Walking adaptability in polio survivors

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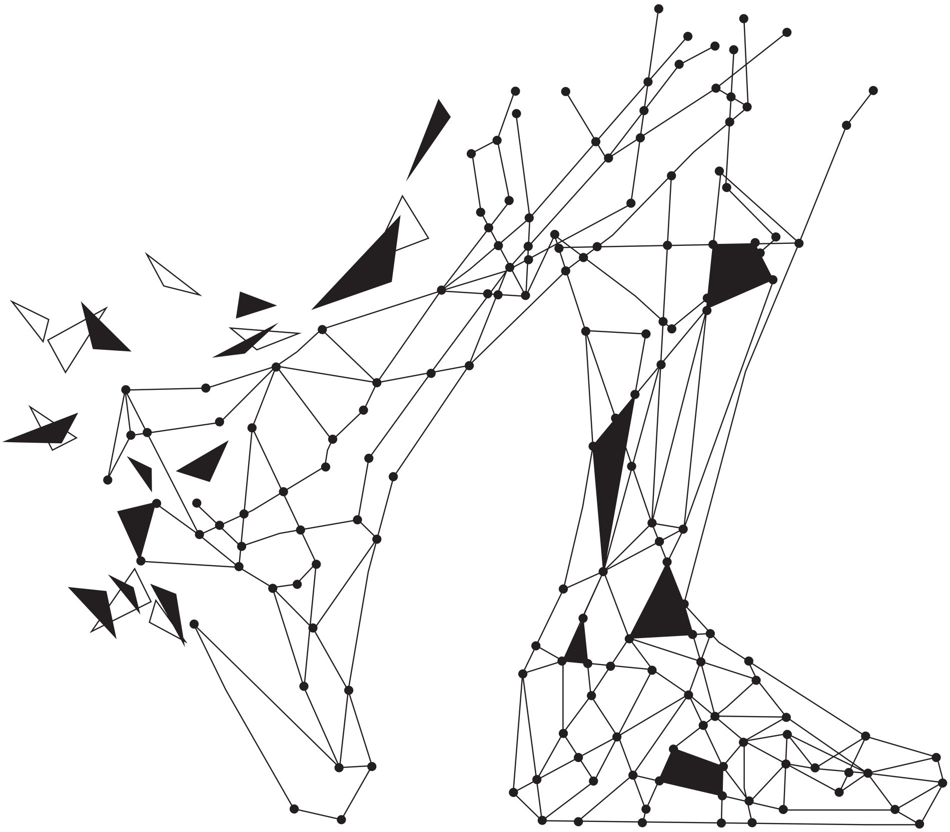

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CHAPTER 1

INTRODUCTION

Falls among polio survivors happen about two to four times more often than in community-dwelling elderly [1-6] and generally have far-reaching consequences [7]. Therefore, fall prevention is an important goal of the rehabilitation treatment in polio survivors. Falls in polio survivors mostly happen during walking [2, 5], which is an activity of daily life that concerns more than just generating steps to move from A to B. In fact, we constantly need to adjust our steps to environmental circumstances and task goals [8, 9]. This so-called walking adaptability is considered essential for safe and independent mobility [8, 9] and its assessment has therefore gained increasing attention in research as well as in clinical practice. In several populations with gait and balance problems, a reduced walking adaptability has been identified [10-16], which increases the risk of falls [13, 17]. In polio survivors, walking adaptability has not been studied so far, even though slips, trips and missteps are a major cause for falls in this population [2, 3, 5, 18], suggesting a reduced walking adapability. The aim of this thesis was therefore to expand our knowledge on walking adaptability and its assessment in polio survivors.

