Sustained physical activity and health following rehabilitation:

Unravelling the role of perceived fatigue and activity pacing behaviour

Bregje Seves

Table of contents

Chapter 1

General introduction

Physical activity in people with physical disabilities and/or chronic diseases

Worldwide more than one billion people live with some type of disability, which is 15% of the global population [1]. In the Netherlands, 12% of the adult population suffers from a moderate or severe physical disability [2]. It is expected that this number will continue to rise due to population ageing [3] and in higher survival resulting improved healthcare.

Sustainable physical activity has health-influencing effects (e.g., lower risk on non-communicable diseases), is crucial for mobility, participation in everyday life, prevention of secondary health problems and for health-related quality of life (HR-QoL), especially also important in people with physical disabilities and/or chronic diseases. Although sustained physical activity is strongly recommended for people with physical disabilities and/or chronic diseases [4], many of them are assumed not to obtain the recommended amount of physical activity to achieve health benefits, which may lead to serious health problems [5]. Compared to the general healthy population, the low participation in physical activities and high dropout rates while trying to maintain physical activities, suggest that people with physical disabilities and/or chronic diseases experience different and higher barriers to obtain and/or maintain physical activity [6].

Factors related to physical activity are described in the context of the World Health Organization's (WHO) (2001) International Classification of Functioning, Disability and Health (ICF) model [1]. Furthermore, theories exist that specifically explain intentions or motivations towards physical activity (e.g., the Theory of Planned Behaviour) [7] like the stages of change concept of the Transtheoretical model [5] and the Physical Activity for people with a Disability (PAD) model [8] (figure 1). The PAD model is an integration of the Attitude, Social influence and self-Efficacy model into the ICF model [8]. The Transtheoretical model and the PAD model provide insight into the process of behavioural change and the relationships between physical activity behaviour, its determinants, and the daily functioning of people with physical disabilities and/or chronic diseases [8,9].

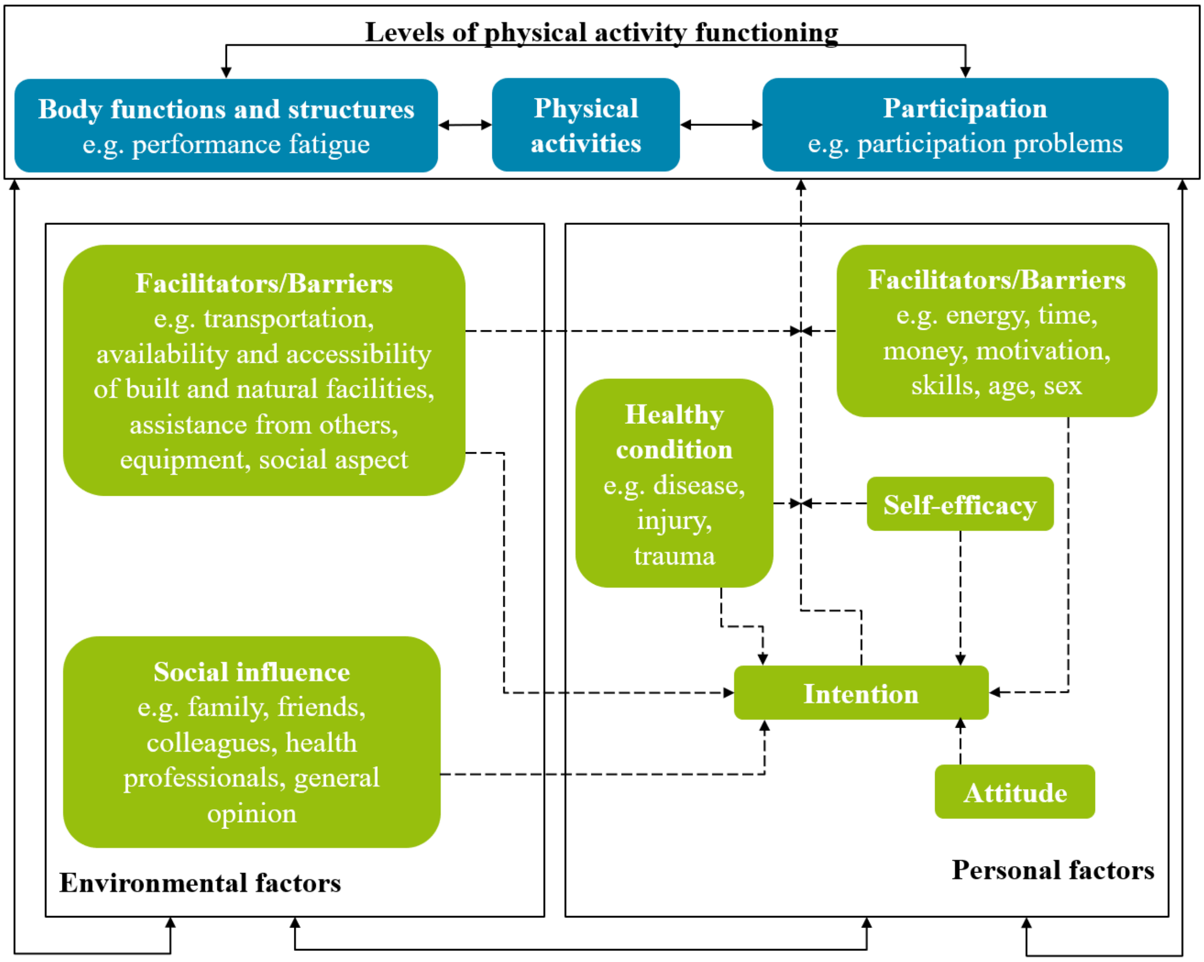


Figure 1 The physical activity for people with a disability model (PAD model), Van der Ploeg et al. (2004) [8]

Physical activity refers to "any bodily movement produced by the muscles that results in increased energy expenditure" [10]. Physical activity can include occupational, sports, conditioning, household, leisure time and other activities [10]. Physical activity can be measured with accelerometers or through self-report. For example, energy expenditure can be measured in (kilo)joules by using an accelerometer or it can be calculated after measuring the frequency, intensity, duration and type of the activity (with a corresponding metabolic equivalent of each individual task [11]) via a questionnaire [10,12,13]. Measuring physical activity in people with physical disabilities and/or chronic diseases is important e.g., for evaluating the effectiveness of physical activity promotion interventions [8] or to monitor whether physical activity guidelines are achieved in the context of sustained health.

There is strong evidence that people with physical disabilities and/or chronic diseases can benefit from motivational interviewing-based counselling on promotion of participation in physical activity during and after rehabilitation [14,15]. Physical activity promotion during and after rehabilitation was found to be effective when people with physical disabilities and/or chronic diseases engage, under supervision of a rehabilitation professional, in physical activities and sports activities as part of the rehabilitation treatment, and when they receive individually tailored counselling [14-16]. Physical activity promotion during and after rehabilitation seems to be a promising period to enhance the motivation towards physical activity and to promote a behaviour change, which are both important factors for sustained physical activity after rehabilitation [6,8,17]. The health-enhancing effects of physical activity together with the high prevalence of inactivity among people with physical disabilities and/or chronic diseases support the important potential of promoting sustained physical activity among this target population but have not hardly been studied over time in a diverse population of people with physical disabilities and/or chronic diseases during and after rehabilitation.

The Rehabilitation, Sports, and Exercise (RSE) program

A person-centred physical activity promotion programme in Dutch rehabilitation care is the Rehabilitation, Sports and Exercise ([RSE] in Dutch: 'Revalidatie, Sport en Bewegen'[1]) programme [9,18]. The RSE programme aims to stimulate an active lifestyle during the

[1] https://specialheroes.nl/revalidatie/programmas-4/revalidatie-sport-en-bewegen/

rehabilitation period and to guide people with physical disabilities and/or chronic diseases in obtaining and/or maintaining physical activity in the home setting after discharge from clinical or ambulant rehabilitation [9,18]. The RSE programme follows a diagnosis-overarching approach since the counselling is tailored to the individual. This approach was found to be effective in targeting a heterogenous population of people with physical disabilities and/or chronic diseases [14-16]. Participants of the RSE programme were referred to a sports counselling desk three to six weeks before discharge from rehabilitation for a face-to-face consultation with a sports counsellor. This was followed by four telephone-based counselling sessions – based on motivational interviewing – up to thirteen weeks after discharge from rehabilitation [9,18] (figure 2). The RSE programme is successfully implemented in Dutch rehabilitation practice [16]. The multicentre longitudinal cohort study 'Rehabilitation, Sports and Active lifestyle' (ReSpAct) was initiated to evaluate this nationwide RSE programme [9,18]. The studies in the current thesis are part of the ReSpAct study.

The ReSpAct study

Participants of the RSE programme from 18 rehabilitation institutes (twelve rehabilitation centres and six rehabilitation departments of hospitals) in the Netherlands were included in the ReSpAct study from May 2013 until August 2015 on a voluntary basis. Participants were monitored with questionnaires at four regular measurement moments over time: at baseline (T0: 3-6 weeks before discharge) and 14 (T1), 33 (T2) and 52 (T3) weeks after discharge from rehabilitation (figure 2). At T4, 5-8 years following discharge from rehabilitation, a selected sample of 15 participants of the ReSpAct study – diagnosed with a stroke – filled in a short questionnaire and participated in a semi-structured individual interview via a video connection[2]. The diagnosis-overarching study population in the ReSpAct study has the advantage to study similarities and differences between different clinical populations. Physical activity was the primary outcome of the ReSpAct study [9]. Besides, HR-QoL was one of the secondary outcomes of the ReSpAct study [9], to evaluate the positive effects of physical activity on HR-QoL [4].

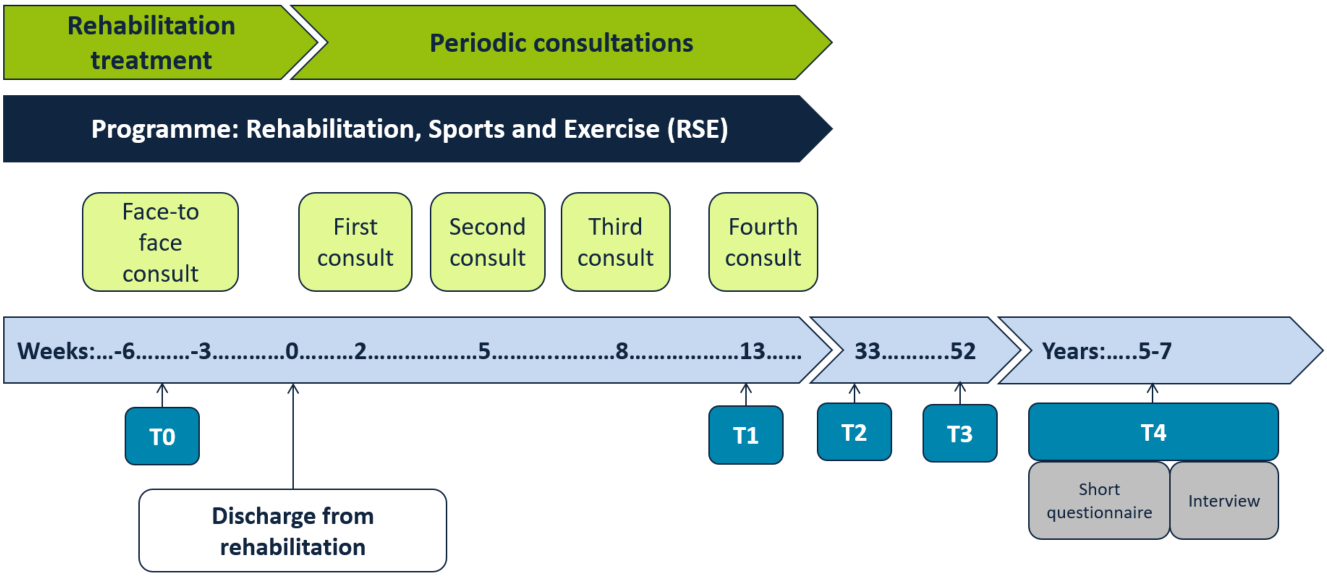


Figure 2 Design of the longitudinal ReSpAct study

Health and Quality of Life

Beyond the levels of physical activity and physical functioning, as described in the PAD model [8], are the overarching dimensions of well-being and HR-QoL, often viewed as the ultimate goals in today's rehabilitation practice and health care. HR-QoL is part of the multidimensional construct of health, which includes distinct domains of an individuals' life (e.g., physical, functional, psychological, and social health) [19]. HR-QoL refers to "how health impacts on an individual's ability to function and his or her perceived well-being in physical, mental, and

[2] Apart from the semi-structured interview and the short questionnaire, all participants of the ReSpAct study received an invitation to fill out a set of questionnaires as part of the ReSpAct 2.0 study, which is beyond the scope of this thesis.

social domains of life" [20]. As already mentioned, promotion of physical activity is assumed to have a positive impact on mobility, participation, secondary health problems and HR-QoL in people with physical disabilities and/or chronic diseases [4,5,17]. Improving HR-QoL is also one of the key objectives in today's rehabilitation practice, in which we can see HR-QoL as an overarching outcome measure. Low levels of HR-QoL are frequently reported during [21] and after rehabilitation in people with physical disabilities and/or chronic diseases [17,22,23]. Furthermore, lower levels of HR-QoL are associated with more frequent secondary health problems (e.g., fatigue, pain, obesity, cardiovascular diseases), while preventing secondary health problems among this target population is an important ambition in rehabilitation and health care [24]. Therefore, it is important to focus on the development of HR-QoL following discharge from rehabilitation, and to consider changeable determinants in this context.

Fatigue

As a primary or secondary health problem, fatigue is assumed to be associated with low levels of HR-QoL [24]. Perceived fatigue is also commonly reported as barrier of functioning and to obtain or maintain physical activity in people with physical disabilities and/or chronic diseases [6,25-27]. This makes fatigue an essential concept in today's rehabilitation practice. Fatigue possibly limits the ability to optimally benefit from rehabilitation programmes, such as the RSE programme, in terms of successfully obtaining sustained physical activity, freedom of movement and mobility, successful participation in social and physical activities, and in reaching high levels of HR-QoL [6,24,28]. According to a Dutch primary care registry, the prevalence of fatigue complaints among patients is estimated 29% [29], which is the second most common symptom presented [30]. Fatigue is a complex phenomenon, often simplified to signals of physical and/or mental fatigue. Fatigue has recently been defined as a two-domain concept “a disabling symptom in which physical and cognitive function is limited by interactions between performance fatigability and perceived fatigability” [31]. Kluger et al. (2013) [32] previously already proposed a taxonomy in which two attributes should be acknowledged in the concept of fatigue: (1) performance fatigability – the decline in an objective measure of performance over a discrete period, and (2) perceived fatigability – the initial value or the rate of change in sensations that regulate the integrity of the performer. The feeling of fatigue, or perceived fatigue, is a non-specific self-reported symptom, which can be quantified at a trait or state level [31]. The trait level represents the average amount of fatigue experienced during a fixed period (e.g. as measured by the self-reported questionnaire such as the Fatigue Severity Scale [33]), while the state level represents the rate of change of perceived fatigability during a fatiguing task (e.g., measured by a Visual Analog Scale [VAS] or Rate of Perceived Exertion [RPE]) [31]. There is a large variability in the perception of fatigue between and within individuals with disabilities due to the subjective character of fatigue and its complex and multidimensional association with biological, psychological, social, and environmental factors [34,35].

Especially stroke survivors, one of the largest populations in rehabilitation [36,37] (and in the cohort of the ReSpAct study) mention fatigue as one of the most common complaints and fatigue appears to be one of the strongest predictors of daily functional limitations [38,39]. Besides, stroke survivors spend long periods being inactive and sedentary, and physical activity levels are lower compared to the general healthy population [40]. This asks for closer observation in the way fatigue impacts on sustained physical activity in stroke survivors and what its consequences are on HR-QoL. Moreover, adequate self-management of fatigue is important for this target population to be able to optimally engage in daily physical activities and participation [41].

Activity Pacing

Activity pacing – as a form of self-management – in people with physical disabilities and/or chronic diseases might be promising in finding a balance between the perceived fatigue and their participation in daily physical activities. From an ecological and psychologic perspective, activity pacing can be seen as a multifaceted goal-directed process of decision-making related to how and when to invest the available energy throughout the day [42]. As such, multiple external and internal factors (e.g., fatigue) play a role in activity pacing. Optimizing activity pacing is proposed to result in optimal performance in a variety of settings, in particular in settings where humans are performing close to their limits and the management of fatigue is of crucial importance, such as in sports or in rehabilitation [41,43].

Activity pacing within the context of rehabilitation represents a potential treatment with supervised pacing instructions for people with physical disabilities and/or chronic diseases on how to manage their fatigue, to accurately distribute the available energy throughout the day, and to alternate physical activities with rest. This potentially allows to gradually increase the participation in daily physical activities [44,45]. Advice on activity pacing might focus on the prevention of symptom exacerbation and on the prevention of overactivity in people at risk of overactivity, which is characterized by an uneven activity pattern consisting of high activity peaks followed by long periods of inactivity [41,46]. Likewise, other individuals, who are at risk of underactivity and are less aware of their energy distribution capacity during the day, might benefit from structured advice on how to manage fatigue and to gradually increase physical activity [28,47,48]. The premise that both avoidance of one's daily activities and overactivity are linked to functional decline and symptoms of fatigue, gives further basis towards activity pacing as a positive coping strategy [45,49]. Naturalistic activity pacing refers to activity pacing strategies an individual implements in daily life without receiving any instructions on activity pacing [48]. Commonly reported activity pacing strategies in people with physical disabilities and/or chronic diseases are based on elements/principles of self-management, such as setting targets, prioritizing activities, adjusting activity level to their reduced energy capacity, budgeting energy, resting and/or sleeping during the day, avoiding stress, taking naps or hot baths, getting help with chores and using assistive devices [47-49]. Activity pacing behaviour can be measured by self-report with a questionnaire or by determining the variability in accelerometer-derived physical activity [50,51]. More insight in the relation between physical activity, fatigue, and activity pacing behaviour in people with physical disabilities and/or chronic diseases might provide input for knowledge-informed advice on activity pacing within the rehabilitation context to help individuals with high levels of perceived fatigue to better manage their fatigue and to enhance and sustain physical activity.

Aims and outline of this thesis

The overall aim of the current thesis is to provide detailed insight in the role of fatigue and activity pacing for sustained physical activity and health among people with physical disabilities and/or chronic diseases following discharge from rehabilitation. The first four studies take a diagnosis-overarching approach. The last three studies specifically focus on the stroke population, since many stroke survivors spend their time inactive and sedentary [40], and since especially stroke survivors, being the largest subpopulation in rehabilitation, mentioned fatigue as one of the most common complaints and one of the strongest predictors of daily functional limitations [38,39]. Figure 3 is a guiding conceptual framework for the thesis and describes in which chapters the core concepts ‘physical activity’, ‘HR-QoL’, ‘fatigue’ and ‘activity pacing’ (presented as circles in the figure) are subject of in this thesis. The overlapping areas of the circles represent the chapters where associations between core concepts are investigated. The framework also includes the individuals' characteristics related to physical activity as described in the PAD model [8].

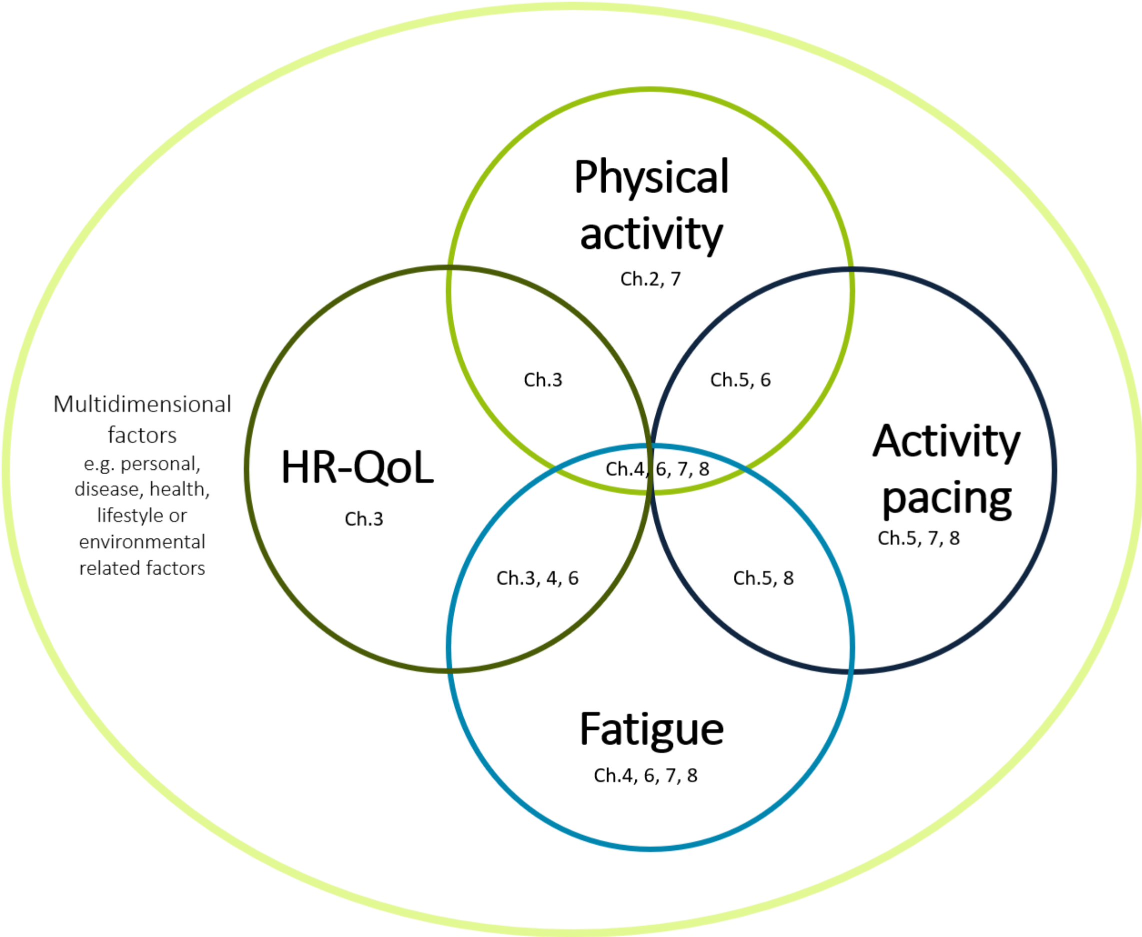


Figure 3 A guiding conceptual framework of this thesis, including the core themes/concepts, chapters (Ch.) and their suggested overlapping associative areas.

People with physical disabilities and/or chronic diseases (a diagnosis-overarching approach)

A self-reported physical activity measure was needed in the ReSpAct study to evaluate physical activity in a large cohort during and after the physical activity stimulation RSE programme. The ReSpAct study used the Adapted Short QUestionnaire to ASsess Health-enhancing physical activity (Adapted-SQUASH), a 19-item self-report recall questionnaire to assess physical activity among people with physical disabilities and/or chronic diseases. The Adapted-SQUASH is based on an average week in the past month as reference period. The original SQUASH [52] was adapted to make the questionnaire more applicable to people with physical disabilities and/or chronic diseases as described in the study protocol of the ReSpAct study [9]. It is relevant for (rehabilitation) practice and research in (adapted) physical activity to determine the psychometric properties of the Adapted-SQUASH among a sample of people with physical disabilities and/or chronic diseases. The study in **chapter 2** – a sub study of the ReSpAct study – aimed to investigate the test-retest reliability and concurrent validity of the Adapted-SQUASH among people with physical disabilities and/or chronic diseases. This study focused on the two main outcome measures of the Adapted-SQUASH, the total activity score and the total minutes of activity per week [52], which were derived from the test and retest of the Adapted-SQUASH, as well as from the Actiheart activity monitor (Cambridge Neurotechnology™ UK) among a convenience sample of adults with a physical disability and/or chronic disease.

Chapter 3 provides an important opportunity to advance the understanding of the natural development of HR-QoL after rehabilitation by using data from the longitudinal cohort study ReSpAct. This study used a diagnosis-overarching prospective analysis of HR-QoL. It aimed to identify trajectories of HR-QoL over time up to one-year after discharge from rehabilitation in people with physical disabilities and/or chronic diseases. Besides, this study aimed to determine person-, disease- and lifestyle-related factors before discharge from rehabilitation that are associated with the HR-QoL trajectories. Thus, it attempts to identify people with physical disabilities and/or chronic diseases at risk for a reduced HR-QoL after discharge of rehabilitation.

Chapter 4 is a narrative review, which adds knowledge to our understanding of fatigue and of its association with physical activity and HR-QoL among people with a wide range of physical disabilities and/or chronic diseases. This knowledge might allow for the development and/or optimization of more focused intervention programs targeting fatigue and bring future patients towards a physically active lifestyle and improved HR-QoL after rehabilitation (e.g., tailored counselling, activity pacing). This narrative review aimed to identify the prevalence and intensity of perceived and performance fatigability in people with physical disabilities and/or chronic diseases during and after rehabilitation, and it aims to explore how perceived and performance fatigability are associated with physical activity and HR-QoL.

Chapter 5 is a cross-sectional study – and a secondary data analysis on data collected in Chapter 2 – which investigates the complex and understudied issue of activity pacing in people with physical disabilities and/or chronic diseases. Activity pacing is assessed with the Actiheart activity monitor and self-report (including perceived attitudes towards activity pacing behaviour) in people with physical disabilities and/or chronic diseases. This study aims to investigate how accelerometer-derived activity pacing behaviour is associated with perceived fatigue, perceived attitudes towards activity pacing behaviour and total self-reported physical activity during the week in people with physical disabilities and/or chronic diseases.

Stroke survivors (a disease specific approach)

Chapter 6 explored the large variability in fatigue among stroke survivors in the longitudinal multicentre study design of the ReSpAct study. It focussed on the evolution over time of a physically active lifestyle up to one year post rehabilitation. This quantitative study aimed (1) to explore perceived fatigue with identifying trajectories of perceived fatigue during and after stroke rehabilitation, (2) to determine which personal, disease/health, psychosocial, lifestyle and environmental characteristics before discharge are associated with the different trajectories of perceived fatigue, and (3) to explore how trajectories of perceived fatigue and activity pacing are associated with physical activity over time up to one year after stroke rehabilitation.

A selected sample (n=15) from the cohort in chapter 6 was invited 5-8 years post stroke rehabilitation for an individual interview through livestream connection to help explain the heterogeneity in the development of perceived fatigue and its interaction with physical activity among stroke survivors. **Chapter 7** is a qualitative study and aims to explore the perceptions and experiences of (1) the impact of perceived fatigue on physical activity 5-8 years after rehabilitation in stroke survivors, and (2) their activity pacing behaviour.

Chapter 8 builds further on the findings in chapter 7 by exploring the experiences and perceptions on fatigue management after stroke in stroke survivors and health professionals. Qualitative studies have the advantage of providing a comprehensive understanding of a specific topic under study since the researcher can directly engage with the experts. Experts on fatigue management include both stroke survivors (the people with experience of fatigue and how to manage it) and health professionals (the people with clinical experience how to assist stroke survivors in fatigue management). Therefore, this qualitative focus group study aims to explore experiences and perceptions of stroke survivors and health professionals on post-stroke fatigue guidance in Dutch care.

Chapter 9 summarizes and critically discusses the main findings of the studies in this thesis. It presents future perspectives on rehabilitation research and practice, and it provides overall conclusions of this thesis.

References

1. World Health O, World B. World report on disability. Geneva; Washington, DC: World Health Organization ;; World Bank; 2011. Engels. (Book, Whole).
2. von Heijden A, van den Dool R, van Lindert C, et al. (On)beperkt sportief 2013: monitor sport- en beweegdeelname van mensen met een handicap. Stichting onbeperkt sportief; 2013.
3. Seeman TE, Merkin SS, Crimmins EM, et al. Disability trends among older Americans: National Health And Nutrition Examination Surveys, 1988-1994 and 1999-2004. American Journal of Public Health. 2010;100(1):100-107.
4. Haskell WL, Lee IM, Pate RR, et al. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. Circulation. 2007;116(9):1081-1093.
5. Carroll DD, Courtney-Long EA, Stevens AC, et al. Vital signs: disability and physical activity--United States, 2009-2012. MMWRMorbidity and mortality weekly report. 2014;63(18):407-413.
6. Martin Ginis KA, Ma JK, Latimer-Cheung AE, et al. A systematic review of review articles addressing factors related to physical activity participation among children and adults with physical disabilities. Health psychology review. 2016;10(4):478-494.
7. Ajzen I. The theory of planned behaviour: reactions and reflections. Psychology & Health. 2011;26(9):1113-1127.
8. van der Ploeg HP, van der Beek AJ, van der Woude LH, et al. Physical activity for people with a disability: a conceptual model. Sports medicine (Auckland, NZ). 2004;34(10):639-649.
9. Alingh RA, Hoekstra F, van der Schans CP, et al. Protocol of a longitudinal cohort study on physical activity behaviour in physically disabled patients participating in a rehabilitation counselling programme: ReSpAct. BMJ open. 2015;5(1):e007591-2015-007591.
10. Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. Public health reports (Washington, DC: 1974). 1985;100(2):126-131.
11. Ainsworth BE, Haskell WL, Herrmann SD, et al. 2011 Compendium of Physical Activities: a second update of codes and MET values. Medicine and science in sports and exercise. 2011;43(8):1575-1581.

12. Booth M. Assessment of physical activity: an international perspective. Research quarterly for exercise and sport. 2000;71(2 Suppl):S114-20.

13. Cervantes CM, Porretta DL. Physical activity measurement among individuals with disabilities: a literature review. Adapted physical activity quarterly : APAQ. 2010;27(3):173-190.

14. van der Ploeg HP, Streppel KR, van der Beek AJ, et al. Successfully improving physical activity behavior after rehabilitation. American Journal of Health promotion : AJHP. 2007;21(3):153-159.

15. van der Ploeg HP, Streppel KR, van der Beek AJ, et al. Counselling increases physical activity behaviour nine weeks after rehabilitation. British journal of sports medicine. 2006;40(3):223-229.

16. Hoekstra F, Hoekstra T, van der Schans CP, et al. The implementation of a physical activity counseling program in rehabilitation care: findings from the ReSpAct study. Disability and rehabilitation. 2019:1-12.

17. Rimmer JH. Getting beyond the plateau: bridging the gap between rehabilitation and community-based exercise. PM & R : the journal of injury, function, and rehabilitation. 2012;4(11):857-861.

18. Hoekstra F, Alingh RA, van der Schans CP, et al. Design of a process evaluation of the implementation of a physical activity and sports stimulation programme in Dutch rehabilitation setting: ReSpAct. Implementation science : IS. 2014;9:127-014-0127-7.

19. Post MW. Definitions of quality of life: what has happened and how to move on. Topics in spinal cord injury rehabilitation. 2014;20(3):167-180.

20. Coons SJ, Rao S, Keininger DL, et al. A comparative review of generic quality-of-life instruments. PharmacoEconomics. 2000;17(1):13-35.

21. Krops LA, Jaarsma EA, Dijkstra PU, et al. Health Related Quality of Life in a Dutch Rehabilitation Population: Reference Values and the Effect of Physical Activity. PloS one. 2017;12(1):e0169169.

22. Kaske S, Lefering R, Trentzsch H, et al. Quality of life two years after severe trauma: a single-centre evaluation. Injury. 2014;45 Suppl 3:S100-5.

23. Estrella-Castillo DFPD, Gómez-de-Regil LPD. Quality of life in Mexican patients with primary neurological or musculoskeletal disabilities. Disability and Health Journal. 2016;9(1):127-133.

24. Rimmer JH, Chen MD, Hsieh K. A conceptual model for identifying, preventing, and managing secondary conditions in people with disabilities. Physical Therapy. 2011;91(12):1728-1739.

25. Veldhuijzen van Zanten JJ, Rouse PC, Hale ED, et al. Perceived Barriers, Facilitators and Benefits for Regular Physical Activity and Exercise in Patients with Rheumatoid Arthritis: A Review of the Literature. Sports medicine (Auckland, NZ). 2015;45(10):1401-1412.

26. Keogh JW, Patel A, MacLeod RD, et al. Perceived barriers and facilitators to physical activity in men with prostate cancer: possible influence of androgen deprivation therapy. European journal of cancer care. 2014;23(2):263-273.

27. Newitt R, Barnett F, Crowe M. Understanding factors that influence participation in physical activity among people with a neuromusculoskeletal condition: a review of qualitative studies. Disability and rehabilitation. 2016;38(1):1-10.

28. Nijs J, Paul L, Wallman K. Chronic fatigue syndrome: an approach combining self-management with graded exercise to avoid exacerbations. Journal of Rehabilitation Medicine. 2008;40(4):241-247.

29. Foets M, Sixma M. Basisrapport gezondheid en gezondheidsgedrag in de praktijkpopulatie. Een nationale studie van ziekten en verrichtingen in de huisartspraktijk. Utrecht: NIVEL; 1991.

30. Okkes IM, Oskam SK, Lamberts H. The probability of specific diagnoses for patients presenting with common symptoms to Dutch family physicians. The Journal of family practice. 2002;51(1):31-36.

31. Enoka RM, Duchateau J. Translating Fatigue to Human Performance. Medicine and science in sports and exercise. 2016;48(11):2228-2238.

32. Kluger BM, Krupp LB, Enoka RM. Fatigue and fatigability in neurologic illnesses: proposal for a unified taxonomy. Neurology. 2013;80(4):409-416.

33. Fleurke AM, Goossen WTF, Hoijtink EJ, et al. Fatigue Severity Scale (FSS). 2004.

34. Kratz AL, Murphy SL, Braley TJ, et al. Development of a person-centered conceptual model of perceived fatigability. Qual Life Res. 2019 May;28(5):1337-1347.

35. Skogestad IJ, Kirkevold M, Larsson P, et al. Post-stroke fatigue: an exploratory study with patients and health professionals to develop a patient-reported outcome measure. Journal of patient-reported outcomes. 2021;5(1):35-021-00307-z.

36. Billinger SA, Arena R, Bernhardt J, et al. Physical activity and exercise recommendations for stroke survivors: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2014;45(8):2532-2553.

37. Ma VY, Chan L, Carruthers KJ. Incidence, prevalence, costs, and impact on disability of common conditions requiring rehabilitation in the United States: stroke, spinal cord injury, traumatic brain injury, multiple sclerosis, osteoarthritis, rheumatoid arthritis, limb loss, and back pain. Archives of Physical Medicine and Rehabilitation. 2014;95(5):986-995.e1.

38. Obembe AO, Olaogun MM, Olalemi AE. Functional limitations due to fatigue among independently ambulant stroke survivors in Osun, South-Western Nigeria. Physiother Res Int. 2015 Mar;20(1):54-9.

39. Schillinger A, Becker F. Fatigue in patients following traumatic brain injury and stroke. Tidsskrift for den Norske laegeforening : tidsskrift for praktisk medicin, ny raekke. 2015;135(4):331-335.

40. Fini NA, Holland AE, Keating J, et al. How Physically Active Are People Following Stroke? Systematic Review and Quantitative Synthesis. Physical Therapy. 2017;97(7):707-717.

41. Abonie US, Edwards AM, Hettinga FJ. Optimising activity pacing to promote a physically active lifestyle in medical settings: A narrative review informed by clinical and sports pacing research. Journal of sports sciences. 2020;38(5):590-596.

42. Smits BL, Pepping GJ, Hettinga FJ. Pacing and decision making in sport and exercise: the roles of perception and action in the regulation of exercise intensity. Sports medicine (Auckland, NZ). 2014;44(6):763-775.

43. Hettinga F. Revalidatie is topsport! In: Bongers RM, Caljouw S, Hartman E, et al., editors. Smart Movements. Groningen: University of Groningen, University Medical Center Groningen, Center for Human Movement Sciences; 2010. p. 66-68.

44. Gill JR, Brown CA. A structured review of the evidence for pacing as a chronic pain intervention. European journal of pain (London, England). 2009;13(2):214-216.

45. Andrews NE, Strong J, Meredith PJ. Activity pacing, avoidance, endurance, and associations with patient functioning in chronic pain: a systematic review and meta-analysis. Archives of Physical Medicine and Rehabilitation. 2012;93(11):2109-2121.e7.

46. White PD, Goldsmith KA, Johnson AL, et al. Comparison of adaptive pacing therapy, cognitive behaviour therapy, graded exercise therapy, and specialist medical care for chronic fatigue syndrome (PACE): a randomised trial. Lancet (London, England). 2011;377(9768):823-836.

47. Antcliff D, Keeley P, Campbell M, et al. Activity pacing: moving beyond taking breaks and slowing down. Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation. 2018.

48. Nielson WR, Jensen MP, Karsdorp PA, et al. Activity pacing in chronic pain: concepts, evidence, and future directions. The Clinical journal of pain. 2013;29(5):461-468.

49. Birkholtz M, Aylwin L, Harman RM. Activity Pacing in Chronic Pain Management: One Aim, but Which Method? Part One: Introduction and Literature Review. British Journal of Occupational Therapy. 2004;67(10):447-452.

50. Murphy SL, Smith DM, Alexander NB. Measuring activity pacing in women with lower-extremity osteoarthritis: a pilot study. The American Journal of Occupational Therapy : Official Publication of the American Occupational Therapy Association. 2008;62(3):329-334.

51. Murphy SL, Kratz AL. Activity pacing in daily life: A within-day analysis. Pain. 2014;155(12):2630-2637.

52. Wendel-Vos GC, Schuit AJ, Saris WH, et al. Reproducibility and relative validity of the short questionnaire to assess health-enhancing physical activity. Journal of clinical epidemiology. 2003;56(12):1163-1169.

Chapter 2

Test-retest reliability and concurrent validity of the Adapted Short QUestionnaire to ASsess Health-enhancing physical activity (Adapted-SQUASH) in adults with disabilities

Seves BL, Hoekstra F, Schoenmakers JWA, Brandenbarg P, Hoekstra T, Hettinga FJ, Dekker R, van der Woude LHV, van der Schans CP.

Journal of Sports Sciences, 2021; Apr;39(8):875-886

Abstract

The current study determined the test-retest reliability and concurrent validity of the Adapted Short QUestionnaire to ASsess Health-enhancing physical activity (Adapted-SQUASH) in adults with disabilities. Before filling in the Adapted-SQUASH twice with a recall period of two weeks, participants wore the Actiheart activity monitor up to one week. For the test-retest reliability (N=68), Intraclass correlation coefficients (ICCs) were 0.67 ($p<0.001$) for the total activity score (min x intensity/week) and 0.76 ($p<0.001$) for the total minutes of activity (min/week). For the concurrent validity (N=58), the Spearman correlation coefficient was 0.40 ($p=0.002$) between the total activity score of the first administration of the Adapted-SQUASH and activity energy expenditure from the Actiheart (kcals kg^{-1} min^{-1}). The ICC was 0.22 ($p=0.027$) between the total minutes of activity assessed with the first administration of the Adapted-SQUASH and Actiheart. The Adapted-SQUASH is an acceptable measure to assess self-reported physical activity in large populations of adults with disabilities but is not applicable at the individual level due to wide limits of agreement. Self-reported physical activity assessed with the Adapted-SQUASH does not accurately represent physical activity assessed with the Actiheart in adults with disabilities, as indicated with a systematic bias between both instruments in the Bland-Altman analysis. We recommend using both self-reported and accelerometer-derived physical activity to understand physical activity behaviour in adults with disabilities.

Key words

Physical activity assessment, accelerometer, chronic disease, rehabilitation, health promotion

Introduction

Measuring patients' physical activity behaviour is important for evaluating effectivity of physical activity promotion interventions and, ideally, individually tailoring rehabilitation programmes among adults suffering from a physical disability and/or chronic disease that impairs mobility (further: adults with disabilities) [1]. Therefore, an accurate and efficient measurement instrument for assessing (self-reported) physical activity in people with physical disabilities is essential. Although multiple measures of physical activity (e.g. accelerometer-derived in combination with self-report) might be preferred [2], mostly it is not practically feasible, and it is too expensive among large scale populations in interventions and/or observational cohort studies [3]. Self-reports are frequently used measurement tools to assess physical activity in disabled populations, both in rehabilitation practice and in research [2,4]. Also, questionnaires are easy to fill in [3,5,6]. However, self-reported physical activity depends on the persons' recall and mostly is not sensitive for light physical activities at home (e.g. walking from the bedroom to the toilet and from the kitchen to the dining table) or outside (e.g. walking to the mailbox to post a letter), as was found in adults with spinal cord injury [7].

A self-reported physical activity measure was needed in the multicentre longitudinal cohort study Rehabilitation, Sports and Active lifestyle (ReSpAct) to evaluate physical activity during and after the physical activity stimulation programme Rehabilitation, Sports and Exercise (RSE; Dutch: 'Revalidatie, Sport en Bewegen') [8,9]. The RSE programme was successfully implemented in eighteen rehabilitation institutions in the Netherlands [10]. The questionnaire was required to be suitable for the target population: adults with disabilities (18 years and older). There are few physical activity questionnaires available specifically developed for adults with disabilities [2]. The Physical Activity Scale for Individuals with Physical Disabilities (PASIPD) [11] was considered for the ReSpAct study, since it is commonly used amongst the target population. To precisely assess the physical activity behaviour before and after a physical activity promotion intervention [3], and to clarify the dose-response relationship between physical activity and the received counselling during the intervention [12], frequency, intensity, duration and type of the activity should be measured. The PASIPD assesses duration and type of physical activities but does not specifically assess the frequency and intensity of physical activities, whereby it was considered not applicable for the ReSpAct cohort. The Short Questionnaire to Assess Health-enhancing physical activity (SQUASH) developed for healthy adults does measure frequency, intensity, duration and type of physical activities [5]. The SQUASH is widely used, for example by governmental agencies to monitor large scale physical activity behaviour among the Dutch population and to monitor whether physical activity guidelines are achieved. Studies on the psychometric properties of the SQUASH have supported the appropriateness of the SQUASH to measure the level of weekly physical activity in a healthy adult population [5], in patients after a total hip arthroplasty [13] and in outpatients with ankylosing spondylitis [14].

When assessing physical activity in adults with disabilities, it needs to be taken into account that this target population may have a different perceived intensity of activities compared to a healthy population [15]. It is expected that adults with a disability experience activities as more intense, because activities often cost (absolutely and relatively) more energy compared to healthy adults [16,17]. Therefore, the ReSpAct research team converted the original SQUASH [5] into a measurement tool (mentioned from here: the Adapted-SQUASH) that was expected to better meet the perceived intensity of activities among adults with disabilities compared with the original SQUASH, by using appropriate metabolic equivalent of task (MET) values for this target population [9]. Also, the SQUASH was adapted to better match the activity pattern of wheelchair users by including common physical activity behaviours: wheelchair sports (e.g. wheelchair basketball) and questions concerning wheelchair propulsion and handcycling [9]. The SQUASH has two main outcome measures: the activity score, measuring a combination of intensity and duration of physical activity per week, and total minutes of activity per week (duration).

It is relevant for (rehabilitation) practice and research in (adapted) physical activity to determine the psychometric properties of the Adapted-SQUASH among a sample of adults with disabilities. Apart from test-retest reliability, concurrent validity is deemed an important asset. The Actiheart (Cambridge Neurotechnology™ UK), an uniaxial activity monitor, was identified by the research team as a suitable criterion measure to compare with the outcomes of the Adapted-SQUASH. Since the Actiheart is a medical device, it is suitable for ambulant people with disabilities. The Actiheart is accurate in measuring physical activity energy expenditure (AEE) in free living conditions, and ideally it combines its measured heart rate and movement sensor information improving the prediction of AEE in daily physical activities [6,18].

The current study aims to determine the test-retest reliability and concurrent validity of the Adapted-SQUASH among adults with disabilities. We focused on the two main outcome measures of the Adapted-SQUASH, the total activity score and the total minutes of activity per week [5], which were derived from the test and retest of the Adapted-SQUASH as well as from the Actiheart activity monitor among a convenience sample of adults with disabilities.

Methods

Study population

Participants were recruited through patient activity groups in hospitals, rehabilitation centres, sport clubs and patient associations in the northern and eastern provinces in the Netherlands.

We aimed at a sample size between 50 and 100 participants, as recommended in literature for validation studies and reliability studies, in order to provide an appropriate number of dots with estimated limits of agreement in the Bland-Altman plot and to obtain an acceptable confidence interval around the reliability parameter [19]. Inclusion criteria were being at least eighteen years of age, having a physical disability and/or chronic disease (e.g. stroke, heart failure, Parkinson's disease) and being able to read and write the Dutch language. Participants were excluded when they were still receiving inpatient or outpatient rehabilitation care, were participating in the ReSpAct study [8,9], were completely wheelchair dependent (because of the use of the Actiheart), or were not able to complete the questionnaires even with help. The data collection took place from November 2014 till June 2016.

Study procedures

This study consisted of a test-retest reliability study and a validity study. For the test-retest reliability study, the participants filled out the first Adapted-SQUASH twice, with approximately two weeks between the measurement occasions.

For the validity study, the participant was asked to wear an Actiheart activity monitor (Cambridge Neurotechnology™ UK) to objectively measure physical activity levels during the week prior to administration of the first Adapted-SQUASH. Two researchers visited the participants in their free-living home situation twice, to install and attach the Actiheart to the participants' chest, and to collect the Actiheart after one week. The Actiheart measurement started at 00:00 AM and continued for the next seven consecutive days, both day and night. The participant was instructed to remove the Actiheart during showering, bathing, or swimming. In addition, the participant filled out a diary in which noncompliance to the Actiheart was noted. Measurements were included in the validity study when a minimum registration of the Actiheart of at least four days valid acceleration data (at least 75% activity data registration of 24 hours) for each participant was present [20].

Participants' general characteristics were obtained by using a questionnaire. Participant's body weight (kg) and height (m) were measured by researchers by using a personal scale and measuring tape, respectively. The study was approved by the Ethics Committee of the Center of Human Movement Sciences (ECB/2014.06.30_1) at the University of Groningen, University Medical Center Groningen. All participants voluntarily signed an informed consent.

The Adapted Short QUestionnaire to ASssess Health-enhancing physical activity (Adapted-SQUASH)

The 19-item Adapted-SQUASH (see supplemental file on osf.io/rtz5y/) is a self-reported recall questionnaire to assess physical activity among adults with disabilities based on an average week in the past month as reference period. Equal to the original SQUASH [5], the Adapted-SQUASH is pre-structured in four main domains outlining types and settings of activity: 'commuting traffic', 'activities at work and school', 'household activities' and 'leisure time activities' including 'sports activities'. The frequency in days per week, the duration in average hours and minutes per day and the perceived intensity were asked.

Several adjustments have been made to make the original SQUASH applicable for people with disabilities, as described in the study protocol of the ReSpAct study [9]. First, the items 'wheelchair riding' and 'handcycling' were added in the domains 'commuting activities and leisure-time' and 'sports activities'. Second, the self-reported intensity of the activity was categorised into 'light', 'moderate' and 'vigorous', instead of 'slow', 'moderate' and 'fast'. Third, the syntax to determine the outcome measures of the Adapted-SQUASH includes a large range of Adapted sports (e.g. wheelchair basketball/rugby/tennis) for the item 'sports activities'. The MET-values in the syntax were updated based on the most recent version of the Ainsworth' compendium of physical activities [21] and MET-values for wheelchair riding, handcycling and adapted sports were added based on a compendium of energy costs of physical activities for wheelchair dependent individuals [22]. Lastly, in the examples of different sports 'tennis' was replaced by '(wheelchair) tennis'.

The total activity score per week (Adapted-SQUASH)

For practical use of the questionnaire all outcome measures of the Adapted-SQUASH were calculated by using a syntax. The total activity score and the total minutes of activity per week are the main outcomes of the Adapted-SQUASH. The total activity score (min x intensity/week) was calculated following the procedure described by Wendel-Vos et al. (2003). First, all the questions in the Adapted-SQUASH were assigned to a MET-value representing the intensity of this task, based on the Ainsworth' compendium of physical activities [21] and based on a compendium of energy costs of physical activities for wheelchair dependent individuals [22]. Second, an activity score was calculated for each domain by multiplying the total minutes of activity with a self-reported intensity score, which is based on age and MET-values [5]. Lastly, the total activity score was calculated by summing up the activity scores of the four domains. In accordance with the original SQUASH, data were excluded if the total minutes of activity a day exceeded 960 minutes or if values were missing [5].

The total minutes of activity per week (Adapted-SQUASH)

The total minutes of activity per week (min/week) assessed with the Adapted-SQUASH were calculated by summing up the total minutes of physical activity per week reported in the Adapted-SQUASH. Also, the total minutes of light, moderate and vigorous intensity activities per week (min/week) were calculated, using MET-value cut-off points based on the Dutch physical activity guidelines [23].

The Actiheart activity monitor

The Actiheart (Cambridge Neurotechnology™ UK) activity monitor is a combined uniaxial accelerometer and heart rate monitor, which was used to measure accelerometer-derived physical activity. Acceptable reliability and validity (when compared with Electrocardiography [ECG] [24] and indirect calorimetry [25]) were found for the Actiheart among adults, and was deemed appropriate for our target population, because the combination of accelerometer data with heart rate data would be better able to determine the intensity of physical activities [24]. The Actiheart was attached to the participation's chest by using two ECG electrodes. The Actiheart is a lightweight (8gram) and compact (7x33mm) device, connected to the two ECG electrode and capable of storing time-sequenced data. Acceleration (1D, vertical axis) was measured with a 15-second epoch by a piezoelectric element within the unit with a frequency range of 1-7Hz. The Actiheart output provides activity counts and heart rate data per minute, simultaneously.

Activity energy expenditure (Actiheart)

Based on the Actiheart data, AEE estimates in kcals kg^{-1} min^{-1} were calculated for each minute by combining activity counts and heart rate in a branched equations model as described in literature [24,25] and as proposed by the Actiheart software for AEE (see supplemental file on osf.io/rtz5y/). A branched equation model allows the Actiheart to accurately assess AEE even when there is low body movement, but high heart rate during an activity. The combined activity and heart rate algorithm to calculate AEE needs the individual's sleeping heart rate.

The sleeping heart rate was calculated by averaging the minute-to-minute heart rate between 2.00-5.00am on the first day the Actiheart was worn.

When heart rate was missing, AEE was calculated based on the activity algorithm only for the specific missing minute. The total AEE per week was calculated by summing up the AEE minute-to-minute data, divided by the number of valid days the Actiheart was worn and multiplied by seven (assuming that the average amount of physical activity a day is representative for all weekdays and weekend days).

In addition, MET values were calculated for each minute based on the AEE minute-to-minute data, following the Ainsworth' compendium of physical activities [21]. In the next step, MET values per minute were categorised in the following MET categories: sedentary behaviour (1.0-1.5 METs), light intensity (1.6-2.9 METs), moderate intensity (3.0-5.9 METs) and vigorous intensity (≥6 METs). Sum scores of all minutes in each MET category were calculated. Also, a sum score for al minutes of physical activity was calculated (≥1.6 METs). Sum scores were divided by the number of valid days the Actiheart was worn and multiplied by seven for week scores.

Statistical analysis

Descriptive statistics were used to describe the demographic characteristics of the study population. Test-retest reliability of the Adapted-SQUASH was determined by calculating Intraclass correlation coefficients (ICCs) (two-way random, absolute agreement, single measures) for the total activity score (total, four main domains separately and all individual item separately), as well for the total minutes of activity (total and separately per intensity category) between the first and second measurement occasion. The ICC quantifies the degree to which the two measurements are absolutely related [26]. Since there is no widely accepted criterion for defining the strength of a correlation, we used a general guideline for clinical research: a correlation below 0.25 indicates little or no agreement, a correlation between 0.25 and 0.50 indicates fair agreement, a correlation between 0.50 and 0.75 indicates moderate to good agreement and a correlation higher than 0.75 indicates good to excellent agreement [27]. Also, confidence intervals were calculated for the ICCs. Additionally, Bland-Altman analyses were performed to illustrate the agreement between the first and second measurement of the Adapted-SQUASH [28,29]. Subsequently, a one-sample t-test was performed to determine any systematic bias.

Concurrent validity of the Adapted-SQUASH was determined by calculating a Spearman correlation coefficient between the total activity score (min x intensity/week) based on the baseline administration of the Adapted-SQUASH and the total AEE (kcals kg^{-1}/week) based on the Actiheart data. Non-parametric Spearman correlation coefficients were chosen because assumptions of normality were not met for the outcomes of the Adapted-SQUASH and the two continuous outcome variables do not have the same measurement unit. In addition, concurrent validity of the Adapted-SQUASH was determined by calculating an ICC between the total minutes of activity (min/week) based on the baseline administration of the Adapted-SQUASH and the total minutes of activity (min/week) based on the Actiheart data, and by performing a Bland-Altman analysis. Although ICCs are preferred if the two measurement instruments are expressed in the same units (min/week) [19], a Spearman correlation coefficient was also calculated between the total minutes of activity assessed with the Adapted-SQUASH and Actiheart to compare our correlation with previous literature [5,11,13,14]. There is no consensus on how high correlations should be in order to demonstrate acceptable validity of a physical activity questionnaire [30]. The same interpretation of correlations as mentioned above is used for the validity of the Adapted-

SQUASH. The level of significance was set at 0.05. Data were analysed using the Statistical Package for the Social Science (IBM SPSS Statistics, version 24).

Results

A convenience sample of adults with disabilities (N=80) was approached. Finally, 68 participants were included in the test-retest reliability study and 58 in the validity study (see supplemental file on osf.io/rtz5y/ for a flow diagram of the included and excluded participants). Twelve out of 80 participants were excluded from the test-retest reliability study because they did not fill out the second questionnaire due to illness (N=1), surgery (N=1) or unknown reasons (N=10). Based on the characteristics, the included and excluded sample for the test-rest reliability study only statistically significantly differed in average body weight (see supplemental file on osf.io/rtz5y/). Body weight was on average 89.8±3.2 kg in the excluded sample (N=12) and 79.1±14.7 kg in the included sample (N=68). However, body height and Body Mass Index were not significantly different between the included and excluded sample. Based on the criterion of a minimum of four days valid Actiheart accelerometer data, 22 out of 80 participants were excluded from the validity study. We included participants with four days (N=5), five days (N=1), six days (N=6), and seven days (N=46) of valid Actiheart accelerometer data, whereof all participants had at least three weekdays and one weekend day available. Based on the characteristics, the included and excluded sample only significantly differed in the use of mobility aid (see supplemental file on osf.io/rtz5y/). In the excluded sample, more people used a mobility aid (32%) compared to the included sample (17%). The characteristics of the participants for the test-retest reliability (N=68) and the validity (N=58) studies are presented in Table 1. The Adapted-SQUASH was completed for a second time after a mean period of 17±4 days.

Table 1 Characteristics of the participants for the test-retest reliability study (N=68) and the validity study (N=58)

	Test-retest reliability study (N=68) Mean±SD or N(%)	**Validity study (N=58)** Mean±SD or N(%)
Gender (% male)	31 (46)	27 (47)
Age (years)	56.9 ± 17.6	54.7 ± 18.7
Body height (m)	1.73 ± 0.10	1.74 ± 0.09
Body weight (kg)	79.1 ± 14.7	80.8 ± 14.3
Body Mass Index (kg/m^2)	26.6 ± 4.7	26.7 ± 4.5
Drug use (% yes)	60 (88)	48 (83)
Use of mobility aid (% yes)	17 (25)	10 (17)
Diagnosis[a]		
Musculoskeletal disease	2 (3)	2 (3)
Brain disorder	22 (32)	15 (26)
Neurologic disease	5 (7)	5 (9)
Organ disease	31 (46)	29 (50)
Other diseases	6 (9)	7 (12)

SD=standard deviation, N=number of participants

[a] Diagnoses included in the study: Rheumatoid arthritis (N=1), Chronic progressive external ophthalmoplegia (N=1), Cerebral Palsy (N=2), Stroke (N=18), Traumatic brain injury (N=2), Guillain–Barré syndrome (N=1), Fibromyalgia (N=1), Parkinson’s’ disease (N=3), Heart disease (N=15), Chronic obstructive pulmonary disease (N=7), Asthma (N=3), Diabetes mellitus (N=5), Crohn's disease (N=1), Atherosclerosis (N=5), Hip replacement (N=1), Ménière’s disease (N=1), Hereditary Motor and Sensory Neuropathy type II (N=1), worn neck vertebrae (N=1), low-back pain (N=1), amputation lower extremity (N=1), upper limb disability (N=1).

Test-retest reliability

The ICC for the repeated Adapted-SQUASH measurements was 0.67 (p<0.001) for the total activity score, and 0.76 (p<0.001) for the total minutes of activity per week, which respectively indicated a moderate to good and good to excellent agreement [26] (Table 2). Test-retest reliability within the light, moderate and vigorous intensity categories were respectively 0.89

(p<0.001), 0.64 (p<0.001), and 0.32 (p=0.004). ICCs for the separate activity categories were: 0.39 (p<0.001) for commuting activities, 0.77 (p<0.001) for activities at work, 0.41 (p<0.001) for household activities, and 0.44 (p<0.001) for leisure-time activities. Test-retest reliability of the separate items of the questionnaire ranged from 0.00 for intense activities at work to 0.81 for walking during commuting (Table 2). Test-retest reliability of the new added items for handcycling activities during commuting and leisure time and wheelchair riding during commuting could not be determined because too few participants reported this activity. Test-retest reliability for wheelchair riding in leisure time was 0.27 (p=0.011).

Table 2 Intraclass correlation coefficients (ICC) between the first and second measurement of the Adapted-SQUASH (N=68)

	Physical activity levels		**Test-retest reliability**		
	First test Median (IQR)	Second test Median (IQR)	ICC	95%CI	p
Main outcomes					
Total activity score[a]	1706 (658 – 4151)	1950 (900 – 3864)	.67	.51-.78	<.001
Total minutes of activity/week	379 (189 – 861)	473 (246 – 939)	.76	.64-.85	<.001
Intensity categories (min/week)					
Light	86 (30 – 233)	90 (30 – 278)	.89	.83-.93	<.001
Moderate	68 (3 – 308)	119 (30 – 366)	.64	.48-.76	<.001
Vigorous	53 (30 – 131)	78 (30 – 135)	.32	.09-.51	.004
Item activity scores[a]					
Commuting	0 (0 – 10)	0 (0 – 15)	.39	.17-.57	<.001
Walking	0 (0 – 0)	0 (0 – 0)	.81	.72-.88	<.001
Bicycling	0 (0 – 8)	0 (0 – 0)	.29	.06-.50	.007
Handcycling	0 (0 – 0)	0 (0 – 0)		NA	
Wheelchair riding	0 (0 – 0)	0 (0 – 0)		NA	
Activities at work	0 (0 – 705)	0 (0 – 525)	.77	.65- .85	<.001
Light	0 (0 – 705)	0 (0 – 450)	.78	.67-.86	<.001
Vigorous	0 (0 – 0)	0 (0 – 0)	.00	-.24-.24	.499

Household activities	53 (21 – 116)	54 (16 – 112)	.41	.20-.59	<.001
Light	45 (16 – 60)	33 (15 – 75)	.43	.21-.61	<.001
Vigorous	0 (0 – 15)	0 (0 – 30)	.20	-.03-.42	.044
Leisure time	136 (73 – 238)	178 (91 – 244)	.44	.23-.61	<.001
Walking	19 (0 – 45)	21 (8 – 45)	.21	-.03-.42	.046
Bicycling	15 (0 – 30)	24 (0 – 38)	.15	-.09-.38	.110
Handcycling	0 (0 – 0)	0 (0 – 0)		NA	
Wheelchair riding	0 (0 – 0)	0 (0 – 0)	.27	.04-.48	.011
Gardening	0 (0 – 28)	0 (0 – 30)	.19	-.05-.41	.059
Odd jobs	0 (0 – 6)	0 (0 – 26)	.50	.30-.66	<.001
Sports	45 (0 – 105)	45 (23 – 105)	.76	.64-.85	<.001

IQR=Inter Quartile Range, ICC=Intraclass Correlation Coefficient, CI=Confidence Interval, NA=not applicable due to too low response on this item.

[a] Activity score = minutes x intensity

Bland-Altman analyses showed that the mean difference between the first and second measurement was not significantly different from zero for both the total activity score (t_{67}=-0.03, p=0.98) and for the total minutes of activity (t_{67}=0.11, p=0.92), indicating no systematic bias between the two measurements. We found wide Limits of Agreement (LOA) with 95% of the measurements of the total activity score within the boundaries of 4072 activity score above and below the mean difference (figure 1), and with 95% of the measurements of the total minutes of activity within the boundaries of 945 minutes activity above and below the mean difference (figure 2). Besides, based on the Bland-Altman plots the absolute amount of time spent on physical activity and the total activity score were higher at the second measurement occasion than at the first measurement occasion, while the total activity score was lower at the second measurement than at the first measurement occasion. Also, a Spearman correlation coefficient of -0.08 (p=.526) between the x and y axis of the Bland-Altman analysis for the total activity score derived from the Adapted-SQUASH was found (figure 1), and a Spearman correlation coefficient of -0.10 (p=.431) between the x and y axis of the Bland-Altman analysis for the total minutes of activity per week derived from the Adapted-SQUASH (figure 2) was found, which indicated homoscedasticity of the data.

