Chapter 1

General introduction and outline
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GENERAL INTRODUCTION

Walking dysfunction is one of the most common consequences of stroke, often displayed by asymmetrical stepping patterns (e.g. step length and time), reduced gait speed, increased energy cost and higher risk of falling [1-6]. As walking ability is an important aspect of independent functioning and participation [7-8], the restoration of gait represents a key rehabilitation goal for stroke patients [9].

Human walking is characterized by bipedal movements in which one leg acts as a support base, while the other is moved forward for progression to end at a new support area [10]. In this brief period of bilateral support, weight is transferred from one leg to the other, and the legs reverse their roles. These procedures are repeated with reciprocal timing until the walker reaches his or her destination [10]. A simple mechanism, one would think, but in order to produce successful and safe stepping, leg movements are controlled by not only the brain e.g. for initiation of gait, but also by the spinal cord to produce oscillating muscle patterns for walking, and by peripheral proprioceptive sensors to modulate these patterns in context of environmental constraints [11]. As such, the re-learning of walking includes developing relatively stable changes at both the spinal and supra-spinal level. And, in order for this to be efficient and functionally useful, changes need to be formed based on task-specific sensory information of functional motor performance [12].

A relatively new approach for re-learning of walking is the use of robotics, such as the Lokomat exoskeleton (Hocoma AG, Volketswil, Switzerland), which is combined with a treadmill and a bodyweight support (BWS) system (see Figure 1). By robotically guiding the legs of the patient along a pre-defined pattern, the Lokomat provides the experience of successful stepping and may induce gait-specific sensory input to potentially guide locomotor related neuroplasticity [13-15]. However, in order to purposefully exploit this potential, knowledge is needed on how robotically guided gait is controlled.

During Lokomat guided walking the amount of robotic guidance, as well as the level of BWS and treadmill speed, can be selected by the therapist to tailor therapy to the needs and possibilities of the individual patient. Selective and well-dosed usage of these training parameters requires knowledge on how they shape locomotor control.

To this end, the present thesis aims to examine the neuromuscular control of Lokomat guided walking, and to establish whether and how variations in Lokomat training parameters (i.e. guidance, BWS and treadmill speed) can be used to shape the neuromuscular control of walking.
Guidance by the Lokomat.

The Lokomat uses an exoskeleton to provide robotic movement guidance throughout the gait cycle. The exoskeleton includes two orthoses that are attached to the legs of the walker by means of cuffs and straps (see Figure 1B). As the hip and knee joints of the exoskeleton are actuated by linear drives, both the exoskeleton and the legs of the walker are moved through the gait cycle in the sagittal plane, following a predefined pattern that is based on the kinematics of healthy walkers [13, 16]. This ‘guidance’ by the exoskeleton is a key feature of Lokomat training, and was initially generated by a position controller. This type of controller imposes the predefined pattern on the legs, with minimal kinematic variability [13]. However, merely imposing fixed patterns allows the walker to remain passive [17], which may negatively affect therapy outcome as active contribution is an important prerequisite for motor learning [18-20]. Therefore, an impedance control strategy was implemented; allowing adjustment of the amount of guidance in accordance with the patient’s walking abilities [14]. With this strategy a virtual coupling between the actual and the predefined pattern is created, and torques are only generated to redirect the legs when deviations occur [15, 21-22]. The selected level of guidance determines the permitted amount of deviation in leg movement. When guidance is set to 100% (i.e. its maximum), the walker is forced to strictly follow the predefined pattern, similar to
the position control strategy. However, when guidance level is lowered, more freedom of movement is allowed, presumably requiring more active involvement of the walker to adhere to the required pattern. Guidance can even be set to 0%, where free limb movements are allowed and torques by the exoskeleton are only generated to correct for the exoskeleton inertia [15-16].

**Rationale for using robotic guidance.**

Current strategies applied in gait rehabilitation often rely on principles emerging from animal studies, as humans are believed to coordinate bipedal walking similar to quadrupeds [23-24]. As such, the idea of providing robotic guidance to induce sensory information of normative walking is primarily driven by work on cat locomotion.

