	0.51

The table presents results of the post hoc t-tests, with the t-value (t(df)), the p-value and the differences (Diff) between the two phases that were tested. Diff values are mean ± standard deviations. P-values are highlighted in bold if the phases were significantly different after the Holm-Bonferroni correction. Abbreviations: Diff = difference score; BL = baseline; EA = early adaptation; LA = late adaptation; EP = early post-adaptation; SLS = step length symmetry; LES = limb excursion symmetry; DSS = double support symmetry; SWT = swing time; SwS = swing speed.

There were no main effects of group for the gait variables, but Phase by Group interactions were significant for LES ($F_{(1,8,35)} = 4.4$; $p = 0.024$), SWT_{fast} ($F_{(3,60)} = 4.8$; $p = 0.006$), SwS_{fast} ($F_{(3,60)} = 5.3$; $p = 0.003$) and SwS_{slow} ($F_{(2,2,44)} = 4.2$; $p = 0.018$). Post-hoc testing revealed that during baseline (BL) there was a slight asymmetry of LES in opposite directions in young and older adults ($t_{(20)} = 2.3$; $p = 0.033$; see Fig. 4). In early adaptation there was a difference of 0.06 greater asymmetry in LES in older vs. young adults ($t_{(20)} = -2.5$; $p = 0.023$). SWT_{fast} showed that young adults had a trend of ±2% higher swing time of the

fast leg compared to older adults during early ($t_{(20)} = 1.8$; $p = 0.094$) and late adaptation ($t_{(20)} = 1.7$; $p = 0.100$). During both early and late adaptation older vs. young adults had respectively a 0.13 and 0.10 m/s higher swing speed of the fast leg (respectively $t_{(20)} = -2.3$; $p = 0.034$ and $t_{(20)} = -2.3$; $p = 0.032$; see Fig. 4). Older compared to young adults had a 0.09 m/s higher swing speed of the slow leg during baseline ($t_{(20)} = -3.0$; $p = 0.006$).

DIFFERENCE BETWEEN SINGLE AND DUAL-TASK SPLIT-BELT WALKING

No significant effects for dual-task cost were found between the single and dual-task condition, except for LES during early post-adaptation ($t_{(21)} = 2.3$; $p = 0.033$). During motor-cognitive dual-tasking, the aftereffects of LES were lower than during the single-task.

DUAL-TASK SPLIT-BELT ADAPTATION FOR YOUNG AND OLDER ADULTS

There was a significant main effect of Phase for both symmetry, SLS ($F_{(2,3,47)} = 28.3$; $p < 0.001$), LES ($F_{(1,8,35)} = 130.8$; $p < 0.001$) and DSS ($F_{(2,1,42)} = 46.0$; $p < 0.001$), and strategy gait variables, SwT_{fast} ($F_{(3,60)} = 122.6$; $p < 0.001$), SwT_{slow} ($F_{(2,3,46)} = 23.0$; $p < 0.001$), SwS_{fast} ($F_{(3,60)} = 102.5$; $p < 0.001$) and SwS_{slow} ($F_{(2,2,44)} = 64.1$; $p < 0.001$), similar to the single-task condition. Post hoc testing revealed that the symmetry variables SLS and DSS showed a similar pattern of asymmetry during early adaptation and re-established symmetry during late adaptation, with opposite aftereffects during early post-adaptation (see Table 2 for the direction and post hoc statistics of all gait variables). Thus, there was still adaptation during this second exposure of split-belt walking necessary for testing task prioritization (see Fig. 5-6). No significant age or interaction effects were found in any of the gait variables.

Table 2. Post hoc tests for the main effect of phase in the dual-task split-belt condition.

Variable	Post hoc tests for the main effect of phase								
	EA - BL			LA - EA			EP - BL		
	Diff	$t_{(21)}$	p	Diff	$t_{(21)}$	p	Diff	$t_{(21)}$	p
SLS	-0.03 ± 0.05	-2.45	0.023	0.10 ± 0.04	11.28	<0.001	0.11 ± 0.14	3.57	0.002
LES	0.17 ± 0.04	19.31	<0.001	0.06 ± 0.03	8.72	<0.001	0.05 ± 0.03	7.96	<0.001
DSS	0.12 ± 0.13	4.04	0.001	-0.11 ± 0.13	-3.83	0.001	-0.08 ± 0.10	-3.75	0.001
SwT_{fast} (%)	9.01 ± 3.77	11.21	<0.001	-1.77 ± 3.87	-2.15	0.04	-0.05 ± 1.95	-0.13	0.90
SwT_{slow} (%)	-3.40 ± 2.80	-5.70	<0.001	1.99 ± 3.54	2.64	0.015	1.98 ± 2.38	3.91	0.001
SwS_{fast} (m/s)	0.32 ± 0.14	11.14	<0.001	0.06 ± 0.15	1.80	0.09	0.09 ± 0.07	5.61	<0.001
SwS_{slow} (m/s)	0.29 ± 0.08	16.84	<0.001	-0.14 ± 0.10	-6.61	<0.001	-0.02 ± 0.09	-0.80	0.43

The table presents results of the post hoc t-test, with the t-value ($t(df)$), the p-value and the differences (Diff) between the two phases that were tested. Diff values are mean ± standard deviations. P-values are highlighted in bold if the phases were significantly different after the Holm-Bonferroni correction. Abbreviations: Diff = difference score; BL = baseline; EA = early adaptation; LA = late adaptation; EP = early post-adaptation; SLS = step length symmetry; LES = limb excursion symmetry; DSS = double support symmetry; SwT = swing time; SwS = swing speed.

Fig. 4. Bar plots of the symmetry (SLS, LES, DSS) and the strategy variables (Swing time, Swing speed) for young and older adults on the single-task split-belt condition. The four phases: baseline (BL), early adaptation (EA), late adaptation (LA) and early post-adaptation (EP) are shown next to each other. The bar plots show the median, the upper and lower quartiles and the min and max value of the age groups. The dots show the individual data of the young (black) and older adults (orange). There were interaction effects for LES, Swing time of the fast leg, and Swing speed of both legs. Abbreviations: SLS = step length symmetry; LES = limb excursion symmetry; DSS = double support symmetry.

Fig. 5. Adaptation plots of the symmetry variables for young and older adults during the dual-task split-belt condition. The adaptation plot shows the development of the mean and standard deviation of the symmetry variables over the split-belt condition, starting with the 90 steps of the slow baseline, then 230 steps of the adaptation phase and then the post-adaptation phase with 180 steps. The symmetry values for step length (A-B), limb excursion (G-H) and double support time (M-N) and the separate values for the fast and slow leg (step length (C-F), limb excursion (I-L) and double support time (O-R)) are shown for young (left) and older adults (right).

Fig. 6. Adaptation plots of the strategy variables for young and older adults during the dual-task split-belt condition. The adaptation plot shows the development of the mean and standard deviation of the strategy variables swing time (A-B) and swing speed (C-D) over the split-belt condition. The adaptation plot starts with the 90 steps of the slow baseline, then 230 steps of the adaptation phase and then the post-adaptation phase with 180 steps. Values of the fast leg are shown in black, values of the slow leg are shown in grey.

Fig. 7. Bar plot of cognitive task performance for young and older adults. Values are shown for the control condition, sitting, and the four phases of the split-belt paradigm: baseline (BL), early adaptation (EA), late adaptation (LA) and early post-adaptation (EP). The bar plots show the median, the upper and lower quartiles and the min and max value of the age groups. The dots show the individual data of the young (black) and older adults (orange). A value of one on cognitive task performance indicates perfect performance.

DIFFERENCES IN COGNITIVE TASK PERFORMANCE BETWEEN YOUNG AND OLDER ADULTS

In the seated control condition, the two age groups did not differ in cognitive task performance (CTP; Young: 0.95 ± 0.05 , Old: 0.96 ± 0.07 ; see Fig. 7). During motor-cognitive dual-tasking, there was a significant main effect of phase for CTP ($F_{(2,3,46)} = 6.5$; $p = 0.002$). Post hoc testing showed that all adults made on average 5-6% more errors on the Auditory Stroop task during early adaptation compared to their performance during baseline ($t_{(21)} = 3.0$; $p = 0.006$) and late adaptation ($t_{(21)} = -3.1$; $p = 0.006$). There was a significant main effect of group on CTP over all the split-belt phases (BL-EA-LA-EP). Young vs. old adults performed better on the cognitive task ($F_{(1,20)} = 11.0$; $p = 0.003$; see Fig. 7), with the largest difference of 11% seen in EA.

DISCUSSION

The overall aim of the present study was to gain insight into the effects of age and dual-tasking on adaptation to a perturbation induced by a split-belt treadmill and task prioritization. More specifically, we examined the effects of age and dual-tasking on gait symmetry and strategy. Both young and older adults adapted to split-belt walking and re-established gait symmetry, but the two age groups achieved this using a different strategy. Older adults increased swing speed of the fast leg, whereas young adults showed a trend of increased swing time of the fast leg. Dual-tasking compared with single-task split-belt walking did not affect gait adaptation strategies, but only affected limb excursion symmetry during the early post-adaptation phase, as indicated by smaller aftereffects. The lack of dual-task effects on all other gait variables and phases is likely due to task prioritization. Task prioritization is clearly present within the dual-task condition in the early adaptation phase, as revealed by worse cognitive task performance, even more so for older compared to young adults. We discuss these results with a perspective on how healthy older adults retain the ability to adapt to the split-belt perturbation.

In line with results of previous research [9,14], both young and older adults re-established symmetry in step length and double support time after the initial perturbation. The re-established symmetry by the older adults in this study indicates a retained ability to continuously adapt to split-belt walking. Although symmetry variables are widely reported and nicely reflect short as well as longer term split-belt adaptation, it is nevertheless important to examine the contribution of both legs (fast and slow) to clearly show the effects of gait adaptation [10]. The effects on gait symmetry can be harder to distinguish at lower speeds or speed ratios, like the 1:2 speed ratio of 0.5-1 m/s used in this study for feasibility. In the current study, we found most of the well-documented adaptation effects on gait symmetry, even with the limitations of these lower speeds and a small sample size with some variation within the age groups (see Fig. 4). It would, therefore, be interesting to further examine adaptive gait and the variation between participants with a larger sample size at slightly higher speeds to show even clearer differences within and between groups.

While both age groups adapt to split-belt walking, our results confirm previous data showing that the adaptation strategies were age-dependent [11]. Swing time of the fast leg showed a trend with a 2% larger increase for young compared to older adults, while swing speed of the fast leg increased 0.10-0.13 m/s more for older than young adults. With the limitation of a small sample size in the current study, only a trend of adaptation in 'timing' for young adults was found, but a larger sample size in future studies could further confirm the adaptation strategies. The current results do agree with

the concept that adaptations occur in ‘timing’ and ‘speed’ in young and older adults, respectively [11]. However, we found the ‘timing’ and ‘speed’ effects for the fast instead of the slow leg, possibly due to the treadmill being stopped between the baseline and adaptation phase in the previous study, while our participants continued walking. This causes a difference in acceleration of the belts between the two studies in that in our study only one belt accelerated with max 0.5 m/s^2 , while in the previous study both belts accelerated with max 0.3 m/s^2 [11].

The age-related change in adaptation strategy might be beneficial for older adults. Switching from a time to a speed strategy in response to a split-belt perturbation decreases the time spent in swing and thus decreases single leg stance, which increases gait stability during split-belt walking, especially immediately after the perturbation [11]. Maintaining dynamic stability during split-belt walking is also important over the longer period of adaptation, as shown by the adaptation of gait stability during the continuous perturbation of split-belt walking [23,24]. Furthermore, asymmetry in gait is associated with poor dynamic stability in stroke survivors [25]. In the context of the present study, the age-related differences in strategy to re-establish gait symmetry might be essential for older adults to maintain gait stability while walking on the split-belt to prevent falling.

Beyond gait stability, age-related decreases in neuromuscular function could contribute to the age-related differences in timing and speed strategies. The age-related reductions in leg muscle strength [26,27] and power [28] are associated with changes in the walking pattern including a slowing of gait speed, an increase in stance and double support time, and a decrease in swing time [29–31]. The neuromuscular changes might thus limit swing time during split-belt walking in old adults. Future research should determine the relationship between the age-related changes in neuromuscular function and the gait adaptation strategies observed in the present study. A comprehensive analysis of muscle activation patterns during split-belt walking, in both timing and contributions of muscles, could provide further insights into neuromuscular mechanisms underlying the age-dependent variations in gait adaptations.

Dual-tasking did not affect gait adaptation as there were no significant effects on dual-task cost, except for the aftereffects of limb excursion symmetry. The smaller aftereffects could be due to the fact that the dual-task caused participants to retain less of the split-belt adaptation. Since there was no randomization between the two conditions, we cannot exclude that fatigue might have had effects on the dual-task results, which is a limitation of the study. The lack of further dual-task effects is in contrast to the previously discussed motor-cognitive dual-tasking studies during split-belt walking [13–16]. We, however, propose that participants prioritized gait over the cognitive task, minimizing any effects of the secondary cognitive task on the gait variables.

At the onset of the speed differences between the belts, the early adaptation phase, both young and older adults performed worse on the cognitive task, as indicated by fewer responses to the Auditory Stroop stimuli compared to baseline and late adaptation. This result suggests that immediately after being exposed to split-belt walking there is a need to prioritize gait over performing the cognitive task for the sake of safety. Our findings support the theory of task prioritization [17] that people tend to prioritize the motor task over the cognitive task in a more challenging environment, in this case, a challenging motor task, which requires attentional capacity to maintain gait.

Furthermore, during dual-task split-belt walking older vs. young adults had 3-11% fewer correct responses on the cognitive task, with the largest differences also during the early adaptation phase. This implies that performing an additional task while reacting to the split-belt perturbation is harder for older adults. Therefore, it seems that older adults even more than young adults need to prioritize gait. The increased need to prioritize gait may be due to age-related changes. Interference from dual-tasking on walking ability starts at a lower level for individuals with less task-relevant resources, like older adults [19]. Older adults might also have a higher need to focus their attention on foot placement in response to the split-belt perturbation since afferent feedback is impaired in old age [32]. Afferent feedback facilitates adaptive gait, and a reduction in feedback from muscles leads to a poorer detection of errors that are important for accurate gait adaptation [33]. By prioritizing the motor task over the cognitive task during split-belt walking, older adults show that they have retained the ability to compensate for the age-related neuromuscular decline, which could help in preventing adverse reactions to perturbations.

CONCLUSIONS

Age did not affect gait symmetry after a split-belt perturbation but did affect adaptation strategy, with young and older adults adapting through “timing” and “speed” respectively. The role of this change in adaptation strategy is likely to increase gait stability in older adults to prevent falling. Task prioritization of the motor over the cognitive task may underlie the lack of dual-tasking effects on gait adaptation. This is supported by a decline in cognitive task performance during early adaptation, more so in older compared with young adults. We conclude that healthy older adults retain the ability to adapt to split-belt perturbations, but interestingly they adapt through a different adaptation strategy. Moreover, in challenging motor tasks, like split-belt adaptation, this requires task prioritization to prevent adverse outcomes. This suggests that task prioritization and adaptation strategy should be a focus in fall prevention interventions. Furthermore, future research should determine the relationship between gait adaptation strategies, gait stability, and neuromuscular function to understand the underlying mechanisms of age-related differences in split-belt adaptation.

REFERENCES

1. Bierbaum S, Peper A, Karamanidis K, Arampatzis A. Adaptive feedback potential in dynamic stability during disturbed walking in the elderly. *J Biomech.* 2011;44: 1921–1926.
2. McCrum C, Epro G, Meijer K, Zijlstra W, Brüggemann GP, Karamanidis K. Locomotor stability and adaptation during perturbed walking across the adult female lifespan. *J Biomech.* 2016;49: 1244–1247.
3. DeVita P, Hortobagyi T. Age causes a redistribution of joint torques and powers during gait. *J Appl Physiol.* 2000;88: 1804–1811.
4. Schmitz A, Silder A, Heiderscheit B, Mahoney J, Thelen DG. Differences in lower-extremity muscular activation during walking between healthy older and young adults. *J Electromyogr Kinesiol.* 2009;19: 1085–1091.
5. Hortobágyi T, Finch A, Solnik S, Rider P, DeVita P. Association between muscle activation and metabolic cost of walking in young and old adults. *Journals Gerontol Ser A.* 2011;66A: 541–547.
6. Weerdesteyn V, Nienhuis B, Duysens J. Advancing age progressively affects obstacle avoidance skills in the elderly. *Hum Mov Sci.* 2005;24: 865–880.
7. Weerdesteyn V, Nienhuis B, Mulder T, Duysens J. Older women strongly prefer stride lengthening to shortening in avoiding obstacles. *Exp brain Res.* 2005;161: 39–46.
8. McCrum C, Gerards MHG, Karamanidis K, Zijlstra W, Meijer K. A systematic review of gait perturbation paradigms for improving reactive stepping responses and falls risk among healthy older adults. *Eur Rev aging Phys Act.* 2017;14.
9. Reisman DS, Block HJ, Bastian AJ. Interlimb coordination during locomotion: what can be adapted and stored? *J Neurophysiol.* 2005;94: 2403–2415.
10. Hoogkamer W, Bruijn SM, Duysens J. Stride length asymmetry in split-belt locomotion. *Gait Posture.* 2014;39: 652–654.
11. Bruijn SM, Van Impe A, Duysens J, Swinnen SP. Split-belt walking: adaptation differences between young and older adults. *J Neurophysiol.* 2012;108: 1149–1157.
12. Vasudevan EVL, Torres-Oviedo C, Morton SM, Yang JF, Bastian AJ. Younger is not always better: Development of locomotor adaptation from childhood to adulthood. *J Neurosci.* 2011;31: 3055–3065.
13. Malone LA, Bastian AJ. Thinking about walking: effects of conscious correction versus distraction on locomotor adaptation. *J Neurophysiol.* 2010;103: 1954–1962.
14. Malone LA, Bastian AJ. Age-related forgetting in locomotor adaptation. *Neurobiol Learn Mem.* 2016;128: 1–6.
15. McFadyen BJ, Hegeman J, Duysens J. Dual task effects for asymmetric stepping on a split-belt treadmill. *Gait Posture.* 2009;30: 340–344.
16. Saito M, Hyodo M, Masakado Y, Tomita Y, Ushiba J. Age-related differences in cognitive function for interlimb coordination during split-belt walking: a pilot study. *Somatosens Mot Res.* 2013;30: 56–63.
17. Yogev-Seligmann G, Hausdorff JM, Giladi N. Do we always prioritize balance when walking? Towards an integrated model of task prioritization. *Mov Disord.* 2012;27: 765–770.
18. Raffegau TE, Haddad JM, Huber JE, Rietdyk S. Walking while talking: young adults flexibly allocate resources between speech and gait. *Gait Posture.* 2018;64: 59–62.
19. Huxhold O, Li SC, Schmiedek F, Lindenberger U. Dual-tasking postural control: aging and the effects of cognitive demand in conjunction with focus of attention. *Brain Res Bull.* 2006;69: 294–305.
20. Mersmann F, Böhm S, Bierbaum S, Dietrich R, Arampatzis A. Young and old adults prioritize dynamic stability control following gait perturbations when performing a concurrent cognitive task. *Gait Posture.* 2013;37: 373–377.
21. Schaefer S, Schellenbach M, Lindenberger U, Woollacott M. Walking in high-risk settings: do older adults still prioritize gait when distracted by a cognitive task? *Exp brain Res.* 2015;233: 79–88.
22. Malone LA, Vasudevan EVL, Bastian AJ. Motor adaptation training for faster relearning. *J Neurosci.* 2011;31: 15136–15143.
23. Buurke TJW, Lamoth CJC, Vervoort D, Van der Woude LH V, Den Otter AR. Adaptive control of dynamic balance in human gait on a split-belt treadmill. *J Exp Biol.* 2018;221.
24. Park S, Finley JM. Characterizing dynamic balance during adaptive locomotor learning. 2017 International Conference of the IEEE Engineering in Medicine and Biology Society. IEEE; 2017. pp. 50–53.
25. Lewek MD, Bradley CE, Wutzke CJ, Zinder SM. The relationship between spatiotemporal gait asymmetry and balance in individuals with chronic stroke. *J Appl Biomech.* 2014;30: 31–36.
26. Hayashida I, Tanimoto Y, Takahashi Y, Kusabiraki T, Tamaki J. Correlation between muscle strength and muscle mass, and their association with walking speed, in community-dwelling elderly Japanese individuals. *PLoS One.* 2014;9.
27. Nigg BM, Fisher V, Ronsky JL. Gait characteristics as a function of age and gender. *Gait Posture.* 1994;2: 213–220.
28. Bean JF, Kiely DK, Herman S, Leveille SG, Mizer K, Frontera WR, et al. The relationship between leg power and physical performance in mobility-limited older people. *J Am Geriatr Soc.* 2002;50: 461–467.
29. Laufer Y. Effect of age on characteristics of forward and backward gait at preferred and accelerated walking speed. *Journals Gerontol Ser A.* 2005;60: 627–632.
30. Samson MM, Crowe A, De Vreede PL, Dessens JA, Dursma SA, Verhaar HJ. Differences in gait parameters at a preferred walking speed in healthy subjects due to age, height and body weight. *Aging Clin Exp Res.* 2001;13: 16–21.
31. Winter DA, Patla AE, Frank JS, Walt SE. Biomechanical walking pattern changes in the fit and healthy elderly. *Phys Ther.* 1990;70: 340–347.
32. Goble DJ, Coxon JP, Wenderoth N, Van Impe A, Swinnen SP. Proprioceptive sensibility in the elderly: degeneration, functional consequences and plastic-adaptive processes. *Neurosci Biobehav Rev.* 2009;33: 271–278.
33. Bastian AJ. Moving, sensing and learning with cerebellar damage. *Curr Opin Neurobiol.* 2011;21: 596–601.

