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The effect of physical exercise on functional recovery following a peripheral nerve lesion in the rat

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Preliminary results of the effects of physical exercise on recovery of function of peripheral nerves following a crush lesion are reported. The right sciatic nerves of 30 Wistar rats were crushed. They were then randomised over three groups: one group was kept in standard cages (control), one group was kept in an enriched environment (enriched cage) and one group was trained 5 × 7 min per day in a drink-trainer (drink-training). Evaluations of walking pattern (functional motor behaviour) and reactions to a mild electric stimulus to the sole of the foot (sensory function) were used to quantify the recovery of function. Both the 'enriched environment' and 'trained' groups of rats showed enhanced recovery as compared to the control group. The results of this experiment suggest a neurotrophic effect of physical exercise on peripheral nerves after a crush lesion.

INTRODUCTION

Walking up a flight of stairs, opening doors, waving to someone or drinking a cup of tea are all activities that make demands on our musculoskeletal system. Every moment of the day we make movements which set off an exchange of information between the central nervous system and the peripheral receptors and effectors. The transport of this information to and from the target organs takes place in part along a so-called 'hard-wired' system: the peripheral nerves. An intact peripheral nervous system is of vital importance for optimal functional use of the musculoskeletal system.

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Trauma, compression, neurovegetative disorders, intoxications and some chronic illnesses such as diabetes mellitus can cause damage to a peripheral nerve (Van der Linden, 1982; De Witte and Van der Werken, 1983; Van Gelder et al, 1985; Kooiker-Swart, 1989; Van der Zee, Gerritsen van der Hoop and Gispen, 1989; Gispen, 1990). Such damage commonly leads to a disruption in the transfer of sensory and motor information and will often result in functional disorders of the musculoskeletal system.

The damaged nerve recovers in certain cases (often depending on the kind of lesion), with recovery being influenced by many intrinsic and extrinsic factors. The recovery process implies the reconstruction of morphological and functional properties of the damaged axons and the recovery of motor function and sensitivity (Vitadello et al, 1986). Insight into the recovery process and the factors influencing this process make therapeutic intervention possible (for extensive coverage of the peripheral nerve, see Lundborg, 1988a).

It has been shown that some therapies, especially drug therapy using compounds such as ORG 2766 (a derivative of ACTH), nimodipine (a calcium entry blocker), ACTH4-10 and alpha-MSH (neuropeptides), gangliosides (a group of complex lipids found mainly in the neural cells and cell structures) and nerve growth factor (a trophic protein molecule) have neurotrophic properties that facilitate recovery of the peripheral nerve, or restrict the sensorimotor effects of a neuropathy (Vitadello et al, 1986; Kuiters, Brakkee, Van der Zee and Gerritsen van der Hoop, 1988; Taniuchi, Brent Clark, Schweitzer and Johnson, 1988; Van der Zee et al, 1989; Gispen, 1990; Gispen, Sporel-Özakat, Duckers and Edwards, 1990).

Seen from the concept of stress-exercise capacity (Bernards, 1988), training, if correctly geared to exercise capacity, could favourably influence the recovery of tissue injuries (such as a crush lesion of the peripheral nerve). Herbison investigated the effect of exercise training on the morphology of denervated muscles immediately before and after reinnervation. He found that exercise training had a favourable effect, especially when started immediately following reinnervation and that overworking the injury endangered the recovery process (Herbison, Jaweed, Ditunno and Scott, 1973; Herbison, Jaweed and Ditunno, 1974, 1980a, 1980b, 1981).

Only one article could be found in the literature on the effect of training activity (intensive swimming) on axonal outgrowth following peripheral nerve damage in rats. This research showed increased axonal outgrowth after 3 days of training with reference to the damage. Follow-up of recovery did not exceed 3 days. In cases where exercise continued for 35 days following crush, a decrease in the mean diameter of the myelinated axons was found. Functional sensorimotor recovery of the experimental group was in agreement with that of the control group, which could indicate a corresponding linear growth of the axons (Gutmann and Jakoubek, 1963).

