Chapter 7

General discussion
This thesis addresses the temporal structure of gait related muscle activity in patients with post stroke hemiparesis. The main goal of the studies presented here was to provide information on the patterning of muscle activity in the lower extremities and on how these patterns change over the course of gait recovery. It was found that the temporal patterns of muscle activity associated with hemiplegic gait show a number of abnormalities, particularly during the stance phase, in the paretic as well as in the non-paretic leg (chapter 3). Despite clear improvements in the gait ability of patients during the subacute phase of stroke, the global temporal characteristics of muscle activity did not change, not even in patterns that were classified as ‘abnormal’ early after inclusion (chapter 4). However, the stride to stride consistency in the production of neuromuscular patterns may increase during subacute rehabilitation, most notably in the paretic BF (chapter 5). These results suggest that aberrant patterns of muscle activity develop early after stroke, that the global temporal characteristics of these patterns are stable over the course of recovery, and that patients may learn to produce these patterns with a greater consistency.

1. Altered temporal control of muscle activity following stroke

Chapter 3 showed that the patterning of gait related muscle activity in a number of important muscle groups of stroke patients differs from those observed in healthy persons. For a good understanding of the altered neuromuscular control after stroke, we need to know which mechanisms play a role in the development of these patterns, and whether or not patterning abnormalities impair gait ability in post stroke hemiparesis.

A possible explanation for the temporal abnormalities that were found in the muscle activity patterns in patients with stroke is that hemiparesis involves a neuromuscular timing disorder for gait. Although the role of higher cerebral centers in human gait is still poorly understood, experimental studies on cats indicate that locomotor centers of the brain are likely to be important for the initiation and termination of gait, as well as for the voluntary modification of ongoing gait activity (Drew et al., 2004). However, for cats and primates alike, there are as yet no indications that the cortical areas involved in walking play a major role in the temporal regulation of gait related muscle activity. On the other hand, there is general agreement that task-specific neural networks in the spinal cord are much
more important for the basic phasing of gait related muscle activity (See Duysens and van de Crommert (1998), van de Crommert et. al (1998) for reviews).

Although there is no evidence that the temporal regulation of human locomotor activity involves a 'cerebral conductor' to keep time, stroke induced damage to cortical gait centers may have indirect effects on timing control through alterations in the gain of spinal reflexes. Reflexes are important for updating ongoing muscle activity with instantaneous information on joint positioning and leg loading, and therefore play a crucial role in the temporal organization of gait (see Duysens et al. (2000), Dietz (2002), and Zehr and Duysens (2004) for reviews). Alterations in the gain of these reflexes (e.g. through disinhibition of central pathways) results in spasticity, which is often considered to be one of the main sources of temporal disregulation in stroke (Perry, 1978, 1993; Lamontagne et al., 2001; Burridge et al. 2001) and other neurological diseases (see Dietz (2001) for a review).

Another potential source of timing abnormalities are the secondary adaptive strategies that are used by patients to attain locomotor tasks goals when faced with primary impairments in muscle force output. In principle, the task structure contained in walking does not prescribe one single neuromuscular solution, and numerous configurations of muscle activity can result in functionally equivalent gait movements (cf. Gelfand and Latash, 1998). This abundance of locomotor solutions can be exploited to optimize gait performance in response to changes in the neurological, physiological, and biomechanical constraints of gait. The proper selection of adaptive patterns involves the development of neuromuscular preferences that are appropriate for given sets of constraints. As such, adaptation represents a general feature of neuromuscular organization in both healthy and pathological gait, with different set of constraints leading to different neuromuscular timing preferences.

Following stroke, decreased muscle force output, increased stiffness and altered biomechanical properties (e.g. due to lower walking speeds) may necessitate a change in coordinative preferences. Indeed, a number of aberrations that have been reported in hemiparetic gait may be related to optimization strategies. For instance, the prolonged activity of quadriceps and hamstring muscles during stance (Hirschberg and Nathanson, 1952; Peat et al., 1976; Knutson and Richards, 1979; Shiavi et al., 1987; Buurke, 2005; chapter 3, this thesis) is likely to be related to a neuromuscular preference in which muscles of the upper leg assist the calf muscles in the supply of support. In this context it is interesting to note that similar
abnormalities have been observed in persons with neuropathic diabetes (Kwon et al., 2003), spinal cord injury (Leroux et al., 1999), and in toddlers (Okamoto et al. 2003). In case of premature calf muscle activity during stance (Perry, 1978, 1993; Knutson and Richards, 1979; chapter 3, this thesis), a sign that is commonly associated with the presence of disinhibited stretch reflexes, it is unclear whether it is directly related to spasticity or whether it reflects an adaptive strategy that is used to prevent foot collapse when landing in a plantarflexed position (see Perry et al., (2003) for similar observations in habitual toe walkers).