CHAPTER 4

Do gait and muscle activation patterns change at middle-age during split-belt adaptation?

Journal of Biomechanics (2020). 99:109510.

Danique Vervoort^{1,2}, Rob den Otter¹, Tom J.W. Buurke¹, Nicolas Vuillerme^{2,3}, Tibor Hortobágyi¹, Claudine JC Lamoth¹

¹University of Groningen, University Medical Center Groningen, Center for Human Movement Sciences, Groningen, The Netherlands

²University Grenoble-Alpes, AGEIS, Grenoble, France

³Institut Universitaire de France, Paris, France

ABSTRACT

Advancing age affects gait adaptability, but it is unclear if such adaptations to split-belt perturbations are already affected at middle-age. Changes in neuromuscular control, that already start at middle-age, may underlie the age-related changes in gait adaptation. Thus, we examined the effects of age on adaptations in gait and muscle activation patterns during split-belt walking in healthy young and middle-aged adults. Young (23.3 ± 3.13 years) and middle-aged adults (55.3 ± 2.91 years) walked on an instrumented split-belt treadmill. Both age groups adapted similarly by reducing asymmetry in step length and double support time. Surface EMG was recorded from eight leg muscles bilaterally. Principal Component Analysis (PCA) was applied to the EMG data of all subjects, for the fast and slow leg separately, to identify muscle activation patterns. The principal components consisted of i.e. temporal projections that were analyzed with Statistical Parametric Mapping (SPM). The functional muscle groups, identified by PCA, increased activation during early adaptation and post-adaptation, and decreased activation over time similarly in both age groups. Extra activation peaks of the plantar- and dorsiflexors suggest a role in gait modulation during split-belt walking. Both young and middle-aged adults re-established gait symmetry and showed adaptation effects in the muscle activation patterns. Since the adaptation of muscle activation patterns parallels adaptation of gait symmetry, changes in muscle activation likely underlie the changes in step parameters during split-belt adaptation. In conclusion, split-belt adaptation, in terms of gait and muscle activation patterns, is still preserved at middle-age, suggesting that age-related differences occur later in the lifespan.

KEYWORDS: Split-belt walking, Gait adaptation, Muscle activation patterns, Middle-aged adults, Statistical Parametric Mapping

INTRODUCTION

Advancing chronological age reduces the ability to adapt to changes in the environment [1]. Preserving gait adaptability seems crucial in preventing adverse outcomes, such as falls [2,3]. The nature of why, and at what age gait adaptability becomes compromised remains unclear. A popular paradigm to examine gait adaptability is split-belt walking, where gait is perturbed by imposing asymmetric belt speeds [4]. Directly after the belt speed perturbation, step length and double support time become asymmetric. After several minutes, symmetry is re-established through bilateral adjustments in these variables [4–6].

Data on age-related changes in split-belt adaptations so far have been inconsistent. Step length symmetry remained unaffected by age in some studies [7–9], while others reported age-effects on adaptation rate of step length symmetry [10,11]. If age effects exist, its underlying mechanism may relate to modifications in timing and amplitude of muscle activation. Immediately after the split-belt perturbation, leg muscle activation increases, and then decreases as adaptation progresses [12,13]. Also, changes in stance times were associated with an earlier onset and higher amplitude of m. gastrocnemius activation in the fast leg, higher m. tibialis anterior activation in the slow leg and higher m. tibialis anterior - m. gastrocnemius co-activation in the slow leg [14]. While these individual muscles show adaptations to split-belt walking, when faced with adaptive challenges, different neuromuscular control strategies could operate. Assessment of such strategies involves the identification of functional muscle groups, muscles that are activated simultaneously and generate specific movements, which are controlled by a common activation pattern that allows the central nervous system to simplify neuromuscular control [15]. These strategies can be measured with EMG.

Using pattern recognition methods, young adults' split-belt gait was previously characterized by four activation patterns. A temporal shift to 3-4% earlier in the gait cycle was observed in two uni- and bilateral activation patterns, likely due to changes in gait cycle timing [13]. Split-belt walking causes an asymmetry in muscle activation, which may be most accurately reflected by unilateral activation patterns. The control strategies of each leg could be autonomous, but the ipsilateral leg needs to interact with the contralateral leg to flexibly control walking and adapt to belt speed differences [16].

At older age, these activation patterns might be affected differently, because age increases the level of co-activation between agonist-antagonist muscle pairs [17] and decreases the onset latency between the tibialis anterior and gastrocnemius muscles [18]. Already during middle-age, there are several neuromuscular changes that arguably affect muscle activation during split-belt walking. During the 5th decade of human life, muscle mass starts to decline by 1-2% per year [19] and leg muscle strength, muscle power, and muscle quality decline, respectively, by 0.7-0.9%, 1.2-1.9% and 1.5-2.4% per year [20]. As expected based on such structural changes in muscle size, maximal voluntary force of the quadriceps is 30% lower in middle-aged compared with young adults [21]. It is conceivable that changes in muscle activation patterns associated with split-belt perturbations are already present at middle-age. Detecting age-related differences in the ability to adapt to split-belt perturbations before gait adaptability is impaired, might help preserve gait adaptability with older age without the presence of other factors that could affect this relationship, like deconditioning or disease.

The aim of this study is to examine the effect of age on adaptations of gait and muscle activation patterns induced by split-belt walking. We hypothesize that even if gait adaptation to the split-belt

perturbation is unaffected by age, its underlying neuromuscular control may still differ between age groups. We expect the muscle activation patterns to change over the course of adaptation, to modulate changes in gait cycle timing. The functional muscle groups will increase activation during early adaptation and post-adaptation. Finally, we hypothesize that middle-aged adults increase the activation and change the timing of functional muscle groups compared to young adults.

METHODS

PARTICIPANTS

Eleven healthy young (23.3 ± 3.13 years, 5 females, BMI = 23.3 ± 2.93 , hours participated in sports/week = 4.5 ± 3.10) and ten middle-aged adults (55.3 ± 2.91 years, 6 females, BMI = 23.1 ± 2.43 , hours participated in sports/week = 4.1 ± 1.49) participated in this study. Participants could walk outdoors without aids and understand verbal instructions. Exclusion criteria were previous experience with split-belt walking, orthopedic surgery of the lower extremities in the last two years, and neurological disorders, psychiatric disorders and/or medication use that might affect postural control and gait. The study protocol was approved by the local Ethical Committee of the Center of Human Movement Sciences of the University Medical Center Groningen. All participants signed a written informed consent before participating.

INSTRUMENTATION AND PROCEDURE

Participants walked on an instrumented split-belt treadmill (Motek, Amsterdam, The Netherlands). Embedded force plates measured ground reaction forces and center of pressure at 1000 Hz. Surface EMG was measured with a Trigno wireless system (bandwidth: 20-450 Hz; Delsys, Natick, MA, USA) at 2000 Hz on eight leg muscles bilaterally: Gluteus Medius (GM), Biceps Femoris (BF), Semitendinosus (ST), Rectus Femoris (RF), Vastus Medialis (VM), Medial Gastrocnemius (GAS), Soleus (SOL) and Tibialis Anterior (TA). Electrode placement locations were determined using SENIAM guidelines [22].

During the split-belt protocol participants first walked tied-belt with a fast (1.4 m/s) and slow baseline (0.7 m/s). During adaptation, one belt was accelerated from 0.7 m/s to 1.4 m/s, while the other belt stayed at 0.7 m/s. Participants returned to tied-belt walking at 0.7 m/s during post-adaptation (Fig. 1). The fast and slow belts were randomly assigned per participant.

Fig. 1. Split-belt protocol. Healthy young and middle-aged adults walked on a split-belt treadmill with tied- and split-belt phases. During the split-belt phase, the fast and slow belt were randomly assigned to left or right per participant. Abbreviations: BL = late slow baseline, EA = early adaptation, LA = late adaptation, EP = early post-adaptation, LP = late post-adaptation.

DATA ANALYSIS

Data were analyzed off-line with custom-made Matlab algorithms (R2015b, MathWorks, Natick, MA, USA). Force plate data were recursively filtered with a 15 Hz second-order low-pass Butterworth filter. Gait events were determined when the vertical ground reaction forces crossed the 50 N threshold. Gait parameters were averaged over the first and last five steps of each phase, late slow baseline (BL), early adaptation (EA), late adaptation (LA), early post-adaptation (EP) and late post-adaptation (LP).

EMG data were high-pass filtered using a 30 Hz second-order Butterworth filter, full-wave rectified using an absolute Hilbert transform, and low-pass filtered (10 Hz second-order recursive Butterworth filter). EMG data were down-sampled to 1000 Hz to obtain similar sample frequencies for the EMG and force plate data. EMG and force plate data were manually synchronized by aligning the moment of heel-strike of the left leg with the peak in TA EMG activation of the left leg.

EMG data were time normalized with 100 data points per gait cycle, 60 data points for the stance phase and 40 data points for the swing phase, starting at heel-strike [23]. Amplitude normalization was done by dividing the EMG signal by the maximum amplitude of the fast baseline EMG for each individual muscle. EMG was averaged for the first (EA, EP) or last five strides of the phases (BL, LA, LP). EMG data of one young subject was not included in the analysis.

GAIT PARAMETERS

Step Length (SL) was defined as the anterior-posterior distance between anteroposterior COP position of the left and right leg at contralateral toe-off [5]. Double Support time (DS) was defined as the time both feet were in contact with the ground, with the fast DS starting at heel-strike of the fast leg [4]. Symmetry for SL (SLS) and DS (DSS) was calculated as:

$$Symmetry(i) = \frac{Fast(i) - Slow(i)}{Fast(i) + Slow(i)}$$

PRINCIPAL COMPONENT ANALYSIS

Principal Component Analysis (PCA) was applied to study differences in amplitude or timing of the overall muscle activation pattern, by reducing the original individual EMG signals to a lower number of principal components (PCs) [24].

The input in the PCA was the combined EMG data of all phases and all participants, for the fast and slow leg separately. For each participant, an EMG matrix ($X_{m,c}$) was created by concatenating the phases (c) of each muscle (m). Then all subjects were included in one matrix (X_{EMC} ; formulas see Appendix).

Based on X_{EMC} , the covariance matrix was estimated. The eigenvectors and eigenvalues were calculated and sorted in descending order of eigenvalues. The temporal projections were determined by projecting the original EMG data onto the eigenvectors (Appendix). The number of PCs was established using the eigenvalue spectrum, with as cut-off criterion the gap between eigenvalues on a log-log scale [24].

STATISTICAL ANALYSIS

GAIT PARAMETERS

Two repeated measures ANOVAs were performed for the dependent variables SLS and DSS, with within-subjects factor Phase (BL, EA, LA, EP, LP) and between-subjects factor Group (young vs. middle-aged adults). Post-hoc testing was done with dependent t-tests with Holm-Bonferroni correction for the Phase comparisons: BL vs. EA (effect of perturbation), EA vs. LA (adaptive change), BL vs. EP (aftereffects) and BL vs. LP (return to baseline). Statistical analysis was performed in SPSS 24.0 (IBM, Armonk, NY, USA). Level of significance was set at $p < 0.05$.

STATISTICAL PARAMETRIC MAPPING ON PCA OUTCOMES

The temporal projections of the PCs were analyzed with Statistic Parametric Mapping (SPM). SPM uses random field theory to make statistical inferences regarding time-series data [see 25–27].

In SPM, test statistics are calculated for every data point of the time series to obtain a statistical parametric map. Based on the temporal gradients, the temporal smoothness of the SPM trajectory is estimated [28]. A critical threshold is calculated using random field theory, so only 5% (α) of the smooth random trajectory is expected to cross this threshold. These supra-threshold clusters correspond to time frames where statistically significant effects are detected. For each supra-threshold cluster, an individual probability (p) value is calculated [29]. Occasionally small supra-threshold clusters (<5% of cycle) are detected that are less likely to contain meaningful information. These clusters are reported in Table 3, but not discussed in the text.

The temporal projections were the input in the repeated measures ANOVA SPM, with within-subjects factor Phase (BL, EA, LA, EP, LP) and between-subjects factor Group (young vs. middle-aged). Post-hoc testing was done with an SPM t-test with Bonferroni correction, for the phase comparisons: BL vs. EA, EA vs. LA, BL vs. EP and BL vs. LP. The SPM analyses were performed in Matlab with open-source spm1d code (version M.0.1, www.spm1d.org).

RESULTS

GAIT PARAMETERS

The effect of Phase was significant for SLS and DSS. Post-hoc testing revealed that SLS and DSS showed asymmetry in EA, with a negative asymmetry for SLS (larger steps of the fast leg), and a positive asymmetry for DSS (larger double support times of the slow leg; see Fig. 2 and Table 1). This asymmetry leveled out towards LA, and the aftereffects in EP are in the opposite direction, i.e. a positive SLS and a negative DSS (see Fig. 2 and Table 1). No group effects were found.

MUSCLE ACTIVATION PATTERNS

Results of the PCA for the fast and slow leg revealed three PCs, explaining $\pm 77\%$ of data's variance. Fig. 3 illustrates the reconstruction of the EMG signal, based on the temporal projections and eigenvectors of the individual PCs. These reconstructions show which part of the original EMG signal is captured by each PC. The reconstruction of all PCs together shows that three PCs represent the original EMG signal well (Appendix Fig. A1). The PCs of the fast leg explained respectively 37.1%, 26.7%, and 12.5%, and the PCs of the slow leg explained 43.1%, 19.3%, and 15.1%. The associated eigenvectors of the muscles are presented in Table 2.

Fig. 2. Adaptation in step length and double support symmetry for young (black) and middle-aged adults (blue). Step length and double support symmetry are averaged over 3 steps and show the development over the entire split-belt protocol. For the figure, all phases consist of the lowest number of steps per phase, thus the baseline consists of 110 steps, the adaptation phase of 460 steps and the post-adaptation phase of 215 steps.

Table 1. The main effect of Phase and post-hoc testing for the gait parameters.

Gait parameters	Mean $\pm$ sd for the five phases					Main effect of Phase		
	BL	EA	LA	EP	LP	F-value	p-value	ES
SLS	0.01 $\pm$ 0.04	-0.41 $\pm$ 0.08	-0.16 $\pm$ 0.04	0.26 $\pm$ 0.13	0.02 $\pm$ 0.05	$F_{(2,03,39)} = 242.02$	<0.001	0.93
DSS	0.00 $\pm$ 0.04	0.16 $\pm$ 0.06	0.02 $\pm$ 0.05	-0.14 $\pm$ 0.08	0.00 $\pm$ 0.04	$F_{(2,44,46)} = 74.91$	<0.001	0.80
Post-hoc testing	BL vs. EA		EA vs. LA		BL vs. EP		BL vs. LP	
	t ₍₂₁₎	p	t ₍₂₁₎	p	t ₍₂₁₎	p	t ₍₂₁₎	p
SLS	25.29	<0.001	-12.21	<0.001	-8.10	<0.001	-1.52	0.14
DSS	-10.61	<0.001	7.94	<0.001	7.83	<0.001	-0.42	0.68

The table presents results of the repeated measures ANOVA (phase effect) and the post-hoc t-test comparisons between phases, with the F/t-values (F/t(df)) and the p-values. Gait parameter values of the five tested phases are given with mean $\pm$ standard deviation. P-values are highlighted in bold if the phases were significantly different (after Holm-Bonferroni correction). Abbreviations: BL = late slow baseline; EA = early adaptation; LA = late adaptation; EP= early post-adaptation; LP = late post-adaptation; SLS = step length symmetry; DSS = double support symmetry; ES = effect size.

Fig. 3. EMG profiles and reconstructions of PC1-3 for all muscles during baseline, early-adaptation, and post-adaptation. The original EMG signal (blue) is shown next to the signals that were reconstructed from the temporal projections and eigenvectors of the PCs as follows: $x_{rec}(j) = \sum V_m(j) * Y_k(j)$ [24]. The reconstructions show which part of the original EMG signal is captured within each PC. The data of all subjects are pooled since there were no group differences. Abbreviations: TA = Tibialis Anterior; SOL = Soleus; GAS = Gastrocnemius Medialis; BF = Biceps Femoris; ST = Semitendinosus; RF = Rectus Femoris; VM = Vastus Medialis; GM = Gluteus Medius.

Table 2. Eigenvectors of all 8 muscles for the three PCs of the fast and slow leg. The muscles that contribute to that PC are highlighted (>0.25).

Muscles	Fast leg			Slow leg		
	PC1	PC2	PC3	PC1	PC2	PC3
TA	0.14	0.49	0.03	0.35	0.26	0.11
SOL	0.42	0.41	0.09	0.09	0.43	0.31
GAS	0.42	0.60	0.01	0.07	0.63	0.30
BF	0.27	0.13	0.51	0.35	0.20	0.43
ST	0.38	0.17	0.66	0.35	0.31	0.61
RF	0.38	0.32	0.40	0.60	0.38	0.38
VM	0.31	0.25	0.16	0.39	0.05	0.08
GM	0.41	0.13	0.34	0.32	0.25	0.29

Abbreviations: TA = Tibialis Anterior; SOL = Soleus; GAS = Gastrocnemius Medialis; BF = Biceps. Femoris; ST = Semitendinosus; RF = Rectus Femoris; VM = Vastus Medialis; GM = Gluteus Medius.