One of the major findings was that completely spinalized cats are able to produce stepping movements with their paralyzed hind limbs when their bodyweight is supported during walking on a moving treadmill [25-28]. In complete spinalization the supra-spinal drive is missing, which leads to the conclusion that circuitries within the spinal cord must exist that are capable of generating the basic oscillating muscle patterns to produce gait [11]. In spinalized cats these Central Pattern Generators (CPG’s) can be reactivated or reorganized by sensory information [11], resulting in recovery of gait-like movement of the hind limbs after a period of training. The importance of afferent input is underlined by cat studies that showed reduced effectiveness of treadmill training when sensory feedback was diminished [29-31]. In addition, the finding that spinalized cats that were trained to walk were more capable at walking than the cats trained to stand [32-33], strongly suggests that spinal learning can be enhanced when the afferent input is task-specific.

Motivated by these findings, Bodyweight Supported Treadmill Training (BWSTT) was implemented in human gait rehabilitation for amongst others stroke patients. During this type of training, the patient wears a harness that can (partially) support the patient’s body weight during treadmill walking [34-35]. By removing weight from the legs, task demands such as weight bearing, transfer and balance control are assisted, aiding walking in patients who are unable to bear their full weight [36]. In addition, pelvic and leg movements can be manually assisted by physiotherapists when needed, to ensure sensory input of successful and normative stepping [13]. BWSTT is believed to be more intensive than conventional overground walking, as patients are capable of producing more stepping movements when BWS is provided [37]. This is beneficial as intensive training can optimize the outcome of gait therapy [38-40].

However, two important drawbacks may limit the intensiveness and task-specificity of BWSTT. First, the training approach can be physically demanding and strenuous for
both the patient and therapist [13, 15-16], in particular for patients with little walking ability who need constant assistance of two, or even three therapists [41]. Second, the quality of the movement guidance relies on the therapist’s experience and judgement, which does not only vary among therapists [22], but also over training sessions. In order to improve BWSTT and to reduce the workload of therapists, the past decade researchers have focused on the development of robotics to apply automated locomotor training. And what began as proof-of-concept testing in the 90s, has led to robotic devices such as the Lokomat that are already commercially available. In essence, the manual support provided by the therapist during BWSTT is replaced by robotics that can support the stepping movement throughout the gait cycle. As such, even patients with no or very low ambulatory skills can be trained, the therapist is unburdened and training sessions can be prolonged to increase duration and intensity (i.e. more movement repetitions). In addition, as the Lokomat uses reference patterns of healthy walkers to guide the legs of the patient [13, 16], trained movements are believed to be standardized and the quality of each step guaranteed.

Questions regarding Lokomat guided gait.

Despite clear advantages for unburdening the therapist when using the Lokomat for gait rehabilitation, the argument of increased task-specificity and intensity is less self-evident. First, during human walking multiple task constraints are linked to specific phases of the gait cycle, e.g. weight acceptance, provision of support, and dynamic balance during stance, whereas progression and foot clearance is necessary during swing [10]. When fixed in the Lokomat, the leg of the walker is mechanically coupled to the exoskeleton. This coupling may modify the task constraints, as the exoskeleton imposes impedance to the legs and restricts movements to the sagittal plane. Therefore, the question remains whether Lokomat guided walking is representative for unrestrained walking. If not, transfer of learned gait ability to overground walking may be limited.

In addition, although the use of robotics may prolong training sessions and therefore increase the number of steps practiced, the intensity of the therapy may be limited due to decreased active participation of the walker when robotically guided. Indeed, studies showed that walking in the Lokomat is more passive then treadmill walking in terms of energy consumption [42-44]. As active contribution to a task is an important prerequisite to learn the particular task [18-20], the effectiveness of the Lokomat as a gait rehabilitation tool may rely on the extent to which the walker actively contributes to the production of gait.
Moreover, implied in the use of the Lokomat is that the parameter space is reduced during therapy to only three dimensions: the amount of guidance, the level of BWS and selected treadmill speed. These three parameters can be set by the therapist to tailor Lokomat therapy to each individual patient. In addition, these are the only parameters available to physically affect the gait pattern and the level of active contribution. The effectiveness of Lokomat therapy may rely on the extent to which the parameters are capable to do so.