POLIOMYELITIS

Acute anterior poliomyelitis (in short acute polio) is caused by the highly infectious poliovirus that spreads from person to person through the fecal-oral route and, in endemic areas, mainly affects children under the age of 5 [19, 20]. The vast majority of polio infections is asymptomatic or passes by with (mild) symptoms like fever, fatigue and headache [19]. However, in 0.1-2% of all infections, the poliovirus invades the central nervous system and predominantly affects the motor neurons of the spinal cord. Poliovirus-induced destruction of these motor neurons leads to denervation of muscle fibers and subsequent muscle paresis or paralysis. Usually, the paresis or paralysis is asymmetrically distributed, affecting a varying number of muscle groups and resulting in a condition in which the ability to perform voluntary movements ranges from limited to completely impaired [21].

Until today, there is no cure for the effects of acute polio, but polio vaccinations contribute to the fight against polio by protecting children life-long. In 1988, a global initiative started to eradicate polio worldwide (the Global Polio Eradication Initiative, GPEI), which has achieved great successes by vaccinating an approximate 2.5 billion children, decreasing the polio incidence by 99% and saving an estimated 16 million people from being paralyzed [22]. Yet, even though two of the three existing wild-type polioviruses have been eradicated completely [19, 23] and very recently, on August 25th 2020, Africa has been declared free of all wild-type polioviruses [24], the last wild poliovirus, type 1, is still endemic in two countries: Afghanistan and Pakistan [20]. Since virus transmission is not bounded by national borders, massive and frequent immunization campaigns remain of vital importance to eliminate polio worldwide. However, during the recent COVID-19 outbreaks, polio vaccination campaigns in Afghanistan and Pakistan were suspended [22, 25] and many children missed their (repeated) polio vaccinations [26, 27]. This led to an increase in cases of acute polio in partially immunized children due to circulating vaccine-derived polioviruses [27], emphasizing the importance of continuation of the polio

eradication program to achieve the ultimate aim: a world free of polio.
In the Netherlands, acute polio became a rare disease after the polio vaccination became part of the national immunization program in 1957. Since then, except for some minor local outbreaks, two larger outbreaks have occurred: one in 1978 (110 cases) and one in 1992-1993 (71 cases). Most individuals who were infected with the poliovirus during these outbreaks were part of a community that refused vaccination because of their religion [28, 29]. Even though no new polio cases have been reported in the Netherlands since 1994 [29], and Europe was declared free of polio in 2002, many individuals who have been infected with the poliovirus are still experiencing the consequences of their polio sequelae every day. Worldwide, an estimated 12 to 20 million individuals are living with serious lasting consequences of their polio infection [30].

RECOVERY AND DETERIORATION

Several weeks to months after the acute phase of the polio infection, a process of partial and sometimes full recovery starts that helps to restore (some) muscle activation. Motor neurons affected by the primary infection regain (part of) their function and motor neurons that were not affected start sprouting to reinnervate muscle fibres from lost motor neurons [31, 32], leading to the development of enlarged motor units [33]. Even though these large motor units are rather unstable, characterized by a constant process of denervation and re-innervation of muscle fibres [34], they are often able to generate up to normal muscle forces [35]. Yet, after several decades, the process of denervation dominates, and the size of enlarged motor units gradually declines [34, 36]. As a result, many polio survivors experience new or increased neuromuscular symptoms [33, 37]. The exact reason for this degeneration remains unclear, but the prevailing hypothesis is that enlarged motor units are unable to maintain the increased metabolic demands due to chronic overuse [38]. New neuromuscular symptoms mostly include new or increased muscle weakness, increased muscle fatigability, generalized fatigue and joint and/or muscle pain [37, 39, 40], which is known as post-polio syndrome (PPS) [37] and usually leads to a decrease in physical functioning [41].

FALLS IN POLIO SURVIVORS

Residual muscle weakness or paralysis following acute polio and PPS-induced muscle weakness often involves the legs [39, 42, 43], which has a great impact on physical mobility and daily functioning [41]. Leg muscle weakness causes gait problems, like slower walking, increased walking energy cost [44] and dependency on assistive devices [45-47], and is a known risk factor for falling in polio survivors [2, 4, 48, 49]. The fall frequency among polio survivors is considerably high, with 55-84% of polio survivors reporting at least one fall annually [1-5, 50, 51] and more than half of them reporting to fall more frequently [2]. In comparison, in community-dwelling adults of 55 years and older, 25% reported one fall annually [6] and in community-dwelling adults of 65 years and older, 28-33% falls annually [52]. Falls in polio survivors have far-reaching consequences, like (severe) injuries that may require medical care, fear of falling [2, 5, 18, 50] and reduced independent mobility and quality of life [2, 45, 53]. Fall prevention thus is an important treatment goal in this population.