SPM ANALYSIS

Table 3 shows the results of the SPM {F} and post-hoc SPM {t} tests on the temporal projections of the three extracted PCs. For the fast leg, the projections of all three PCs showed an effect of Phase. For the slow leg, the projection of the first and second PC showed an effect of Phase. No group or interaction effects were found.

POST-HOC SPM COMPARISON ACROSS PHASES

Fig. 4 shows the post-hoc test for the effect of phase for PC1 of the fast and slow leg, with the temporal projections of the phases (first and third row of graphs) and the SPM results of the post-hoc comparison between phases (second and fourth row). Post-hoc testing for PC1 of the fast leg showed increased activation in EA compared to BL and LA (Table 3; Fig. 4). During EA, there was an extra peak around 15% of the gait cycle, related to the extra activation peaks of the GAS, SOL, BF, ST (Fig. 3). These muscles could be activated to stabilize the leg while suddenly moving at a faster speed. Muscle activation during EP was significantly larger compared to BL. LP did not significantly differ from BL, suggesting a complete return to normal walking.

Similar effects were seen for PC1 of the slow leg (Table 3). During EA, muscle activation was significantly higher than BL and LA, and had an extra peak around 60% of the gait cycle (Fig. 4). During EP, muscle activation was significantly higher and had an extra peak around 60% compared to BL. The extra peak at 60% was related to the peak in RF and TA activation (Fig. 3). Possibly, the slow leg requires more control during swing initiation. LP and BL did not differ significantly.

Table 3. Results of the SPM {F} and post-hoc SPM {t} tests on the temporal projections of the fast (top panel) and slow leg (bottom panel).

SPM	DF	<i>PC1</i>			<i>PC2</i>			<i>PC3</i>		
		CT	Supra-threshold clusters	p-values	CT	Supra-threshold clusters	p-values	CT	Supra-threshold clusters	p-values
<i>Fast leg</i>										
Phase	F(4,72)	4.48	1) 0-69.4% 2) 72.8-100%	p<0.001 p<0.001	4.76	1) 6.0-43.7% 2) 52.2-65.3% 3) 82.4-84.5%	p<0.001 p<0.001 <i>p=0.039</i>	4.89	1) 59.5-62.8% 2) 71.0-82.3%	<i>p=0.02</i> p<0.001
EA vs. BL	t(1,38)	3.83	1) 0-100%	p<0.001	3.90	1) 0-4.1% 2) 10.6-17.8% 3) 40.4-44.5% 4) 53.0-100%	<i>p=0.003</i> p<0.001 <i>p=0.003</i> p<0.001	3.92	1) 12.0-21.0% 2) 69.4-82.8%	p<0.001 p<0.001
LA vs. EA	t(1,38)	3.83	1) 0-2.6% 2) 7.1-83.7% 3) 95.6-100%	<i>p=0.009</i> p<0.001 <i>p=0.005</i>	3.88	1) 52.8-82.4%	p<0.001	3.92	1) 15.5-19.7% 2) 69.5-81.7%	<i>p=0.003</i> p<0.001
EP vs. BL	t(1,38)	3.83	1) 0-66.2% 2) 76.5-100%	p<0.001 p<0.001	3.94	1) 7.4-41.1% 2) 53.8-65.6% 3) 79.5-95.5%	p<0.001 p<0.001 p<0.001	3.96	1) 13.8-19.2% 2) 44.4-45.6% 3) 59.1-64.3%	p<0.001 <i>p=0.011</i> p<0.001
LP vs. BL	t(1,38)	3.89	-	-	3.94	-	-	3.92	-	-
<i>Slow leg</i>										
Phase	F(4,72)	4.39	1) 0-100%	p<0.001	4.75	1) 0-19.6% 2) 28.7-40.4% 3) 45.1-51.4% 4) 95.5-100%	p<0.001 p<0.001 p=0.005 <i>p=0.017</i>	4.85	-	-
EA vs. BL	t(1,38)	3.78	1) 0-100%	p<0.001	3.85	1) 0-3.4% 2) 12.4-39.0% 3) 44.5-51.4% 4) 57.5-67.5% 5) 94.7-100%	<i>p=0.006</i> p<0.001 p<0.001 p<0.001 p=0.002	-	-	-
LA vs. EA	t(1,38)	3.79	1) 0-100%	p<0.001	3.85	1) 0-4.3% 2) 15.3-19.3% 3) 24.3-38.3% 4) 44.1-52.5% 5) 59.2-67.3% 6) 95.2-100%	<i>p=0.004</i> <i>p=0.005</i> p<0.001 p<0.001 p<0.001 <i>p=0.003</i>	-	-	-
EP vs. BL	t(1,38)	3.76	1) 0-90.8% 2) 91.1-100%	p<0.001 p<0.001	3.93	1) 6.8-21.6% 2) 63.5-76.2%	p<0.001 p<0.001	-	-	-
LP vs. BL	t(1,38)	3.79	-	-	3.95	-	-	-	-	-

The table presents results of the repeated measures SPM {F} analysis (phase effect) and the post-hoc SPM {t} tests, with the F/t-values (F/t(df)), the critical threshold, the supra-threshold clusters, and the p-values. The p-values of the clusters that are discussed in the text are highlighted in bold. Small supra-threshold clusters and p-values that likely do not represent meaningful results are given in italic. Abbreviations: DF = degrees of freedom, CT = critical threshold; BL = late slow baseline; EA = early adaptation; LA = late adaptation; EP= early post-adaptation; LP = late post-adaptation.

PC 1: Fast leg

PC 1: Slow leg

Fig. 4. Post-hoc SPM t-tests (SPM {t}) for PC1 of the fast (A) and slow leg (B), showing the changes in temporal projections across phases of the split-belt protocol. For both panels, the upper graphs (1-4) show the temporal projections of the phases that are compared to each other, with the SPM {t} results of that comparison shown in the graphs below (5-8). A larger temporal projection shows an increase in overall muscle activation, while a lower temporal projection shows a decrease in overall muscle activation. At a corrected level of $\alpha = 0.013$, the red dotted line indicates the critical threshold of significance. The vertical black dotted line shows the stance (0-60%) and swing phase (60-100%). Abbreviations: BL = late slow baseline, EA = early adaptation, LA = late adaptation, EP = early post-adaptation, LP = late post-adaptation, CT = critical threshold.

PC 2: Fast leg

PC 2: Slow leg

Percentage of Gait cycle

Fig. 5. Post-hoc SPM t -tests (SPM $\{t\}$) for PC₂ of the fast (A) and slow leg (B), showing the changes in temporal projections across phases of the split-belt protocol. For both panels, the upper graphs (1-4) show the temporal projections of the phases that are compared to each other, with the SPM $\{t\}$ results of that comparison shown in the graphs below (5-8). A larger temporal projection shows an increase in overall muscle activation, while a lower temporal projection shows a decrease in overall muscle activation. At a corrected level of $\alpha = 0.013$, the red dotted line indicates the critical threshold of significance. The vertical black dotted line shows the stance (0-60%) and swing phase (60-100%). Abbreviations: BL = late slow baseline, EA = early adaptation, LA = late adaptation, EP = early post-adaptation, LP = late post-adaptation, CT = critical threshold.

Fig. 5 shows the post-hoc test for the effect of phase for PC2 of the fast and slow leg, with the temporal projections of the phases (first and third row of graphs) and the SPM results of the post-hoc comparison between phases (second and fourth row). Post-hoc testing for PC2 of the fast leg showed significantly increased activation during EA compared to BL (53.0-100%; Table 3; Fig. 5), and an extra activation peak (10.6-17.8%), due to GAS and SOL activation (Fig. 3). Muscle activation during EA was significantly higher than LA (52.8-82.4%). Two supra-threshold clusters showed increased activation in EP compared to BL (53.8-65.6%, 79.5-95.5%), while the other cluster showed an extra activation peak (7.4-41.1%), which is likely due to TA activation during the stance phase. LP did not significantly differ from BL.

For PC2 of the slow leg, EA differed from BL with decreased activation from 12.4-39.0% of the gait cycle, a delayed activation peak from 44.5-51.4% and increased activation from 57.5-67.5% (Table 3; Fig. 5). Muscle activation was significantly lower in EA compared to LA from 24.3-38.3% of the gait cycle, had a delayed peak from 44.1-52.5%, and an extra peak from 59.2-67.3%. EP significantly differed from BL during stance with an extra burst (6.8-21.6%) and increased activation (63.5-76.2%) likely associated with GAS and SOL activation (Fig. 3). LP and BL did not differ significantly.

Post-hoc testing for PC3 of the fast leg showed supra-threshold clusters with increased activation in EA compared to BL (12.0-21.0%, 69.4-82.8%) and LA (69.5-81.7%; Table 3), due to BF and ST activation (Fig. 3). During EP, two small clusters showed increased activation compared to BL (13.8-19.2%, 59.1-64.3%). LP and BL did not differ significantly.

DISCUSSION

We studied the effects of age on adaptations of gait and muscle activation patterns induced by split-belt walking. Young and middle-aged adults adapted step lengths and double support times to split-belt walking. The functional muscle groups, identified by PCA, increased activation during early adaptation and post-adaptation, and decreased activation over time. The adaptations in these patterns might contribute to the restoration of step symmetry during split-belt adaptation. Contrary to our hypothesis, both age groups adapted gait features as well as muscle activation patterns in a similar way during all phases of split-belt walking.

In agreement with previously reported data, split-belt walking modified walking, and both age groups decreased asymmetry in step length and double support time during adaptation [4,5,12]. There are mixed results on the effects of age on gait adaptation with regards to gait symmetry, with some studies reporting age-related decline in step length symmetry [10,11] and others reporting no effects [8,9]. We extend this literature by showing that middle-aged adults exhibited similar (de-)adaptations as young adults, suggesting that gait adaptability remains intact in middle-age. The mixed results could be due to differences between studies in subject characteristics, split-belt conditions, and data analysis. To reduce inconsistencies, future studies should examine how gait adaptations evolve across the lifespan using uniform methods. Such an approach could determine which outcome is the most sensitive to detect the onset of slow or aberrant adaptation caused by natural aging.

Although gait adaptation is not different at middle-age, the underlying neuromuscular control might be different. We, however, found that adaptations in muscle activation to split-belt walking were also

independent of age. During early adaptation, the first activation pattern showed increased activation, followed by a decrease in activation as adaptation progressed. The decrease in muscle activation over the course of adaptation was previously suggested to parallel the decrease in gait asymmetry and thus show a more efficient gait pattern [12,13]. Similar adaptation effects are seen in platform perturbation studies, with increased muscle activation in response to unexpected perturbations, which decreased with repetitions of the perturbation [30,31]. In the current study, the decrease in muscle activation with adaptation parallels the decrease in gait asymmetry. Since muscle activation reflects the neural drive, we suggest that changes in activation patterns underlie the changes in gait during the adaptation process.

Plantarflexors and dorsiflexors emerged as key functional regulators of adaptation to split-belt walking. These muscle groups were involved in the modulation of gait cycle timing during split-belt (de-) adaptation. A unique adaptive role for the plantarflexors and dorsiflexors was previously identified during split-belt walking [14]. The plantarflexors provide push-off power [32], regulate step length [33], and contribute to restraining falls [34]. During normal walking, aging increases (co-)activation of agonist-antagonist muscles, e.g. the plantarflexors and dorsiflexors [17,18]. This change in muscle (co-)activation might affect the ability of older adults to modulate gait during split-belt walking.

One possible reason for a lack of age effects is that the locomotor challenge created by these speeds of split-belt walking was insufficient in proportion to the level of neuromuscular dysfunction at middle-age in terms of muscle strength and quality [19,20]. It is also possible that the neuromuscular changes at middle-age are not large enough to cause differences, because the adaptive responses needed are well within the neuromuscular reserve present at middle-age.

If split-belt adaptation is within the neuromuscular reserve at middle-age, this places the split-belt paradigm between some other paradigms that test dysfunction in adaptability. Middle-aged adults were able to adapt their margin of stability to perturbed walking with an ankle strap resistance [1] but needed more recovery steps to adapt [35]. During a slip and fall protocol, middle-aged adults experienced slightly more falls than younger adults but generally could recover quite similarly [36]. Middle-aged adults also had delayed muscle activation peaks compared to young adults during platform perturbations [37]. Thus, while the continuous perturbation of split-belt walking does not show any aging effects at middle-age, these perturbation models with sudden, short perturbations show some small signs of dysfunction of adaptability. That could indicate that the split-belt paradigm appears to be at the easier end of the perturbation continuum for middle-aged adults.

In the current study, we used a task-specific maximum peak amplitude value for the EMG amplitude normalization. This method is an alternative to MVIC-based normalization of EMG data [38]. With this method, we created an EMG template of the specific task, i.e., walking, used frequently in locomotion studies [12,13,17]. Such normalization of EMG activity does not affect timing of muscle activation but could reduce age-differences in the magnitude of activation.

CONCLUSIONS AND RECOMMENDATIONS

Adaptations in gait and muscle activation patterns during split-belt walking are still preserved at middle-age. Both young and middle-aged adults re-established gait symmetry and showed adaptations in the muscle activation patterns. Since the adaptations in muscle activation patterns parallel the adaptation of gait symmetry, changes in muscle activation likely underlie the changes in step parameters during split-belt adaptation. Future studies should consider using a lifespan approach to examine gait and muscle activation adaptations to split-belt perturbations. This will provide information about when advancing age starts to affect adaptability in terms of gait and muscle activation, which could form a basis for fall prevention interventions and suggested target groups with aging.

REFERENCES

1. McCrum C, Epro G, Meijer K, Zijlstra W, Brüggemann GP, Karamanidis K. Locomotor stability and adaptation during perturbed walking across the adult female lifespan. *J Biomech.* 2016;49: 1244–1247.
2. Lurie JD, Zagaria AB, Pidgion DM, Forman JL, Spratt KF. Pilot comparative effectiveness study of surface perturbation treadmill training to prevent falls in older adults. *BMC Geriatr.* 2013;13: 49.
3. Pai Y-C, Bhatt T, Yang F, Wang E, Kritchevsky S. Perturbation training can reduce community-dwelling older adults' annual fall risk: a randomized controlled trial. *Journals Gerontol Ser A.* 2014;69: 1586–1594.
4. Reisman DS, Block HJ, Bastian AJ. Interlimb coordination during locomotion: what can be adapted and stored? *J Neurophysiol.* 2005;94: 2403–2415.
5. Buurke TJW, Lamothe CJC, Vervoort D, Van der Woude LH V, Den Otter AR. Adaptive control of dynamic balance in human gait on a split-belt treadmill. *J Exp Biol.* 2018;221.
6. Malone LA, Bastian AJ. Thinking about walking: effects of conscious correction versus distraction on locomotor adaptation. *J Neurophysiol.* 2010;103: 1954–1962.
7. Malone LA, Bastian AJ. Age-related forgetting in locomotor adaptation. *Neurobiol Learn Mem.* 2016;128: 1–6.
8. Roemmich RT, Nocera JR, Stegelmöller EL, Hassan A, Okun MS, Hass CJ. Locomotor adaptation and locomotor adaptive learning in Parkinson's disease and normal aging. *Clin Neurophysiol.* 2014;125: 313–319.
9. Vervoort D, den Otter AR, Buurke TJW, Vuillerme N, Hortobágyi T, Lamothe CJC. Effects of Aging and Task Prioritization on Split-Belt Gait Adaptation. *Front Aging Neurosci.* 2019;11: 10.
10. Bruijn SM, Van Impe A, Duysens J, Swinnen SP. Split-belt walking: adaptation differences between young and older adults. *J Neurophysiol.* 2012;108: 1149–1157.
11. Sombric CJ, Harker HM, Sparto PJ, Torres-Oviedo G. Explicit Action Switching Interferes with the Context-Specificity of Motor Memories in Older Adults. *Front Aging Neurosci.* 2017;9: 40.
12. Finley JM, Bastian AJ, Gottschall JS. Learning to be economical: the energy cost of walking tracks motor adaptation. *J Physiol.* 2013;591: 1081–1095.
13. MacLellan MJ, Ivanenko YP, Massaad F, Bruijn SM, Duysens J, Lacquaniti F. Muscle activation patterns are bilaterally linked during split-belt treadmill walking in humans. *J Neurophysiol.* 2014;111: 1541–1552.
14. Dietz V, Zijlstra W, Duysens J. Human neuronal interlimb coordination during split-belt locomotion. *Exp Brain Res.* 1994;101: 513–520.
15. Ivanenko YP, Poppele RE, Lacquaniti F. Motor control programs and walking. *Neurosci.* 2006;12: 339–348.
16. Choi JT, Bastian AJ. Adaptation reveals independent control networks for human walking. *Nat Neurosci.* 2007;10: 1055–1062.
17. Schmitz A, Silder A, Heiderscheit B, Mahoney J, Thelen DG. Differences in lower-extremity muscular activation during walking between healthy older and young adults. *J Electromyogr Kinesiol.* 2009;19: 1085–1091.
18. Hortobágyi T, Solnik S, Gruber A, Rider P, Steinweg K, Helseth J, et al. Interaction between age and gait velocity in the amplitude and timing of antagonist muscle coactivation. *Gait Posture.* 2009;29: 558–564.
19. Muscaritoli M, Lucia S, Molfino A, Cederholm T, Fanelli FR. Muscle atrophy in aging and chronic diseases: is it sarcopenia or cachexia? *Intern Emerg Med.* 2013;8: 553–560.
20. Kennis E, Verschueren S, Van Roie E, Thomis M, Lefevre J, Delecluse C. Longitudinal impact of aging on muscle quality in middle-aged men. *Age (Omaha).* 2014;36: 9689.
21. Chuang Y-F, Chen C-C, Hsu M-J, Huang N-J, Huang Y-Z, Chan H-L, et al. Age related changes of the motor excitabilities and central and peripheral muscle strength. *J Electromyogr Kinesiol.* 2019;44: 132–138.
22. Hermens HJ, Freriks B, Merletti R, Stegeman D, Blok J, Rau G, et al. European recommendations for surface electromyography. Roessingh research and development. 1999.
23. Den Otter AR, Geurts ACH, Mulder T, Duysens J. Speed related changes in muscle activity from normal to very slow walking speeds. *Gait Posture.* 2004;19: 270–278.
24. Daffertshofer A, Lamothe CJC, Meijer OG, Beek PJ. PCA in studying coordination and variability: a tutorial. *Clin Biomech.* 2004;19: 415–428.
25. Friston KJ, Holmes AP, Worsley KJ, Poline J, Frith CD, Frackowiak RSJ. Statistical parametric maps in functional imaging: a general linear approach. *Hum Brain Mapp.* 1995;2: 189–210.
26. Pataky TC. Generalized n-dimensional biomechanical field analysis using statistical parametric mapping. *J Biomech.* 2010;43: 1976–1982.
27. Pataky TC, Robinson MA, Vanrenterghem J. Vector field statistical analysis of kinematic and force trajectories. *J Biomech.* 2013;46: 2394–2401.
28. Penny WD, Friston KJ, Ashburner JT, Kiebel SJ, Nichols TE. Statistical parametric mapping: the analysis of functional brain images. Elsevier; 2011.
29. Cao J, Worsley KJ. The detection of local shape changes via the geometry of Hotelling's T² fields. *Ann Stat.* 1999;27: 925–942.
30. Horak FB, Diener HC, Nashner LM. Influence of central set on human postural responses. *J Neurophysiol.* 1989;62: 841–853.
31. Oude Nijhuis LB, Allum JHJ, Borm GF, Honegger F, Overeem S, Bloem BR. Directional Sensitivity of "First Trial" Reactions in Human Balance Control. *J Neurophysiol.* 2009;101: 2802–2814.
32. Neptune RR, Kautz SA, Zajac FE. Contributions of the individual ankle plantar flexors to support, forward progression and swing initiation during walking. *J Biomech.* 2001;34: 1387–1398.
33. Varraine E, Bonnard M, Pailhous J. Intentional on-line adaptation of stride length in human walking. *Exp Brain Res.* 2000;130: 248–257.
34. Honeine J-L, Schieppati M, Gagey O, Do M-C. The Functional Role of the Triceps Surae Muscle during Human Locomotion. *PLoS One.* 2013;8.
35. Süptitz F, Catalá MM, Brüggemann GP, Karamanidis K. Dynamic stability control during perturbed walking can be assessed by a reduced kinematic model across the adult female lifespan. *Hum Mov Sci.* 2013;32: 1404–1414.
36. Lockhart TE, Smith JL, Woldstad JC. Effects of aging on the biomechanics of slips and falls. *Hum Factors.* 2005;47: 708–729.
37. de Freitas PB, Knight CA, Barela JA. Postural reactions following forward platform perturbation in young, middle-age, and old adults. *J Electromyogr Kinesiol.* 2010;20: 693–700.
38. Burden A. How should we normalize electromyograms obtained from healthy participants? What we have learned from over 25 years of research. *J Electromyogr Kinesiol.* 2010;20: 1023–1035.