To summarize, the abnormalities that are found in the temporal patterning of muscle activity are most likely to be related either to the disinhibition of reflexes or to secondary adaptive mechanisms rather than to a locomotor timing disorder. An important question is whether these timing abnormalities impede gait performance. Because neuromuscular adaptations are developed to accommodate locomotor task demands under different sets of constraint they are expected to optimize rather than to impede gait performance. However, premature development of such strategies may get in the way of further recovery and the development of new (i.e. more optimal) adaptive preferences. The role of spasticity related timing abnormalities is less clear. Despite clinical emphasis on the reduction of spasticity to promote gait ability, clear empirical support for the assumption that spasticity impedes gait function is still lacking (Ada et al., 1998; Vattanasilp et al., 2000). In fact, it has been suggested that the more simple regulation of muscle tension associated with spasticity can be advantageous for patients because it may help them to maintain support during the stance phase (Dietz, 1999, 2003). In conclusion, there is as yet no convincing empirical evidence showing that muscular timing abnormalities impair gait performance in hemiplegic walkers. Further support for the idea that timing abnormalities are not causally related to gait dysfunctions was presented in chapter 4 of this thesis, which dealt with the patterning of muscle activity during gait recovery in the subacute phase of stroke. Although gait ability increased quite dramatically over time, no systematic changes could be detected in the temporal layout of gait related muscle activity. This finding will be discussed in more detail in the following section.

2. The patterning of muscle activity during gait recovery in the subacute phase
The study described in chapter 4 shows that the gross temporal structure of gait related muscle activity does not change during the subacute phase of stroke despite
substantial improvements in terms of body mobility, ambulatory independence, and maximum gait speed. How can these results be explained? In order to better understand why the gross temporal patterning of muscle activity does not change during recovery, I will first try to make clear why particular interventions are successful in modifying the temporal patterning of gait related muscle activity.

In chapter 1 and in the previous paragraph it was argued that patterns of muscle activity (denoted as ‘neuromuscular preferences’) develop in the interplay between an invariant locomotor task set, and a set of constraints that is imposed upon possible coordinative solutions. One implication of this idea is that alterations in the temporal patterning of activity can be induced by changing the neurological, physiological or biomechanical constraints of walking. Indeed, several studies have shown that changes in the muscular patterning of hemiparetic subjects can be realized e.g. by constraining the range of ankle motion by means of an orthosis (Hesse et al., 1999; Geboers et al., 2002), by surgically altering muscle length (Buurke et al., 2004), or by reducing muscle force output through neurolytic intervention (Hesse et al., 1996). These studies show that rather immediate changes in neuromuscular patterning can be brought about by directly interfering with the biomechanical or physiological properties of the walker.

Studies on the time course of motor recovery generally agree that the major portion of physiological recovery occurs within the first 6 weeks after stroke, although functional improvements have been reported up to 2 years after stroke (Richards and Olney, 1996). During this early period the development of muscle function stabilizes, although this does not exclude that some further improvements can be made during later phases of recovery. Therefore, it can be assumed that the primary (neuro-)physiological and biomechanical determinants of gait are established during the early phase post stroke. Consequently, the temporal patterns of muscle activity are not likely to undergo any major changes beyond this period.

However, because changes in gait function cannot be established without alterations in neuromuscular control, this raises the question what aspects of muscle control are subject to change during recovery. There is evidence to show that alterations in important gait parameters can be realized by a local scaling of the amplitude of activity within a stable temporal organization. Recent studies have pointed out that substantial changes in gait speed (Hof et al., 2002; chapter 2, this thesis) and body loading (Ivanenko et al., 2004) do not alter the basic temporal layout of muscle coordination, showing that a single stereotyped temporal structure may be sufficient for a wide range of parameter settings. In line with this notion, it
can be assumed that recovery related changes in the quality of the gait pattern are not necessarily associated with a reorganization of the gross temporal coordination of muscle activity, and that local tuning of the amplitude of activity perhaps plays a more important role in establishing improved gait function.

