SUMMARY

Peripheral nerve injury is a frequently occurring complication of trauma due to traffic accidents, sports accidents or otherwise. Particularly if such injuries involve a disruption of the nerve, surgical intervention is needed in order to restore the continuity. In cases of a larger gap the transplantation of an autologous nerve graft, or the implantation of an artificial nerve guide is required. Despite advanced surgical techniques, however, functional outcome generally is poor. Literature on plexus lesions in babies, or nerve lesions in children suggests an improved recovery. Others, however, do not share this optimism.

My thesis consists of a number of articles and essays on experimental studies in rats into problems on the recovery after nerve transections. In one hindleg, we transected the sciatic nerve, proximally to the bifurcation into the tibial and common peroneus nerves, and the defect was repaired by means of an autologous nerve transplant. The first problem of my thesis was,

What are the effects of a transection of the sciatic nerve in adult rats on the morphology of three major hindleg muscles, as well as the time courses of denervation and reinnervation.

In the second part we transected this same nerve, but in rats at the 10th day after birth and in this part, the question was ,

Do the effects of a transection of the sciatic nerve at the 10th postnatal day on motor performance and on muscle morphology indicate a better recovery compared to those in adult rats.

In chapter 2 we studied the effects after a transection of the sciatic nerve in adult rats on morphological aspects of the gastrocnemius and soleus muscles (both hindleg extensors) and the anterior tibial muscle (a hindlimb flexor). Reinnervation has started before 7 weeks after the transection, and this induced changes in the fibre type composition of the muscles. The tibial and gastrocnemius muscles initially contained increased percentages of type I muscle fibers, but this had decreased again at 21 weeks. The soleus muscle, which normally contains 80 – 85% type I muscle fibers, however, now had around 80% of type II muscle fibers. We discussed that these shifts in muscle fibre distributions may be explained by an at-random reinnervation of these muscles.

In chapter 3 we studied the consequences of axotomy on the motor endplates. In cases in which we prevented reinnervation, all motor endplates had disappeared by 7 weeks. In other rats, however, where reinnervation was allowed, we detected new motor endplates already at 7 weeks. Remarkably at this age, 20% of the endplates in the gastrocnemius and tibial muscles were polineurally innervated and this even was the case in 40% of the endplates in the soleus muscle. At 21 weeks, the percentages in all three muscle had decreased to around 10%.
In chapter 4 we described the long term effects of a sciatic nerve transection on the muscle fiber composition and on innervation patterns. Even after one year, the soleus muscle contained 80% of type II muscle fibers, a similar percentage as that found at 21 weeks after the operation. Remarkably we observed an increased percentage of polyneurally innervated motor endplates. It the leg in which the sciatic nerve was transected, around 20% of the motor endplates were polyneurally innervated, but we also found at the control side 10% of polyneurally innervated endplates, both probably because of an aging process.

In the second part we studied whether sciatic nerve transections at the 10th day after birth has less serious effects on motor performance and also, less drastic effects on muscle fiber composition.

As peripheral nerve transection at neonatal age in rats induces massive motoneuronal cell death, we studied in chapter 5 at which young age still an appreciable number of motoneurones survived axotomy. Investigations in a time series indicated that transections at the 10th postnatal day left 50 – 60% of the motoneurones alive, and that age was chosen in further experimentation.

In chapter 6 we studied motor performance after a transection at the 10th postnatal day. Initially performance was only moderately disturbed but from around 20 days after the operation, walking became seriously impaired, by dragging of the affected hindleg, marked exorotation of the hind foot. We suppose that from this age aberrant reinnervation started to establish.

In chapter 7 EMG recordings were made during walking and the patterns from the gastrocnemius and tibial muscle, showed coactivation of both muscles at all stages of walking, and this is indicative for an at-random reinnervation of the muscles. These results were supported by a study in which we retrogradely traced the motoneurones, innervating these muscles. Often, labeled motoneurones were found far outside the normal territories of the respective muscles. Obviously, also after a transection at early age, the outgrowing axons were unable to relocate their own muscle and in stead major portions of them connected to the wrong muscles. This in turn, induced abnormal activation patterns of the muscles.

In chapter 8 we studied the morphology of the soleus muscle after a transection at the 10th day. Similar to findings after transection at adult age, we observed that the soleus muscle had shifted into a muscle with mainly type II muscle fibers.

In chapter 9 we discussed the results of my thesis. After a transection of the sciatic nerve at a proximal level, beit at adult age, or at the 10th postnatal day, the outgrowing axons are unable to relocate their own muscle or muscle fibers. In stead they randomly reinnervate the muscles which were denervated by the transection. This in turn leads to all affected muscle having a similar fibre type composition.

We put forward a few suggestions for further research. We advocate that in
future research the factors are identified which at embryonic stages effect the outgrowth of the axons to flexor muscle and extensor muscles. Such research probably should be performed in tissue cultures. Hopefully, such factors might be identified and these should then be tested in *in-vivo* experiments after transection and subsequent outgrowth of the axons to flexors and extensors.