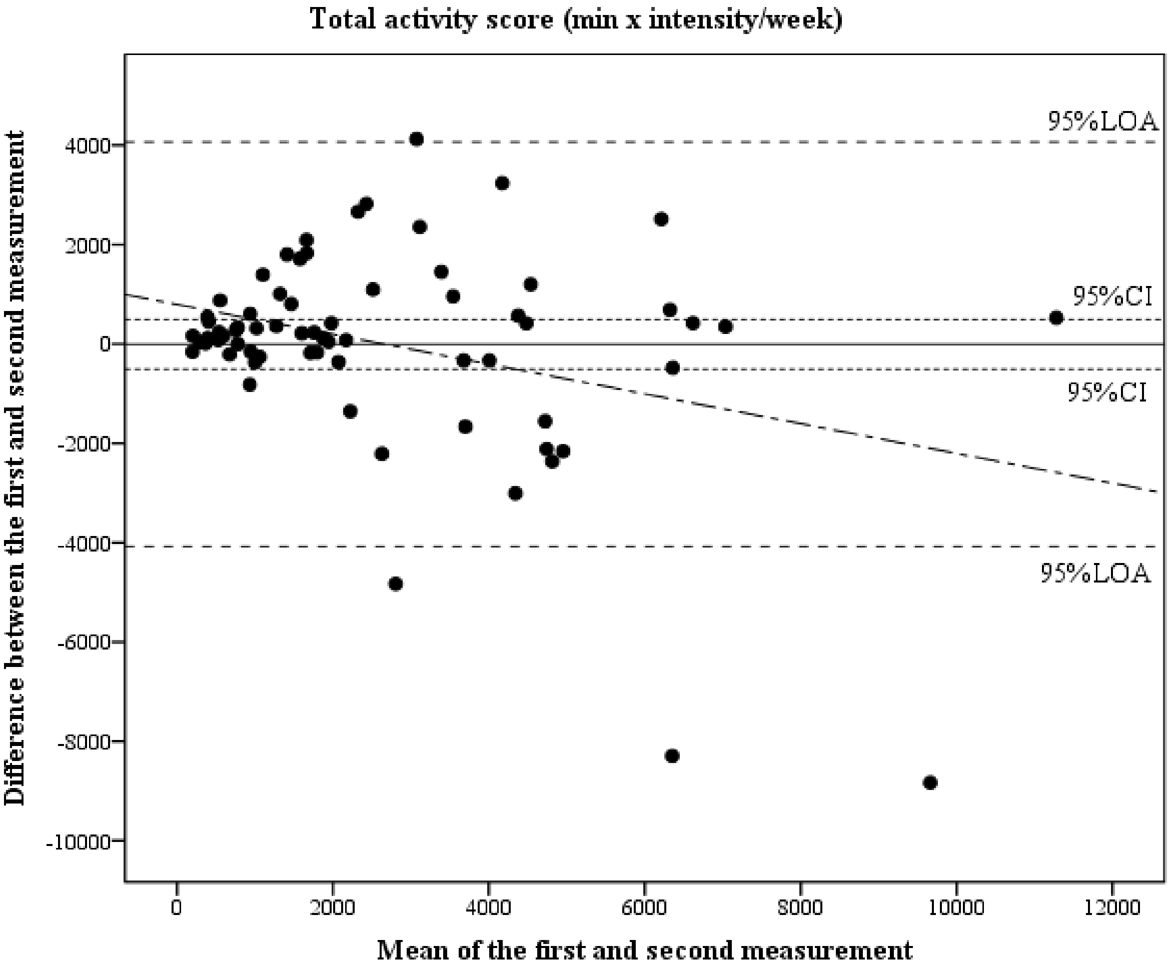


Figure 1 The differences between the total activity scores on the first and second measurement of the Adapted-SQUASH, plotted against their mean for each participant, together with the 95% confidence interval (CI) and the 95% Limits of Agreement (LOA) (N=68), with the diagonal line representing the correlation between the x and y axis (ρ=-0.08, p=.526), indicating homoscedasticity.

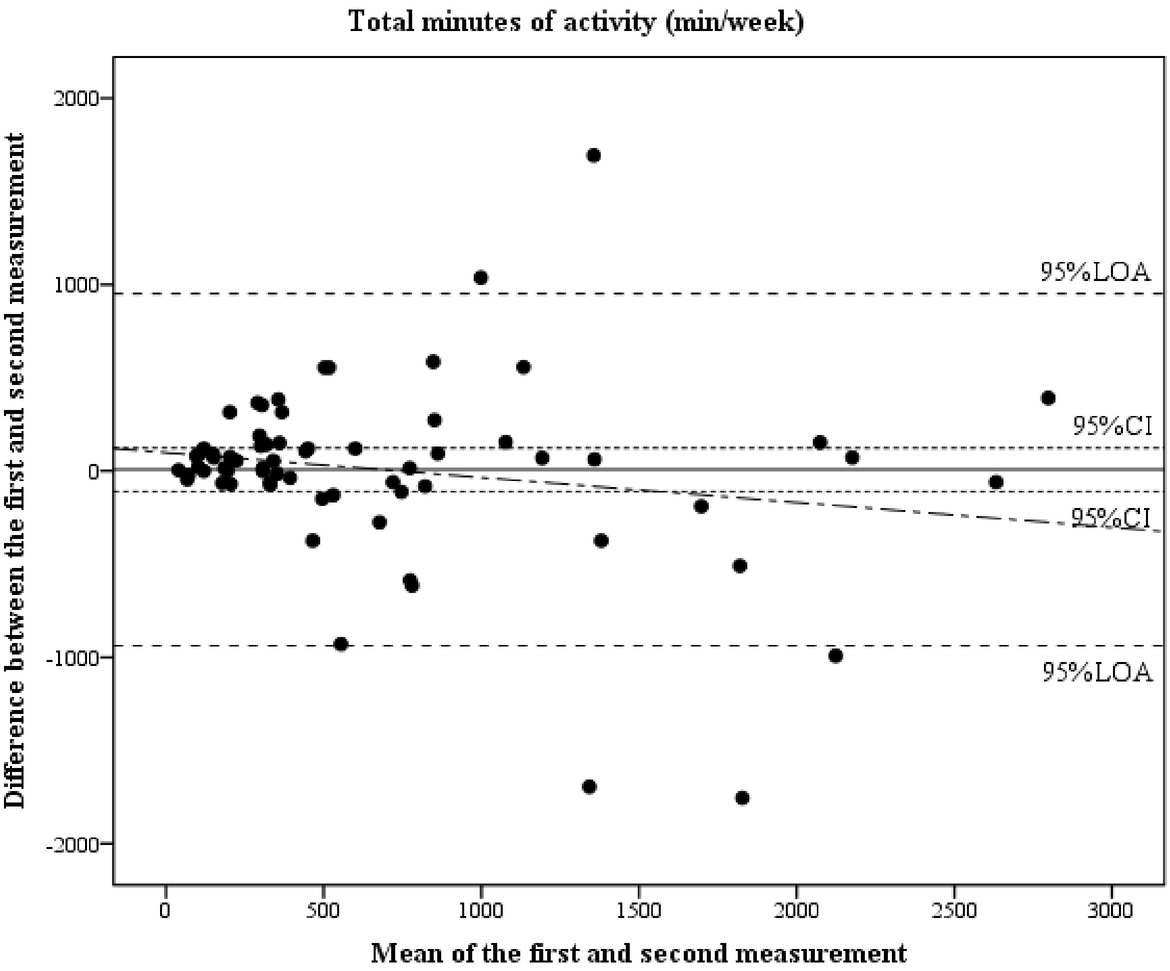


Figure 2 The differences between the total minutes of activity on the first and second measurement of the Adapted-SQUASH, plotted against their mean for each participant, together with the 95% confidence interval (CI) and the 95% Limits of Agreement (LOA) (N=68), with the diagonal line representing the correlation between the x and y axis (ρ=-0.10, p=.431), indicating homoscedasticity.

Concurrent validity

Correlation coefficients for the concurrent validity are presented in Table 3. A significant Spearman correlation coefficient was found between the total activity score from the Adapted-SQUASH and the AEE from the Actiheart (ρ=0.40, p=0.002). A significant ICC of 0.22 was found between the total minutes of activity per week from the Adapted-SQUASH and the total minutes of activity per week from the Actiheart (p=0.027). The correlation coefficients indicated fair and little agreement, respectively. No significant ICCs were found between the total minutes of light and moderate activity per week calculated with the Adapted-SQUASH and Actiheart. Only a significant ICC of 0.21 (p=0.046) was found between the total minutes of vigorous activity per week from the Adapted-SQUASH and Actiheart, indicating little agreement between the two measurement tools.

Bland-Altman analysis showed that the mean difference between the total minutes of activity calculated with the Adapted-SQUASH and Actiheart was significantly different from zero (t_{57}=3.48, p=0.001), indicating systematic bias between the two. We found wide LOA with 95% of the measurements of the total minutes of activity within the boundaries of 1485 minutes above and below the mean difference (figure 3). Besides, based on the Bland-Altman plot the absolute amount of time spent on physical activity was higher reported in the Adapted-SQUASH questionnaire compared to physical activity assessed with the Actiheart. Also, a Spearman correlation coefficient of 0.418 (p=.001) between the x and y axis of the Bland-Altman analysis for the total minutes of activity per week derived from the Actiheart and Adapted-SQUASH was found (figure 3), which indicated heteroscedasticity of the data.

Table 3 Correlation coefficients between the first measurement of the Adapted-SQUASH and the Actiheart (N=58)

	Physical activity levels		Concurrent validity		
	First test	Actiheart[b]	$r_{spearman}$		p
Outcomes Adapted-SQUASH	Median (IQR)	Median (IQR)			
Total activity score[a]	1903 (958 – 4260)	49 (26 – 74)	.40		.002
Total minutes of activity/week	454 (231 – 1073)	341 (106 – 727)	.36		.006
			ICC	95%CI	p
Total minutes of activity/week	454 (231 – 1073)	341 (106 – 727)	.22	-.01-.44	.027
Total minutes of light activity/week	83 (43 – 369)	223 (91 - 548)	.05	-.21-.31	.346

Total minutes of moderate activity/week	101 (0 – 371)	31 (10 – 114)	.03	-.17-.24	.401
Total minutes of vigorous activity/week	60 (30 – 136)	27 (10 – 92)	.21	-.03-.43	.046

IQR=Inter Quartile Range, ICC=Intraclass Correlation Coefficient, CI=Confidence Interval; p<0.05: significantly different from zero.

[a] Activity score = minutes x intensity

[b] Values are in total minutes per week, only the total activity score of the Adapted-SQUASH is compared with activity energy expenditure in kcals kg^{-1} min^{-1}.

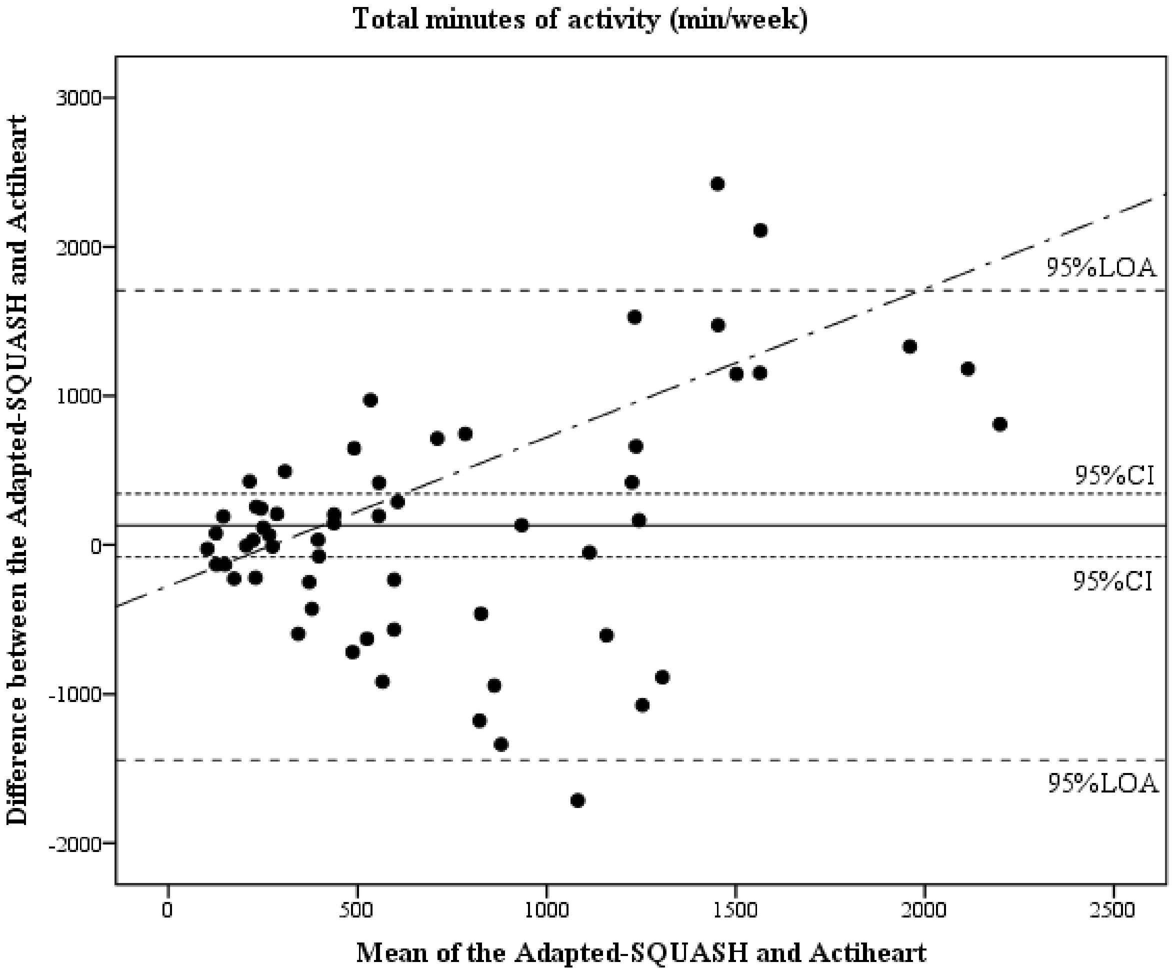


Figure 3 The differences between the total minutes of activity calculated with the Adapted-SQUASH and Actiheart, plotted against their mean for each participant, together with the 95% confidence interval (CI) and the 95% Limits of Agreement (LOA). (N=58), with the diagonal line representing the correlation between the x and y axis (ρ=0.418, p=.001), indicating heteroscedasticity.

Discussion

The current study showed good reproducibility of the Adapted SQUASH to assess self-reported physical activity in populations of people with disabilities, but not at the individual level since the Bland-Altman analyses found wide LOA. In addition, the current study showed fair validity of the Adapted SQUASH and the Bland-Altman analysis showed wide LOA, which indicates that self-reported physical activity individually assessed with the Adapted-SQUASH does not accurately represent individually accelerometer-derived physical activity assessed with the Actiheart in this sample of people with disabilities.

Test-retest reliability

The test-retest reliability of the total activity score per week (ICC=0.67, p<.001) of the Adapted-SQUASH is slightly higher compared to the Spearman correlation coefficients found in studies of the original SQUASH among 50 healthy adults (ρ=0.58) [5], among 44 patients after a total hip arthroplasty (ρ=0.57) [13], but slightly lower compared to a study among 52 patients with ankylosing spondylitis (ρ=0.89) [14]. Also, our result of the test-retest reliability of the total minutes per week (ICC=0.76, p<.001) of the Adapted-SQUASH is comparable to the Spearman correlation coefficient for the test-retest reliability of the PASIPD in similar populations with a disability (ρ=0.77) [11]. A special note when comparing the test-retest reliability of our study to others is that we examined the test-retest reliability by using ICCs, while others used Spearman correlation coefficients [5,13,14]. ICCs give lower correlation coefficients compared to Spearman correlation coefficients, because an ICC is the absolute agreement between the first and second measurement, which does not correct for systematic differences. In accordance with previous studies [13,14], the Bland-Altman analysis showed no systematic bias on total activity scores between test and retest. Although the Adapted-

SQUASH has good test-retest reliability and the mean differences between the first and second measurement are close to zero, relatively wide LOA are found for the total activity score and the total minutes of activity, which indicated that the degree of repeatability is insufficient at the individual level and/or that levels of physical activity fluctuate over time. Therefore, the Adapted-SQUASH can be used to assess self-reported physical activity behaviour in large (patient) populations but is not acceptable to monitor individual physical activity levels. Also, it indicates that large changes in the outcomes of the Adapted-SQUASH should be found when interested in the course of self-reported physical activity over time (e.g. before and after an intervention or treatment).

The Adapted-SQUASH also calculated the total minutes of light, moderate and vigorous activity per week. In previous literature, Wendel-Vos et al. (2003) and Wagenmakers et al. (2008) found the highest Spearman correlation coefficient for the total minutes of vigorous activity per week, respectively 0.92[5] and 0.85[13], while we found the lowest correlation for the total minutes of vigorous activity per week (ICC=0.32, p=.004). Explanation of this outcome is that vigorous intensity activities, such as weekly scheduled sports activities, are the easiest to recall for healthy adults [31], while intermittent light intensity activities (e.g. walking) are more difficult to recall [32,33]. However, adults with disabilities might experience activities as more intense, since activities often cost more energy compared to healthy adults [16,17] and may be more variable over the day due to fatigue and lack of appropriate pacing behaviour [34-37]. Therefore, temporal fluctuation in light intensity activities in healthy adults, may be similar to temporal fluctuation in moderate or vigorous intensity activities in our target population. Furthermore, our sample reported less minutes of vigorous intensity activities (so a lower between subjects' variance) compared to light intensity activities, which might give a lower ICC.

The Adapted-SQUASH provides information of different settings of physical activity (commuting activities, activities at work/school, household activities and leisure time activities including different sports). We found low test-retest reliability for leisure-time activities, which might be explained by the non-regular frequency of this type of activities per week, due to barriers to physical activity such as the amount of leisure-time, tiredness, or bad weather conditions [38]. The quite low correlation for intense activities at work could be due to a small percentage of the population who can perform intense activities at work and the high variability in vigorous activities. The two newly added items ‘wheelchair riding’ and ‘handcycling’ in the Adapted-SQUASH had low response, because our study excluded people who were completely wheelchair dependent. However, our study population did mention adapted sports in the category ‘sports activities’ (e.g. wheelchair basketball).

Another interesting variable is the sport outcome measure indicating good test-retest reliability (ICC=0.76, $p<0.001$), probably because sports activities are often easy to recall, and sports participation is a stable behaviour with scheduled regular practice. This variable is often used in clinical settings, as well as in policy making and governmental guidelines worldwide. Insight in sports activities can be used for a tailored advice regarding an active lifestyle during or after rehabilitation, which has health-influencing effects, is crucial for quality of life, mobility and participation in everyday life and is strongly recommended for adults with disabilities [39].

Concurrent validity

The concurrent validity of the total activity score per week of the Adapted-SQUASH ($\rho=0.40$, $p=.002$), when compared with the total AEE per week assessed with the Actiheart, is lower compared to the Spearman correlation coefficients found in studies of the original SQUASH among 50 healthy adults (ρ=0.45, physical activity was assessed with the computer science and applications activity monitor) [5], among 44 patients after a total hip arthroplasty (ρ=0.67, physical activity was assessed with an Actigraph accelerometer) [13], but higher compared to a study among 52 patients with ankylosing spondylitis (ρ=0.35, physical activity was assessed with an Actigraph accelerometer) [14]. Also, the concurrent validity of the total minutes of activity per week of the Adapted-SQUASH (ICC=0.22, p=.027 and ρ=0.36, p=.006), when compared with the total minutes of activity assessed with the Actiheart, is lower compared to the Spearman correlation coefficient found in the study of the original SQUASH among 50 healthy adults (ρ=0.56) [4], but higher compared to the Spearman correlation coefficient for the validity of the PASIPD among people with disabilities (ρ=0.30, physical activity was assessed with an Actigraph accelerometer) [11]. The lower concurrent validity of physical activity questionnaires in people with disabilities compared to healthy adults might be due to variation of the questionnaire and variation of the standard. Also, cognitive function, which is sometimes affected in people with disabilities, might influence the recall of activities and thereby might explain the differences between self-reported and accelerometer-derived physical activity [32].

In addition, the Bland-Altman analysis showed systematic bias between the total minutes of activity per week assessed with the Adapted-SQUASH and Actiheart and the LOA were wide. This indicated that the Adapted-SQUASH does not accurately represent accelerometer-derived physical activity assessed with the Actiheart in individuals with disabilities. Previous literature also found that individual self-reported physical activity compared to physical activity assessed with an accelerometer was not accurate in people after joint arthroplasty [40] and in people with spinal cord injury [7]. Besides, the mean difference between the Adapted-SQUASH and Actiheart was 346 minutes per week, which indicates that people with disabilities seem to overestimate their self-reported physical activity assessed with the Adapted-SQUASH compared to accelerometer-derived physical activity assessed with the Actiheart. Also, based on the Bland-Altman analysis for the total minutes of activity per week assessed with the Adapted-SQUASH and Actiheart, heteroscedasticity in the data was found, which indicates a tendency to overestimate self-reported physical activity when higher mean levels of physical activity were measured of the Adapted-SQUASH and Actiheart. This is in agreement with previous literature [41-43]. This overestimation of actual time spent being physically active is probably attributable to recall bias, such as the difficulty in recalling short breaks during physical activity (e.g. socializing or refreshment during the reported time doing sports, or taking rest during the reported time doing gardening or household activities) [7], while the Actiheart does measure all sorts of short breaks during physical activity and over the day. Another potential bias between self-reported and accelerometer-derived physical activity outcomes may reside in the appreciation and perception of physical activities and their intensities, which notions may be quite different in our population in the context of their often low physical work capacity [44] and phenomena of fatigue during the day [35,36]. This introduces a difference in what one does and what one perceives.

Consequently, for the total minutes of vigorous activities per week low or little agreement was found between the Adapted-SQUASH and Actiheart (ICC=0.21, p=.046), while no agreement was found for the total minutes of light (ICC=0.05, p=.346) and moderate (ICC=0.03, p=.401) activities per week. This suggests that the perceived intensity of activities in people with disabilities is not in agreement with the accelerometer-derived intensities of activities assessed with the Actiheart. Therefore, we suggest to use the total minutes of physical activity per week assessed with the Adapted-SQUASH when interested in dose-response relationships among for instance physical activity and health outcomes, or between physical activity and the received intervention/treatment in people with disabilities.

Limitations

A few limitations need to be considered. First, the Adapted-SQUASH used MET values from the Ainsworth compendium of physical activities, which were derived from and intended for use in able-bodied adults [21]. This limitation could have overestimated the total activity score for each intensity category [21,45], because our target population probably experiences activities as more intense compared to healthy adults [16,17], as well as less consistent during the day. Also, the Adapted-SQUASH is sensitive to overestimation of frequency and/or duration of the activities, due to recall bias. A more or less similar limitation is however true for the Actiheart device, where the used sensor algorithms are not specific to people with disabilities, but have been derived from the general healthy population [24,25]. This stresses the need for more population-specific validation studies also of objective physical activity measurement tools in the future [46].

Thirdly, the test-retest period was on average seventeen days. This duration could be too short to prevent participants from copying the Adapted-SQUASH from memory. However, following the recommendations of Matthews et al. (2012), we have consciously chosen for this short recall period to decrease the reporting error of activities, since physical activity levels tend to fluctuate between days and weeks due to weather conditions [47] and/or due to fluctuating experienced health or fatigue conditions among this population of persons with a disability [37]. Furthermore, we did not check at the participant if the week the Actiheart was worn was a representative week of their physical activity behaviour.

Lastly, the Actiheart is a device capable of measuring heart rate and acceleration, and combines these variables in a branched equation model to calculate AEE [24,25]. However, we found a large amount of missing heart rate data in our sample, while calculating AEE based on the heart rate and combined algorithm is preferred [25]. The median percentage of missing heart rate was 22% (inter quartile range: 10% - 42%). The unsuccessful measurement of heart rate may have happened due to malfunction of the battery or the electrodes. However, if during the week participants felt that the electrodes loosened or if the electrodes had not been replaced by the fourth day, the instruction was given to replace the electrodes. As stated above another limitation is that the algorithm from the Actiheart to calculate AEE has not been validated among adults with deviating movement patterns and adults using drugs against high blood pressure, who are included in our target population. This is however the case for most of the activity monitor devices currently available [48]. In addition, the Actiheart was validated among healthy adults within the age range of 26-50 years [24] and the algorithm of the Actiheart was validated among adults within the age range of 21-55 years [25], while the current study population had an age range of 19-85 years.

Practical implications and further research

The Adapted-SQUASH provides information on various dimensions (frequency, duration and intensity) and settings (e.g. household, leisure time), is inexpensive, and has low burden for participants to fill in. Together this turns the Adapted-SQUASH into a useful tool to assess self-reported physical activity among adults with disabilities in large population studies. Firstly, the Adapted-SQUASH can be used in community and health-care settings, like rehabilitation centres, to monitor physical activity levels in large heterogeneous populations with disabilities. For this practical use, the Adapted-SQUASH is distinctive compared with other physical activity questionnaires (e.g. PASIPD), because even though the questionnaire specifically assesses type, frequency and intensity of activities, it is short and quick to fill in and it includes physical activities for wheelchair users and adapted sports. Secondly, the Adapted-SQUASH can be used for large longitudinal cohort studies or intervention studies to evaluate self-reported physical activity. For example, the Adapted-SQUASH has already been used in the longitudinal cohort study ReSpAct, which aimed to evaluate physical activity in people with disabilities during and after a physical activity stimulation programme [8,9]. When accurate and complete measures of physical activity are preferred in further research among large populations with disabilities, we suggest using both the Adapted-SQUASH (in the total sample) and an activity monitor (in a sub-sample). The Adapted-SQUASH provides information on the setting of the activity, while an activity monitor provides information on intermittent activities (e.g. walking at home and taking rest during activities) [7,33]. So, selection of the best measurement to assess physical activity depends on the purpose, construct, measurement unit, population, setting etc. [3].

For practical implications, we recommend using the total minutes of activity per week or the total activity score, which were the two main outcome measures of the Adapted-SQUASH, to assess self-reported physical activity in people with disabilities. The test-retest reliability of the total minutes of activity per week was good but systematic bias with the Actiheart was found. The test-retest reliability of the total activity score per week was lower and the perceived intensity of activities (light, moderate and vigorous) was not in agreement with the Actiheart. However, outcomes should be interpreted with caution since our sample of people with disabilities overestimated their physical activity. Also, for future research it is recommended to assess the validity and test-retest reliability of the Adapted-SQUASH among people who are completely wheelchair dependent.

Conclusion

The Adapted-SQUASH is an acceptable measure to assess self-reported physical activity in large populations of people with disabilities but is not applicable at the individual level due to the wide LOA. Self-reported physical activity assessed with the Adapted-SQUASH does not accurately represent accelerometer-derived physical activity assessed with the Actiheart in individuals with disabilities. They seem to overestimate their physical activity and find it difficult to recall the perceived intensity of the activity. The test-retest reliability and concurrent validity of the Adapted-SQUASH are comparable to other physical activity questionnaires among people with disabilities. We recommend using the total minutes of activity per week and/or total activity score, derived from the Adapted-SQUASH, - preferably in combination with measurements with an activity monitor in a sub-sample - to evaluate physical activity in large populations of people with disabilities in rehabilitation practice and beyond as well as in (cohort) research.

Acknowledgements

The authors wish to thank the participating subjects and the students in the bachelor and master Human Movement Sciences at the University of Groningen who contributed to the data collection. The authors would like to thank Leonie A. Krops for her critical reading and comments on a draft of the manuscript. This study is funded by Stichting Beatrixoord Noord-Nederland and a personal grant received from the University of Groningen, University Medical Center Groningen (grant date 1-9-2018).

References

1. van der Ploeg HP, van der Beek AJ, van der Woude LH, van Mechelen W. Physical activity for people with a disability: a conceptual model. Sports Med 2004;34(10):639-649.

2. Cervantes CM, Porretta DL. Physical activity measurement among individuals with disabilities: a literature review. Adapt Phys Activ Q 2010 Jul;27(3):173-190.

3. Nigg CR, Fuchs R, Gerber M, Jekauc D, Koch T, Krell-Roesch J, et al. Assessing physical activity through questionnaires - A consensus of best practices and future directions. Psychology of Sport & Exercise 2020.

4. Booth M. Assessment of physical activity: an international perspective. Res Q Exerc Sport 2000 Jun;71(2 Suppl):S114-20.

5. Wendel-Vos GC, Schuit AJ, Saris WH, Kromhout D. Reproducibility and relative validity of the short questionnaire to assess health-enhancing physical activity. J Clin Epidemiol 2003 Dec;56(12):1163-1169.

6. Rennie KL, Wareham NJ. The validation of physical activity instruments for measuring energy expenditure: problems and pitfalls. Public Health Nutr 1998 Dec;1(4):265-271.

7. Ma JK, McCracken LA, Voss C, Chan FHN, West CR, Martin Ginis KA. Physical activity measurement in people with spinal cord injury: comparison of accelerometry and self-report (the Physical Activity Recall Assessment for People with Spinal Cord Injury). Disabil Rehabil 2020 Jan;42(2):240-246.

8. Hoekstra F, Alingh RA, van der Schans CP, Hettinga FJ, Duijf M, Dekker R, et al. Design of a process evaluation of the implementation of a physical activity and sports stimulation programme in Dutch rehabilitation setting: ReSpAct. Implement Sci 2014 Sep 20;9:127-014-0127-7.

9. Alingh RA, Hoekstra F, van der Schans CP, Hettinga FJ, Dekker R, van der Woude LH. Protocol of a longitudinal cohort study on physical activity behaviour in physically disabled patients participating in a rehabilitation counselling programme: ReSpAct. BMJ Open 2015 Jan 29;5(1):e007591-2015-007591.

10. Hoekstra F, Hoekstra T, van der Schans CP, Hettinga FJ, van der Woude LHV, Dekker R, et al. The implementation of a physical activity counseling program in rehabilitation care: findings from the ReSpAct study. Disabil Rehabil 2019 Oct 17:1-12.

11. van der Ploeg HP, Streppel KR, van der Beek AJ, van der Woude LH, Vollenbroek-Hutten M, van Mechelen W. The Physical Activity Scale for Individuals with Physical Disabilities: test-retest reliability and comparison with an accelerometer. J Phys Act Health 2007 Jan;4(1):96-100.

12. Prince SA, Adamo KB, Hamel ME, Hardt J, Connor Gorber S, Tremblay M. A comparison of direct versus self-report measures for assessing physical activity in adults: a systematic review. Int J Behav Nutr Phys Act 2008 Nov 6;5:56-5868-5-56.

13. Wagenmakers R, van den Akker-Scheek I, Groothoff JW, Zijlstra W, Bulstra SK, Kootstra JW, et al. Reliability and validity of the short questionnaire to assess health-enhancing physical activity (SQUASH) in patients after total hip arthroplasty. BMC Musculoskelet Disord 2008 Oct 17;9:141-2474-9-141.

14. Arends S, Hofman M, Kamsma YP, van der Veer E, Houtman PM, Kallenberg CG, et al. Daily physical activity in ankylosing spondylitis: validity and reliability of the IPAQ and SQUASH and the relation with clinical assessments. Arthritis Res Ther 2013 Aug 23;15(4):R99.

15. Dawes HN, Barker KL, Cockburn J, Roach N, Scott O, Wade D. Borg's rating of perceived exertion scales: do the verbal anchors mean the same for different clinical groups? Arch Phys Med Rehabil 2005 May;86(5):912-916.

16. Waters RL, Mulroy S. The energy expenditure of normal and pathologic gait. Gait Posture 1999 Jul;9(3):207-231.

17. Wezenberg D, van der Woude LH, Faber WX, de Haan A, Houdijk H. Relation between aerobic capacity and walking ability in older adults with a lower-limb amputation. Arch Phys Med Rehabil 2013 Sep;94(9):1714-1720.

18. Strath SJ, Bassett DR,Jr, Swartz AM, Thompson DL. Simultaneous heart rate-motion sensor technique to estimate energy expenditure. Med Sci Sports Exerc 2001 Dec;33(12):2118-2123.

19. Vet HCWd, Terwee CB, Mokkink LB, Knol DL. Measurement in medicine : a practical guide. Cambridge: Cambridge University Press; 2011.

20. Klaren RE, Hubbard EA, Zhu W, Motl RW. Reliability of Accelerometer Scores for Measuring Sedentary and Physical Activity Behaviors in Persons With Multiple Sclerosis. Adapt Phys Activ Q 2016 Apr;33(2):195-204.

21. Ainsworth BE, Haskell WL, Herrmann SD, Meckes N, Bassett DR,Jr, Tudor-Locke C, et al. 2011 Compendium of Physical Activities: a second update of codes and MET values. Med Sci Sports Exerc 2011 Aug;43(8):1575-1581.

22. Conger SA, Bassett DR. A compendium of energy costs of physical activities for individuals who use manual wheelchairs. Adapt Phys Activ Q 2011 Oct;28(4):310-325.

23. Hildebrandt V, Ooijendijk W, Stiggelhout M. Trendrapport bewegen en gezondheid 1998/1999. 1999;p. 23-9.

24. Brage S, Brage N, Franks PW, Ekelund U, Wareham NJ. Reliability and validity of the combined heart rate and movement sensor Actiheart. Eur J Clin Nutr 2005 Apr;59(4):561-570.

25. Crouter SE, Churilla JR, Bassett DR,Jr. Accuracy of the Actiheart for the assessment of energy expenditure in adults. Eur J Clin Nutr 2008 Jun;62(6):704-711.

26. Cicchetti DV. Guidelines, criteria, and rules of thumb for evaluating normed and standardized assessment instruments in psychology. Psychological Assessment 1994;6(4):284-290.

27. Portney LG, Watkins MP. Foundations of Clinical Research: Applications to Practice. : Upper Saddle River, NJ: Pearson/Prentice Hall; 2009.

28. Bland JM, Altman DG. Measuring agreement in method comparison studies. Stat Methods Med Res 1999 Jun;8(2):135-160.

29. Giavarina D. Understanding Bland Altman analysis. Biochem Med (Zagreb) 2015 Jun 5;25(2):141-151.

30. Terwee CB, Mokkink LB, van Poppel MN, Chinapaw MJ, van Mechelen W, de Vet HC. Qualitative attributes and measurement properties of physical activity questionnaires: a checklist. Sports Med 2010 Jul 1;40(7):525-537.

31. Jacobs DR,Jr, Ainsworth BE, Hartman TJ, Leon AS. A simultaneous evaluation of 10 commonly used physical activity questionnaires. Med Sci Sports Exerc 1993 Jan;25(1):81-91.

32. Herbolsheimer F, Riepe MW, Peter R. Cognitive function and the agreement between self-reported and accelerometer-accessed physical activity. BMC Geriatr 2018 Feb 21;18(1):56-018-0747-x.

33. Skender S, Ose J, Chang-Claude J, Paskow M, BrÃ¼hmann B, Siegel EM, et al. Accelerometry and physical activity questionnaires - a systematic review. BMC Public Health 2016 Jun 16;16:515-016-3172-0.

34. Murphy SL, Kratz AL. Activity pacing in daily life: A within-day analysis. Pain 2014 Dec;155(12):2630-2637.

35. Rimmer JH, Chen MD, Hsieh K. A conceptual model for identifying, preventing, and managing secondary conditions in people with disabilities. Phys Ther 2011 Dec;91(12):1728-1739.

36. Martin Ginis KA, Ma JK, Latimer-Cheung AE, Rimmer JH. A systematic review of review articles addressing factors related to physical activity participation among children and adults with physical disabilities. Health Psychol Rev 2016 Dec;10(4):478-494.

37. Abonie US, Edwards AM, Hettinga FJ. Optimising activity pacing to promote a physically active lifestyle in medical settings: A narrative review informed by clinical and sports pacing research. J Sports Sci 2020 Mar;38(5):590-596.

38. King AC. Intervention strategies and determinants of physical activity and exercise behavior in adult and older adult men and women. World Rev Nutr Diet 1997;82:148-158.

39. Haskell WL, Lee IM, Pate RR, Powell KE, Blair SN, Franklin BA, et al. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. Circulation 2007 Aug 28;116(9):1081-1093.

40. Vaughn NH, Dunklebarger MF, Mason MW. Individual Patient-reported Activity Levels Before and After Joint Arthroplasty Are Neither Accurate nor Reproducible. Clin Orthop Relat Res 2019 Mar;477(3):536-544.

41. Feuering R, Vered E, Kushnir T, Jette AM, Melzer I. Differences between self-reported and observed physical functioning in independent older adults. Disabil Rehabil 2014;36(17):1395-1401.

42. Chinapaw MJ, Slootmaker SM, Schuit AJ, van Zuidam M, van Mechelen W. Reliability and validity of the Activity Questionnaire for Adults and Adolescents (AQuAA). BMC Med Res Methodol 2009 Aug 10;9:58-2288-9-58.

43. Sebastiao E, Gobbi S, Chodzko-Zajko W, Schwingel A, Papini CB, Nakamura PM, et al. The International Physical Activity Questionnaire-long form overestimates self-reported physical activity of Brazilian adults. Public Health 2012 Nov;126(11):967-975.

44. Carroll DD, Courtney-Long EA, Stevens AC, Sloan ML, Lullo C, Visser SN, et al. Vital signs: disability and physical activity--United States, 2009-2012. MMWR Morb Mortal Wkly Rep 2014 May 9;63(18):407-413.

45. Rikli RE. Reliability, validity, and methodological issues in assessing physical activity in older adults. Res Q Exerc Sport 2000 Jun;71(2 Suppl):S89-96.

46. Lankhorst K, Oerbekke M, van den Berg-Emons R, Takken T, de Groot J. Instruments Measuring Physical Activity in Individuals Who Use a Wheelchair: A Systematic Review of Measurement Properties. Arch Phys Med Rehabil 2020 Mar;101(3):535-552.

47. Matthews CE, Moore SC, George SM, Sampson J, Bowles HR. Improving self-reports of active and sedentary behaviors in large epidemiologic studies. Exerc Sport Sci Rev 2012 Jul;40(3):118-126.

48. Van Remoortel H, Giavedoni S, Raste Y, Burtin C, Louvaris Z, Gimeno-Santos E, et al. Validity of activity monitors in health and chronic disease: a systematic review. Int J Behav Nutr Phys Act 2012 Jul 9;9:84-5868-9-84.

Chapter 3

Trajectories of Health-related Quality of Life among people with a physical disability and/or chronic disease during and after rehabilitation: a longitudinal cohort study.

Seves BL, Hoekstra F, Hettinga FJ, Dekker R, van der Woude LHV, Hoekstra T.

Quality of Life Research, 2021; Jan;30(1):67-80

Abstract

Purpose: To identify Health-related Quality of Life (HR-QoL) trajectories in a large heterogeneous cohort of people with a physical disability and/or chronic disease during and after rehabilitation, and to determine which factors before discharge are associated with longitudinal trajectory membership.

Methods: A total of 1100 people with a physical disability and/or chronic disease were included from the longitudinal cohort study Rehabilitation, Sports and Active lifestyle. All participants participated in a physical activity promotion programme in Dutch rehabilitation care. HR-QoL was assessed using the RAND-12 Health Status Inventory questionnaire at baseline (T0: 3-6 weeks before discharge) and at 14 (T1), 33 (T2) and 52 (T3) weeks after discharge from rehabilitation. A data-driven approach using Latent Class Growth Mixture modelling was used to determine HR-QoL trajectories. Multiple binomial multivariable logistic regression analyses were used to determine person-, disease- and lifestyle-related factors associated with trajectory membership.

Results: Three HR-QoL trajectories were identified: moderate (N=635), high (N=429), and recovery (N=36). Trajectory membership was associated with person-related factors (age and body mass index), disease-related factors (perceived fatigue, perceived pain and acceptance of the disease) and one lifestyle-related factor (alcohol consumption) before discharge from rehabilitation.

Conclusions: Most of the people who participated in a physical activity promotion programme obtained a relatively stable but moderate HR-QoL. The identified HR-QoL trajectories among our heterogeneous cohort are disease-overarching. Our findings suggest that people in rehabilitation may benefit from person-centred advice on management of fatigue and pain (e.g. activity pacing) and the acceptance of the disability.

Key words

Quality of Life, Active lifestyle, Health promotion, Rehabilitation, Latent class growth (mixture) models, activity pacing.

Introduction

Improving health-related quality of life (HR-QoL) is one of the key objectives in today's rehabilitation practice. When evaluating rehabilitation treatments, interventions taking place in rehabilitation practice and policy in health care, HR-QoL is often used as an outcome measure [1, 2]. In people with a physical disability and/or chronic disease, HR-QoL during rehabilitation is lower than in the nondisabled population [3]. More importantly, after rehabilitation, low levels of HR-QoL are commonly reported in people with a physical disability and/or chronic disease [4-6], and HR-QoL is poorer compared to a healthy reference population [7]. Low levels of HR-QoL are associated with secondary health conditions (e.g. fatigue, pain, obesity and cardiovascular diseases), whereby preventing secondary health conditions among this target population is an important step towards sustainable health [8] and healthy ageing. Furthermore, low levels of HR-QoL are associated with inactivity and sedentary behaviour in healthy adults [9, 10]. Also, previous literature found that physical activity is positively associated with all components of HR-QoL, except for mental health in people after rehabilitation [7]. Physical activity promotion programmes in rehabilitation care could have positive impact on improving HR-QoL by reducing secondary health conditions during but also after treatment has finished [4, 11, 12].

According to literature, there is large heterogeneity in HR-QoL development among people with disabilities [7]. Therefore, investigating HR-QoL by looking at average levels within the sample is not as useful as by investigating subgroups with distinct developmental trajectories of HR-QoL. Previous studies already identified several trajectories of HR-QoL in people during or after rehabilitation from breast cancer or stroke, which were related to the proposed characteristic trajectories of level of dysfunction: high, recovery, decline and low HR-QoL [13-15].

Cross-sectional research into the determinants of HR-QoL has found that personal factors (e.g. age and gender) are associated with HR-QoL in people with heart diseases [16] and in aneurysmal subarachnoid haemorrhage (SAH) survivors [17]. Psychosocial factors (e.g. self-efficacy, acceptance, passive coping) are associated with longitudinal HR-QoL in breast cancer survivors [13], in people post stroke [18] and in SAH survivors [17]. Psychological factors (e.g. depression, anxiety and fatigue) predict longitudinal trajectory membership of HR-QoL trajectories in people post stroke [14] and in SAH survivors [19], and predict cross-sectional HR-QoL in people with renal cell carcinoma [20]. Disease-related factors such as disease awareness in people after traumatic brain injury [21] and having comorbidities in people with renal cell carcinoma [20] were associated with respectively cross-sectional and longitudinal HR-QoL.

Most rehabilitation treatments or interventions to promote physical activity have not been evaluated for effectiveness on sustainable HR-QoL after rehabilitation treatment [2, 22]. So far, very little attention has been paid to a disease-overarching mechanism in the heterogeneous course of HR-QoL after rehabilitation. Previous research on HR-QoL development usually focussed on specific disease populations. The current longitudinal study provides an important opportunity to advance the understanding of the course of HR-QoL after rehabilitation, by undertaking a disease-overarching prospective analysis of HR-QoL. In addition, more insight into relevant determinants, such as person-, disease- and lifestyle-related factors is needed to identify vulnerable people with a physical disability and/or chronic disease at risk to experience a reduced HR-QoL after discharge already in the early stages of rehabilitation. These determinants can be non-modifiable (e.g. gender, age, severity of the disability) or modifiable (e.g. physical activity behaviour, acceptance of the disability, the use of tobacco and alcohol). Modifiable factors should be targeted by rehabilitation professionals, to improve patients' HR-QoL. The findings of this study may support the need for more person-centred care to help people to obtain and maintain sustainable high levels of HR-QoL after rehabilitation.

Therefore, the purposes of this study were (1) to identify trajectories of HR-QoL up to one-year after discharge from rehabilitation in people with a physical disability and/or chronic disease and (2) to determine person-, disease- and lifestyle-related factors before discharge from rehabilitation that are associated with longitudinal trajectory membership.

Methods

Context

The current study is part of the multicentre longitudinal cohort study Rehabilitation, Sports and Active lifestyle (ReSpAct) that was initiated to evaluate the nationwide programme Rehabilitation, Sports and Exercise (RSE; Dutch: 'Revalidatie, Sport en Bewegen') [23, 24]. The RSE programme has been implemented in eighteen rehabilitation institutions in the Netherlands (twelve rehabilitation centres and six rehabilitation departments of hospitals). The RSE programme aims to stimulate an active lifestyle during the rehabilitation period and to guide people with a physical disability and/or chronic disease in maintaining a physically active lifestyle in the home setting after discharge from rehabilitation [23, 24]. Participants of the RSE programme were referred to a sports counselling counter three to six weeks before discharge from rehabilitation for a face-to-face consultation with a sports counsellor, followed by four telephone-based counselling sessions up to thirteen weeks after discharge from rehabilitation [23, 24]. All sessions were based on motivational interviewing [25] (see Online Resource 2 for a schematic overview of the RSE programme and the ReSpAct study).

Participants were included in the ReSpAct-study from May 2013 until August 2015. Participants were monitored with questionnaires at given regular measurement times: at baseline (T0: 3-6 weeks before discharge) and 14 (T1), 33 (T2) and 52 (T3) weeks after discharge from rehabilitation (Online Resource 2). The study was approved by the ethics committee of the Center for Human Movement Sciences of the University Medical Center Groningen (reference: ECB/2013.02.28_1). All participants voluntarily participated after signing an informed consent.

Study population

Inclusion criteria were: (1) being at least eighteen years of age, (2) having a chronic disease or physical disability (e.g. stroke, heart failure, Parkinson's disease, spinal cord injury), (3) receiving inpatient or outpatient rehabilitation care or treatment at one of the participating rehabilitation departments or institutions, (4) participating in the RSE programme [24] and (5) filling in the RAND-12 Health Status Inventory (RAND-12) at two or more measurement occasions. Participants were excluded if they were not able to complete the questionnaires, even with help, or were participating in another physical activity stimulation programme.

HR-QoL

HR-QoL was assessed by using the self-reported RAND-12 questionnaire [26], an adapted, abbreviated version of the RAND-36 Health Status Inventory (RAND-36) [27]. The RAND-12 contains at least one item from each of the eight subscales of the RAND-36, so that it adequately represents the wide range of relevant aspects of health status [28]. Six items of the RAND-12 contribute to the physical health composite (how health limits a person in activities, or how a person's physical health causes problems with work or other activities) and six other items contribute to the mental health composite (how a person feels and how a person's mental health causes problems with work or other activities) [27, 28]. All twelve items contribute to the general health composite, which represents all relevant aspects of health status [28]. We used an age-corrected general health composite score for this study [27]. A higher score on the RAND-12 indicated better HR-QoL. Because the RAND-12 only contains twelve items of the RAND-36 (range 0-100), scores on the RAND-12 range from 0 to 65. We found good reliability (internal consistency) of the RAND-12 based on the study sample at T0 (Cronbach's alpha = .85, N=974), at T1 (Cronbach's alpha = .87, N=957), at T2 (Cronbach's alpha = .88, N=861) and at T3 (Cronbach's alpha = .88, N=780). Previous literature supports acceptable construct validity and test-retest reliability of the RAND-12 in among others clinical populations [28, 29].

Person-, disease- and lifestyle-related factors

All independent variables were measured at baseline (T0: 3-6 weeks before discharge). Person-related factors included gender, age, body mass index (BMI) and level of education, which was dichotomized into low (up to completed secondary education) and high (completed applied University or higher) to make it internationally comparable.

Disease-related factors included the type of disease divided into eight categories: musculoskeletal disease, amputation, brain disorder (e.g. stroke or other non-congenital brain defects), spinal cord injury, other neurologic disease, organ disease, chronic pain and other diseases. Also, disease-related factors included the number of comorbidities dichotomized into no comorbidities and one or more comorbidities, because this variable included all diseases and disabilities reported by a participant. The level of acceptance of the disability or disease was assessed on a four-point Likert scale (1-4, no acceptance to complete acceptance), with a higher score indicating better acceptance of the disability or disease. The level of acceptance was dichotomized into no (no or little acceptance) and yes (acceptance to a large extent or completely), because when entering the level of acceptance as categorical variable in the logistic regression, we found that the odds ratios (ORs) did not linearly increased/decreased. Perceived fatigue was assessed with the 9-item Fatigue Severity Scale (FSS) [30], which is a valid and reliable questionnaire to determine the impact of perceived fatigue in clinical populations (in people with systematic lupus erythematosus $r_{validity}$=0.81 and $r_{reliability}$=0.89, and in people with multiple sclerosis $r_{validity}$= 0.47 and $r_{reliability}$=0.81) [30-32]. The FSS score ranges from 1 to 7, with a higher score indicating more perceived fatigue [30]. We found good reliability (internal consistency) of the FSS based on the study sample at T0 (Cronbach's alpha = .91, N=1044). The FSS includes items like "Exercise brings on my fatigue." and "I am easily fatigued" [30]. The level of perceived pain was assessed on a six-point Likert scale (1-6, from no pain to severe pain), with a higher score indicating more perceived pain. The level of pain was dichotomized into no (no to light pain: score 1 -3) and yes (moderate to severe pain: score: 4 - 6), because when entering perceived pain as categorical variable in the logistic regression, we found that the ORs did not linearly increased/decreased. Also, too few people reported severe pain (perceived pain = 6).

Lifestyle-related factors included the dichotomous variables smoking and alcohol use ("Do you smoke currently?" and "Do you consume alcohol currently?": yes or no). In addition, the total minutes of physical activity per week was assessed by using the Adapted Short Questionnaire to Assess Health-enhancing physical activity (Adapted-SQUASH), a 19-item self-reported recall questionnaire. In a previous study, the Adapted-SQUASH has been shown to be a sufficiently reliable (intraclass correlation coefficient = 0.76, p<.001) and valid - compared to the Actiheart activity monitor – (intraclass correlation coefficient = 0.22, p=.027) questionnaire to determine self-reported physical activity in a similar sample (people with a physical disability and/or chronic disease) [33]. The Adapted-SQUASH is pre-structured in four main domains outlining types and settings of activity: 'commuting traffic', 'activities at work and school', 'household activities' and 'leisure time activities' including 'sports activities' [34]. The SQUASH [34] was adapted to make the questionnaire more applicable for this population (Adapted-SQUASH), as described in the study protocol of the ReSpAct study [24]. First, the items 'wheeling in a wheelchair' and 'handcycling' were added in the domains 'commuting activities and leisure-time' and 'sports activities'. Second, the self-reported intensity of the activity was categorised in 'light', 'moderate' and 'vigorous', instead of 'slow', 'moderate' and 'fast'. Third, a large range of adapted sports (e.g. wheelchair basketball/ruby/tennis) were included for the item 'sports activities'. Lastly, in the examples of different sports 'tennis' was replaced by '(wheelchair) tennis'. Information on sports participation (yes/no) was obtained from the Adapted-SQUASH. If the participant reported to perform at least one sports activity per week, than they were coded as ´yes', if not as ´no´.

Statistical analysis

Analyses were conducted in a two-step approach. First, trajectories of HR-QoL during and after rehabilitation among participants with two or more valid measurements over time were identified using Latent Class Growth Mixture (LCGM) modelling with quadratic (assuming non-linear change over time), linear (assuming linear change over time) and latent class analyses (lca) models [35], using the Mplus software program 7.11. The choice for linear and quadratic models was made based on previous research [14], showing trajectories of HR-QoL to be both linear as well as quadratic (non-linear). Additionally, latent class analyses were conducted for descriptive purposes. These analyses gave us insight in the (heterogeneity of) patterns of change in HR-QoL without a-priori assuming a trajectory shape. LCGM models are regression-based models that assume that individuals in the sample do not necessarily come from one underlying population but might come from multiple underlying (or latent) subpopulations. LCGM modelling aims to find the optimal number and characteristics of these subpopulations. Common, stepwise modelling strategies were applied [34, 35], using the Guidelines for Reporting on Latent Trajectory Studies (GRoLTS) as well [36]. A one-class model was first determined, thus assuming one underlying population, and subsequently more classes were added one at a time and model fit indices were inspected. The optimal number of classes was determined according to the following model fit criteria: (1) a lower Bayesian Information Criterion (BIC), where a difference of 10 points lower is usually regarded as sufficient improvement [37], (2) a higher entropy (range from 0 to 1), a standardized measure of how accurately individuals' trajectories are classified, where higher values indicate better classification [38, 39] and (3) average posterior probabilities of ≥0.80 [35]. The choice for the optimal number of classes was additionally made considering clinical interpretation (rejecting solutions that do not make clinical sense) and class size. Finally, individuals were classified into their most likely class based on their posterior probability.

Second, multiple binomial multivariable logistic regression analyses were performed to assess associations between the previously described person-, disease- and lifestyle-related factors and trajectory membership using version 24 of the Statistical Package for the Social Science (SPSS). The outcome of the LCGM modelling, the nominal variable of trajectory membership, was used as dependent variable.

Independent variables at baseline were all entered block wise (block 1: person-related factors, block 2: disease-related factors and block 3: lifestyle-related factors) in multivariable models. Descriptive statistics of these variables were analysed at baseline. Assumptions of normality and linearity were checked. The continuous independent variables age, BMI, fatigue, and physical activity/week were standardized. Results of the multiple binomial multivariable logistic regression analyses are presented as OR and corresponding 95% confidence interval (CI). Because three comparisons between two trajectories were needed to compare all HR-QoL trajectories, a Bonferroni-corrected p-value, to correct for multiple testing, of 0.017 (0.05/3=0.017) was used to give a 95% probability of correctly concluding not to reject the null hypothesis [40].

To facilitate transparency and reproducibility, additional information is available on: (a) the dataset of the HR-QoL (Online Resource 1) and (b) the Mplus syntax of the LCGM modelling and the SPSS syntax of the multiple binomial multivariable logistic regression analyses (Online Resource 2).

Results

Characteristics of participants

In total 1100 participants were included in this study. Participants had an average age of 51.0 ± 13.5 years and 52.0% were female. The three most common disease groups were brain disorder (26.0%, N=286), musculoskeletal disease (18.1%, N=199) and chronic pain (15.6%, N=172) (Table 1).

Based on descriptive characteristics at baseline (Table 1), participants excluded for the LCGM modelling analyses were on average more often female, younger, lower educated, lived less independently, had worse acceptance of their disease, perceived more fatigue, smoked less, received less counselling moments and had lower levels of HR-QoL. Descriptive characteristics at baseline were missing of around 250 excluded participants, which might give skewed descriptive characteristics.

Table 1 Participants' descriptive statistics at baseline for participants included (N=1100) and excluded (N=617) in the latent class growth mixture modelling analyses.

Characteristic	**Included in LCGMM** Mean ± SD or % (N)	**Excluded for LCGMM** Mean ± SD or % (N)
Personal related factors		
Gender (% female)	52.0 (572)	57.8 (358)*
Age in years	51.0 ± 13.5	47.8 ± 13.9**
Body mass index (kg/m^2)	27.2 ± 5.5	27.6 ± 6.2
Education level (% high)[a]	24.5 (270)	11.5 (71)*
Living situation (% independent)	88.7 (976)	53.0 (328)*
Disease related factors		
Disease group		
Brain disorders	26.0 (286)	27.1 (168)
Musculoskeletal disease	18.1 (199)	19.2 (119)
Chronic pain	15.6 (172)	17.8 (110)
Neurologic disease	15.5 (171)	12.1 (75)
Organ disease	12.0 (132)	10.7 (66)
Amputation	4.5 (50)	4.4 (27)
Other symptoms	4.0 (44)	3.1 (19)
Spinal cord injury	2.8 (31)	4.4 (27)
Acceptance (% yes)	54.3 (597)	28.4 (176)*
Comorbidities (% yes)	41.3 (454)	28.1 (174)
Fatigue (FSS score)	4.3 ± 1.5	4.5 ± 1.5*
Pain (% yes)	46.2 (508)	25.7 (159)
Lifestyle related factors		
Smoking (% yes)	16.4 (180)	13.7 (85)*
Alcohol use (% yes)	39.1 (430)	18.6 (115)
Total minutes of PA/week	1081.1 ± 919.5	1120.8 ± 966.8
Sports participation (% yes)	54.5 (600)	45.6 (282)
Institutional level		
Treatment form (% outpatient)[c]	90.4 (994)	89.0 (551)
Treatment context (% hospital)	28.1 (309)	26.2 (162)
Amount of physical activity counselling moments after rehabilitation[d]	2.6 ± 1.4	2.1 ± 1.5*

Health-related quality of life (RAND-12)		
Mental health composite	40.3 ± 9.4	38.5 ± 9.3*
Physical health composite	36.2 ± 10.3	33.6 ± 9.4**
General health composite	37.2 ± 9.3	34.7 ± 8.8**

[a] Completed applied University or higher

[b] Percentage of participants with one or more comorbidities

[c] Treatment form includes outpatient and inpatient

[d] Participants in the Rehabilitation, Sports and Exercise programme received four telephone-based counselling sessions with a sports counsellor

Standard deviation (SD); Number of participants (N); Latent Class Growth Mixture Modelling (LCGMM); Fatigue Severity Scale (FSS)

* and **: the characteristic is significantly different (* p<0.05, ** p<0.01) between the participants included and excluded for the LCGMM based on independent sample t-tests for continuous variables and based on Chi-squared tests for categorical variables.

HR-QoL trajectories

The results of the fit indices for quadratic, linear and lca models with one to six trajectories of HR-QoL are presented in Table 2. Comparing these models with the model fit criteria alone proved to be complicated, as the model fit criteria were not always in agreement, which is a common finding in LCGM modelling [41]. After careful consideration, we chose the three-class quadratic model as the optimal model in this sample, although the average posterior probabilities were slightly below 0.80, indicating possibly less distinct trajectories and subsequent fuzzy classification, yet it avoids inclusion of an extremely small class, as is the case in the four-class and five-class quadratic models. The three-trajectory model consisted of two large and stable, but distinctly different trajectories: moderate (N=635, 55.1%) and high (N=429; 40.9%) trajectory. In addition, one smaller intermediate trajectory is provided, which increases between 3-6 weeks before discharge from rehabilitation and 33 weeks post rehabilitation and then stabilizes (i.e., recovery) (N=36; 4.0%) (Figure 1).

Descriptive statistics of the mental, physical and general health composites for the three trajectories at each measurement time are presented in Table 3. Overall, mental health followed the same but higher course and physical health followed the same but lower course compared to general health. Supplementary figures are given in the supplemental file on osf.io/rtz5y/, including estimated mean trajectories for each model, estimated means with individual trajectories for each latent class and the estimated with observed means for the final model. Although the plots with estimated means with individual trajectories for each latent class show large heterogeneity in individual trajectories of HR-QoL, all individual trajectories follow the same growth pattern over time for each latent class.

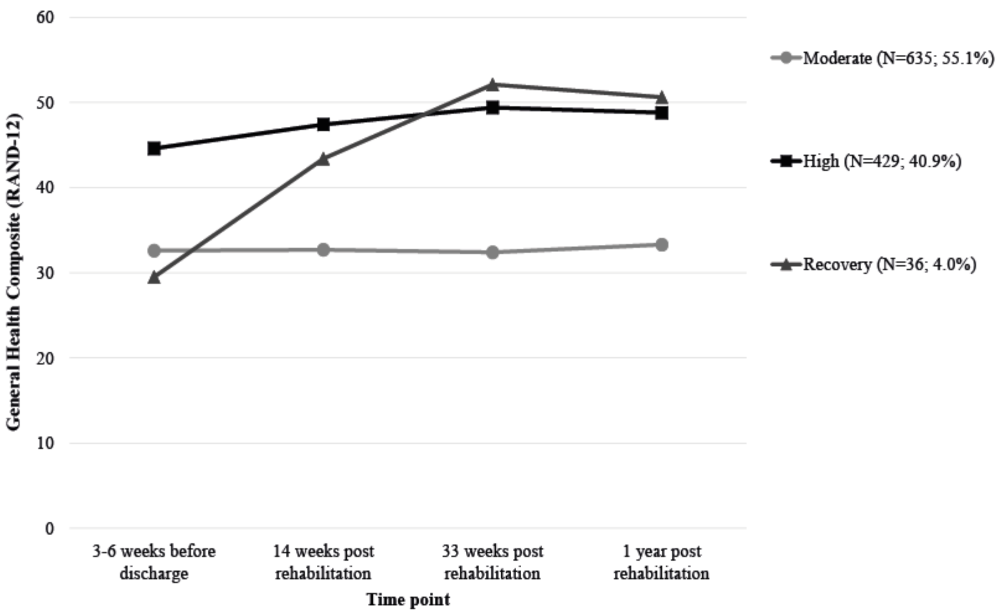


Figure 1 Three trajectory model of HR-QoL (N=1100), based on the general health composite (RAND-12)

Table 2 Fit indices for quadratic, linear and lca models with 1-6 trajectories of HR-QoL

Health-related Quality of Life									
				Number of participants in each trajectory class					
Number of classes	BIC	Entropy	Average posterior probability (min-max)	1	2	3	4	5	6
Quadratic analyses									
1	24301.36	NA	1.0	1100					
2	24227.49	.87	.90 (.83 - .97)	1058	42				
3	**24198.33**	**.61**	**.79 (.76 - .83)**	**36**	**635**	**429**			
4	24201.32	.67	.83 (.77 - .95)	2	640	42	416		
5	24196.12	.69	.78 (.72 - .83)	620	55	31	3	391	
6	24204.48	.65	.78 (.64 - .98)	53	595	2	34	370	46
Linear analyses									
1	24254.81	NA	1.0	1100					
2	24224.64	.98	.94 (.87 – .99)	1093	7				
3	24225.76	.64	.85 (.81 - .90)	636	7	457			
4	24228.39	.79	.84 (.80 - .90)	993	71	7	30		
5	24221.44	.63	.80 (.72 - .90)	629	331	6	31	103	
6	24237.72	.66	.78 (.71 - .86)	5	320	32	126	615	2
lca analyses									
1	26708.06	NA	1.0	1100					
2	25283.89	.79	.94 (.94 - .94)	603	497				
3	24698.63	.81	.91 (.91 - .91)	354	509	237			
4	24504.05	.79	.88 (.86 - .90)	229	119	414	338		
5	24400.27	.78	.86 (.83 - .91)	76	288	355	279	102	
6	24367.06	.80	.85 (.76 - .91)	79	16	352	286	265	102

Bayesian Information Criterion (BIC); Not applicable (NA); Latent class analyses (lca)

Note: in bold are the values of the chosen model

Table 3 Mental, physical and general HR-QoL for the three trajectories at baseline (T0: 3-6 weeks before discharge) and at 14 (T1), 33 (T2) and 52 (T3) weeks after discharge from rehabilitation.

	T0 Mean ± SD	T1 Mean ± SD	T2 Mean ± SD	T3 Mean ± SD
Mental health composite				
Moderate (N=635)	36.2 ± 7.8	36.3 ± 7.7	35.9 ± 7.3	37.1 ± 8.4
High (N=429)	46.9 ± 7.8	49.6 ± 7.5	51.2 ± 6.3	49.8 ± 7.9
Recovery (N=36)	35.1 ± 7.5	46.7 ± 9.0	55.2 ± 6.2	53.9 ± 7.5
Physical health composite				
Moderate (N=635)	32.0 ± 8.6	32.0 ± 8.6	31.9 ± 8.4	32.2 ± 8.9
High (N=429)	43.1 ± 8.5	45.4 ± 8.0	47.3 ± 7.2	47.5 ± 7.5
Recovery (N=36)	28.2 ± 10.6	41.1 ± 11.9	48.3 ± 8.2	46.9 ± 9.3
General health composite				
Moderate (N=635)	32.6 ± 7.2	32.7 ± 7.0	32.4 ± 6.4	33.3 ± 7.6
High (N=429)	44.6 ± 7.2	47.4 ± 6.9	49.4 ± 5.7	48.8 ± 7.0
Recovery (N=36)	29.5 ± 7.1	43.4 ± 10.5	52.1 ± 6.0	50.6 ± 7.9

Standard deviation (SD); Number of participants (N)

Range: Mental health composite (13-66), Physical health composite (0-63), General health composite (6-65)

Determinants of HR-QoL trajectories

Descriptive statistics of possible determinants before discharge from rehabilitation for the HR-QoL trajectories are presented in Table 4. Multiple binomial multivariable logistic regression analyses were performed to determine associations among the personal-, disease- and lifestyle-related factors before discharge from rehabilitation and the HR-QoL trajectories (Table 5).