APPENDIX

PRINCIPAL COMPONENT ANALYSIS (PCA)

The concatenated EMG matrix ($X_{m,c}$) of one participant consists of 100 data points per phase (k) of all 5 phases (c) of 8 muscles (m) = 500 samples of 8 muscles.

$$X_{m,c} = \left(\begin{pmatrix} X_{1,1} & \dots & X_{1,k} \\ \vdots & \dots & \vdots \\ X_{m,1} & \dots & X_{m,k} \end{pmatrix}_1 \dots \begin{pmatrix} X_{1,1} & \dots & X_{1,k} \\ \vdots & \dots & \vdots \\ X_{m,1} & \dots & X_{m,k} \end{pmatrix}_c \right)$$

The final EMG matrix for the PCA analysis consists of all included participants, with k (100 samples) * c (5 phases) * p (20 participants) = 10,000 samples of 8 muscles ($X_{8,10000}$).

$$X_{EMG} = \left((X_{m,c})_1 \dots (X_{m,c})_p \right)$$

Based on the EMG matrix ($X_{8,10000}$), the covariance matrix can be defined as [24]:

$$Cov_X = \frac{1}{N-1} \sum_{i=1}^N (X_{m,i} - \overline{X_m})(X_{k,i} - \overline{X_k}) \text{ with } \overline{X_m} = \frac{1}{N} \sum_{i=1}^N X_{m,i}$$

With N as the number of samples and i as the sample.

Based on the covariance matrix, the eigenvectors (V) and eigenvalues (λ) of each PC (j) are determined [24].

$$D = V * V^{-1} * Cov_X \text{ with } D_{jk} = \lambda_j \text{ for } j=k$$

With D as the diagonal matrix of eigenvalues (λ). The eigenvalues show the amount of variance of the original data set that is explained by a specific PC. The eigenvector of each PC is build up by m muscles, with the nth eigenvector representing the amount that that specific muscle contributed to that PC. If the eigenvector value exceeds 0.25, that muscle is important for that PC.

The temporal projections (Y) were determined by projecting the original EMG set (X) onto the eigenvectors (V) [24].

$$Y_k^{(j)} = \sum_{m=1}^{16} V_m^{(j)} * X_{m,k}$$

FIGURE

Fig. A1. EMG profiles and the reconstruction of the PCs for all muscles during baseline, early-adaptation, and post-adaptation. The original EMG signal (blue) is shown next to the signal that was reconstructed (red) from the temporal projections and eigenvectors of the PC as follows: $X_{rec} = \sum_{j=1}^3 V_m(j) * Y_k(j)$ [24]. The data of all subjects are pooled since there were no group differences. Abbreviations: TA = Tibialis Anterior; SOL = Soleus; GAS = Gastrocnemius Medialis; BF = Biceps Femoris; ST = Semitendinosus; RF = Rectus Femoris; VM = Vastus Medialis; GM = Gluteus Medius.

CHAPTER 5

Adaptive control of dynamic balance across the adult lifespan

Revised version in *Medicine and Science in Sports and Exercise* (2020). 52(10): 2270-2277.

Danique Vervoort^{1,2*}, Tom J.W. Buurke^{1*}, Nicolas Vuillerme^{2,3}, Tibor Hortobágyi¹, Rob den Otter¹, Claudine JC Lamoth¹

¹ University of Groningen, University Medical Center Groningen, Center for Human Movement Sciences, Groningen, The Netherlands

² University Grenoble-Alpes, AGEIS, Grenoble, France

³ Institut Universitaire de France, Paris, France

* Contributed equally to this work

ABSTRACT

INTRODUCTION: The ability to adapt dynamic balance to perturbations during gait deteriorates with age. To prevent age-related decline in adaptive control of dynamic balance, we must first understand how adaptive control of dynamic balance changes across the adult lifespan. We examined how adaptive control of the MoS changes across the lifespan during perturbed and unperturbed walking on the split-belt treadmill.

METHODS: Seventy-five healthy adults (age range: 18-80 years old) walked on an instrumented split-belt treadmill with and without split-belts. Linear regression analyses were performed for the MedioLateral (ML) and AnteroPosterior (AP) Margin of Stability (MoS), step length, single support time, step width, double support time and cadence during unperturbed and perturbed walking (split-belt perturbation), with age as predictor.

RESULTS: Age did not significantly affect dynamic balance during unperturbed walking. However, during perturbed walking, the ML MoS of the leg on the slow belt increased across the lifespan due to a decrease in bilateral single support time. The AP MoS did not change with aging despite a decrease in step length. Double support time decreased and cadence increased across the lifespan when adapting to split-belt walking. Age did not affect step width.

CONCLUSION: Aging affects the adaptive control of dynamic balance during perturbed but not unperturbed treadmill walking with controlled walking speed. The ML MoS increased across the lifespan, while bilateral single support times decreased. The lack of aging effects on unperturbed walking suggests that participants' balance should be challenged to assess aging effects during gait. The decrease in double support time and increase in cadence suggests that older adults use the increased cadence as a balance control strategy during challenging locomotor tasks.

KEYWORDS: Aging, Split-belt walking, Margin of Stability, Locomotion

INTRODUCTION

Control of dynamic balance maintains erect posture during walking. There is a need for continuous, online supervision of dynamic balance because the vertical projection of the Center of Mass (CoM) is outside the Base of Support (BoS) for ~80% of the gait cycle during walking [1]. Adaptive control of dynamic balance helps cope with internal and external perturbations that the locomotor system encounters in daily life [2]. The ability to adapt dynamic balance deteriorates with age, due to age-related changes in the sensorimotor system [3,4]. To prevent age-related decline in adaptive control of dynamic balance during gait, we must first understand how adaptive control of dynamic balance changes across the adult lifespan.

One way to examine adaptability of dynamic balance is to have a continuous change in the speed of one of the two belts while walking on a split-belt treadmill. The difference in speed between the two belts initially causes an asymmetry in gait and requires adjustments in the movements of each leg. That is, adaptive control of dynamic balance is necessary to avoid a loss of balance and continue walking [5,6]. Split-belt gait is an attractive perturbation paradigm to probe locomotor adaptability because it is sufficiently challenging yet virtually all healthy adults are able to complete the task [7,8].

Stable locomotion necessitates a spatial margin between the Extrapolated CoM (XCoM), a parameter that incorporates CoM position and velocity, and the BoS called the Margin of Stability (MoS) [5,6,9,10]. A positive MoS indicates stable gait and a negative MoS indicates unstable walking, with a possible loss of balance that would require a corrective step [11]. The MoS can be influenced by multiple gait variables [12,13]. The AnteroPosterior (AP) MoS tends to increase with decreasing walking speed, by which AP XCoM excursion is reduced, or by increasing step length, by which the AP BoS is increased [13]. The MedioLateral (ML) MoS can become larger by decreasing bilateral single support time, by which ML XCoM excursion is reduced, and by increasing step width, by which the ML BoS is increased [10,12,13]. Understanding adaptive control during gait of MoS, therefore, requires an understanding of changes in the variables that can influence MoS, i.e., gait speed, step length, single support time, cadence, and step width.

Adaptive control of dynamic balance deteriorates with age. In the present study, a lifespan approach will be used to investigate age-related changes in adaptive control of dynamic balance. A previous lifespan study [14] and a review [15] showed a gradual decline in ML local dynamic stability after age 40 and a gradual decline in AP root mean square trunk acceleration while walking. These studies provide novel insights into age-related change in balance control but did not control for walking speed, which declines with increasing age and affects MoS. Older adults' gait is characterized by shorter and wider steps and increased stance and double support times [3,16] and these spatiotemporal parameters are closely related to walking speed [17]. Therefore, to fully capture changes in adaptive control of dynamic balance across the lifespan, we used a fixed treadmill speed. Furthermore, although not directly related to MoS, adaptive balance mechanisms could involve a shift in the time spent in single support time and double support time with age. With aging, there could be a shortening of single support time and a prolongation of double support time. Alternatively, cadence could be increased to cope with timing differences.

The present study aims to determine the effects of aging on: 1) AP and ML MoS during unperturbed walking at a fixed treadmill speed; 2) AP and ML MoS when gait is perturbed during split-belt walking; 3) the variables (step length, single support time, step width) that influence the MoS, and 4) the variables double support time and cadence to investigate a possible shift in timing as a balance mechanism.

Fig. 1 shows the hypotheses in graphical format. We hypothesize that: 1) AP MoS and ML MoS will, respectively, gradually decrease and increase with age during unperturbed walking; 2) When gait is perturbed by split-belt walking, AP MoS will decrease and ML MoS will gradually increase with age; 3) If there are age-related changes in gait parameters when walking speed is fixed, we expect step length and single support time to gradually decrease and step width to gradually increase with age, and 4) An increase in double support time or cadence with age.

Fig. 1. Graphical representation of the hypothesized changes across the lifespan. During unperturbed and perturbed walking, we expect step width to increase and bilateral single support time to decrease with increasing age. These age-related changes will cause the MedioLateral Margin of Stability to increase. With increasing age, step length will decrease, which will cause the Anteroposterior Margin of Stability to decrease. The * next to the line from age to walking speed indicates that although there is a well-documented effect of age on walking speed, walking speed is fixed throughout the experiment and thus there are no effects on walking speed.

METHODS

PARTICIPANTS

Healthy adults, 12-13 per decade, participated in the study (N = 75, age range: 18-79 years). The table in Supplemental Digital Content 1 shows participant characteristics. Male and female participants were included if they were able to walk without walking aids and understood verbal instructions. Exclusion criteria were: 1) previous experience with split-belt walking; 2) orthopedic surgery in the last two years; 3) neurological disorders; 4) (neuro)psychiatric disorders; 5) use of medication that might affect gait. The local Ethical Committee of the Center for Human Movement Sciences of the University Medical Center Groningen approved the study protocol. Before the measurements, all participants signed a written informed consent.

INSTRUMENTATION AND PROTOCOL

Participants walked on an instrumented split-belt treadmill (Motek, Amsterdam, The Netherlands). The embedded force plates measured three-dimensional ground reaction forces and the Center of Pressure (CoP) at 1000 Hz.

Participants walked on the split-belt treadmill for 22 minutes, starting with the belts tied at 0.7 m/s and 1.4 m/s (Slow and Fast Baseline) for 3 minutes at each speed. Next, participants walked for 10 minutes with split-belts with one belt on 1.4 m/s, while the speed of the other belt was kept at 0.7 m/s. The first five steps of this adaptation phase are from here on referred to as Initial Perturbation and steps 6-30 are termed Early Change [18]. After 16 minutes, participants returned to tied-belt walking at 0.7 m/s. The fast and slow speeds were randomly assigned to the left or right side per participant during split-belt walking. Participants were instructed to look straight ahead and not touch the handrails throughout the experiment [19].

DATA ANALYSIS

All data were analyzed off-line with a custom Matlab code (R2015b, MathWorks, Natick, MA, USA). Vertical ground reaction forces were filtered with a 15 Hz second-order low-pass Butterworth filter and missing data were interpolated. Gait events were determined at the moment when the vertical ground reaction forces crossed the threshold of 50 N on either force plate. To determine balance parameters, the CoM velocity and CoM position were obtained from the ground reaction forces which were divided by body mass to obtain the CoM acceleration (m/s^2). The CoM acceleration was double-integrated to obtain CoM position (m) and was high-pass filtered to prevent integration drift. For the absolute CoM position, the previously obtained CoM position was supplemented with the 0.2 Hz low-pass Butterworth filtered CoP signal [20,21].

The XCoM position was determined with Equation 1 for both the AP as the ML directions [9]. With l as leg length (m) and g as gravitational acceleration (9.81 m/s^2).

$$XCoM = CoM + \frac{v_{CoM}}{\sqrt{g/l}}$$

The MoS was defined as the distance between the COP position and the XCoM position at contralateral toe-off for each step. The AP MoS is calculated along the x-axis and the ML MoS along the z-axis [5].

Step length was defined as the AP distance between the COPx position of the left and right leg at heel-strike. Step length was normalized for leg length by dividing step length through leg length [22]. Single support time was defined as the time from contralateral toe-off to contralateral heel-strike [12]. Double support time was defined as the time from unilateral heel-strike to contralateral toe-off. Step width was specified as the difference between minimum/maximum ML COP position of the ipsilateral single support, and minimum/maximum ML COP of the consecutive contralateral single support for each step. Cadence was defined as the number of steps per minute.

Balance parameters were averaged over a number of steps for each of the four phases, Fast Baseline (last 5 steps), Slow Baseline (last 5 steps), Initial Perturbation (first 5 steps of adaptation) and Early Change (steps 6-30 of the adaptation) [18]. During the baselines (Fast, Slow) all variables (except step width) were calculated for the left and right leg, and during split-belt walking (Initial Perturbation, Early Change) variables were calculated for the leg on the fast belt (fast leg) and the leg on the slow belt (slow leg).

STATISTICAL ANALYSIS

To determine the effects of aging on AP and ML MoS during unperturbed walking (aim 1), a linear regression analyses were performed for both parameters (AP/ML MoS) at baseline (Fast, Slow; controlled walking speed) with age as the predictor. To address the second research question, i.e., effects of aging on adaptive control of the MoS, linear regression analyses were performed for AP and ML MoS during Initial Perturbation and Early Change with age as predictor. To address research questions 3 and 4, a similar linear regression analyses were performed on the variables that can influence the MoS (step length, single support time, double support time, step width and cadence) during the four phases (Fast Baseline, Slow Baseline, Initial Perturbation, Early Change) with age as predictor. The data of all participants was checked for outliers through inspection of the normal probability plots of the residuals. No data was excluded from the analyses. To account for the 48 linear regression analyses that were performed, the critical p-value was set at a Bonferroni-corrected $\alpha = 0.05 / 48 \text{ tests} = 0.001042$. The variance explained by the linear regression models was expressed with a coefficient of determination (R^2).

RESULTS

TIED-BELT WALKING AT FIXED SPEEDS

When walking on tied-belts during the Fast Baseline, cadence increased with 0.14 steps/min per year from 18 to 79 years old ($F(1,73) = 13.03$, $p < 0.001$; Table 1). During the Slow Baseline, double support time of the left leg significantly decreased with 0.0007 s per year from 18 to 79 years ($F(1,73) = 12.55$, $p < 0.001$) and cadence significantly increased with 0.18 steps/min per year from 18 to 79 years ($F(1,73) = 11.77$, $p < 0.001$).

Table 1. Statistics (R^2 and p-values) of the linear regression models of the balance parameters with age as predictor for the four phases.

Variable		Fast Baseline		Slow Baseline			Initial Perturbation		Early Change	
		R^2 -value	p-value	R^2 -value	p-value		R^2 -value	p-value	R^2 -value	p-value
AP MoS	Left	0.0007	0.81	0.0003	0.88	Fast	0.05	0.05	0.08	0.02
	Right	0.02	0.27	0.006	0.52	Slow	0.06	0.03	0.10	0.005
Step Length	Left	0.01	0.35	0.005	0.54	Fast	0.07	0.02	0.19	<0.001
	Right	0.00002	0.97	0.02	0.22	Slow	0.13	0.0013	0.15	<0.001
ML MoS	Left	0.07	0.02	0.12	0.003	Fast	0.03	0.17	0.09	0.008
	Right	0.02	0.18	0.04	0.07	Slow	0.16	<0.001	0.22	<0.001
	Left	0.14	0.00109	0.09	0.008	Fast	0.08	0.01	0.26	<0.001
Single Support	Right	0.13	0.0015	0.04	0.07	Slow	0.17	<0.001	0.31	<0.001
	Left	0.04	0.10	0.15	<0.001	Fast	0.09	0.008	0.22	<0.001
Double Support	Right	0.01	0.34	0.10	0.007	Slow	0.18	<0.001	0.21	<0.001
Step Width	-	0.04	0.08	0.05	0.06	-	0.03	0.14	0.07	0.03
Cadence	-	0.15	<0.001	0.14	<0.001	-	0.23	<0.001	0.36	<0.001

R^2 and p-values are highlighted in bold if the regression line was significant after Bonferroni correction ($\alpha=0.001042$). During the Fast and Slow Baseline, the variables were calculated for the left and right leg. During Initial Perturbation and Early Change, the variables were calculated for the fast and slow leg. Abbreviations: ML = MedioLateral; AP = AnteroPosterior; MoS = Margin of Stability.

EFFECTS OF AGING ON ADAPTIVE CONTROL OF THE MOS DURING SPLIT-BELT WALKING

During adaptation to walking with split-belts, the regression models for ML MoS of the slow leg revealed an increase of 0.035 cm per year from 18 to 79 years old in both the Initial Perturbation ($F(1,73) = 13.46$, $p < 0.001$) and Early Change phase ($F(1,73) = 20.25$, $p < 0.001$; Table 1, Fig. 2). Age explained respectively 16% and 22% of the variance in ML MoS slow during Initial Perturbation and Early Change. Aging did not affect AP MoS ($p > 0.05$).

Fig. 2. Linear regression models of ML MoS of the slow leg with age as predictor during the Initial Perturbation (steps 1-5 of split-belt walking; left panel) and Early Change (steps 6-30; right panel) phases. The color of the data points changes with increasing age. The formula of the regression line is given at the top of each graph. When the models were significant, the p-value and R^2 value of the model are given in bold. Abbreviations: ML MoS = MedioLateral Margin of Stability.

EFFECTS OF AGING ON THE VARIABLES THAT CONTROL THE MOS

During Early Change, step length of the fast leg ($F(1,73) = 19.52$, $p < 0.001$; Table 1, Fig. 3) and step length of the slow leg ($F(1,73) = 22.24$, $p < 0.001$) decreased with 0.002 m per year across the lifespan.