One of the conclusions from the study presented in chapter 4 is that the abnormal temporal patterns that are observed in hemiparesis develop early after stroke, probably within the first 6 weeks post stroke. In fact, it can be hypothesized that such temporal reorganizations take place almost immediately after stroke. They may occur already during the first steps that are made post stroke, as an emergent property of the coupled activity of leg muscles that participate in a single, locomotor specific, coordinative structure. A general characteristic of motor learning is that gross approximations of newly learned patterns develop in the early phases of learning, and that the major portion of skill learning is concerned with the further optimization of this pattern and with the reduction of trial to trial variability (Lee et al., 1995; Wenderoth and Bock, 2001). In line with this, we hypothesized that gait recovery is associated with a decrease in the stride to stride variability of muscle activation patterns. The results described in chapter 5 provide support for this idea. The typical pattern of prolonged stance activity of the Biceps femoris that has been reported on several occasions in the literature (Hirschberg and Nathanson, 1952; Peat et al., 1976; Knutson and Richards, 1979; Shiavi et al., 1987; Buurke, 2005; chapter 3, this thesis) showed a significant linear reduction in the stride to stride gain (i.e. amplitude) variability of the pattern over the course of recovery, despite the fact that the global temporal characteristics remained unaltered. These results suggest that gait recovery in hemiparetic stroke is associated with the more consistent production of newly formed neuromuscular patterns, and not with the construction of these patterns per se.

It is useful to point out a few potential limitations of the studies on gait recovery presented in this thesis. The results that have been described in chapters 4 and 5 do not exclude that changes in lower extremity muscle activity did in fact take place during gait recovery. There is evidence that recovery is associated with increases in the force output of muscles (Buurke, 2005) suggesting that increases in the amplitude of muscle activity may have occurred over the course time. Obviously, due to the analytical strategy used (dichotomization of the signal to quantify temporal characteristics) such changes would have been missed. However, multi-session comparisons of EMG amplitude is difficult due to possible variations in electrode placement, properties of the skin tissue, and environmental conditions.
Another limitation concerns the continuous nature of neuromuscular coordination and the methods used to describe the temporal coordination of muscle activity. As in the majority of studies on the patterning of muscle activity, local variations in the variance of the electromyographic signal are estimated by means of step functions: muscles are supposed to be either 'on' or 'off'. Clearly, such a dichotomization of the signal is a gross abstraction in which potentially valuable information on the continuous nature of muscle activity is lost. Intermuscular coordination does not involve timekeeping of discrete neuromuscular events, but is a continuous process in which the force levels generated by individual muscles are weighed continuously to produce the adequate joint moments necessary to accommodate time varying task demands. Future development of analytical techniques that are able to capture the continuous nature of multichannel electromyographic signals may lead to a more precise view of the muscle coordination that underlies gait. New approaches may also include the use of inverse dynamics to better understand the nature of gait impairments and the role of adaptive processes in the formation of neuromuscular patterns in hemiplegic gait.

3. Clinical implications
A clinically important question is whether treatment aimed at the re-acquisition of gait ability should attempt to modify the temporal structure of gait related muscle activity. Evidently, ‘treatment’ of the temporal coordination of muscle activity will only be fruitful if temporal abnormalities are causally related to gait impairments. As was pointed out in the first paragraph of this chapter, there is as yet no evidence to support the idea that temporal abnormalities in muscle activity patterns are an important cause of gait problems, indicating that changing the gross temporal coordination of muscle activity should not be an important goal in rehabilitation. Instead, therapeutic efforts should be focused on changing the (physiological or biomechanical) constraints of gait coordination which, in turn, may (or may not) result in a changed temporal structure of gait related muscle activity.

As was stated in chapter 1 of this thesis, the majority of clinical interventions in gait rehabilitation is aimed at changing the control processes that underlie gait coordination. The formation of coordinative patterns is constrained by biomechanical, physiological, and neurological factors, and changing these constraints provides clinical opportunities to alter coordinative control. Biomechanical interventions (e.g. the prescription of orthoses, the use of walking aids), surgical interventions (e.g. split anterior tibial tendon transfer, hamstring
lengthening), neurochemical interventions (e.g. botulinum toxin, phenol) are examples of effectively altering constraints which may result in changed gait control and better gait performance. An important role for physiotherapy is to effectively incorporate these altered constraints into new coordinative patterns by means of intensive and supervised gait training.

The results reported in chapter 5 provided evidence for the idea that recovery during the subacute phase of stroke is associated with the automatization of newly developed patterns of muscle activity. Because the speed of automatization of patterns is a function of repetition frequency, training intensity may be an important factor in the development of more automatic production of neuromuscular patterns. In addition, because optimization and automatization of motor patterns can only occur when pattern specific efferent and afferent information is available, more consistent production of locomotor patterns can be promoted through task specific training. These ideas are in line with clinical studies that show that outcome is positively correlated with training intensity and that task specific training results in better outcome than non task specific training (see van Peppen et al. (2004) for a review).

References
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