Herbison and co-workers, as well as Gutmann and Jakoubek, concluded that exercise has an unfavourable influence on nerve recovery after damage. In the research cited, the effect of intensive exercise training was measured. However, this research was not directed towards finding an experimental form of training to produce a positive effect. We presume that a different, less strenuous training programme can facilitate recovery following a crush lesion to the nerve. The present article presents the initial results of our findings on the effect of physical exercise on the recovery of a peripheral nerve lesion in the rat.

MATERIALS AND METHODS

A total of 30 male Wistar rats (weight 140–160 g, age 6–7 weeks) were randomised into three groups: an enriched cage group, a drink-training group and a control group. Following a standardised procedure described by Brakkee, De Koning and Gispen (1987), the right n. ischiadicus was crushed under anaesthesia (Hypnorm®: Duphar, Weesp, Netherlands; dosage: 1.0 ml/kg body weight, administered i.m.). Immediately following operation, the rats were returned to their respective cages for recovery. Ethical approval for the research was granted by the Commission for Animal Experiments, University of Utrecht.

Enriched cage group

The rats were housed in a cage measuring 120 × 40 × 70 cm (Fig. 1). Food (commercial pellets; Hope Farms Ltd, Woerden, Netherlands) and water were accessible by following an ob-

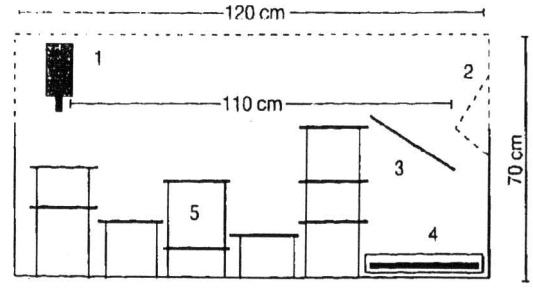

Fig. 1 Diagram of the enriched cage showing: (1) adjustable water tank; (2) food; (3) 35° sloping run; (4) plexiglass container with sawdust; (5) the obstacle course for reaching food and water.

stacle course set at different heights. Food was accessible when standing on a 35° sloping run. The water tank was fixed in such a way that the rats had to stand on their hindlegs to drink. In order to both eat and drink, the rats had to walk and climb back and forth over the obstacle course. The cage offered ample space for play.

Drink-training group

The drink-training was housed in Makrolon cages (Type III, RUCO, Netherlands) on sawdust in groups of 2×3 and 1×4 rats per cage. Access to food was *ad libitum*. Access to water was controlled and the Makrolon cages were kept water-free throughout the experiment. The rats were kept thirsty to motivate them for drink-training. They were placed in an enclosure with water for 7 min five times per day (9:00, 10:30, 12:00, 13:30 and 15:00 h). In this enclosure, the thirsty rats had access to water by standing on their hindlegs (Fig. 2). The height of the water tank with its drinking spout was adjustable and was elevated gradually during the experiment.

To maintain a basic acceptable weight level in this group (a maximum of 10% weight loss with respect to the control group), the rats were provided with water in their Makrolon cages for 10 min at the end of each day.

Control group

The control group ($n = 10$) was housed in Makrolon cages (corresponding to the drink-training group) on sawdust. Access to food and water was *ad libitum*.

To ensure consistency between the three groups, the control group and the enriched cage group were also placed in the drink-training enclosure 5×7 min per day. The height of the water tank was consistent for all three groups.

Ten rats were housed together in the enriched cage, which induced social behaviour. Food and drink were only available by following the obstacle course. The rats in the drink-training group were forced to make an effort five times per day from day 1 following crush to satisfy their thirst. To drink they had to stand on both hindlegs, at optimal stretch with, seemingly, extensive muscular activity (Fig. 2). In the control group, however, drinking and eating required only slight effort, as food and drink were placed in such a way that the rat only had to move its head.