Compared with participants in the moderate HR-QoL trajectory (N=635), participants with a higher BMI (OR=0.77, 95%CI=0.64-0.94), participants who perceive fatigue (OR=0.47, 95%CI=0.39-0.58) and/or participants who perceive pain (OR=0.22, 95%CI=0.15-0.33) are less likely to belong to the latent class with a high HR-QoL trajectory (N=429), while participants who accept their physical disability and/or chronic disease (OR=3.25, 95%CI=2.25-4.68) are more likely to belong to the latent class with a high HR-QoL trajectory. Also compared to the moderate HR-QoL trajectory, based on the limits of the 95% CI which both lie above or below one (but not significant), participants who are older (OR=1.27, 95%CI=1.04-1.55), participants who drink alcohol (OR=1.44, 95%CI=1.01-2.05) and/or participants who are more physically active (OR=1.21, 95%CI=1.01-1.44) are more likely to belong to the latent class with a high HR-QoL trajectory, while participants who smoke (OR=0.58, 95%CI=0.35-0.94) are less likely to belong to this latent class.

There were no significant determinants before discharge to distinguish between the moderate HR-QoL (N=635) and the recovery HR-QoL (N=36) trajectories. But, based on the limits of the 95% CI which both lie above one (but not significant), participants who drink alcohol (OR=3.05, 95%CI=1.09-8.53) are more likely to belong to the latent class with a moderate HR-QoL trajectory, compared to the recovery HR-QoL trajectory.

A comparison of the recovery HR-QoL trajectory (N=36) and the high HR-QoL trajectory (N=429) showed that participants who are older (OR=1.97, 95%CI=1.18-3.29), participants who accept their physical disability and/or chronic disease (OR=5.09, 95%CI=2.04-12.69) and/or participants who drink alcohol (OR=4.60, 95%CI=1.53-13.83) are more likely to belong to the latent class with a high HR-QoL trajectory (N=429).

Remarkably, gender, education level, type of disease, having comorbidities, level of physical activity and sports participation before discharge were not significant determinants to distinguish between trajectories of HR-QoL.

In addition, we checked whether the found significant determinants in the multiple binomial multivariable logistic regression analyses were still found after controlling for general HR-QoL scores at baseline (Table 5). HR-QoL scores at baseline were found to be significant determinants in the comparisons between the moderate and high HR-QoL trajectories (OR=5.86, 95%CI=4.14-8.30) and between the recovery and high HR-QoL trajectories (OR=45.24, 95%CI=10.26-199.47). When controlling for HR-QoL score at baseline, only perceived fatigue (OR=0.69, 95%CI=0.55-0.87) and perceived pain (OR=0.56, 95%CI=0.35-0.88) remain significant determinants when comparing the moderate and high HR-QoL trajectories (Table 5).

Table 4 Person-, disease- and lifestyle-related factors at baseline for the three trajectories of HR-QoL

	Moderate (N=635) Mean ± SD or % (N)	High (N=429) Mean ± SD or % (N)	Recovery (N=36) Mean ± SD or % (N)
Personal related factors			
Gender (% female)	57.2 (363)	43.6 (187)	61.1 (22)
Age in years	50.3 ± 13.3	52.8 ± 13.5	42.8 ± 14.5
Body Mass Index (kg/m^2)	27.9 ± 5.6	26.2 ± 5.0	27.4 ± 6.5
Education level (% high)	21.3 (135)	28.9 (124)	30.6 (11)
Disease related factors			
Disease group			
Muscoloskeletal disease	20.0 (127)	13.5 (58)	38.9 (14)
Amputation	2.7 (17)	7.5 (32)	2.8 (1)
Brain disease	23.3 (148)	30.5 (131)	19.4 (7)
Neurologic disease	17.0 (108)	13.5 (58)	13.9 (5)
Spinal cord injury	2.4 (15)	3.7 (16)	0 (0)
Organ disease	9.6 (61)	15.9 (68)	8.3 (3)
Chronic pain	19.5 (124)	10.0 (43)	13.9 (5)
Other disease	3.8 (24)	4.4 (19)	2.8 (1)
Acceptance (% yes)	42.0 (267)	74.4 (319)	30.6 (11)
Comorbidities (% yes)	47.1 (299)	33.3 (143)	33.3 (12)
Fatigue (FSS score)	4.8 ± 1.3	3.6 ± 1.4	4.3 ± 1.3
Pain (% yes)	60.5 (384)	23.3 (100)	66.7 (24)
Lifestyle related factors			
Smoking (% yes)	19.4 (123)	12.1 (52)	13.9 (5)
Alcohol use (% yes)	34.6 (220)	47.1 (202)	22.2 (8)
Total minutes of PA/week	1031.0 ± 884.9	1137.6 ± 956.8	1294.5 ± 1021.2
Sports participation (% yes)	52.3 (332)	58.5 (251)	47.2 (17)

a Completed applied University or higher

Standard deviation (SD); Number of participants (N); Physical activity (PA); Fatigue Severity Scale (FSS)

Table 5 Multiple binomial multivariable logistic regression analyses at baseline to distinguish between three pairs of three HR-QoL trajectories, and the same comparisons with correction for general HR-QoL scores at baseline.

	HR-QoL						HR-QoL, after correcting for baseline HR-QoL					
	Moderate (ref) vs. High		Recovery (ref) vs. Moderate		Recovery (ref) vs. High		Moderate (ref) vs. High		Recovery (ref) vs. Moderate		Recovery (ref) vs. High	
	Odds ratio (95% CI)	p	Odds ratio (95% CI)	p	Odds ratio (95% CI)	p	Odds ratio (95% CI)	p	Odds ratio (95% CI)	p	Odds ratio (95% CI)	p
HR-QoL 3-6 weeks before discharge	NA		NA		NA		**5.80 (4.10 – 8.21)**	**<.001**	2.05 (1.05 – 3.97)	.034	**45.18 (10.26 – 198.98)**	**<.001**
Personal related factors												
Gender (female)	0.90 (0.62 – 1.31)	.584	1.47 (0.65 – 3.34)	.352	1.70 (0.62 – 4.67)	.308	0.93 (0.61 – 1.42)	.739	1.34 (0.59 – 3.04)	.489	2.24 (0.52 – 9.60)	.279
Age	1.27 (1.04 – 1.55)	.020	1.48 (0.94 – 2.33)	.094	**1.97 (1.18 – 3.29)**	**.010**	1.03 (0.82 – 1.29)	.815	1.22 (0.75 – 1.78)	.427	1.30 (0.67 – 2.52)	.438
Body Mass Index	**0.77 (0.64 – 0.94)**	**.009**	1.04 (0.69 – 1.56)	.849	0.80 (0.53 – 1.20)	.272	0.88 (0.71 – 1.09)	.249	1.09 (0.72 – 1.66)	.690	0.80 (0.46 – 1.39)	.423
Education (high)	1.41 (0.95 – 2.10)	.089	0.79 (0.32- 1.95)	.602	0.70 (0.26 – 1.89)	.477	1.26 (0.81 – 1.96)	.312	0.76 (0.30 – 1.92)	.555	0.62 (0.15 – 2.68)	.526
Disease related factors												
Disability (ref=musculoskeletal disease)		.549		.303		.874		.408		.265		.351
Amputation	1.86 (0.72 – 4.80)	.202	2.34 (0.23 – 24.04)	.473	2.63 (0.22 – 31.64)	.447	1.88 (0.63 – 5.58)	.257	2.54 (0.25 – 26.12)	.434	16.46 (0.62 – 437.36)	.094
Brain disorders	0.82 (0.46 – 1.47)	.505	5.10 (1.34 – 19.44)	.017	3.03 (0.72 – 12.67)	.129	0.78 (0.41 – 1.50)	.459	**5.23 (1.36 – 20.12)**	**.016**	6.03 (0.95 – 38.49)	.057
Neurologic disease	0.96 (0.51 – 1.80)	.886	2.49 (0.73 – 8.45)	.143	1.52 (0.39 – 6.04)	.548	0.97 (0.48 – 1.96)	.927	2.73 (0.81 – 9.20)	.106	2.17 (0.34 – 13.91)	.415
Spinal cord injury	2.07 (0.72 – 5.99)	.180	NA	.999	NA	.998	2.17 (0.69 – 6.83)	.186	NA	.999	NA	.998
Organ disease	1.02 (0.51 – 2.05)	.959	1.89 (0.41 – 8.81)	.418	1.19 (0.23 – 6.10)	.839	0.66 (0.30 – 1.47)	.312	1.74 (0.37 – 8.16)	.485	0.58 (0.07 – 5.18)	.628
Chronic pain	0.97 (0.52 – 1.82)	.926	4.02 (1.04 – 15.45)	.043	2.17 (0.46 – 10.23)	.328	0.78 (0.39 – 1.55)	.476	4.16 (1.06 – 16.29)	.040	2.27 (0.35 – 14.86)	.393
Other symptoms	0.75 (0.29 – 1.89)	.538	2.95 (0.31 – 28.27)	.348	1.47 (0.12 – 17.45)	.760	0.75 (0.26 – 2.15)	.594	3.09 (0.31 – 30.70)	.337	0.63 (0.04 – 9.89)	.740
Acceptance (yes)	**3.25 (2.25 – 4.68)**	**<.001**	1.65 (0.73 – 3.76)	.231	**5.09 (2.04 – 12.69)**	**<.001**	1.46 (0.96 – 2.23)	.077	1.14 (0.46 – 2.80)	.775	0.58 (0.15 – 2.34)	.447
Comorbidities (yes)	0.79 (0.55 – 1.16)	.228	1.55 (0.62 – 3.86)	.346	0.66 (0.23 – 1.91)	.443	0.90 (0.59 – 1.37)	.631	1.70 (0.70 – 4.32)	.265	1.49 (0.38 – 5.90)	.570
Fatigue (FSS score)	**0.47 (0.39 – 0.58)**	**<.001**	1.32 (0.87 – 2.00)	.200	0.67 (0.40 – 1.12)	.126	**0.69 (0.55 – 0.87)**	**.001**	1.54 (0.99 – 2.40)	.056	1.60 (0.74 – 3.44)	.229
Pain (yes)	**0.22 (0.15 – 0.33)**	**<.001**	1.59 (0.62 – 4.09)	.332	0.39 (0.14 – 1.98)	.072	**0.56 (0.35 – 0.88)**	**.011**	2.19 (0.80 – 5.94)	.125	2.16 (0.54 – 8.67)	.280
Lifestyle related factors												
Smoking (yes)	0.58 (0.35 – 0.94)	.027	2.05 (0.64 – 6.59)	.226	1.00 (0.24 – 4.14)	.999	0.53 (0.30 – 0.94)	.028	2.02 (0.62 – 6.65)	.246	0.53 (0.10 – 2.73)	.450
Alcohol use (yes)	1.44 (1.01 – 2.05)	.043	3.05 (1.09 – 8.53)	.033	**4.60 (1.53 – 13.83)**	**.007**	1.41 (0.95 – 2.09)	.088	2.61 (0.92 – 7.42)	.071	2.62 (0.71 – 9.66)	.149
Total minutes of PA/week	1.21 (1.01 – 1.44)	.043	0.82 (0.57 – 1.19)	.303	1.12 (0.70 – 1.81)	.630	1.00 (0.81 – 1.24)	.976	0.77 (0.53 – 1.12)	.170	0.97 (0.56 – 1.70)	.921
Sports participation (yes)	1.11 (0.78 – 1.58)	.555	1.19 (0.53 – 2.66)	.669	1.28 (0.52 – 3.19)	.594	1.03 (0.70 – 1.53)	.871	1.17 (0.52 – 2.66)	.706	1.49 (0.47 – 4.70)	.495

Health-related Quality of Life (HR-QoL); Confidence Interval (CI); reference (ref); Fatigue Severity Scale (FSS); Physical activity (PA); Not applicable (NA)

Note: values in bold are significant (p<0.017)

Discussion

This study identified three distinct trajectories of HR-QoL up to one year after rehabilitation in a large heterogeneous cohort of people with a physical disability and/or chronic disease: moderate, high and recovery. The two large and stable trajectories of HR-QoL (moderate and high) among our sample are similar to the large HR-QoL trajectories identified in specific disease populations (e.g. stroke patients [14] and breast cancer survivors [13]), which might indicate that HR-QoL trajectories are not necessarily disease specific. However, we did not identify a decline HR-QoL trajectory in our sample. Although a considerable group of our sample (40.9%) obtained stable high HR-QoL after participating in the physical activity promotion programme [23, 24], most of the sample (55.1%) did not.

This study determined which person-, disease- and lifestyle-related factors at discharge from rehabilitation are associated with trajectories of HR-QoL after rehabilitation. The following modifiable disease-related factors were determinants of trajectory membership: acceptance of the disability, perceived fatigue and pain before discharge from rehabilitation. These factors could be explored further for possibilities to modify the vulnerable trajectories into more favourable trajectories of HR-QoL. Acceptance of the disability before discharge from rehabilitation distinguished people in the high HR-QoL trajectory from people in both the moderate and the recovery HR-QoL trajectories. Van Mierlo et al. (2017) also found that the acceptance of the disability is a determinant for stable high HR-QoL compared with low HR-QoL in stroke patients [14]. This finding indicates the importance of paying attention to the acceptance of the disability during rehabilitation (e.g. focus on self-management and social/family support [42]), so that people are able to obtain and/or maintain high HR-QoL during and after rehabilitation.

In addition, less perceived fatigue and pain at discharge from rehabilitation strongly distinguishes people in the high HR-QoL trajectory from those in the moderate HR-QoL trajectory, even after controlling for baseline general HR-QoL scores. Fatigue is a distressing secondary health condition that is commonly reported in rehabilitation [43, 44]. Psychological/behavioural treatment (e.g. coping or activity pacing) has been found to be beneficial for reducing fatigue and/or pain by stimulating a more regular pattern of activities and rest [45], and could play a role in optimising HR-QoL during and after rehabilitation. Activity pacing is a multifaceted coping strategy [46, 47], wherein people who perceive fatigue divide their energy and daily physical activities during the day. Activity pacing can be beneficial for: (1) people at risk of under activity and less aware of their energy distribution during the day [48] and (2) people at risk of over activity characterized by an uneven activity pattern consisting of high activity peaks followed by long periods of inactivity [49]. Health-care professionals (e.g. sports counsellors or physiotherapists) may improve person-centred advice by motivational interviewing with a focus on activity pacing to reduce perceived fatigue and pain for sustained levels of high HR-QoL after rehabilitation.

Furthermore, we found that 'not consuming alcohol' distinguishes people in the recovery HR-QoL trajectory from people in the high HR-QoL trajectory before discharge. Also, we found confidence that people who do not smoke and/or drink alcohol were more likely to belong to the high HR-QoL trajectory compared to the moderate HR-QoL trajectory, but this finding was not statistically significant. This might be an indication of consequences of unhealthy lifestyle habits, like smoking and alcohol use, not sufficiently addressed during the rehabilitation treatment. More guidance, information and awareness related to general healthy lifestyle behaviours could potentially optimise rehabilitation programmes.

Finally, we did not find physical activity to be statistically significantly associated with HR-QoL trajectories. However, the direction of the association indicates that people who were more physically active before discharge from rehabilitation were more likely to follow the high HR-QoL trajectory compared to people in the moderate HR-QoL trajectory. This might imply that more physical activity is associated with higher HR-QoL, which supports previous literature [7, 9, 50, 51].

Lastly, no significant determinants were found to distinguish between the moderate versus recovery HR-QoL trajectories, probably because these trajectories had comparable HR-QoL scores at baseline. When we control for HR-QoL scores at baseline in the multiple binomial multivariable logistic regression analyses, we see that most significant determinants become non-significant. This implies that especially HR-QoL scores at baseline (the intercepts) of the moderate, high and recovery HR-QoL trajectories can be determined, while most personal-, disease- and lifestyle-related determinants are not able to differentiate between the course (slopes) of the HR-QoL trajectories up to one year after discharge from rehabilitation. Only perceived fatigue and pain are still significant determinants to distinguish between the moderate and high HR-QoL trajectories.

Some strengths and limitations of this study need to be addressed. HR-QoL scores (mean ± standard deviation) found in our cohort before discharge from rehabilitation (physical health: 36.2±10.3; mental health: 40.3±9.4) are comparable to a cohort of primary care patients with chronic diseases (physical health: 36.1±10.8; mental health: 40.0±10.8) [26]. However, HR-QoL scores in our sample are lower compared to people with type 2 diabetes (physical health: 43.5±10.8; mental health: 44.8±10.2) and people after total joint arthroplasty (physical health: 32.1±8.1; mental health: 50.0±9.2) [29].

In addition, we used LCGM models to unravel heterogeneity in HR-QoL after rehabilitation and to understand the underlying mechanisms for different subgroups in the population, which has some important advantages. First, this methodological technique categorises people based on their development pattern, a data-driven approach, instead of on a priori classification in theory-driven predefined groups [35, 52]. Furthermore, this LCGM approach categorises people in homogenous subgroups that represent different profiles of HR-QoL and subsequent health outcomes. This data-driven approach fits with the research design, an observational cohort study, but differs from the traditional way of summarising patient data into 'the average patient' [41]. An important point of discussion is the decision on the optimal number of classes, with respect to both the model fit criteria and clinical interpretation. Also, the sample size and the number of measurement occasions have been shown to influence the number and characteristics of the identified classes in the final model [53-56]. Choices made during the modelling process (e.g. model with the lowest BIC) may influence the interpretation of the models and subsequent implications. For example, the five-class quadratic model had a decline HR-QoL trajectory, but also a very small distinct strong recovery HR-QoL trajectory.

In addition, we used the two-step approach to evaluate the characteristics of the latent classes. In step one, we obtained the classes and assigned individuals to their most likely class. In step two, we assessed factors associated with class membership. These steps can also be combined into a one-step approach, where the extra variables are already included in the model during the (conditional) class formation process. Neither approach is right or wrong. The two-step approach for example ignores class assignment error, but does estimate the classes without covariates clouding the class formation [57, 58]. The one-step approach does incorporate the class assignment uncertainty, but covariates can influence the class formation process [57, 58]. Our posterior probabilities were relatively high and indicative of low membership error and the one step-approach does not always improve model fit.

Also, we used the RAND-12 questionnaire, which is not preferred over the extended, original RAND-36 questionnaire, nor over more disease-specific HR-QoL questionnaires. However, disease-specific questionnaires were not feasible in our heterogeneous cohort and the shorter RAND-12 version provided a solution to the problem to restrict the length of the questionnaire in the ReSpAct study in order to reduce the load for participants [24], which advances the commitment to participate in this longitudinal study.

Furthermore, we found differences between the sample included versus the sample excluded in the current study. Of interest are the acceptance of the disease, fatigue and smoking behaviour. These variables differed statistically significantly between the included and excluded sample as well as between the trajectories. Unfortunately, we were unable to determine the missing at random mechanism, because baseline variables of almost half of the excluded participants were missing.

Implications for practice and research

More than one third of our sample obtained a relatively stable high HR-QoL, but more than half obtained moderate HR-QoL after participating in a person-centred physical activity promotion programme; the RSE programme. We found several modifiable disease-related factors to be important in determining HR-QoL, which emphasizes the importance for optimising person-centred advice in focusing on fatigue and pain management and on better acceptance of the disability during rehabilitation. Also, the identified HR-QoL trajectories are not disease specific, which might imply a disease-overarching mechanism.

Furthermore, to make the LCGM modelling more transparent, the data, syntax and results are available in the supplemental file on osf.io/rtz5y/. Especially in latent trajectory studies, open communication is important due to the data-driven aspect of the analyses and the difficult choices made to find the optimal model fit. We would like to encourage other researchers in the field of latent trajectory studies, to provide open communication of their analyses and results, and to use the GRoLTS checklist [36] in reporting the analysis of the latent trajectory study. This will benefit comparison of the results in different study populations.

Conclusion

This study identified three trajectories of HR-QoL after rehabilitation among a large heterogeneous cohort of people with a physical disability and/or chronic disease, of which there were two large stable trajectories (high and moderate), and one small intermediate trajectory (recovery). Our identified HR-QoL trajectories are comparable to HR-QoL trajectories identified in specific disease populations, which might indicate that HR-QoL trajectories are not disease specific. More than half of our sample obtained a relatively stable but moderate HR-QoL after rehabilitation, while 40.9% obtained a stable high HR-QoL. Membership of these HR-QoL trajectories were associated with a limited extend of personal-related factors (age and BMI), disease-related factors (perceived fatigue, perceived pain and acceptance of the disability) and one lifestyle-related factor (alcohol use) before discharge. The moderate HR-QoL trajectory may benefit from person-centred advice during rehabilitation on management of fatigue and pain (e.g. activity pacing), and the acceptance of the disability.

Acknowledgements

The authors would like to thank all participants for their contribution to the ReSpAct study. Furthermore, we would like to thank the following organisations for their support in the ReSpAct study: Adelante Zorggroep (Hoensbroek, the Netherlands), Merem behandelcentra, De Trappenberg (Almere, the Netherlands), Vogellanden (Zwolle, the Netherlands), Maasstad Ziekenhuis (Rotterdam, the Netherlands), Noordwest Ziekenhuisgroep (Alkmaar, the Netherlands), Militair Revalidatiecentrum Aardenburg (Doorn, the Netherlands), Rehabilitation Center Leijpark (Tilburg, the Netherlands), Rehabilitation Center Reade (Amsterdam, the Netherlands), Revalidatie Friesland (Heerenveen, the Netherlands) ,Revant (Breda, the Netherlands), Rijnlands Rehabilitation Center (Leiden, the Netherlands), Klimmendaal (Arnhem, the Netherlands), Treant Zorggroep (Hoogeveen and Emmen, the Netherlands), Sint Maartenskliniek (Nijmegen, the Netherlands), Sophia Rehabilitation Center (Den Haag, the Netherlands), Tolbrug Rehabilitation ('s Hertogenbosch, the Netherlands), Klimmendaal, Sport Variant (Apeldoorn, the Netherlands). The authors would like to thank Leonie A. Krops and Pim Brandenbarg for their critical reading and comments on a draft of the manuscript.

This study was funded by the Dutch Ministry of Health, Welfare and Sports (Grant No. 319758), Stichting Beatrixoord Noord-Nederland (grant date 19-2-2018) and a personal grant received from the University Medical Center Groningen, and supported by the Knowledge Center of Sport Netherlands and Stichting Special Heroes Nederland (before January 2016: Stichting Onbeperkt Sportief).

References

1. Hays, R.D., Hahn H., Marshall G. (2002). Use of the SF-36 and other health-related quality of life measures to assess persons with disabilities. *Arch Phys Med Rehabil* Dec;83(12 Suppl 2):S4-9.

2. Gellert, G.A. (1993). The importance of quality of life research for health care reform in the USA and the future of public health. *Qual Life Res* Oct;2(5):357-61.

3. Schrier, E., Schrier I., Geertzen J.H., Dijkstra P.U. (2016). Quality of life in rehabilitation outpatients: Normal values and a comparison with the general dutch population and psychiatric patients. *Qual Life Res* Jan;25(1):135-42.

4. Rimmer, J.H. (2012). Getting beyond the plateau: Bridging the gap between rehabilitation and community-based exercise. *PM R* Nov;4(11):857-61.

5. Estrella-Castillo, D.F.P.D., Gómez-de-Regil L.P.D. (2016). Quality of life in mexican patients with primary neurological or musculoskeletal disabilities. *Disability and Health Journal*;9(1):127-133.

6. Kaske, S., Lefering R., Trentzsch H., Driessen A., Bouillon B., Maegele M., et al. (2014). Quality of life two years after severe trauma: A single-centre evaluation. *Injury* Oct;45 Suppl 3:S100-5.

7. Krops, L.A., Jaarsma E.A., Dijkstra P.U., Geertzen J.H., Dekker R. (2017). Health related quality of life in a dutch rehabilitation population: Reference values and the effect of physical activity. *PLoS One* Jan 6;12(1):e0169169.

8. Rimmer, J.H., Chen M.D., Hsieh K. (2011). A conceptual model for identifying, preventing, and managing secondary conditions in people with disabilities. *Phys Ther* Dec;91(12):1728-39.

9. Feeny, D., Garner R., Bernier J., Thompson A., McFarland B.H., Huguet N., et al. (2014). Physical activity matters: Associations among body mass index, physical activity, and health-related quality of life trajectories over 10 years. *J Phys Act Health* Sep;11(7):1265-75.

10. Sawatzky, R., Liu-Ambrose T., Miller W.C., Marra C.A. (2007). Physical activity as a mediator of the impact of chronic conditions on quality of life in older adults. *Health Qual Life Outcomes* Dec 19;5:68,7525-5-68.

11. Haskell, W.L., Lee I.M., Pate R.R., Powell K.E., Blair S.N., Franklin B.A., et al. (2007). Physical activity and public health: Updated recommendation for adults from the american college of sports medicine and the american heart association. *Circulation* Aug 28;116(9):1081-93.

12. Carroll, D.D., Courtney-Long E.A., Stevens A.C., Sloan M.L., Lullo C., Visser S.N., et al. (2014). Vital signs: Disability and physical activity--united states, 2009-2012. *MMWR Morb Mortal Wkly Rep* May 9;63(18):407-13.

13. Goyal, N.G., Levine B.J., Van Zee K.J., Naftalis E., Avis N.E. (2018). Trajectories of quality of life following breast cancer diagnosis. *Breast Cancer Res Treat* Jan 24.

14. van Mierlo, M., van Heugten C., Post M.W.M., Hoekstra T., Visser-Meily A. (2017). Trajectories of health-related quality of life after stroke: Results from a one-year prospective cohort study. *Disabil Rehabil* Mar 13:1-10.

15. Bonanno, G.A., Mancini A.D. (2008). The human capacity to thrive in the face of potential trauma. *Pediatrics* Feb;121(2):369-75.

16. Lee, D.T., Choi K.C., Chair S.Y., Yu D.S., Lau S.T. (2014). Psychological distress mediates the effects of socio-demographic and clinical characteristics on the physical health component of health-related quality of life in patients with coronary heart disease. *Eur J Prev Cardiol* Jan;21(1):107-16.

17. Passier, P.E., Visser-Meily J.M., van Zandvoort M.J., Rinkel G.J., Lindeman E., Post M.W. (2012). Predictors of long-term health-related quality of life in patients with aneurysmal subarachnoid hemorrhage. *NeuroRehabilitation*;30(2):137-45.

18. Teoh, V., Sims J., Milgrom J. (2009). Psychosocial predictors of quality of life in a sample of community-dwelling stroke survivors: A longitudinal study. *Top Stroke Rehabil* Mar-Apr;16(2):157-66.

19. Visser-Meily, J.M., Rhebergen M.L., Rinkel G.J., van Zandvoort M.J., Post M.W. (2009). Long-term health-related quality of life after aneurysmal subarachnoid hemorrhage: Relationship with psychological symptoms and personality characteristics. *Stroke* Apr;40(4):1526-9.

20. Beisland, E., Beisland C., Hjelle K.M., Bakke A., Aarstad A.K., Aarstad H.J. (2015). Health-related quality of life, personality and choice of coping are related in renal cell carcinoma patients. *Scand J Urol*;49(4):282-9.

21. Grauwmeijer, E., Heijenbrok-Kal M.H., Ribbers G.M. (2014). Health-related quality of life 3 years after moderate to severe traumatic brain injury: A prospective cohort study. *Arch Phys Med Rehabil* Jul;95(7):1268-76.

22. White, G.W., Gonda C., Peterson J.J., Drum C.E., RRTC Expert Panel on Health Promotion Interventions. (2011). Secondary analysis of a scoping review of health promotion interventions for persons with disabilities: Do health promotion interventions for people with mobility impairments address secondary condition reduction and increased community participation? *Disabil Health J* Apr;4(2):129-39.

23. Hoekstra, F., Alingh R.A., van der Schans C.P., Hettinga F.J., Duijf M., Dekker R., et al. (2014). Design of a process evaluation of the implementation of a physical activity and sports stimulation programme in dutch rehabilitation setting: ReSpAct. *Implement Sci* Sep 20;9:127,014-0127-7.

24. Alingh, R.A., Hoekstra F., van der Schans C.P., Hettinga F.J., Dekker R., van der Woude L.H. (2015). Protocol of a longitudinal cohort study on physical activity behaviour in physically disabled patients participating in a rehabilitation counselling programme: ReSpAct. *BMJ Open* Jan 29;5(1):e007591,2015-007591.

25. Miller, W.R., Rose G.S. (2009). Toward a theory of motivational interviewing. *Am Psychol* Sep;64(6):527-37.

26. Feeny, D., Farris K., Cote I., Johnson J.A., Tsuyuki R.T., Eng K. (2005). A cohort study found the RAND-12 and health utilities index mark 3 demonstrated construct validity in high-risk primary care patients. *J Clin Epidemiol* Feb;58(2):138-41.

27. Hays, R.D., Morales L.S. (2001). The RAND-36 measure of health-related quality of life. *Ann Med* Jul;33(5):350-7.

28. Ware, J.,Jr, Kosinski M., Keller S.D. (1996). A 12-item short-form health survey: Construction of scales and preliminary tests of reliability and validity. *Med Care* Mar;34(3):220-33.

29. Maddigan, S.L., Feeny D.H., Johnson J.A., DOVE Investigators. (2004). Construct validity of the RAND-12 and health utilities index mark 2 and 3 in type 2 diabetes. *Qual Life Res* Mar;13(2):435-48.

30. Krupp, L.B., LaRocca N.G., Muir-Nash J., Steinberg A.D. (1989). The fatigue severity scale. application to patients with multiple sclerosis and systemic lupus erythematosus. *Arch Neurol* Oct;46(10):1121-3.

31. Whitehead, L. (2009). The measurement of fatigue in chronic illness: A systematic review of unidimensional and multidimensional fatigue measures. *J Pain Symptom Manage* Jan;37(1):107-28.

32. Elbers, R.G., Rietberg M.B., van Wegen E.E., Verhoef J., Kramer S.F., Terwee C.B., et al. (2012). Self-report fatigue questionnaires in multiple sclerosis, parkinson's disease and stroke: A systematic review of measurement properties. *Qual Life Res* Aug;21(6):925-44.

33. Seves, B.L., Hoekstra F., Schoenmakers J.W., Brandenbarg P., Hoekstra T., Hettinga F.J., et al. (2020). Test-retest reliability and concurrent validity of the adapted short QUestionnaire to ASsess health-enhancing physical activity (adapted-SQUASH) in adults with disabilities. *medRxiv* Cold Spring Harbor Laboratory Press:2020.09.09.20190371.

34. Wendel-Vos, G.C., Schuit A.J., Saris W.H., Kromhout D. (2003). Reproducibility and relative validity of the short questionnaire to assess health-enhancing physical activity. *J Clin Epidemiol* Dec;56(12):1163-9.

35. Jung, T., Wickrama K.A.S. (2008). An introduction to latent class growth analysis and growth mixture modeling. *Social and Personality Psychology Compass*;2(1):302-317.

36. van de Schoot, R., Sijbrandij M., Winter S.D., Depaoli S., Vermunt J.K. (2017). The GRoLTS-checklist: Guidelines for reporting on latent trajectory studies. *Structural Equation Modeling: A Multidisciplinary Journal*;24(3):451-467.

37. Raftery, A.E. (1995). Bayesian model selection in social research. *Sociological Methodology*;25:111.

38. Ramaswamy, V., Desarbo W.S., Reibstein D.J., Robinson W.T. (1993). An empirical pooling approach for estimating marketing mix elasticities with PIMS data. *Marketing Science*;12(1):103-124.

39. Carragher N, Adamson G, Bunting B, McCann S. (2009). Subtypes of depression in a nationally representative sample. *J Affect Disord*;113(1-2):88-99.

40. Brown, B.W., Russell K. (1997). Methods correcting for multiple testing: Operating characteristics. *Stat Med*;16(22):2511-2528.

41. Hoekstra T. Applied latent class models for epidemiology [dissertation]. S.l.: Amsterdam: VU University; 2013.

42. Li L, Moore D. (1998). Acceptance of disability and its correlates. *J Soc Psychol*;138(1):13-25.

43. Clark, L.V., White P.D. (2009). The role of deconditioning and therapeutic exercise in chronic fatigue syndrome (CFS). *Journal of Mental Health*;14(3):237-252.

44. Nijs, J., Paul L., Wallman K. (2008). Chronic fatigue syndrome: An approach combining self-management with graded exercise to avoid exacerbations. *J Rehabil Med* Apr;40(4):241-7.

45. Acciarresi, M., Bogousslavsky J., Paciaroni M. (2014). Post-stroke fatigue: Epidemiology, clinical characteristics and treatment. *Eur Neurol*;72(5-6):255-61.

46. Antcliff, D., Keeley P., Campbell M., Woby S., Keenan A.M., McGowan L. (2018). Activity pacing: Moving beyond taking breaks and slowing down. *Qual Life Res* Feb 2.

47. Abonie, U.S., Sandercock G.R.H., Heesterbeek M., Hettinga F.J. (2018). Effects of activity pacing in patients with chronic conditions associated with fatigue complaints: A meta-analysis. *Disabil Rehabil* Nov 18:1-10.

48. Gill, J.R., Brown C.A. (2009). A structured review of the evidence for pacing as a chronic pain intervention. *Eur J Pain* Feb;13(2):214-6.

49. Antcliff, D., Keeley P., Campbell M., Oldham J., Woby S. (2013). The development of an activity pacing questionnaire for chronic pain and/or fatigue: A delphi technique. *Physiotherapy* Sep;99(3):241-6.

50. Marck, C.H., Hadgkiss E.J., Weiland T.J., van der Meer D.M., Pereira N.G., Jelinek G.A. (2014). Physical activity and associated levels of disability and quality of life in people with multiple sclerosis: A large international survey. *BMC Neurol* Jul 12;14:143,2377-14-143.

51. Farris, M.S., Kopciuk K.A., Courneya K.S., McGregor S.E., Wang Q., Friedenreich C.M. (2017). Identification and prediction of health-related quality of life trajectories after a prostate cancer diagnosis. *Int J Cancer* Apr 1;140(7):1517-27.

52. Muthen, B. (2006). The potential of growth mixture modelling. *Infant and Child Development*;15(6):623-625.

53. Connell, A.M., Frye A.A. (2006). Response to commentaries on target paper, 'Growth mixture modeling in developmental psychology'. *Infant and Child Development*;15(6):639-642.

54. Stanger, C. (2006). Latent growth mixture models: An important new tool for developmental researchers. *Infant and Child Development*;15(6):635-637.

55. Bauer DJ, Curran PJ. (2003). Distributional assumptions of growth mixture models: Implications for overextraction of latent trajectory classes. *Psychol Methods*;8(3):338-63.

56. Nagin, D.S., Tremblay R.E. (2001). Analyzing developmental trajectories of distinct but related behaviors: A group-based method. *Psychol Methods*;6(1):18-34.

57. Huang, D., Brecht M.L., Hara M., Hser Y.I. (2010). Influences of a covariate on growth mixture modeling. *J Drug Issues* Winter;40(1):173-94.

58. Muthén B. (2003). Statistical and substantive checking in growth mixture modeling: Comment on bauer and curran (2003). *Psychol Methods*;8(3):369-77.

Chapter 4

Perceived and performance fatigability associated with physical activity and health-related quality of life in people with physical disabilities and/or chronic diseases: a narrative review

Seves BL, van der Woude LHV, Zijdewind CAT, Hettinga FJ.

In preparation for submission

Abstract

Purpose: The aims of this narrative review were to provide a comprehensive knowledge from current literature on (1) the prevalence and intensity of fatigue in terms of perceived and performance fatigability in a wide range of adults with physical disabilities and/or chronic diseases, and (2) the associations between perceived and performance fatigability and physical activity and health-related quality of life (HR-QoL) in this population.

Method: Databases PubMed and PsycINFO were searched by combining variations of the terms fatigue and disease. In this narrative review, 113 studies were included.

Results and Conclusions: Several diseases were associated with greater levels of perceived and performance fatigability. Subsequently, higher levels of perceived fatigability were associated with lower physical activity and lower HR-QoL. These findings indicate the urgent need for further research on fatigue and fatigability, the determinants there-off, and on the role of rehabilitation programmes aiming to reduce fatigue by promoting a physically active lifestyle and improving HR-QoL. Finally, studies that assessed both perceived and performance fatigability are deemed relevant in understanding fatigue in people with physical disabilities and/or chronic diseases.

Keywords

Fatigue, Rehabilitation, Disability, Health, Chronic disease, Physical activity, Quality of life

Introduction

Fatigue is one of the most commonly reported, often disabling, symptoms in people with physical disabilities and/or chronic diseases [1-3]. A disease refers to “a condition of a person in which his/her body or structure is harmed because an organ or part is unable to work as it usually does” [4]. For standardisation in health care and international literature, diseases are often classified according to the International Classification of Diseases (ICD-11) [5]. In today’s health care, primary hospitalisation in serious disease or trauma is often followed by in- or outpatient rehabilitation to treat the functional consequences of the disease or trauma. The consequences of a disease or trauma are commonly described in terms of physical functioning, impairment, disability participation, and health, according to the World Health Organization’s (WHO) model ‘International Classification of Functioning, Disability and Health (ICF)’ [5]. Worldwide, more than one billion people, 15% of the world’s population, live with a disability due to a trauma or chronic health condition [5]. In this narrative review, we shift from the ICD-11 (focus on disease) to the ICF, where we focus on the consequences of the disease (formal WHO terminology: impairment, disability and participation), such as fatigability which plays a large role in the ICF model [5]. In this narrative review, fatigue refers to a nonspecific, self-reported symptom, which can be quantified as either a trait or a state variable [6]. The trait level represents the average amount of perceived fatigue experienced during a fixed period (e.g., as measured by self-reported questionnaires, such as Fatigue Severity Scale [7] and Fatigue Impact Scale [8]). The state level represents the rate of change of perceived fatigability during a fatiguing task (e.g., measured by the Visual Analog Scale and Rated Perceived Exertion) [6].

Fatigue is an important concept in today’s rehabilitation care, because fatigue is a strong predictor of functional disability [1-3, 9], and as such a barrier for functioning and physical activities in people with chronic diseases [10-15]. Therefore, fatigue might limit the ability to optimally benefit from rehabilitation programmes in terms of successfully attaining a physically active lifestyle, freedom of movement and mobility, participation, and health-related quality of life (HR-QoL) [16-18]. Physical activity has health-stimulating effects, may improve fitness, is crucial for participation, mobility and HR-QoL, and is strongly recommended for people with chronic diseases [19-21]. Improving HR-QoL is one of the overarching dimensions in today's rehabilitation practice, often viewed as the optimal goal in rehabilitation and health care [22].

Fatigue is a strong contributor to consequences of disease on disability, health and physical functioning. To identify the extent of this problem, it is important to ascertain the prevalence and intensity of fatigue in those diseases, and to study the association between fatigue and physical activity, as well as with HR-QoL. However, comparing the current literature on fatigue is a major challenge due to the wide variety in definitions of fatigue used, and the large overlap among different definitions (e.g. motor, mental, peripheral, and central fatigue) [6], often lacking a clear conceptual framework. Although fatigue is a commonly reported symptom in diseases with a large impact on daily life, it is still an elusive concept. With the review by Enoka and Duchateau (2016) [23] in which they make a distinction between fatigue and fatigability such a framework has become available (figure 1). The operationalisation of fatigue towards fatigability has the major advantage of quantification. Fatigability is defined in the ICF model as "the susceptibility to fatigue at any level of exertion" [5]. The recently proposed taxonomy identifies two types of fatigability: perceived fatigability and performance fatigability [6, 23] (figure 1). Perceived fatigability is the initial value or the rate of change in sensations that regulate the integrity of the performer [23], and depends on the psychological state of the performer and the physiological capacity of the body to maintain homeostasis (figure 1) [6]. Performance fatigability is the decline in an objective measure of performance over a discrete period [23], including reductions in muscle contraction force (e.g. maximal voluntary contraction [MVC]), and limitations in the muscle capacity (N; Nm) during an ongoing task (e.g. the time to complete a prescribed task [s], and the decline in power production [W]).

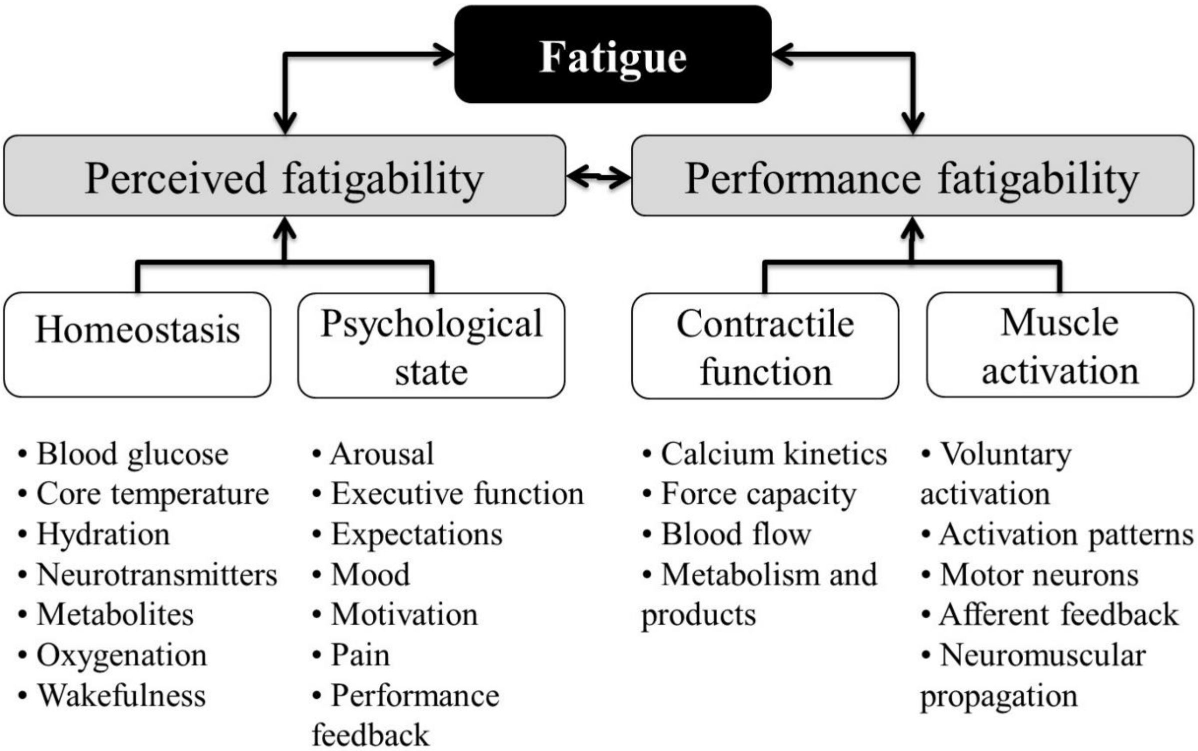


Figure 1 Two-domain concept of fatigue: proposed taxonomy of Kluger et al. (2013), adapted by Enoka and Duchateau (2016) [6, 23]

This proposed taxonomy of fatigue and fatigability allows to potentially cluster previous literature on fatigue and fatigability into the domains perceived fatigue (trait level), perceived fatigability (state level) and performance fatigability [6, 23]. This will help systemizing, integrating, as well as clarifying and understanding scientific knowledge on fatigue and fatigability. Although extensive research has been carried out on fatigue in people with physical disabilities and/or chronic diseases, including many literature reviews [23-25], there has been no literature review taking a broader approach, overarching different diseases. In addition, this narrative review opens up and connects with the notions of functional recovery and rehabilitation within the framework of the ICF [5].

With this narrative review we attempt to advance the understanding and consequences of symptoms of fatigue in a wide range of chronic diseases. This knowledge might allow to develop and/or optimize more focused (physical activity promotion) intervention programs targeting fatigue and bring future patients towards a physically active lifestyle and HR-QoL after rehabilitation (e.g., tailored counselling, activity pacing [26]). Therefore, the aim of this narrative review is to identify the prevalence and intensity of perceived and performance fatigability in people with chronic diseases during and after rehabilitation. Secondly, we explored how perceived and performance fatigability are associated with physical activity and HR-QoL. We hypothesized that people with chronic diseases would report increased levels of fatigue due to specific disturbances in the domains of perceived fatigability and/or performance fatigability (figure 1) [27]. We also expected higher levels of perceived and performance fatigability to have a negative association with daily physical activity and/or HR-QoL.

Methods

Search strategy

A narrative review of the literature was conducted by researcher BLS . A literature search was performed in the databases PubMed and PsycINFO until January 2019. The following keywords were combined to define the search term: ‘fatigue complications’ (MeSH term), ‘muscle fatigue/physiology’(MeSH term), ‘fatigue symptom’ or ‘fatigue complaint’, ‘adults’(MeSH term), ‘diseases categories’(MeSH term), ‘disabled persons’(MeSH term) or ‘chronic disease’(MeSH term), and ‘humans’(MeSH term). See Appendix A for a more precise search strategy.

Inclusion and exclusion criteria

Inclusion criteria were: (1) the study was written in English, and (2) the study reported on a target group of adults (>18 years) with physical disabilities and/or chronic diseases. In addition, this review excluded studies if: (1) the fatigue measurement was not the main outcome of the study or was not one of the main determinants of physical activity or HR-QoL, (2) the study aimed to investigate psychometric properties of a tool to measure perceived or performance fatigability, (3) the study included people with chronic fatigue syndrome (because we are interested in fatigue as a symptom instead of the disease), (4) the study aimed to investigate fatigue as an effect on an intervention or (pharmacological) treatment (because we are interested in fatigue not mediated by a treatment), and (5) the study aimed to investigate the relation between perceived and performance fatigability and another dependent variable than physical activity and/or HR-QoL (because a second aim of this narrative review was to explore how perceived and/or performance fatigability are associated with physical activity and HR-QoL).

Selection of studies

The initial literature search resulted in 988 articles. A flow chart of our literature search can be found in figure 2. A first selection of studies was made by screening the titles and/or abstract of the studies. At this stage, 830 articles were excluded based on the inclusion and exclusion criteria above mentioned. Secondly, after reading the full text of the study, 45 articles were excluded based on the inclusion and exclusion criteria. Eventually, 113 articles were included in this literature review (figure 2).

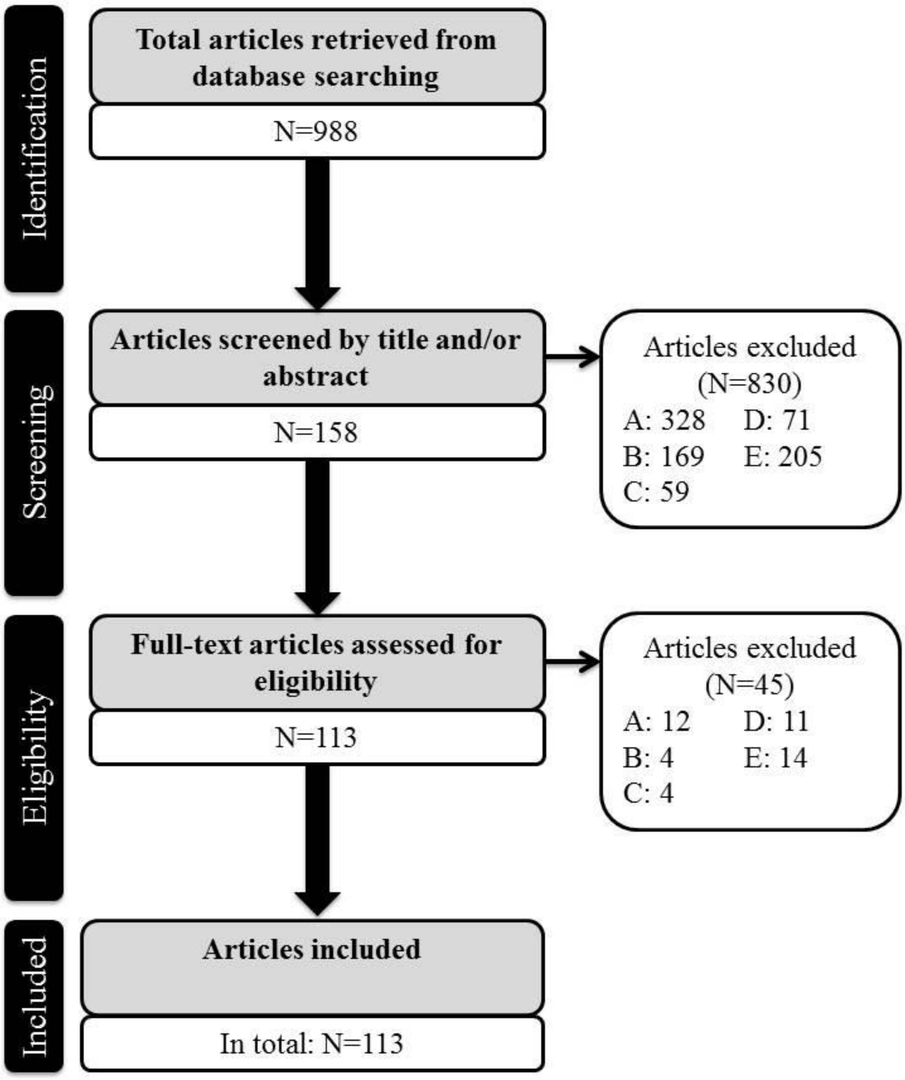


Figure 2 Flow diagram of the literature search and the number of articles (N) after each stage. Articles excluded based on (A) study population, (B) not reporting on fatigue symptoms, (C) investigating psychometric properties of a tool to measure fatigue, (D) investigating fatigue as an effect on an intervention or pharmacological treatment, and (E) investigating the relation between fatigue and other variable than physical activity and/or HRQoL.

Description of perceived and performance fatigability

Findings of the included articles in this narrative review were presented in table 1, including characteristics of the study design, the study population (e.g. age and sex), perceived or performance fatigability (including trait or state variable and frequency). Different measurement tools have been used to assess perceived or performance fatigability. Therefore, to better compare the intensity of perceived and performance fatigability measured with a large variety of questionnaires and muscle activity tests, we have visualized the different outcome measures on a self-designed scale (table 1). The circle marker indicated the fatigue intensity for the study group and the triangle indicated the fatigue intensity for the control group if applicable. The closed marker indicated pre-test and the open marker indicated post-test, if applicable. The notation of the intensity of fatigue was presented below the scale line for the study group and above the scale line for the control group.

Results

General description

All 113 included articles are categorized according to the disease of the study population in table 1. Characteristics of the included articles are presented in table 1. From the included articles 37% was cross-sectional, 34% experimental, 13% descriptive, 13% a cohort study, and 4% qualitative (not in table). The included articles reported on study populations with on average 45% (range from 0% to 100%) male participants. Seven studies included only male participants and thirteen studies included only female participants. The study populations comprised individuals of an average age of 49 years, ranging from 24 to 72 years. The studies investigated perceived and/or performance fatigability among several diseases, with most studies reporting on fatigue in multiple sclerosis (MS) (number of articles [N]=14), cancer (N=9), spinal cord injury (N=7), Parkinson's disease (N=7) and fibromyalgia (N=5).

From the 113 included articles, 56 studies reported only on perceived fatigability, 41 studies only reported on performance fatigability and 16 studies reported on perceived as well as on performance fatigability (table 1). Most studies reporting on perceived fatigability assessed it at a trait level (95%), and 5% at a state level. Only 13% of the included articles reported on perceived fatigability associated with physical activity, while 28% reported on perceived fatigability associated with HR-QoL. No articles were found reporting on the association between performance fatigability and physical activity or HR-QoL.

Firstly, we will summarize the main results of this narrative review regarding the prevalence of fatigue, as well as the intensity of fatigue for both perceived and/or performance fatigability in several diseases. Secondly, we will present how perceived fatigability is associated with physical activity and HR-QoL.

Prevalence of perceived and/or performance fatigability in several diseases

Table 1 gives an overview of the percentages of persons with a certain disease that complain about fatigue. An indication of the level of fatigue is also presented, often in relation to values obtained by control participants.

Cardiovascular diseases

People with cardiovascular diseases experience high levels of perceived fatigability [28-30] (table 1), with women reporting higher levels, and more women reporting clinically meaningful levels of perceived fatigability (Fatigue Symptom Inventory (FSI) Interference Scale score ≥3) compared with men [28]. The perceived fatigue intensity ranged from 2.9 [29] to 3.8

[28] on a scale from 0 to 10 (FSI). More than half of the people with cardiovascular diseases reported perceived fatigability on 3.5 days a week (FSI) [28].

Measures of performance fatigability (quadriceps MVC, twitch force and voluntary muscle activation) in people with cardiovascular diseases did not significantly differ from healthy adults [31].

Pulmonary diseases

High levels of perceived fatigability were found in people with chronic obstructive pulmonary disease (COPD) [33, 34]. Performance fatigability was an important limiting factor in people with COPD during exercise [35, 36]. Greater performance fatigability was found in people with COPD compared to healthy adults [37, 38], while in cystic fibrosis performance fatigability and muscle endurance were similar compared to controls [39].

Liver diseases

Perceived fatigability was the most commonly reported symptom (97%) in people with chronic hepatitis C virus [40]. The average intensity of perceived fatigability ranged from 33 [41] to 36 [42] in people with primary biliary cirrhosis, and was 78 [40] in people with chronic hepatitis C virus on a scale from 0 to 160 (Fatigue Impact Scale) (table 1). No studies were found on performance fatigability in people with liver diseases.

Diabetes

High perceived fatigability was found in women with type II diabetes, with an intensity of 13 (±5) on the Multidimensional Fatigue Inventory-20 ranging from 4 to 20 [43]. Perceived fatigability was, however, not associated with fasting blood glucose levels [43], representing ‘homeostasis’ of perceived fatigability (see also figure 1). Measures of performance fatigability (changes in conduction velocity and motor unit discharge frequency) were significantly larger in people with diabetes type I compared to healthy adults [44]. In people with type II diabetes, performance fatigability (quadriceps muscle) was significantly larger in terms of reductions in power during a fatiguing task and reduced MVC torque after the fatiguing task. However, similar voluntary muscle activation was found compared to healthy controls [45].

Other organ diseases

Perceived fatigability is a common and distressful symptom in daily life for people with organ diseases, such as renal disease [46, 47], inflammatory bowel disease [48, 49], kidney disease [47], and Crohn’s disease [49, 50]. Perceived fatigability in people with kidney disease and renal disease ranged from 34 [47] to 39 [46] on a scale from 0 to 52 (Functional Assessment of Chronic Illness Therapy Fatigue Scale) (table 1), and was prevalent in 54% of people with inflammatory bowel disease, whereof 11% indicating severe perceived fatigability [49].

Although, maximum muscle force was decreased in people with sepsis and multi-organ failure, no difference was found in performance fatigability compared to healthy adults [51]. Similar results were obtained in people with sickle cell disease [52]; MVC was reduced, but performance fatigability was comparable to healthy controls. Both increased perceived and performance fatigability was observed in people with Crohn’s disease compared with healthy adults during MVCs of the knee extensors [50]. Measures of perceived and performance fatigability showed a significant association (r=0.52), people with higher levels of perceived fatigue demonstrated more performance fatigue.

Perceived fatigability in people with sarcoidosis in clinical remission is a frequent symptom and can be characterized as a severe and long-lasting problem. Of the total study population, 76% perceived severe fatigability during the onset and active phase of the sarcoidosis and 56% perceived that this fatigability persisted[53].

Neurological diseases

Perceived fatigability is very common in people with Parkinson's disease and it is one of the three most disabling symptoms [14]. The prevalence of perceived fatigability (Fatigue Severity Scale [FSS] score ≥4) in people with Parkinson's disease varied from 34% [54], 45% [55], 59% [56], 70% [57] to 76% [14]. Using a cut-off score of five (FSS score ≥5), the prevalence of perceived fatigability in people with Parkinson's disease was 69%, which is comparable to that in people with spinocerebellar ataxia. Perceived fatigability was classified in nearly 70% of the people among their three most disabling symptoms [58]. Performance fatigability in people with Parkinson's disease was high (during a continuous, maximal, isometric forearm flexion), often asymmetric and more noticed on the side more affected by the disease [59, 60].

The intensity of perceived fatigability in people after stroke was 32±12 on the Modified Fatigue Impact Scale (range: 0-84) [61]. People post-stroke reported higher levels of perceived fatigability [62], and higher levels of performance fatigability were observed compared with healthy adults [63]. Performance fatigability was significantly greater in the paretic limb than in the non-paretic limb [62].

People with spinal cord injury (SCI) had significantly and clinically elevated levels of perceived fatigability compared to able-bodied adults [64]. The prevalence of perceived fatigability in people with SCI was more than 50% [64] and the perceived intensity of fatigue was 4±3 on a scale from 0 to 10 [65]. Also the performance fatigability was significantly higher in people with SCI compared with healthy adults during MVC [66]. Contradictory findings were found in people with SCI showing more performance fatigability (lower fatigue index) [67], or less performance fatigability (higher fatigue index) [68] compared with healthy adults during repetitive muscle contractions. Poor recovery in the quadriceps after electrically stimulated contractions in people with SCI indicated that they are more susceptible to performance fatigability than healthy adults [69]. In addition, no significant differences in performance fatigability could be observed between people with SCI early in rehabilitation, trained and untrained people with SCI [70].

In people with multiple sclerosis (MS), high levels of perceived fatigability were found [71-77]. People with MS had greater performance fatigability compared with healthy adults [73, 75-81]. In contrast, two studies did not find differences in performance fatigability between people with MS and healthy adults [81, 82]. Already at an early stage of MS (clinically isolated syndrome), perceived fatigability is a very common symptom with a severity similar to people with MS [83]. Almost half of them (47%) suffer from perceived fatigability and performance fatigability at this early stage of clinically isolated syndrome [84].

Performance fatigability was significantly higher in people with amyotrophic lateral sclerosis (ALS) compared with healthy adults [85, 86]. However, no studies were included reporting on perceived fatigability in people with ALS.

Perceived fatigability was on average 33±13, determined with the Functional Assessment of Chronic Illness Therapy Fatigue Scale (FACIT-F), in adults with neuromyelitis optica spectrum disorder [87]. Perceived fatigability seemed to be a common symptom in this population with a prevalence of 71% [87].

In people with post/prior-poliomyelitis [88, 89] and people with Guillain-Barre syndrome [90] no significant difference in performance fatigability (MVC) during the fatigue protocol was found [88, 90]. Performance fatigability, in terms of voluntary activation, in people with poliomyelitis was significantly different compared with healthy adults [89]. In people with post-polio syndrome, no significant differences were found in performance fatigability (maximal voluntary ventilation) compared with healthy controls [91].

Adults with spastic bilateral cerebral palsy were severely affected by perceived fatigability (FSS was 4.4 ± 1.3 [mean ±SD]).

The prevalence of perceived fatigability in people with chronic headache was 70% with an intensity of 4.1 ± 3.3 (mean ±SD) on the VAS scale ranging from 1 to 10, with highest perceived fatigability in women [92] (table 1). Similar findings were found in people with migraine (FSS was 3.6 ± 1.5 [mean ±SD]) [93].

People with neuromuscular diseases experienced a higher level of perceived fatigability than healthy adults [94-96]. People with muscular dystrophy had an average perceived fatigability over the past week of 5.0 on a scale between 0 and 10 [97]. Perceived fatigability was reported in 53% of people with non-dystrophic myotonia [98], and in more than 90% of people with myotonic dystrophy [99]. In people with neuromuscular diseases greater performance fatigability was found compared with healthy adults during a sustained MVC protocol [94]. In contrast, people with myotonic dystrophy showed similar performance fatigability compared with healthy adults [100]. People with myasthenia gravis showed performance fatigability in both arm movement test (not in table 1) and 6-minute walk test (in table 1), but that did not correlate with perceived fatigability scores [96].

Cancer

The prevalence of perceived fatigability among people with cancer varied between 15% [104], 22% [103], 50% [101], 56% [102], and 57% [103] (table 1). People with cancer reported frequent perceived fatigability, whereof 86% reported having at least two weeks of perceived fatigability in the past month [101]. The occurrence of perceived fatigability was high in both people with breast and prostate cancer [105], but people with breast cancer reported significantly higher occurrence rates during the evening and morning compared to people with prostate cancer [105]. Also, performance fatigability was higher in people with cancer compared with healthy adults [106].

Perceived fatigability seems to be a chronic symptom among cancer survivors. A total of 74% of cancer survivors reported perceived fatigability, with 57% experiencing it daily [107]. In lung cancer, almost half of the people with cancer reported perceived fatigability during five years after diagnosis [108]. The prevalence of chronic perceived fatigability in lymphoma survivors was 27% [109].

Immunological disease

The prevalence of a moderate level of perceived fatigability in men with human immunodeficiency virus (HIV) was 98% with an intensity of 2 on a scale from 1 to 3 [110] and the intensity of perceived fatigability in women with HIV was 43 (± 23) on a scale from 0 to 130 (Fatigue Symptom Inventory (FSI)) [111]. No studies were found on performance fatigability in people with HIV.

Elevated levels of perceived fatigability were found during the day in people with primary Sjögren syndrome, systematic lupus erythematosus [112, 113] and rheumatoid arthritis [113]. In people with systematic lupus erythematosus, 95% reported perceived fatigability, which was variable in terms of severity and frequency [114].

High intensity perceived fatigability was reported in women with fibromyalgia [115, 116]. The severity of fatigue in people with fibromyalgia was comparable with the fatigue among people with rheumatoid arthritis [116], the prevalence in people with rheumatoid arthritis ranging from 65% [117] to 81% [118] (table 1). However, people with fibromyalgia showed similar performance fatigability (MVC of the quadriceps, and EMG) compared with healthy adults [125, 126].

Musculoskeletal disorders

No studies were found reporting on perceived fatigability among people with (chronic) neck pain. However, high performance fatigability was found in the superficial cervical flexor muscles ipsilateral to the side of pain [119]. Overall, there is greater performance fatigability of the superficial cervical flexors in people with neck pain compared with healthy adults [120]. In contrast, performance fatigability did not differ on neck muscle endurance between people with neck pain and healthy adults [121].

In people with symptomatic femoroacetabular impingement [122], people with chronic ankle instability [123], and people with thoracic outlet syndrome [124] the performance fatigability did not differ compared with healthy adults.

Severe perceived fatigability was least prevalent in people with osteoarthritis (35%) and most prevalent in people with fibromyalgia (82%) [117]. One out of every two persons with a rheumatic disease is severely fatigued [117]. Most people with knee or hip osteoarthritis indicated that they had experienced notable perceived fatigability [127]. People reported perceived fatigability intensity of 31 (± 9) on a scale from 0 to 52 [127]. Also, the performance fatigability was higher in people with knee osteoarthritis compared with healthy adults during repetitive muscle contractions [128].

Perceived fatigability was very common in people with severe ankylosing spondylitis with severe functional impairment [129], with a prevalence ranging from 40% [130] to 60% [129] and high levels of performance fatigability (MVC, ankle muscle) [131].

Association between perceived fatigability and physical activity

Fifteen studies investigated the association between perceived fatigability and physical activity, including aspects such as activities of daily living, leisure-time activities and occupational physical activities. Physical activity was measured with self-reported questionnaires, interviews or accelerometers. Diseases in which perceived fatigability was related to reduced physical activity were diabetes ($r=-.28$, $p<.05$) [43], ankylosing spondylitis [129, 130], cancer [108, 109, 132], rheumatoid arthritis[118, 133] ($r=.21$, $p=.02$ [118]), systemic lupus erythematosus[112, 114] ($r=-.40$, $p<.001$ [112]), and sarcoidosis [53]. In contrast, one study did not find a significant association between the severity of perceived fatigability and reductions in objectively measured physical activity in people with cancer[102].