Single support time of the fast leg decreased with 0.001 s per year from 18 to 79 years old in Early Change ($F(1,73) = 24.99$, $p < 0.001$; Table 1, Fig. 3). Single support of the slow leg decreased across the lifespan with 0.002 s per year in the Initial Perturbation ($F(1,73) = 14.45$, $p < 0.001$) and with 0.003 s in the Early Change phase ($F(1,73) = 32.19$, $p < 0.001$). No significant age effects were found for step width.

Double support of the fast leg decreased with 0.0006 s per year from 18 to 79 years old in Early Change ($F(1,73) = 20.29$, $p < 0.001$; Table 1, Fig. 4). The regression models for double support of the slow leg showed that double support time decreased with 0.001 s per year across the lifespan in both the Initial Perturbation ($F(1,73) = 16.36$, $p < 0.001$) and the Early Change phase ($F(1,73) = 19.88$, $p < 0.001$).

Cadence increased across the lifespan with 0.57 steps/min per year in Initial Perturbation ($F(1,73) = 21.29$, $p < 0.001$) and with 0.68 steps/min in Early Change ($F(1,73) = 40.66$, $p < 0.001$; Table 1, Fig. 4).

Fig. 3. Linear regression models of step length and single support time of the fast and slow leg, with age as predictor during the Initial Perturbation (steps 1-5 of split-belt walking; left panel) and Early Change (steps 6-30 of split-belt walking; right panel) phases. The color of the data points changes with increasing age. The formula of the regression line is given at the top of each graph. When the models were significant, the p-value and R^2 value of the model are given in bold. Abbreviations: SL = step length; SS = single support time.

Fig. 4. Linear regression models of double support time of the fast and slow leg and cadence, with age as predictor during the Initial Perturbation (steps 1-5 of split-belt walking; left panel), Early Change (steps 6-30 of split-belt walking; middle panel) and Fast/Slow Baseline (right panel). The color of the data points changes with increasing age. The formula of the regression line is given at the top of each graph. When the models were significant, the p-value and R^2 value of the model are given in bold. Abbreviations: DS = double support time; Cad = cadence.

DISCUSSION

We examined how adaptive control of the MoS changes across the lifespan during perturbed and unperturbed walking on the split-belt treadmill. Aging did not affect the ML and AP MoS during unperturbed walking. When balance was challenged by split-belt walking, aging affected the adaptive control of the ML MoS for the leg on the slow belt. This indicates that gait must be perturbed to assess age-related changes in adaptive control of dynamic balance, as these effects might not surface during unperturbed walking. Interestingly, step length, single support time and double support time decreased across the lifespan when adapting to split-belt walking, while cadence increased with age. The cadence data suggest that as healthy humans age, they shorten their steps and their single and double support time to cope with balance perturbations. Fig. 5 summarizes an interpretation of the results.

CHANGES IN ADAPTIVE CONTROL OF DYNAMIC BALANCE DURING WALKING ACROSS THE LIFESPAN

During unperturbed walking with controlled walking speed, no age-related changes were found for the ML and AP MoS. The effects that were found, were that left leg double support time decreased and cadence increased with age, suggesting that increasing cadence might be an age-specific strategy for the control of dynamic balance. Since walking speed is controlled, increasing cadence might resemble a similar strategy as decreasing walking speed with advancing age. Older adults could

increase cadence as a way to reduce the propulsive impulse and to reduce the braking impulse [23]. With increasing age, it may be more difficult to produce a propulsive impulse as there is an age-related distal-to-proximal shift [24] that may change the way older adults can use the plantarflexors, that provide forward propulsion [25]. With increasing age, adults may reduce the braking impulse to more easily facilitate the contralateral forward propulsion and to reduce internal balance perturbations.

During perturbed walking, we observed that step length decreased 12 cm on average from 18 to 79 years old for both the fast and slow legs. This age-related decrease in step length, however, did not affect the AP MoS. As walking speed was similar for all participants, this, interestingly, means that the changes in step length were canceled out by reduced AP XCoM excursion, but not through reduced walking speed. This indicates that excursion of whole body AP momentum may be reduced with age, leading to a reduction in AP XCoM excursion with age. Another possibility could be that the changes in step length are canceled out by the shortening of the single and double support duration.

During perturbed walking, the ML MoS of the slow leg increased 2 cm from age 18 to 79 years. Single and double support time of both legs decreased with age, cadence increased with age and no changes were seen across the lifespan for step width. The results suggest that the changes in ML MoS were due to age-related changes in bilateral single support times, as bilateral single support times are known to affect the ML MoS [12]. The age-related increase in cadence and decrease in single support time during perturbed walking may offer more opportunity to actively control dynamic balance and decrease the time adults have to use the 'inverted pendulum' aspect of dynamic balance. Since the time that balance is passively controlled by the inverted pendulum is decreased, this increases the time that balance can be actively controlled by foot placement. No age-related changes were found for step width, but any change in step width might be limited in this study, as walking on a split-belt treadmill already causes adults to walk with wider steps [26]. The data thus suggests that changes in single support time in the slow and fast leg coincide with changes in adaptive control of the ML MoS across the lifespan. Future research is necessary to assess whether participants actively modify single support time to control the MoS, or if such changes are instead a side effect of changes in the temporal regulation of the gait cycle. The increase in ML MoS with advancing age may feel counterintuitive. Balance usually deteriorates with increasing age, and thus it may be expected that the ML MoS decreases with age. However, the magnitude of the ML MoS does not reflect balance quality per se, as a positive ML MoS is a condition for dynamic stability [9], but a large positive ML MoS may very well be a strategy to compensate poor balance control at the cost of a wide and inefficient gait pattern.

Fig. 5. Graphical representation of the changes across the lifespan during perturbed walking (split-belt walking). With increasing age, the MedioLateral Margin of Stability of the slow leg increased due to decreased bilateral single support time. Step length decreased with age but did not cause the Anteroposterior Margin of Stability to change across the lifespan. The * next to the line from age to walking speed indicates that although there is a well-documented effect of age on walking speed, walking speed is fixed throughout the experiment and thus there are no effects on walking speed.

Unexpectedly, the age-related changes in the ML MoS, step length, single support time, double support time and cadence were linear. These findings contrast the previous balance research that found either exponential changes [15] or quadratic changes after the age of 40 [14]. The difference may be that both these studies did not control for walking speed, which affects how the age-related changes on other parameters progress.

Age-related changes in adaptive control of dynamic balance were most prominent in parameters of the limb that stood on the slow-belt during split-belt walking. For the slow leg, ML MoS increased, while step length, single support time and double support time decreased. Indeed, during split-belt walking, the slow leg has a longer stance time than the fast leg [27] and therefore there is more time available to adjust balance parameters. Alternatively, with increasing age, humans may unload the perturbed leg (on the fast belt) more. The majority of weight-bearing during adaptive walking is then performed with the leg on the slow belt. While both the single support time of the fast and slow leg decreased with age, the single support time is still longer on the slow vs. fast side during split-belt walking.

Age-related changes were more prominent during Early Change (steps 6-30 of split-belt adaptation) than during Initial Perturbation (first five steps of split-belt adaptation). With increasing age, adults may need more steps to overcome the initial perturbation of changing belt speeds, while young adults start adapting to split-belt walking during early change. Such a longer lower rate of adaptation was previously found for the rate of adaptation of step length asymmetry [28,29]. This could explain the most prominent age-related changes in the early change phase. Further research is necessary to investigate the rate of adaptation of dynamic balance, for instance by assessing the number of steps necessary to overcome the initial perturbation.

CONTROLLING WALKING SPEED AFFECTS AGE-RELATED CHANGES IN OTHER GAIT PARAMETERS

Walking speed tends to decrease in old age [30]. Because walking speed affects AP MoS, we fixed walking speed. We found no changes across the lifespan in AP MoS, ML MoS, single support time, step length and step width during unperturbed treadmill walking. In overground walking studies with self-selected gait speed, age-related changes were reported, such as changes in step length, stride length, step width, stance time and double support time [30–32]. The difference between the present study and these overground studies could be due to the between-subject differences in walking speed in the overground studies. Therefore, the results of the current study emphasize the need to control walking speed to accurately assess age-related changes in adaptive control of dynamic balance. Since we controlled for walking speed, this allows us to unambiguously interpret changes in other gait parameters due to age, with only age-related changes in double support time and cadence.

The lack of age-related changes in balance parameters during normal walking could also be because walking at comfortable speed or in a controlled lab environment is not challenging enough to show age effects on dynamic balance in a healthy population. Age-related changes were seen during perturbed walking but not during unperturbed walking. This suggests that when older adults face a task that more specifically requires a skill, in this case, maintaining dynamic balance, like walking with a visual perturbation [33], reacting to an ankle resistance perturbation while walking [34] or during split-belt walking [28,29], age-related changes in dynamic balance emerge that are not seen during

unperturbed walking due to the age-related deteriorations in this particular skill. This should be taken into account in future studies designed to decipher how balance and gait changes across the healthy lifespan.

CONCLUSIONS

Aging affects the adaptive control of dynamic balance during perturbed treadmill walking. The ML MoS increased across the lifespan due to a decrease in bilateral single support times, i.e., increased cadence, while aging did not affect AP MoS despite changes in step length. Furthermore, the age-related decreases in double support time along with the increases in cadence that were observed suggest that older adults prefer an increase of cadence as balance control strategy during challenging locomotor tasks. The finding that aging affects the adaptive control of dynamic balance during perturbed but not unperturbed treadmill walking, suggests that adult's balance should be challenged by a task that targets this specific skill to assess aging effects in dynamic balance.

REFERENCES

1. Winter DA. The biomechanics and motor control of human gait: normal, elderly and pathological. 2nd ed. University of Waterloo Press; 1991.
2. Patla AE. Strategies for dynamic stability during adaptive human locomotion. *IEEE Eng Med Biol Mag*. 2003;22: 48–52.
3. Winter DA, Patla AE, Frank JS, Walt SE. Biomechanical walking pattern changes in the fit and healthy elderly. *Phys Ther*. 1990;70: 340–347.
4. Woollacott MH, Tang P-F. Balance control during walking in the older adult: research and its implications. *Phys Ther*. 1997;77: 646–660.
5. Buurke TJW, Lamothe CJC, Vervoort D, Van der Woude LH V, Den Otter AR. Adaptive control of dynamic balance in human gait on a split-belt treadmill. *J Exp Biol*. 2018;221.
6. Park S, Finley JM. Characterizing dynamic balance during adaptive locomotor learning. 2017 International Conference of the IEEE Engineering in Medicine and Biology Society. IEEE; 2017. pp. 50–53.
7. Vervoort D, den Otter AR, Buurke TJW, Vuillerme N, Hortobágyi T, Lamothe CJC. Effects of Aging and Task Prioritization on Split-Belt Gait Adaptation. *Front Aging Neurosci*. 2019;11: 10.
8. Vervoort D, den Otter AR, Buurke TJW, Vuillerme N, Hortobágyi T, Lamothe CJC. Do gait and muscle activation patterns change at middle-age during split-belt adaptation? *J Biomech*. 2020;99: 109510.
9. Hof AL, Gazendam MGJ, Sinke WE. The condition for dynamic stability. *J Biomech*. 2005;38: 1–8.
10. Hof AL, van Bockel RM, Schoppen T, Postema K. Control of lateral balance in walking. Experimental findings in normal subjects and above-knee amputees. *Gait Posture*. 2007;25: 250–258.
11. Hof AL. The “extrapolated center of mass” concept suggests a simple control of balance in walking. *Hum Mov Sci*. 2008;27: 112–125.
12. Buurke TJW, Lamothe CJC, Van der Woude LH V, Hof AL, den Otter R. Bilateral temporal control determines mediolateral margins of stability in symmetric and asymmetric human walking. *Sci Rep*. 2019;9: 12494.
13. Hak L, Houdijk H, Beek PJ, van Dieën JH. Steps to take to enhance gait stability: the effect of stride frequency, stride length, and walking speed on local dynamic stability and margins of stability. *PLoS One*. 2013;8.
14. Terrier P, Reynard F. Effect of age on the variability and stability of gait: a cross-sectional treadmill study in healthy individuals between 20 and 69 years of age. *Gait Posture*. 2015;41: 170–174.
15. Iosa M, Fusco A, Morone G, Paolucci S. Development and decline of upright gait stability. *Front Aging Neurosci*. 2014;6.
16. Schrager MA, Kelly VE, Price R, Ferrucci L, Shumway-Cook A. The effects of age on medio-lateral stability during normal and narrow base walking. *Gait Posture*. 2008;28: 466–471.
17. Kirtley C, Whittle MW, Jefferson RJ. Influence of walking speed on gait parameters. *J Biomed Eng*. 1985;7: 282–288.
18. Roemmich RT, Bastian AJ. Two ways to save a newly learned motor pattern. *J Neurophysiol*. 2015;113: 3519–3530.
19. Buurke TJW, Lamothe CJC, van der Woude LH V., den Otter AR. Handrail holding during treadmill walking reduces locomotor learning in able-bodied persons. *IEEE Trans Neural Syst Rehabil Eng*. 2019;27: 1753–1759.
20. Schepers HM, van Asseldonk E, Buurke JH, Veltink PH. Ambulatory estimation of center of mass displacement during walking. *IEEE Trans Biomed Eng*. 2009;56: 1189–1195.
21. Hof AL. Comparison of three methods to estimate the center of mass during balance assessment. *J Biomech*. 2005;38: 2134–2135.
22. Hof AL. Scaling gait data to body size. *Gait Posture*. 1996;4: 222–223.
23. Goldberg EJ, Kautz SA, Neptune RR. Can treadmill walking be used to assess propulsion generation? *J Biomech*. 2008;41: 1805–1808.
24. DeVita P, Hortobágyi T. Age causes a redistribution of joint torques and powers during gait. *J Appl Physiol*. 2000;88: 1804–1811.
25. Neptune RR, Kautz SA, Zajac FE. Contributions of the individual ankle plantar flexors to support, forward progression and swing initiation during walking. *J Biomech*. 2001;34: 1387–1398.
26. Zeni JA, Higginson JS. Gait parameters and stride-to-stride variability during familiarization to walking on a split-belt treadmill. *Clin Biomech*. 2010;25: 383–386.
27. Reisman DS, Block HJ, Bastian AJ. Interlimb coordination during locomotion: what can be adapted and stored? *J Neurophysiol*. 2005;94: 2403–2415.
28. Bruijn SM, Van Impe A, Duysens J, Swinnen SP. Split-belt walking: adaptation differences between young and older adults. *J Neurophysiol*. 2012;108: 1149–1157.
29. Sombric CJ, Harker HM, Sparto PJ, Torres-Oviedo G. Explicit action switching interferes with the context-specificity of motor memories in older adults. *Front Aging Neurosci*. 2017;9: 40.
30. Samson MM, Crowe A, De Vreede PL, Dessens JA, Dursma SA, Verhaar HJ. Differences in gait parameters at a preferred walking speed in healthy subjects due to age, height and body weight. *Aging Clin Exp Res*. 2001;13: 16–21.
31. McKay MJ, Baldwin JN, Ferreira P, Simic M, Vanicek N, Wojciechowski E, et al. Spatiotemporal and plantar pressure patterns of 1000 healthy individuals aged 3–101 years. *Gait Posture*. 2017;58: 78–87.
32. Herssens N, Verbecque E, Hallemans A, Vereeck L, Van Rompaey V, Saeyns W. Do spatiotemporal parameters and gait variability differ across the lifespan of healthy adults? A systematic review. *Gait Posture*. 2018;64: 181–190.
33. Francis CA, Franz JR, O'Connor SM, Thelen DG. Gait variability in healthy old adults is more affected by a visual perturbation than by a cognitive or narrow step placement demand. *Gait Posture*. 2015;42: 380–385.
34. McCrum C, Epro G, Meijer K, Zijlstra W, Brüggemann GP, Karamanidis K. Locomotor stability and adaptation during perturbed walking across the adult female lifespan. *J Biomech*. 2016;49: 1244–1247.

SUPPLEMENTAL DIGITAL CONTENT

Table 1. Participant characteristics. The characteristics are shown for the entire groups of participants and per decade.

Age groups	Age (mean ± sd)	N (M/F)	Height (m) (mean ± sd)	BMI (mean ± sd)	Sport hours per week (mean ± sd)
All participants	48.1 ± 17.95	75 (34/41)	1.75 ± 0.10	24.1 ± 3.53	3.89 ± 3.35
18-29 years	21.4 ± 2.18	13 (6/7)	1.77 ± 0.08	21.6 ± 2.02	5.42 ± 4.29
30-39 years	33.8 ± 3.26	13 (6/7)	1.81 ± 0.10	23.8 ± 4.36	3.65 ± 3.37
40-49 years	44.3 ± 3.31	12 (5/7)	1.74 ± 0.07	25.1 ± 4.10	3.79 ± 2.89
50-59 years	53.7 ± 2.42	12 (5/7)	1.78 ± 0.09	24.5 ± 2.91	3.71 ± 2.41
60-69 years	64.1 ± 2.47	13 (5/8)	1.73 ± 0.09	24.4 ± 3.21	2.81 ± 2.59
70-79 years	73.2 ± 2.79	12 (7/5)	1.69 ± 0.11	25.2 ± 3.42	3.92 ± 4.16

Abbreviations: sd = standard deviation, N = number of participants, M = male, F = female.

CHAPTER 6

General Discussion

This thesis focused on adaptability of gait and balance performance across the adult lifespan. 'Healthy aging', or the effects of age, has been a focus point of the last decades. In the days of the *Homo erectus*, the average life expectancy of humans was around 30 years old [1], while the average life expectancy nowadays is above 80 years old in the Netherlands [2]. Of those 80 years, on average 62-64 years of human life are spent in good health, while the next 8-10 years are spent with minor health problems [3]. This means that there is still some room left to extend the period spent in excellent health or with minor health problems, which is a focus point of the World Health Organization [4]. One of the factors that can influence and be influenced by healthy aging, is walking ability. That is why this thesis aimed to shed light on how adaptation of gait and balance changes across the healthy adult lifespan.

MAIN FINDINGS

Changes in gait and balance across the lifespan were firstly investigated during a clinical task that includes several elements performed in daily life, the Timed-Up-and-Go (TUG). The TUG was measured with a smart device to objectively quantify the movements, which is then called the instrumented Timed-Up-and-Go (iTUG). Healthy adults across the lifespan could be distinguished in two age groups, above and below 45 years of age, based on 27 outcome measures that show a change in performance. These outcome measures mainly concern the turns, walking and the stand-to-sit movement. The overall classification accuracy of the model classifying healthy young and healthy older adults was AUC = 94.7%, and the sensitivity and specificity of the classification model were respectively 90% and 85%. These results show that the iTUG can accurately distinguish young and older adults and that the combination of a mobility test and smart technology can be used in clinical practice to distinguish age groups (Chapter 2).