Fig. 2 In the drink-trainer, the rat is offered water from above. The animal must stand on its hindlegs to reach the water tank.

Measurement methods

Motor function was measured and quantified on the basis of the unconstrained walking pattern of the rat. The hindfeet of the rats were dipped in photographic developer after which the rats were made to walk along a 50 cm long, slightly inclined (10°) walkway. The walkway floor was covered with photographic paper and recorded the hind (foot)prints almost immediately in black. A number of parameters can be calculated from this print pattern. The parameter used for this test was the Sciatic Functional Index (SFI)

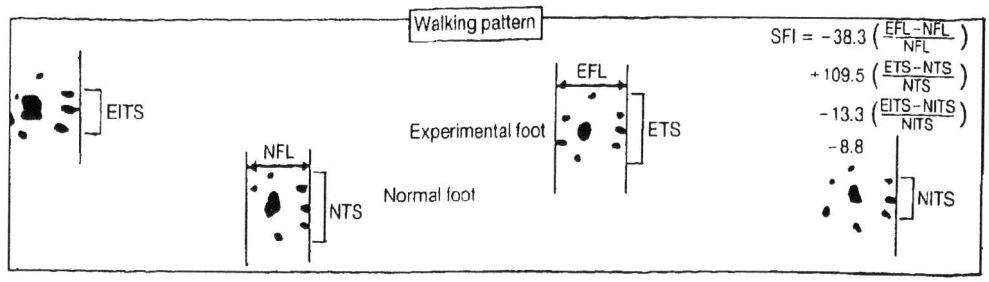

Fig. 3 Walking pattern using Bain's SFI. EFL, experimental foot length; NFL, normal foot length; ETS, experimental toe spread; NTS, normal toe spread; EITS, experimental intermediate toe spread; NITS, normal intermediate toe spread.

described by Bain, Mackinnon and Hunter (1989), a functional index of the n. ischiadicus whereby measurements such as toe-spread, step-length and intermediate toe-spread are calculated (Fig. 3).

Quantification of the recovery of sensory function was assessed by using the 'footshock' method. The sole of the foot is stimulated by an electric current, varying in strength from 0.1–0.6 mA, applied locally to the skin of the sole innervated by the n. ischiadicus (point 3; Fig. 4). In the intact nerve, a retractive reflex action occurs; after crush lesion, this reflex action is absent. Return of the reflex action marks re-innervation of the relevant point 3 on the skin, which with the lesions used here occurred at the earliest 16–17 days post-operation. Measurements are taken daily from day 15 and current strength necessary for reflex action is recorded. Current strength is then expressed in terms of recovery percentage (0.6 mA: 17%, 0.5 mA: 33%, etc., through 0.1 mA: 100%) (Brakkee et al, 1987).

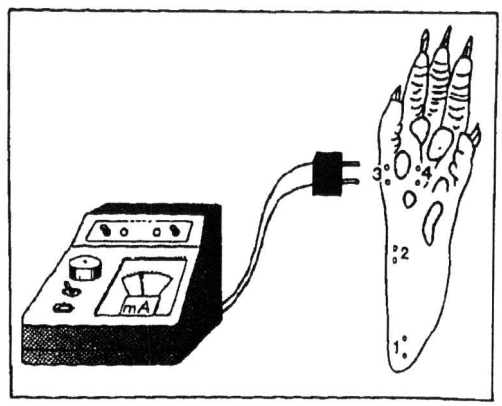

Fig. 4 Footshock: an electrical stimulus to point 3 of the sole of the rat.

Statistics

The data were analysed using repeated measures analysis of variance (ANOVAR).

RESULTS

Motor recovery

A crush lesion impedes use of the injured hindfoot. This is expressed by a sharp change in the walking pattern, which was quantified here with the aid of Bain's SFI. The SFI of rats with completely damaged n. ischiadicus axons after crush lesion shows a value of from -100 to -140; a SFI of 0 indicates an intact nerve function (Bain et al, 1989). Calculations using the day 4 walking pattern show that the crush was successful; there is almost no measurable print of the damaged hindfoot (SFI < -100).