Perceived fatigability was one of the top ten barriers that often interfered with exercise participation in people with cancer[107]. Other barriers of physical activity were mainly health-related or environmental factors. Furthermore, managing perceived fatigability was also one of the four motivators of being physically active[107]. Improving physical activity reduced perceived fatigability in people with cancer[132]. There were no studies investigating the association between performance fatigability and physical activity.

Association between perceived fatigability and HR-QoL

Thirty-one articles reported on the association between perceived fatigability and HR-QoL. HR-QoL was mostly assessed with a questionnaire, such as the Medical Outcome Study Short Form 36 (SF-36) [134] with the separated constructs physical health, mental health, and general health. All 31 studies found a major negative association of perceived fatigability with HR-QoL in several diseases: COPD (odds ratio:.91, 95% confidence interval:.89-.93) [33], Parkinson's disease [14, 54, 56] (r=.74, p<.05 [56]; r=-.49, p<.01 [54]), SCI [64, 65], other neurological diseases [58, 97] (r=-.37, p<.001 [97]), cancer [102, 104, 107, 108, 132, 135, 136], cardiovascular diseases [28, 29] (r=-.39, p<.001 [29]), ankylosing spondylitis [129, 130], fibromyalgia [115, 116], other musculoskeletal diseases [98, 127], HIV [40, 110, 111], neuromyelitis optica spectrum disorder ($r_{physicalComponent}$=.59, p<.001; $r_{mentalComponent}$=.52, p=.002) [87], inflammatory bowel diseases (odds ratio:.82, 95% confidence interval:.74-.93) [49], migraine [93], and renal diseases (r=.51, p<.001 [46], and r=.81, p<.001 [47]). Other studies found significantly lower levels of HR-QoL in fatigued persons compared with non-fatigued persons, e.g. in sarcoidosis [53] and COPD [34]. In contrast, in people with SCI perceived fatigability was not significantly related to worse scores on 'physical functioning' [65].

Discussion

In this narrative review, we sought (1) to identify the prevalence and intensity of fatigue in terms of perceived and performance fatigability in a wide range of diseases, and (2) to determine how perceived and performance fatigability are associated with physical activity and health-related quality of life (HR-QoL) in people with physical disabilities and/or chronic diseases. We classified disease populations according to the ICD-11 on symptoms of fatigue and shifted to the ICF model [5] and beyond, where we found fatigue to play an important role in in physical activity and/or HR-QoL. Both perceived and performance fatigability are strong contributors to consequences of disease on disability. Also, perceived fatigability was negatively associated with measures of physical activity and HR-QoL.

Firstly, this narrative review identified both high perceived and performance fatigability in a wide range of diseases, including diabetes, Parkinson's disease, SCI, MS, ankylosing spondylitis, cancer, myasthenia gravis, and knee/hip osteoarthritis. In contrast, we found disease populations reporting high perceived fatigability but normal patterns (like healthy adults) of performance fatigability, e.g. in cardiovascular diseases, organ diseases, myotonic dystrophy and fibromyalgia (table 1). Probably, based on the prevalence of either or both perceived and performance fatigability in populations with different diseases, tailored treatments in rehabilitation practice and/or health care are required in order to reduce the perceived and/or performance fatigability, albeit through pharmacological or non-pharmacological treatment (including tailored counselling, activity pacing, self-management, behavioural therapy) [21, 137-140].

Furthermore, perceived fatigability was found to be associated with lower levels of physical activity in diabetes, ankylosing spondylitis, cancer, rheumatoid arthritis, systemic lupus erythematosus, renal disease and sarcoidosis. These findings further support the idea that fatigue is a barrier to participate in physical activity in people with physical disabilities and/or chronic diseases [15, 141]. In turn, improving physical activity reduced perceived fatigability in people with cancer [132] and reduced performance fatigability in people with MS [75], which strengthens the importance of rehabilitation programmes aiming to promote fitness and a physically active lifestyle. Furthermore, perceived fatigability has been found to consistently be associated with a lower HR-QoL in a wide array of diseases: Parkinson's disease, SCI, other neurological diseases, cancer, cardiovascular diseases, ankylosing spondylitis, fibromyalgia, other musculoskeletal diseases, HIV, sarcoidosis, inflammatory bowel diseases, and renal diseases (table 1). Thus, reducing symptoms of fatigue is assumed to improve HR-QoL in people with physical disabilities and/or chronic diseases.

This narrative review used the proposed unified taxonomy of Enoka and Duchateau (2016), adapted from the study of Kluger et al. (2013) [6, 23], which was a relevant method to cluster research on fatigue and fatigability in people with physical disabilities and/or chronic diseases into perceived or performance fatigability. More than half of the included studies reported on perceived fatigability, possibly because perceived fatigability is assessed with questionnaires and thus more easy and less expensive. Some questionnaires were commonly used in specific disease populations, for example the validated functional assessment of chronic illness therapy-fatigue, for people with organ diseases [142]. In studies on perceived fatigability in people with liver diseases, only the validated Fatigue Impact Scale was used as assessment tool [143]. We agree with Elbers et al. (2012) that questionnaires that include both general and disease-specific aspects of perceived fatigability specifically developed for one disease population are valuable [144]. Clearly, disease-specific questionnaires make it hard to compare research in different disease populations. Therefore, we recommend researchers to add a more general (non disease-specific) questionnaire assessing perceived fatigability, to enable comparison reported intensity of perceived fatigability across disease populations. On another note, while cut-off scores to separate persons on basis of their score of perceived fatigability in fatigued or non-fatigued individuals differ across studies, this requires international debate and consensus-based decisions.

Most of the included studies on performance fatigability assessed performance fatigability during sustained or repeated motor tasks on basis of a force parameter, e.g. decline in MVC, which is a very common and valid assessment tool in exercise sciences [145]. Also, performance fatigability was mainly assessed in a muscle which was most affected by the disease, which could explain some of the inconsistencies in the findings. Besides, performance fatigability is known to be task and muscle specific [146], which again requires international consensus in the context of clinical assessment.

A few limitations of this narrative review need to be considered. Firstly, it was hard to discuss the results of the prevalence and intensity of both perceived and performance fatigability for all included studies together, due to the wide range of different diseases and the high variability in measurement tools to assess fatigue. Therefore, we reported the intensity of perceived fatigability on a self-designed scale in the results table, which gave a better overview of the intensity of perceived fatigability. Furthermore, questionnaires which assess fatigue were mostly specific for one disease population and reported levels of perceived fatigability on a wide variation of scales. For example, the FSS was used in a wide range of diseases. However, caution is warranted when comparing FSS scores directly across disease populations using the FSS 7-items version, where different item hierarchies were found across disease populations [147]. Consequently, some results from the included articles reporting on perceived fatigability, and its prevalence and intensity were contradictory in the same disease population (table 1). This highlights the large variety in questionnaires used and/or the disease status potentially expressed in the large heterogeneity in fatigue among people with physical disabilities and/or chronic diseases. This problem was already addressed in research among healthy older adults [148]. They developed the Pittsburgh Fatigability scale, which is a valid and reliable measurement tool to assess perceived fatigability in older adults [148]. Further research should investigate if the Pittsburgh Fatigability scale is also suitable for people with physical disabilities and/or chronic diseases. Also, previous research found that perceived fatigability scales are mostly developed for older adults [149]. Moreover, no gold standard yet exist for measuring perceived fatigability [149].

This narrative review describes just a limited part of a multidisciplinary and complex phenomenon of fatigue and fatigability in people with physical disabilities and/or chronic diseases. This review excluded articles reporting on fatigability included in a cluster of symptoms (e.g. pain, depression, insomnia and mood disturbances) [150, 151], or fatigability during and/or after surgery or treatment/interventions, such as in people with cancer during and after chemotherapy, which is also a disease population suffering from high levels of fatigue. Furthermore, we did not take into account factors such as personal characteristics (e.g. age, sex, body weight), depression [150, 151], sleep [152-154], or pain [151, 155, 156], which might be confounders in the association between on the one hand perceived and performance fatigability and on the other hand physical activity and HR-QoL.

This narrative review gives a valuable overview of fatigue and fatigability in people with physical disabilities and/or chronic diseases for rehabilitation practice, health care and science. Measures for perceived and/or performance fatigability should be more systematically introduced in rehabilitation and health care in order to more profoundly understand these limiting barriers of functioning as well as how to optimize individually tailored treatments. The prevalence and intensity of either or both perceived and performance fatigability in disease populations are valuable in developing or optimizing programmatic interventions targeting fatigue towards a physically active lifestyle and HR-QoL after rehabilitation. Several included studies emphasised the need to offer non-pharmacological programmes (e.g. tailored counselling, activity pacing, behavioural therapy or self-management) to give advice on managing fatigue during and after rehabilitation in people with ankylosing spondylitis [129], fibromyalgia [116], cancer [104, 107], rheumatic diseases [113] and SCI [65]. Activity pacing techniques as self-management contain among others setting targets, prioritizing activities, adjusting activity level to their reduced energy capacity, budgeting energy, resting and/or sleeping during the day, avoiding stress, getting help with chores and using assistive devices and must be better understood in populations with chronic diseases [48, 127, 130, 157]. There were similarities regarding managing daily activities in persons with ankylosing spondylitis, fibromyalgia, multiple sclerosis and stroke. The reported high levels of perceived and/or performance fatigability in disease population warrant increased clinical awareness and may allow professionals to offer adequate information and methods of managing fatigue [157]. Abonie et al. already concluded in their meta-analysis that both perceived fatigability severity and levels of physical activity improved after activity pacing interventions [158]. However, more research is needed to develop appropriate interventions focussing on activity pacing as a solution to the high prevalence of perceived fatigability in several disease populations.

A scientific implication is that we recommend researchers in the area of fatigue to measure both perceived and performance fatigability in a standardised consensus-based manner. This narrative review found sixteen studies that assessed both perceived and performance fatigability in several disease populations, which were relevant in understanding the concept of fatigue in different disease populations. Firstly, these studies provided insight in the association between perceived and performance fatigability in people with Crohn's disease, people with MS and people with fibromyalgia. We see that several studies failed to find a significant association between perceived and performance fatigability [72, 73, 76, 77], in contrast to studies who did find a significant association [75]. This apparent controversy needs further experimental research. Secondly, these studies provided insight into disease populations that reported high perceived fatigability but normal performance fatigability, e.g. in neuromuscular diseases and fibromyalgia. In addition, we recommend researchers in the area of fatigue to specify which concept of fatigue they measured (perceived and/or performance fatigability), and to specify the measurement tool they used to assess fatigue.

Considerable gaps in knowledge remain to be studied on perceived fatigability in people with ALS, COPD and chronic neck pain, and on performance fatigability in people with liver diseases and HIV. Also, in people with SCI much research has already been done on performance fatigability and little on perceived fatigability, while in people with cancer much research has been done on perceived fatigability and little on performance fatigability. In addition, literature on perceived and performance fatigability in several disease populations is lacking, such as in people with viral infections (e.g. Pfeiffer's disease, Epstein–Barr virus), bacterial infections (e.g. tuberculosis, Lyme disease), and metabolic disorders (e.g. Cushing's syndrome, hyper- and hypothyroidism).

Conclusion

Literature showed that a broad range of diseases were associated with greater levels of perceived and performance fatigability. Higher levels of perceived fatigability in turn were associated with lower levels of physical activity and/or lower HR-QoL. These findings indicate the urgent need for further research on fatigue, factors influencing fatigue, and rehabilitation programmes aiming to reduce fatigue, to promote physical activity and HR-QoL. Until then, clinicians should take the above concluding notions into account in their daily practice.

Acknowledgements

This review was not supported by sources of funding. The authors declare no potential conflicts of interest that are directly relevant to the content of this review.

References

1. Whitehead L. The measurement of fatigue in chronic illness: A systematic review of unidimensional and multidimensional fatigue measures. J Pain Symptom Manage. 2009 Jan;37(1):107-28.

2. Swain MG. Fatigue in chronic disease. Clin Sci (Lond). 2000 Jul;99(1):1-8.

3. De Groot MH, Phillips SJ, Eskes GA. Fatigue associated with stroke and other neurologic conditions: Implications for stroke rehabilitation. Arch Phys Med Rehabil. 2003 Nov;84(11):1714-20.

4. Scully JL. What is a disease? EMBO Rep. 2004 07;5(7):650-3.

5. World Health Organisation (Geneva)., World Bank (Washington D. World report on disability. Geneva; Washington, DC: World Health Organization; World Bank; 2011.

6. Enoka RM, Duchateau J. Translating fatigue to human performance. Med Sci Sports Exerc. 2016 Nov;48(11):2228-38.

7. Fleurke A, Goossen W, Hoijtink E, Van der Kooij J, Vlastuin M. Fatigue severity scale (FSS). 2004.

8. Fisk JD, Ritvo PG, Ross L, Haase DA, Marrie TJ, Schlech WF. Measuring the functional impact of fatigue: Initial validation of the fatigue impact scale. Clin Infect Dis. 1994 Jan;18 Suppl 1:S79-83.

9. Murphy SL, Lyden AK, Clary M, Geisser ME, Yung RL, Clauw DJ, et al. Activity pacing for osteoarthritis symptom management: Study design and methodology of a randomized trial testing a tailored clinical approach using accelerometers for veterans and non-veterans. BMC Musculoskelet Disord. 2011 Aug 2;12:177,2474-12-177.

10. Veldhuijzen van Zanten JJ, Rouse PC, Hale ED, Ntoumanis N, Metsios GS, Duda JL, et al. Perceived barriers, facilitators and benefits for regular physical activity and exercise in patients with rheumatoid arthritis: A review of the literature. Sports Med. 2015 Oct;45(10):1401-12.

11. Keogh JW, Patel A, MacLeod RD, Masters J. Perceived barriers and facilitators to physical activity in men with prostate cancer: Possible influence of androgen deprivation therapy. Eur J Cancer Care (Engl). 2014 Mar;23(2):263-73.

12. Newitt R, Barnett F, Crowe M. Understanding factors that influence participation in physical activity among people with a neuromusculoskeletal condition: A review of qualitative studies. Disabil Rehabil. 2016;38(1):1-10.

13. Crane PB, Abel WM, McCoy TP. Fatigue and physical activity after myocardial infarction. Biol Res Nurs. 2015 May;17(3):276-84.

14. Dogan VB, Koksal A, Dirican A, Baybas S, Dirican A, Dogan GB. Independent effect of fatigue on health-related quality of life in patients with idiopathic parkinson's disease. Neurol Sci. 2015 Dec;36(12):2221-6.

15. Martin Ginis KA, Ma JK, Latimer-Cheung AE, Rimmer JH. A systematic review of review articles addressing factors related to physical activity participation among children and adults with physical disabilities. Health Psychol Rev. 2016 Dec;10(4):478-94.

16. Belza BL. Comparison of self-reported fatigue in rheumatoid arthritis and controls. J Rheumatol. 1995 Apr;22(4):639-43.

17. Nijs J, Paul L, Wallman K. Chronic fatigue syndrome: An approach combining self-management with graded exercise to avoid exacerbations. J Rehabil Med. 2008 Apr;40(4):241-7.

18. Clark LV, White PD. The role of deconditioning and therapeutic exercise in chronic fatigue syndrome (CFS). Journal of Mental Health. 2009;14(3):237-252.

19. Haskell WL, Lee IM, Pate RR, Powell KE, Blair SN, Franklin BA, et al. Physical activity and public health: Updated recommendation for adults from the american college of sports medicine and the american heart association. Circulation. 2007 Aug 28;116(9):1081-93.

20. Rimmer JH, Marques AC. Physical activity for people with disabilities. The Lancet. 2012;380(9838):193-195.

21. Rimmer JH, Chen MD, Hsieh K. A conceptual model for identifying, preventing, and managing secondary conditions in people with disabilities. Phys Ther. 2011 Dec;91(12):1728-39.

22. World Health Organization. World report on disability. Geneva, Switzerland: WHO Press; 2011.

23. Kluger BM, Krupp LB, Enoka RM. Fatigue and fatigability in neurologic illnesses: Proposal for a unified taxonomy. Neurology. 2013 Jan 22;80(4):409-16.

24. Daniels LA, Oerlemans S, Krol AD, van de Poll-Franse LV, Creutzberg CL. Persisting fatigue in hodgkin lymphoma survivors: A systematic review. Ann Hematol. 2013 Aug;92(8):1023-32.

25. van Langenberg DR, Gibson PR. Systematic review: Fatigue in inflammatory bowel disease. Aliment Pharmacol Ther. 2010 Jul;32(2):131-43.

26. Abonie US, Sandercock GRH, Heesterbeek M, Hettinga FJ. Effects of activity pacing in patients with chronic conditions associated with fatigue complaints: A meta-analysis. Disabil Rehabil. 2018 Nov 18:1-10.

27. Zijdewind I, Prak RF, Wolkorte R. Fatigue and fatigability in persons with multiple sclerosis. Exerc Sport Sci Rev. 2016 Oct;44(4):123-8.

28. Eckhardt AL, Devon HA, Piano MR, Ryan CJ, Zerwic JJ. Fatigue in the presence of coronary heart disease. Nurs Res. 2014 Mar-Apr;63(2):83-93.

29. Fink AM, Sullivan SL, Zerwic JJ, Piano MR. Fatigue with systolic heart failure. J Cardiovasc Nurs. 2009 Sep-Oct;24(5):410-7.

30. Plach SK, Heidrich SM, Jeske L. Fatigue representations in women with heart failure. Res Nurs Health. 2006 Oct;29(5):452-64.

31. Hopkinson NS, Dayer MJ, Antoine-Jonville S, Swallow EB, Porcher R, Vazir A, et al. Central and peripheral quadriceps fatigue in congestive heart failure. Int J Cardiol. 2013 Sep 10;167(6):2594-9.

32. Weiss K, Schar M, Panjrath GS, Zhang Y, Sharma K, Bottomley PA, et al. Fatigability, exercise intolerance, and abnormal skeletal muscle energetics in heart failure. Circ Heart Fail. 2017 Jul;10(7):10.1161/CIRCHEARTFAILURE.117.004129.

33. Stridsman C, Svensson M, Johansson Strandkvist V, Hedman L, Backman H, Lindberg A. The COPD assessment test (CAT) can screen for fatigue among patients with COPD. Ther Adv Respir Dis. 2018 Jan-Dec;12:1753466618787380.

34. Kentson M, Todt K, Skargren E, Jakobsson P, Ernerudh J, Unosson M, et al. Factors associated with experience of fatigue, and functional limitations due to fatigue in patients with stable COPD. Ther Adv Respir Dis. 2016 Oct;10(5):410-24.

35. Gagnon P, Saey D, Vivodtzev I, Laviolette L, Mainguy V, Milot J, et al. Impact of preinduced quadriceps fatigue on exercise response in chronic obstructive pulmonary disease and healthy subjects. J Appl Physiol (1985). 2009 Sep;107(3):832-40.

36. Saey D, Cote CH, Mador MJ, Laviolette L, LeBlanc P, Jobin J, et al. Assessment of muscle fatigue during exercise in chronic obstructive pulmonary disease. Muscle Nerve. 2006 Jul;34(1):62-71.

37. Allaire J, Maltais F, Doyon JF, Noel M, LeBlanc P, Carrier G, et al. Peripheral muscle endurance and the oxidative profile of the quadriceps in patients with COPD. Thorax. 2004 Aug;59(8):673-8.

38. Cannon DT, Coelho AC, Cao R, Cheng A, Porszasz J, Casaburi R, et al. Skeletal muscle power and fatigue at the tolerable limit of ramp-incremental exercise in COPD. J Appl Physiol (1985). 2016 Dec 1;121(6):1365-73.

39. Gruet M, Decorte N, Mely L, Vallier JM, Camara B, Quetant S, et al. Skeletal muscle contractility and fatigability in adults with cystic fibrosis. J Cyst Fibros. 2016 Jan;15(1):e1-8.

40. Goh J, Coughlan B, Quinn J, O'Keane JC, Crowe J. Fatigue does not correlate with the degree of hepatitis or the presence of autoimmune disorders in chronic hepatitis C infection. Eur J Gastroenterol Hepatol. 1999 Aug;11(8):833-8.

41. Biagini MR, Tozzi A, Milani S, Grippo A, Amantini A, Capanni M, et al. Fatigue in primary biliary cirrhosis: A possible role of comorbidities. Eur J Gastroenterol Hepatol. 2008 Feb;20(2):122-6.

42. Jones DE, Bhala N, Burt J, Goldblatt J, Prince M, Newton JL. Four year follow up of fatigue in a geographically defined primary biliary cirrhosis patient cohort. Gut. 2006 Apr;55(4):536-41.

43. Fritschi C, Quinn L, Hacker ED, Penckofer SM, Wang E, Foreman M, et al. Fatigue in women with type 2 diabetes. Diabetes Educ. 2012 Sep-Oct;38(5):662-72.

44. Almeida S, Riddell MC, Cafarelli E. Slower conduction velocity and motor unit discharge frequency are associated with muscle fatigue during isometric exercise in type 1 diabetes mellitus. Muscle Nerve. 2008 Feb;37(2):231-40.

45. Senefeld J, Magill SB, Harkins A, Harmer AR, Hunter SK. Mechanisms for the increased fatigability of the lower limb in people with type 2 diabetes. J Appl Physiol (1985). 2018 Aug 1;125(2):553-66.

46. Wang SY, Zang XY, Fu SH, Bai J, Liu JD, Tian L, et al. Factors related to fatigue in chinese patients with end-stage renal disease receiving maintenance hemodialysis: A multi-center cross-sectional study. Ren Fail. 2016;38(3):442-50.

47. Jhamb M, Liang K, Yabes J, Steel JL, Dew MA, Shah N, et al. Prevalence and correlates of fatigue in chronic kidney disease and end-stage renal disease: Are sleep disorders a key to understanding fatigue? Am J Nephrol. 2013;38(6):489-95.

48. Czuber-Dochan W, Dibley LB, Terry H, Ream E, Norton C. The experience of fatigue in people with inflammatory bowel disease: An exploratory study. J Adv Nurs. 2013 Sep;69(9):1987-99.

49. Villoria A, Garcia V, Dosal A, Moreno L, Montserrat A, Figuerola A, et al. Fatigue in out-patients with inflammatory bowel disease: Prevalence and predictive factors. PLoS One. 2017 Jul 27;12(7):e0181435.

50. van Langenberg DR, Della Gatta P, Warmington SA, Kidgell DJ, Gibson PR, Russell AP. Objectively measured muscle fatigue in crohn's disease: Correlation with self-reported fatigue and associated factors for clinical application. J Crohns Colitis. 2014 Feb;8(2):137-46.

51. Eikermann M, Koch G, Gerwig M, Ochterbeck C, Beiderlinden M, Koeppen S, et al. Muscle force and fatigue in patients with sepsis and multiorgan failure. Intensive Care Med. 2006 Feb;32(2):251-9.

52. Waltz X, Pichon A, Lemonne N, Mougenel D, Lalanne-Mistrih ML, Lamarre Y, et al. Normal muscle oxygen consumption and fatigability in sickle cell patients despite reduced microvascular oxygenation and hemorheological abnormalities. PLoS One. 2012;7(12):e52471.

53. Korenromp IH, Heijnen CJ, Vogels OJ, van den Bosch JM, Grutters JC. Characterization of chronic fatigue in patients with sarcoidosis in clinical remission. Chest. 2011 Aug;140(2):441-7.

54. Tu XJ, Hwang WJ, Ma HI, Chang LH, Hsu SP. Determinants of generic and specific health-related quality of life in patients with parkinson's disease. PLoS One. 2017 Jun 26;12(6):e0178896.

55. Tanaka K, Wada-Isoe K, Yamamoto M, Tagashira S, Tajiri Y, Nakashita S, et al. Clinical evaluation of fatigue in japanese patients with parkinson's disease. Brain Behav. 2014 Sep;4(5):643-9.

56. Gallagher DA, Lees AJ, Schrag A. What are the most important nonmotor symptoms in patients with parkinson's disease and are we missing them? Mov Disord. 2010 Nov 15;25(15):2493-500.

57. Goulart FO, Godke BA, Borges V, Azevedo-Silva SM, Mendes MF, Cendoroglo MS, et al. Fatigue in a cohort of geriatric patients with and without parkinson's disease. Braz J Med Biol Res. 2009 Aug;42(8):771-5.

58. Brusse E, Brusse-Keizer MG, Duivenvoorden HJ, van Swieten JC. Fatigue in spinocerebellar ataxia: Patient self-assessment of an early and disabling symptom. Neurology. 2011 Mar 15;76(11):953-9.

59. Ziv I, Avraham M, Michaelov Y, Djaldetti R, Dressler R, Zoldan J, et al. Enhanced fatigue during motor performance in patients with parkinson's disease. Neurology. 1998 Dec;51(6):1583-6.

60. Santos PC, Gobbi LT, Orcioli-Silva D, Simieli L, van Dieen JH, Barbieri FA. Effects of leg muscle fatigue on gait in patients with parkinson's disease and controls with high and low levels of daily physical activity. Gait Posture. 2016 Jun;47:86-91.

61. Obembe AO, Olaogun MM, Olalemi AE. Functional limitations due to fatigue among independently ambulant stroke survivors in osun, south-western nigeria. Physiother Res Int. 2015 Mar;20(1):54-9.

62. Knorr S, Ivanova TD, Doherty TJ, Campbell JA, Garland SJ. The origins of neuromuscular fatigue post-stroke. Exp Brain Res. 2011 Oct;214(2):303-15.

63. Rybar MM, Walker ER, Kuhnen HR, Ouellette DR, Berrios R, Hunter SK, et al. The stroke-related effects of hip flexion fatigue on over ground walking. Gait Posture. 2014 Apr;39(4):1103-8.

64. Wijesuriya N, Tran Y, Middleton J, Craig A. Impact of fatigue on the health-related quality of life in persons with spinal cord injury. Arch Phys Med Rehabil. 2012 Feb;93(2):319-24.

65. Alschuler KN, Jensen MP, Sullivan-Singh SJ, Borson S, Smith AE, Molton IR. The association of age, pain, and fatigue with physical functioning and depressive symptoms in persons with spinal cord injury. J Spinal Cord Med. 2013 Sep;36(5):483-91.

66. Pelletier CA, Hicks AL. Muscle fatigue characteristics in paralyzed muscle after spinal cord injury. Spinal Cord. 2011 Jan;49(1):125-30.

67. Klein CS, Hager-Ross CK, Thomas CK. Fatigue properties of human thenar motor units paralysed by chronic spinal cord injury. J Physiol. 2006 May 15;573(Pt 1):161-71.

68. Lin KH, Chen YC, Luh JJ, Wang CH, Chang YJ. H-reflex, muscle voluntary activation level, and fatigue index of flexor carpi radialis in individuals with incomplete cervical cord injury. Neurorehabil Neural Repair. 2012 Jan;26(1):68-75.

69. Mahoney E, Puetz TW, Dudley GA, McCully KK. Low-frequency fatigue in individuals with spinal cord injury. J Spinal Cord Med. 2007;30(5):458-66.

70. Mayer F, Billow H, Horstmann T, Martini F, Niess A, Rocker K, et al. Muscular fatigue, maximum strength an stress reactions of the shoulder musculature in paraplegics. Int J Sports Med. 1999 Oct;20(7):487-93.

71. Steens A, de Vries A, Hemmen J, Heersema T, Heerings M, Maurits N, et al. Fatigue perceived by multiple sclerosis patients is associated with muscle fatigue. Neurorehabil Neural Repair. 2012 Jan;26(1):48-57.

72. Sheean GL, Murray NM, Rothwell JC, Miller DH, Thompson AJ. An electrophysiological study of the mechanism of fatigue in multiple sclerosis. Brain. 1997 Feb;120 (Pt 2)(Pt 2):299-315.

73. Scheidegger O, Kamm CP, Humpert SJ, Rosler KM. Corticospinal output during muscular fatigue differs in multiple sclerosis patients compared to healthy controls. Mult Scler. 2012 Oct;18(10):1500-6.

74. Koch M, Mostert J, Heerings M, Uyttenboogaart M, De Keyser J. Fatigue, depression and disability accumulation in multiple sclerosis: A cross-sectional study. Eur J Neurol. 2009 Mar;16(3):348-52.

75. Wolkorte R, Heersema DJ, Zijdewind I. Reduced dual-task performance in MS patients is further decreased by muscle fatigue. Neurorehabil Neural Repair. 2015 Jun;29(5):424-35.

76. Iriarte J, de Castro P. Correlation between symptom fatigue and muscular fatigue in multiple sclerosis. Eur J Neurol. 1998 Nov;5(6):579-85.

77. Sharma KR, Kent-Braun J, Mynhier MA, Weiner MW, Miller RG. Evidence of an abnormal intramuscular component of fatigue in multiple sclerosis. Muscle Nerve. 1995 Dec;18(12):1403-11.

78. de Haan A, de Ruiter CJ, van Der Woude LH, Jongen PJ. Contractile properties and fatigue of quadriceps muscles in multiple sclerosis. Muscle Nerve. 2000 Oct;23(10):1534-41.

79. Wolkorte R, Heersema DJ, Zijdewind I. Reduced voluntary activation during brief and sustained contractions of a hand muscle in secondary-progressive multiple sclerosis patients. Neurorehabil Neural Repair. 2016 May;30(4):307-16.

80. Skurvydas A, Brazaitis M, Andrejeva J, Mickeviciene D, Streckis V. The effect of multiple sclerosis and gender on central and peripheral fatigue during 2-min MVC. Clin Neurophysiol. 2011 Apr;122(4):767-76.

81. Hameau S, Bensmail D, Roche N, Zory R. Fatigability in patients with multiple sclerosis during maximal concentric contractions. Arch Phys Med Rehabil. 2017 Jul;98(7):1339-47.

82. de Ruiter CJ, Jongen PJ, van der Woude LH, de Haan A. Contractile speed and fatigue of adductor pollicis muscle in multiple sclerosis. Muscle Nerve. 2001 Sep;24(9):1173-80.

83. Runia TF, Jafari N, Siepman DA, Hintzen RQ. Fatigue at time of CIS is an independent predictor of a subsequent diagnosis of multiple sclerosis. J Neurol Neurosurg Psychiatry. 2015 May;86(5):543-6.

84. Kalron A, Achiron A, Dvir Z. Muscular and gait abnormalities in persons with early onset multiple sclerosis. J Neurol Phys Ther. 2011 Dec;35(4):164-9.

85. Kent-Braun JA, Miller RG. Central fatigue during isometric exercise in amyotrophic lateral sclerosis. Muscle Nerve. 2000 Jun;23(6):909-14.

86. Sanjak M, Konopacki R, Capasso R, Roelke KA, Peper SM, Houdek AM, et al. Dissociation between mechanical and myoelectrical manifestation of muscle fatigue in amyotrophic lateral sclerosis. Amyotroph Lateral Scler Other Motor Neuron Disord. 2004 Mar;5(1):26-32.

87. Seok JM, Choi M, Cho EB, Lee HL, Kim BJ, Lee KH, et al. Fatigue in patients with neuromyelitis optica spectrum disorder and its impact on quality of life. PLoS One. 2017 May 23;12(5):e0177230.

88. Sunnerhagen KS, Carlsson U, Sandberg A, Stalberg E, Hedberg M, Grimby G. Electrophysiologic evaluation of muscle fatigue development and recovery in late polio. Arch Phys Med Rehabil. 2000 Jun;81(6):770-6.

89. Allen GM, Gandevia SC, Neering IR, Hickie I, Jones R, Middleton J. Muscle performance, voluntary activation and perceived effort in normal subjects and patients with prior poliomyelitis. Brain. 1994 Aug;117 (Pt 4)(Pt 4):661-70.

90. Garssen MP, Schillings ML, Van Doorn PA, Van Engelen BG, Zwarts MJ. Contribution of central and peripheral factors to residual fatigue in guillain-barre syndrome. Muscle Nerve. 2007 Jul;36(1):93-9.

91. Shoseyov D, Cohen-Kaufman T, Schwartz I, Portnoy S. Comparison of activity and fatigue of the respiratory muscles and pulmonary characteristics between post-polio patients and controls: A pilot study. PLoS One. 2017 Jul 27;12(7):e0182036.

92. Spierings EL, van Hoof MJ. Fatigue and sleep in chronic headache sufferers: An age- and sex-controlled questionnaire study. Headache. 1997 Oct;37(9):549-52.

93. Seo JG, Park SP. Significance of fatigue in patients with migraine. J Clin Neurosci. 2018 Apr;50:69-73.

94. Schillings ML, Kalkman JS, Janssen HM, van Engelen BG, Bleijenberg G, Zwarts MJ. Experienced and physiological fatigue in neuromuscular disorders. Clin Neurophysiol. 2007 Feb;118(2):292-300.

95. Symonette CJ, Watson BV, Koopman WJ, Nicolle MW, Doherty TJ. Muscle strength and fatigue in patients with generalized myasthenia gravis. Muscle Nerve. 2010 Mar;41(3):362-9.

96. Jordan B, Mehl T, Schweden TLK, Menge U, Zierz S. Assessment of physical fatigability and fatigue perception in myasthenia gravis. Muscle Nerve. 2017 May;55(5):657-63.

97. Alschuler KN, Jensen MP, Goetz MC, Smith AE, Verrall AM, Molton IR. Effects of pain and fatigue on physical functioning and depression in persons with muscular dystrophy. Disabil Health J. 2012 Oct;5(4):277-83.

98. Trip J, de Vries J, Drost G, Ginjaar HB, van Engelen BG, Faber CG. Health status in non-dystrophic myotonias: Close relation with pain and fatigue. J Neurol. 2009 Jun;256(6):939-47.

99. Heatwole C, Bode R, Johnson N, Quinn C, Martens W, McDermott MP, et al. Patient-reported impact of symptoms in myotonic dystrophy type 1 (PRISM-1). Neurology. 2012 Jul 24;79(4):348-57.

100. Boerio D, Lefaucheur JP, Bassez G, Hogrel JY. Central and peripheral components of exercise-related fatigability in myotonic dystrophy type 1. Acta Neurol Scand. 2012 Jan;125(1):38-46.

101. Yeh ET, Lau SC, Su WJ, Tsai DJ, Tu YY, Lai YL. An examination of cancer-related fatigue through proposed diagnostic criteria in a sample of cancer patients in taiwan. BMC Cancer. 2011 Sep 6;11:387,2407-11-387.

102. Fernandes R, Stone P, Andrews P, Morgan R, Sharma S. Comparison between fatigue, sleep disturbance, and circadian rhythm in cancer inpatients and healthy volunteers: Evaluation of diagnostic criteria for cancer-related fatigue. J Pain Symptom Manage. 2006 Sep;32(3):245-54.

103. Johnsen AT, Petersen MA, Pedersen L, Groenvold M. Symptoms and problems in a nationally representative sample of advanced cancer patients. Palliat Med. 2009 Sep;23(6):491-501.

104. So WK, Dodgson J, Tai JW. Fatigue and quality of life among chinese patients with hematologic malignancy after bone marrow transplantation. Cancer Nurs. 2003 Jun;26(3):211,9; quiz 220-1.

105. Garrett K, Dhruva A, Koetters T, West C, Paul SM, Dunn LB, et al. Differences in sleep disturbance and fatigue between patients with breast and prostate cancer at the initiation of radiation therapy. J Pain Symptom Manage. 2011 Aug;42(2):239-50.

106. Kisiel-Sajewicz K, Siemionow V, Seyidova-Khoshknabi D, Davis MP, Wyant A, Ranganathan VK, et al. Myoelectrical manifestation of fatigue less prominent in patients with cancer related fatigue. PLoS One. 2013 Dec 31;8(12):e83636.

107. Blaney JM, Lowe-Strong A, Rankin-Watt J, Campbell A, Gracey JH. Cancer survivors' exercise barriers, facilitators and preferences in the context of fatigue, quality of life and physical activity participation: A questionnaire-survey. Psychooncology. 2013 Jan;22(1):186-94.

108. Cheville AL, Novotny PJ, Sloan JA, Basford JR, Wampfler JA, Garces YI, et al. The value of a symptom cluster of fatigue, dyspnea, and cough in predicting clinical outcomes in lung cancer survivors. J Pain Symptom Manage. 2011 Aug;42(2):213-21.

109. Kiserud CE, Seland M, Holte H, Fossa A, Fossa SD, Bollerslev J, et al. Fatigue in male lymphoma survivors differs between diagnostic groups and is associated with latent hypothyroidism. Acta Oncol. 2015 Jan;54(1):49-59.

110. Buseh AG, Kelber ST, Stevens PE, Park CG. Relationship of symptoms, perceived health, and stigma with quality of life among urban HIV-infected african american men. Public Health Nurs. 2008 Sep-Oct;25(5):409-19.

111. Marion I, Antoni M, Pereira D, Wohlgemuth W, Fletcher MA, Simon T, et al. Distress, sleep difficulty, and fatigue in women co-infected with HIV and HPV. Behav Sleep Med. 2009;7(3):180-93.

112. Da Costa D, Dritsa M, Bernatsky S, Pineau C, Menard HA, Dasgupta K, et al. Dimensions of fatigue in systemic lupus erythematosus: Relationship to disease status and behavioral and psychosocial factors. J Rheumatol. 2006 Jul;33(7):1282-8.

113. van Oers ML, Bossema ER, Thoolen BJ, Hartkamp A, Dekkers JC, Godaert GL, et al. Variability of fatigue during the day in patients with primary sjogren's syndrome, systemic lupus erythematosus, and rheumatoid arthritis. Clin Exp Rheumatol. 2010 Sep-Oct;28(5):715-21.

114. Sterling K, Gallop K, Swinburn P, Flood E, French A, Al Sawah S, et al. Patient-reported fatigue and its impact on patients with systemic lupus erythematosus. Lupus. 2014 Feb;23(2):124-32.

115. Segura-Jimenez V, Alvarez-Gallardo IC, Carbonell-Baeza A, Aparicio VA, Ortega FB, Casimiro AJ, et al. Fibromyalgia has a larger impact on physical health than on psychological health, yet both are markedly affected: The al-andalus project. Semin Arthritis Rheum. 2015 Apr;44(5):563-70.

116. Oncu J, Basoglu F, Kuran B. A comparison of impact of fatigue on cognitive, physical, and psychosocial status in patients with fibromyalgia and rheumatoid arthritis. Rheumatol Int. 2013 Dec;33(12):3031-7.

117. Overman CL, Kool MB, Da Silva JA, Geenen R. The prevalence of severe fatigue in rheumatic diseases: An international study. Clin Rheumatol. 2016 Feb;35(2):409-15.

118. Mancuso CA, Rincon M, Sayles W, Paget SA. Psychosocial variables and fatigue: A longitudinal study comparing individuals with rheumatoid arthritis and healthy controls. J Rheumatol. 2006 Aug;33(8):1496-502.

119. Falla D, Jull G, Rainoldi A, Merletti R. Neck flexor muscle fatigue is side specific in patients with unilateral neck pain. Eur J Pain. 2004 Feb;8(1):71-7.

120. Falla D, Rainoldi A, Merletti R, Jull G. Myoelectric manifestations of sternocleidomastoid and anterior scalene muscle fatigue in chronic neck pain patients. Clin Neurophysiol. 2003 Mar;114(3):488-95.

121. Edmondston S, Bjornsdottir G, Palsson T, Solgard H, Ussing K, Allison G. Endurance and fatigue characteristics of the neck flexor and extensor muscles during isometric tests in patients with postural neck pain. Man Ther. 2011 Aug;16(4):332-8.

122. Casartelli NC, Leunig M, Item-Glatthorn JF, Lepers R, Maffiuletti NA. Hip flexor muscle fatigue in patients with symptomatic femoroacetabular impingement. Int Orthop. 2012 May;36(5):967-73.

123. Webster CA, Nussbaum MA. Localized ankle fatigue development and fatigue perception in adults with or without chronic ankle instability. J Athl Train. 2016 Jun 2;51(6):491-7.

124. Ozcakar L, Inanici F, Kaymak B, Abali G, Cetin A, Hascelik Z. Quantification of the weakness and fatigue in thoracic outlet syndrome with isokinetic measurements. Br J Sports Med. 2005 Mar;39(3):178-81.

125. Bandak E, Amris K, Bliddal H, Danneskiold-Samsoe B, Henriksen M. Muscle fatigue in fibromyalgia is in the brain, not in the muscles: A case-control study of perceived versus objective muscle fatigue. Ann Rheum Dis. 2013 Jun;72(6):963-6.

126. Mengshoel AM, Saugen E, Forre O, Vollestad NK. Muscle fatigue in early fibromyalgia. J Rheumatol. 1995 Jan;22(1):143-50.

127. Power JD, Badley EM, French MR, Wall AJ, Hawker GA. Fatigue in osteoarthritis: A qualitative study. BMC Musculoskelet Disord. 2008 May 1;9:63,2474-9-63.

128. Elboim-Gabyzon M, Rozen N, Laufer Y. Quadriceps femoris muscle fatigue in patients with knee osteoarthritis. Clin Interv Aging. 2013;8:1071-7.

129. Ibn Yacoub Y, Amine B, Laatiris A, Abouqal R, Hajjaj-Hassouni N. Assessment of fatigue in moroccan patients with ankylosing spondylitis. Clin Rheumatol. 2010 Nov;29(11):1295-9.

130. Farren W, Goodacre L, Stigant M. Fatigue in ankylosing spondylitis: Causes, consequences and self-management. Musculoskeletal Care. 2013 Mar;11(1):39-50.

131. Sahin N, Ozcan E, Baskent A, Karan A, Ekmeci O, Kasikcioglu E. Isokinetic evaluation of ankle muscle strength and fatigue in patients with ankylosing spondylitis. Eur J Phys Rehabil Med. 2011 Sep;47(3):399-405.

132. Buffart LM, De Backer IC, Schep G, Vreugdenhil A, Brug J, Chinapaw MJ. Fatigue mediates the relationship between physical fitness and quality of life in cancer survivors. J Sci Med Sport. 2013 Mar;16(2):99-104.

133. Hammer NM, Midtgaard J, Hetland ML, Krogh NS, Esbensen BA. Physical activity behaviour in men with inflammatory joint disease: A cross-sectional register-based study. Rheumatology (Oxford). 2018 May 1;57(5):803-12.

134. McHorney CA, Ware JE,Jr, Raczek AE. The MOS 36-item short-form health survey (SF-36): II. psychometric and clinical tests of validity in measuring physical and mental health constructs. Med Care. 1993 Mar;31(3):247-63.

135. Annunziata MA, Muzzatti B, Mella S, Bidoli E. Fatigue, quality of life, and mood states during chemotherapy in italian cancer patients. Tumori. 2013 Jan-Feb;99(1):e28-33.

136. Alibhai SM, Breunis H, Timilshina N, Brignardello-Petersen R, Tomlinson G, Mohamedali H, et al. Quality of life and physical function in adults treated with intensive chemotherapy for acute myeloid leukemia improve over time independent of age. J Geriatr Oncol. 2015 Jul;6(4):262-71.

137. Hoekstra F, Hettinga FJ, Alingh RA, Duijf M, Dekker R, van der Woude LH, et al. The current implementation status of the integration of sports and physical activity into dutch rehabilitation care. Disabil Rehabil. 2015 Aug 10:1-6.

138. Murphy SL, Lyden AK, Clary M, Geisser ME, Yung RL, Clauw DJ, et al. Activity pacing for osteoarthritis symptom management: Study design and methodology of a randomized trial testing a tailored clinical approach using accelerometers for veterans and non-veterans. BMC Musculoskelet Disord. 2011 Aug 2;12:177,2474-12-177.

139. Birkholtz M, Aylwin L, Harman RM. Activity pacing in chronic pain management: One aim, but which method? part one: Introduction and literature review. British Journal of Occupational Therapy. 2004 10/01; 2017/02;67(10):447-52.

140. Murphy SL, Kratz AL. Activity pacing in daily life: A within-day analysis. Pain. 2014 Dec;155(12):2630-7.

141. Moffat F, Paul L. Barriers and solutions to participation in exercise for moderately disabled people with multiple sclerosis not currently exercising: A consensus development study using nominal group technique. Disabil Rehabil. 2018 Jun 29:1-9.

142. Tinsley A, Macklin EA, Korzenik JR, Sands BE. Validation of the functional assessment of chronic illness therapy-fatigue (FACIT-F) in patients with inflammatory bowel disease. Aliment Pharmacol Ther. 2011 Dec;34(11-12):1328-36.

143. Lundgren-Nilsson A, Tennant A, Jakobsson S, Simren M, Taft C, Dencker A. Validation of fatigue impact scale with various item sets - a rasch analysis. Disabil Rehabil. 2017 Dec 12:1-7.

144. Elbers RG, Rietberg MB, van Wegen EE, Verhoef J, Kramer SF, Terwee CB, et al. Self-report fatigue questionnaires in multiple sclerosis, parkinson's disease and stroke: A systematic review of measurement properties. Qual Life Res. 2012 Aug;21(6):925-44.

145. Wilson GJ, Murphy AJ. The use of isometric tests of muscular function in athletic assessment. Sports Med. 1996 Jul;22(1):19-37.

146. Enoka RM, Duchateau J. Muscle fatigue: What, why and how it influences muscle function. J Physiol. 2008 Jan 1;586(1):11-23.

147. Johansson S, Kottorp A, Lee KA, Gay CL, Lerdal A. Can the fatigue severity scale 7-item version be used across different patient populations as a generic fatigue measure--a comparative study using a rasch model approach. Health Qual Life Outcomes. 2014 Feb 22;12:24,7525-12-24.

148. Glynn NW, Santanasto AJ, Simonsick EM, Boudreau RM, Beach SR, Schulz R, et al. The pittsburgh fatigability scale for older adults: Development and validation. J Am Geriatr Soc. 2015 Jan;63(1):130-5.

149. Kim I, Hacker E, Ferrans CE, Horswill C, Park C, Kapella M. Evaluation of fatigability measurement: Integrative review. Geriatr Nurs. 2018 Jan - Feb;39(1):39-47.

150. Laird BJ, Scott AC, Colvin LA, McKeon AL, Murray GD, Fearon KC, et al. Pain, depression, and fatigue as a symptom cluster in advanced cancer. J Pain Symptom Manage. 2011 Jul;42(1):1-11.

151. Cheng KK, Lee DT. Effects of pain, fatigue, insomnia, and mood disturbance on functional status and quality of life of elderly patients with cancer. Crit Rev Oncol Hematol. 2011 May;78(2):127-37.

152. Vitkova M, Gdovinova Z, Rosenberger J, Szilasiova J, Nagyova I, Mikula P, et al. Factors associated with poor sleep quality in patients with multiple sclerosis differ by disease duration. Disabil Health J. 2014 Oct;7(4):466-71.

153. Mermigkis C, Stagaki E, Amfilochiou A, Polychronopoulos V, Korkonikitas P, Mermigkis D, et al. Sleep quality and associated daytime consequences in patients with idiopathic pulmonary fibrosis. Med Princ Pract. 2009;18(1):10-5.

154. Laberge L, Dauvilliers Y, Begin P, Richer L, Jean S, Mathieu J. Fatigue and daytime sleepiness in patients with myotonic dystrophy type 1: To lump or split? Neuromuscul Disord. 2009 Jun;19(6):397-402.

155. Riemsma RP, Rasker JJ, Taal E, Griep EN, Wouters JM, Wiegman O. Fatigue in rheumatoid arthritis: The role of self-efficacy and problematic social support. Br J Rheumatol. 1998 Oct;37(10):1042-6.

156. Nijrolder I, van der Windt DA, Twisk JW, van der Horst HE. Fatigue in primary care: Longitudinal associations with pain. Pain. 2010 Aug;150(2):351-7.

157. Eilertsen G, Ormstad H, Kirkevold M, Mengshoel AM, Soderberg S, Olsson M. Similarities and differences in the experience of fatigue among people living with fibromyalgia, multiple sclerosis, ankylosing spondylitis and stroke. J Clin Nurs. 2015 Jul;24(13-14):2023-34.

158. Abonie U, Heesterbeek M, Sandercock G, Hettinga F. Effects of activity pacing in patients with chronic conditions associated with fatigue complaints: A meta-analysis. BASES 2016 Nottingham. 2016.

159. Juengst S, Skidmore E, Arenth PM, Niyonkuru C, Raina KD. Unique contribution of fatigue to disability in community-dwelling adults with traumatic brain injury. Arch Phys Med Rehabil. 2013 Jan;94(1):74-9.

160. Prak RF, Doestzada M, Thomas CK, Tepper M, Zijdewind I. Reduced voluntary drive during sustained but not during brief maximal voluntary contractions in the first dorsal interosseous weakened by spinal cord injury. J Appl Physiol (1985). 2015 Dec 1;119(11):1320-9.

161. de Haan A, de Ruiter CJ, van Der Woude LH, Jongen PJ. Contractile properties and fatigue of quadriceps muscles in multiple sclerosis. Muscle Nerve. 2000 Oct;23(10):1534-41.

162. Wolkorte R, Heersema DJ, Zijdewind I. Muscle fatigability during a sustained index finger abduction and depression scores are associated with perceived fatigue in patients with relapsing-remitting multiple sclerosis. Neurorehabil Neural Repair. 2015 Sep;29(8):796-802.

163. Schubert M, Wohlfarth K, Rollnik JD, Dengler R. Walking and fatigue in multiple sclerosis: The role of the corticospinal system. Muscle Nerve. 1998 Aug;21(8):1068-70.

164. Van Der Slot WM, Nieuwenhuijsen C, Van Den Berg-Emons RJ, Bergen MP, Hilberink SR, Stam HJ, et al. Chronic pain, fatigue, and depressive symptoms in adults with spastic bilateral cerebral palsy. Dev Med Child Neurol. 2012 Sep;54(9):836-42.

165. Mengshoel AM, Norheim KB, Omdal R. Primary sjogren's syndrome: Fatigue is an ever-present, fluctuating, and uncontrollable lack of energy. Arthritis Care Res (Hoboken). 2014 Aug;66(8):1227-32.

166. Bachasson D, Guinot M, Wuyam B, Favre-Juvin A, Millet GY, Levy P, et al. Neuromuscular fatigue and exercise capacity in fibromyalgia syndrome. Arthritis Care Res (Hoboken). 2013 Mar;65(3):432-40.

Appendix A

Search terms

The following search term for articles reporting on perceived and/or performance fatigability was used in PubMed: ((("muscle fatigue/physiology"[MeSH Major Topic]) OR "fatigue/complications"[MeSH Major Topic])) AND ((("diseases category"[MeSH Major Topic]) AND adults[MeSH Terms]) AND humans[MeSH Terms]). This search was performed in January 2019 and resulted in 865 articles.

We used the search term (MA (disabled or disability or disabilities) OR MA chronic disease) AND (Muscle fatigue OR fatigue symptoms) AND (human AND adults) in PsycINFO, resulting in 123 articles.

Table 1 Overview with characteristics of the included studies (N=113) in this narrative review

Study	Study population					Fatigue					Relation[h]	
Author (year)[a]	Design[b]	Disease[c]	N	Age Mean (SD)	Male (%)	Assessment[d]	Freq. (%)[e]	Trait/ State[f]	Intensity[g] Perceived	Intensity[g] Performance	PA	HR-QoL
Cardiovascular diseases												
Eckhardt (2014)[28]	CSS; QS	Coronary heart disease	102	65 (11)	64	FSI	Men 57 Women78	T	0 – 3.4 (2.2) – 10 0 – 4.4 (2.2) – 10		0	1
Fink (2009)[29]	CSS	Heart failure	87	57 (14)	44	FSI	33	T	0 – 2.9 (0.3) – 10		0	1
Hopkinson (2013)[31]	ES	Heart failure	10	55 (12)	100	MVC					0	0
Plach (2006)[30]	CSS	Heart failure	169	69 (12)	0	SRQ		T			0	0
Pulmonary diseases												
Stridsman (2018)[33]	CS	COPD	367	72 (9)	56	FACIT-F	37	T	0 – 47; 48 – 52		0	1
Kentson (2016)[34]	CSS	COPD	101	68 (7)	49	FIS	56	T	0 – 26; 60 – 160		0	1
Saey (2006)[36]	CSS	COPD	30	67	100	MVC					0	0
Allaire (2004)[37]	ES	COPD	29	65	69	MVC (kg)				0 – 28 (2); 45 (3) – 50	0	0
Gagnon (2009)[35]	ES	COPD	15	67	100	MVC (kg)				0 – 36 (3) -17%; 46 (2) -25% – 50	0	0
Cannon (2016)[38]	CSS	COPD	13	65 (11)	85	P_{iso}				0 – 72 (34); 212 (84); 350 (162); 498 (160) – 500	0	0
Gruet (2015)[39]	ES	CF	15	28 (6)	80	MVC				0 – 197 (76) -62%; 245 (101) -60% – 250	0	0
Liver diseases												
Biagini (2008)[41]	ES	PBC	49	59	10	FIS; MFIS; FSS		T	0 – 25; 33 – 160		0	0
Jones (2006)[42]	CS	PBC	108	62	9	FIS		T	0 – 36 – 160		0	0
Goh (1999)[40]	CS	Hepatitis C	66	48	0	FIS		T	0 – 31 (24); 78 (36) – 160		0	0

Study		Study population				Fatigue					Relation[h]	
Author (year)[a]	Design[b]	Disease[c]	N	Age Mean (SD)	Male (%)	Assessment[d]	Freq. (%)[e]	Trait/ State[f]	Intensity[g] Perceived	Performance	PA	HR-QoL
Diabetes												
Fritschi (2012)[43]	CSS; DS	Diabetes TII	83	53 (7)	0	MFI-20		T	4 ● 20; 13 (5)		1	0
Almeida (2008)[44]	ES	Diabetes TI	10	26 (11)	90	MVC				0 △○ ▲● 60; 55 (25) -33%; 56 (17) -30%	0	0
Senefeld (2018)[45]	ES	Diabetes TII	17	60 (9)	60	FIS; MVC		T	0 ▲● 160; 7; 24		0	0
Other organ diseases												
Wang (2016)[46]	CSS	RD	345	56 (13)	63	FACIT-F		T	0 ● 52; 39		0	1
Czuber-Dochan (2013)[48]	DS	Bowel disease	46	55 (14)	33	Interview	100	T			0	0
Villoria (2017)[49]	CSS	IBD	177	39 (12)	58	FACIT-F	54	T	0 ● 52; 38 (12)		0	1
Jhamb (2013)[47]	CSS	Kidney disease	87	49 (14)	68	FACIT-F		T	0 ● 52; 34 (11)		0	1
		RD	86	54 (15)	66				0 ● 52; 35 (11)			
van Langenberg (2014)[50]	CSS	Crohn's disease	27	43	44	FIS, MVC		T	0 ● 160; 45		0	0
Eikermann (2006)[51]	CS	Organ failure	13	58 (14)		MVC	100			0 ○● △ ▲ 70; 65 (19) -32%; 20 (16) -28%	0	0
Waltz (2012)[52]	ES	Sickle cell disease	20	36 (12)	50	MVC				0 ○ △● ▲ 20; 18 (3) -22%; 15 (4) -18%	0	0
		Sickle cell anemia	16	33 (14)	50					0 ○ ●△ ▲ 20; 18 (3) -22%; 13 (3) -17%		
Korenromp (2011)[53]	ES	Sarcoidosis	75	47 (8)	44	CIS	76	T			1	1
Neurological diseases												
Dogan (2015)[14]	DS	PD	86	64 (11)	54	FSS	76	T			0	1
Tanaka (2014)[55]	DS	PD	110	70 (7)	45	J-PFS	53	T			0	0
Gallagher (2010)[56]	DS	PD	94	68 (10)	69	FSS	59	T			0	1
Goulart (2009)[57]	CS	PD	50	71	44	FSS, MFIS	70	T			0	0
Ziv (1998)[59]	ES	PD	17	56 (9)	59	MVC				0 ○ △●▲ 20; 18 (2) -16%; 16 (2) -54%	0	0

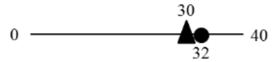
Study			Study population			Fatigue					Relation[h]	
Author (year)[a]	Design[b]	Disease[c]	N	Age Mean (SD)	Male (%)	Assessment[d]	Freq. (%)[e]	Trait/ State[f]	Intensity[g] Perceived	Intensity[g] Performance	PA	HR-QoL
Tu (2017)[54]	CSS	PD	92	65 (10)	65	FSS	34	T	1 – 3 (2) – 7		0	1
Santos (2016)[60]	CSS	PD				MVC				1500; 1593 (404); 1786 (560); 2446 (554); 2576 (624); 2500	0	0
Brusse (2011)[58]	CSS	SCA	123	58 (13)	41	FSS	69	T			0	1
Knorr (2011)[62]	ES	Stroke	10	59 (16)	50	FAS, MVC		T	10; 14 (3); 21 (4); 50	0; 17 -29%; 22 -59%; 25	0	0
Obembe (2015)[61]	ES	Stroke	63	54 (11)	56	MFIS		T	0 – 32 (12) – 84		0	0
Rybar (2014)[63]	ES	Stroke	10	62 (8)	50	MVC				0; 221 (68) -80%; 368 (137) -76%; 370	0	0
Juengst (2013)[159]	CSS; CS	TBI	50	48 (16)	80	MFIS	48	T	0 – 36 (21) – 84		0	0
Alschuler (2013)[65]	CSS	SCI	481	50 (14)	67	NRSs		T	0 – 4 (3) – 10		0	1
Wijesuriya (2012)[64]	ES	SCI	41	47 (12)	95	Iowa FS	56	T	11; 22 (5.6); 26 (7.5); 55		0	1
Pelletier (2011)[66]	CSS	SCI	6	44 (14)	83	MVC				0; 22 -14%; 57 -20%; 60	0	0
Mahoney (2007)[69]	ES	SCI	9	35 (11)	78	Force				0; -50%; -50%; 100	0	0
Lin (2012)[68]	ES	SCI	9	36 (10)	89	MVC				0; 4 (2) – 37%; 9 (3) – 48%; 10	0	0
Mayer (1999)[70]	CS	SCI early	13	31 (11)	100	EQ					0	0
		SCI trained	16	37 (10)	100							
		SCI untrained	12	38 (13)	100							
Klein (2006)[67]	ES	SCI	7	34	71	EMG				0; 0.31; 0.85; 1	0	0
Prak (2015)[160]	ES	SCI	17	52 (10)	76	MVC				0; 38 (10) -57% (13); 20 (7) -58% (15); 40	0	0
Sheean (1997)[72]	ES	MS	21	40	43	FSS, MVC	95	T	1 – 5.9 (0.9) – 7	0; 2.3 (1.2); 4.0 (0.9); 4.2 (1.2); 5.0 (1.2); 5	0	0

Study			Study population				Fatigue				Relation[h]	
Author (year)[a]	Design[b]	Disease[c]	N	Age Mean (SD)	Male (%)	Assessment[d]	Freq. (%)[e]	Trait/ State[f]	Intensity[g] Perceived	Intensity[g] Performance	PA	HR-QoL
Sharma (1995)[77]	ES	MS	28	44	25	VAS, MVC		S	0; 6.5; 10	357.9 (19.7); 0; 400; 223.1 (17.0)	0	0
Iriarte (1998)[76]	ES	MS	50	32 (10)	48	FSS, MVS		T	1; 7; 3.4 (1.5)	94.2 (10.2); 0; 100; 98.1 (13.6)	0	0
Steens (2012)[71]	CSS	MS	20		35	FSS, MVC		T	2.9 (0.6); 1; 7; 5.3 (0.9)	35 (9) -63% (12); 0; 40; 31 (9) -63% (12)	0	0
de Haan (2000)[161]	ES	MS	17	42 (8)	47	MVC				0; 370; 364 (174) -31%	0	0
de Ruiter (2001)[82]	ES	MS	12	42 (7)	50	MVC				0; 70; 61 (18)	0	0
Wolkorte (2015)[75]	ES	MS	19	39	61	FSS, MVC		T	2.4; 1; 7; 3.9	61.0 (12.2) 70.7 (8.0); 0; 80; 67.0 (12.4) 76.1 (7.1)	0	0
Wolkorte (2015)[162]	CSS	MS	86	41	39	FSS, MFIS, MVC	75	T	1; 7; 4.6 (1.4) 0; 84; 38.3	0; 100; 29.7% (10.2) 100%	0	0
Koch (2009)[74]	CS	MS	412	49	30	FSS		T	1; 7; 5.4 (1.4)		0	0
Scheidegger (2012)[73]	ES	MS	23	40(11)	83	FSS, MVC		T	1; 7; 5.3 (2.1)	44 (9); 0; 100; 36 (16)	0	0
Skurvydas (2011)[80]	ES	MS	18	43 (5)	50	FSS, MVC	100	T			0	0
Schubert (1997)[163]	ES	MS	11	34	36	MEPs				-42%; 0; 100; -19%	0	0
Wolkorte (2016)[79]	ES	MS	25	53	32	MVC				32 -63%; 0; 40; 25 -73%	0	0
Hameau (2017)[81]	CSS	MS	38	50 (10)	34	MVC				46 (11); 0; 50; 33 (21)	0	0
Kalron (2011)[84]	ES	CIS	52	35 (7)	31	MVC				-19%; 0; 100; -27%	0	0
Runia (2015)[83]	CS	CIS	127	34 (9)	23	FSS	47	T	2.9 (1.1); 1; 7; 4.3 (1.9)		0	0
Kent-Braun (2000)[85]	ES	ALS	7	50 (3)	86	MVC				148 (22) -53% (10); 0; 150; 110 (16) -43% (8)	0	0

Study		Study population					Fatigue				Relation[h]	
Author (year)[a]	Design[b]	Disease[c]	N	Age Mean (SD)	Male (%)	Assessment[d]	Freq. (%)[e]	Trait/ State[f]	Intensity[g] Perceived	Intensity[g] Performance	PA	HR-QoL
Sanjak (2004)[86]	CSS	ALS	13	51 (12)	77	MVC				0 – 28 – 43 – 50	0	0
Seok (2017)[87]	CS	NMOSD	35	47 (14)	17	FACIT-F	71	T	0 – 33 (13) – 52		0	1
Sunnerhagen (2000)[88]	CSS	Post-poliomyelitis	10	54 (5)	50	MVC				0 – 124 -45% – 185 -37% – 200	0	0
Allen (1994)[89]	ES	Prior-poliomyelitis	21	51	48	MVC				0 – 78 (12) % – 78 (12) % – 100	0	0
Shoseyov (2017)[91]	CSS	Post-polio syndrome	12	62 (12)	50	EMG				10 – 11 (4) – 11 (8) – 12 (8) – 12 (5) – 15	0	0
Garssen (2006)[90]	ES	Guillain-Barré	10	56	50	FSS, MVC		T	1 – 4.9 (1.3) – 7	0 – 178 (74) -40% – 180	0	0
Van der Slot (2012)[164]	CSS	Cerebral palsy	56	36 (6)	63	FSS		T	1 – 4.4 (1.3) – 7		0	0
Spierings (1997)[92]	ES	Chronic headache	113	44 (11)	52	VAS	70	S	0 – 4 (3) – 10		0	0
Seo (2018)[93]	CS	Migraine	226	42 (12)	16	FSS	60	T	1 – 3.6 (1.5) – 7		0	1
Heatwole (2012)[99]	CSS	MD	278	47 (11)	53	Interview	91	T			0	0
Boërio (2012)[100]	ES	MD	10	44 (14)	20	MVC				0 – 9 (3) -4% – 10	0	0
Trip (2009)[98]	CSS	NDM	62	42 (11)	53	FAS	53	T		10 – 27 (4) – 50	0	1
Schillings (2007)[94]	CSS	FD	65	43 (10)	59	AFQ, MVC		T	4 – 14 (6) – 28	0 – 134 (66) – 210 (65) – 210	0	0
		MD	79	41 (10)	56				4 – 16 (6) – 28	0 – 131 (65) – 210 (65) – 210		
		HMSN-1	73	42 (10)	41				4 – 17 (6) – 28	0 – 148 (79) – 210 (65) – 210		
Alschuler (2012)[97]	CSS	MD	332	53 (13)	42	NRSs		T	0 – 5 – 10		0	1
Symonette (2010)[95]	ES	MG(decrement)	12	53 (17)	50	MGFS, MVC		T	25 – 71 (23) – 130	0 – 24 -15% – 41 -10% – 60	0	0
		MG(no decrement)	8	54 (17)	75				25 – 57 (13) – 130	0 – 43 -23% – 52 -22% – 60	0	0