WALKING ADAPTABILITY

Falls in polio survivors mostly happen during walking [2, 5], which is an activity of daily life that is more complex than just placing one foot in front of the other. Recently, three essential aspects for walking have been described in a tripartite model of locomotor control (Figure 1), comprising the ability to 1) generate stepping movements, 2) maintain balance while walking, and 3) adapt walking (i.e. walking adaptability) [9]. In this model, these three abilities partially overlap and the extent to which each ability is involved in walking depends on the environmental circumstances and behavioral task goals. When walking in a simple and predictable environment, basic stepping can suffice while the center of mass is kept within a constantly moving base of support. However, in daily life, environmental circumstances are rarely simple and predictable, but challenging and variable. These more complex situations (e.g. crossing a busy road, avoiding a loose paving slab while carrying a shopping bag) require higher levels of balance control to keep the body upright in space and walking adaptability to meet environmental requirements. Yet, despite the importance of all three abilities for safe and independent walking in daily life, clinical tests used to define fall risk in polio survivors mainly focus on the abilities to generate stepping movements and to maintain balance while walking [47, 48, 54, 55], whereas the assessment of walking adaptability has received no attention so far.

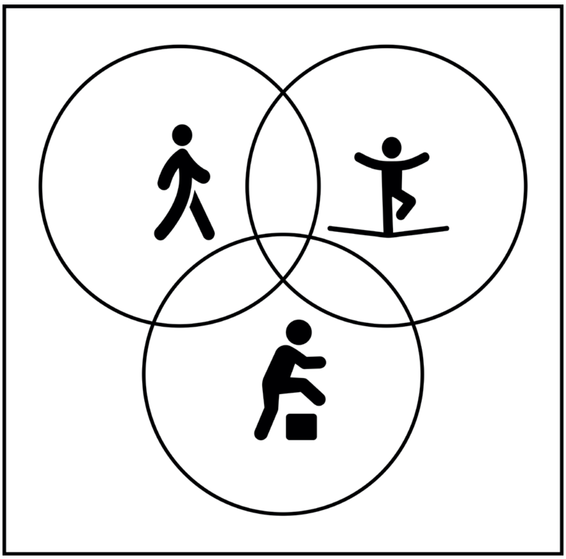

Figure 1. *The tripartite model of locomotor control, as described in [9], shows the partial overlap in three core abilities of locomotor control: to generate stepping movements (upper left circle), to maintain balance (the upper right circle) and to adapt walking to the environment (lower circle). Figure is based on [9].*

WALKING ADAPTABILITY ASSESSMENT IN CLINICAL PRACTICE: THE C-MILL

The construct of walking adaptability covers a broad spectrum of everyday life situations, environments and task goals that all require (slightly) different aspects of walking adaptability. In order to facilitate walking adaptability assessment in clinical practice, the concept of walking adaptability has been narrowed down into nine aspects, comprising: 1) obstacle negotiation, 2) time constraints, 3) cognitive dual tasking, 4) motor dual tasking, 5) terrain demands (e.g. walking on uneven surfaces), 6) ambient demands (e.g. light, temperature, noise), 7) postural transitions during walking, 8) physical load (e.g. carrying a bag) and 9) maneuvering during walking (e.g. avoiding other people or vehicles) [8, 9]. The C-Mill is an instrumented treadmill that was developed specifically to assess and practice several of these walking adaptability aspects in a challenging though safe environment (Figure 2). Step adjustments are elicited on the C-Mill by a visual environment projected onto the treadmill belt. A force platform that is embedded in the C-Mill treadmill registers the course of the center of pressure during walking, which is used online to estimate instants and locations of foot placement without needing extensive marker-based 3D motion-registration systems that are often used in gait analysis laboratories [56]. Based on the estimated timing and location of foot placement, objects can be projected onto the treadmill belt mimicking different aspects of walking adaptability, such as i) precision stepping, in which foot placement has to be adjusted to a sequence of (ir)regularly spaced stepping targets (Figure 2, lower-left panel), and ii) obstacle avoidance, in which step adjustments are required to avoid projected obstacles (Figure 2, lower-right panel). The difficulty of such walking adaptability tasks can be adjusted and tailored to the patient's ability and/or training goals.