Secondly, the effects of aging on adaptability of gait and balance were assessed with split-belt walking. Young and older adults (65+) could both re-establish symmetry in step length and double support time following the split-belt perturbation. The two age groups, however, differed in the strategy they used to adapt. Young adults increased swing time more, while older adults increased swing speed more. This difference in the strategy to adapt possibly reflects a need to increase gait stability to prevent falling. When a cognitive dual-task was added to split-belt adaptation, older adults showed a decrease in the performance of the cognitive task. This indicates that older adults need to prioritize adapting to split-belt walking over the simultaneously performed cognitive task to maintain walking and prevent adverse outcomes (Chapter 3). Investigating age-related changes in gait adaptation during split-belt walking also necessitates the examination of muscle activation. Young and middle-aged (± 55 years old) adults were perturbed by split-belt walking and re-established symmetry in step length and double support time. Both age groups activated similar functional muscle groups to cope with the perturbation and adjusted their gait, showing that the ability to adapt gait to split-belt walking is still preserved at middle-age. The muscle activation patterns did show adaptation effects, with increased muscle activation immediately after the split-belt perturbation, which decreased over time. This adaptation of muscle activation patterns paralleled the adaptation of gait symmetry, suggesting that the changes in muscle activation underlie the changes in step symmetry during split-belt adaptation (Chapter 4). Another factor related to adaptation that could be influenced by aging is the control of dynamic balance. Thus, we examined how adaptive control of the dynamic balance, represented by the Margin of Stability (MoS), changed across the adult lifespan (18-80 years old) during perturbed and unperturbed walking on the split-belt treadmill. Aging affected adaptive control of

dynamic balance during perturbed but not unperturbed treadmill walking with controlled walking speed. This confirms the importance of controlling for walking speed when investigating age effects on gait and suggests that dynamic balance should be challenged to assess aging effects on gait adaptation. During perturbed, split-belt, walking, the ML MoS increased across the lifespan, while bilateral single support times decreased and cadence increased. The decrease in single support time and double support time and the increase in cadence suggests that older adults prefer an increase of cadence as a balance control strategy during challenging locomotor tasks (Chapter 5).

USE OF SMART DEVICES TO DISTINGUISH AGE GROUPS BASED ON GAIT AND BALANCE

A large part of the population nowadays has a smart device or even several smart devices, like a smartphone or tablet. This makes the use of a smart device in clinical practice easier than it has ever been, especially since recent research has shown that the sensors, e.g. accelerometers, embedded in these devices, in combination with distinctive algorithms, are reliable and valid in gait and balance research, both for healthy adults [5–7] and in patient populations [8–10].

Using a smart device during the performance of a clinical test, such as the TUG might be even more powerful. Patients already perform these tests in the clinic, which would eventually make it easier to generalize the use of smart devices in the clinic. In this thesis we have shown that we can make a good classification model using the instrumented TUG (iTUG), with appropriate algorithms, that can differentiate age groups. When we zoom into the elements of the iTUG that the algorithms identified as good classifiers, the subsections of the iTUG that represent daily tasks in which adaptation in both gait and balance is necessary (turns, walking and the stand-to-sit) best classified the age groups. Healthy adults above 45 years old showed larger variability during the stand-to-sit, lower variability during walking and longer and less smooth turns (Chapter 2; see Figure 1 for a schematic overview of main findings). The reason why these elements might differentiate is that the stand-to-sit can be related to strength or power differences between age groups [11], walking could be related to differences in the ability to vary their gait pattern, and the turns require a larger degree of planning and spatial orientation that may be more cognitively demanding [12].

Other studies have shown that some of the elements of the iTUG that differentiate age groups (walking, turning, stand-to-sit) can also differentiate healthy older adults from fallers [13,14], patients with Parkinson's disease [15–17], mild cognitive impairment [18], mobility disability [11], and patients post-stroke [9]. If this knowledge would be combined, a more precise classification model could be made that can classify different age groups and patient populations based on iTUG variables. This would make the iTUG a strong diagnostic tool in clinical practice. However, while the iTUG and the use of a smart device are quite accessible, there has not been that much cross over to clinical practice. While IMU's are popular in human research [14,15,18], the number of doctors that use an IMU on a daily basis as a diagnostic tool is quite limited. A requirement for the use of IMU's in clinical practice is an adequate, automated algorithm that can immediately analyze the data and provide the clinician information on a patient's gait performance. Until now, that last requirement has not yet been achieved. As such, there is a need to develop sufficient algorithms that translate the outcomes to clinically relevant information in order to implement smart devices in the standard daily clinical practice to further this line of research and the use of gait analysis in clinical practice.

BROADER PERSPECTIVE ON ADAPTABILITY OF GAIT AND BALANCE ACROSS THE LIFESPAN

Adaptability of gait and balance is necessary since this allows us to react to internal and external perturbations [19]. The ability to adapt gait and balance could be essential for healthy adults to respond to the perturbation and maintain walking balance. However, much is still uncertain about how aging affects this ability to adapt gait and balance to sustained perturbations.

With increasing age, several changes in the ability to adapt to split-belt walking were found in this thesis (schematic overview see Fig. 1). Older adults changed the strategy to adapt to split-belt walking (increase in swing speed vs. swing time), and needed to prioritize adaptation to split-belt walking over performing the cognitive task (Chapter 3). In addition, with increasing age, the balance control strategy was altered, with a preference to increase cadence and decrease single support time, which leads to an increased mediolateral margin of stability (Chapter 5). We also uncovered an intact ability to adapt gait symmetry at middle and older age (Chapter 3 and 4) and no age-related changes were found in muscle activation patterns between young and middle-aged adults (Chapter 4).

Fig. 1. Schematic overview of the main findings in this thesis. Adaptability of gait and balance and its underlying mechanisms were studied in Chapters 2-5. In Chapter 2, iTUG performance distinguished age groups (healthy adults above and below 45 years old). In Chapters 3-5, adaptability of gait and balance was tested with the split-belt paradigm. Adaptation strategies and the ability to adapt gait with and without a cognitive dual-task were studied in Chapter 3. In Chapter 4, we investigated muscle activation patterns and gait symmetry in young and middle-aged adults. Finally, adaptive control of dynamic balance was studied across the lifespan in Chapter 5. Abbreviations: ML = mediolateral; MoS = margin of stability.

We expected aging effects on gait adaptability due to age-related changes in the sensorimotor system that might affect gait and balance performance. As can be seen in Figure 1, increasing age affected certain features of adaptability of gait and balance, and left other features unaffected. When challenging healthy individuals to adapt their gait pattern to our sustained perturbation, we did not find age effects on the symmetry outcomes that are standardly used in split-belt research (Chapters 3 and 4). These symmetry outcomes might show the ability to re-establish symmetry in step length

and double support time [20–22], but do not show how aging affects gait adaptability. To show how aging affects gait adaptability, more attention might need to be directed at how older adults reach that symmetry in split-belt gait. In Chapter 3, we showed that older adults use a different adaptation strategy to adapt to split-belt walking, with a preference of increasing swing speed instead of further increasing swing time. This was suggested to show their need to increase gait stability [23].

We continued on this line of thinking in Chapter 5, where we investigated the effects of age on adaptive control of dynamic balance during perturbed and unperturbed treadmill walking. Aging affected adaptive control of dynamic balance during perturbed but not unperturbed treadmill walking with controlled walking speed (0.7 m/s and 1.4 m/s). With controlled treadmill walking, the results are thus different compared to many overground walking studies, that showed older adults have shorter and wider steps, prolonged stance and double support times, and shortened swing times, along with a decrease in gait speed [24,25]. Firstly, this confirms the importance of controlling for walking speed when investigating age effects on gait. Secondly, healthy older adults presumably have more walking capacity than previously thought. Consequently, we need to challenge dynamic balance during gait to get insight into gait adaptability in older adults. Indeed, when we perturbed walking (Chapter 5), we found an effect of increasing age on dynamic balance during gait adaptation. With increasing age, healthy adults increased their mediolateral margin of stability through a decrease in single support time, i.e. increased cadence to adapt to split-belt walking. In addition, double support time and step length decreased. The increased cadence suggests that older adults cope with balance perturbations through shortened steps along with decreases in single and double support time. Healthy older adults thus seem to adopt an increased cadence as a balance control strategy. This may be done to reduce the propulsive impulse and reduce the braking impulse during walking [26], which would be one avenue worth exploring in future aging research on gait adaptability.

In this thesis, we also explored the contribution of the neuromuscular system to adaptability of gait, by examining the effects of aging on muscle activation patterns (Chapter 4). With increasing age, there is a shift in muscle activation from distal-to-proximal muscles and there is larger co-activation during walking [27,28]. However, we showed that all functional muscle groups were similarly activated between young and middle-aged adults, suggesting that adapting gait was still within the neuromuscular reserve at middle-age. Chapter 4 did show that the plantarflexors and dorsiflexors were key functional regulators of gait adaptation, as was also previously shown [29]. Since the plantarflexors play a large role in providing push-off power [30] and preventing falls [31], future research could look into these muscles specifically to investigate if and how these muscles perhaps influence age-related changes in gait adaptability.

One theory that did show merit was that older adults may need more cognitive resources to adapt gait. When humans walk and perform a cognitive task at the same time, gait can be modified because gait and cognitive function partly rely on the same cortical resources [32], while it is also possible that healthy adults prioritize gait over the cognitive task, minimizing any effects of the secondary cognitive task on the gait variables [33]. In Chapter 3, we showed that older adults needed to prioritize adapting gait over performing the cognitive dual-task. Under challenging circumstances, older adults thus need more attentional capacity to maintain walking ability and adapt gait. We speculated that a possible reason for this increased need to focus attention on responding to the split-belt perturbation could be impaired afferent feedback at older age [34]. In unpublished work, we did see a trend

toward a decreased perception of belt speed differences at middle-age (poster EWEP), but we have not investigated if this could be linked to afferent feedback or gait adaptability. Further research is necessary to (dis)prove that afferent feedback could play an important role in age-related changes in gait adaptability.

LIFESPAN APPROACH

The effects of age on gait are typically studied by comparing two age groups, young (18-30) vs. older adults (65+). Aging is, however, a continuous process across the adult lifespan. In order to investigate the development of changes in gait adaptability, and more specifically adaptive control of dynamic balance, over the age continuum, a lifespan approach was used in Chapter 5. The expectation was that adaptive control of dynamic balance would gradually decline across the lifespan, but what kind of relationship that would be was uncertain. Previous lifespan research showed different kinds of relationships between gait and age, from linear relationships [24,35] to exponential [36] and quadratic functions [37,38]. Many physiological functions, such as muscle mass and function, also show a quadratic relationship with age [39,40]. Therefore, we also expected a quadratic relation between adaptability of gait and balance and age. However, in Chapter 5 of this thesis, we showed that the control of dynamic balance and several gait parameters changed linearly across the lifespan. Thus, there is not an age threshold after which dynamic balance started to decline, but dynamic balance gradually changed from age 18 to 80 years old. To further our understanding of the relationship between age and changes in gait and balance, more research needs to be done with either a lifespan approach or even by using a longitudinal design. Using a longitudinal design is an avenue of research that is still relatively unused to study the effects of aging on gait and balance, while it would provide necessary longitudinal data. Recently, several research programs have started to collect and publish longitudinal data of individuals, such as Lifelines [41], the Rotterdam study [42] and the Longitudinal Aging Study Amsterdam [43]. Ideally, the assessment of gait and balance should be added to such research programs to study aging effects on gait and balance longitudinally in the future.

CHALLENGES IN HEALTHY AGING RESEARCH

Researching the effects of healthy aging on gait and balance also brings about some challenges. The first challenge is the inclusion bias of mainly including very active healthy older adults. These adults are generally more interested and willing to participate in research. However, to really understand the effects of aging on adaptability of gait and balance, also less active and sedentary older adults need to be studied. At old age, activity level affects physical functioning [44–46], and physical activity could possibly preserve gait and balance performance with increasing age [45]. Also including less active older adults in future studies could give a complete view of the effects of aging on gait.

Another discussion point is the normative values that are used to compare older adults with. These normative values generally come from the first age-related research, which has been done about 30 years ago [25,47]. For example, the values for gait speed, which was ± 1.3 m/s at 65 years old [47,48] and ± 1.2 m/s at 80 years old [24], might not be indicative for older adults' gait speed these days. Since there has been a lot of attention for 'healthy aging' for the last few years, e.g. by the WHO [4], older adults these days might be 'fitter' than their counterparts 30 years ago. Older adults nowadays are generally more aware of the positive effect of exercise and the importance of staying active. As previously

mentioned, physical activity might influence gait and balance performance [45], which is why older adults might have a 'better' gait performance, such as higher gait speed. Future research should look into updating normative values on gait parameters, perhaps in the longitudinal design suggested earlier.

CONCLUDING REMARKS

This thesis increased our understanding of changes in adaptability of gait and balance across the adult lifespan. The natural, healthy aging process affected gait adaptation strategy, dynamic balance and the ability to perform a dual-task during split-belt adaptation. We were also able to develop a model using gait and balance parameters of the iTUG that can discriminate healthy young and older adults. In contrast to our expectations, healthy aging did not affect gait symmetry or muscle activation patterns (at middle-age). In conclusion, this thesis showed how increasing age affected certain features of adaptability of gait and balance, and left other features unaffected. Future research should utilize similar larger cohorts with different age groups or along the age continuum to further increase our understanding of healthy aging and the changes that occur in gait and balance performance.

REFERENCES

- Curven M, Kaplan H. Longevity among hunter-gatherers: a cross-cultural examination. *Popul Dev Rev*. 2007;33: 321–365.
- Poos MJJC. Levensverwachting | Cijfers & Context | Huidige situatie. In: *Volksgezondheid en Zorg*. 2018.
- Poos MJJC, Bruggink JW, Nusselder WJ. Gezonde levensverwachting | Cijfers & Context | Huidige situatie. In: *Volksgezondheid en Zorg*. 2018.
- World Health Organization. What is Healthy Ageing? In: *World Health Organization*. 2018.
- Kosse NM, Caljouw S, Vervoort D, Vuillerme N, Lamoth CJC. Validity and reliability of gait and postural control analysis using the tri-axial accelerometer of the iPod touch. *Ann Biomed Eng*. 2015;43: 1935–1946.
- Mellone S, Tacconi C, Chiari L. Validity of a Smartphone-based instrumented Timed Up and Go. *Gait Posture*. 2012;36: 163–165.
- Galán-Mercant A, Barón-López FJ, Labajos-Manzaneres MT, Cuesta-Vargas AI. Reliability and criterion-related validity with a smartphone used in timed-up-and-go test. *Biomed Eng Online*. 2014;13: 156.
- Salarian A, Russmann H, Vingerhoets FJG, Dehollain C, Blanc Y, Burkhard PR, et al. Gait assessment in Parkinson's disease: toward an ambulatory system for long-term monitoring. *IEEE Trans Biomed Eng*. 2004;51: 1434–1443.
- Wüest S, Massé F, Aminian K, Conzenbach R, de Bruin ED. Reliability and validity of the inertial sensor-based Timed "Up and Go" test in individuals affected by stroke. *J Rehabil Res Dev*. 2016;53: 599–610.
- van Lummel RC, Walgaard S, Hobert MA, Maetzler W, van Dieën JH, Galindo-Garre F, et al. Intra-rater, inter-rater and test-retest reliability of an instrumented Timed Up and Go (iTUG) test in patients with Parkinson's disease. *PLoS One*. 2016;11.
- Weiss A, Mirelman A, Buchman AS, Bennett DA, Hausdorff JM. Using a body-fixed sensor to identify subclinical gait difficulties in older adults with IADL disability: maximizing the output of the timed up and go. *PLoS One*. 2013;8.
- Herman T, Giladi N, Hausdorff JM. Properties of the "Timed Up and Go" test: more than meets the eye. *Gerontology*. 2011;57: 203–210.
- Weiss A, Herman T, Plotnik M, Brozgov M, Giladi N, Hausdorff JM. An instrumented timed up and go: the added value of an accelerometer for identifying fall risk in idiopathic fallers. *Physiol Meas*. 2011;32: 2003–2018.
- Jackson K, Sample R, Bigelow K. Use of an instrumented Timed Up and Go (iTUG) for fall risk classification. *Phys Occup Ther Geriatr*. 2018;36: 354–365.
- Palmerini L, Mellone S, Avanzolini G, Valzania F, Chiari L. Quantification of motor impairment in Parkinson's disease using an instrumented timed up and go test. *IEEE Trans Neural Syst Rehabil Eng*. 2013;21: 664–673.
- Herman T, Weiss A, Brozgov M, Giladi N, Hausdorff JM. Identifying axial and cognitive correlates in patients with Parkinson's disease motor subtype using the instrumented Timed Up and Go. *Exp Brain Res*. 2014;232: 713–721.
- Salarian A, Horak FB, Zampieri C, Carlson-Kuhta P, Nutt JC, Aminian K. iTUG, a sensitive and reliable measure of mobility. *IEEE Trans Neural Syst Rehabil Eng*. 2010;18: 303–310.
- Mirelman A, Weiss A, Buchman AS, Bennett DA, Giladi N, Hausdorff JM. Association between performance on Timed Up and Go subtasks and mild cognitive impairment: further insights into the links between cognitive and motor function. *J Am Geriatr Soc*. 2014;62: 673–678.
- Woollacott MH, Tang P-F. Balance control during walking in the older adult: research and its implications. *Phys Ther*. 1997;77: 646–660.
- Reisman DS, Block HJ, Bastian AJ. Interlimb coordination during locomotion: what can be adapted and stored? *J Neurophysiol*. 2005;94: 2403–2415.
- Malone LA, Bastian AJ. Age-related forgetting in locomotor adaptation. *Neurobiol Learn Mem*. 2016;128: 1–6.
- Finley JM, Bastian AJ, Gottschall JS. Learning to be economical: the energy cost of walking tracks motor adaptation. *J Physiol*. 2013;591: 1081–1095.
- Bruijn SM, Van Impe A, Duysens J, Swinnen SP. Split-belt walking: adaptation differences between young and older adults. *J Neurophysiol*. 2012;108: 1149–1157.
- Samson MM, Crowe A, De Vreede PL, Dessens JA, Duursma SA, Verhaar HJ. Differences in gait parameters at a preferred walking speed in healthy subjects due to age, height and body weight. *Aging Clin Exp Res*. 2001;13: 16–21.
- Winter DA, Patla AE, Frank JS, Walt SE. Biomechanical walking pattern changes in the fit and healthy elderly. *Phys Ther*. 1990;70: 340–347.
- Goldberg EJ, Kautz SA, Neptune RR. Can treadmill walking be used to assess propulsion generation? *J Biomech*. 2008;41: 1805–1808.
- Schmitz A, Silder A, Heiderscheit B, Mahoney J, Thelen DG. Differences in lower-extremity muscular activation during walking between healthy older and young adults. *J Electromyogr Kinesiol*. 2009;19: 1085–1091.
- Hortobágyi T, Solnik S, Gruber A, Rider P, Steinweg K, Helseth J, et al. Interaction between age and gait velocity in the amplitude and timing of antagonist muscle coactivation. *Gait Posture*. 2009;29: 558–564.
- Dietz V, Zijlstra W, Duysens J. Human neuronal interlimb coordination during split-belt locomotion. *Exp Brain Res*. 1994;101: 513–520.
- Neptune RR, Kautz SA, Zajac FE. Contributions of the individual ankle plantar flexors to support, forward progression and swing initiation during walking. *J Biomech*. 2001;34: 1387–1398.
- Honeine J-L, Schieppati M, Gagey O, Do M-C. The functional role of the triceps surae muscle during human locomotion. *PLoS One*. 2013;8.
- Holtzer R, Epstein N, Mahoney JR, Izzetoglu M, Blumen HM. Neuroimaging of mobility in aging: a targeted review. *Journals Gerontol Ser A*. 2014;69: 1375–1388.
- Yogev-Seligmann G, Hausdorff JM, Giladi N. Do we always prioritize balance when walking? Towards an integrated model of task prioritization. *Mov Disord*. 2012;27: 765–770.
- Goble DJ, Coxon JP, Wenderoth N, Van Impe A, Swinnen SP. Proprioceptive sensibility in the elderly: degeneration, functional consequences and plastic-adaptive processes. *Neurosci Biobehav Rev*. 2009;33: 271–278.
- Herssens N, Verbecque E, Hallemans A, Vereeck L, Van Rompaey V, Saeyns W. Do spatiotemporal parameters and gait variability differ across the lifespan of healthy adults? A systematic review. *Gait Posture*. 2018;64: 181–190.
- Iosa M, Fusco A, Morone G, Paolucci S. Development and decline of upright gait stability. *Front Aging Neurosci*. 2014;6.
- Terrier P, Reynard F. Effect of age on the variability and stability of gait: a cross-sectional treadmill study in healthy individuals between 20 and 69 years of age. *Gait Posture*. 2015;41: 170–174.
- Frimenko R, Goodyear C, Bruening D. Interactions of sex and aging on spatiotemporal metrics in non-pathological gait: a descriptive meta-analysis. *Physiotherapy*. 2015;101: 266–272.