Study		Study population				Fatigue					Relation[h]	
Author (year)[a]	Design[b]	Disease[c]	N	Age Mean (SD)	Male (%)	Assessment[d]	Freq. (%)[e]	Trait/ State[f]	Intensity[g] Perceived	Performance	PA	HR-QoL
Jordan (2017)[96]	CSS	MG	32	56 (17)	28	LT-6MWT; MGFS	100	T	25 ▲40(9) ●62 (24) 130	-1 ●-0.6 (1) ▲0.2 (1) 1	0	0
Cancer												
Yeh (2011)[101]	DS	Cancer	265		36	ICD-10	50	T			0	0
Garrett (2011)[105]	DS	Breast;	78	55 (11)	0	LFS			0 ●3.5 10		0	0
		Prostate cancer	82	67 (8)	100				0 ●3.2 10			
Cheville (2011)[108]	CS	Lung cancer	2405	65 (11)	50	Baecke	47	T			1	1
So (2003)[104]	CSS	Cancer	157	40 (10)	54	RPFS		T	0 ●5 (2) 10		0	1
Fernandes (2006)[102]	ES	Cancer	25	67	0	EORTC QLQ-C30	56	T	0 ▲22 (22) ●78 (47) 100		1	1
Johnsen (2009)[103]	CSS	Cancer	977		44	EORTC QLQ-C30	57	T	0 ●37 100		0	0
Kiserud (2015)[109]	CSS	Lymphoma	233	48	100	FQ	27	T	0 ●14.2 (4.7) 33		0	1
Blaney (2013)[107]	DS	Cancer	456	61	24	MFSI	74	T	0 ●27 84		1	1
Kisiel-Sajewicz (2013)[106]	ES	Cancer	12	59 (10)	33	MVC				0 ○191 (71) -18% ● △ ▲245 (76) -14% 250	0	0
Immunological disorders												
Buseh (2008)[110]	CSS; DS	HIV	55	49 (8)	100	SSC-HIVrev	98	T	0 ●2 (1) 3		0	1
Marion (2009)[111]	DS	HIV and HPV	60	31 (9)	0	FSI		T	0 ●43 (23) 130		0	0
Da Costa (2006)[112]	DS	SLE	130	45 (14)	0	MFI-20		T	4 ●11 (4) 20		1	0
Sterling (2014)[114]	CSS; QS	SLE	22	46 (13)	5	Interview	95	T			1	0
van Oers (2010)[113]	DS	PSS	29	53 (14)	0	MFI			0 ●2.3 4		0	0
		SLE	23	44 (12)	0				0 ●1.9 4			
		RA	19	55 (13)	0				0 ●2.3 4			
Mengshoel (2014)[165]	DS	PSS	9		44	Interview	100	T			0	0
Öncü (2013)[116]	CSS	RA	44	55 (10)	0				1 ●5 (1) 7		0	1
Mancuso (2006)[118]	CS	RA	122	49 (12)	16	FSS	81	T	1 ●4 (1) 7		1	0

Study		Study population						Fatigue			Relation[h]	
Author (year)[a]	Design[b]	Disease[c]	N	Age Mean (SD)	Male (%)	Assessment[d]	Freq. (%)[e]	Trait/ State[f]	Intensity[g] Perceived	Performance	PA	HR-QoL
Overman (2016)[117]	CSS	RA	6120	47 (12)	12	SF-36	65	T			0	0
Hammer (2018)[133]	CSS	RA	325	54	100	VAS		S	0–100; 31.0		1	0
Musculoskeletal disorders												
Falla (2003)[120]	ES	Chronic NP	10	29 (9)	10	MVC				0–60; 52 (16); 54 (13)	0	0
Falla (2004)[119]	ES	Unilateral NP	10	32 (7)	0	MVC				0–130; 108 (18); 127 (18)	0	0
Edmondston (2011)[121]	ES	Postural NP	13	29 (13)	0	EMG				0–250; 240 -21%; 240 -54%	0	0
Webster (2016)[123]	ES	CAI	11	24 (3)	9	MVC				0–50; 41 (14) -22%; 39 (11) -22%	0	0
Casartelli (2012)[122]	ES	FAI	15	32 (10)	40	MVC				0–1.5; 1.2 (0.4); 1 (0.4)	0	0
Özçakar (2005)[124]	ES	TOS	23	42 (12)	26	MVC	91			0–40; 22 (13); 35 (28)	0	0
Mengshoel (1995)[126]	CSS	Fibromyalgia	9	29 (5)	0	MVC				0–370; 365 (23) -36%	0	0
Bandak (2012)[125]	CSS	Fibromyalgia	25	44 (9)	0	FIQ, MVC		T	0–10; 7.5 (2.3)		0	0
Segura-Jiménez (2015)[115]	CSS	Fibromyalgia	459	52 (7)	0	MFI-S		T	4–20; 10.6; 17.9		0	1
Bachasson (2013)[166]	CSS	Fibromyalgia	11	44 (9)	0	FSS, MVC		T	1–7; 2.4 (1.3); 5.4 (1.7)	0–120; 120 (24) -19%; 102 (18) -24%	0	0
Öncü (2013)[116]	CSS	Fibromyalgia;	45	40 (8)	0	FSS		T	1–7; 6 (1)		0	1
Elboim-Gabyzon (2013)[128]	DS	Osteoarthritis	62	68 (8)	18	MVC				0–20; 17 (7) -26%; 14 (7) -15%	0	0
Power (2008)[127]	QS	Osteoarthritis	46	72 (8)	61	FACIT		T	0–52; 31 (9)		0	1
Farren (2013)[130]	CS; QS	AS	10	52 (13)	60	Interview	40	T			1	1
Yacoub (2010)[129]	CSS	AS	100	38 (13)	67	MAF	60	T	0–50; 32 (20)		1	1

Study			Study population			Fatigue					Relation[h]	
Author (year)[a]	Design[b]	Disease[c]	N	Age Mean (SD)	Male (%)	Assessment[d]	Freq. (%)[e]	Trait/ State[f]	Intensity[g] Perceived	Intensity[g] Performance	PA	HR-QoL
Sahin (2011)[131]	ES	AS	26	37 (9)	100	MVC					0	0

a First author and publication year

b Cross-sectional study (CSS); Qualitative study (QS); Cohort study (CS); descriptive study (DS); experimental study (ES).

c Primary biliary cirrhosis (PBC); Renal disease (RD); Inflammatory bowel disease (IBD); Chronic obstructive pulmonary disease (COPD); Cystic Hibrosis (CF); Parkinson's disease (PD); Hereditary motor and sensory neuropathy type I (HMSI-1); Spinocerebellar ataxia (SCA); Traumatic brain injury (TBI); Spinal cord injury (SCI); Multiple sclerosis (MS); Clinically isolated syndrome (CIS); Amyotrophic lateral sclerosis (ALS); Neuromyelitis optica spectrum disorder (NMOSD); Muscular dystrophy (MD); Non-dystrophic myotonia (NDM); Facioscapulohumeral dystrophy (FD); Myasthenia gravis (MG); Human immunodeficiency virus (HIV); Human papillomavirus (HPV); Neck pain (NP); Chronic ankle instability (CAI); Femeroacetabular impingement (FAI); Thoracic outlet syndrome (TOS); Systemic lupus erythematosus (SLE); Primary Sjögren's syndrome (PSS); Rheumatoid arthritis (RA); Ankylosing spondylitis (AS).

d Fatigue Severity Scale (FSS); Fatigue Symptom Inventory (FSI); Symptom Representation Questionnaire (SRQ); Vigor subscale of POMS (POMS-V); Multidimensional Fatigue Inventory-20 (MFI-20); Fatigue Questionnaire (FQ); Japanese version of the Parkinson Fatigue Scale (J-PFS); Modified Fatigue Impact Scale (MFIS); Spanisch version of the Multidimensional Fatigue Inventory (MFI-S); Numerical Rating Scales (NRSs); Lee Fatigue Scale (LFS); Revised Piper Fatigue Scale (RPFS); Bidimensional Fatigue Scale (BFS); Revised Piper Fatigue Scale (PFS-R); International Classification of Diseases (ICD-10); Multidimensional assessment of fatigue (MAF); Asthma Symptom Checklist (ASC); Fatigue impact scale (FIS); Multidimensional Fatigue Symptom Inventory (MFSI); Checklist Individual Strength (CIS); European Organization for Research and Treatment of Cancer Fatigue Subscale (EORTC QLQ-C30); Fasting Blood glucose meter (FBGm); Cancer Fatigue Scale (CFS); Functional Assessment of Chronic Illness Therapy Fatigue Scale (FACIT-F); Functional Assessment of Cancer Therapy fatigue subscale (FACT-F); Holzemer Sings and Symptoms Checklist for HIV (SSC-HIVrev); Self-administered Comorbidity Questionnaire (SACQ); Abbreviated fatigue questionnaire (AFQ); Myasthenia gravis fatigue survey (MGFS); Fatigue Assessment Scale (FAS); Force decline during Maximal Voluntary Contraction (MVC); Linear trend in 6-minute walk test (LT-6MWT); Motor Evoked Potentials (MEPs); Endurance quotient (EQ); Peak isokinetic contraction (P_{iso})

e Prevalence of fatigue reported by the study population

f T=trait level and S=state variable

g Intensity of fatigue on a scale with (if applicable) ● = patient group at baseline, ○ = patient group after fatiguing task, ▲ = control group at baseline, △ = control group after fatiguing task; with notation of the intensity of fatigue below the scale line for the patient group and above the scale line for the control group.

h The relation between fatigue and physical activity (PA) and/or health-related quality of life (HR-QoL) is investigated (1) or not (0)

Chapter 5

Associations of perceived fatigue, perceived activity pacing and physical activity with accelerometer-derived activity pacing behaviour in people with physical disabilities and/or chronic diseases.

Barakou I*, Seves BL*, Hoekstra T, Hoekstra F, Krops LA, Brandenbarg P, van der Woude LHV, Dekker R, Hettinga FJ.

*Equal contributions

Submitted

Abstract

Purpose: To investigate how perceived fatigue, perceived activity pacing, and total physical activity are associated with accelerometer-derived activity pacing behaviour during the week among people with physical disabilities and/or chronic diseases.

Methods: Fifty-eight participants with physical disabilities and/or chronic diseases wore an Actiheart monitor for one week and filled in the Fatigue Severity Scale, the Adapted-SQUASH, and a questionnaire assessing perceived activity pacing. Accelerometer-derived activity pacing behaviour (outcome measure) was defined by the standard deviation of activity energy expenditure (SD of AEE) in the morning, afternoon, and evening for each day. Univariable and multivariable (corrected for sex, age, body mass index, drug use and use of a mobility aid) longitudinal mixed model analyses were performed to associate perceived fatigue, perceived activity pacing and total physical activity with accelerometer-derived activity pacing behaviour during the week.

Results: In the multivariable models, higher levels of total physical activity scores were on average over time associated with higher levels of SD of AEE (B[SE]=.151[.066], 95%CI=.018-.284), while perceived fatigue and perceived activity pacing were on average over time not significantly associated with SD of AEE.

Conclusion: The current study suggests that higher levels of physical activity were associated with activity pacing behaviour with higher activity peaks during the week after correction for confounders, while perceived fatigue was not associated with activity pacing behaviour. People who pace their activities less over the day might not realize that activity bursts could relate to

longer recovery periods, which supports patients' needs for fatigue guidance during and after rehabilitation.

Keywords

Energy distribution, health promotion, chronic disease, rehabilitation, activity monitors

Implications for rehabilitation

- People with physical disabilities and/or chronic diseases with an evenly distributed activity pacing behaviour might benefit from activity pacing advice to manage their perceived fatigue and to gradually enhance physical activity.
- People with activity pacing behaviour with high activity peaks during the day might participate in even more physical activity when receiving appropriate pacing advice, since they may not realize that activity bursts could relate to longer recovery periods.

Introduction

Perceived fatigue is an important denominator of limitations in functional independence, participation in physical activities and society, and health-related quality of life [1]. Fatigue is a major problem for many individuals with physical disabilities and/or chronic diseases and can be chronic and severe [2-4]. It is also a multidimensional symptom concerning physical fatigue, mental fatigue, cognitive fatigue, emotional fatigue, and motivational fatigue [5-8]. Hence, there are several definitions across the literature regarding fatigue [3,9]. It is commonly defined as a feeling of lack of energy, weariness, and aversion to effort [10] or as a disruptive and severe non-motor symptom with cognitive and emotional elements [11-13]. It has been reported in different diagnostic groups with a prevalence varying from 39 to 80% [4,10,14-16]. Perceived fatigue has a significant impact on activities in daily life, exercise engagement and choice of activities [1,10], while daily physical activity improves the health and quality of life [17-19]. It is often reported that people with physical disabilities and/or chronic diseases are struggling with dividing physical activities over the day [2,20-23], which results in uneven pacing patterns with long recovery periods or avoidance of activities due to fatigue or prevention thereof [24]. Hence, adequate management of daily physical activities and perceived fatigue in people with disabilities is important to increase participation and reduce health risks [2,25].

Activity pacing is defined in medical settings as a strategy to divide one's daily physical activities into smaller, more manageable, portions, in a way that should not exacerbate their symptoms, which then allows gradual progressive increases in physical activity [20]. Activity pacing can thereby be the basis of a promising intervention that can be used to anticipate fatigue by reducing activity levels before strong fatigue levels occur while promoting physical activity

[2,26]. Furthermore, pacing advice could also be oriented towards reducing avoidance of physical activity related to fear of symptoms occurring [27]. People who suffer from fatigue typically adopt a more responsive approach to physical activity behaviour and fatigue because of symptom-contingency, yet a more anticipatory approach could be beneficial in many cases [24,25,27,28]. In a recent interview study, stroke survivors reported that they need guidance and instructions on activity pacing – through taking a more anticipatory approach – to better manage fatigue and engage more in physical activity [29]. To be able to provide advice to people on how to optimally manage fatigue, tailored advice is needed. Before tailored advice can be given or even before optimal activity pacing interventions can be developed, challenges related to activity pacing behaviour need to be explored and understood among people with physical disabilities and/or chronic diseases who may either be inclined to be overactive or avoid activity. So far, the number of studies exploring activity pacing is limited and inconclusive [24,26,27,30].

Some of those studies are aiming at understanding activity pacing patterns or developing activity pacing interventions as part of fatigue management programs in a limited number of chronic conditions (e.g., people with osteoarthritis, rheumatoid arthritis, and chronic pain) [2,22-26]. A pilot study on activity pacing patterns in women with osteoarthritis [26] defined activity pacing as a strategy for going slower and taking breaks or dividing activities into smaller pieces while they examined activity pacing by measuring the variation of physical activity by using an Actigraph watch. The results showed that people with a more evenly paced activity pattern during the day showed lower levels of physical activity and higher levels of perceived fatigue and pain compared to people with unevenly divided activities during the day. This finding highlights the symptom contingency strategy occurring in activity pacing since fatigue symptoms are associated with more awareness of pacing and deliberately lower participation in physical activity. Thus, it is essential to explore which factors are significantly associated with activity pacing among individuals with physical disabilities and/or chronic diseases. Exploring these factors will help to identify where to focus on the next step, which is the development of a rigorous optimised activity pacing intervention.

The current study is an attempt to better understand activity pacing behaviour during the week in a heterogeneous group of people with physical disabilities and/or chronic diseases. Activity pacing was derived by calculating the standard deviation of activity energy expenditure (SD of AEE) assessed with the Actiheart activity monitor (Cambridge Neurotechnology™ UK) and via self-reporting questionnaires (including perceived activity pacing). The purpose of this study was to investigate among people with physical disabilities and/or chronic diseases who lived independently how perceived fatigue, perceived activity pacing, and self-reported physical activity are associated with activity pacing behaviour during the week. We expect that lower variance in AEE (so an evenly distributed activity pacing behaviour) is associated with higher levels of fatigue and lower levels of physical activity, since we know from previous literature that people with physical disabilities and/or chronic diseases are more aware of activity pacing strategies and lower their physical activity levels to reduce or prevent fatigue symptoms [24]. Besides, we expect that lower variance in AEE is associated with more perceived activity pacing, and that higher variance in AEE (with high activity peaks during the day) is associated with more perceived risk of overactivity [30].

Methods

Study overview

This secondary data analyses study used data from the reliability and validity study of the Adapted Short Questionnaire to Assess Health-enhancing physical activity (Adapted-SQUASH) [31]. We used data collected at the first questionnaire measurement (including questions on participants' general characteristics, self-reported physical activity, perceived fatigue, and self-reported activity pacing) and the Actiheart (Cambridge Neurotechnology™ UK)-based accelerometer data, which ideally was worn and monitored daily activities for seven consecutive days. The existing dataset provided the opportunity to explore activity pacing based on accelerometer-derived physical activity data and questionnaire data in people with physical disabilities and/or chronic diseases. The study was approved by the Ethics Committee of the Center for Human Movement Sciences (ECB/2014.06.30_1) at the University Medical Center Groningen, University of Groningen, The Netherlands. All participants voluntarily participated and signed informed consent prior to testing.

Study population

Participants were adults with a chronic physical disability and/or disease who lived independently. Participants were recruited via sport and exercise groups in rehabilitation centres, sport clubs and patient associations in the northern and eastern provinces in the Netherlands. Inclusion criteria were being at least eighteen years of age, having a physical disability and/or chronic disease (e.g., stroke, heart disease, Parkinson's disease) and being able to read and write the Dutch language. Participants were excluded when they were still receiving inpatient or outpatient rehabilitation care, were participating in the Rehabilitation, Sports and Active lifestyle (ReSpAct) study [32,33], were completely wheelchair dependent (because of the use of the Actiheart), were not able to complete the questionnaire even with help, or when participants did not have a minimum registration of the Actiheart of at least four days of valid acceleration data (with at least 75% of activity data registration of each single day) [34,35]. The data collection took place between November 2014 and June 2016.

Study procedure

Each participant was asked to wear an Actiheart (Cambridge Neurotechnology™ UK) activity monitor for one week. Two researchers visited the participants in their home situation twice: (1) to install and attach the Actiheart to the participants' chest, and (2) to collect the Actiheart device after one week. The Actiheart measurement started at 00:00 AM and continued for the next seven consecutive days, both day and night. The participant was instructed to remove the Actiheart during showering, bathing, or swimming. During the week, the participant filled out a diary in which non-compliance to the Actiheart was noted.

After wearing the Actiheart activity monitor for one week, the participants filled in a set of questionnaires. These questionnaires included questions on participants' self-reported physical activity during the past week, perceived fatigue, self-reported activity pacing and general characteristics. The researchers measured participants' body weight (kg) and height (m).

Outcome measure

Accelerometer-derived activity pacing

(1) Activity Energy Expenditure:

The Actiheart (Cambridge Neurotechnology™ UK) activity monitor is a combined uniaxial accelerometer and heart rate monitor, which we used in the current study to measure accelerometer-derived activity pacing. The Actiheart is a reliable and valid measurement device [34] and was deemed appropriate for the target population since the combination of accelerometer data with heart rate data would be better able to determine the intensity of physical activities. The Actiheart was attached to the participation's chest by using two Electrocardiography (ECG) electrodes. The Actiheart is a lightweight (8gram) and compact (7x33mm) device, connected to the two ECG electrodes and capable of storing time-sequenced data. Acceleration (1D, vertical axis) was measured with a 1-minute epoch by a piezoelectric element within the unit with a frequency range of 1-7Hz.

The Actiheart reported activity counts and heart rate data per minute, simultaneously. Based on these Actiheart outputs, AEE estimates in $kcals \cdot kg^{-1} \cdot min^{-1}$ were calculated for each minute by combining activity counts and heart rate in a branched equations model as described in the literature [34,35] and as proposed by the Actiheart software for AEE. A branched equation model allows the Actiheart to accurately assess AEE even when there is low body movement, but high heart rate during an activity. This combined activity and heart rate algorithm to calculate AEE is based on an individual's sleeping heart rate. The sleeping heart rate was calculated by averaging the minute-to-minute heart rate between 2.00-5.00 AM on the first day the Actiheart was worn. When heart rate data was missing, AEE was calculated based on the activity algorithm only for the specific missing minute [34].

(2) Variation in physical activity (standard deviation of Activity Energy Expenditure):

Accelerometer-based activity pacing – as the outcome measure – was derived by first calculating the standard deviation (SD) of the regular outcome AEE in the morning (6:00 AM-12:00 PM), afternoon (12:00 PM-06:00 PM) and evening (06:00 PM-12.00 AM) for each measured day. The SD of activity counts has been used in the literature as a measure of accelerometer-derived activity pacing and signifies a way of probing the variability of physical activity during the monitoring period [24,36], which provides insight into the distribution of activities over the day, i.e., commonly defined as activity pacing behaviour.

Determinants

Perceived fatigue

Perceived fatigue on average in the week was assessed by using the Fatigue Severity Scale (FSS) [37]. The FSS (range: 1-7) is a valid and reliable questionnaire to determine the impact of perceived fatigue in several patient populations (e.g., stroke) [38,39] and to detect change over time [38]. A higher score on the FSS indicated greater perceived fatigue severity, in which an FSS score of 4 or greater indicates severe perceived fatigue [40].

Perceived activity pacing

Perceived activity pacing was assessed by using a self-constructed seven-item questionnaire based on the literature [41-43]. The questionnaire includes two constructs of perceived activity pacing: (1) a two-item construct on persons' perceptions of being at risk of overactivity (Cronbach's alpha = .71), and (2) a five-item construct on persons' awareness of their engagement in activity pacing (Cronbach's alpha = .78). Participants scored the seven items of the questionnaire on a scale of 1-5 (1=never, 2=rarely, 3=sometimes, 4=often, 5=very often). Sum scores were calculated for each construct (range from 2-10 and from 5-25 respectively). Reliability and construct validity have been investigated by the ReSpAct research team and a paper is in preparation.

Self-reported physical activity

Self-reported physical activity - in total physical activity score per week - was assessed using the Adapted-SQUASH, a 19-item self-reported recall questionnaire. The Adapted-SQUASH has been shown to be sufficiently reliable (intraclass correlation coefficient = 0.67, $p<0.001$) and valid - compared to the Actiheart activity monitor – (intraclass correlation coefficient = 0.40, $p=0.002$) questionnaire to determine self-reported physical activity in the same study population as in the current study [31]. The Adapted-SQUASH is pre-structured in four main domains outlining types and settings of activity: 'commuting traffic', 'activities at work and school', 'household activities' and 'leisure time activities' including 'sports activities'.

The total physical activity score (min x intensity/week) was calculated following the procedure described by Wendel-Vos et al. (2003) [44]. First, all the questions in the Adapted-SQUASH were assigned to a MET-value representing the intensity of this task, based on the Ainsworth' compendium of physical activities [45] and based on a compendium of energy costs of physical activities for wheelchair dependent individuals [46]. Second, an activity score was calculated for each domain by multiplying the total minutes of activity with a self-reported intensity score, which is based on age and MET-values [44]. Lastly, the total activity score was calculated by summing up the activity scores of the four domains. In accordance with the original SQUASH, data were excluded if the total minutes of activity a day exceeded 960 minutes or if values were missing [44].

Personal characteristics

Personal characteristics included sex, age at inclusion, Body Mass Index (BMI) in kg/m^2, drug use (yes or no), use of mobility aid (yes or no), and the diagnosis divided into the categories: musculoskeletal disease, brain disorder, neurologic disease, organ disease, other diseases. Sex, age, BMI, drug use and mobility aid were added as confounders in the association models. Brandenbarg et al. showed that age, sex and BMI had an significant effect on physical activity levels in people with a physical disability and/or chronic disease [47]. Besides, older participants could be more experienced in effective pacing patterns to avoid or minimize fatigue in daily life than younger participants [48] or older participants are less bound to work activities and other scheduled activities in the week compared to younger participants. Also, previous literature shows sex differences in self-reported fatigue [49].

Statistical analysis

Descriptive statistics of the included sample and the excluded sample were analysed with independent samples t-tests for continuous variables and with Chi-squared tests for categorical variables. Initially, data were explored to check the assumptions for a linear mixed model. The data adhered to the following assumptions: the determinants are linearly related to the outcome measure, the residuals have constant variance, the residuals are independent, and the residuals are normally distributed [50]. First, univariable longitudinal mixed model analyses were performed, in which the repeated measures over time of the day (morning, afternoon and evening) and different days were used as outcome measure. So the repeated measures over the day (morning, afternoon and evening) (level 1), were clustered within days (level 2) and were clustered within participants (level 3) in the longitudinal mixed model analyses. Each of the following determinants were separately associated with activity pacing behaviour (SD of AEE) in the univariable models: perceived fatigue, perceived activity pacing, and self-reported total physical activity. Subsequently we corrected for confounders: sex, age, body mass index, drug use and use of a mobility aid in multivariable longitudinal mixed model analyses. Random intercepts at participant level were added to the models. No random slopes were added to the models, since models with random slopes did not converge. All statistical analyses were performed using version 29 of the Statistical Package for the Social Science (SPSS). A p-value <.05 was interpreted as statistically significant.

Results

Out of a total of 80 participants who volunteered, 58 participants filled in the questionnaire, had at least four days of valid Actiheart data and were thus included in the current study. We included participants with four (N=5), five (N=1), six (N=6), and seven days (N=46) of valid Actiheart accelerometer data; thereof all participants had at least data of three weekdays and one weekend day available. Participants had an average age of 54.7 ± 18.7 years and 47% were male (Table 1). All but one of the personal factors were similar between the included and excluded samples. They only differed in the use of a mobility aid, where the excluded participants made more use of mobility aid compared to the included participants.

Table 1 Characteristics of the included participants (N=58) and excluded participants (N=22).

	Included participants (N=58)	**Excluded participants (N =22)**	
	Mean±SD or N (%)	Mean±SD or N (%)	p
Sex (% male)	27 (47)	9 (41)	.651
Age (years)	54.7 ± 18.7	61.8 ± 12.4	.255
Body height (m)	1.74 ± 0.1	1.68 ± 0.1	.068
Weight (kg)	80.8 ± 14.3	79.9 ± 16.5	.961
Body Mass Index (kg/m^2)	26.7 ± 4.5	28.4 ± 5.4	.276
Drug use (% yes)	48 (83)	13 (59)	.633
Use of mobility aid (% yes)	10 (17)	7 (32)	**.024**
Diagnosis			NA
Musculoskeletal disease	2 (3)	0 (0)	
Brain disorder	15 (26)	8 (36)	
Neurologic disease	5 (9)	3 (14)	
Organ disease	29 (50)	8 (36)	
Other diseases[a]	7 (12)	0 (0)	

SD=standard deviation, N=number of participants, NA=not applicable

[a] E.g., Ménière’s disease, Hereditary Motor and Sensory Neuropathy type II, worn neck vertebrae, low-back pain.

Values in bold: the characteristic is significantly different (p<0.05) between the participants included and excluded based on independent samples t-tests for continuous variables and based on Chi-squared tests for categorical variables.

Univariable longitudinal mixed models

Without adjusting for confounders in the univariable models, higher levels of the total physical activity score (B[SE]= .211[.074], 95%CI=.062-.360) were on average over time associated with higher levels of SD of AEE (Table 2). Without adjusting for confounders, perceived fatigue, perceived risk of overactivity and perceived awareness of activity pacing were on average over time not significantly associated with SD of AEE.

Multivariable longitudinal mixed models

After adjusting for sex, age, body mass index, drug use and use of a mobility aid, higher levels of the total physical activity score were on average over time associated with higher levels of SD of AEE (B[SE]=.151[.066], 95%CI=.018-.284) (Table 2). Perceived fatigue, perceived risk of overactivity and perceived awareness of activity pacing were on average over time not significantly associated with SD of AEE after adjusting for the confounders.

Table 2 Univariable and multivariable longitudinal mixed models separately for the four determinants (perceived fatigue, perceived risk of overactivity, perceived awareness of activity pacing, Total physical activity score) of accelerometer-derived activity pacing behaviour (defined as standard deviation of activity energy expenditure during the week) (N=58)

		Univariable models			Multivariable models adjusted for confounders*		
Model		B (SE)	95% CI	p-value	B (SE)	95% CI	p-value
1	Perceived fatigue	-.090 (.047)	-.185 - .005	.064	-.033 (.048)	-.129 - .064	.502
2	Perceived risk of overactivity	.018 (.077)	-.136 - .172	.816	.041 (.072)	-.103 - .186	.569
3	Perceived awareness of activity pacing	-.035 (.089)	-.212 - .143	.695	-.018 (.079)	-.177 - .141	.821
4	Total physical activity score (z-score)	.211 (.074)	.062 - .360	**.006**	.151 (.066)	.018 - .284	**.027**

*Confounders in the model are sex, age, body mass index, drug use and use of a mobility aid

B = regression coefficients, SE = standard error, CI = confidence interval

Values in bold: significant association (p<.05)

Discussion

The current study investigated how perceived fatigue, perceived activity pacing, and physical activity are associated with activity pacing behaviour during the week among people with physical disabilities and/or chronic diseases. Higher levels of physical activity were associated with higher variability in AEE during the week, even after adjusting for sex, age, body mass index, drug use and use of a mobility aid. Perceived fatigue and perceived activity pacing were not associated with variability in AEE after adjusting for the confounders. This may indicate that low variability in AEE – an evenly distributed activity pacing behaviour – is used to regulate fatigue through lowering physical activity peaks as a reactive response to symptom occurrence.

High levels of perceived fatigue were expected to be associated with low levels of variability in AEE, indicating an evenly distributed activity pacing behaviour, since previous studies of Murphy and Cuperus [24,26,51] found that a more stable pattern of activity pacing was associated with higher levels of fatigue, showing a symptom contingency response. The current study found that higher levels of fatigue were almost significantly associated with lower variability in AEE in the univariable models, but after correcting for sex, age, body mass index, drug use and use of a mobility aid in the multivariable model, perceived fatigue was far from a significant association with variability in AEE. So the corrected multivariable models in the current study might explain why our results are not in accordance with the results of Murphy and Cuperus [24,26,51].

The outcome variable variability of AEE was calculated as a measure of accelerometer derived activity pacing. However, perceived activity pacing was not significantly associated with the variability of AEE. Some factors might have influenced the perceived activity pacing including scheduled activities during the day or the week such as working hours or even the opening hours of sports facilities. So the people with physical disabilities and/or chronic diseases with higher levels of variability of AEE - having higher peaks in physical activity during the week (based on accelerometer data) - did not perceive a higher risk of overactivity. This finding may suggest that the people with physical disabilities and/or chronic diseases with higher levels of variability of AEE do not realize that activity bursts might relate to longer recovery periods since they did not receive any information and/or guidance on fatigue management. They might be able to manage more activity because of a better physical condition, or might be able to become even more physically active when receiving appropriate pacing advice [52].This was also found in an interview study among stroke survivors in which they reported that they need activity pacing advice to manage fatigue and to engage in physical activity [29]. The current study found this interesting discrepancy between perceived activity pacing measured with self-report and actual activity pacing patterns measured with an accelerometer, which was also found in previous literature [30]. Moreover, the current study investigated two activity pacing subscales 'awareness of pacing related decisions' and 'perceived risk of overactivity'. In future research, it might be interesting to investigate if accelerometer-derived activity pacing behaviour is associated with another subscale of activity pacing such as quota contingent (to increase function) versus symptom contingent (to reduce fatigue or pain) activity pacing behaviour [53].

Furthermore, this study found that higher levels of self-reported physical activity behaviour were significantly associated with higher variability of AEE. The low levels of physical activity found in people with a more evenly distributed activity pacing behaviour are similar to the finding of Murphy et al. [26] among women with lower-extremity osteoarthritis and Abonie et al. [30] among people with multiple sclerosis. Hence, people with an evenly distributed activity pacing behaviour might avoid physical activity in anticipation to fatigue, which was also found in a previous study among individuals with rheumatoid arthritis [51]. Overall, an evenly distributed activity pacing behaviour occurring in people with physical disabilities and/or chronic diseases is not associated with higher levels of physical activity. Some pilot studies in previous literature already showed promising effects of activity pacing interventions to improve physical activity behaviour [30,54,55].

People with physical disabilities and/or chronic diseases with an evenly distributed activity pacing behaviour might need advice on activity pacing strategies to change their beliefs that they should perform less if they are tired in order to engage more in physical activity [27,54]. However, we do not know the individuals' load-capacity ratio, which means that we do not know if they can become more physically active due to their condition and/or disabilities. On the other hand, people with high activity peaks during the day and week might need advice on how to be more aware of anticipatory ways in activity pacing in order to have a more even pacing pattern [27].

Strengths and limitations

This diagnosis-overarching study investigated perceived fatigue, perceived activity pacing and self-reported physical activity associated with accelerometer-derived activity pacing patterns from a new perspective by looking at longitudinal fluctuations of physical activity during the week. The current study findings provide valuable knowledge for designing tailored interventions on activity pacing in people with physical disabilities and/or chronic diseases. The outcomes of the current study build on existing evidence on activity pacing among people with physical disabilities and/or chronic diseases [24,26,27,56]. The data contribute to a clearer understanding of how individuals with physical disabilities and/or chronic diseases pace their activities on average over the week without receiving any fatigue guidance. This is highly relevant for designing successful interventions to manage fatigue and improve quality of life [2,25]. The fact that we investigated people with diverse physical disabilities and/or chronic diseases might help the understanding of diagnosis-overarching activity pacing and fatigue symptoms across different conditions.

Some limitations should also be kept in mind when interpreting our results. Firstly, we collected at least four consecutive days of Actiheart data for all participants, so for some participants their average activity pacing pattern during the week was based on four days which might not be a good representation of their activity pacing pattern during a full week. Consequently, this could have influenced the outcome variable variability of AEE. Additionally, we used the Actiheart activity monitor to study *fluctuations* of physical activity during the day, while the Actiheart is only validated to measure the *total amount of* physical activity over a day or week [34,35]. The Actiheart can be used to measure changes in sedentary behaviour, and light and moderate/vigorous activities in people without physical disabilities; however, it is not assessed on reliability and validity in people with physical disabilities yet [34]. Another limitation is that the participants were recruited from sport and exercise groups in rehabilitation centres and sport clubs, which might not be a representative sample of people with physical disabilities and/or chronic diseases, since these participants were relatively active. The participants also used drugs, inducing beta-blockers. This might have influenced the Actiheart outcome since it is not validated for people using beta-blockers, and beta-blockers influence heart rate, on which physical activity behaviour is partly calculated by the Actiheart. However, it was important for the study to include participants with heart diseases or stroke survivors, who might have used beta-blockers because these individuals commonly reported fatigue complaints and might benefit from advice on activity pacing. Moreover, this is a cross-sectional study, therefore intervention studies are needed to establish potential effects of activity pacing.

Future research and practical implications

We investigated the association between variability of AEE on different time points during the week and the average level of perceived fatigue. In future research it might be relevant to measure perceived fatigue on the different timepoints during the week, instead of measuring the average perceived fatigue over the week. This might give a more comprehensive picture of the association between activity pacing and perceived fatigue in people with physical disabilities and/or chronic diseases and might help to understand this association further. Furthermore, for future research, it is recommended to measure both accelerometer-derived activity pacing and perceptions of activity pacing by using a questionnaire, as we did in the current study, to better understand the overall sense of activity pacing. Moreover, although the included diverse population is a strength as mentioned above, our sample was too small to look at activity pacing behaviour in separate diagnosis groups. Potentially, interventions are needed to establish effects and future research in a larger cohort of people with physical disabilities and/or chronic diseases is needed to study whether the association between activity pacing behaviour, perceived fatigue, perceived awareness of activity pacing and physical activity is diagnosis-specific or more symptom-specific. Furthermore, the device-based approach on activity pacing requires validation since this technology has been validated only for physical activity. Intervention research is needed to explore the potential beneficial effects of appropriate advice and tailored guidance related to activity pacing and fatigue management. Based on these steps, strategies for fatigue management and a balanced healthy active lifestyle may benefit from activity pacing training programs in rehabilitation.

Conclusion

The current study found that higher levels of self-reported physical activity were associated with activity pacing behaviour with more activity peaks during the day – and in turn that lower levels of self-reported physical activity were associated with more evenly distributed activity pacing behaviour – after correcting for sex, age, body mass index, drug use and use of a mobility aid in people with physical disabilities and/or chronic diseases. However, we did not find an association between perceived fatigue and perceived activity pacing and the dependent variable accelerometer-derived activity pacing. This might indicate a reactive response to symptom occurrence. People with physical disabilities and/or chronic diseases might not realize that activity bursts could relate to longer recovery periods, which supports patients' needs for fatigue guidance during and after rehabilitation. Results suggested the potential of device-based activity pacing research among people with physical disabilities and/or chronic diseases. Future longitudinal and intervention research should investigate the potential and effect of tailored advice on activity pacing to improve physical activity behaviour in people with a physical disability and/or chronic disease, and eventually to improve health and well-being.

Acknowledgements

The authors want to thank the participants of the current study and the students in the bachelor and master Human Movement Sciences at the University of Groningen who contributed to the data collection. This study was funded by Stichting Beatrixoord Noord-Nederland. Bregje L. Seves received a 3-year personal grant from the University Medical Center Groningen to perform the current study (grant date 1-9-2018). Femke Hoekstra is supported by a Craig H. Neilsen Foundation Postdoctoral Fellowship (#719049) and Michael Smith Foundation for Health Research (MSFHR) Trainee Award (#RT-2020-0489).

References

1. Martin Ginis KA, Ma JK, Latimer-Cheung AE, et al. A systematic review of review articles addressing factors related to physical activity participation among children and adults with physical disabilities. Health psychology review. 2016;10(4):478-494.

2. Abonie US, Sandercock GRH, Heesterbeek M, et al. Effects of activity pacing in patients with chronic conditions associated with fatigue complaints: a meta-analysis. Disability and rehabilitation. 2018:1-10.

3. Swain MG. Fatigue in chronic disease. Clinical science (London, England : 1979). 2000;99(1):1-8.

4. De Groot MH, Phillips SJ, Eskes GA. Fatigue associated with stroke and other neurologic conditions: Implications for stroke rehabilitation. Archives of Physical Medicine and Rehabilitation. 2003;84(11):1714-1720.

5. Acciarresi M, Bogousslavsky J, Paciaroni M. Post-stroke fatigue: epidemiology, clinical characteristics and treatment. European neurology. 2014;72(5-6):255-261.

6. Alikari V, Sachlas A, Giatrakou S, et al. Fatigue in Arthritis: A Multidimensional Phenomenon with Impact on Quality of Life : Fatigue and Quality of Life in Arthritis. Adv Exp Med Biol. 2017;987:243-256.

7. Bruera E. Cancer-related fatigue: a multidimensional syndrome. J Support Oncol. 2010 Jul-Aug;8(4):175-6.

8. Da Costa D, Zummer M, Fitzcharles MA. Biopsychosocial determinants of physical and mental fatigue in patients with spondyloarthropathy. Rheumatol Int. 2011 Apr;31(4):473-80.

9. Kluger BM, Krupp LB, Enoka RM. Fatigue and fatigability in neurologic illnesses: proposal for a unified taxonomy. Neurology. 2013;80(4):409-416.

10. Enoka RM, Duchateau J. Translating Fatigue to Human Performance. Medicine and science in sports and exercise. 2016;48(11):2228-2238.

11. Falup-Pecurariu C. Fatigue assessment of Parkinson's disease patient in clinic: specific versus holistic. J Neural Transm (Vienna). 2013 Apr;120(4):577-81.

12. Billones R, Liwang JK, Butler K, et al. Dissecting the fatigue experience: A scoping review of fatigue definitions, dimensions, and measures in non-oncologic medical conditions. Brain Behav Immun Health. 2021 Aug;15:100266.

13. Adamowicz JL, Vélez-Bermúdez M, Thomas EBK. Fatigue severity and avoidance among individuals with chronic disease: A meta-analysis. J Psychosom Res. 2022 Aug;159:110951.

14. MacIntosh BJ, Edwards JD, Kang M, et al. Post-stroke Fatigue and Depressive Symptoms Are Differentially Related to Mobility and Cognitive Performance. Front Aging Neurosci. 2017;9:343.

15. Kluger BM, Pedersen KF, Tysnes OB, et al. Is fatigue associated with cognitive dysfunction in early Parkinson's disease? Parkinsonism Relat Disord. 2017 Apr;37:87-91.

16. Aldughmi M, Bruce J, Siengsukon CF. Relationship Between Fatigability and Perceived Fatigue Measured Using the Neurological Fatigue Index in People with Multiple Sclerosis. Int J MS Care. 2017 Sep-Oct;19(5):232-239.

17. Segura-Jiménez V, Estévez-López F, Castro-Piñero J, et al. Association of Patterns of Moderate-to-Vigorous Physical Activity Bouts With Pain, Physical Fatigue, and Disease Severity in Women With Fibromyalgia: the al-Ándalus Project. Arch Phys Med Rehabil. 2019 Jul;100(7):1234-1242.e1.

18. Haskell WL, Lee IM, Pate RR, et al. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. Circulation. 2007;116(9):1081-1093.

19. Bull FC, Al-Ansari SS, Biddle S, et al. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. Br J Sports Med. 2020 Dec;54(24):1451-1462.

20. Andrews NE, Strong J, Meredith PJ. Activity pacing, avoidance, endurance, and associations with patient functioning in chronic pain: a systematic review and meta-analysis. Archives of Physical Medicine and Rehabilitation. 2012;93(11):2109-2121.e7.

21. Antcliff D, Keeley P, Campbell M, et al. Activity pacing: moving beyond taking breaks and slowing down. Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation. 2018.

22. Nijs J, van Eupen I, Vandecauter J, et al. Can pacing self-management alter physical behavior and symptom severity in chronic fatigue syndrome? A case series. J Rehabil Res Dev. 2009;46(7):985-96.

23. Kos D, van Eupen I, Meirte J, et al. Activity Pacing Self-Management in Chronic Fatigue Syndrome: A Randomized Controlled Trial. Am J Occup Ther. 2015 Sep-Oct;69(5):6905290020.

24. Murphy SL, Kratz AL. Activity pacing in daily life: A within-day analysis. Pain. 2014;155(12):2630-2637.

25. Abonie US, Edwards AM, Hettinga FJ. Optimising activity pacing to promote a physically active lifestyle in medical settings: A narrative review informed by clinical and sports pacing research. Journal of sports sciences. 2020;38(5):590-596.

26. Murphy SL, Smith DM, Alexander NB. Measuring activity pacing in women with lower-extremity osteoarthritis: a pilot study. The American Journal of Occupational Therapy : Official Publication of the American Occupational Therapy Association. 2008;62(3):329-334.

27. Abonie US, Hoekstra F, Seves BL, et al. Associations between Activity Pacing, Fatigue, and Physical Activity in Adults with Multiple Sclerosis: A Cross Sectional Study. Journal of Functional Morphology and Kinesiology. 2020;5(2):43.

28. Nielson WR, Jensen MP, Karsdorp PA, et al. Activity pacing in chronic pain: concepts, evidence, and future directions. The Clinical journal of pain. 2013;29(5):461-468.

29. Seves BL H, T, Hettinga FJ, Brandenbarg P, Dekker R, Krops LA, van der Woude LHV, Hoekstra F. Perceptions and experiences of the impact of fatigue on physical activity 5-8 years after stroke rehabilitation: an interview study. 2023.

30. Abonie US, Saxton J, Baker K, et al. Objectively-assessed physical activity and self-reported activity pacing in adults with multiple sclerosis: A pilot study. Clin Rehabil. 2021 Dec;35(12):1781-1788.

31. Seves BL, Hoekstra F, Schoenmakers JWA, et al. Test-retest reliability and concurrent validity of the Adapted Short QUestionnaire to ASsess Health-enhancing physical activity (Adapted-SQUASH) in adults with disabilities. medRxiv. 2020:2020.09.09.20190371.

32. Hoekstra F, Alingh RA, van der Schans CP, et al. Design of a process evaluation of the implementation of a physical activity and sports stimulation programme in Dutch rehabilitation setting: ReSpAct. Implementation science : IS. 2014;9:127-014-0127-7.

33. Alingh RA, Hoekstra F, van der Schans CP, et al. Protocol of a longitudinal cohort study on physical activity behaviour in physically disabled patients participating in a rehabilitation counselling programme: ReSpAct. BMJ open. 2015;5(1):e007591-2015-007591.

34. Brage S, Brage N, Franks PW, et al. Reliability and validity of the combined heart rate and movement sensor Actiheart. European journal of clinical nutrition. 2005;59(4):561-570.

35. Crouter SE, Churilla JR, Bassett DR, Jr. Accuracy of the Actiheart for the assessment of energy expenditure in adults. European journal of clinical nutrition. 2008;62(6):704-711.

36. Murphy SL, Smith DM, Lyden AK. Type of activity pacing instruction affects physical activity variability in adults with symptomatic knee or hip osteoarthritis. Journal of physical activity & health. 2012;9(3):360-366.

37. Fleurke AM, Goossen WTF, Hoijtink EJ, et al. Fatigue Severity Scale (FSS). 2004.

38. Whitehead L. The measurement of fatigue in chronic illness: a systematic review of unidimensional and multidimensional fatigue measures. Journal of pain and symptom management. 2009;37(1):107-128.

39. Elbers RG, Rietberg MB, van Wegen EE, et al. Self-report fatigue questionnaires in multiple sclerosis, Parkinson's disease and stroke: a systematic review of measurement properties. Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation. 2012;21(6):925-944.

40. Krupp LB, LaRocca NG, Muir-Nash J, et al. The fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. Arch Neurol. 1989 Oct;46(10):1121-3.

41. Smits BL, Pepping GJ, Hettinga FJ. Pacing and decision making in sport and exercise: the roles of perception and action in the regulation of exercise intensity. Sports medicine (Auckland, NZ). 2014;44(6):763-775.

42. Goudsmit EM, Nijs J, Jason LA, et al. Pacing as a strategy to improve energy management in myalgic encephalomyelitis/chronic fatigue syndrome: a consensus document. Disability and rehabilitation. 2012;34(13):1140-1147.

43. White PD, Goldsmith KA, Johnson AL, et al. Comparison of adaptive pacing therapy, cognitive behaviour therapy, graded exercise therapy, and specialist medical care for chronic fatigue syndrome (PACE): a randomised trial. Lancet (London, England). 2011;377(9768):823-836.

44. Wendel-Vos GC, Schuit AJ, Saris WH, et al. Reproducibility and relative validity of the short questionnaire to assess health-enhancing physical activity. Journal of clinical epidemiology. 2003;56(12):1163-1169.

45. Ainsworth BE, Haskell WL, Herrmann SD, et al. 2011 Compendium of Physical Activities: a second update of codes and MET values. Medicine and science in sports and exercise. 2011;43(8):1575-1581.

46. Conger SA, Bassett DR. A compendium of energy costs of physical activities for individuals who use manual wheelchairs. Adapted physical activity quarterly : APAQ. 2011;28(4):310-325.

47. Brandenbarg P, Hoekstra F, Krops LA, et al. Physical activity behaviour up to 1 year post-rehabilitation among adults with physical disabilities and/or chronic diseases: results of the prospective cohort study ReSpAct. BMJ Open. 2022 Jun 15;12(6):e056832.

48. Menting SGP, Edwards AM, Hettinga FJ, et al. Pacing Behaviour Development and Acquisition: A Systematic Review. Sports Med Open. 2022 Dec 9;8(1):143.

49. Pawlikowska T, Chalder T, Hirsch SR, et al. Population based study of fatigue and psychological distress. BMJ : British Medical Journal. 1994;308(6931):763-766.

50. Twisk JWR. Applied Longitudinal Data Analysis for Epidemiology: A Practical Guide. Second edition ed. New York: Cambridge University Press; 2013. (Book, Whole).

51. Cuperus N, Hoogeboom TJ, Neijland Y, et al. Are people with rheumatoid arthritis who undertake activity pacing at risk of being too physically inactive? Clinical rehabilitation. 2012;26(11):1048-1052.

52. Antcliff D, Keenan AM, Keeley P, et al. "Pacing does help you get your life back": The acceptability of a newly developed activity pacing framework for chronic pain/fatigue. Musculoskeletal care. 2021.

53. Antcliff D, Campbell M, Woby S, et al. Assessing the Psychometric Properties of an Activity Pacing Questionnaire for Chronic Pain and Fatigue. Physical Therapy. 2015;95(9):1274-86.

54. Abonie US, Hettinga FJ. Effect of a Tailored Activity Pacing Intervention on Fatigue and Physical Activity Behaviours in Adults with Multiple Sclerosis. Int J Environ Res Public Health. 2020 Dec 22;18(1).

55. Gill JR, Brown CA. A structured review of the evidence for pacing as a chronic pain intervention. European journal of pain (London, England). 2009;13(2):214-216.

56. Seves BL, Hoekstra T, Hoekstra F, et al. Unravelling perceived Fatigue and Activity pacing in maintaining a physically active Lifestyle after Stroke Rehabilitation: a longitudinal cohort study. Disability and rehabilitation (submitted). 2020.

Chapter 6

Unravelling perceived fatigue and activity pacing in maintaining a physically active lifestyle after stroke rehabilitation: a longitudinal cohort study

Seves BL, Hoekstra T, Hoekstra F, ReSpAct group, Hettinga FJ, Dekker R, van der Woude LHV.

Disability and Rehabilitation, 2021; Dec;43(24):3492-3502

Abstract

Purposes: To identify fatigue trajectories during/after stroke rehabilitation, to determine characteristics associated with trajectory membership before discharge and to investigate how these trajectories and activity pacing are associated with sustained physical activity after rehabilitation.

Methods: People after stroke (N=206) were followed from 3-6 weeks before discharge (T0) to 14 (T1), 33 (T2) and 52 (T3) weeks after discharge from rehabilitation in the ReSpAct study. Latent Class analysis was used to identify trajectories of perceived fatigue. Binomial multivariable regression analyses were performed to determine characteristics associated with trajectory membership (T0). Multilevel analyses were used to investigate how perceived fatigue and activity pacing were associated with self-reported physical activity (T0-T3).

Results: Three fatigue trajectories were identified: high (N=163), low (N=41) and recovery (N=2). Compared with the high fatigue trajectory, people in the low fatigue trajectory were more likely to report higher levels of health-related quality of life (HR-QoL) (OR=3.07, 95%CI=1.51-6.26) and physical activity (OR=1.93, 95%CI=1.07-3.47). Sustained high levels of physical activity after rehabilitation were significantly associated with low perceived fatigue and high perceived risk of overactivity.

Conclusions: Three fatigue trajectories after stroke rehabilitation were identified. High levels of HR-QoL and physical activity before discharge identified people in the low fatigue trajectory. A physically active lifestyle after rehabilitation was associated with low perceived fatigue and perceived risk of overactivity.

Key words

Stroke, Physical activity, Perceived fatigue, Activity Pacing, Latent class analyses, Health promotion, Quality of life.

Implications for rehabilitation

- Since almost 80% of people after stroke in this study perceived severe fatigue up to 1 year after stroke rehabilitation, activities focusing on the management of fatigue symptoms should be integrated in general stroke rehabilitation.
- In clinical practice, low levels of health-related quality of life and low levels of self-reported physical activity before discharge from stroke rehabilitation should be considered by rehabilitation professionals (e.g., physicians, physiotherapists, and physical activity counsellors) since these characteristics can predict chronic perceived fatigue up to 1 year after stroke rehabilitation.
- A physical activity counselling programme delivered during and after stroke rehabilitation may be improved by incorporating tailored advice regarding the management of fatigue.

Introduction

It is worrisome that most people after stroke, one of the largest populations in rehabilitation [1, 2], spend their time inactive and sedentary [3]. This is the more so, since a physically active lifestyle contributes to the improvement of functioning and health (e.g. reducing the risk of new cardiovascular events and maintaining functional autonomy), encourages socialization (e.g. participating in sports groups), and is deemed crucial for quality of life [1, 3-5]. Promoting physical activity during and after stroke rehabilitation seems to be promising and is therefore recommended [6-9]. Although research has shown that tailored physical activity counselling sessions can increase physical activity levels in people after stroke [6, 7], these increased physical activity levels are not always sustained at the longer term. A possible reason for this is that people after stroke may experience barriers to obtain and maintain a physically activity lifestyle [10, 11].

A common and distressing personal barrier that is often reported by people after stroke is (perceived) fatigue, which is also one of the strongest predictors of daily functional limitations [12, 13]. Indeed, people after stroke reported higher levels of fatigue compared with healthy adults [14]. However, there is a large variability in fatigue levels reported by and measured in people after stroke [15, 16]. The wide variability in fatigue (wide range of prevalence and intensity) in people after stroke is potentially driven by population heterogeneity [13], for example age, sex, depression, pain, anxiety symptoms, employment status before stroke, pre-stroke fatigue and excessive daytime sleepiness [17-20]. Furthermore, the variability in (perceived) fatigue can be due to the large variation in measurement tools to assess fatigue (e.g. maximal voluntary contractions versus surveys) [13, 21] and/or the large variation in definitions of fatigue [16]. Enoka and Duchateau (2016) previously raised this terminology issue and defined fatigue as “a disabling symptom in which physical and cognitive function is limited by interactions between performance fatigue and perceived fatigue” [22, 23]. The current study only focused on perceived fatigue assessed with a questionnaire (the fatigue severity scale). It explores the large variability in fatigue among people after stroke in a longitudinal multicentre study design focussed on the evolution over time of a physically active lifestyle after rehabilitation [15, 16, 24]. This prospective questionnaire-based cohort study provided the opportunity to explore perceived fatigue patterns over time (trajectories of perceived fatigue) in people after stroke [16, 25] (by performing latent class growth mixture modelling) in the context of a physically active lifestyle, personal, disease/health, psychosocial, lifestyle and environmental characteristics.

How people effectively manage their fatigue during the day, e.g. by dividing their daily activities into smaller, more manageable, portions, is called activity pacing behaviour. Questions raised when unravelling fatigue in the context of a physically active lifestyle in general are: how do people deal with their fatigue during the day, and how do people divide their energy and daily physical activities during the day in order to reduce fatigue? Two different attitudes towards activity pacing behaviour can be identified: (1) people are at risk of underactivity and probably more aware of how they divide their energy and activities during the day, as they are afraid to overdo the activities [26] and (2) people are at risk of overactivity characterized by an un-even activity pattern consisting of high activity peaks followed by long periods of inactivity [27-33]. Literature on activity pacing in rehabilitation populations today is scarce [34, 35]. A better understanding of activity pacing behaviour in people after stroke with varying levels of perceived fatigue might provide new directions for more person-specific physical activity stimulation programmes in rehabilitation.

The physical activity and sport stimulation programme Rehabilitation, Sports and Exercise (RSE; Dutch: ‘Revalidatie, Sport en Bewegen’) is a programme in rehabilitation practice aiming to stimulate an active lifestyle in adults with a physical disability and/or chronic disease [36, 37]. The Rehabilitation, Sports and Active lifestyle study (ReSpAct) is a multicentre longitudinal cohort study (with people after stroke as largest subgroup), that was designed to evaluate the RSE programme [36, 37] within the context of the International Classification of Disability, Functioning and Health [38].

The current study is part of the ReSpAct study and aimed (1) to explore perceived fatigue with identifying trajectories of perceived fatigue during and after stroke rehabilitation, (2) to determine which personal, disease/health, psychosocial, lifestyle and environmental characteristics before discharge are associated with the different trajectories of perceived fatigue (also called trajectory membership of perceived fatigue) and (3) to explore how trajectories of perceived fatigue and activity pacing are associated with physical activity over time up to one year after stroke rehabilitation. In the current study associations between physical activity, perceived fatigue and activity pacing will be studied in separate statistical models to help understand the independent role of perceived fatigue as well as in combination with activity pacing. In this context the following hypotheses were formulated: firstly, we hypothesized that most people after stroke perceive chronic high fatigue levels even up till one year after rehabilitation [1, 13]. Secondly, we expected personal related and disease/health related characteristics to be associated with trajectory membership of perceived fatigue. Thirdly, we hypothesized that high perceived fatigue is associated with maintaining a lower physically active lifestyle after stroke rehabilitation [39, 40]. Finally, we expected that when people after stroke are aware of their activity pacing related decisions, it allows them to gradually enhance physical activity after stroke rehabilitation [41-43].

Methods

Context and theoretical framework

This study is part of the multicentre longitudinal cohort study ReSpAct that was designed to evaluate the RSE programme [36, 37]. This motivational interview-based physical activity and sport stimulation RSE programme aims to stimulate an active lifestyle in people with a physical disability and/or chronic disease during the rehabilitation period and to guide them in maintaining a physically active lifestyle in the home setting after discharge from rehabilitation [36, 37]. Three to six weeks before discharge from rehabilitation, participants in the RSE programme were referred to a physical activity counselling centre for a face-to-face consultation with a physical activity and sports counsellor, followed by four telephone-based counselling sessions (based on motivational interviewing) up to thirteen weeks after discharge from rehabilitation [36, 37]. The RSE programme was successfully implemented in Dutch rehabilitation practice [8].

The stages of change concept of the Transtheoretical model and the Physical Activity for people with a Disability (PAD) model [44] formed the theoretical basis for the RSE programme [37]. These models provide insight into the process of behavioural change and the relationships between physical activity behaviour, its determinants and the daily functioning of people with a disability [44]. The PAD model is an integration of the Attitude, Social influence and self-Efficacy model in the International Classification of Functioning, Disability and Health (ICF) model [44].

Participants were included in the ReSpAct study from May 2013 till August 2015. Participants were followed over time: at baseline (T0: 3-6 weeks before discharge) and at 14 (T1), 33 (T2) and 52 (T3) weeks after discharge from clinical rehabilitation [37]. Each measurement consisted of filling out a set of questionnaires. The study was approved by the ethics committee of the Center for Human Movement Sciences of the University Medical Center Groningen (reference: ECB/2013.02.28_1, which can be found on the Open Science Framework: osf.io/f4hjc/). All participants signed an informed consent.

Study population

Participants were recruited through seventeen rehabilitation institutions across the Netherlands (11 rehabilitation centres and 6 rehabilitation departments of hospitals). Inclusion criteria for the current study were (1) being at least eighteen years of age, (2) having been diagnosed with stroke, (3) receiving inpatient or outpatient rehabilitation care or treatment within one of the participating rehabilitation institutions, (4) participating in the RSE programme, and (5) filling in the Fatigue Severity Scale (FSS) at two or more measurement occasions. Participants were excluded when they were not able to complete the questionnaires, even with help, or were participating in another physical activity stimulation programme [37]. The current study concerns the cohort of those persons with a stroke.

Measures

Self-reported physical activity

Physical activity was assessed with the Short Questionnaire to Assess Health-enhancing physical activity (SQUASH) [45], a 19-item self-reported recall questionnaire, which is a valid and reliable measurement tool to assess the total minutes of physical activity in healthy adults [45] and in patient populations [46, 47] based on an average week in the past month. The SQUASH is pre-structured in four main domains outlining types and settings of activity: 'commuting traffic', 'activities at work and school', 'household activities' and 'leisure time activities' including 'sports activities' [45]. The ReSpAct research team adapted the SQUASH to make it applicable for people with a physical disability and/or chronic disease as described elsewhere [37]. The intraclass correlation coefficient for the test-retest reliability of the Adapted-SQUASH was 0.73 ($p<0.001$) for the total minutes of activity. A significant Spearman correlation coefficient was found for the total minutes of activity ($\rho=0.34$, $p=0.008$) between the Actiheart and the Adapted-SQUASH. A scientific paper is in preparation.

Perceived fatigue

Perceived fatigue severity was assessed by using the FSS questionnaire [48, 49]. The FSS (range: 1-7) is a valid and reliable questionnaire to determine the impact of perceived fatigue in several patient populations (e.g. stroke) [50, 51] and to detect change over time [50]. A higher score on the FSS indicated greater fatigue severity, in which a FSS score of 4 or greater indicates severe fatigue [48].

Activity pacing

Activity pacing was assessed by using a self-constructed seven-item questionnaire based on literature [52-54]. This questionnaire assessed the two different attitudes of activity pacing and evaluated how and based on what aspects people modify their physical activity behaviour over the day. The questionnaire includes two constructs of attitudes towards engagement in activity pacing: (1) a two-item construct on persons' perceptions of being at risk of overactivity (Cronbach's alpha = .71), and (2) a five-item construct on persons' awareness of their engagement in activity pacing (Cronbach's alpha = .78). The participants scored the seven items of the questionnaire on a scale of 1-5 (1=never, 2=rarely, 3=sometimes, 4=often, 5=very often). Sum scores were calculated for each construct (range from 2-10 and from 5-25 respectively). Reliability and construct validity have been investigated by the ReSpAct research team and a paper is in preparation [55].

Personal characteristics

Personal characteristics include sex, age at inclusion, Body Mass Index (BMI) in kg/m^2, living situation and level of education dichotomized into low (up to completed secondary education) and high (completed applied University or higher) to make it internationally comparable.

Disease/Health characteristics

Disease/health characteristics include the number of comorbidities dichotomized into no comorbidities and one or more comorbidities, because this variable included all kind of diseases and disabilities reported by a participant, which makes this value hard to compare between people. The level of acceptance of the stroke was assessed on a four-point Likert scale (1-4, no acceptance to complete acceptance), with a higher score indicating better acceptance of the stroke. The level of acceptance was dichotomized into no (no or little acceptance) and yes (acceptance to a large extent or completely), because the assumption for linearity was not met. Health-related quality of life (HR-QoL) was assessed by using the self-reported RAND-12 questionnaire [56], an adapted, abbreviated version of the RAND-36 [57-59]. We used an age-corrected general health score for this study [57]. A higher score on the RAND-12 (range 0-65) indicated better quality of life [57, 58].

