Summary

Functional muscle characteristics after stroke and unloading

The general objective of this thesis was to investigate muscle adaptations occurring in patients after a cerebral vascular accident (stroke). The specific aims of this thesis were to assess how the maximal muscle strength and speed, and fatigue properties of the knee extensor muscles of both legs had changed in patients with subacute stroke and to investigate whether strength is more impaired at shorter muscle lengths (chapter 2-4). Furthermore, we correlated activation capacity, contractile speed and muscle strength with functional performance in subacute patients and investigated how these variables developed during the first year after stroke (chapter 5).

In patients with stroke not only the direct effects of the disorder can affect the working muscles, but also the indirect effect of lower activity levels. To be able to differentiate between these effects, we performed two unloading studies (unilateral lower limb suspension (chapter 6) and bed rest (chapter 7)) in healthy people to investigate which adaptations could be (partly) attributed to the lower physical activity, which goes together with a stroke mainly as a consequence of hemi paresis, and to investigate whether this could be prevented or attenuated by training.

Chapter 2 shows significant adaptations in both central neural activation and more intrinsic muscle properties in individuals 3.5 months after stroke. Weakness was observed in both paretic and non- paretic knee-extensors and –flexors. In the non-paretic lower limb the strength was 56% of control. This seemed primarily due to impaired voluntary activation, whereas in the paretic lower limb (28% of control) both impaired voluntary activation as well as reduced intrinsic torque capacity seemed responsible for the reduced strength.

The high correlations found between strength and voluntary activation, and functional performance, indicate that these variables mainly determine performance.
The results clearly indicate that both muscle strength and voluntary activation are important variables, which can potentially be fruitful subjects for rehabilitation programs following stroke. In addition to a severe reduction in maximal isometric strength, the knee extensors of patients with subacute stroke also demonstrated severe impairment in the rate of torque development (chapter 3). Interestingly, whereas in the paretic lower limb both changes in the intrinsic muscle (fiber) characteristics and impaired neural activation seem responsible, in the non-paretic lower limb reduced rate of torque development seems primarily related to neural activation changes, precisely as was found for MVC in chapter 2. In addition, both paretic and non-paretic muscles relaxed more slowly than control as indicated by significantly higher half relaxation times. The paretic lower limb fatigued more and faster than control and both the paretic and non-paretic lower limbs recovered slower from fatigue. Thus, these changes suggest adaptations in muscle properties of both lower limbs towards slower, less fatigue resistant muscles, which develop shortly after stroke.

The most important finding in the fourth chapter was the selectively impaired muscle function at lower muscle lengths of both knee extensors and flexors of the paretic lower limb, but not the non-paretic lower limb of individuals after stroke. For the knee extensors, this can be attributed to a length-dependent lower voluntary activation capacity, which may also be the case for the flexor muscles. Co-activation did not seem to play a significant role in the length-dependency of muscle weakness after stroke.

Improvements in functional performance up to 9 months after stroke were shown in chapter 5. There was a substantial variation between subjects with respect to the muscle variables at the start of the study as well with respect to the changes in these variables over time. Most importantly, changes in muscle variables correlated significantly with improvements in functional performance of patients with stroke.
Plantar flexor (calf) and quadriceps (thigh) maximal voluntary contraction torque decreased after 3 weeks of unilateral lower limb suspension, as did electrically evoked (triplet) torque of the thigh, whereas activation did not (chapter 6). Absolute maximal rate of torque development during voluntary and electrically evoked contractions decreased. However, maximal rate of torque development normalized for maximal torque did not change after unloading, indicating that the reduction in maximal rate of torque development could be fully accounted for by the reduction in maximal torque. Following unilateral lower limb suspension, 2-leg jump height and 1-leg jump height with the suspended leg decreased significantly, whereas 1-leg jump height with the non-suspended leg did not. The torque decreases were significantly related to the decreases in the more complex jump task, although, similar to the literature, torque in itself (without intervention) was not related to jump performance.

The primary findings of chapter 7 showed unchanged maximal rate of torque development for calf and thigh, but increased initial torque development (impulse) for the calf in the inactive control group after 60 days of bed rest. During the performance of explosive isometric contractions, suppression of agonist activity was only seen in the calf for the controls, but also in the thigh in the trained individuals. Regardless of whether resistance training during the bed rest was augmented by vibration exposure, loss in muscle size and strength was fully prevented for the thigh, yet only mitigated for the calf after 60 days of bed rest.

**Conclusions and implications**

The most important implications of the studies described in this thesis are that patients with stroke show decreased maximal torque in both lower limbs. We showed impaired intrinsic muscle strength, neural activation and fatigue resistance in the paretic lower limb and impaired neural activation and fatigue resistance in the non-paretic lower limb. These adaptations are partly related to the effects of reduced physical activity. After limb suspension and bed rest we also found a decrease in maximal torque, but no changes in activation capacity. The reduction in voluntary maximal rate of torque development after unloading could be fully accounted for by
the reduction in maximal torque, whereas decreased maximal rate of torque development in patients with stroke seemed to be a result of a lower activity level. Additionally, in the paretic lower limb also reduced intrinsic speed characteristics or tendon properties could contribute to a lower maximal rate of torque development. The changes in muscle characteristics may be counteracted if these aspects are included in a training/rehabilitation program. For improvement of neural activation it can be advised to combine resistance training with task-specific functional training and/or e.g. mirror training or transcranial magnetic stimulation (facilitating brain plasticity), since activation deficit is the most important underlying factor in muscle weakness after stroke. This may lead to decreased fall risk and improved performance of daily life activities. Improved strength will also result in decreased relative load during weight bearing activities such as walking and climbing and descending stairs, resulting in less fatigability. The clinical applications of this thesis can be likely extended to other neurological conditions that induce a decreased activity level and abnormal neural innervation such as closed head injury, spinal cord injury and multiple sclerosis.