39. Lexell J, Taylor CC, Sjöström M. What is the cause of the ageing atrophy? Total number, size and proportion of different fiber types studied in whole vastus lateralis muscle from 15- to 83-year-old men. *J Neurol Sci.* 1988;84: 275–294.
40. Hughes VA, Frontera WR, Roubenoff R, Evans WJ, Singh MAF. Longitudinal changes in body composition in older men and women: role of body weight change and physical activity. *Am J Clin Nutr.* 2002;76: 473–481.
41. Kuiper JS, Oude Voshaar RC, Zuidema SU, Stolk RP, Zuidersma M, Smidt N. The relationship between social functioning and subjective memory complaints in older persons: a population-based longitudinal cohort study. *Int J Geriatr Psychiatry.* 2017;32: 1059–1071.
42. Koolhaas CM, Dhana K, Schoufour JD, Ikram MA, Kavousi M, Franco OH. Impact of physical activity on the association of overweight and obesity with cardiovascular disease: the Rotterdam study. *Eur J Prev Cardiol.* 2017;24: 934–941.
43. Wouters H, Hilmer SN, Gnjdijic D, Van Campen JP, Teichert M, Van Der Meer HG, et al. Long-term exposure to anticholinergic and sedative medications and cognitive and physical function in later life. *Journals Gerontol Ser A.* 2019;75: 357–365.
44. Shah KN, Lin F V., Yu F, McMahon JM. Activity engagement and physical function in old age sample. *Arch Gerontol Geriatr.* 2017;69: 55–60.
45. Morie M, Reid KF, Miciek R, Lajevardi N, Choong K, Krasnoff JB, et al. Habitual physical activity levels are associated with performance in measures of physical function and mobility in older men. *J Am Geriatr Soc.* 2010;58: 1727–1733.
46. Hillsdon MM, Brunner EJ, Guralnik JM, Marmot MG. Prospective study of physical activity and physical function in early old age. *Am J Prev Med.* 2005;28: 245–250.
47. Hageman PA, Blanke DJ. Comparison of gait of young women and elderly women. *Phys Ther.* 1986;66: 1382–1387.
48. Bohannon RW. Comfortable and maximum walking speed of adults aged 20-79 years: reference values and determinants. *Age Ageing.* 1997;26: 15–19.

CHAPTER 7

Appendices

—

Summary

Samenvatting

Résumé

Dankwoord

About the author

Scientific output

Conference contributions

Research institute SHARE

SUMMARY

Human walking has evolved from mammalian quadrupedal gait to our current bipedal gait. During bipedal gait, there is a prolonged period of pivoting over one foot that challenges balance control, especially in the presence of internal and external perturbations. Gait adaptability, the ability to adjust walking to a potential loss of balance, is needed for ambulation. An impaired ability to adapt gait makes walking more vulnerable to internal and external perturbations and increases the risk of falling. With increasing age, gait adaptability might be affected due to changes in gait and balance performance, which would make older adults more vulnerable to a loss of balance. Therefore, the main objective of the present thesis was to shed light on the effects of age on adaptability of gait and balance. Adaptability of gait and balance was assessed by two different tasks: the instrumented Timed-Up-and-Go (iTUG) and split-belt walking, where gait is perturbed by imposing asymmetric belt speeds. The effects of age were assessed in cross-sectional studies comparing age groups and by comparing adults across the lifespan (**Chapter 1**).

Age-related changes in gait and balance were firstly investigated during the iTUG using an inertial measurement unit for objective quantification of movement. The aim of **Chapter 2** was to develop a model based on gait and balance parameters of the iTUG that can discriminate different age groups. Healthy adults across the lifespan could be distinguished in two age groups, above and below 45 years of age, based on 27 outcomes associated with turning, walking and the stand-to-sit during the iTUG. The overall accuracy of the classification model was $AUC = 94.7\%$, and the sensitivity and specificity were respectively 90% and 85%. A model of iTUG variables could thus accurately distinguish healthy young and older adults. The combination of a clinical test and smart technology shows promise for being used in clinical practice to classify different groups.

Secondly, the effects of aging on adaptability of gait and balance were assessed with split-belt walking. In **Chapter 3**, we studied the effects of age on adaptability of gait and task prioritization. Both healthy young and older adults could re-establish symmetry in step length and double support time following the split-belt perturbation, but differed in the strategy they used to adapt. Young adults increased swing time of the fast leg more, while older adults increased swing speed of the fast leg more. When a cognitive dual-task was added to split-belt adaptation, older adults needed to prioritize adapting to split-belt walking over performing the cognitive task, to maintain walking and prevent adverse outcomes.

In **Chapter 4**, we investigated the effects of age on adaptation of gait symmetry and muscle activation patterns. Both age groups, healthy young and middle-aged adults, could re-establish symmetry in step length and double support time and activated similar functional muscle groups to cope with the split-belt perturbation. Thus, the ability to adapt gait to split-belt walking is still preserved at middle-age. The muscle activation patterns did show adaptation effects, with increased activation immediately after the split-belt perturbation, which decreased over time. The adaptation of muscle activation patterns paralleled the adaptation of gait symmetry, suggesting that the changes in muscle activation underlie the changes in gait symmetry during split-belt adaptation.

Chapter 5 examined how adaptive control of dynamic balance changed across the adult lifespan during perturbed and unperturbed walking on the split-belt treadmill. Increasing age did not affect adaptive control of dynamic balance during unperturbed treadmill walking at a controlled gait speed. This confirms the importance of controlling for walking speed when investigating age effects on gait. Advancing age did affect adaptive control of dynamic balance during perturbed walking, suggesting that dynamic balance should be challenged to assess aging effects on gait adaptation. During split-belt walking, the mediolateral margin of stability increased across the lifespan, due to a decrease in bilateral single support times, i.e. an increased cadence. The increased cadence suggests that older adults cope with challenging balance perturbations through shortened steps along with decreases in single and double support time. With increasing age, healthy adults thus adopt an increased cadence as a balance control strategy.

Chapter 6 summarizes and discusses the findings of this thesis. Increasing age alters gait adaptation strategy and dynamic balance during split-belt adaptation, while gait symmetry and muscle activation patterns remain unaffected by age. Using gait and balance parameters of the iTUG, an accurate classification model could discriminate healthy young and older adults. The cross-sectional assessment of adaptive control of dynamic balance across the lifespan shows promise to further our understanding of age-related changes in gait and balance performance. Ideally, future research would adopt a longitudinal design to study aging effects, and follow adults over a longer period to capture gait and balance performance along the age continuum.

SAMENVATTING

Menselijk lopen is geëvolueerd van het lopen op vier poten naar het huidige lopen op twee benen, waarbij er in verhouding een langere periode is waarbij je op een voet staat. Dit daagt balanscontrole uit, zeker tijdens interne of externe verstoringen. Adaptatie, het vermogen om het lopen aan te passen aan mogelijk balansverlies, is nodig tijdens het lopen. Een verminderd adaptatievermogen maakt het lopen vatbaarder voor interne en externe verstoringen en verhoogt het valrisico. Naarmate mensen ouder worden, kan adaptatie worden beïnvloed door veranderingen in het looppatroon en de balans, waardoor ouderen vatbaarder worden voor evenwichtsverlies. Het doel van dit proefschrift was daarom om de effecten van leeftijd op adaptatie van lopen en balans te onderzoeken. Adaptatie van lopen en balans werd bestudeerd met behulp van twee taken: de instrumented Timed-Up-and-Go (iTUG) en het split-belt lopen. Split-belt lopen is een taak waarbij mensen lopen op een split-belt loopband, die twee banden heeft waarvan de snelheid afzonderlijk aangestuurd kan worden. De effecten van leeftijd werden bestudeerd in cross-sectioneel onderzoek waarbij leeftijdsgroepen met elkaar werden vergeleken en in een studie waar volwassenen over de levensduur (18-80 jaar oud) werden vergeleken (**Hoofdstuk 1**).

Leeftijdsgebonden veranderingen in het lopen en de balans werden eerst onderzocht tijdens de iTUG. Tijdens de iTUG wordt er gemeten met een inertial measurement unit (IMU) voor objectieve kwantificatie van bewegingen. Het doel van **Hoofdstuk 2** was om een model te ontwikkelen op basis van loop- en balansparameters van de iTUG die verschillende leeftijdsgroepen kunnen onderscheiden. Gezonde volwassenen in twee leeftijdsgroepen, boven en onder de 45 jaar, werden onderscheiden op basis van 27 parameters die geassocieerd zijn met het draaien, lopen en staan tijdens de iTUG. De nauwkeurigheid van het classificatiemodel was $AUC = 94,7\%$ en de sensitiviteit en specificiteit waren respectievelijk 90% en 85%. Een model van iTUG-variabelen kan dus nauwkeurig gezonde jongeren en ouderen classificeren. De combinatie van een klinische test en technologie is veelbelovend om in de klinische praktijk verschillende groepen te onderscheiden.

Ten tweede werden de effecten van veroudering op adaptatie van lopen en balans bestudeerd met het split-belt lopen. In **Hoofdstuk 3** zijn de effecten van leeftijd op adaptatie van het looppatroon en het prioriteren van taken bestudeerd. Zowel gezonde jongeren als ouderen konden symmetrie in staplengte en dubbele standtijd herstellen na de split-belt verstoring, maar verschilden in de strategie die ze gebruikten. Jongeren verhoogden de zwaaitijd van het snelle been meer, terwijl ouderen de zwaaisnelheid van het snelle been meer verhoogden. Toen het split-belt lopen met een cognitieve dubbel taak werd uitgevoerd, moesten ouderen prioriteit geven aan adaptatie van het split-belt lopen om te blijven lopen en vallen te voorkomen.

In **Hoofdstuk 4** onderzochten we de effecten van leeftijd op adaptatie van loopsymmetrie en spieractivatie patronen. Beide leeftijdsgroepen, gezonde jongeren en volwassenen van middelbare leeftijd, konden symmetrie in staplengte en dubbele standtijd herstellen en activeerden vergelijkbare functionele spiergroepen in reactie op de split-belt verstoring. Het vermogen om te adapteren aan split-belt lopen blijft dus behouden op middelbare leeftijd. De spieractivatie patronen vertoonden effecten van adaptatie, met verhoogde spieractivatie onmiddellijk na de split-belt verstoring en de spieractiviteit nam na verloop van tijd af. De aanpassing van de spieractivatie patronen liep parallel

met de aanpassing van loopsymmetrie, wat suggereert dat de veranderingen in spieractivatie onderliggend zijn aan de veranderingen in loopsymmetrie tijdens de adaptatie aan split-belt lopen.

In **Hoofdstuk 5** onderzochten we hoe adaptieve controle van dynamische balans veranderd over de leeftijden (18-80 jaar oud) tijdens verstoord en onverstoord lopen op de split-belt loopband. Adaptieve controle van dynamische balans tijdens onverstoord lopen met een gecontroleerde loopsnelheid veranderde niet door leeftijd. Dit bevestigt dat het belangrijk is om te controleren voor loopsnelheid wanneer de effecten van leeftijd op het lopen worden bestudeerd. Adaptieve controle van het dynamische balans tijdens verstoord lopen veranderde wel met leeftijd, wat suggereert dat dynamische balans moet worden uitgedaagd om leeftijdseffecten waar te nemen tijdens de adaptatie van het looppatroon. Tijdens het split-belt lopen nam de mediolaterale 'margin of stability' toe over de leeftijden als gevolg van een afname van de bilaterale standtijd, d.w.z. een hogere cadans. De hogere cadans suggereert dat ouderen omgaan met uitdagende balansverstoringen door kortere stappen te nemen in combinatie met een afname in standtijd. Naarmate gezonde volwassenen ouder worden, nemen ze dus een verhoogde cadans aan als strategie voor balanscontrole.

Hoofdstuk 6 vat de bevindingen van dit proefschrift samen en bediscussieert deze bevindingen. Als volwassenen ouder worden, veranderen de adaptatiestrategie en de controle van adaptieve balans tijdens split-belt adaptatie, terwijl loopsymmetrie en spieractivatie patronen niet worden beïnvloed door leeftijd. Met behulp van loop- en balansparameters van de iTUG kan een classificatiemodel accuraat gezonde jongeren en ouderen onderscheiden. Het cross-sectioneel bestuderen van adaptieve controle van dynamische balans over de leeftijden is veelbelovend om ons inzicht te vergroten over leeftijd gerelateerde veranderingen in lopen en balans. Idealiter zou toekomstig onderzoek een longitudinaal design gebruiken om verouderingseffecten te bestuderen en volwassenen gedurende een langere periode te volgen om lopen en balans vast te leggen over het leeftijdscontinuüm.

RÉSUMÉ

Les capacités d'adaptation locomotrice, vues comme la capacité à ajuster sa marche à un environnement ou un contexte changeant, ou bien à une situation de perte d'équilibre, revêtent une importance primordiale pour la réalisation de nos activités quotidiennes. Avec l'âge, ces capacités d'adaptation locomotrice peuvent être affectées. Les causes sont probablement dues aux troubles de l'équilibre et de la marche le plus souvent associés à l'avancée en âge ; les conséquences sont probablement une augmentation des épisodes de perte d'équilibre et le nombre de chutes chez les personnes âgées. Dans ce contexte, l'objectif principal de ce travail doctoral visait à caractériser et mieux comprendre les effets de l'âge sur les adaptations posturales et locomotrices. Pour ce répondre à cet objectif, nous avons conduit des études transversales comparant des groupes d'âge et comparant des adultes à tous les âges de la vie (**Chapitre 1**), au cours desquels il a été demandé aux participants de réaliser les deux tâches suivantes : le test Timed-Up-and-Go instrumenté (iTUG) et le test de marche sur tapis roulant à deux courroies qui permet d'imposer une démarche asymétrique aux participants et d'évaluer les adaptations à cette perturbation.

Dans un premier temps, les effets de l'âge sur la marche et l'équilibre ont été étudiés à travers l'exécution du test iTUG. L'objectif du **Chapitre 2** était, à partir des paramètres posturo-locomoteurs fournis par le test iTUG, de construire un modèle permettant de discriminer différents groupes d'âge. La prise en compte de 27 paramètres associés aux phases de marche, de rotation, et debout-assis du test iTUG a permis aux adultes en bonne santé d'être discriminés, avec précision, en deux groupes d'âges, moins de 45 ans et plus de 45 ans. La précision globale du modèle de classification est très bonne, avec une valeur de l'aire sous la courbe ROC de 94.7% d'une part, et des valeurs de sensibilité et de spécificité respectivement de 90% et 85%, d'autre part.

Dans un second temps, les effets de l'âge sur les capacités d'adaptation posturo-locomotrice ont été évalués à travers l'exécution du test de marche sur tapis roulant à deux courroies. Dans le **Chapitre 3**, nous avons étudié les effets de l'âge sur l'adaptation locomotrice et sur la priorisation de la tâche. Les résultats montrent que les sujets jeunes et âgés sont capables de rétablir une symétrie de longueur de pas et de temps double de double support après la perturbation. Cependant, les stratégies adoptées par les deux groupes d'âge sont différentes : alors que les sujets jeunes augmentent plus le temps d'oscillation de la jambe 'rapide', les sujets âgés augmentent plus la vitesse d'oscillation de la jambe 'rapide'. Enfin, en condition de double tâche cognitive, les résultats montrent que les sujets âgés donnent priorité à la tâche locomotrice au détriment de la tâche concurrente cognitive, ceci sans doute afin de préserver leur patron locomoteur et de prévenir d'éventuelles conséquences néfastes.

Dans le **Chapitre 4**, nous avons étudié les effets de l'âge sur l'adaptation de la symétrie des paramètres locomoteurs et sur les actions musculaires mises en œuvre. Les résultats montrent que les sujets jeunes et les sujets d'âge moyen sont capables de rétablir une symétrie de longueur du pas et de temps de double support. Les résultats montrent également que, pour faire face à la perturbation, les sujets jeunes et les sujets d'âge moyen réorganisent les actions musculaires de la manière similaire.

Autrement dit, ces résultats suggèrent, d'une part que la capacité à adapter sa marche au tapis roulant à double courroie est préservée chez les personnes d'âge moyen, et d'autre part, que les changements des activations musculaires sous-tendent les changements de symétrie des paramètres locomoteurs.

Le **Chapitre 5** évalue si, et dans quelle mesure, l'âge modifie les adaptations posturo-locomotrices en condition de marche non perturbée et perturbée réalisée sur tapis roulant à deux courroies. Les résultats montrent qu'en condition de marche non perturbée réalisée sur tapis roulant à vitesse contrôlée, l'avancée en âge ne modifie pas de manière significative l'adaptation locomotrice. Ce résultat confirme l'importance, et la nécessité, de contrôler la vitesse de marche quand on étudie les effets de l'âge. En condition de marche perturbée réalisée sur tapis roulant, les résultats montrent également que l'avancée en âge ne modifie pas de manière significative l'adaptation locomotrice. Ce résultat suggère que la difficulté de la tâche locomotrice proposée est à considérer pour mettre en évidence les effets de l'âge sur l'adaptation locomotrice. En condition de marche sur tapis roulant à deux courroies, la marge de stabilité médio-latérale augmente avec l'âge, probablement en raison d'une diminution de temps de simple support, autrement dit de l'augmentation de la cadence. Cette augmentation de la cadence suggère que les personnes âgées font face à cette perturbation posturale en diminuant la longueur de leur pas et en réduisant les durées de simple et de double support. Il est dès lors possible que cette augmentation de la cadence avec l'âge puisse être considérée comme une stratégie de contrôle de l'équilibre.

Les résultats de ce travail doctoral sont présentés de manière synthétique et discutés dans le **Chapitre 6**. Les résultats montrent qu'à partir des paramètres posturo-locomoteurs extraits lors de l'exécution du test iTUG, il a été possible de proposer un modèle de classification permettant de discriminer avec précision des personnes en bonne santé, jeunes et âgées. Les résultats montrent en outre que l'avancée en âge modifie les stratégies d'adaptation locomotrice et l'équilibre dynamique en condition de marche sur tapis roulant à deux courroies, alors que la symétrie des paramètres locomoteurs et les actions musculaires mises œuvres ne se sont pas modifiées. Plus largement, ce travail doctoral suggère que l'étude transversale des adaptations posturales et locomotrices tout au long de la vie représente une voie prometteuse pour mieux comprendre les changements associés à l'avancée en l'âge. A l'avenir, et idéalement, des études de type longitudinal seraient des plus appropriées pour étudier, sur des temps plus longs, et sur de plus larges cohortes, les effets de l'âge.