Psychosocial characteristics

Psychosocial characteristics include motivation towards physical activity assessed with the 19-item Behavioural Regulation in Exercise Questionnaire (BREQ-2) (range of the total score from

-80 to 80) [60]. The BREQ-2 is factorially validated among adults who participated in an exercise referral scheme [60]. Self-efficacy towards physical activity (range: 0-70) was assessed by using five items out of an existing questionnaire, which was designed to measure one's ability to maintain physical activity in various situations and showed good internal consistency (Cronbach's α=0.82) [61], and two additional items formulated by the ReSpAct research team in order to assess a more comprehensive self-efficacy construct. The internal consistency of the self-efficacy questionnaire assessed in the ReSpAct cohort (N=1719) improved after adding the two items. More information on the internal consistency of the self-efficacy questionnaire used in this study can be found on the Open Science Framework (osf.io/mg6z9/).

Lifestyle characteristics

Lifestyle characteristics included the dichotomous variables smoking and alcohol use ("Do you currently smoke?" and "Do you currently consume alcohol?": yes or no). Information on sports participation (yes/no) was obtained from an additional question derived from the SQUASH questionnaire. If the participant reported to perform at least one sports activity per week, than they were coded as ´yes', if not as ´no´.

Environmental characteristics

Environmental characteristics include the rehabilitation and treatment context and the number of received physical activity counselling moments as part of the RSE programme.

Statistical analyses

Descriptive statistics at baseline (T0) of the included sample, the excluded sample and for the trajectories of perceived fatigue were analysed using the Statistical Package for the Social Science (IBM SPSS Statistics, version 24). The statistical analyses for the three aims of this study are described below.

Firstly, trajectories of perceived fatigue during and after rehabilitation were identified by fitting Latent Class Growth Mixture (LCGM) models to the data of the FSS score, with quadratic (assuming non-linear change over time), linear (assuming linear change over time) and latent class analyses (LCA) models [62], using the Mplus software programme 7.11 (Muthén & Muthén, Los Angeles, CA). From the ReSpAct study population, only people after stroke with at least two measurement occasions over time were included for these analyses. LCGM models are based on regression and structural equation modelling techniques. These techniques assume that there are multiple underlying subpopulations (or latent classes), that each follow a unique trajectory of perceived fatigue over time, which provide us with insight in the heterogeneity of patterns in perceived fatigue over time. The latent classes to which individuals belong are denoted by the term 'trajectory membership'. The classes in perceived fatigue are based on the total FSS scores at T0, T1, T2 and T3 (dependent variables). Common stepwise modelling strategies were applied [62]. The Guidelines for Reporting on Latent Trajectory Studies (GRoLTS) were used to transparently report the results of the LCGM modelling analyses [63]. First, a one-class model was determined. Subsequently more classes were added one at a time to investigate if the model fit improves due to the additional class [62, 64]. A 1-4 trajectory solution was inspected. The optimal number of classes was determined according to the following model fit criteria: (1) a lower Bayesian Information Criterion (BIC), where a difference of ten points lower is usually regarded as sufficient improvement [65], (2) a higher entropy (range from 0 to 1), a standardized measure of how accurately individuals' trajectories are classified, where higher values indicate better classification [66, 67] and (3) average posterior probabilities of ≥0.80 [62]. In addition, clinical interpretation (rejecting solutions that do not make clinical sense) of the trajectories were considered for the optimal number of classes. Participants were classified into their most likely class (trajectory membership) based on their posterior probabilities.

Secondly, a binomial multivariable logistic regression analysis was performed to assess associations between trajectory membership (dependent variable) and different independent variables: characteristics of the study population (personal, disease/health, psychosocial, lifestyle and environmental), using the Statistical Package for the Social Science (IBM SPSS Statistics, version 24). Descriptive statistics of the independent variables were analysed at baseline. Assumptions of normality and linearity were met. All continuous independent variables were standardized. Independent variables at baseline were all entered block wise based on the PAD model (block 1: personal characteristics, block 2: disease/health characteristics, block 3: psychosocial characteristics, block 4: lifestyle characteristics, block 5: environmental characteristics) in a multivariable model. Results of the binomial multivariable logistic regression analysis were presented as odds ratios (OR) and corresponding 95% confidence intervals (95%CI).

Thirdly, multilevel regression analysis was performed to determine whether and how perceived fatigue and attitudes towards engagement in activity pacing were associated with physical activity up to one year after stroke rehabilitation by using MLwiN 3.0. Total minutes of physical activity based on the SQUASH was the dependent variable in the multilevel regression analysis. A three-level model was used in which repeated measures (Level 1) were clustered within individuals (Level 2), and individuals were clustered within institutions (Level

3). The model was corrected for sex, age, BMI and treatment context at baseline (level two variables), as well as motivation and self-efficacy scores from T0 to T3 (level one variables). These confounders are based on the PAD model. Firstly, perceived fatigue was added in model 1 as independent variable, a dichotomized variable based on the identified high and low fatigue trajectories. Activity pacing for both awareness of engagement in activity pacing and perceived risk of overactivity were entered separately (due to collinearity) in respectively model 2 and model 3. All continuous variables in the multilevel model were standardized. Random intercepts were considered thus allowing a unique intercept for each individual participant [68]. We expected variation in physical activity behaviour between participants. Therefore, random slopes were entered into the model to properly account for correlations amongst repeated measures within individuals. The independent variables were entered separately into the initial model. During each step goodness of fit was evaluated by comparing the -2*Log Likelihood (IGLS deviance) of the previous model, with the most recent model. In general, two-sided p-values were given, where a p-value lower than 0.05 was regarded as statistically significant.

To facilitate transparency and reproducibility, additional information is available in the supplemental file on osf.io/rtz5y/: (a) the dataset of perceived fatigue at T0-T3, (b) the Mplus syntax of the LCGM modelling, the SPSS syntax of the binomial multivariable logistic regression analysis, and the multilevel models in MLwiN, and (c) an overview table of the statistical analyses used in the current study.

Results

Characteristics of the participants

In total 303 persons after stroke were included in the ReSpAct study, whereof data from 206 participants (68%) completed at least two measurement occasions with perceived fatigue data and were included in the LGCM modelling analyses. Participants had an average age of 55.3 ± 10.8 years and 41.7% were female (Table 1). Descriptive statistics at T0 for included (N=206) and excluded (N=97) participants for the LCGM modelling analyses are presented in table 1. Participants excluded for the LGCM modelling analyses lived less independent, had worse acceptance of the stroke, had a lower HR-QoL score, smoked more, and received less physical activity counselling moments after rehabilitation.

Table 1 Participants' descriptive statistics at baseline for participants included (N=206) and excluded (N=97) in the latent class growth mixture modelling analyses.

Characteristics	Included in LCGMM Mean ± SD or % (N)	Excluded for LCGMM Mean ± SD or % (N)	Test value	p-value
Personal				
Sex (% female)	41.7 (86)	45.4 (44)	0.35	.553
Age (years)	55.3 ± 10.8	52.8 ± 11.4	-1.77	.077
Body mass index (kg/m^2)	26.5 ± 4.6	27.1 ± 5.3	0.95	.342
Education level (% high)[a]	20.4 (42)	8.2 (8)	2.97	.085
Living situation (% independent)	88.3 (182)	57.7 (56)	**9.37**	**.002**
Activity pacing				
Perceived risk of overactivity	6.9 ± 1.9	6.9 ± 2.0	0.04	.968
Awareness of activity pacing	17.8 ± 3.4	17.9 ± 3.4	0.30	.768
Psychosocial				
Motivation	45.1 ± 21.5	48.8 ± 21.3	1.34	.181
Self-efficacy	41.1 ± 11.5	39.6 ± 12.9	-0.92	.361
Disease/health				
Fatigue (FSS score)	4.3 ± 1.4	4.6 ± 1.6	1.44	.152
Acceptance (%yes)	51.0 (105)	24.7 (24)	**6.85**	**.009**
Comorbidity (% yes)[b]	33.0 (68)	23.7 (23)	0.01	.951
HR-QoL (general health)	38.6 ± 8.7	35.2 ± 8.3	**-2.30**	**.023**
Lifestyle				
PA (total minutes per week)	963.3 ± 818.0	1049.3 ± 943.4	0.76	.447

Sports participation (%yes)	54.4 (112)	48.5 (47)	0.00	.994
Smoking (% yes)	11.2 (23)	11.3 (11)	**3.87**	**.049**
Alcohol use (% yes)	34.5 (71)	19.6 (19)	0.13	.716
Environmental				
Treatment form (% outpatient)[c]	88.8 (183)	89.7 (87)	0.05	.823
Treatment context (% hospital)	27.7 (57)	25.8 (25)	0.12	.729
Amount of physical activity counselling moments after rehabilitation[d]	2.8 ± 1.4	2.0 ± 1.6	**-3.97**	**<.001**

[a] Completed applied University or higher

[b] Percentage of participants with one or more comorbidities

[c] Treatment form includes outpatient and inpatient

[d] Participants in the Rehabilitation, Sports and Exercise programme received four telephone-based counselling sessions with a sports counsellor

Standard deviation (SD); Number of participants (N); Latent Class Growth Mixture Modelling (LCGMM); Fatigue Severity Scale (FSS); Health-related Quality of Life (HR-QoL); Physical activity (PA)

Values in bold: the characteristic is significantly different ($p<0.05$) between the participants included and those excluded from the LCGMM, based on independent sample t-tests for continuous variables and based on Chi-squared tests for categorical variables.

Trajectories of perceived fatigue

LCGM modelling showed distinct trajectories of perceived fatigue based on the total FSS score after rehabilitation (N=206). The results of the fit indices for quadratic, linear and LCA models with one to four trajectories are presented in table 2. According to the model fit criteria (Table 2) and clinical interpretation the three-trajectory linear model for perceived fatigue was superior. Quadratic and LCA models were considered, but showed worse statistical fit compared with the linear models. Three fatigue trajectories were identified whereof one large and stable trajectory with slightly increasing high perceived fatigue over time (labelled 'high', N=163, 79.1%), one smaller stable trajectory with slightly decreasing low perceived fatigue over time (labelled 'low', N=41, 19.9%), and one very small trajectory with a large decline in perceived fatigue (labelled 'recovery', N=2, 1.0%) (Figure 1). Supplementary figures can be found in the supplemental file on osf.io/rtz5y/, including estimated mean trajectories for each model and the estimated with observed means for the final model. For each trajectory of perceived fatigue, the estimated mean with individual trajectories are presented in figure 2. Although the average course of perceived fatigue is relatively stable over time, figure 2 shows that heterogeneity within the identified trajectories of perceived fatigue is high. Most individual trajectories in the trajectory of high perceived fatigue lie above the cut-off point (FSS>4) for severe fatigue (Figure 2a) and in the trajectory of low perceived fatigue lie below this cut-off point (Figure 2b). The two individual trajectories within the trajectory of recovery perceived fatigue show a large shift from severe fatigue (T0-T1) to low fatigue (T2-T3). The trajectory of recovery perceived fatigue was left out of further analyses due to the too small sample size.

Table 2 Fit indices for Latent Class Growth Mixture models with 1-4 trajectories of perceived fatigue (FSS score) in people after stroke rehabilitation (N=206).

Perceived fatigue (FSS score)							
				Number of participants in each trajectory class			
Number of classes	BIC	Entropy	Average posterior probability (min-max)	1	2	3	4
Linear analyses							
1	5327.57	NA	1.0	206			
2	5301.43	.78	.93 (.91 - .95)	39	167		
3	**5298.09**	**.86**	**.94 (.88 - 1.00)**	**163**	**41**	**2**	
4	5304.35	.85	.89 (.74 - 1.00)	155	42	2	7
Pattern analyses							
1	5647.17	NA	1.0	206			
2	5417.01	.83	.93 (.90 - .97)	61	145		
3	5343.73	.80	.91 (.88 - .92)	30	72	104	
4	5343.08	.82	.88 (.82 - .92)	27	107	65	7
Quadratic analyses							
1	5324.51	NA	1.0	206			
2	5304.46	.78	.93 (.91 - .95)	38	168		
3	5303.18	.83	.91 (.89 - .95)	35	166	5	
4	5306.05	.83	.90 (.77 - 1.00)	36	155	13	2

BIC: Bayesian Information Criterion; NA: Not applicable; FSS: Fatigue Severity Scale

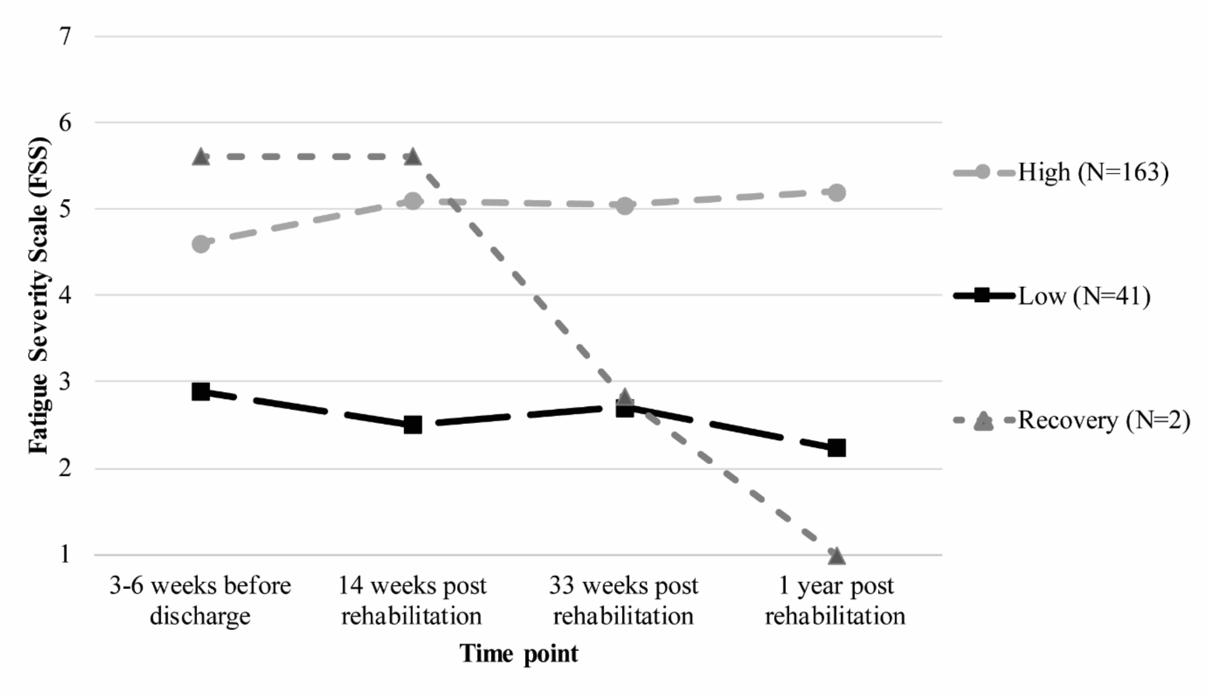


Figure 1 Three trajectory model of perceived fatigue (FSS score) during and after rehabilitation in people after stroke (N=206), based on Latent Class Growth Mixture modelling.

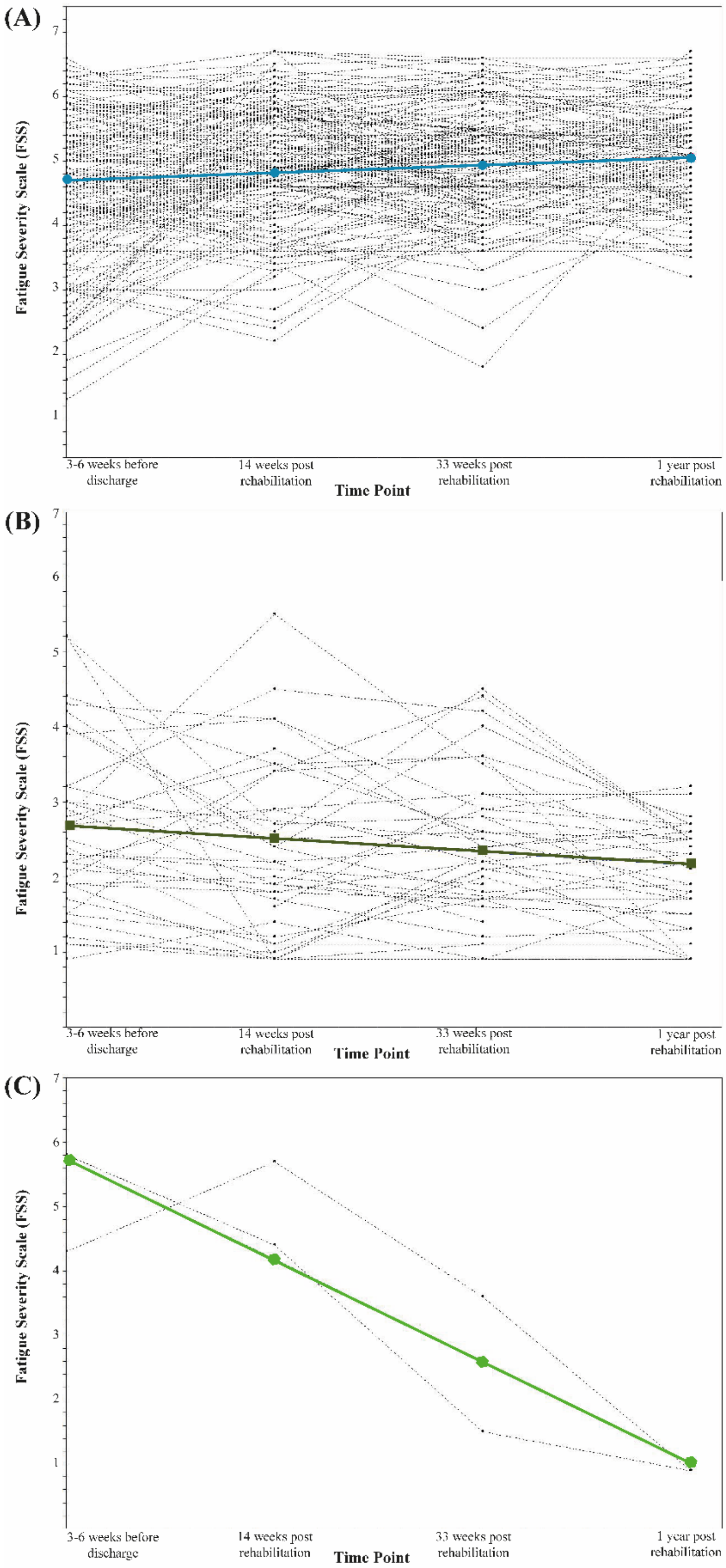


Figure 2 Individual trajectories within each trajectory of perceived fatigue, based on Latent Class Growth Mixture modelling: (A) High, N=163, (B) Low, N=41, (C) Recovery, N=2.

Characteristics of the Trajectories of perceived Fatigue

Baseline descriptive statistics of characteristics – 3-6 weeks before discharge from rehabilitation (T0) – of the trajectories of high and low perceived fatigue are displayed in table 3. Binomial multivariate logistic regression analysis was performed to determine which characteristics (personal, disease/health, psychosocial, lifestyle and environmental) could discriminate between the trajectories of high and low perceived fatigue (Table 3). Compared with the trajectory of high perceived fatigue, people after stroke in the trajectory of low perceived fatigue were more likely to experience high levels of HR-QoL (OR=3.07, 95%CI=1.51-6.26) and were more likely to be physically active (OR=1.93, 95%CI=1.07-3.47) at baseline (T0) (Table 3).

Table 3 Descriptive statistics of characteristics 3-6 weeks before discharge (T0) for the high (N=163) and low (N=41) trajectories of perceived fatigue among people after stroke and binomial multivariate logistic regression analysis to distinguish between those trajectories.

	Descriptive statistics		Test statistics	
Characteristics	High fatigue (N=163)	Low fatigue (N=41)	High (reference) vs. Low	
	mean ± SD or % (N)	mean ± SD or % (N)	Odds ratio (95% CI)	p
Personal				
Sex (% female)	43.6 (71)	34.1 (14)	0.34 (0.10 - 1.15)	.084
Age (years)	55.6 ± 10.7	54.4 ± 11.1	0.65 (0.31 - 1.34)	.243
Body mass index (kg/m^2)	26.8 ± 4.8	25.1 ± 4.0	0.96 (0.45 - 2.08)	.923
Education level (% high)[a]	19.0 (31)	26.8 (11)	1.92 (0.53 - 7.01)	.324
Living situation (% independent)	89.0 (145)	85.4 (35)	2.93 (0.08 - 102.01)	.554
Disease /health				
Acceptance (% yes)	46.6 (76)	65.9 (27)	0.69 (0.21 - 2.29)	.543
Comorbidity (% yes)[b]	33.1 (54)	31.7 (13)	2.59 (0.73 - 9.17)	.139
HR-QoL (general health)	37.0 ± 7.8	45.1 ± 9.2	**3.07 (1.51 - 6.26)**	**.002**
Psychosocial				
Motivation	42.6 ± 22.1	55.7 ± 15.2	1.89 (0.90 – 3.98)	.092
Self-efficacy	39.3 ± 11.4	47.9 ± 9.3	1.84 (0.97 – 3.48)	.061
Lifestyle				
PA (total minutes per week)	884.5 ± 735.5	1294.6 ± 1049.6	**1.93 (1.07 - 3.47)**	**.029**
Sports participation (%yes)	53.4 (87)	61.0 (25)	0.88 (0.30 - 2.64)	.831

Smoking (% yes)	11.7 (19)	9.8 (4)	0.97 (0.17 - 5.50)	.975
Alcohol use (% yes)	36.2 (59)	29.3 (12)	0.41 (0.11 - 1.54)	.185
Environmental				
Treatment form (% outpatient)[c]	91.4 (149)	80.5 (33)	0.28 (0.04 - 1.82)	.183
Treatment context (% hospital)	29.4 (48)	22.0 (9)	0.87 (0.24 - 3.10)	.826
Number of physical activity counselling moments after rehabilitation[d]	2.8 ± 1.4	2.5 ± 1.4	094 (0.62 - 1.43)	.766

[a] Completed applied University or higher

[b] Percentage of participants with one or more comorbidities

[c] Treatment form includes outpatient and inpatient

[d] Participants in the Rehabilitation, Sports and Exercise programme received four telephone-based counselling sessions with a sports counsellor

Standard deviation (SD); Number of participants (N); Fatigue Severity Scale (FSS); Health-related Quality of Life (HR-QoL); Confidence Interval (CI); Reference category (ref)

Characteristics in bold are significantly different; p<.05 based on binomial multivariable logistic regression analysis

Fatigue and Activity pacing associated with Physical activity

Descriptive statistics of physical activity from T0 to T3 are presented in figure 3, both for the trajectories of high and low perceived fatigue. People in the trajectory of low perceived fatigue had higher levels of physical activity over time compared to people in the trajectory of high perceived fatigue (Figure 3). Results of the multilevel regression analysis are presented in table 4. A random intercept model at level 2 did improve the model fit, but a random intercept model for rehabilitation institutions did not improve the model fit. The third multilevel model showed that the trajectory of low perceived fatigue (β=0.57[0.14], 95%CI=0.30-0.84) and higher levels of perceived risk of overactivity (β=0.11[0.05], 95%CI=0.02-0.20) were simultaneously associated with higher levels of self-reported physical activity (min/week) after a correction for sex, age, BMI, treatment context, motivation and self-efficacy (Table 4). People in the trajectory of low perceived fatigue had almost half a standard deviation higher levels of physical activity over time compared to people in the trajectory of high perceived fatigue. High awareness of activity pacing was not significantly associated with physical activity. Random slopes did not improve the model fit.

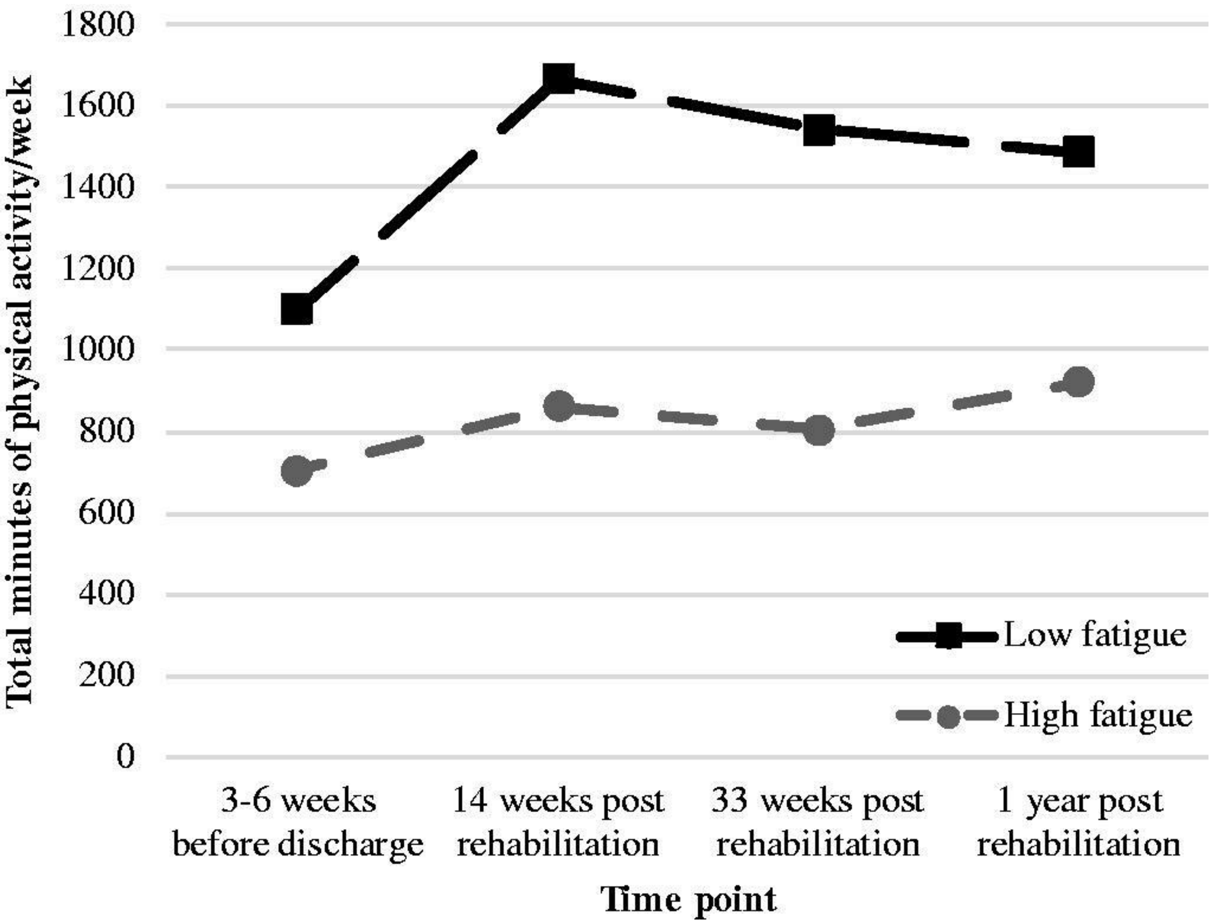


Figure 3 Physical activity (min/week) during and after rehabilitation in the high (N=163) and low (N=41) trajectories of perceived fatigue, based on descriptive statistics (medians).

Table 4 Results of the multilevel regression analyses for the outcome - total minutes of physical activity per week – in three subsequent models for determinants perceived fatigue (model 1), awareness of activity pacing (model 2) and risk of overactivity (model 3) for data from T0 to T3 in people after stroke (N=204).

	Total minutes of physical activity/week								
	Model 1			Model 2			Model 3		
Fixed Factors	Coefficient (SE)	95% CI	*p*	Coefficient (SE)	95% CI	*p*	Coefficient (SE)	95% CI	*p*
Constant	0.00 (0.09)			0.02 (0.08)			0.01 (0.09)		
Fatigue (low)[a]	**0.51 (0.14)**	**0.24 - 0.78**	**<.001**	**0.46 (0.14)**	**0.19 - 0.74**	**.001**	**0.57 (0.14)**	**0.30 - 0.84**	**<.001**
Activity pacing - awareness	n.e.			-0.08 (0.05)	-0.17 - 0.02	.116			
Activity pacing - overactivity	n.e.			n.e.			**0.11 (0.05)**	**0.02 - 0.20**	**.016**
Random effects	Coefficient (SE)			Coefficient (SE)			Coefficient (SE)		
Level 1 (within time points)									
Constant	0.59 (0.04)			0.61 (0.04)			0.60 (0.04)		
Level 2 (between participants)									
Constant	0.32 (0.05)			0.29 (0.05)			0.30 (0.05)		
Level 3 (between institutions)									
Constant	0.00 (0.00)			0.00 (0.00)			0.00 (0.00)		
Δ Deviance	326.16		<0.001	367.03		<0.001	369.35		<0.001
Deviance empty model	1879.60								

a The high fatigue trajectory was used as reference category

The multilevel model included a correction for sex, age, Body Mass Index, treatment context, motivation and self-efficacy

SE=standard error; CI=confidence interval, n.e.=not entered

Discussion

Firstly, the current study aimed to explore perceived fatigue with identifying fatigue trajectories during and after stroke rehabilitation using LCGM. We identified two main trajectories of perceived fatigue (high and low) during and after discharge from stroke rehabilitation and one very small trajectory (recovery). Most people after stroke (79.1%) perceived high fatigue even up to one year after rehabilitation, while 19.9% of the sample indicated a trajectory of low perceived fatigue. This finding highlights that perceived fatigue is a very common and chronic symptom in people after stroke, which is in accordance with previous literature [12, 14]. Although most people after stroke were assigned to stable trajectories of perceived fatigue, high levels of within-person heterogeneity were found, indicating that levels of perceived fatigue might fluctuate over time (Figure 2). On average, the fatigue severity identified in our sample 3-6 weeks before discharge from stroke rehabilitation (FSS score = 4.3 ± 1.4) is lower compared to that in patients with fibromyalgia (FSS score = 6 ± 1) [69] and patients with rheumatoid arthritis (FSS score = 5 ± 1) [69].

Secondly, this study determined which characteristics (personal, disease/health, psychosocial, lifestyle and environmental) before discharge from rehabilitation are associated with the two main trajectories of perceived fatigue. High levels of HR-QoL and high levels of physical activity before discharge distinguished people in the trajectory of low perceived fatigue from people in the trajectory of high perceived fatigue. In general, most personal and disease/health characteristics were not found to be significant characteristics of trajectory membership of perceived fatigue, which contrasts with our hypothesis. A possible explanation for this is that previous literature mostly focused on predictors for fatigue up to 6 months after stroke [70, 71], while the current study determined predictors for fatigue from 3-6 weeks before discharge up to one year after stroke rehabilitation. Probably, predictors for fatigue early after stroke, like personal and disease/health characteristics, are not necessarily predictors for fatigue in the chronic phase after stroke.

Thirdly, this study explored how the trajectories of high and low perceived fatigue and activity pacing are associated with physical activity up to one year after stroke rehabilitation. We found that people after stroke in the trajectory of low perceived fatigue, who participated in the physical activity stimulation RSE programme [36, 37], showed higher levels of physical activity even up to one year after discharge from rehabilitation compared to people in the trajectory of high perceived fatigue. Note: this is not a causal relationship. This finding supports literature on the benefits of counselling on promoting participation in physical activity during and after stroke rehabilitation [6, 7]. However, most of our sample showed high levels of perceived fatigue which in turn were associated with low levels of physical activity up to one year after rehabilitation after correction for several confounders. Although 63% of our sample did receive three or more counselling moments, the content of the counselling from a physical activity and sports counsellor during and after rehabilitation may be improved by providing more targeted advice regarding the management of fatigue. Furthermore, our results did not support our hypothesis that people after stroke who are aware of their engagement in activity pacing are more physically active. We found that people who perceived to be at risk of over activity, are not afraid to overdo, because they reported higher levels of physical activity. However, the RSE programme did not specifically focus on the management of fatigue and/or activity pacing behaviour. We are not sure if advice on fatigue has been provided by rehabilitation professionals during and after rehabilitation. Tailored advice on how to manage fatigue and energy during the day in people after stroke might be recommended. Abonie et al. in their meta-analysis concluded that both perceived fatigue severity and levels of physical activity improved after activity pacing interventions in patients with chronic diseases [35].

Strengths and limitations

The principal strength of the current study lies in its multicentre longitudinal cohort design, including one baseline measurement and three follow-up measurements up to one year after stroke rehabilitation, and the use of LCGM modelling to identify trajectories of perceived fatigue. To our knowledge, a data-driven LCGM modelling has never been used before to analyse the course of perceived fatigue during and after discharge from stroke rehabilitation, which has some advantages compared to the traditional way of summarizing patient-data over time into 'the average of a group' [62]. This specific methodological technique categorises people based on their developmental pattern instead of on a-priori classification in predefined groups [61, 68]. Also, this Latent Class Growth approach categorises people in homogenous subgroups, which might represent different underlying subpopulations requiring different interventions regarding the management of perceived fatigue [62]. To support this data-driven approach, an open communication of the performed analyses and results is important. Therefore, to make the LCGM modelling more transparent, the data, syntax and results are available on the Open Science Framework (osf.io/rtz5y/), and we used the GRoLTS checklist [63] in reporting the results of the LCGM modelling analyses.

Some limitations of this study need to be addressed. An important point of discussion is the decision of the number of classes and the low sample size in one of the classes, when considering both the model fit criteria and clinical interpretation. Choices made during the modelling process based on model fit criteria, but also the sample size and the number of measurement occasions have been shown to influence the number and characteristics of the identified classes in the final model [72-76]. This may influence the interpretation of the models and subsequent implications. The identified ‘recovery’ trajectory consisted of only two people, excluding further secondary statistical analyses .

We are not able to describe our study population in terms of the type of stroke, the severity of the stroke and the side of affection, because these data were not available in more detail in the current study. However, we think that stroke severity would not be a significant determinant for trajectory membership, since a recent study of Chen and Marsh (2018) found that early post stroke fatigue (<6 months after stroke) was largely attributable to characteristics of the stroke (e.g. stroke severity), while chronic fatigue (>6 months after stroke) was not [70]. In the ReSpAct study, fatigue was assessed from 3-6 weeks before discharge up to one year after rehabilitation, which is the chronic phase after stroke. Besides the lack of these stroke related variables, the current study did not use stroke related questionnaires. Also, the multicentre longitudinal cohort study ReSpAct is entirely questionnaire based. Measurements on performance fatigue and objectively measurement physical activity could have improved the current study.

Finally, people after stroke often may have comorbidities such as cognitive impairments and/or communication issues, which are often exclusion criteria in stroke research [77]. The ReSpAct study included in that sense a positive selection of people after stroke, who were – at the time of inclusion, at the end of their rehabilitation – willing to participate on a voluntary basis and were able to fill in the questionnaires by themselves or with help at several measurement moments over a long period of time. This leads to the assumption that the population in the current study was a positive selection and may not have had severe cognitive impairments or communication issues. Besides, the excluded participants in the current study lived less independent and had worse acceptance of the stroke, which stresses the assumption that the persons we finally included may have had a less severe stroke. Therefore, generalizability of the findings of the current study to other stroke populations should be done with caution. Also, our stroke population seems to be on average less physically active before discharge from rehabilitation (963 ± 818 minutes/week assessed with the Adapted-SQUASH) compared with patients after total hip arthroplasty (1694 ± 1173 minutes/week) [50], patients with multiple sclerosis (1815 minutes/week) [71], patients after total knee replacement (1347 ± 1278 minutes/week) [72], and healthy adults (3045 ± 931 minutes/week)[49], all assessed with the self-reported SQUASH.

Practical implications and future directions

We recommend rehabilitation professionals (e.g. physicians, physiotherapist, sports counsellors) to pay attention to fatigue symptoms in people after stroke. Especially people after stroke who are less physically active and perceive low levels of HR-QoL 3-6 weeks before discharge are at risk of perceiving high levels of fatigue even up to one year after rehabilitation.

However, it is still unclear which advice on the management of fatigue (e.g. activity pacing) reduces fatigue and enhances physical activity during and after stroke rehabilitation. Firstly, qualitative research on fatigue and activity pacing in the context of a physically active lifestyle could improve our knowledge on these constructs. Also, to improve our understanding on activity pacing in people after stroke, it is recommended to use objectively measured activity pacing (by using accelerometers) to determine how people divide their physical activities during the day, like in previous studies on people with rheumatoid arthritis [78] and in people with osteoarthritis [79, 80]. Thereafter, more research is needed focusing on the development of treatments aiming to reduce perceived fatigue levels and to enhance physical activity after rehabilitation.

Conclusion

This study identified two main trajectories of perceived fatigue and one very small trajectory during and after stroke rehabilitation: high, low and recovery. Almost 80% of people after stroke perceived severe fatigue even up till one year after rehabilitation. High levels of HR-QoL and high levels of physical activity before discharge identified people after stroke in the low fatigue trajectory. Furthermore, higher levels of physical activity over time after rehabilitation were associated with low perceived fatigue and high perceived risk of overactivity simultaneously. Early identification of perceived fatigue is important in the context of a physically active lifestyle. Future research may consider activity pacing as being of added value to rehabilitation programmes.

Acknowledgement

This study was funded by the Dutch Ministry of Health, Welfare and Sport (grant no. 319758) and supported by Stichting Special Heroes Nederland. The authors would like to thank all participants for their contribution to the ReSpAct study. Furthermore, we would like to thank the following eighteen organizations for their support in the ReSpAct study: Adelante zorggroep, Bethesda Ziekenhuis, De Trappenberg, De Vogellanden, Maasstad Ziekenhuis, Medisch Centrum Alkmaar, Militair Revalidatiecentrum Aardenburg, Revalidatiecentrum Leijpark, Revalidatiecentrum Reade, Revalidatie Friesland, Revant, Rijnlands Revalidatiecentrum, RMC Groot Klimmendaal, Scheper Ziekenhuis, Sint Maartenskliniek, Sophia Revalidatie, Tolbrug Revalidatie, ViaReva.

References

1. Billinger SA, Arena R, Bernhardt J, et al. Physical activity and exercise recommendations for stroke survivors: A statement for healthcare professionals from the american heart association/american stroke association. Stroke. 2014 Aug;45(8):2532-53.

2. Ma VY, Chan L, Carruthers KJ. Incidence, prevalence, costs, and impact on disability of common conditions requiring rehabilitation in the united states: Stroke, spinal cord injury, traumatic brain injury, multiple sclerosis, osteoarthritis, rheumatoid arthritis, limb loss, and back pain. Arch Phys Med Rehabil. 2014 May;95(5):986,995.e1.

3. Fini NA, Holland AE, Keating J, et al. How physically active are people following stroke? systematic review and quantitative synthesis. Phys Ther. 2017 Jul 1;97(7):707-17.

4. Belfiore P, Miele A, Galle F, et al. Adapted physical activity and stroke: A systematic review. J Sports Med Phys Fitness. 2017 Oct 24.

5. Haskell WL, Lee IM, Pate RR, et al. Physical activity and public health: Updated recommendation for adults from the american college of sports medicine and the american heart association. Circulation. 2007 Aug 28;116(9):1081-93.

6. van der Ploeg HP, Streppel KR, van der Beek AJ, et al. Successfully improving physical activity behavior after rehabilitation. Am J Health Promot. 2007 Jan-Feb;21(3):153-9.

7. Morris JH, MacGillivray S, Mcfarlane S. Interventions to promote long-term participation in physical activity after stroke: A systematic review of the literature. Arch Phys Med Rehabil. 2014;95(5):956-967.

8. Hoekstra F, Hoekstra T, van der Schans CP, et al. The implementation of a physical activity counseling program in rehabilitation care: Findings from the ReSpAct study. Disabil Rehabil. 2019 Oct 17:1-12.

9. Lobelo F, Rohm Young D, Sallis R, et al. Routine assessment and promotion of physical activity in healthcare settings: A scientific statement from the american heart association. Circulation. 2018 Apr 4.

10. Martin Ginis KA, Ma JK, Latimer-Cheung AE, et al. A systematic review of review articles addressing factors related to physical activity participation among children and adults with physical disabilities. Health Psychol Rev. 2016 Dec;10(4):478-94.

11. Rimmer JH, Marques AC. Physical activity for people with disabilities. The Lancet. 2012;380(9838):193-195.

12. Obembe AO, Olaogun MM, Olalemi AE. Functional limitations due to fatigue among independently ambulant stroke survivors in osun, south-western nigeria. Physiother Res Int. 2015 Mar;20(1):54-9.

13. Schillinger A, Becker F. Fatigue in patients following traumatic brain injury and stroke. Tidsskr Nor Laegeforen. 2015 Feb 24;135(4):331-5.

14. Knorr S, Ivanova TD, Doherty TJ, et al. The origins of neuromuscular fatigue post-stroke. Exp Brain Res. 2011 Oct;214(2):303-15.

15. Lerdal A, Bakken LN, Kouwenhoven SE, et al. Poststroke fatigue--a review. J Pain Symptom Manage. 2009 Dec;38(6):928-49.

16. Kim I, Hacker E, Ferrans CE, et al. Evaluation of fatigability measurement: Integrative review. Geriatr Nurs. 2018 Jan - Feb;39(1):39-47.

17. Mead GE, Graham C, Dorman P, et al. Fatigue after stroke: Baseline predictors and influence on survival. analysis of data from UK patients recruited in the international stroke trial. PLoS One. 2011 Mar 18;6(3):e16988.

18. Galligan NG, Hevey D, Coen RF, et al. Clarifying the associations between anxiety, depression and fatigue following stroke. J Health Psychol. 2016 Dec;21(12):2863-71.

19. Delva I, Lytvynenko N, Delva M. Factors associated with post-stroke fatigue within the first 3 month after stroke. Georgian Med News. 2017 Jun;(267)(267):38-42.

20. Thilarajah S, Mentiplay BF, Bower KJ, et al. Factors associated with post-stroke physical activity: A systematic review and meta-analysis. Arch Phys Med Rehabil. 2017 Oct 19.

21. Acciarresi M, Bogousslavsky J, Paciaroni M. Post-stroke fatigue: Epidemiology, clinical characteristics and treatment. Eur Neurol. 2014;72(5-6):255-61.

22. Kluger BM, Krupp LB, Enoka RM. Fatigue and fatigability in neurologic illnesses: Proposal for a unified taxonomy. Neurology. 2013 Jan 22;80(4):409-16.

23. Enoka RM, Duchateau J. Translating fatigue to human performance. Med Sci Sports Exerc. 2016 Nov;48(11):2228-38.

24. Duncan F, Kutlubaev MA, Dennis MS, et al. Fatigue after stroke: A systematic review of associations with impaired physical fitness. Int J Stroke. 2012 Feb;7(2):157-62.

25. Twisk J. Applied longitudinal data analysis for epidemiology: A practical guide. Second edition ed. New York: Cambridge University Press; 2013.

26. Gill JR, Brown CA. A structured review of the evidence for pacing as a chronic pain intervention. Eur J Pain. 2009 Feb;13(2):214-6.

27. Murphy SL, Lyden AK, Clary M, et al. Activity pacing for osteoarthritis symptom management: Study design and methodology of a randomized trial testing a tailored clinical approach using accelerometers for veterans and non-veterans. BMC Musculoskelet Disord. 2011 Aug 2;12:177,2474-12-177.

28. Antcliff D, Keeley P, Campbell M, et al. The development of an activity pacing questionnaire for chronic pain and/or fatigue: A delphi technique. Physiotherapy. 2013 Sep;99(3):241-6.

29. Nielson WR, Jensen MP, Hill ML. An activity pacing scale for the chronic pain coping inventory: Development in a sample of patients with fibromyalgia syndrome. Pain. 2001 Jan;89(2-3):111-5.

30. Brown CA. Occupational therapists' beliefs regarding treatment options for people with chronic pain. British Journal of Occupational Therapy. 2002 09/01; 2017/02;65(9):398-404.

31. Dick B, Eccleston C, Crombez G. Attentional functioning in fibromyalgia, rheumatoid arthritis, and musculoskeletal pain patients. Arthritis Rheum. 2002 Dec 15;47(6):639-44.

32. Murphy SL, Kratz AL. Activity pacing in daily life: A within-day analysis. Pain. 2014 Dec;155(12):2630-7.

33. NICE. Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy). London: NICE clinical guideline 53; 2007.

34. Murphy SL, Lyden AK, Smith DM, et al. Effects of a tailored activity pacing intervention on pain and fatigue for adults with osteoarthritis. Am J Occup Ther. 2010 Nov-Dec;64(6):869-76.

35. Abonie US, Sandercock GRH, Heesterbeek M, et al. Effects of activity pacing in patients with chronic conditions associated with fatigue complaints: A meta-analysis. Disabil Rehabil. 2018 Nov 18:1-10.

36. Hoekstra F, Alingh RA, van der Schans CP, et al. Design of a process evaluation of the implementation of a physical activity and sports stimulation programme in dutch rehabilitation setting: ReSpAct. Implement Sci. 2014 Sep 20;9:127,014-0127-7.

37. Alingh RA, Hoekstra F, van der Schans CP, et al. Protocol of a longitudinal cohort study on physical activity behaviour in physically disabled patients participating in a rehabilitation counselling programme: ReSpAct. BMJ Open. 2015 Jan 29;5(1):e007591,2015-007591.

38. World Health Organization. World report on disability. Geneva, Switzerland: WHO Press; 2011.

39. Lerdal A, Gay CL. Acute-phase fatigue predicts limitations with activities of daily living 18 months after first-ever stroke. J Stroke Cerebrovasc Dis. 2017 Mar;26(3):523-31.

40. Duncan F, Lewis SJ, Greig CA, et al. Exploratory longitudinal cohort study of associations of fatigue after stroke. Stroke. 2015 Apr;46(4):1052-8.

41. Andrews NE, Strong J, Meredith PJ. Activity pacing, avoidance, endurance, and associations with patient functioning in chronic pain: A systematic review and meta-analysis. Arch Phys Med Rehabil. 2012 Nov;93(11):2109,2121.e7.

42. Butler, Moseley D, Lucas N. Explain pain. adelaide (australia): Noigroup publications; 2003. Journal of Osteopathic Medicine. 2003;6(2):100-100.

43. Nicholas M, Molloy A, Tonkin L, et al. Manage your pain. sydney (australia): ABC books; 2006. . 2006.

44. van der Ploeg HP, van der Beek AJ, van der Woude LH, et al. Physical activity for people with a disability: A conceptual model. Sports Med. 2004;34(10):639-49.

45. Wendel-Vos GC, Schuit AJ, Saris WH, et al. Reproducibility and relative validity of the short questionnaire to assess health-enhancing physical activity. J Clin Epidemiol. 2003 Dec;56(12):1163-9.

46. Wagenmakers R, van den Akker-Scheek I, Groothoff JW, et al. Reliability and validity of the short questionnaire to assess health-enhancing physical activity (SQUASH) in patients after total hip arthroplasty. BMC Musculoskelet Disord. 2008 Oct 17;9:141,2474-9-141.

47. Arends S, Hofman M, Kamsma YP, et al. Daily physical activity in ankylosing spondylitis: Validity and reliability of the IPAQ and SQUASH and the relation with clinical assessments. Arthritis Res Ther. 2013 Aug 23;15(4):R99.

48. Krupp LB, LaRocca NG, Muir-Nash J, et al. The fatigue severity scale. application to patients with multiple sclerosis and systemic lupus erythematosus. Arch Neurol. 1989 Oct;46(10):1121-3.

49. Fleurke A, Goossen W, Hoijtink E, et al. Fatigue severity scale (FSS). . 2004.

50. Whitehead L. The measurement of fatigue in chronic illness: A systematic review of unidimensional and multidimensional fatigue measures. J Pain Symptom Manage. 2009 Jan;37(1):107-28.

51. Elbers RG, Rietberg MB, van Wegen EE, et al. Self-report fatigue questionnaires in multiple sclerosis, parkinson's disease and stroke: A systematic review of measurement properties. Qual Life Res. 2012 Aug;21(6):925-44.

52. Smits BL, Pepping GJ, Hettinga FJ. Pacing and decision making in sport and exercise: The roles of perception and action in the regulation of exercise intensity. Sports Med. 2014 Jun;44(6):763-75.

53. White PD, Goldsmith KA, Johnson AL, et al. Comparison of adaptive pacing therapy, cognitive behaviour therapy, graded exercise therapy, and specialist medical care for chronic fatigue syndrome (PACE): A randomised trial. Lancet. 2011 Mar 5;377(9768):823-36.

54. Goudsmit EM, Nijs J, Jason LA, et al. Pacing as a strategy to improve energy management in myalgic encephalomyelitis/chronic fatigue syndrome: A consensus document. Disabil Rehabil. 2012;34(13):1140-7.

55. Hettinga FJ, Hoekstra F, Kotte EMG, et al. The development of an activity pacing questionnaire to provide tailored advice on engagement in an active lifestyle and sports for persons with a disability or chronic disease. . Not submitted.

56. Feeny D, Farris K, Cote I, et al. A cohort study found the RAND-12 and health utilities index mark 3 demonstrated construct validity in high-risk primary care patients. J Clin Epidemiol. 2005 Feb;58(2):138-41.

57. Hays RD, Sherbourne CD, Mazel RM. The RAND 36-item health survey 1.0. Health Econ. 1993 Oct;2(3):217-27.

58. Hays RD, Morales LS. The RAND-36 measure of health-related quality of life. Ann Med. 2001 Jul;33(5):350-7.

59. VanderZee KI, Sanderman R, Heyink JW, et al. Psychometric qualities of the RAND 36-item health survey 1.0: A multidimensional measure of general health status. Int J Behav Med. 1996;3(2):104-22.

60. Markland D, Tobin V. A modification to the behavioural regulation in exercise questionnaire to include an assessment of amotivation. J Sport Exerc Psychol. 2004;26(191):6.

61. Marcus BH, Selby VC, Niaura RS, et al. Self-efficacy and the stages of exercise behavior change. Res Q Exerc Sport. 1992 Mar;63(1):60-6.

62. Jung T, Wickrama KAS. An introduction to latent class growth analysis and growth mixture modeling. Social and Personality Psychology Compass. 2008;2(1):302-317.

63. van de Schoot R, Sijbrandij M, Winter SD, et al. The GRoLTS-checklist: Guidelines for reporting on latent trajectory studies. Structural Equation Modeling: A Multidisciplinary Journal. 2017;24(3):451-467.

64. Hoekstra T. Applied latent class models for epidemiology [dissertation]. S.l.: Amsterdam: VU University; 2013.

65. Raftery AE. Bayesian model selection in social research. Sociological Methodology. 1995;25:111.

66. Ramaswamy V, Desarbo WS, Reibstein DJ, et al. An empirical pooling approach for estimating marketing mix elasticities with PIMS data. Marketing Science. 1993;12(1):103-124.

67. Carragher N, Adamson G, Bunting B, et al. Subtypes of depression in a nationally representative sample. J Affect Disord. 2009;113(1-2):88-99.

68. Peugh JL, Enders CK. Using the SPSS mixed procedure to fit cross-sectional and longitudinal multilevel models. Educational and Psychological Measurement. 2005 10/01; 2018/01;65(5):717-41.

69. Oncu J, Basoglu F, Kuran B. A comparison of impact of fatigue on cognitive, physical, and psychosocial status in patients with fibromyalgia and rheumatoid arthritis. Rheumatol Int. 2013 Dec;33(12):3031-7.

70. Chen K, Marsh EB. Chronic post-stroke fatigue: It may no longer be about the stroke itself. Clin Neurol Neurosurg. 2018 Nov;174:192-7.

71. Feigin VL, Barker-Collo S, Parag V, et al. Prevalence and predictors of 6-month fatigue in patients with ischemic stroke: A population-based stroke incidence study in auckland, new zealand, 2002-2003. Stroke. 2012 Oct;43(10):2604-9.

72. Hoeksma JB, Kelderman H. On growth curves and mixture models. Infant and Child Development. 2006;15(6):627-634.

73. Bauer DJ, Curran PJ. Distributional assumptions of growth mixture models: Implications for overextraction of latent trajectory classes. Psychol Methods. 2003;8(3):338-63.

74. Nagin DS, Tremblay RE. Analyzing developmental trajectories of distinct but related behaviors: A group-based method. Psychol Methods. 2001;6(1):18-34.

75. Connell AM, Frye AA. Response to commentaries on target paper, 'Growth mixture modeling in developmental psychology'. Infant and Child Development. 2006;15(6):639-642.

76. Stanger C. Latent growth mixture models: An important new tool for developmental researchers. Infant and Child Development. 2006;15(6):635-637.

77. Nelson MLA, McKellar KA, Yi J, et al. Stroke rehabilitation evidence and comorbidity: A systematic scoping review of randomized controlled trials. Top Stroke Rehabil. 2017 Jul;24(5):374-80.

78. Cuperus N, Hoogeboom TJ, Neijland Y, et al. Are people with rheumatoid arthritis who undertake activity pacing at risk of being too physically inactive? Clin Rehabil. 2012 Nov;26(11):1048-52.

79. Murphy SL, Smith DM, Lyden AK. Type of activity pacing instruction affects physical activity variability in adults with symptomatic knee or hip osteoarthritis. J Phys Act Health. 2012 Mar;9(3):360-6.

80. Murphy SL, Smith DM, Alexander NB. Measuring activity pacing in women with lower-extremity osteoarthritis: A pilot study. Am J Occup Ther. 2008 May-Jun;62(3):329-34.

Chapter 7

Perceptions and experiences of the impact of fatigue on physical activity 5-8 years after stroke rehabilitation: an interview study

Seves BL, Hoekstra, T, Hettinga FJ, Brandenbarg P, Dekker R, Krops LA, van der Woude LHV, Hoekstra F.

Submitted

Abstract

Purpose: To explore perceptions and experiences of stroke survivors on (1) the impact of fatigue on physical activity 5-8 years after rehabilitation, and (2) activity pacing behaviour.

Methods: This interview study is part of the longitudinal cohort study Rehabilitation, Sports, and Active lifestyle (ReSpAct). The ReSpAct cohort was used to purposively sample participants who received stroke rehabilitation. Using existing survey data, individual timelines of perceived fatigue and physical activity were created to guide the interviews. Fifteen semi-structured interviews were conducted 5-8 years after rehabilitation. We analysed the data using reflexive thematic analysis.

Results: Findings were summarized following three themes: *Differences in perceived impact of mental and physical fatigue on physical activity*, *Activity pacing strategies to manage fatigue*, and *Insight in fatigue guidance*. Participants perceived mental fatigue as barrier for *becoming* physically active and physical fatigue as barrier for *maintaining* physical activity. Participants talked about activity pacing strategies as response to perceived fatigue at the short-term after rehabilitation.

Conclusions: This study highlights the importance to provide stroke survivors during and after rehabilitation with instructions – tailored to the notion of perceived fatigue (mental and physical) – on activity pacing to manage fatigue and to engage and persevere in physical activity.

Keywords

Mental fatigue, physical fatigue, activity pacing, fatigue guidance, health, stroke rehabilitation.

Implications for rehabilitation

- The study findings indicated important differences between the impact of *mental fatigue* and *physical fatigue* on physical activity after rehabilitation in stroke survivors, which are important to consider in fatigue guidance.
- Fatigue guidance in survivors with *mental fatigue* might focus on enhancing (self)motivation and providing goal-setting strategies to gradually increase their physical activity levels, while in survivors with *physical fatigue* the fatigue guidance might target increasing physical activity within the boundaries of their physical capacity and disability
- Stroke survivors seem to have the ability to develop self-learned fatigue management skills (e.g., activity pacing) through self-regulation strategies – after years of experience – which makes fatigue guidance during and early after stroke rehabilitation important.
- The study findings form a step-up towards improving tailored guidance on fatigue management to promote sustained participation in physical activity during and after stroke rehabilitation.

Introduction

Perceived fatigue is a heterogeneous and distressing secondary health symptom that is commonly reported in stroke survivors [1-3]. The onset of fatigue typically occurs within the first two weeks after stroke [3,4]. The prevalence of perceived fatigue is slightly reduced at three months after stroke, but fatigue symptoms generally persist over the longer term [4-7]. Fatigue complaints after stroke can limit an individual's participation in activities of daily living including the engagement in physical activity [8,9]. Our recent survey-based Rehabilitation, Sports, and Active lifestyle (ReSpAct) study up to one year after rehabilitation showed that 80% of the stroke survivors perceived moderate to high levels of fatigue up to one year after rehabilitation [2]. Moreover, these high levels of perceived fatigue were associated with low levels of physical activity in our ReSpAct study [2], which is in accordance with a previous longitudinal cohort study and a systematic review [10,11]. This is worrisome since sustained participation in physical activity contributes to the improvement of health and well-being in stroke survivors [12].

A previous study showed that individuals with fatigue complaints manage their perceived fatigue and physical activity in various ways [13]. Some individuals show a behaviour of avoidance of physical activities that exacerbate more severe symptoms of fatigue (underactivity), whereas others persist physical activity while disregarding symptoms of fatigue followed by long periods of rest (overactivity) [13]. A promising self-regulatory approach to manage fatigue and physical activity is activity pacing. Activity pacing is defined as a (sub)conscious behaviour of trying to manage daily physical activities, to divide energy over the day and to plan rest periods [14-16]. The optimal goal of activity pacing is to minimize any overactivity or underactivity and to manage complaints like fatigue and pain while engaging in physical activity [14-16]. Activity pacing seems promising in health care to manage fatigue and to gradually enhance physical activity in people with chronic conditions [16,17]. We do know that stroke survivors use fatigue management strategies (e.g., planning, incorporating rest, activity pacing during the day, energy conservation) to enable to engage in physical activity [18], but knowledge on how activity pacing behaviour develops in the chronic phase after rehabilitation is lacking. Furthermore, considering the high prevalence of perceived fatigue and inactivity in stroke survivors [2,10], it might be profitable to individually tailor and actually train activity pacing strategies in this population.

Many questions still remain regarding why some people experience lower levels of fatigue and are able to engage in physical activity, while others experience the opposite [2]. Most quantitative studies investigating the (longitudinal) interaction between perceived fatigue and physical activity in stroke survivors are survey based [2,10], allowing little room for individual perceptions and the exploration thereof. Personal experiences on how stroke survivors manage their fatigue to participate in physical activity – also experiences on activity pacing behaviour – are important to better understand how perceived fatigue interacts with physical activity, and how this interaction may change during and after rehabilitation in the longer-term chronic phase after stroke. Understanding how perceived fatigue impacts physical activity may help to finetune tailored interventions to guide fatigue management and to promote physical activity during and after rehabilitation.

Therefore, this qualitative study aimed to explore the perceptions and experiences of (1) the impact of perceived fatigue on physical activity 5-8 years after rehabilitation in stroke survivors, and (2) their activity pacing behaviour. The qualitative data from stroke survivors will form a step-up towards improving tailored guidance on fatigue management to promote sustained participation in physical activity during and after stroke rehabilitation.

Methods

Study context and design

This qualitative, explorative study was conducted based on a constructivist approach, since the study aimed to understand the participants' perceptions and experiences on perceived fatigue, physical activity behaviour and fatigue management [19]. The constructivist approach follows an ontological relativist paradigm, which "assumes no single external reality independent of the individual; reality exists in the form of multiple individual mental constructions about the world, which are shaped through lived experiences" [19]. In line with the constructivist approach, this study follows a subjective and transactional epistemology, meaning that "the knowledge is created through transactions between the researcher and the participant; researchers cannot enter a study as a 'blank slate' by separating themselves from their previous experiences and their interpretations of those experiences" [19].

This qualitative study is part of the multicentre longitudinal cohort study ReSpAct [20,21]. The ReSpAct study was designed to evaluate a tailored, nationwide and motivational interviewing-based physical activity and sport stimulation programme called Rehabilitation, Sports and Exercise (RSE; in Dutch: Revalidatie, Sport en Bewegen). The RSE programme was successfully implemented in Dutch rehabilitation practice [22]. In total, the ReSpAct cohort consisted of 1719 people with a physical disability and/or chronic disease, whereof 303 stroke survivors. Participants in the ReSpAct study were asked to fill in a questionnaire at four moments in time: at baseline (T0: 3-6 weeks before discharge) and at 14 (T1), 33 (T2) and 52 (T3) weeks after discharge from rehabilitation.

The ReSpAct study was approved by the ethics committee of the Center for Human Movement Sciences of the University Medical Center Groningen (reference: ECB/2013.02.28_1). The current study as an amendment of the ReSpAct study was approved by the local ethical committee of the University Medical Center Groningen (Reference: 201800894). All participants signed an informed consent prior to the data collection. Information on the research team members can be found in the supplemental file on osf.io/rtz5y/. The consolidated criteria for reporting qualitative research checklist (COREQ) were used to guide the reporting of this qualitative study [23] (see supplemental file on osf.io/rtz5y/).

Participants

Fifty people of the 303 stroke survivors in our ReSpAct study population were invited by email to participate in an individual interview and to fill in a short questionnaire. At the time of invitation, the potential participants were 5-8 years after discharge from rehabilitation. Inclusion criteria for this study were: (1) being at least eighteen years old, (2) being diagnosed with stroke, and (3) completed the ReSpAct surveys at all four measurement points. Exclusion criteria were: (1) having deregistered from the ReSpAct study, or (2) being deceased during the ReSpAct study at the time. Potential participants were selected purposively using maximum variation and criterion-based sampling strategies [24], based on the following participant characteristics: sex, age, rehabilitation centre and their trajectory of perceived fatigue and physical activity behaviour between T0 and T3.

Prework

Individual timelines

The first author (BLS) used the existing survey data from the ReSpAct study [20,21] to create the individual timelines of fatigue and physical activity. Included participants were asked to fill in an additional questionnaire about their personal characteristics (e.g., sex and age), perceived fatigue, physical activity, and activity pacing behaviour. The survey was sent by mail two weeks prior to the interview. For each participant, a timeline was created based on their self-reported fatigue and physical activity data over time up to 5-8 years after rehabilitation. These individual timelines were presented to the participant as a visual guidance during the interview. The supplemental file on osf.io/rtz5y/ describes additional information about how the timelines were created.

Interview guide

An interview guide was created by the first-author (BLS) in collaboration with all co-authors. The questions in the semi-structured interview guide were based on the findings and knowledge gaps in our recent ReSpAct study (e.g., 'Do high levels of perceived fatigue persist in the chronic phase after stroke?', 'Why do perceived fatigue levels change over time?', 'How do perceived fatigue and daily physical activities mutually influence each other?', 'How do people manage their perceived fatigue?') [2], on other previous qualitative studies [9,25] and on intuition. The interview guide was pilot tested by BLS with an occupational therapist working with stroke survivors, a person with a chronic disease and fatigue complaints and a qualitative researcher. After pilot testing, several adaptations were made to the interview guide (e.g., reformulating difficult questions). The final interview guide consisted of four topics: (1) the rehabilitation after stroke, (2) timeline of perceived fatigue, (3) timeline of physical activity, and (4) relation between timelines of perceived fatigue and physical activity (see supplemental file on osf.io/rtz5y/). Example questions were: “What can you tell me about your perceived fatigue?”, “How do your daily physical activities or sports activities influence your perceived fatigue?”, “Since the onset of the stroke, did you find anything that helps to manage your perceived fatigue and energy?”. The interviewer also asked questions about participant’s timeline, such as: “Do you know why this change in perceived fatigue took place?”, “What can you tell me about your physical activity behaviour during this moment?”.