In order to use the C-Mill in clinical practice for walking adaptability assessment in polio survivors, clinimetric properties like the validity and reproducibility of its outcomes should be known. This is essential for adequately distinguishing patients with different levels of walking adaptability or for evaluating patients' progress or decline in walking adaptability over time. Currently, only a few studies investigated validity aspects of C-Mill walking adaptability assessment implicitly [12, 57-60], and previous reproducibility studies of the C-Mill only focused on its step detection algorithm [60, 61], whereas information on the reproducibility of the actual walking adaptability outcomes is lacking.

Figure 2. *Walking adaptability assessment on the C-Mill. The lower-left panel depicts the target stepping task and the lower-right panel depicts the obstacle avoidance task. Participants wear a safety harness to guarantee safety while walking on the treadmill (upper panel).*

WALKING ADAPTABILITY PERFORMANCE IN POLIO SURVIVORS

In several studies, the C-Mill has been used to assess walking adaptability, revealing a reduced walking adaptability for populations with gait and balance disorders, including older adults with lower executive function [11], people walking with a prosthesis [12] and people post stroke [16]. In polio survivors, walking adaptability has not been studied so far. Previous studies that investigated risk factors for falling in this population evaluated intrinsic factors, and found that leg muscle weakness [49] (specifically of the most affected leg [2, 4, 48]), fear of falling [2, 48, 50], self-reported balance problems [2], balance performance [62] and gait variability [62] were associated with an increased fall risk. Yet, risk factors for falling are multifactorial and next to intrinsic factors, extrinsic factors might also be involved [63], as supported by several retrospective surveys reporting that most falls in polio survivors occurred during ambulation and inside the home as a result of trips, slips or missteps [2, 3, 5, 18]. This could be indicative of a reduced walking adaptability in this population. Comparing walking adaptability of polio survivors to that of healthy individuals is important to identify whether their walking adaptability is indeed reduced, as this might limit safe and independent walking [8, 9].

FACTORS ASSOCIATED WITH WALKING ADAPTABILITY

To retain safe and independent walking, early identification of walking adaptability limitations in this population might be of great value. To this end, insight into factors that are associated with walking adaptability in polio survivors is needed. In Parkinson's disease and stroke, balance problems, leg muscle weakness in the hip abductors and quadriceps, previous falls and impaired executive function were found to be associated with a reduced walking adaptability [64, 65]. Yet, these are both neurological disorders, while polio is a neuromuscular disorder characterized by different symptoms. Factors associated with walking adaptability in these populations may thus not be evidently transferable to polio survivors. Furthermore, in community-dwelling elderly [17] and in people with Parkinson's disease [13], a reduced walking adaptability has been shown to be associated with falling, but this association has not yet been confirmed in polio survivors.

THE TIME COURSE OF WALKING ADAPTABILITY

Despite large individual differences based on the severity of, and recovery after acute polio [36], most polio survivors develop new or increased disabilities while they are aging, which is often accompanied by a further decline in independent functioning and physical mobility [66-71]. Based on a ten-year follow-up study in polio survivors, the decline in physical mobility might mainly be determined by increasing self-reported problems with indoor and outdoor walking [71]. An age-related decline in walking adaptability might partly be involved, as could be expected from the normal aging process, leading to an increasing extent of comorbidities with a negative impact on disabilities [70], but also from a polio-specific decline in muscle strength due to the progressive nature of the polio sequelae [35, 68, 70, 72]. Yet, to our knowledge, no longitudinal studies on the time course of walking adaptability have been performed in polio or any other clinical population so far. From cross-sectional studies it is known that walking adaptability limitations are more pronounced for elderly compared to younger adults [73-76], which could indicate an age-related decline in walking adaptability. Knowledge on the course of walking adaptability in aging polio survivors might contribute to a better understanding of the decline in physical mobility in this population.