DANKWOORD

Toen ik ongeveer 9 jaar geleden naar Groningen vertrok om Bewegingswetenschappen te studeren, had ik geen idee dat mijn avontuur bij BW uiteindelijk zou eindigen met dit proefschrift. In dit (meest gelezen) stuk van mijn proefschrift wil ik graag een aantal mensen persoonlijk bedanken die de afgelopen jaren belangrijk voor me zijn geweest, me geholpen/geadviseerd hebben en vertrouwen in me hebben gehad.

First, I would like to address my promotion team, **Dr. Claudine Lamothe, Dr. Rob den Otter, Prof. Dr. Tibor Hortobágyi** and **Dr. Nicolas Vuillerme**. I would like to thank all of you for trusting, guiding and coaching me during my studies and my PhD to become the researcher and the person I am today.

Beste **Claudine**, het is nu ruim 6 jaar geleden dat ik jou kantoor binnen stapte om mijn bachelor project te starten, toen nog totaal niet beseffend waar dit uiteindelijk toe zou leiden. In die 6 jaar kan ik wel zeggen dat je me veel geleerd hebt en me hebt zien groeien als persoon. Naast al je kennis en ervaring binnen het onderzoek, betekende ook de persoonlijke noot in onze overleggen en koffiemomentjes veel voor me. Bedankt dat je er voor me bent geweest, ook als ik het soms nodig had om een schop onder mijn kont te krijgen.

Beste **Rob**, toen je tijdens mijn master aansloot bij mijn project, zorgde je niet alleen voor een nieuwe impuls qua kennis, maar ook meteen voor een vrolijke noot. Ik had altijd het idee dat ik even bij je binnen kon stappen voor een gezellig praatje, of het nu over planten ging of over sport. Ook onze discussies over de data (en alle mooie plaatjes) en hoe je met de 'reviewer bril' naar mijn stukken hebt gekeken, heb ik altijd gewaardeerd. Bedankt voor alles!

Dear **Tibor**, I don't think I would have become the scientist I am today, if you hadn't been involved in my project. You taught me how to look at the big-

ger picture and write with the famous 'helicopter view', even though I sometimes had to close the manuscripts at first since the text was largely red. Over time that improved and I do think I can confidently say that I became a better writer. Thank you for all your encouragement and your extremely quick responses.

Cher **Nicolas**, je vais essayer, et j'insiste bien sur "essayer", d'écrire ceci en français. Bien que je n'ai passé qu'un mois (et deux courts séjours) dans votre laboratoire pendant mon doctorat, j'ai toujours pu compter sur toi, sur ton soutien et ton enthousiasme pour mon projet et mon développement personnel et en tant chercheuse. Pendant nos réunions (Skype), nous avons plus souvent parlé de moi que de la recherche, ce qui m'a toujours aidé à avancer. Merci beaucoup d'avoir été là pour moi ces dernières années.

Je voudrais aussi remercier **les membres du laboratoire AEGIS** pour m'avoir bien accueilliquand je suis venue à Grenoble. Je voudrais surtout remercier **Julie** pour les belles conversations, l'agréable compagnie et de m'avoir emmener dans la prise des mesures.

Dan zijn er nog twee coauteurs die ik persoonlijk wil bedanken, **Dr. Nienke Kosse** en **Dr. Tom Buurke**. Beste **Nienke**, ik weet nog heel goed hoe verbaasd en vereerd ik was toen er voorgesteld werd dat is als coauteur op jou artikel zou komen na aanleiding van mijn bachelor scriptie. Ons contact en jou begeleiding tijdens mijn

bachelor project heeft zeker meegespeeld in mijn keuze om met het MSc-PhD traject te beginnen. Bedankt daarvoor! Beste **Tom**, toen we op het congres in Miami brainstormde over hoe en of we meer samen zouden kunnen werken, wisten we beiden nog niet dat dat het begin zou zijn van een artikelenreeks. Bedankt voor al je input, je hulp en de leuke discussies over de wondere wereld van de dynamische balans en split-belt onderzoek.

Al het onderzoek in dit proefschrift had niet kunnen gebeuren zonder de hulp van een aantal studenten van bewegingswetenschappen. **Anne, Ylva, Marloes, Kas, Tessa, Linda, Timon, Lotte, Rob** en **Jorien**, bedankt voor de leuke samenwerking en jullie hulp tijdens alle metingen, ook al duurde die soms tot laat in de avond. Deze metingen hadden niet door kunnen gaan zonder de mensen die daaraan mee wilden doen. Hierbij wil ik alle **proefpersonen** nogmaals bedanken voor hun tijd en moeite om mee te doen aan de onderzoeken.

Dan zijn er wat mensen bij BW die ik graag wil bedanken. **Wim, Emyl, Dirk** en **Anniek**, bedankt voor al jullie hulp rondom de metingen. Ik kwam regelmatig binnenlopen als er iets was met de loopband, de EMG sensoren, of als we weer eens nieuwe EMG plakkers nodig hadden. Jullie hielpen me niet alleen, maar namen ook de tijd voor een gezellig praatje. **Wia, Dea** en **Nettie**, bedankt voor jullie ondersteuning als ik wat nodig had of dingen niet kon vinden en voor de gezellige gesprekken bij het secretariaat of de koffieautomaat.

(Oud-)PhD-ers van BW, bedankt voor alle gezelligheid tijdens de koffiepauzes, de PhD uitjes, de vrijmibo's en de congressen. In het bijzonder wil ik mijn roomies van het eerste uur noemen: **Tjerk, Lisette** en **Marika**. Ik zal de discussies over airsquats, functies van fruit en groeten, de temperatuur in het kantoor en de discriminatiebriefjes niet snel vergeten. Ook waren jullie zo lief

om langs te komen mijn korfbalwedstrijden (al snaptten jullie er niks van) en ontstonden de tradities van de wodka woensdagen en de jaarlijkse bezoeken aan het bierfestival. Bedankt voor niet alleen de gezelligheid, maar ook jullie steun als ik het even niet zag zitten, het gezamenlijke klagen en jullie altijd goede adviezen. Dan nog een bedankje aan **Tom** en **Sylvana**, jullie hebben me goed opgevangen toen ik in de laatste paar maanden nog kort van kantoor moest wisselen. Ik blijf nog steeds verbaasd over hoe snel de snoep pot soms leeg was.

Ook mijn vriendengroepen van de studie mag ik natuurlijk niet vergeten. De altijd prachtige namen komen nu langs. Lieve **meiden van Nobeltje** en **de hele club van de Roddelboks**, bedankt voor al jullie gezelligheid en steun tijdens niet alleen de studie BW, maar ook tijdens mijn PhD. Ondanks dat we ondertussen verspreid over Nederland wonen en werken, ben ik blij dat we elkaar nog af en toe zien met leuke uitjes of etentjes.

Tijdens mijn studie en PhD heb ik ook redelijk veel tijd op en rond het korfbalveld doorgebracht bij **korfbalvereniging Nic**. Iedereen daar wil ik bedanken voor de leuke tijden in en buiten het veld en de goede afleiding die het korfbal bracht tijdens stressvolle periodes.

Dan een special mention naar de twee vriendinnen die me al het langst kennen. **Monique** en **Renske**, jullie houden het ondertussen zo'n 15 jaar met me vol. Ondanks dat we niet meer dagelijks contact hebben, kan ik altijd bij jullie terecht en weet ik dat het altijd gezellig als ik jullie wel weer zie.

Natascha en **Marika**, bedankt dat jullie op deze mooie dag naast me willen staan tijdens mijn promotie. Bedankt voor jullie hulp en advies tijdens de voorbereidingen, jullie maakten deze periode leuker! **Natascha**, jij bent vaak een van de eerste met wie ik contact heb als er iets

gebeurd en ik kon me dan ook bijna niet voorstellen dat je deze dag niet naast me zou staan. Bedankt voor de goede gesprekken over van alles en nog wat, je steun en je betrokkenheid! **Mari-ka**, ik kan me geen (kamer) 216, en dus een groot deel van mijn promotietraject, voorstellen zonder jou. Bedankt dat ik altijd bij je terecht kon, of dat nu was voor advies of om te klagen of voor een van je prachtige GIFjes!

Jamilla en Colin, jullie zijn er letterlijk (bijna) altijd al bij geweest. Ondanks dat ik aan de andere kant van het land ben gaan wonen, heb ik altijd het idee gehad dat ik bij jullie terecht kon. Bedankt voor jullie steun en betrokkenheid!

Lieve **papa en mama**, ik heb niet genoeg woorden om jullie te bedanken voor alles wat jullie voor me betekenen en gedaan hebben, maar ik ga toch een poging doen. Bedankt dat jullie me altijd gesteund hebben, dat ik altijd bij jullie terecht kan en dat jullie me altijd gemotiveerd hebben om te doen wat ik leuk vind. Ook al begrepen jullie niet altijd waar ik nu weer mee bezig was, kon ik jullie toch altijd bellen voor advies. Bedankt voor alles!

Dan last but not least, **Duco**. De afgelopen jaren heb je wat met me meegemaakt in de route naar mijn promotie. Als ik weer eens ergens over twijfelde of aan het stressen was hielp jou nuchtere blik me (uiteindelijk) om niet zo zwaar aan alles te tillen. Bedankt dat je er voor me bent als ik je nodig heb, maar me ook mijn eigen pad laat kiezen. Samen hebben we al een aantal mooie avonturen meegemaakt en ik hoop dat we de komende jaren nog vele mooie momenten samen hebben.

Bedankt, veel liefs en Hora Finita.
Danique

ABOUT THE AUTHOR

This thesis was authored by me, Danique Vervoort. I was born on September 7th, 1993 in Sint-Oedenrode, the Netherlands. In 2011, I obtained my high school diploma (Gymnasium) with honors from Zwijsen College Veghel. I then moved to Groningen to study Human Movement Sciences at the University of Groningen. After receiving my bachelor's degree in 2014, I continued with the 2-year master program, during which I specialized in Healthy Aging and started my MSc-PhD project. During my studies, I was a member of the Jaarvertegenwoordiging and after that a member of the Opleidingscommissie and Promove, where I represented students' interests within the education program. During the last year of the master's program, I successfully published my first research paper, which led to a fully-funded PhD position at the University Medical Center Groningen, University of Groningen, as part of the Master-PhD program.

During my PhD, I worked on multiple research studies at the Center of Human Movement Sciences focusing on adaptability of gait and balance across the adult lifespan. This research was done in an international team, with a collaboration with the University of Grenoble-Alpes, where I spent one month as a visiting scholar (November-December 2018). During my PhD, I also supervised multiple

students during their graduation projects (bachelor/master). Additionally, I was a PhD representative within the Center for Human Movement Sciences, and in that capacity was a member of the Advisory board and the Research Committee. In 2018, I was part of the organization of the annual SMALLL (Society for Movement Analysis Laboratories in the Low Lands) conference.

Currently, I am continuing my career at IV experts, where I work as Consultant Functioneel Beheer/Data. IV experts is the specialist in the area of Functioneel Beheer and Information Management. IV experts offers advice, support, and aids in the development of organizations and professionals, with the aim to have the information management well organized for every organization.

SCIENTIFIC OUTPUT

Vervoort D, Buurke TJW, Vuillerme N, Hortobágyi T, den Otter AR, Lamothe CJC (2020). Adaptive control of dynamic balance across the adult lifespan. *Medicine and Science in Sports and Exercise*, 52(10): 2270-2277.

Vervoort D, den Otter AR, Buurke TJW, Vuillerme N, Hortobágyi T, Lamothe CJC (2020). Do gait and muscle activation patterns change at middle-age during split-belt adaptation? *Journal of Biomechanics*, 99: 109510.

Vervoort D, den Otter AR, Buurke TJW, Vuillerme N, Hortobágyi T, Lamothe CJC (2019). Effects of aging and task prioritization on split-belt gait adaptation. *Frontiers in Aging Neuroscience*, 11: 10.

Buurke TJW, Lamothe CJC, **Vervoort D**, van der Woude LHV, den Otter AR (2018). Adaptive control of dynamic balance in human gait on a split-belt treadmill. *Journal of Experimental Biology*, 22(13): jeb-174896.

Vervoort D, Vuillerme N, Kosse N, Hortobágyi T, Lamothe CJC (2016). Multivariate analyses and classification of inertial sensor data to identify aging effects on the Timed-Up-and-Go test. *PLoS One*, 11(6): e0155984.

Kosse NM, Caljouw S, **Vervoort D**, Vuillerme N, Lamothe CJC (2015). Validity and reliability of gait and postural control analysis using the tri-axial accelerometer of the iPod Touch. *Annals of Biomedical Engineering*, 43(8): 1935-1946.

CONFERENCE CONTRIBUTIONS

Vervoort D, den Otter AR, Buurke TJW, Vuillerme N, Hortobágyi T, Lamothe CJC. Changes in muscle activation patterns underlie split-belt gait adaptation. *Poster presentation at the 24th ISGR world congress. July 2019, Edinburgh, United Kingdom.*

Vervoort D, den Otter AR, Buurke TJW, Vuillerme N, Hortobágyi T, Lamothe CJC. Gait adaptation differs from explicit perception of split-belt speed differences in young and middle-aged adults. *Poster presentation at the 8th SMALLL year congress. November 2018, Groningen, Netherlands.*

Buurke TJW, Lamothe CJC, **Vervoort D**, van der Woude LHV, den Otter AR. Changes in medio-lateral dynamic balance control during imposed gait asymmetry on a split-belt treadmill strongly depend on passive dynamics in gait. *Oral presentation at the 8th World congress of Biomechanics. July 2018, Dublin, Ireland.*

Buurke TJW, Lamothe CJC, **Vervoort D**, van der Woude LHV, den Otter AR. Long-term retention of split-belt walking reveals differences in spatio-temporal gait adaptation and dynamic balance control. *Oral presentation at the 22th ISEK congress. June 2018, Dublin, Ireland.*

Vervoort D, den Otter AR, Buurke TJW, Vuillerme N, Hortobágyi T, Lamothe CJC. Gait adaptation differs from explicit perception of split-belt speed differences in young and middle-aged adults. *Poster presentation at the 15th EWEP congress. June 2018, Toulouse, France.*

Vervoort D, den Otter AR, Buurke TJW, Hortobágyi T, Lamothe CJC. Muscle synergies during split-belt walking in young and middle-aged adults. *Poster presentation at the VvBN PhD day. December 2017, Rotterdam, Netherlands.*

Buurke TJW, Lamothe CJC, **Vervoort D**, van der Woude LHV, den Otter AR. Three week retention of a single split-belt adaptation session: Effects on gait symmetry and balance control. *Poster presentation at the 7th SMALLL year congress. November 2017, Leuven, Belgium.*

Vervoort D, den Otter AR, Buurke TJW, Hortobágyi T, Lamothe CJC. Muscle synergies during split-belt walking in young and middle-aged adults. *Poster presentation at the 7th SMALLL year congress. November 2017, Leuven, Belgium.*

Lamothe CJC, **Vervoort D**. Aging effects on muscle synergies during split-belt walking. *Oral presentation at the 26th ESMAC congress. September 2017, Trondheim, Norway.*

Lamothe CJC, **Vervoort D**, den Otter AR. Aging effects on the temporal modification of muscle activation patterns during split-belt treadmill walking. *Poster presentation at the 23rd ISGR world congress. June 2017, Fort Lauderdale, USA.*

Vervoort D, den Otter AR, Vuillerme N, Hortobágyi T, Lamothe CJC. Age and dual task effects on gait adaptability during split-belt walking. *Oral presentation at the 23rd ISGR world congress. June 2017, Fort Lauderdale, USA.*

RESEARCH INSTITUTE SHARE

This thesis is published within the Research Institute SHARE (Science in Healthy Ageing and health-care) of the University Medical Center Groningen / University of Groningen.

Further information regarding the institute and its research can be obtained from our internet site: <http://www.share.umcg.nl/>

More recent theses can be found in the list below.
(supervisors are between brackets)

2020

Renting N

Clinical workplace learning today; how competency frameworks inform clinical workplace learning (and how they do not)
(*prof ROB Gans, prof ADC Jaarsma, prof JCC Borlefs*)

Kramer T

How to develop a Grand Slam winner...: physical and psychological skills in Dutch junior tennis players
(*dr MT Elferink-Gemser, prof C Visscher, dr BCH Huijgen*)

Raven D

Where's the need? The use of specialist mental health services in adolescence and young adulthood
(*prof AJ Oldehinkel, prof RA Schoevers, dr F Jörg*)

Stoter IK

Staying on track; the road to elite performance in 1500 m speed skating
(*dr MT Elferink-Gemser, prof C Visscher, prof FJ Hettinga*)

Silva Lagos LA

Gestational diabetes mellitus and fetoplacental vasculature alterations; exploring the role of adenosine kinase in endothelial (dys)function
(*dr MM Faas, prof T Plösch, prof P de Vos, prof L Sobrevia*)

Reints R

On the design and evaluation of adjustable footwear for the prevention of diabetic foot ulcers
(*prof ir GJ Verkerke, prof K Postema, dr JM Hijmans*)

Bekhuis E

A body-mind map; epidemiological and clinical aspects of the relation between somatic, depressive and anxiety symptomatology
(*prof JCM Rosmalen, prof RA Schroevers, dr L Boschloo*)

Havinga PJ

Breaking the cycle? Intergenerational transmission of depression/anxiety and opportunities for intervention
(*prof RA Schoevers, prof CA Hartman, dr L Boschloo*)

Geer SJ van der

Trismus in head and neck cancer patients
(*prof PU Dijkstra, prof JLN Rodenburg, dr H Reintsema*)

Salavati N

Preconception environmental factors and placental morphometry in relation to pregnancy outcome
(*prof JHM Erwich, prof RM van der Beek, dr MK Bakker, dr SJ Gordijn*)

Fels IMJ van der

Movement, cognition and underlying brain functioning in children
(*dr E Hartman, prof C Visscher, prof RJ Bosker, dr J Smith*)

Braaksma P

Moving matters for children with developmental coordination
(*prof R Dekker, prof CK van der Sluis, dr MM Schoemaker, dr I Stuive*)

Akkerman M

Functioning beyond pediatric burns
(*prof LHV van der Woude, dr LJ Mouton, dr MK Nieuwenhuis*)

Buurke TJW

Adaptive control of dynamic balance in human walking
(*dr CJC Lamoth, prof LHV van der Woude, dr AR den Otter*)

Bos CJFJ

Physical activity and physical fitness in children with chronic conditions
(*prof PU Dijkstra, prof JHB Geertzen*)

Heugten P van

Talent in international business defined: implications and applications for honours education
(*prof ADC Jaarsma, dr MVC Wolfensberger, dr M Heijne-Penninga*)

Kranenburg HA

Adverse effects following cervical manual physical therapy techniques
(*prof CP van der Schans, dr MA Schmidt, dr GJR Luijckx*)

Lameijer CM

Perspectives on outcome following hand and wrist injury in non-osteoporotic patients
(*prof CK van der Sluis, prof HJ ten Duis, dr M El Moumni*)

For earlier theses visit our website