Data collection

Qualitative data collection took place from November 2020 till March 2021. Due to Covid-19 restrictions, all interviews were conducted via a livestream connection by author BLS (Blackboard Collaborate©, Educational technology, Washington, D.C., U.S.), and were audio and video recorded. Field notes were made by the interviewer during and after the interviews. A written summary of the transcript and the constructed timeline were shared with the participant after the interview and the participant was asked if any relevant experiences or perceptions arose in their mind after the interview. Participants did not have any additions to the summary and timeline.

Analyses

Audio and video recordings of the interviews were transcribed non-verbatim, with identifying data removed. All data were pseudonymized by using a participant fictional name. We analysed the data using reflexive thematic analysis [26] to explore patterns of meaning (themes) in participants’ experiences on fatigue, physical activity and activity pacing in the chronic phase after rehabilitation [26]. The analyses were performed using Atlas.ti (version 8.3; GmbH, Berlin, Germany) software for data storage, coding, and theme development. The qualitative analysis started with the exploration of the data by reading through the transcripts, looking at the constructed timelines and making notes. Second, open coding of the data was performed by BLS through segmenting and labelling the text, followed by axial and selective coding of the data. During this process, some codes were edited or merged with others. Themes were derived from the data by aggregating similar codes together. Parallel to this, the codes and themes were developed and connected through constructive and critical discussions with co-authors – for their reflections and perspectives – to ensure the quality and rigor of the coding process [27]. Further information on these discussions was described in the supplemental on osf.io/rtz5y/. Memo writing was performed during the qualitative analysis to structure thoughts, adaptations, and reflections.

Results

Fifty potential participants were invited, 35 of them did not respond to the invitation. Fifteen participants, 9 males and 6 females, between 25 and 77 years old participated in the study (Table 1). Participants were previously treated in inpatient and/or outpatient rehabilitation in the Netherlands and were between 5-8 years post stroke rehabilitation. Eleven participants were low educated (up to completed secondary education) and four participants were high educated (completed applied University or higher) (not in table). The interviews lasted on average 53 minutes each (range: 42-64 minutes).

We identified the following three themes from the interviews: (1) differences in perceived impact of mental and physical fatigue on physical activity, (2) activity pacing strategies to manage fatigue, and (3) insight in fatigue guidance. Within each theme distinct sub-themes were identified. All themes and subthemes are summarized in table 2. The (sub)themes are described below and are illustrated with quotes from participants.

Table 1 Participants' personal characteristics (N=15)

ID	Sex	Age (Years)	**Years after rehabilitation**	**Treatment context** (Duration in days)	
				Inpatient	Outpatient
William	M	72	5	77	29
Amy	F	52	6		239
Jessica	F	25	6		149
Jacob	M	53	5		99
Jennifer	F	33	5		155
Bob	M	56	8		578
George	M	61	6	77	71
Steven	M	73	6		98
Paul	M	77	5		109
Harry	M	52	7		136
Charlotte	F	48	5	70	98
Emily	F	41	6		142
Richard	M	76	5	20	71
Thomas	M	58	6	93	59
Margaret	F	63	6		53

Participant's fictional name (ID), Male (M), Female (F)

Table 2 – An overview of themes and related subthemes with a short description and supporting quotes.

Theme	Short description	Subthemes	Quotes
Differences in perceived impact of mental and physical fatigue on physical activity	The positive and negative perceived impacts of fatigue on physical activity levels after rehabilitation. The different influences of mental and physical fatigue on physical activity after rehabilitation.	Perceived impact of mental fatigue on physical activity	*"What I have noticed very much myself is that the threshold to be physically active is very difficult, because you are tired, you do not have the energy for it. But when you once do it, you quickly notice that it gives you energy."* (Jennifer)
		Perceived impact of physical fatigue on physical activity	*"It' is officially called muscle pain. But I just notice, as my left leg is not as strong as my right leg. My right leg is not affected and my left leg is called the affected leg so to speak. That is really fatigue in the muscle strength so to speak."* (George)
Activity pacing strategies to manage fatigue	Activity planning, setting boundaries, and incorporating rest are key fatigue management strategies. Activity pacing strategies shift from symptom response at the short-term to more symptom	Activity pacing behaviour at the short-term after rehabilitation	*"I often go beyond my boundaries; I think for that matter. I am still learning to clearly indicate those boundaries in terms of fatigue and my abilities."* (Jennifer)

Theme	Short description	Subthemes	Quotes
	prevention at the long-term after rehabilitation.	Activity pacing behaviour in the chronic phase after rehabilitation	*"[in the present] You are more aware of what you want to do and what you can do. You get to know your own boundaries a bit and you can respond to them with what you do."* (Emily)
Insight in fatigue guidance	The need for fatigue guidance during and after stroke rehabilitation. Suggestions to improve fatigue guidance.	Guidance during and/or after rehabilitation	"*I never received a booklet about fatigue complaints and physical fatigue and mental fatigue. I never knew there was a difference, they did not teach me that in the rehabilitation centre*". (Charlotte)
		Improvement of fatigue guidance	*"That it [the fatigue] literally controls your life. I now know that from experience, but it has never been said that it has really become a pillar of your life."* (Amy)

Differences in perceived impact of mental and physical fatigue on physical activity

All participants perceived fatigue after stroke, but their perceptions of fatigue were diverse in notion (mental versus physical) and intensity. The quote below shows that Charlotte perceived the fatigue as a severe residual phenomenon after stroke.

"I will just have to learn to live with it, because fatigue is just one of the highest negative things left after my stroke." (Charlotte)

The subtheme *Perceived impact of mental fatigue on physical activity* describes how mental fatigue mainly impacts physical activity when stroke survivors start to engage in physical activities during and after rehabilitation. The subtheme *Perceived impact of physical fatigue on physical activity* describes how physical fatigue mainly impacts physical activity when stroke survivors try to maintain their physical activities and sports during and after rehabilitation.

Perceived impact of mental fatigue on physical activity

Participants made the distinction between *mental fatigue* and *physical fatigue* (perceived as fatigue in the leg muscles). Participants talked about their experiences with mental fatigue after the stroke and described mental fatigue as having little sense of doing anything, feeling that you can go to sleep at any time, and/or having headaches. The participants experiencing mental fatigue said that they suffered from mental/cognitive complaints, such as balance struggles, aphasia, concentration disturbances and memory problems. Participants experienced that these mental/cognitive complaints have an impact on the perceived mental fatigue. Some participants experienced mental fatigue as the worst type of fatigue, while others experienced physical fatigue as the worst fatigue. Besides, participants experienced that the intensity of mental fatigue and physical fatigue sometimes changed over time after rehabilitation. This is explained in more detail by Jennifer.

"I think the ratio is different. I also walked a lot worse; I hadn't had surgery on my leg and I didn't exercise either. After I started exercising and after the surgery, I was able to move more easily. So I think that at the time of registering at the sports centre[1] my physical fatigue was higher, I had much more trouble moving than now. … So my mental load was minimal. While I now have a lot on my mind with my work, sports, a little one and household. Now my mental load is a bit bigger." (Jennifer)

Most participants who experienced mental fatigue perceived their fatigue as a barrier for starting to engage in physical activity, such as sports activities, leisure time activities, but also social activities. Jennifer experienced this for example. But when they could motivate themselves to do these activities, and actually did, they experienced lower mental fatigue and/or had more energy after the activity. This was for example experienced by George.

"The more you are able to be physically active, the more you will be physically active. Because if you are seriously tired, let me call it that, dead tired sounds so macabre, if you are seriously tired, you do not tend to be very physically active of course." (George)

Participants perceived that too many stimuli (e.g., loud music and a crowded environment) in a fitness centre or in a swimming pool caused mental fatigue and resulted in not being able to maintain regular engagement in fitness or swimming. Also, participants experienced a lot of stimuli (e.g., traffic and a crowded environment) during walking, running, or cycling outside, which made these activities very tiring for them due to the increased levels of perceived mental fatigue. For example, Amy experienced that too many stimuli during physical activity had an impact on perceived mental fatigue.

[1] A sports centre is a "Physical Activity Counseling Centre" in which stroke survivors received face-to-face consultation and telephone-based counselling on active lifestyle after rehabilitation [21].

"I have swum for a while in a regular swimming pool, that is way too many stimuli, with all those water waves, wrong acoustics and much more, way too many people... But then comes the [mental] fatigue again." (Amy)

Perceived impact of physical fatigue on physical activity

Participants described physical fatigue as wanting to sit down and take rest and/or experiencing muscle pain/exhaustion. Amy felt that the physical fatigue was her greatest barrier to continue walking. Some of the stroke survivors rarely experienced physical fatigue; only after a very long walk for example. Participants experienced that since the stroke the time to recover from physical fatigue after physical activities or sports is longer compared to before their stroke.

Some participants experienced that their perceived level of physical fatigue remained stable following their stroke. However, although the level remained stable, they experienced to be able to engage in more physical activity, which they experienced as an improvement. They also noticed that the moments of rest in between activities became shorter after rehabilitation. Participants experienced the highest levels of physical fatigue during rehabilitation. Most of the participants experienced that the physical fatigue decreased over time, since they gradually recovered from their physical complaints. Jennifer experienced that the physical fatigue remained stable after rehabilitation.

"[after some time daily activities are less tiring], which means that you start doing more. So the overall fatigue remains the same." (Jennifer)

Participants felt that participating in physical activities and sports directly enhanced their physical fatigue and that they needed to take extra rest to recover. For example, William perceives physical fatigue very soon when they go out for a walk.

“I notice that I intend to go for a walk and then unfortunately I have to sit down after one kilometre. That only has to be ten seconds, but then I am also very tired. Then I can walk again, for a while, but then I have to sit down again.” (William)

Participants experienced that their physical complaints due to the stroke could be the cause of their physical fatigue. Participants who perceived severe physical fatigue had physical complaints in the affected side of the body, such as limited functionality of the arm, hand and/or leg. For example, the affected side caused problems during walking, with a drop foot that hampered them to walk long distances or created a risk of falling, leading to increased physical fatigue. Especially shortly after rehabilitation, participants experienced high levels of physical fatigue due to physical complaints after the stroke. They perceived that the physical fatigue hindered them to start or maintain to engage in physical activity. Emily experienced that the affected side of her body caused physical fatigue during physical activity or sports.

Shortly after rehabilitation, most participants received physiotherapy. The participants experienced that the physical activity during for example leisure time, physiotherapy or sports activities helped them to improve endurance, strength and/or physical fitness and to reduce physical fatigue, which enabled them to better maintain to engage in physical activity. Participants experienced that the daily burden due to these physical complaints decreased over time after rehabilitation, but it did not entirely disappear. For example, Jacob experienced that on the long-term higher levels of physical activity resulted in experiencing less physical fatigue.

“Then [after rehabilitation] I started at the gym and then you see a year after rehabilitation I was exercising and the more I exercised, the better I felt, the more energy I had… Now I am doing nothing [no physical activity] or little at the moment, so I notice that I am having more trouble on the right side. So for me, I get rid of some of my [physical] fatigue by being active.” (Jacob)

Activity pacing strategies to manage fatigue

The subtheme *activity pacing behaviour at the short-term after rehabilitation* describes that activity pacing strategies in stroke survivors were mostly a response on fatigue symptoms. Participants talked about different activity pacing strategies which they (sub)conscious used in daily life to manage fatigue. Also, the subtheme *activity pacing behaviour in the chronic phase after rehabilitation* describes how participants learned and developed activity pacing strategies through years of experience to prevent fatigue symptoms. The following activity pacing strategies were reported by participants: planning activities over the day and over the week, setting boundaries, and incorporating rest.

Activity pacing behaviour at the short-term after rehabilitation

At the short-term after rehabilitation, participants perceived difficulties with planning their physical and social activities during the day and week. Participants talked how they learned activity pacing strategies by themselves, since not all participants received fatigue guidance during or after rehabilitation. Participants stated that they sometimes planned too many activities, which resulted in higher experienced burden of their physical impairments.

Participants experienced that they often crossed their fatigue boundaries at the short-term after rehabilitation. Although they perceived fatigue during an activity (e.g. walking outside, gardening) they felt they should continue. Participants mentioned that they needed to incorporate rest to recover when they crossed their fatigue boundaries. Besides, participants felt that trying to expand their fatigue boundaries through enhancing physical activity mostly resulted in perceiving more physical complaints, as illustrated by Amy:

"It is a matter of planning and sometimes that goes better than other times, because then you think: that can also be done for a while. That does not actually work, even though you actually know that. Still you sometimes try to broaden a boundary, but that just does not actually happen." (Amy)

Participants talked about the incorporated rest – varying from several minutes to hours – to recover from physical activity. Their rest consisted of drinking coffee, lying on the couch, sleeping, meditating, or clearing the mind. At the short-term after rehabilitation, most participants incorporated rest as a response to perceived fatigue. For example, William, incorporated rest when perceiving fatigue during a walk.

"If I then [when feeling fatigued during a walk outside] wait 10 seconds, or if I sit on a stone and after a few seconds say: come on, let's go further. And then I can go hundreds of meters forward again." (William)

Activity pacing behaviour in the chronic phase after rehabilitation

Participants talked about their activity pacing strategies which they learned from a therapist or which they learned themselves after rehabilitation. Participants who learned activity pacing strategies themselves experienced that their activity pacing strategies improved after rehabilitation, but this took several years of practice. When participants incorporated rest in the chronic phase after rehabilitation, they mostly incorporated rest to prevent fatigue complaints. Most participants said that in the chronic phase after rehabilitation they were better able to plan activities, were more aware of their activity pacing behaviour and better understand their own limits. Jacob for example experienced this.

"Well, somehow I might have become quite an expert in combining things. If I know I am going to have a rough day, I might subconsciously do less the day before. I am very good at adjusting things, which goes very automatically, not that I think of it a lot or something, but that goes very naturally in one way or another… I think I have learned that [planning activities] myself in that whole process from stroke to today." (Jacob)

Participants experienced that their activity pacing strategies were not always applicable when participating in work activities. Participants mentioned that they perceived *more* fatigue on days when they were unable to balance activity and rest. The younger participants who worked several days a week reported that they felt fatigued after a long or intensive day at work, where it is somewhat crowded with colleagues and where they cannot take rest when they need to. One participant worked at home due to the Covid-19 measures and was able to schedule her work and rest during the day, which eventually reduced perceived fatigue. The older participants experienced that their perceived fatigue levels reduced when they stopped working.

Insight in fatigue guidance

A subtheme of this theme describes the experiences of participants who received *fatigue guidance during and/or after rehabilitation*. Also, perceptions of fatigue guidance of participants who did not receive fatigue guidance are described. This theme ends with a subtheme describing several points for *improvement of fatigue guidance*.

Guidance during and/or after rehabilitation

Participants had mixed experiences and perceptions on fatigue guidance during rehabilitation. Participants who perceived low levels of fatigue during rehabilitation did not receive any fatigue guidance during rehabilitation and reported that they did not feel the need. However, other participants mentioned that they did not receive any fatigue guidance during the rehabilitation, while they did perceive fatigue during rehabilitation and did feel the need for fatigue guidance. Some participants felt the need for fatigue guidance and received this guidance from an occupational therapist or a social worker during rehabilitation. They received information on post-stroke fatigue and guidance in planning activities and dividing energy during the day. Jessica for example was very positive about this received guidance.

"Fatigue is really an underestimated part [of the stroke] … I can manage it [the fatigue] a lot more, and I have really learned that during rehabilitation." (Jessica)

Some participants who still perceived fatigue after rehabilitation sought behavioural support to better manage the fatigue. Examples mentioned were psychotherapy, mindfulness therapy, social work counselling, or therapy sessions at a care institution, which is illustrated by a quote from Charlotte.

"*I had to weigh energy guzzlers and energy givers against each other [in the therapy] and I have found my place in that"* (Charlotte)

Improvement of fatigue guidance

The participants found it hard to mention suggestions for improvement of fatigue guidance. Even the participants who did not receive any fatigue guidance, but still perceived fatigue in the chronic phase after stroke were sceptic if any sort of fatigue guidance would have helped them to better manage fatigue. For example, Amy found it hard to give suggestions for improvement.

In retrospect, some participants found the information provision of fatigue and fatigue management very limited. Charlotte preferred to receive information on the difference between physical fatigue and mental fatigue. Amy preferred to receive information on the chronic aspect of fatigue and its large impact in daily life. Participants suggested that more structured information during rehabilitation might help to better guide the transition to the home situation. This was for example mentioned by Jennifer.

"I think more information provision. Also that you are sent back to your own life again, that you are released … Maybe it was also because I did not have many complaints during the rehabilitation, but that there is attention for: listening, realize that you will get of track, that you are tired when you go

back to your own life. And attention for: these are ways to deal with it, you can go here if you want to talk about it or if you want to chat with someone." (Jennifer)

Also, during rehabilitation, some participants missed emphasizing the importance of engaging in physical activity to improve their recovery at the short term after rehabilitation, but also for their recovery many years beyond rehabilitation. Jacob for example said that the chronic phase after stroke rehabilitation should be emphasized more already during rehabilitation.

"I have not seen the importance of going to rehabilitation the periods after a stroke. The first time is of course very important, the sooner the fewer complaints perhaps. The first half year, from half year to one year [after stroke], but also from year to year onwards, what you can possibly achieve. And I think that [the chronic phase after stroke] should be emphasized much more to people who have had a stroke." (Jacob)

Besides points for improvement of fatigue guidance during rehabilitation, participants mentioned a point for improvement in the period after rehabilitation. Participants perceived the need for evaluation moments or periodic consultations with a rehabilitation professional after rehabilitation to have the opportunity to ask, inform and exchange experiences in daily life regarding their fatigue and other complaints. Some participants thought that it might be informative to receive tips on fatigue guidance from peers, such as: (1) keep doing things, (2) participate in social activities, (3) stay stimulated, (4) try to perform (physical) tasks yourself if possible and do not lean too quickly on your disabilities, and (5) do not focus on things you cannot do anymore due to the stroke, but rather think in possibilities. An example of these tips was given by Steven.

"Think in your own possibilities. Do not think: I would like to run because that is not possible. But you can walk. People who say: I cannot do that anymore. Then do something else. Just do something." (Steven)

Discussion

The findings of this qualitative study form a step-up towards improving tailored guidance on fatigue management to promote sustained participation in physical activity during and after stroke rehabilitation. The results of the first study aim indicated important differences between perceptions and experiences of the impact of *mental fatigue* and *physical fatigue* on physical activity after rehabilitation in stroke survivors. *Mental fatigue* was mainly a barrier for *becoming* physically active, but after being active the individuals perceived lower levels of mental fatigue and increased energy levels. This finding is supported by a previous review in adults without disabilities in which they found decreased levels of intrinsic motivation towards an upcoming physical activity when mentally fatigued [28] and that the effects of mental fatigue can be counteracted when increasing motivation [29]. In other words, mental fatigue has mainly an impact on the motivation towards physical activity instead of the physical activity itself. This finding is substantiated by the COM-B model of Behaviour Change, which suggests that capability, opportunity and motivation are essential to change any – in this context physical activity – behaviour [30]. This can also be explained by findings from the systematic review of Van Cutsem et al. (2017) where they concluded that physiological variables – such as maximal strength, power and anaerobic work – were not affected by mental fatigue in healthy adults [29]. Besides, our finding is supported by a recent systematic review of Casson et al. (2022) in patients with chronic fatigue syndrome where they concluded that gradually increasing daily physical activities is effective in reducing fatigue in general [31]. For stroke survivors perceiving mental fatigue it might be effective to provide external motivation in the (social) environment or to provide goal setting strategies to improve self-motivation and to maintain physical activity [32,33].

Besides, participants reported that *physical fatigue* was mainly a barrier for *maintaining* physical activity. Stroke survivors perceived physical fatigue as fatigue in their (leg) muscles. A reduction in e.g. muscle force during an ongoing performance is described as performance fatigability in the taxonomy of fatigue and fatigability proposed by Kluger et al. (2013) [34]. The stroke survivors who perceived physical fatigue also perceived muscular pain and exhaustion (performance fatigability) during physical activities or sports activities, which was mostly attributable to severe physical disabilities in the affected side of the body. Probably, these physical disabilities explain the impact of physical fatigue as a barrier for maintaining physical activity. This can be explained by the fact that a limited functionality in the affected side of the body can limit endurance and walking capacity due to increased energy costs in the lower extremities [35,36]. Also, previous studies found that at a certain level of performance fatigability the walking function was decreased in stroke survivors compared to healthy individuals [37,38]. However, participants in our study indicated that physical activity and especially sports activities had a positive effect in stroke survivors perceiving physical fatigue, since those activities increased strength and physical fitness, which gradually enhanced their physical activity behaviour and reduced their perceived physical fatigue. This finding is also found in previous qualitative studies in stroke survivors [25,39]. The positive impact of physical activity on reduced long term levels of physical fatigue can be explained by the theory of energy envelope, which posits that "maintaining expended energy levels consistent with available energy levels may reduce the frequency and severity of symptoms" in persons with chronic fatigue syndrome [40]. Moreover, through participating in physical activity the perceived energy levels may increase over time, allowing an individual to engage in higher levels of physical activity at the long-term [16,40]. Health professionals working in stroke rehabilitation or follow-up care should be aware of the distinct impact of mental fatigue versus physical fatigue on physical activity in stroke survivors, to be able to tailor fatigue guidance during and after stroke rehabilitation. Future research is needed to investigate if fatigue guidance focusing on enhancing (self)motivation and providing goal-setting strategies [32,33] is effective to target fatigue in stroke survivors perceiving *mental fatigue* to gradually enhance and persevere physical activity. Besides, future research is needed to investigate if fatigue guidance focusing on structured physical activity aiming to improve strength and physical fitness is effective to target fatigue in stroke survivors perceiving *physical fatigue,* also to gradually enhance and persevere physical activity.

The second study aim focused on perceptions and experiences of activity pacing behaviour after rehabilitation in stroke survivors. Most stroke survivors did not receive any guidance in fatigue management, but gradually learned how to manage their fatigue in daily life themselves by trial and error, which indicates that their used fatigue management strategies are a self-learned skill or behaviour. A previous systematic review on pacing behaviour development stressed that pacing behaviour development follows an established process of (self-learned) skills acquisition through gathered experience on pacing [41]. Besides, self-regulation is an important strategy in self-learned activity pacing behaviour. Elferink-Gemser & Hettinga described that aspects of self-regulation in activity pacing behaviour are making adequate choices concerning the distribution of available energy during the activity and reflecting on the learning process to analyse the stronger and weaker skills in activity pacing [42]. This enables an individual to use gathered experiences to develop and/or improve activity pacing strategies for future activities [42]. Activity pacing behaviour based on self-learned skills has also been called naturalistic activity pacing behaviour – the pacing behaviour that people exert without receiving any intervention to reduce fatigue – in previous literature. Shortly after the stroke, people showed more symptom-contingent behaviour, such as slowing down or taking rest after physical activity when perceiving fatigue. This naturalistic activity pacing behaviour is similar to a previous study among people with osteoarthritis reporting pain and fatigue [14]. In the chronic phase (5-8 years) after rehabilitation people's behaviour shifted to more pre-planned behaviour, such as pre-planning rest and dividing physical and social activities during the day and week. This is also called quota-contingent behaviour, in which an individual sets meaningful and realistic goals towards activity and is pre-planning activities [43]. Moreover, their activity pacing behaviour shifted from more intuitive activity pacing in the acute phase after rehabilitation to more deliberative activity pacing in the chronic phase after rehabilitation [44]. The dual process theory distinguishes between intuitive and deliberative decisions in activity pacing [44]. The dual process theory describes "a multidimensional process of decision-making in the context of regulating exercise intensity" [44]. Probably, the shift from intuitive to deliberative decision-making in activity pacing in our stroke survivors arose due to their experience on activity pacing. Stroke survivors seem to have the ability to develop self-learned activity pacing skills, but it requires years of experience. Therefore, structured advice on activity pacing behaviour [45] might be beneficial for stroke survivors to reduce the time to develop activity pacing strategies to manage fatigue and to gradually enhance physical activity.

Implications and future directions

The findings of this study provided valuable information for improving stroke rehabilitation programmes. First, our findings indicated that different perceived impact of mental fatigue and physical fatigue on physical activity are important to consider when promoting physical activity during and after rehabilitation by providing tailored advice on fatigue guidance. Fatigue guidance in survivors with mental fatigue might focus on enhancing (self)motivation and providing goal-setting strategies to gradually increase their physical activity levels, while in survivors with physical fatigue the fatigue guidance might target increasing physical activity within the boundaries of their physical capacity and disability. Future research is needed to advance our understanding of distinct impact of mental and physical fatigue on physical activity in stroke survivors by measuring perceived mental fatigue and performance fatigability using both qualitatively and quantitively [46]. Subsequently, these insights can be used to inform development of fatigue management interventions for stroke survivors.

Second, we found that activity pacing behaviour in stroke survivors shifted from intuitive to deliberative decision-making in activity pacing, but this took several years of experience after stroke rehabilitation. Incorporating standardised instructions on activity pacing is a promising strategy to reduce the time of this shift. When stroke survivors are better able to manage fatigue symptoms and to gradually enhance physical activity shortly after stroke rehabilitation, they will be able to improve health and well-being sooner [12]. Previous studies show examples of activity pacing interventions to guide patients with chronic fatigue and/or pain symptoms [43,45] or patients with multiple sclerosis [47] to manage fatigue symptoms. Further research should investigate the feasibility and effectivity of application of these types of activity pacing interventions in stroke rehabilitation.

Third, our findings indicated that stroke survivors needed more information on the chronic aspect of fatigue, the distinct notions of fatigue and how to deal with fatigue in daily life. Providing this information during rehabilitation or shortly before discharge from rehabilitation might help them to better guide the transition from rehabilitation to home. Also, individuals needed an evaluation moment or periodic counselling in stroke after-care with a rehabilitation professional. Since stroke survivors reported to advance the peer-support, it might be valuable to include peers in providing tips and information during rehabilitation and after-care. However, these suggestions for rehabilitation practice should be investigated further in co-creation with experts on fatigue and physical activity during and/or after stroke rehabilitation by performing qualitative studies and/or a Delphi study with stroke survivors and rehabilitation professionals, before an intervention among fatigue management can be developed.

In sum, our findings provide directions to improve tailored guidance on fatigue management to promote participation in physical activity during and after stroke rehabilitation. Our findings can be used to inform the development of interventions on fatigue guidance targeting fatigue to enhance physical activity in stroke survivors by using intervention development strategies [48]. A next step is to explore wishes and ideas of stakeholders on fatigue guidance interventions targeting fatigue to enhance physical activity to implement in stroke rehabilitation and stroke follow-up care.

Strengths and limitations

This qualitative study provided a rich overview of perceptions and experiences on fatigue, physical activity and activity pacing behaviour from the rehabilitation treatment till the chronic phase after rehabilitation in stroke survivors. The following limitations may influence the generalization of the findings to inactive stroke survivors, to old female survivors and young male survivors who were underrepresented in the present sample. It is possible that the fifteen included participants are motivated and interested in physical activity and sports activities, since these individuals were selected from the larger ReSpAct cohort and filled in the ReSpAct questionnaire at four moments in time. Even more, the fifteen included participants might be more motivated towards physical activity compared to the fifty invited persons, which might explain the very active stroke sample in our study. Also, despite the purposive sampling strategy, the older participants in this study were more often males and the younger participants were more often females. Older females were invited to participate in the study but did not respond.

Based on quantitative data of self-reported physical activity and perceived fatigue of the ReSpAct study [20,21], individual timelines from the rehabilitation period until the present were created prior to the interview. We consciously choose to create the basis of the timeline without co-creation with individuals to reduce the duration of the interview and to prevent fatigue during the interview. The participant was allowed to adapt and reflect on the timeline during the interview. It is hard to suppose if participants responded on the interview questions based on their memory or if they were guided towards the data presented on the timeline. Also, this quantitative data of the ReSpAct study did not include information on the background of the stroke, such as the severity, aetiology or location of the stroke. However, the duration of inpatient and/or outpatient rehabilitation gave an indication of the severity of the stroke.

Conclusion

We found that the distinction between mental fatigue and physical fatigue perceived in stroke survivors is important to consider when providing tailored advice to reduce fatigue and to promote a physically active lifestyle in stroke survivors. Mental fatigue was reported mostly as a barrier for *becoming* physically active and physical fatigue was mostly reported as a barrier for *maintaining* physical activity. Most individuals showed symptom-contingent activity pacing behaviour with intuitive decision-making at the short-term after stroke. This shifted to more pre-planned activity pacing behaviour with deliberative decision-making at the long-term after stroke. Stroke survivors seem to have the ability to develop self-learned fatigue management skills (e.g. activity pacing) through self-regulation strategies, but this requires years of experience. Therefore, it is recommended to focus future research on intervention development in fatigue guidance and to investigate the effectivity of standardised instructions – adapted to the perceived mental and/or physical fatigue of the survivor – on activity pacing provided during and after stroke rehabilitation.

Acknowledgements

The authors would like to thank all participants for their contribution to the current study. We wish to thank dr. Anja de Kruif for her assistance with the qualitative research methodology. Bregje L. Seves received a personal grant from the University Medical Center Groningen to perform the current study. Femke Hoekstra is supported by a Craig H. Neilsen Foundation Postdoctoral Fellowship (#719049) and Michael Smith Foundation for Health Research (MSFHR) Trainee Award (#RT-2020-0489).

References

1. Schillinger A, Becker F. Fatigue in patients following traumatic brain injury and stroke. Tidsskrift for den Norske laegeforening : tidsskrift for praktisk medicin, ny raekke. 2015;135(4):331-335.
2. Seves BL, Hoekstra T, Hoekstra F, et al. Unravelling perceived fatigue and activity pacing in maintaining a physically active lifestyle after stroke rehabilitation: a longitudinal cohort study. Disability and rehabilitation. 2020:1-11.
3. Cumming TB, Packer M, Kramer SF, et al. The prevalence of fatigue after stroke: A systematic review and meta-analysis. International journal of stroke : official journal of the International Stroke Society. 2016;11(9):968-977.
4. Christensen D, Johnsen SP, Watt T, et al. Dimensions of post-stroke fatigue: a two-year follow-up study. Cerebrovasc Dis. 2008;26(2):134-41.
5. Duncan F, Wu S, Mead GE. Frequency and natural history of fatigue after stroke: a systematic review of longitudinal studies. Journal of psychosomatic research. 2012;73(1):18-27.
6. Duncan F, Greig C, Lewis S, et al. Clinically significant fatigue after stroke: a longitudinal cohort study. J Psychosom Res. 2014 Nov;77(5):368-73.
7. Lerdal A, Lee KA, Bakken LN, et al. The Course of Fatigue during the First 18 Months after First-Ever Stroke: A Longitudinal Study. Stroke Res Treat. 2012;2012:126275.
8. Obembe AO, Olaogun MM, Olalemi AE. Functional limitations due to fatigue among independently ambulant stroke survivors in Osun, South-Western Nigeria. Physiother Res Int. 2015 Mar;20(1):54-9.
9. White JH, Gray KR, Magin P, et al. Exploring the experience of post-stroke fatigue in community dwelling stroke survivors: a prospective qualitative study. Disability and rehabilitation. 2012;34(16):1376-1384.
10. Duncan F, Lewis SJ, Greig CA, et al. Exploratory longitudinal cohort study of associations of fatigue after stroke. Stroke. 2015 Apr;46(4):1052-8.
11. Thilarajah S, Mentiplay BF, Bower KJ, et al. Factors Associated With Post-Stroke Physical Activity: A Systematic Review and Meta-Analysis. Archives of Physical Medicine and Rehabilitation. 2017.
12. Belfiore P, Miele A, Galle F, et al. Adapted physical activity and stroke: a systematic review. The Journal of sports medicine and physical fitness. 2017.
13. Birkholtz M, Aylwin L, Harman RM. Activity Pacing in Chronic Pain Management: One Aim, but Which Method? Part One: Introduction and Literature Review. British Journal of Occupational Therapy. 2004;67(10):447-452.
14. Murphy SL, Kratz AL. Activity pacing in daily life: A within-day analysis. Pain. 2014;155(12):2630-2637.
15. Antcliff D, Keeley P, Campbell M, et al. Activity pacing: moving beyond taking breaks and slowing down. Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation. 2018.
16. Abonie US, Sandercock GRH, Heesterbeek M, et al. Effects of activity pacing in patients with chronic conditions associated with fatigue complaints: a meta-analysis. Disability and rehabilitation. 2018:1-10.

17. Abonie US, Edwards AM, Hettinga FJ. Optimising activity pacing to promote a physically active lifestyle in medical settings: A narrative review informed by clinical and sports pacing research. Journal of sports sciences. 2020;38(5):590-596.
18. Skogestad IJ, Kirkevold M, Larsson P, et al. Post-stroke fatigue: an exploratory study with patients and health professionals to develop a patient-reported outcome measure. Journal of patient-reported outcomes. 2021;5(1):35-021-00307-z.
19. Poucher Zoë A. Thinking through and designing qualitative research studies: a focused mapping review of 30 years of qualitative research in sport psychology. International Review of Sport and Exercise Psychology.13(1):163-186.
20. Alingh RA, Hoekstra F, van der Schans CP, et al. Protocol of a longitudinal cohort study on physical activity behaviour in physically disabled patients participating in a rehabilitation counselling programme: ReSpAct. BMJ open. 2015;5(1):e007591-2015-007591.
21. Hoekstra F, Alingh RA, van der Schans CP, et al. Design of a process evaluation of the implementation of a physical activity and sports stimulation programme in Dutch rehabilitation setting: ReSpAct. Implementation science : IS. 2014;9:127-014-0127-7.
22. Hoekstra F, Hoekstra T, van der Schans CP, et al. The implementation of a physical activity counseling program in rehabilitation care: findings from the ReSpAct study. Disability and rehabilitation. 2019:1-12.
23. Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. International Journal for Quality in Health Care. 2007;19(6):349-357.
24. Sparkes AC, Smith B. Qualitative research methods in sport, exercise and health: from process to product. Routledge; 2014. (Book, Whole).
25. Barbour VL, Mead GE. Fatigue after Stroke: The Patient's Perspective. Stroke Res Treat. 2012;2012:863031.
26. Braun V, Clarke V. Reflecting on reflexive thematic analysis. Qualitative Research in Sport, Exercise and Health. 2019 2019/08/08;11(4):589-597.
27. Smith B, McGannon KR. Developing rigor in qualitative research: problems and opportunities within sport and exercise psychology. International review of sport and exercise psychology. 2018;11(1):101-121.
28. Martin K, Meeusen R, Thompson KG, et al. Mental Fatigue Impairs Endurance Performance: A Physiological Explanation. Sports Med. 2018 Sep;48(9):2041-2051.
29. Van Cutsem J, Marcora S, De Pauw K, et al. The Effects of Mental Fatigue on Physical Performance: A Systematic Review. Sports Med. 2017 Aug;47(8):1569-1588.
30. Michie S, van Stralen MM, West R. The behaviour change wheel: a new method for characterising and designing behaviour change interventions. Implementation science : IS. 2011;6:42-5908-6-42.
31. Casson S, Jones MD, Cassar J, et al. The effectiveness of activity pacing interventions for people with chronic fatigue syndrome: a systematic review and meta-analysis. Disabil Rehabil. 2022 Nov 8:1-15.

32. Sakalidis KE, Menting SGP, Elferink-Gemser MT, et al. The Role of the Social Environment in Pacing and Sports Performance: A Narrative Review from a Self-Regulatory Perspective. Int J Environ Res Public Health. 2022 Dec 2;19(23).

33. Mozafarinia M, Mate KKV, Brouillette MJ, et al. An umbrella review of the literature on the effectiveness of goal setting interventions in improving health outcomes in chronic conditions. Disabil Rehabil. 2023 Jan 27:1-11.

34. Kluger BM, Krupp LB, Enoka RM. Fatigue and fatigability in neurologic illnesses: proposal for a unified taxonomy. Neurology. 2013;80(4):409-416.

35. Novak AC, Li Q, Yang S, et al. Energy flow analysis of the lower extremity during gait in persons with chronic stroke. Gait Posture. 2015 Feb;41(2):580-5.

36. Olney SJ, Monga TN, Costigan PA. Mechanical energy of walking of stroke patients. Arch Phys Med Rehabil. 1986 Feb;67(2):92-8.

37. Kuhnen HR, Rybar MM, Onushko T, et al. Stroke-related effects on maximal dynamic hip flexor fatigability and functional implications. Muscle Nerve. 2015 Mar;51(3):446-8.

38. Rybar MM, Walker ER, Kuhnen HR, et al. The stroke-related effects of hip flexion fatigue on over ground walking. Gait Posture. 2014 Apr;39(4):1103-8.

39. Flinn NA, Stube JE. Post-stroke fatigue: qualitative study of three focus groups. Occupational therapy international. 2010;17(2):81-91.

40. Jason LA, Brown M, Brown A, et al. Energy Conservation/Envelope Theory Interventions to Help Patients with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. Fatigue : biomedicine, health & behavior. 2013;1(1-2):27-42.

41. Menting SGP, Edwards AM, Hettinga FJ, et al. Pacing Behaviour Development and Acquisition: A Systematic Review. Sports Med Open. 2022 Dec 9;8(1):143.

42. Elferink-Gemser MT, Hettinga FJ. Pacing and Self-regulation: Important Skills for Talent Development in Endurance Sports. Int J Sports Physiol Perform. 2017 Jul;12(6):831-835.

43. Antcliff D, Keenan AM, Keeley P, et al. Testing a newly developed activity pacing framework for chronic pain/fatigue: a feasibility study. BMJ open. 2021;11(12):e045398-2020-045398.

44. Micklewright D, Kegerreis S, Raglin J, et al. Will the Conscious–Subconscious Pacing Quagmire Help Elucidate the Mechanisms of Self-Paced Exercise? New Opportunities in Dual Process Theory and Process Tracing Methods.

45. Antcliff D, Keenan AM, Keeley P, et al. "Pacing does help you get your life back": The acceptability of a newly developed activity pacing framework for chronic pain/fatigue. Musculoskeletal care. 2021.

46. Enoka RM, Duchateau J. Translating Fatigue to Human Performance. Medicine and science in sports and exercise. 2016;48(11):2228-2238.

47. Abonie US, Hettinga FJ. Effect of a Tailored Activity Pacing Intervention on Fatigue and Physical Activity Behaviours in Adults with Multiple Sclerosis. Int J Environ Res Public Health. 2020 Dec 22;18(1).

48. Bartholomew LK, Parcel GS, Kok G. Intervention mapping: a process for developing theory- and evidence-based health education programs. Health Educ Behav. 1998 Oct;25(5):545-63.

Chapter 8

Getting the right people to the right care at the right time: Exploring experiences and perceptions of stroke survivors and health professionals on post-stroke fatigue guidance

Jacobi M*, van der Schuur L*, Seves BL, Brandenbarg P, Dekker R, Hettinga FJ, Hoekstra F, Krops LA, van der Woude LHV, Hoekstra, T.

Equal contributions

Under review

Abstract

Purpose: This focus group study aimed to explore experiences and perceptions on post-stroke fatigue guidance in Dutch rehabilitation and follow-up care among stroke survivors and health professionals.

Methods: Ten stroke survivors and twelve health professionals with different professions within stroke rehabilitation or follow-up care in the Netherlands were purposively sampled and included. Eight online focus group interviews were conducted. We analysed the data using reflexive thematic analysis.

Results: Three themes were identified. *Guidance in fatigue management* did not always match survivors' needs. However, professionals were positive about the provided fatigue guidance (e.g., advice on activity pacing), but it could be better tailored to the survivors' situation. Professionals believe *the right time for post-stroke fatigue guidance* is when survivors are motivated to change physical activity behaviour to manage fatigue – mostly several months after stroke – while survivors preferred information on post-stroke fatigue well before discharge. *Follow-up care and suggestions for improvement* described that follow-up support after rehabilitation by a stroke coach is not implemented nationwide, while survivors and professionals expressed a need for it.

Conclusions: The study findings will help guide improvement of fatigue guidance in stroke rehabilitation programmes and stroke follow-up care aiming to improve physical activity, functioning, participation, and health.

Keywords

Rehabilitation, participation, physical activity, health, activity pacing, information provision

Implications for rehabilitation

- To improve fatigue guidance, we suggest providing information on post-stroke fatigue to stroke survivors and their relatives, well before discharge from stroke rehabilitation.
- Tailored advice on activity pacing during and after stroke rehabilitation is important to fill the current unmet need of stroke survivors to manage fatigue and to gradually improve participation, physical activity behaviour and health.
- In fatigue guidance, we suggest to consider the acceptance of the stroke, capability, opportunity and motivation to change physical activity behaviour and participation as focus points.
- We suggest to offer follow-up support on fatigue guidance, including peer support, to all stroke survivors after rehabilitation.

Introduction

Fatigue is a common and debilitating symptom after stroke [1]. The prevalence of post-stroke fatigue ranges between 25% and 85% [1,2]. More specifically, our recent study among 206 Dutch stroke survivors found that almost 80% suffered from severe fatigue problems up to one year after rehabilitation [3]. This is problematic as post-stroke fatigue is reported as a barrier to participate in physical activity promotion programmes [4], to resume social, familial and work-related activities [5], and to maintain physical activity after stroke rehabilitation [3]. Moreover, post-stroke fatigue often leads to physical, mental and social impairment [6,7], reduced quality of life [8] and higher mortality risk [4,5,9]. Hence, early detection and effective interventions for post-stroke fatigue are of immense importance to manage fatigue and to gradually improve physical activity, participation, and overall health [4,10].

A recent meta-analysis described and compared non-pharmacological interventions for alleviating fatigue and – compared to usual care – found six out of only eight interventions significantly benefiting post-stroke fatigue [10]. The largest fatigue reduction was seen in a community health management intervention consisting of a multidimensional intervention including drug management, fatigue education, community activities and psychological care. Another promising pilot randomized trial, although not included in the review, found a large reduction in fatigue in stroke survivors who received a newly developed fatigue management counselling programme compared to survivors receiving regular stroke education [11]. This fatigue management programme consisted of an introduction to fatigue management, sleep/relaxation, exercise, nutrition, mood and future focus [11].

The limited number of evidence-based interventions on fatigue management to obtain and/or sustain physical activity in stroke survivors impedes clinical practice. Research on health professionals' perspectives on post-stroke fatigue further showed a lack of consistency regarding key features of post-stroke fatigue (e.g., terminology use, treatment and prognosis) and its impact on physical activity, participation, and health [12,13]. Although Dutch guidelines on neuropsychological rehabilitation after stroke do provide some recommendations on fatigue management to promote physical activity [14], structured advice on fatigue management in Dutch clinical stroke rehabilitation is currently lacking.

Moreover, studies show a discrepancy between stroke survivors' needs in rehabilitation and their experience of the received care [15-17]. With regard to stroke recovery in general, stroke survivors described their challenges in rehabilitation in relation to social and emotional functioning, in particular related to long term difficulties in terms of quality of life, life satisfaction and social reintegration [18-20]. This stresses the need for a multidisciplinary approach in stroke rehabilitation [18]. To the dismay of stroke survivors, health providers approach recovery mainly from a biomedical point of view [19,20]. With relevance to fatigue guidance, stroke survivors reported the need to gain knowledge on (managing) fatigue [21]. This can be considered as an unmet need since stroke survivors stated that education concerning post-stroke fatigue is often not provided during rehabilitation [21]. It is problematic because stroke survivors often think that fatigue is normal and comes with stroke recovery [22]. Hinkle et al. [23] acknowledged this unmet need and pleaded that health professionals need to have a better understanding of post-stroke fatigue in order to properly advise stroke survivors in managing fatigue.

The findings of the current study will help guide improvement of fatigue management in stroke rehabilitation programmes and stroke follow-up care aiming to improve physical activity, functioning, participation, and health. Therefore, experiences and perceptions of experts of current stroke rehabilitation programmes and in stroke follow-up care are vital to help guide improvement of fatigue management in those programmes. Experts on fatigue management in stroke rehabilitation and stroke follow-up care include both stroke survivors (the people with experience of fatigue and how to manage it) and health professionals working in stroke rehabilitation or stroke follow-up care (the people with clinical experience how to assist stroke survivors in fatigue management). A qualitative study has the advantage of providing a comprehensive description of stroke survivors' as well as professionals' experiences of fatigue management during and after stroke rehabilitation since the researcher can directly engage with the experts. Therefore, this qualitative, exploratory focus group study aimed to explore experiences and perceptions of stroke survivors and health professionals on post-stroke fatigue guidance during and after stroke rehabilitation. By drawing on perspectives of stroke survivors and health professionals, we hope to support professionals in the guidance of their patients on post-stroke fatigue at all stages of the clinical pathway to improve physical activity, functioning, participation, and health.

Methods

Design

The study was designed as a qualitative, exploratory study with a constructivist approach, since the study aimed to explore stroke survivors' and health professionals' perceptions and experiences of the concept 'post-stroke fatigue guidance' [24]. The constructivist approach follows an ontological relativist paradigm, which "assumes no single external reality independent of the individual; reality exists in the form of multiple individual mental constructions about the world, which are shaped through lived experiences" [24]. In line with the constructivist approach, this study follows a subjective and transactional epistemology, meaning that "the knowledge is created through transactions between the researcher and the participant; researchers cannot enter a study as a 'blank slate' by separating themselves from their previous experiences and their interpretations of those experiences" [24]. A focus group methodology was used to collect experiences and information on the guidance of post-stroke fatigue in stroke care and to generate ideas for improving this guidance. Focus group settings create an environment for participants to share and consider their experiences which often result in rich information about social norms and the variety of opinions and views in a population [25].

Focus groups with stroke survivors and health professionals were held separately in small groups to ensure that stroke survivors and health professionals felt comfortable and not inhibited to share their positive and/or negative experiences of fatigue guidance during and after stroke rehabilitation.

Ethical considerations

The study was approved by the Local Ethics Committee of the University Medical Center Groningen based on the current legislation in the Netherlands and additional regulations (Research register number: 201800894). All voluntary participants signed the informed consent, either by email or written, prior to their focus group participation. The information letter emphasized the voluntary nature of the participation, the right to refuse participation at any moment and the accurate handling of the data. Names and other identifying information were deleted from the transcripts. The video and audiotapes were erased after finalizing the transcripts.

Participant selection

Stroke survivors

Ten stroke survivors were included through purposive, convenience and snowball sampling strategies. Two participants were purposefully sampled at the Centre for Rehabilitation of the University Medical Center Groningen in the Netherlands. These patients were selected by a rehabilitation physician and a psychologist. Seven participants were recruited through convenience sampling via the Facebook page of the largest patient association for stroke survivors in the Netherlands (In Dutch: Hersenletsel.nl). Snowball sampling was also used because a number of ambassadors of this association forwarded the call to other potentially suitable participants. One participant was recruited through snowball sampling via a research team member. Inclusion criteria were: *(1)* the availability of a computer, microphone, and camera, *(2)* being aged eighteen years or older, *(3)* being diagnosed with stroke in the past, *(4)* speaking the Dutch language, and *(5)* not suffering from severe aphasia or impeding cognitive problems.

Health professionals

Twelve health professionals with different professions within stroke rehabilitation or stroke follow-up care in the Netherlands were included through a purposive sampling strategy. More specifically, maximum variation sampling (in sex, age and profession of the participant, and province where the participant worked) was applied aiming to capture a comprehensive insight of perspectives on fatigue guidance. Inclusion criteria were: *(1)* the availability of a computer, microphone and camera, *(2)* speaking the Dutch language, *(3)* performing at least one of the following professions: rehabilitation physician, neurology nurse, physiotherapist, occupational therapist, speech therapist, psychologist, sports- and exercise consultant, social worker or another relevant position in stroke care and *(4)* the profession being currently (also) practised on stroke survivors in the Netherlands.

Data collection

Eight online focus groups were conducted between April and June 2021 via Zoom Cloud Meetings. The focus groups were held in multiple and smaller groups than usual, because of the online setting of the focus groups due to COVID-19 restrictions and to avoid overstimulation in stroke survivors as much as possible. All focus groups were audio and videotaped with participants' consent. The focus groups of the stroke survivors were moderated by LS and the focus groups of the health professionals by MJ (both female, and with a background in health sciences). The researcher who was not moderating (MJ or LS) was responsible for the recording, kept track of time and took field notes.

Two semi-structured interview guides, for respectively stroke survivors and health professionals, were created by LS and MJ. The interview guides were developed by building upon interview guides used in previous qualitative studies [21,26] that were closely related to the current study as they also investigated the experiences of stroke survivors on post stroke fatigue but in a different country. Besides, the interview guides were adapted based on intuition and the current context. Example questions included: 'What could be improved in the management of fatigue in stroke patients in rehabilitation programs?' and 'Suppose you are a health professional in stroke care, what tips would you like to give yourself to deal with the perceived fatigue?'. After development, the interview guides were thoroughly discussed and refined by authors MJ, LS, BLS and TH. The emerged versions of the interview guides were pilot tested in a practice focus group with a general practitioner and a nurse. Their provided feedback to reformulate several questions led to the final revision of the interview guides. The prepared questions of the interview guides and the entire interview guides in Dutch can be obtained in the supplemental file on osf.io/rtz5y/.

Data analysis

Data analysis and collection was an iterative process. A reflexive thematic analysis was used for analysing the focus groups [27]. The data analysis was continued in the computer programme MAXQDA Plus 2020, where the transcripts were coded in three phases: open coding, axial coding, and selective coding. The first step in this process was familiarisation with the data through reading transcripts. Secondly, LS coded the transcripts of the focus groups with stroke survivors and MJ coded the transcripts of the focus groups with health professionals. Thus, the data of the focus groups with stroke survivors and the data of the focus groups with health professionals were first analysed separately. During axial coding, connections were made between the codes by looking at their interrelationship which ultimately resulted in concepts [28]. The code tree demonstrates the results from the axial coding in Dutch and the code trees from both stroke survivors and health professionals can be obtained in the supplemental on osf.io/rtz5y/. During selective coding, codes from the focus groups with stroke survivors were merged with codes from the focus groups with health professionals and connections were made between the concepts resulting in themes and subthemes. Finally, themes and subthemes were described in the results section of this study. The supplemental file on osf.io/rtz5y/ provides more background information of all authors and describes how all authors provided their reflections on the themes and subthemes.

Trustworthiness

Green & Thorogood [28] explain that credibility, transferability, dependability, confirmability and reflexivity should be followed to ensure the trustworthiness of qualitative findings. Strategies like immersion in the data, reflexive analysis, peer debriefing and an audit trail ensured that MJ and LS were open to the data and minimized the chance of bias during data analysis because of preconceived notions based on their clinical status and experience. The collaboration of MJ and LS during data collection by making field notes and keeping track of the interview guides during the focus groups improved the depth of the data analysis.

The current study is reported according to the consolidated criteria for reporting qualitative research (COREQ) checklist [29]. The completed checklist can be found in the supplemental file on osf.io/rtz5y/. Finally, the translation of the quotes from Dutch to English were checked by MJ or LS for accuracy. Editorial changes were made to the quotes to improve the readability. The Dutch quotes can be obtained in the supplemental file on osf.io/rtz5y/.

Results

Four focus groups with stroke survivors took place consisting of two to three stroke survivors each. These focus groups lasted 62-76 minutes (median of 69 minutes). Four focus groups with health professionals took place consisting of three health professionals each. These focus groups lasted 82-96 minutes (median of 85 minutes). Participants' characteristics are presented in tables 1 and 2. The age of the stroke survivors ranged between 30 and 62, the majority was female and the years out of rehabilitation varied from 0 (still involved in clinical/ambulant rehabilitation) to twelve years beyond rehabilitation. The age of the health professionals ranged between 25 and 65 and the majority was female. The health professionals worked in stroke rehabilitation or in stroke follow-up care e.g., as rehabilitation physician, neurology nurse, physiotherapist, occupational therapist or speech therapist. All participants were pseudonymized in the current study.

Table 1. Stroke survivors' (N=10) characteristics

Focus group	Pseudonym	Sex	Age range (years)	Stroke onset	Years out of rehabilitation	Received PSF guidance
1	Caroline	F	55-60	2009	12	No
1	Francis	F	50-55	2014, 2019	1	Yes
1	Daniel	M	30-35	2008	9	Yes
2	Caitlyn	F	30-35	2013	7	No
2	Lex	M	55-60	2013, 2017, 2018	3	Yes
2	Juliet	F	55-60	2006	NR	No
3	Abigail	F	55-60	2017	3	Yes
3	Mathilda	F	55-60	2015	4.5	Yes
4	Thom	M	50-55	2020	0	Yes
4	Harry	M	60-65	2014	SR	No

F = Female; M = Male; NR = Did not receive any rehabilitation; SR= Still in rehabilitation; PSF = Post-stroke fatigue

Table 2. Health professionals' (N=12) characteristics

Focus group	Pseudonym	Sex	Age range (years)	Profession
1	Susan	F	40-45	Geriatric physiotherapist
1	Hannah	F	50-55	Neurology nurse
1	Emily	F	35-40	Cognitive therapist
2	Diana	F	50-55	Speech therapist
2	Robert	M	30-35	Occupational therapist
2	Jessica	F	25-30	Speech therapist
3	Sarah	F	50-55	Rehabilitation physician
3	Carl	M	40-45	Neurology nurse & follow-up care nurse for stroke survivors

3	Eleanor	F	30-35	Outpatient attendant
4	Rosanna	F	50-55	Cognitive rehabilitation therapist & TBI-coach
4	Ellen	F	35-40	Speech therapist
4	Elisabeth	F	60-65	Physiotherapist

F = Female; M = Male; TBI = Traumatic brain injury

Based on the focus groups of both stroke survivors and health professionals, we identified three main themes (*guidance in fatigue management, the right time for post-stroke fatigue guidance,* and *follow-up care and suggestions for improvement*) with subthemes. The themes and sub-themes are presented in table 3 and are described in more detail below.

Table 3. Identified themes and subthemes

Theme	Subtheme
Guidance in fatigue management	Fatigue guidance: not a common good Incorporating pacing activities One size does not fit all
The right time for post-stroke fatigue guidance	Post-stroke fatigue realization Struggling finding the right time for information provision on fatigue guidance
Follow-up care and suggestions for improvement	Follow-up care after discharge? Not a guarantee! The need for a linking pin

First a brief description of participants´ perception on post-stroke fatigue. Most stroke survivors reported that they suffered from post-stroke fatigue. They mentioned fatigue having a substantial impact on their physical activities (e.g. leisure time activities and work activities) and participation in society. Stroke survivors also felt they were dealing with the consequences of a physically invisible disability. On the one hand, they liked that outsiders could not tell by their appearance that they had had a stroke or suffered from fatigue. On the other hand, the physical invisibility led to incomprehension because from the outside they are not considered to be disabled as their medical conditions (e.g. fatigue) are not immediately apparent. This struggle was discussed by a stroke survivor and her general practitioner, illustrated in the following quote:

“Several times a day, I hear from others: you got off so well! I once said that to my previous general practitioner and she almost fell of her chair. She said: you are one of the most disabled people in my practice, but you can't see it from the outside." (Francis, stroke survivor)

Guidance in fatigue management

The main theme *Guidance in fatigue management* can be divided into three subthemes. The subtheme *fatigue guidance: not a common good* describes that not every participating stroke survivor received fatigue guidance, although all professionals agreed on the importance and the potential benefits of fatigue guidance. Professionals indicated that the acceptance of the stroke and its consequences are crucial for dealing with post-stroke fatigue, although stroke survivors found that fatigue was underestimated or not always recognized by stroke care professionals. Most stroke survivors who did not receive fatigue guidance would have liked it. Fatigue guidance often includes the provision and assistance in *incorporating pacing activities*. The last subtheme emphasized that *one size does not fit all* when it comes to fatigue guidance.

Fatigue guidance: not a common good

Both professionals and stroke survivors indicated that fatigue guidance was not offered to everyone during rehabilitation. A few stroke survivors did not receive any guidance because they were not treated in a rehabilitation centre or because it was simply not part of their rehabilitation treatment. These stroke survivors were not aware of the existence of fatigue guidance, and some felt that they had not received fatigue guidance because they had not specifically asked for help, even though they were suffering from fatigue. Some professionals confirmed this thought and explained that fatigue management consists of changing behaviours and only when survivors are motivated to change their behaviours, fatigue guidance can help. Occupational therapist Robert explained in the following quote that behaviour change is hard to instigate when the request for help does not come from the survivor themselves:

"There are clients who ask for help for themselves and there are clients who are sent by their general practitioner. Or like, "my daughter thinks I am..." In the latter case, behaviour change is very difficult to achieve which I understand. Because if I do not want to change something myself, I am not going to change it. So, I only treat stroke survivors when the survivor himself indicates they suffer from their fatigue." (Robert, occupational therapist)

Stroke survivors explained that they struggled with adjustments in daily life to be compliant with their need for rest and had difficulty with accepting the *'second version'* of themselves: a version which is unable to fully participate in social- and work activities. Older stroke survivors seemed to better accept their new version than younger stroke survivors, as thirty-something year old Caitlyn indicates in the quote below:

“'I cannot really accept that I am different from what I used to be. I would have liked to have more energy and be a different mother than I am now. Although I really can do a lot, I find it regrettable that I just miss a few hours a day because I sleep.” (Caitlyn, stroke survivor)

Health professionals emphasised that acceptance of the *‘second version’* is crucial for dealing with post-stroke fatigue. They also agreed with the survivors that adjustments in daily life were inevitable for their need for rest. Professionals indicated that the acceptance of the stroke and its consequences can reduce the burden of fatigue.

Contrastingly, the stroke survivors mentioned that the impact of post-stroke fatigue was underestimated by health professionals who work in stroke care. Survivors declared that fatigue was sometimes recognized by professionals, but found it was given little attention in general or not taken seriously. Stroke survivor Francis, for example, experienced this underestimation by her rehabilitation physician:

“My rehabilitation physician became seriously ill at one point. And he said: now I understand, I really get it now. That fatigue is not normal.” (Francis, stroke survivor)

However, all health professionals did portray post-stroke fatigue as a very debilitating and common consequence after stroke. They claimed to be able to oversee the burden that comes with post stroke fatigue and reported that they do not underestimate their patients.

Incorporating pacing activities

Health professionals agreed on the importance of incorporating pacing activities to manage post-stroke fatigue. The professionals, such as Robert, were clear that this guidance does not resolve the stroke survivors' fatigue but that by pacing activities the fatigue may be experienced as less limiting:

"It definitely does not solve the fatigue. But it really does lessen the limitations it imposes." (Robert, occupational therapist)

The most mentioned pacing activity by the professionals was balancing between activity and rest. They explained that fatigued stroke survivors often become engaged in a boom-and-bust cycle, where they are likely to do too much on one day and because of that have too little energy to do anything the next day.

The professionals described different behavioural strategies which could be used to balance between activity and rest, such as limiting the activities performed, prioritizing, planning, and incorporating rest during the day. The stroke survivors who did receive fatigue guidance confirmed these strategies and explained that the guidance was focused on energy distribution, where mapping activities was the most mentioned tool used. Stroke survivors found rearranging daily activities useful and most of them still made a daily schedule for proper energy distribution. Professionals also advised stroke survivors to make their physical activities less tiring by, for example, moving around in a wheelchair instead of going on foot or wearing sunglasses or earplugs to reduce the amount of stimuli. Some of the survivors were indignant about the rehabilitation schedule as it did not match what they were taught during fatigue guidance. A day in rehabilitation was fully planned and did not include any rest moments. This led to incomprehension among the survivors. For example, Harry experienced the rehabilitation schedule as too full without sufficient rest moments, as he said in the quote below:

''Well, the fatigue problem is not picked up by therapists. Every therapist [in rehabilitation centre] has a task, you are there as a patient and the physiotherapist must get you to walk. He will chase you through the entire building. […] When you see the schedule that you get every day there, it is unbelievable. There is no resting moment in between." (Harry, stroke survivor)

One size does not fit all

The professionals regularly emphasized the importance of tailoring fatigue guidance to the individual, noting the individualized nature of post-stroke fatigue as well as the multiple factors that can contribute to or cause it. Professionals mentioned that in each stroke survivor, fatigue has its unique package of contributing factors and potential causes that should be explored before guidance is provided. For example, the age of the survivor, the occurrence of other major life events or whether someone suffered from co-morbidities. Hence every survivor requires a unique tailored approach to their fatigue. Therefore, professionals, for example Eleanor, struggled with following standardized guidelines for post-stroke fatigue guidance:

"There are guidelines, but every survivor has his/her own problems, their own family and based on that we try to do what is best, but not really based on a fixed protocol or methodology." (Eleanor, outpatient attendant)

The opinions of the stroke survivors regarding the effectiveness of the fatigue guidance were also diverse. Most stroke survivors were somewhat negative about the received fatigue guidance and explained that the provided information did not match their wishes or needs. For example Mathilda thought the explanation about mapping activities sounded as an academic approach and found it to be very technical.

Theme: The right place and time for post-stroke fatigue guidance

Within this theme, the first subtheme describes that *post-stroke fatigue realisation* often occurs in the home setting. Professionals are *struggling with finding the right time for information provision on fatigue guidance.* Survivors, however, have clear ideas on the timing of information provision and want to be informed from the very beginning in the hospital.

Post-stroke fatigue realisation

The professionals mentioned that most stroke survivors experience fatigue during rehabilitation but are not always aware of the duration and severity of the fatigue. They mentioned that inpatient stroke survivors are in a survival mode, mainly focusing on initial recovery (e.g. walking ability, going to the bathroom) and going back home as soon as possible. At that point they expect the fatigue to resolve itself after discharge. Once they return to the home setting with the expectation to take up their pre-stroke life including all daily activities (e.g. work, childcare, visiting friends/family), it becomes clear that their energy levels conflict with their expectations and pre-stroke life. Professional Rosanna explains that when survivors must resume their pre-stroke responsibilities, the (chronic) nature of the fatigue becomes evident:

"I often hear [from my patients] that especially in the outpatient phase or afterwards, when they have to participate again at work or at home with small children, that the fatigue hits them hard." (Rosanna, cognitive rehabilitation therapist & TBI-coach)

Struggling finding the right time for information provision on fatigue guidance

Professionals were aware of the importance of the right time for information provision on fatigue guidance, but they struggled with finding this right moment. Professionals experienced that ideally the information provision should be aligned to the moment when stroke survivors perceive the impact of fatigue on their daily lives. They agreed that this moment occurs mostly several months after rehabilitation. Sarah, for example, experienced that from that moment stroke survivors are motivated to cope with the fatigue and to change their pre-stroke behaviours:

"I recognise that sometimes after rehabilitation, stroke survivors first have to actually face some problems before they are motivated for something, for a next step." (Sarah, rehabilitation physician)

Besides, professionals wonder how useful the information provision on fatigue guidance is during rehabilitation as they feel that most survivors cannot retrieve this information after discharge when they need it. Eleanor, for example, experienced that information provision by handing out leaflets does not always have the desired effect, illustrated in the following quote:

"If you give them leaflets, well, they disappear into the closet. And when they are needed, when they actually need the information because they are struggling with something, they often forget that they have them. And then they do not know where to go for help" (Eleanor, outpatient attendant).

Some professionals attribute this difficulty in obtaining information to secondary stroke effects, such as cognitive problems, which may negatively impact the survivors' comprehension of information. Others ascribe it to the so-called "information-overload" the stroke survivors received during inpatient rehabilitation. According to them, the survivors are only receptive to information that is interesting for them at that time.