THE EFFECT OF FATIGUE ON WALKING ADAPTABILITY

Next to aging, another factor that could affect walking adaptability in polio survivors is fatigue. Fatigue is a very common symptom after polio [37, 39, 40, 77-80] and is mostly described as 'an increasing loss of strength during exercise' or 'a heavy sensation in the muscles' [79]. This suggests that localized muscle fatigue plays a prominent role in causing fatigue complaints. Yet, increased muscle fatigue in polio survivors compared with healthy individuals has only been confirmed in studies with isometric contractions [81, 82] even though fatigue after isometric contractions likely differs from the muscle fatigue experienced during daily life activities such as walking. Fatigue during walking in polio survivors has rarely been studied despite their high energy cost of walking [44, 83], which makes walking fatiguing [84]. So far, two studies evaluated fatigue during walking with the rate of perceived exertion and heart rate [84, 85] and one study reported a significant reduction in walking speed during six-minutes walking [85], possibly due to fatigue. Yet, none of these outcome measures reflect leg muscle fatigue during walking. In other clinical populations, such as people with multiple sclerosis [86] and cerebral palsy [87], leg muscle fatigue occurred during walking, affecting gait and increasing fall risk. The same may hold for polio survivors, since both fatigue [79] and fall rate [2, 50] have been shown to increase during the day in this population. Considering the high number of falls among polio survivors, and especially during walking after trips, slips or missteps [2, 3, 5, 18], it is pertinent to evaluate the effect of leg muscle fatigue on walking adaptability in this population, since a fatigue-induced reduction in walking adaptability might increase their fall risk.

GOAL AND AIMS OF THIS THESIS

Walking adaptability in polio survivors has not been investigated so far, even though a reduced walking adaptability might be involved in their high number of falls. The goal of this thesis is therefore to expand our knowledge on walking adaptability and its assessment in polio survivors. To this end, the first aim of the thesis is to determine the validity and reproducibility of walking adaptability assessment. The second aim is to investigate whether walking adaptability in polio survivors differs from healthy individuals. The third aim is to identify factors associated with walking adaptability and its association with falling in polio survivors. The final aim is to evaluate whether walking adaptability in polio survivors worsens over time and decreases with fatigue. To address these aims, walking adaptability is operationalized throughout the thesis as the ability to precisely step onto a sequence of (ir)regularly spaced stepping targets and as the ability to avoid (suddenly) projected obstacles (i.e., respectively target stepping and obstacle avoidance tests; Figure 2). In the last chapter of this thesis, next to target stepping, the ability to walk on a narrow-beam projection is evaluated (i.e. narrow-beam walking).

OUTLINE OF THIS THESIS

In **Chapter 2**, the face, construct and content validity of C-Mill walking adaptability assessment in polio survivors with a history of falls and/or fear of falling are determined. Furthermore, the reproducibility of walking adaptability outcomes is evaluated for target stepping and obstacle avoidance tests. The cross-sectional study in **Chapter 3** describes differences in walking adaptability between polio survivors and community-dwelling healthy individuals of similar age to identify whether walking adaptability limitations in polio survivors are present. In the cross-sectional study in **Chapter 4,** factors associated with walking adaptability performance in polio survivors and its association with falling in this population are explored. In the longitudinal study in **Chapter 5**, the two-year course of walking adaptability in polio survivors is evaluated. In **Chapter 6**, the effects of six minutes walking on physical fatigue and walking adaptability is evaluated in both polio survivors and healthy individuals. In **Chapter 7**, the main findings and overarching scientific and methodological considerations and clinical implications of these studies are discussed and directions for future research are given.

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