**Neuromuscular control of Lokomat guided gait.**

Taken together, knowledge is needed on (1) whether Lokomat guided gait patterns are similar to unrestrained walking, (2) to what extent the walker actively contributes to the production of gait and (3) the effects of the three available training parameters on neuromuscular control. When addressing these questions, the study of surface electromyography is particularly interesting as the timing of activity of lower limb muscles relates to control strategies and the amplitude to the level of active contribution to the production of gait [45]. However, knowledge on the neuromuscular control of Lokomat guided gait is limited. During treadmill walking, muscle activity typically follows characteristic patterns as the muscles of both limbs need to be well coordinated to achieve the temporally fixed task constraints [46]. A few studies on healthy walkers showed that, overall, the modular ordering of muscle activity remains stable when walking in the Lokomat [47-48]. At the level of individual muscles alterations are observed, such as increased activity in the upper leg muscles and decreased activity in lower leg muscles [49]. Although these studies indicate that the neuromuscular control of gait is altered during Lokomat guided walking, little information is available on how the neuromuscular control is affected by the training parameters (i.e. guidance, BWS and speed). In addition, the only study focusing on neuromuscular control of stroke patients showed that gait-related muscle patterns were more symmetrical and similar to healthy walkers during Lokomat guided walking, compared to treadmill walking [50]. However, training parameters (i.e. guidance and BWS) were set differently for each individual patient and no evaluation of the effects of the training parameters was done.
GENERAL OUTLINE

This thesis aims to provide a more complete account of the neuromuscular control of Lokomat guided gait. Even when the exoskeleton is not actuated, the mechanical coupling between the leg of the walker and the Lokomat exoskeleton may modify gait related task constraints, possibly necessitating adaptation in the neuromuscular control of gait. Therefore, Chapter 2 describes whether and how the Lokomat exoskeleton affects typical muscle activity, by evaluating the differences in neuromuscular control of healthy young adults between unrestrained treadmill walking and walking in the Lokomat exoskeleton without movement guidance. In addition, it is studied whether observed differences depend on the level of BWS or the set treadmill speed. Subsequently, the effects of robotic movement guidance are studied in Chapter 3, gaining insight in how guidance provided by the Lokomat affects the neuromuscular control of healthy gait, and how the nature and magnitude of its effects depend on BWS and speed.

The study of healthy subjects is beneficial as it enables free variation and exploration of the training parameters while studying the effects in a relatively homogeneous population. However, generalization of established results to stroke patients is not self-evident for two important reasons. First, post-stroke hemiparetic gait is often altered due to muscle weakness, insufficient spinal drive and spasticity [4, 10, 51]. As a result the neuromuscular control of both the affected and unaffected leg is altered and muscular patterns often deviate from the characteristic healthy patterns in both the amplitude and timing of activity [4, 52-54]. Lokomat guided gait in hemiparetic stroke patients may thus require a different control strategy then previously observed in healthy walkers. Second, whereas free exploration of the full range of settings for guidance, BWS and speed is possible in healthy walkers, patients may not tolerate all levels. Therefore, the following two chapters focus on the neuromuscular control of Lokomat guided walking in post-stroke hemiparetic patients. More specifically, Chapter 4 describes the differences between unrestrained treadmill walking and Lokomat guided walking in the neuromuscular control of gait in chronic stroke patients (FAC 2-4), and evaluates whether and how abnormalities in neuromuscular control of patients are altered during Lokomat guided gait. Thereupon the effects of a clinically relevant range of settings for guidance, BWS and treadmill speed on the neuromuscular control of post-stroke hemiparetic gait are evaluated in Chapter 5.

To end, the results will be summarized and discussed in Chapter 6.
REFERENCES