Stroke survivors highlighted, in contrast to the thoughts of the health professionals, specifically that they would have liked more information at discharge (e.g. by handing out leaflets or a conversation with a health professional) about post-stroke fatigue, and to go home more prepared. Several stroke survivors thought it would be of added value if their partner or child would also be informed on post-stroke fatigue. Abigail explained she would have liked to have left the hospital better informed:

''I think the health professional should have told me beforehand: madam, your body is doing quite well again, but remember, a stroke involves a lot more. You have a few tough weeks ahead. Lie down every afternoon. Either dose activities or take it easy. At that moment, I needed that." (Abigail, stroke survivor)

Theme: Follow-up stroke care and suggestions for improvement

The theme describes that *follow-up care after discharge* is *not a guarantee* in the Netherlands. Fatigue guidance follow-up exists but varies among rehabilitation centres and hospitals. Professionals and survivors discuss in the second theme the *need for a linking pin:* someone who gets the survivors to the right care.

Follow-up care after discharge? Not a guarantee!

For some survivors, a follow-up appointment with a stroke professional was arranged, but others received no follow-up care at all. The survivors who received follow-up care did not experience this as coherent care because they thought the care was not useful for them. There seemed to be no clear difference in follow-up care between survivors after hospital discharge and survivors after rehabilitation discharge. When it comes to seeking help for their fatigue after discharge, survivors admitted being reluctant, which was recognised by the professionals as stated by Eleanor:

"I think that if survivors have to take active steps themselves to get that help, many people drop out because they can't oversee the steps they have to take." (Eleanor, outpatient attendant)

Even though health professionals were quite positive about the arranged follow-up care, they were clear that coherent follow-up care should be accessible to all discharged (both hospital and rehabilitation) stroke survivors. They noted that in rehabilitation centres where follow-up support was well-arranged, the follow-up only occurred during the first year after discharge and did not provide continuity for longer support. Financial constraints and limited staff resources kept them from providing longer-term support.

The survivors who were treated in a rehabilitation centre reported they would have liked their relatives to be more involved in rehabilitation since their fatigue has a substantial impact on their relatives and because they play a vital role in care after discharge. One way to include relatives in rehabilitation is by providing education, for instance, through conversations with professionals. Lex illustrated that the impact of a stroke is larger than just the person who suffers the stroke by the following quote:

"I always say: you never get a stroke all by yourself" (Lex, stroke survivor)

The need for a linking pin

Professionals and stroke survivors agreed upon the importance of linking a stroke survivor to a 'coach' in follow-up care after rehabilitation discharge. When discussing the activities of such a 'coach', the professionals recommend that this person should perform follow-up visits in the home environment, recognise when someone suffers from fatigue, and if necessary, refers the survivor to the right fatigue management programme(s). Stroke survivor Francis, for example, explained that the consultations with this linking pin should start during rehabilitation and not after discharge:

''There actually should be some consultations during the rehabilitation process. When the end of the trajectory approaches, the frequency should be increased a bit. Instead of once a month,

once every two weeks or once a week. And at the end you can ask, can we continue?'' (Francis, stroke survivor)

Some professionals specifically mentioned that the general practitioner is the first contact point for medical matters and is therefore expected to take the responsibility for the signalling of fatigue and referring to fatigue management programmes. However, health professionals experienced that most general practitioners have limited time available and limited knowledge on post-stroke fatigue and fatigue management programmes. Robert explained that not all general practitioners refer fatigued patients to fatigue management programmes:

"When I look at the referrals we get from the general practitioners, they are often from the same general practitioners and many general practitioners do not come with these kinds of referrals. They should stop categorizing post-stroke fatigue as a symptom that 'just comes' with the stroke." (Robert, occupational therapist).

Most stroke survivors, on the other hand, preferred contact with peer support workers rather than health professionals, as support workers draw upon their own experiences. They also had a need for support groups where themes as fatigue, work and family life were addressed. The lack of these support groups in most of the survivors' rehabilitation was experienced as a major shortcoming. Mathilda explained in the following quote the preference on hearing information from a peer support worker over a professional:

''I think it would have benefited me more to hear it from a peer support worker. Because they have experienced the same, they don't have it from a book." (Mathilda, stroke survivor)

Discussion

This qualitative focus group study explored experiences and perceptions of stroke survivors and health professionals on post-stroke fatigue guidance in Dutch rehabilitation and follow-up care. We found that providing fatigue guidance (e.g., tailored advice on pacing activities) during and after stroke rehabilitation could fill the current unmet need of stroke survivors for coping with fatigue to improve participation, physical activity and health. Moreover, information provision at the optimal time and extensive follow-up support for all stroke survivors after rehabilitation may help to get *the right people, to the right care* at *the right time*.

The right people

According to health professionals, the right people (stroke survivors) who are able to receive fatigue guidance are the stroke survivors who accept their 'second version' (according to stroke survivors: 'a version which is unable to fully participate in social- and work activities'), because the health professionals think that acceptance of the second version and the fatigue is crucial for dealing with post-stroke fatigue. Two recent studies found comparable results and reported that not accepting post-stroke fatigue worsened the fatigue [17,30]. Skogestad et al. [17] distinguished behavioural- and emotional strategies to manage fatigue and lists acceptance among the latter. However, all stroke survivors (including stroke survivors who struggled with accepting their 'second version') stressed their need for fatigue guidance during rehabilitation and during follow-up care. Therefore, we recommend health professionals working with stroke survivors that fatigue guidance should be accessible to all stroke survivors, but that in some cases attention should be paid to the acceptance of the 'second version' before fatigue guidance is provided.

Also, some professionals explained that fatigue management consists of changing behaviours and only when survivors are motivated to change their behaviours, fatigue guidance can help. The behaviour where we are referring to is the survivors' physical activity behaviour and his/her participation in e.g. social- and work activities. These findings are supported by the COM-B model for Behavior Change, in which capability, opportunity and motivation are the three key factors capable of changing behaviour [31] (in the current context: physical activity behaviour and participation). The acceptance of the 'second version' aligns with the factor capability since capability comprises among other the mental state of an individual. Health professionals are the right people to play a vital role in the key factor opportunity since health professionals should provide or refer to the right fatigue guidance. Besides, the motivation to learn how to deal with fatigue fits with the key factor motivation to change behaviour. But again, fatigue guidance should be accessible to all stroke survivors, since they feel the need for it. We recommend to consider the key factors capable of changing behaviour according to the COM-B model [31] in fatigue guidance to change stroke survivors' behaviour into a behaviour wherein the stroke survivors is trying to manage fatigue complaints while engaging in physical activity and while participating in e.g. social- and work activities; so-called activity pacing behaviour. Activity pacing is defined as a (sub)conscious behaviour of trying to manage daily physical activities, to divide energy over the day and to plan rest periods [32-34]. When considering the above mentioned suggestions regarding tailored fatigue guidance, all stroke survivors are the right people for fatigue guidance.

Furthermore, stroke survivors stressed their need of follow-up care, which is not offered to all stroke survivors. This finding is in line with a previous focus group study [16]. A systematic review reported that stroke survivors and their caregivers expect ongoing follow-up care after rehabilitation to be facilitated by the general practitioner, but limited support from the general practitioner was experienced in practice [35]. The difference between the expectations of health professionals concerning the follow-up support from the general practitioner and the actual support provided by the general practitioner was also mentioned in this study. Most stroke survivors preferred to be linked to a peer during rehabilitation to whom they could turn after discharge. A recent study found that talking to a peer was helpful in learning how to manage fatigue for both caregivers as stroke survivors [36]. For that matter, peers are 'the right people' to play a vital role in stroke follow-up care. Moreover, research showed that peer support for stroke survivors has positive influence on loneliness, enhances hope and positivity, enables coping through knowledge exchange and promotes community reintegration [49,50]. Further research is needed to investigate whether a peer as coach is a feasible and effective in fatigue guidance in follow-up care.

The right care

The quality and content of the fatigue guidance was considered important according to the stroke survivors and health professionals. In line with the current study, multiple previous studies indicated that stroke survivors were not satisfied with the information they received [37-40]. Stroke survivors in the study of Ablewhite et al. [36] did not know that fatigue could be a consequence after stroke. A recent study specifically indicated that information should concern what post-stroke fatigue means, how it manifests itself and why rest is important [37]. In line with our study, this study highlighted the importance of including relatives in the information provision, to improve understanding of post-stroke fatigue and the support from relatives. Survivors in that study experienced more support from relatives who had been educated about rest than from relatives who were not educated. According to them, relatives should be informed at the same time as the survivors. In the study of Blackwell et al. [41] and in our study, health professionals also acknowledge the importance of post-stroke fatigue education to both survivors and their support network. Hence, there seems to be a discrepancy between the received education of the survivors and the provided education of the professionals.

Furthermore, the survivors in our study felt that both leaflets and a conversation with a health professional would have benefited them to better deal with perceived fatigue. In contrast to our findings, a recent systematic review showed that active information provision (programme of lectures and services with an opportunity to answer questions) for stroke survivors may improve quality of life and may slightly reduce anxiety and depression, while passive information provision (generic information, booklets and leaflets) does not lead to any reduction [42]. Further research should investigate if active information provision on fatigue is effective in stroke survivors to reduce fatigue and to enhance physical activity.

During rehabilitation, some of the survivors were indignant about the rehabilitation schedule as it did not match what they were taught during fatigue guidance. A day in rehabilitation was fully planned and did not include any rest moments, although they strongly had a need for rest. This is in line with previous qualitative studies, who reported survivors found rehabilitation exhausting, and challenging when experiencing fatigue [43,44].Therefore, we recommend health professionals working in stroke rehabilitation to tailor the rehabilitation schedule to the patients' energy level and perception of fatigue.

The finding that many stroke survivors did not receive fatigue guidance is in line with the qualitative study of Bicknell et al. [43], who reported that stroke survivors mostly had to learn to manage fatigue by themselves by using trial and error and receiving fatigue education was considered as 'an exception rather than a rule'. Stroke survivors' caregivers in the study of Ablewhite et al. [36] revealed that if they had not advocated for fatigue guidance on behalf of the survivors, it was unlikely that the survivors would have received support.

Without fatigue guidance, stroke survivors become engaged in an overactivity-underactivity cycle. Previous literature found that such an overactivity-underactivity cycle in fatigued people with chronic conditions can lead to reduced participation in physical activity [45,46]. Therefore, in accordance with the health professionals, we suggest that fatigue guidance should include advice to incorporate pacing activities to manage post-stroke fatigue. The finding that health professionals experienced that activity pacing does not solve the fatigue in stroke survivors but that it does reduce limitations in physical activity and participation, is in accordance with previous literature on activity pacing [45-48]. A promising concept to implement structured advice on activity pacing in fatigue guidance in rehabilitation is the Activity Pacing Framework of Antcliff et al. (2021) [47]. “This Activity Pacing framework recognises pacing as a multidimensional concept that involves different facets, such as breaking down tasks, finding baselines of tolerable activities, implementing consistent levels of activities, planning activities, setting goals of meaningful activities, accepting activity levels and gradually increasing activities” [47]. Further research is needed to evaluate the effectiveness of this Activity Pacing framework during and after stroke rehabilitation.

The right time

The professionals feel that the optimal time for information provision on fatigue guidance is aligned to the moment when survivors are motivated to (learn to) manage their fatigue while engaging in physical activity and while participating in e.g. social- and work activities, which is often when the impact of fatigue becomes evident, often several months after rehabilitation. This finding is supported by the contemplation phase in the transtheoretical model of health behaviour, which hypothesised that behaviour change is more likely when educational strategies are tailored to an individual's current state of readiness for change [49]. A previous systematic review acknowledged this specifically for stroke care, reporting that the timing of information provision should be tailored to the stage of recovery [35].

Stroke survivors highlighted that they would have liked more information well before discharge about post-stroke fatigue, to go home better prepared. This is supported by previous studies that reported that stroke survivors felt commonly unprepared for *what was going to come* after rehabilitation [30,35,42,50]. All survivors in the study of Eriksson et al. [37] emphasised the need of receiving information shortly after the stroke, to better understand post-stroke fatigue and to receive support from their relatives. This 'right time' shortly after stroke is supported by a previous study that found that assessing and treating post-stroke fatigue in the acute phase remains important because post-stroke fatigue in the acute phase is an independent risk factor for poor physical health at 18 months following stroke [51].We recommend health professionals working in stroke rehabilitation to provide information on post-stroke fatigue, its chronic aspect and how to manage the fatigue well before discharge – even though the patient may not be in the contemplation phase yet – to prevent stroke survivors that they are overwhelmed by the fatigue when they try to (re)engage in physical activities. Further research, like intervention studies, are needed to confirm the optimal time well before discharge for information provision on post-stroke fatigue.

Strengths and limitations

The current qualitative study provided rich data on post-stroke fatigue guidance in Dutch health care. The integration of perceptions of health professionals and experiences of stroke survivors provided novel insight in discrepancies concerning post-stroke fatigue guidance, which resulted in important implications to improve stroke rehabilitation programs and stroke follow-up care. An important strength of the study is the involvement of a large variety of health professionals working in different disciplines, at distinct stages in recovery and in different regions in the Netherlands. This variety of health professionals, besides the stroke survivors, led to a comprehensive insight into the different perspectives on post-stroke fatigue guidance to inform future optimisation of fatigue management programmes in healthcare. Furthermore, the online setup could be considered as a strength as it made it easier to combine participants from different geographical areas in the same focus group. This facilitated the discussion and interest in one another and may therefore have led to richer data [51].

This study has some limitations that must be considered. First, multiple professionals had clear expectations of the role of the general practitioner in stroke follow-up care, the inclusion of a general practitioner would have provided a more comprehensive perception of fatigue guidance in the Netherlands. However, the heterogeneous group of professionals included in this study is a good representation of health professionals in post-stroke care as stroke survivors must deal with multiple different disciplines [18]. For the generalizability of the study findings, it is important to note that the majority of the included stroke survivors have had a mild stroke, were female, and many were ambassadors of the patient stroke association. So the study findings lack experiences of stroke survivors after severe stroke and male stroke survivors.

Implications for rehabilitation practice and further research

The following implications will help guide improvement of fatigue guidance in stroke rehabilitation programmes and stroke follow-up care aiming to improve physical activity, functioning, participation, and health. First, we suggest that fatigue guidance should be accessible to all stroke survivors, but to pay attention to the acceptance of the stroke and/or 'the second version' and to consider the key factors capability, opportunity and motivation [31] to change physical activity behaviour and participation in e.g., social and work activities. We suggest embedding knowledge on fatigue guidance in education of health professionals working in stroke rehabilitation and/or stroke follow-up care. Further research is needed to investigate whether a peer as coach is a feasible and effective in fatigue guidance in follow-up care.

We suggest tailoring the rehabilitation schedule to the patients' energy level and perception of fatigue. Besides, we suggest that fatigue guidance should include advice to incorporate pacing activities to manage post-stroke fatigue, e.g. standardised instructions in the Activity Pacing framework [47], but further research is need to test the effectivity of this framework in stroke care because advice on activity pacing should be tailored to the stroke survivors' situation. Furthermore, we recommend to provide information on post-stroke fatigue, its chronic aspect and how to manage the fatigue well before discharge, to both survivors and relatives, but further research is needed to confirm this 'right time' for information provision.

The insights of this study contribute to a growing recognition of post-stroke fatigue guidance and are valuable for health professionals and decision makers in health care to improve fatigue guidance in stroke care. However, this study is relatively small and to our knowledge it is the first study on perceptions of post-stroke fatigue guidance in the

Netherlands. Hence, more research on post-stroke fatigue guidance is required for specific recommendations and/or implementation.

Conclusion

The study findings of this focus group study will help guide improvement of fatigue guidance in stroke rehabilitation programmes and stroke follow-up care aiming to improve physical activity, functioning, participation, and health. We suggest providing information on post-stroke fatigue to stroke survivors and their relatives, well before discharge from stroke rehabilitation. Besides, tailored advice on activity pacing during and after stroke rehabilitation is important to fill the current unmet need of stroke survivors to manage fatigue and to gradually improve participation, physical activity behaviour and health. Also, in fatigue guidance, we suggest to consider the acceptance of the stroke, capability, opportunity and motivation to change physical activity behaviour and participation as focus points. In addition, we suggest to offer follow-up support on fatigue guidance, including peer support, to all stroke survivors after rehabilitation.

Acknowledgements

The authors would like to thank all participants for their contribution to the current study. We wish to thank dr. Hella Brand for her assistance with the qualitative research methodology. Bregje L. Seves received a personal grant from the University Medical Center Groningen to perform the current study. Femke Hoekstra is supported by a Craig H. Neilsen Foundation Postdoctoral Fellowship (#719049) and Michael Smith Foundation for Health Research (MSFHR) Trainee Award (#RT-2020-0489).

References

1. Cumming TB, Packer M, Kramer SF, et al. The prevalence of fatigue after stroke: A systematic review and meta-analysis. International journal of stroke : official journal of the International Stroke Society. 2016;11(9):968-977.
2. van der Werf SP, van den Broek HL, Anten HW, et al. Experience of severe fatigue long after stroke and its relation to depressive symptoms and disease characteristics. Eur Neurol. 2001;45(1):28-33.
3. Seves BL, Hoekstra T, Hoekstra F, et al. Unravelling perceived fatigue and activity pacing in maintaining a physically active lifestyle after stroke rehabilitation: a longitudinal cohort study. Disability and rehabilitation. 2020:1-11.
4. Wu S, Chalder T, Anderson KE, et al. Development of a psychological intervention for fatigue after stroke. PLoS One. 2017;12(8):e0183286.
5. Choi-Kwon S, Kim JS. Poststroke fatigue: an emerging, critical issue in stroke medicine. Int J Stroke. 2011 Aug;6(4):328-36.
6. Staub F, Bogousslavsky J. Post-stroke depression or fatigue. Eur Neurol. 2001;45(1):3-5.
7. Fini NA, Holland AE, Keating J, et al. How Physically Active Are People Following Stroke? Systematic Review and Quantitative Synthesis. Physical Therapy. 2017;97(7):707-717.
8. Pedersen SG, Anke A, Aadal L, et al. Experiences of quality of life the first year after stroke in Denmark and Norway. A qualitative analysis. Int J Qual Stud Health Well-being. 2019 Dec;14(1):1659540.
9. Mead GE, Graham C, Dorman P, et al. Fatigue after stroke: baseline predictors and influence on survival. Analysis of data from UK patients recruited in the International Stroke Trial. PloS one. 2011;6(3):e16988.
10. Su Y, Yuki M, Otsuki M. Non-Pharmacological Interventions for Post-Stroke Fatigue: Systematic Review and Network Meta-Analysis. Journal of Clinical Medicine. 2020;9(3):. doi:10.3390/jcm9030621.
11. Clarke A, Barker-Collo SL, Feigin VL. Poststroke fatigue: does group education make a difference? A randomized pilot trial. Top Stroke Rehabil. 2012 Jan-Feb;19(1):32-9.
12. Thomas K, Hjalmarsson C, Mullis R, et al. Conceptualising post-stroke fatigue: a cross-sectional survey of UK-based physiotherapists and occupational therapists. BMJ Open. 2019 Dec 10;9(12):e033066.
13. Thomas K, Gamlin C, De Simoni A, et al. How is poststroke fatigue understood by stroke survivors and carers? A thematic analysis of an online discussion forum. BMJ Open. 2019 Jul 9;9(7):e028958.

14. Van Heugten C, Bertens, D., Spikman, J. Richtlijn Neuropsychologische Revalidatie 2017.

15. Satink T, Cup EH, Ilott I, et al. Patients' views on the impact of stroke on their roles and self: a thematic synthesis of qualitative studies. Arch Phys Med Rehabil. 2013 Jun;94(6):1171-83.

16. Kjörk EK, Gunnel C, Lundgren-Nilsson Å, et al. Experiences, needs, and preferences for follow-up after stroke perceived by people with stroke and healthcare professionals: A focus group study. PloS one. 2019;14(10):e0223338.

17. Skogestad IJ, Kirkevold M, Larsson P, et al. Post-stroke fatigue: an exploratory study with patients and health professionals to develop a patient-reported outcome measure. Journal of patient-reported outcomes. 2021;5(1):35-021-00307-z.

18. Clarke DJ, Forster A. Improving post-stroke recovery: the role of the multidisciplinary health care team. J Multidiscip Healthc. 2015;8:433-42.

19. van Eeden M, van Heugten C, van Mastrigt GA, et al. The burden of stroke in the Netherlands: estimating quality of life and costs for 1 year poststroke. BMJ Open. 2015 Nov 27;5(11):e008220.

20. Winstein CJ, Stein J, Arena R, et al. Guidelines for Adult Stroke Rehabilitation and Recovery: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke. 2016 Jun;47(6):e98-e169.

21. White JH, Gray KR, Magin P, et al. Exploring the experience of post-stroke fatigue in community dwelling stroke survivors: a prospective qualitative study. Disability and rehabilitation. 2012;34(16):1376-1384.

22. Nadarajah M, Goh HT. Post-stroke fatigue: a review on prevalence, correlates, measurement, and management. Top Stroke Rehabil. 2015 Jun;22(3):208-20.

23. Hinkle JL, Becker KJ, Kim JS, et al. Poststroke Fatigue: Emerging Evidence and Approaches to Management: A Scientific Statement for Healthcare Professionals From the American Heart Association. Stroke. 2017 Jul;48(7):e159-e170.

24. Poucher Zoë A. Thinking through and designing qualitative research studies: a focused mapping review of 30 years of qualitative research in sport psychology. International Review of Sport and Exercise Psychology.13(1):163-186.

25. Mack N, Woodsong, C., Macqueen, K.M., Guest, G., Namey, E. Qualitative Research Methods: A data collector’s field guide. . 2011.

26. Flinn NA, Stube JE. Post-stroke fatigue: qualitative study of three focus groups. Occupational therapy international. 2010;17(2):81-91.

27. Braun V, Clarke V. Reflecting on reflexive thematic analysis. Qualitative Research in Sport, Exercise and Health. 2019 2019/08/08;11(4):589-597.

28. J GN, Thorogood;. Qualitative Methods for Health Research. 3rd Edition ed. Los Angeles: Sage; 2014.

29. Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. International Journal for Quality in Health Care. 2007;19(6):349-357.

30. Turner GM, McMullan C, Atkins L, et al. TIA and minor stroke: a qualitative study of long-term impact and experiences of follow-up care. BMC Family Practice. 2019;20(1).

31. Michie S, van Stralen MM, West R. The behaviour change wheel: a new method for characterising and designing behaviour change interventions. Implementation science : IS. 2011;6:42-5908-6-42.

32. Abonie US, Sandercock GRH, Heesterbeek M, et al. Effects of activity pacing in patients with chronic conditions associated with fatigue complaints: a meta-analysis. Disability and rehabilitation. 2018:1-10.

33. Antcliff D, Keeley P, Campbell M, et al. Activity pacing: moving beyond taking breaks and slowing down. Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation. 2018.

34. Murphy SL, Kratz AL. Activity pacing in daily life: A within-day analysis. Pain. 2014;155(12):2630-2637.

35. Pindus DM, Mullis R, Lim L, et al. Stroke survivors' and informal caregivers' experiences of primary care and community healthcare services - A systematic review and meta-ethnography. PLoS One. 2018;13(2):e0192533.

36. Ablewhite J, Nouri F, Whisker A, et al. How do stroke survivors and their caregivers manage post-stroke fatigue? A qualitative study. Clin Rehabil. 2022 Oct;36(10):1400-1410.

37. Eriksson G, Larsson I, Guidetti S, et al. Handling fatigue in everyday activities at five years after stroke: A long and demanding process. Scand J Occup Ther. 2022 Jun 25:1-11.

38. Manola M, Petropoulou K, Calogero F. Gap in stroke patients' and carers' education. J Frailty Sarcopenia Falls. 2019 Mar;4(1):26-28.

39. Guo Y, Zhang Z, Lin B, et al. The Unmet Needs of Community-Dwelling Stroke Survivors: A Systematic Review of Qualitative Studies. Int J Environ Res Public Health. 2021 Feb 22;18(4).

40. Davoody N, Koch S, Krakau I, et al. Post-discharge stroke patients' information needs as input to proposing patient-centred eHealth services. BMC Med Inform Decis Mak. 2016 Jun 7;16:66.

41. Blackwell S, Crowfoot G, Davey J, et al. Management of post-stroke fatigue: an Australian health professional survey. Disabil Rehabil. 2022 Nov 11:1-7.

42. Crocker TF, Brown L, Lam N, et al. Information provision for stroke survivors and their carers. Cochrane Database Syst Rev. 2021 Nov 23;11(11):Cd001919.

43. Bicknell ED, Said CM, Haines KJ, et al. "I Give It Everything for an Hour Then I Sleep for Four." The Experience of Post-stroke Fatigue During Outpatient Rehabilitation Including the Perspectives of Carers: A Qualitative Study. Front Neurol. 2022;13:900198.

44. Purcell S, Scott P, Gustafsson L, et al. Stroke survivors' experiences of occupation in hospital-based stroke rehabilitation: a qualitative exploration. Disabil Rehabil. 2020 Jun;42(13):1880-1885.

45. Abonie US, Edwards AM, Hettinga FJ. Optimising activity pacing to promote a physically active lifestyle in medical settings: A narrative review informed by clinical and sports pacing research. Journal of sports sciences. 2020;38(5):590-596.

46. Antcliff D, Keenan AM, Keeley P, et al. "Pacing does help you get your life back": The acceptability of a newly developed activity pacing framework for chronic pain/fatigue. Musculoskeletal care. 2021.

47. Antcliff D, Keenan AM, Keeley P, et al. Testing a newly developed activity pacing framework for chronic pain/fatigue: a feasibility study. BMJ open. 2021;11(12):e045398-2020-045398.

48. Abonie US, Hettinga FJ. Effect of a Tailored Activity Pacing Intervention on Fatigue and Physical Activity Behaviours in Adults with Multiple Sclerosis. Int J Environ Res Public Health. 2020 Dec 22;18(1).

49. Prochaska JO, Velicer WF. The transtheoretical model of health behavior change. Am J Health Promot. 1997 Sep-Oct;12(1):38-48.

50. Shipley J, Luker J, Thijs V, et al. The personal and social experiences of community-dwelling younger adults after stroke in Australia: a qualitative interview study. BMJ Open. 2018 Dec 16;8(12):e023525.

51. Lerdal A, Gay CL. Fatigue in the acute phase after first stroke predicts poorer physical health 18 months later. Neurology. 2013 Oct 29;81(18):1581-7.

Chapter 9

General discussion

This thesis provided detailed insight and evidence that fatigue and activity pacing play an important role to reach sustained physical activity and health among people with physical disabilities and/or chronic diseases following discharge from rehabilitation, and especially in stroke survivors. This thesis took a diagnosis-overarching and disease-specific (stroke) approach to investigate this aim. Moreover, this aim was investigated by using divers methodologies, including quantitative study designs (cohort studies and cross-sectional studies), a narrative literature review and qualitative study designs (a semi-structured interview study and a focus group study).

Summary and discussion of the main findings

A summary of the main findings in this thesis is described following the guiding conceptual framework for this thesis as presented in the general introduction. This thesis investigated the four core concepts 'physical activity', 'Health-related Quality of Life (HR-QoL)', 'fatigue', and 'activity pacing' separately, which are subject in several chapters of this thesis. In addition, all overlapping associations between these four core concepts are investigated. The conceptual framework in figure 1 changed compared to the one presented in the general introduction. First, circles are now filled areas with colours, representing the obtained knowledge in this thesis. Second, the overlapping associative areas between physical activity and HR-QoL, and between activity pacing and fatigue are smaller, since these associations are not as great as expected.

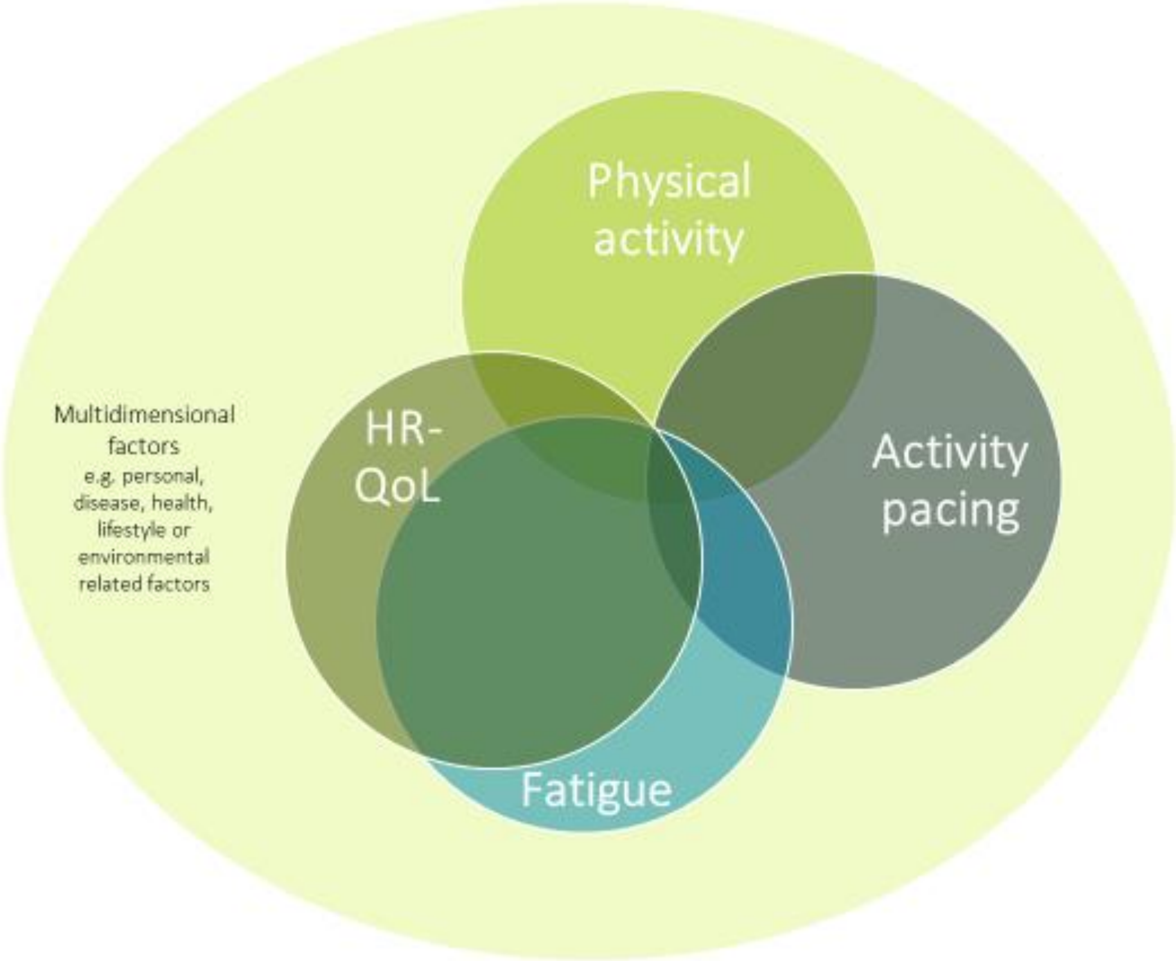


Figure 1 A conceptual framework of this thesis, including the core themes/concepts and their suggested overlapping associative areas.

Physical activity

Physical activity, being the key focus point of the ReSpAct study and the RSE programme, was studied with the Adapted Short QUestionnaire to ASsess Health-enhancing physical activity (Adapted-SQUASH). Whether the Adapted-SQUASH catches the construct of physical activity among a diverse group of persons with physical disabilities and/or chronic diseases was assessed in chapter 2. The results of chapter 2 revealed that the Adapted-SQUASH is an acceptable measure to assess self-reported physical activity in large populations of people with physical disabilities and/or chronic diseases but is not applicable at the individual level due to wide limits of agreement. The test-retest reliability and concurrent validity of the Adapted-SQUASH are comparable to other physical activity questionnaires among people with physical disabilities and/or chronic diseases [1-5]. Self-reported physical activity assessed with the Adapted-SQUASH does not accurately represent accelerometer-derived physical activity assessed with the Actiheart in individuals with disabilities, since these individuals seem to overestimate their physical activity and find it difficult to recall the perceived intensity of the activity. I would like to advice researchers and clinicians working with people with physical disabilities and/or chronic diseases to carefully consider which construct of physical activity they want to measure – self reported or accelerometer-derived physical activity – because both measure different aspects of physical activity (e.g., type of activity, duration, frequency, intensity), most self-reported physical activity questionnaires are not applicable at the individual level, and accelerometers are very expensive among large scale populations in intervention studies or cohort studies.

Physical activity associated with HR-QoL

Sustained physical activity is one of the key goals in today's rehabilitation practice and health care. Beyond the sustained levels of physical activity is the overarching key goal to improve HR-QoL. Chapter 3 provides evidence that 41% of the people with disabilities and/or chronic diseases who participated in the physical activity promotion programme RSE obtained high levels of HR-QoL up till one year after discharge from rehabilitation. However, chapter 3 does not provide evidence that the obtained high levels of HR-QoL are significantly associated with high levels of physical activity in this target population. The findings in chapter 3 did support a trend that implies that more physical activity is associated with higher levels of HR-QoL, since the direction of the observed (almost significant) association indicates that people who were more physically active before discharge from rehabilitation were more likely to obtain high levels of HR-QoL compared to people who obtained moderate levels of HR-QoL after discharge from rehabilitation. Previous literature did find an association between higher levels of physical activity and higher levels of HR-QoL in people with disabilities and/or chronic diseases [6-9]. I believe that physical activity promotion alone during and after rehabilitation is not the holy grail to obtain and maintain high levels of HR-QoL after rehabilitation, because chapter 3 provided important insight in people with a worse acceptance of the disease and having secondary health problems (high body mass index, perceived fatigue and perceived pain), showing a more vulnerable course of moderate levels of HR-QoL after rehabilitation. These findings have important implications for rehabilitation, which are discussed hereafter in the discussion.

Physical activity associated with fatigue

The association between physical activity and fatigue – in terms of perceived and performance fatigability – in people with physical disabilities and/or chronic diseases, was investigated in the narrative review in chapter 4. As expected, low levels of physical activity were found to be associated with high levels of perceived fatigability in specific diseases (diabetes, ankylosing spondylitis, cancer, rheumatoid arthritis, systemic lupus erythematosus, renal disease and sarcoidosis). In turn, improving physical activity reduced perceived fatigability in cancer and performance fatigability in multiple sclerosis.

In addition, chapter 6 found that low perceived fatigue was associated with sustained high levels of physical activity up to one year after stroke rehabilitation, which is supported by previous literature [10,11]. The relation between fatigue and physical activity in stroke survivors is further explored in the qualitative study in chapter 7. Chapter 7 found that the differences in this interaction between individuals were mainly attributable to the different perceptions of fatigue (mental versus physical fatigue). Mental fatigue was mainly a barrier for becoming physically active, but after being active the individuals perceived lower levels of mental fatigue and increased energy levels. A literature review in people without disabilities found decreased levels of intrinsic motivation towards an upcoming physical activity when mentally fatigued [12] and found that the effects of mental fatigue can be counteracted when increasing motivation [13]. Hence, mental fatigue seems to have an impact on the motivation towards physical activity instead of the physical activity itself, which is an important finding to consider in tailored advice on fatigue guidance in rehabilitation practice. Physical fatigue was mostly a barrier for *maintaining* physical activity, due to perceived pain and exhaustion in the muscles during physical activity, which was mostly attributable to severe physical complaints. Physical fatigue levels decreased after sustained physical activity, possibly due to more strength and physical fitness, and recovery of the affected side of the body. These findings are also found in previous qualitative studies among stroke survivors [14,15]. Chapter 4 and chapter 6 provide evidence for the existence of different notions of fatigue, which are disease-specific in several disease populations. This is important to consider in person-centred advice on fatigue management to enhance physical activity during and after rehabilitation practice.

Physical activity associated with activity pacing

Chapter 5 found that higher levels of self-reported physical activity were associated with activity pacing behaviour with high activity peaks during the week in people with physical disabilities and/or chronic diseases, even after adjusting for sex, age, body mass index, drug use and use of a mobility aid. They might become even more physically activity when receiving appropriate pacing advice, since they may not realize that activity bursts could relate to longer recovery periods. The association in the opposite direction means that lower levels of self-reported physical activity were associated with a more evenly distributed activity pacing behaviour. They might avoid physical activity in anticipation to fatigue, which was also found in a previous study among individuals with rheumatoid arthritis [16]. Therefore, the ones with a more evenly distributed activity pacing behaviour might benefit activity pacing advice to manage their perceived fatigue and to sustain physical activity. In addition, chapter 6 found that stroke survivors who perceived to be at risk of overactivity, are not afraid to overdo, because they reported higher levels of physical activity up to one year after stroke rehabilitation. An explanation for this association might be that their physical capacity and their load-capacity ratio allows them to participate in physical activity. That's also what I have heard during the individual interviews with stroke survivors. Some stroke survivors are very active, know that sometimes they do too much activities in a row, and know that it sometimes results in long periods of rest.

Health-related Quality of Life

Chapter 3 found that more than one third of the ReSpAct cohort obtained a relatively stable high HR-QoL, which is a very positive finding since improving HR-QoL is one of the key objectives in today's rehabilitation practice. However, more than half of the participants obtained only moderate HR-QoL after participating in the person-centred physical activity promotion Rehabilitation, Sports and Exercise (RSE) programme (chapter 3). This is worrisome since it is known that lower levels of HR-QoL are associated with secondary health problems (e.g., fatigue, pain, obesity, cardiovascular diseases) [17]. Also in chapter 3, we found that the secondary health problems perceived fatigue, perceived pain and a high body mass index – that were already present just before discharge from rehabilitation – explained the distinct moderate and high HR-QoL trajectories. Besides, people who had a better acceptance of the disease had a higher change to follow the high HR-QoL trajectory after rehabilitation, compared to the moderate HR-QoL trajectory. These findings indicate the importance of paying attention to the acceptance of the disease during rehabilitation (e.g., focus on self-management or self-regulation strategies) and to provide advice on activity pacing to manage fatigue and pain for sustained high levels of HR-QoL after rehabilitation.

In addition, a small group (4%) obtained a recovery trajectory of HR-QoL following a large increase of HR-QoL after discharge from rehabilitation. Based on the study findings in chapter 3 we cannot explain why these people obtained such a large increase in levels of HR-QoL from discharge till one year after rehabilitation. Future research might investigate the obtained steep increase in levels of HR-QoL in more detail, for example by performing individual interviews with these people. Furthermore, the identified high, moderate and recovery HR-QoL trajectories are comparable to HR-QoL trajectories identified in specific disease populations (e.g., in stroke [18] and in breast cancer survivors [19]), which might indicate that HR-QoL trajectories are not disease specific.

HR-QoL associated with fatigue

HR-QoL was associated with perceived fatigue as mentioned above in a diagnosis-overarching population of people with physical disabilities and/or chronic diseases (chapter 3). In more detail, people with less perceived fatigue at discharge had a higher odds to follow the high HR-QoL trajectory after rehabilitation, compared to the moderate HR-QoL trajectory, even after controlling for the level of HR-QoL before discharge from rehabilitation. In addition, the association between HR-QoL and fatigue – in terms of perceived and performance fatigability – was analysed in the narrative review in chapter 4. Low levels of HR-QoL were associated with high levels of perceived fatigability in a wide array of diseases. The association between HR-QoL and performance fatigability was however not systematically studied in the reviewed literature (chapter 4). Chapter 6 investigated a diagnosis-specific association between HR-QoL and fatigue in stroke survivors. Stroke survivors with high levels of HR-QoL before discharge from rehabilitation had a higher odds to follow the low perceived fatigue trajectory after rehabilitation, compared to the high perceived fatigue trajectory. These findings support the importance to pay attention to manage perceived fatigue to obtain sustained higih levels of HR-QoL after rehabilitation, not only in stroke survivors but across all patient populations in rehabilitation practice.

Fatigue

Fatigue is one of the most important health problems in people with physical disabilities and/or chronic diseases [17,20]. Perceived fatigue was investigated in several chapters in this thesis; in both quantitative and qualitative study designs. Chapter 4 aimed to provide a comprehensive review regarding the prevalence and intensity of fatigue in terms of perceived and performance fatigability in people with physical disabilities and/or chronic diseases. This narrative review identified both high perceived and performance fatigability in a wide array of diseases, including stroke (chapter 4). In contrast, this review found disease populations reporting high perceived fatigability but normal patterns (like in healthy adults) of performance fatigability. This might be due to some disease populations having more impaired physical capacity due to severe physical disabilities compared to other disease populations. For example in stroke survivors, the limited functionality in the affected side of the body can limit endurance and walking capacity due to increased energy costs in the lower extremities [21,22].

This thesis provided a deeper understanding of fatigue in stroke survivors, since stroke survivors are one of the largest populations in rehabilitation [23,24] (and in the cohort of the ReSpAct study), and since they mention fatigue as one of the most common complaints impacting on daily functioning [25,26]. Chapter 6 found that most stroke survivors in the ReSpAct cohort (79.1%) perceived high fatigue even up to one year after rehabilitation, while 19.9% of the sample followed a trajectory of low perceived fatigue. This finding highlights that perceived fatigue is a very common and chronic symptom in stroke survivors, which is in accordance with previous literature [25,27]. Although most stroke survivors followed stable trajectories of perceived fatigue, high levels of within-person heterogeneity were found, indicating that levels of perceived fatigue might fluctuate over time (chapter 6).

Furthermore, chapter 6 found that personal factors, disease-related, psychosocial and environmental factors before discharge from rehabilitation did not distinguish stroke survivors with sustained high levels of fatigue from those with sustained low levels of fatigue till one year after rehabilitation, while previous literature did find that personal factors and disease-related factors predicted fatigue up to 6 months after stroke [28,29]. Probably, personal and disease/health characteristics predict fatigue early after stroke, but are not necessarily predictors for fatigue in the chronic phase after stroke. This is important to consider when providing tailored advice in stroke follow-up care to manage fatigue.

In addition to this quantitative study, chapter 7 used a qualitative study design to explore experiences and perspectives of stroke survivors on fatigue, physical activity and activity pacing from rehabilitation till the chronic phase after stroke. Chapter 7 found that stroke survivors perceived different notions of fatigue after stroke: mental fatigue (perceived as having little sense of doing anything, feeling that you can go to sleep at any time, and/or having headaches) and physical fatigue (perceived as wanting to sit down and take rest and/or experiencing muscle pain/exhaustion). These distinct notions of fatigue can be linked to the different constructs of fatigue (perceived fatigue and performance fatigability respectively) as described in the narrative review in chapter 4.

Fatigue associated with activity pacing

High levels of perceived fatigue were expected to be associated with a more evenly distributed activity pacing behaviour, since previous studies of Murphy and Cuperus [16,30,31] found that a more stable pattern of activity pacing was associated with higher levels of fatigue, showing a symptom contingency response. The association between fatigue and activity pacing was quantitatively investigated in chapter 5 in people with physical disabilities and/or chronic disease. In chapter 5, we did not find a significant association between perceived fatigue and activity pacing behaviour, which might indicate that perceived fatigue levels are similar in people with a more evenly distributed activity pacing behaviour and in people with high activity pacing in their activity pacing behaviour. Another explanation for this non-significant association is the large variability between diseases in this diagnose-overarching design compared to the previous disease specific studies [16,30,31].

Activity pacing

Chapter 5 investigated accelerometer-derived activity pacing behaviour by using the variability in activity energy expenditure during the week in people with physical disabilities and/or chronic diseases. In this chapter, we associated two perceived attitudes of activity pacing – perceived awareness of activity pacing and the perceived risk of overactivity – with accelerometer-derived activity pacing behaviour. However, we did not find a significant association between the perceived attitudes of activity pacing and accelerometer-derived activity pacing. In other words, the ones with activity pacing behaviour with high activity peaks during the week (based on accelerometer data), did not perceive a higher risk of overactivity. This finding may suggest that those people do not realize that activity bursts might relate to longer recovery periods since they did not receive any information and/or guidance on fatigue management. This interesting discrepancy between perceived activity pacing measured with self-report and actual activity pacing patterns measured with an accelerometer was also found in previous literature [32] and is important to consider when measuring activity pacing in rehabilitation practice and research.

Activity pacing is further explored in chapter 7 that aimed to explore the experiences on fatigue management in individuals after stroke, in particular regarding activity pacing behaviour. When individuals after stroke did not receive any guidance in fatigue management during or after rehabilitation, they gradually learned how to manage their fatigue in daily life themselves by trial and error (chapter 7). This findings indicates that their used fatigue management strategies are a self-learned skill or behaviour. Common fatigue management strategies after stroke were planning activities during the day/week, setting boundaries and incorporating rest breaks during the day (chapter 7), which were also found in previous literature in stroke survivors [14,15,33-35]. Most individuals showed symptom-contingent activity pacing behaviour with intuitive decision-making at the short-term after stroke. This shifted to more pre-planned activity pacing behaviour with deliberative decision-making at the long-term after stroke. Hence, stroke survivors seem to have the ability to develop self-learned activity pacing skills, but it requires years of experience which is absolutely worrisome. The sooner a stroke survivor learns how to manage fatigue, the sooner the stroke survivor is able to sustain physical activity and health. Therefore, structured advice on activity pacing behaviour [36] might be beneficial for stroke survivors to reduce the time to develop activity pacing strategies to manage fatigue and to gradually enhance physical activity.

The focus group study in chapter 8 explored the experiences and perceptions on post-stroke fatigue guidance in Dutch rehabilitation and follow-up care in stroke survivors and health professionals. The health professionals were positive about the provided fatigue guidance and suggested that fatigue guidance should include advice to incorporate pacing activities to manage post-stroke fatigue, but it could be better tailored to the survivors' situation. In addition, health professionals experienced that activity pacing does not solve the fatigue in stroke survivors but that it does reduce limitations in physical activity and participation, is in accordance with previous literature on activity pacing. I believe that this is an important finding to consider in rehabilitation practice, since the perceived fatigue might not disappear in stroke survivors when receiving fatigue guidance (e.g., advice on activity pacing) but the fatigue guidance should help them to manage fatigue which will allow them to gradually increase physical activity.

Strengths

The principal strength of the current thesis lies in its divers appropriate methodological techniques used throughout the thesis to unravel the role of fatigue and activity pacing for sustained physical activity and health among people with physical disabilities and/or chronic diseases following discharge from rehabilitation. Quantitative studies provided knowledge on the four core concepts (physical activity, HR-QoL, fatigue and activity pacing) under study in this thesis and their mutual associations. The quantitative studies included both cross-sectional studies and prospective cohort studies (the ReSpAct study), which are first desired to understand the association between de four core concepts of this thesis, before we can develop interventions targeting fatigue to improve physical activity and health during and after rehabilitation practice. A prospective cohort study has the advantage to investigate the aims under study in a real world setting instead of a controlled setting. Valuable additions in this thesis were the two qualitative studies that provided detailed insight in the relation between physical activity and fatigue, and insight on activity pacing and fatigue guidance in Dutch rehabilitation care.

Furthermore, a strength of the used unique dataset of the ReSpAct study is the large sample size of 1719 people with physical disabilities and/or chronic diseases. A large sample size is important for high statistical power when investigating cross-sectional and longitudinal associations between several concepts. This large unique cohort in the ReSpAct study enabled diagnosis-overarching analyses, but also a disease-specific analysis in stroke survivors (the largest population of the ReSpAct cohort). These diagnosis-overarching and stroke-specific studies provide valuable input for intervention development of fatigue guidance to improve physical activity and health, e.g., should the intervention be stroke-specific or is the intervention applicable for a wide array of disease populations in rehabilitation practice?

Limitations

Several limitations of this thesis need to be addressed. First, the participants in the ReSpAct study participated in the RSE programme that aimed to stimulate an active lifestyle during the rehabilitation period [37,38]. The included counselling sessions were tailored to the individual and did not specifically focus on advice on activity pacing behaviour. Therefore, activity pacing measured in the ReSpAct study was identified as naturalistic activity pacing behaviour (a self-learned activity pacing behaviour without receiving any advice or information on fatigue guidance) [30], but it is uncertain if specific information or guidance has been given on activity pacing to obtain/maintain physical activity during the RSE programme. If so, that might have reduced the perceived fatigue levels in the ReSpAct cohort.

Second, the ReSpAct study is entirely questionnaire based, but it did not include disease specific questionnaires since the ReSpAct study included a heterogeneous group of persons with a physical disability and/or chronic disease. Therefore, no stroke specific questionnaires were used in studies among persons after stroke, which makes it harder to compare our results with previous literature in stroke survivors who did use stroke specific questionnaires.

Third, the current thesis used survey data and interviews to gain insight in the four core concepts under study in this thesis, but this knowledge would be more enriched when for example physical activity was also measured with an activity monitor, since self-reported physical activity questionnaires mostly show an overestimation of actual time spent being physically active, which is probably attributable to recall bias, such as the difficulty in recalling short breaks during physical activity (e.g. socializing or refreshment during the reported time doing sports, or taking rest during the reported time doing gardening or household activities) [39], while an activity monitor does measure all sorts of short breaks during physical activity and over the day. Another potential bias between self-reported and accelerometer-derived physical activity outcomes may reside in the appreciation and perception of physical activities and their intensities [40]. Also insight in fatigue would have been enriched when perceived fatigue was not only measured with self-report but also measured during maximal voluntary contractions to gain insight in the different constructs perceived and performance fatigability [41]. However, these measurements are too expensive and time-consuming to measure in such a large cohort.

Fourth, it is likely that selection bias took place during inclusion of participants in the ReSpAct study. It is possible that these participants are motivated and interested in physical activity and sports activities, since these participants filled in the ReSpAct questionnaire at four moments in time, which lasted around 60 minutes per questionnaire. The study of Brandenbarg et al. 2022 [42] confirmed that the ReSpAct cohort seems on average more active compared to similar populations with a physical disability and/or chronic disease [42]. This might influence the generalizability of the findings. The same holds for the participants in the stroke specific studies in this thesis. The ReSpAct study included in that sense a positive selection of stroke survivors, who were willing to participate on a voluntary basis and were able to fill in the questionnaires by themselves or with help at several measurement moments over a long period of time and/or were able to participate in an individual interview or focus group. This leads to the assumption that the stroke participants in the current thesis may not have had severe cognitive impairments or communication issues. These selection biases are important to consider when generalizing the findings in this thesis to the general population of people with physical disabilities and/or chronic disease or in specific to stroke survivors.

Implications for rehabilitation practice

Figure 1 presents the four core concepts and their overlapping associations. Figure 1 includes one small piece – exactly in the middle of the four circles – where alle four core concepts overlap. This small piece includes the knowledge with implications for rehabilitation practice and follow-up care, in which we should strive for an optimum to manage fatigue by incorporating advice on activity pacing to enhance physical activity and health.

First, rehabilitation professionals (e.g. sports counsellors, physiotherapists, physicians) may improve person-centred advice focusing on activity pacing to manage and to obtain/maintain sustained high levels of physical activity and HR-QoL in people with physical disabilities and/or chronic diseases suffering from fatigue symptoms. This especially holds for stroke survivors due to the high prevalence of the chronic and invisible symptom fatigue perceived in this population. The distinct notions of perceived fatigue (mental and physical fatigue) in stroke survivors emphasize the importance of the person-centred aspect of advice on activity pacing. Also, the fatigue guidance should pay attention to the acceptance of the stroke and should consider the key factors capability, opportunity and motivation [43] to change physical activity behaviour. Furthermore, it is important that person-centred advice on activity pacing is provided both during and after stroke rehabilitation (e.g., an evaluation moment or periodic counselling in stroke after-care), since the chronic aspect of perceived fatigue reveals after rehabilitation when stroke survivors try to re-integrate in society (e.g., participation in social and physical activities, work, spend time with family and friends).

Furthermore, based on the findings in the focus group study in chapter 8, I recommend to provide information on post-stroke fatigue, its chronic aspect and how to manage the fatigue well before discharge, to both stroke survivors and relatives, but further research is needed to confirm this optimal timing for information provision. Besides, I would suggest embedding knowledge on fatigue guidance in education of health professionals working in stroke rehabilitation and/or stroke follow-up care.

Implications for future research

The findings in this thesis are based on cross-sectional studies, prospective cohort studies and interview studies. The findings provide valuable recommendations to improve person-centred advice on activity pacing to manage fatigue and to obtain sustained physical activity and health after rehabilitation. The findings in this thesis form a step-up towards future research on intervention development of fatigue guidance by incorporating person-centred advice on activity pacing. The Activity Pacing Framework from Antcliff et al. [36,44] might be a good starting framework in this intervention development, since this framework provides standardised instructions on activity pacing for healthcare professionals to guide patients with chronic fatigue and/or pain symptoms to manage these symptoms. Future research should investigate if the implications of this thesis can be incorporated in the Activity Pacing Framework or in other existing framework, or that a new activity pacing framework should be developed to manage fatigue for sustained physical activity and health in people with physical disabilities and/or chronic diseases.

In addition, when the effectivity of such a (newly developed) activity pacing intervention will be investigated, it is recommended to measure self-reported physical activity with the Adapted-SQUASH and accelerometer-derived physical activity since both measures provide different information on the construct physical activity. Also, it is recommended to measure both perceived and performance fatigability in a standardised consensus-based manner, since these measures provide information on the different notions of fatigue.

General conclusion

High levels of perceived fatigue are associated with low levels of physical activity and low levels of HR-QoL in people with physical disabilities and/or chronic diseases following discharge from rehabilitation, and especially in stroke survivors. Advice on activity pacing seems to have the potential to manage fatigue and to increase physical activity and HR-QoL in this target population in rehabilitation practice and in follow-up care. The findings of this thesis will help guide improvement of fatigue guidance (e.g., advice on activity pacing) in rehabilitation programmes and follow-up care. Especially in stroke survivors, the advice on activity pacing should be person-centred through considering the acceptance of the disease, the capability, opportunity and motivation to change physical activity behaviour, and the distinct notions of perceived fatigue (mental and physical fatigue). Besides, information on post-stroke fatigue should be provided to stroke survivors well before discharge. Also, follow-up support after rehabilitation by a stroke coach should be implemented nationwide, since survivors and professionals expressed a need for it.

References

1. Booth M. Assessment of physical activity: an international perspective. Research quarterly for exercise and sport. 2000;71(2 Suppl):S114-20.
2. Wendel-Vos GC, Schuit AJ, Saris WH, et al. Reproducibility and relative validity of the short questionnaire to assess health-enhancing physical activity. Journal of clinical epidemiology. 2003;56(12):1163-1169.
3. van der Ploeg HP, Streppel KR, van der Beek AJ, et al. The Physical Activity Scale for Individuals with Physical Disabilities: test-retest reliability and comparison with an accelerometer. Journal of physical activity & health. 2007;4(1):96-100.
4. Arends S, Hofman M, Kamsma YP, et al. Daily physical activity in ankylosing spondylitis: validity and reliability of the IPAQ and SQUASH and the relation with clinical assessments. Arthritis research & therapy. 2013;15(4):R99.
5. Wagenmakers R, van den Akker-Scheek I, Groothoff JW, et al. Reliability and validity of the short questionnaire to assess health-enhancing physical activity (SQUASH) in patients after total hip arthroplasty. BMC musculoskeletal disorders. 2008;9:141-2474-9-141.
6. Krops LA, Jaarsma EA, Dijkstra PU, et al. Health Related Quality of Life in a Dutch Rehabilitation Population: Reference Values and the Effect of Physical Activity. PloS one. 2017;12(1):e0169169.
7. Feeny D, Garner R, Bernier J, et al. Physical activity matters: associations among body mass index, physical activity, and health-related quality of life trajectories over 10 years. Journal of physical activity & health. 2014;11(7):1265-1275.

8. Marck CH, Hadgkiss EJ, Weiland TJ, et al. Physical activity and associated levels of disability and quality of life in people with multiple sclerosis: a large international survey. BMC neurology. 2014;14:143-2377-14-143.

9. Farris MS, Kopciuk KA, Courneya KS, et al. Identification and prediction of health-related quality of life trajectories after a prostate cancer diagnosis. International journal of cancer. 2017;140(7):1517-1527.

10. Duncan F, Lewis SJ, Greig CA, et al. Exploratory longitudinal cohort study of associations of fatigue after stroke. Stroke. 2015 Apr;46(4):1052-8.

11. Thilarajah S, Mentiplay BF, Bower KJ, et al. Factors Associated With Post-Stroke Physical Activity: A Systematic Review and Meta-Analysis. Archives of Physical Medicine and Rehabilitation. 2017.

12. Martin K, Meeusen R, Thompson KG, et al. Mental Fatigue Impairs Endurance Performance: A Physiological Explanation. Sports Med. 2018 Sep;48(9):2041-2051.

13. Van Cutsem J, Marcora S, De Pauw K, et al. The Effects of Mental Fatigue on Physical Performance: A Systematic Review. Sports Med. 2017 Aug;47(8):1569-1588.

14. Flinn NA, Stube JE. Post-stroke fatigue: qualitative study of three focus groups. Occupational therapy international. 2010;17(2):81-91.

15. Barbour VL, Mead GE. Fatigue after Stroke: The Patient's Perspective. Stroke Res Treat. 2012;2012:863031.

16. Cuperus N, Hoogeboom TJ, Neijland Y, et al. Are people with rheumatoid arthritis who undertake activity pacing at risk of being too physically inactive? Clinical rehabilitation. 2012;26(11):1048-1052.

17. Rimmer JH, Chen MD, Hsieh K. A conceptual model for identifying, preventing, and managing secondary conditions in people with disabilities. Physical Therapy. 2011;91(12):1728-1739.

18. van Mierlo M, van Heugten C, Post MWM, et al. Trajectories of health-related quality of life after stroke: results from a one-year prospective cohort study. Disability and rehabilitation. 2017:1-10.

19. Goyal NG, Levine BJ, Van Zee KJ, et al. Trajectories of quality of life following breast cancer diagnosis. Breast cancer research and treatment. 2018.

20. Okkes IM, Oskam SK, Lamberts H. The probability of specific diagnoses for patients presenting with common symptoms to Dutch family physicians. The Journal of family practice. 2002;51(1):31-36.

21. Olney SJ, Monga TN, Costigan PA. Mechanical energy of walking of stroke patients. Arch Phys Med Rehabil. 1986 Feb;67(2):92-8.

22. Novak AC, Li Q, Yang S, et al. Energy flow analysis of the lower extremity during gait in persons with chronic stroke. Gait Posture. 2015 Feb;41(2):580-5.

23. Billinger SA, Arena R, Bernhardt J, et al. Physical activity and exercise recommendations for stroke survivors: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2014;45(8):2532-2553.

24. Ma VY, Chan L, Carruthers KJ. Incidence, prevalence, costs, and impact on disability of common conditions requiring rehabilitation in the United States: stroke, spinal cord injury, traumatic brain injury, multiple sclerosis, osteoarthritis, rheumatoid arthritis, limb loss, and back pain. Archives of Physical Medicine and Rehabilitation. 2014;95(5):986-995.e1.

25. Obembe AO, Olaogun MM, Olalemi AE. Functional limitations due to fatigue among independently ambulant stroke survivors in Osun, South-Western Nigeria. Physiother Res Int. 2015 Mar;20(1):54-9.

26. Schillinger A, Becker F. Fatigue in patients following traumatic brain injury and stroke. Tidsskrift for den Norske laegeforening : tidsskrift for praktisk medicin, ny raekke. 2015;135(4):331-335.

27. Knorr S, Ivanova TD, Doherty TJ, et al. The origins of neuromuscular fatigue post-stroke. Exp Brain Res. 2011 Oct;214(2):303-15.

28. Chen K, Marsh EB. Chronic post-stroke fatigue: It may no longer be about the stroke itself. Clin Neurol Neurosurg. 2018 Nov;174:192-197.

29. Feigin VL, Barker-Collo S, Parag V, et al. Prevalence and predictors of 6-month fatigue in patients with ischemic stroke: a population-based stroke incidence study in Auckland, New Zealand, 2002-2003. Stroke. 2012;43(10):2604-2609.

30. Murphy SL, Kratz AL. Activity pacing in daily life: A within-day analysis. Pain. 2014;155(12):2630-2637.

31. Murphy SL, Smith DM, Alexander NB. Measuring activity pacing in women with lower-extremity osteoarthritis: a pilot study. The American Journal of Occupational Therapy : Official Publication of the American Occupational Therapy Association. 2008;62(3):329-334.

32. Abonie US, Saxton J, Baker K, et al. Objectively-assessed physical activity and self-reported activity pacing in adults with multiple sclerosis: A pilot study. Clin Rehabil. 2021 Dec;35(12):1781-1788.

33. White JH, Gray KR, Magin P, et al. Exploring the experience of post-stroke fatigue in community dwelling stroke survivors: a prospective qualitative study. Disability and rehabilitation. 2012;34(16):1376-1384.

34. Skogestad IJ, Kirkevold M, Larsson P, et al. Post-stroke fatigue: an exploratory study with patients and health professionals to develop a patient-reported outcome measure. Journal of patient-reported outcomes. 2021;5(1):35-021-00307-z.

35. Eilertsen G, Ormstad H, Kirkevold M. Experiences of poststroke fatigue: qualitative meta-synthesis. Journal of advanced nursing. 2013;69(3):514-525.

36. Antcliff D, Keenan AM, Keeley P, et al. "Pacing does help you get your life back": The acceptability of a newly developed activity pacing framework for chronic pain/fatigue. Musculoskeletal care. 2021.

37. Hoekstra F, Alingh RA, van der Schans CP, et al. Design of a process evaluation of the implementation of a physical activity and sports stimulation programme in Dutch rehabilitation setting: ReSpAct. Implementation science : IS. 2014;9:127-014-0127-7.

38. Alingh RA, Hoekstra F, van der Schans CP, et al. Protocol of a longitudinal cohort study on physical activity behaviour in physically disabled patients participating in a rehabilitation counselling programme: ReSpAct. BMJ open. 2015;5(1):e007591-2015-007591.

39. Ma JK, McCracken LA, Voss C, et al. Physical activity measurement in people with spinal cord injury: comparison of accelerometry and self-report (the Physical Activity Recall Assessment for People with Spinal Cord Injury). Disability and rehabilitation. 2020;42(2):240-246.

40. Carroll DD, Courtney-Long EA, Stevens AC, et al. Vital signs: disability and physical activity--United States, 2009-2012. MMWRMorbidity and mortality weekly report. 2014;63(18):407-413.

41. Enoka RM, Duchateau J. Translating Fatigue to Human Performance. Medicine and science in sports and exercise. 2016;48(11):2228-2238.

42. Brandenbarg P, Hoekstra F, Krops LA, et al. Physical activity behaviour up to 1 year post-rehabilitation among adults with physical disabilities and/or chronic diseases: results of the prospective cohort study ReSpAct. BMJ Open. 2022 Jun 15;12(6):e056832.

43. Michie S, van Stralen MM, West R. The behaviour change wheel: a new method for characterising and designing behaviour change interventions. Implementation science : IS. 2011;6:42-5908-6-42.

44. Antcliff D, Keenan AM, Keeley P, et al. Testing a newly developed activity pacing framework for chronic pain/fatigue: a feasibility study. BMJ open. 2021;11(12):e045398-2020-045398.