The walking pattern of each rat was recorded every 2 days from day 10 following crush lesion and the SFI calculated. The mean ($\pm$SEM) results for each group are given in Table 1 and Fig. 5. Figure 5 shows the spontaneous, normal course of recovery by the control group ($n = 10$). The SFI of the enriched cage group ($n = 9$; one animal was excluded due to autotomy) and that of the drink-training group ($n = 9$; one animal was excluded due to autotomy) show accelerated recovery with respect to the control group ($F = 6.5$, $P < 0.006$). If we compare the treated groups individually with the control group, it

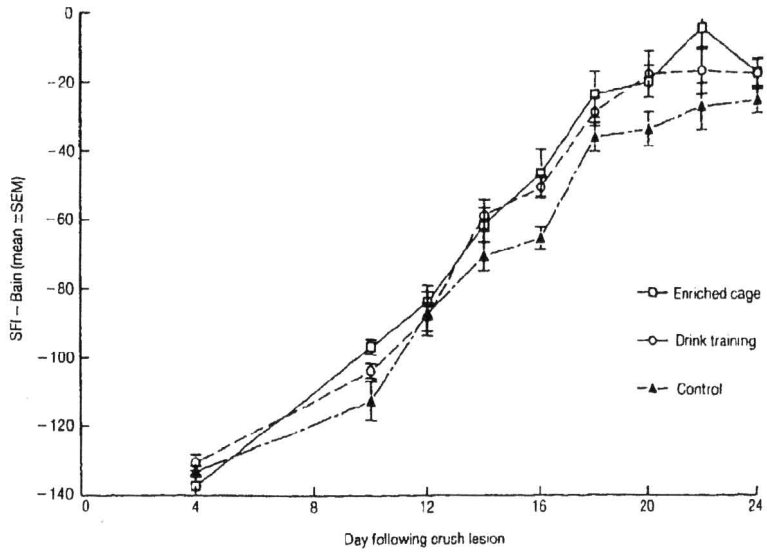

Fig. 5 The recovery of motor function following crush lesion of the n. ischiadicus, based on the analysis of the walking pattern using Bain's SFI.

Table 1
Mean (±SEM) calculations of the walking patterns based on Bain's SFI

Day following crush lesion	Group		
	Control (n=10)	Enriched cage (n=9)	Drink-training (n=9)
4	−132.9±1.53	−135.9±3.31	−130.9±2.35
10	−112.3±5.58	−96.1±2.14	−102.6±2.22
12	−86.8±6.43	−85.1±4.93	−88.3±4.10
14	−70.0±4.22	−63.4±5.06	−58.7±4.68
16	−64.6±3.21	−47.2±6.79	−49.1±3.36
18	−34.9±4.24	−20.1±6.77	−27.6±4.27
20	−32.4±4.96	−17.8±4.71	−16.2±6.84
22	−25.5±6.94	−6.5±6.22	−19.1±6.88
24	−23.7±3.70	−16.0±3.94	−18.6±4.54

appears that both the enriched cage group (F= 14.57, P<0.002) and the drink-training group (F= 6.64, P<0.02) show normal values in their walking patterns sooner. Motor recovery of the enriched cage group and the drink-training group was similar (F= 0.16, P<0.699).

Sensory recovery

Sensory measurement, taken by noci(sensory) electrical stimulation on day 4, showed a complete absence of sensitivity to stimulation of the denervated hindfoot in all animals. From day 15 the animals were tested daily by means of foot-shock. The lowest current strength needed for reflex action was used to determine the recovery percentage. The results are given in Table 2 and Fig. 6. Spontaneous recovery in the control group took 23–24 days. It can be seen from Fig. 6 that the drink-training and enriched cage groups recovered more quickly and gained 100% recovery sooner (F= 5.12, P<0.014) than the controls.

DISCUSSION

In this experiment (using two separate para-

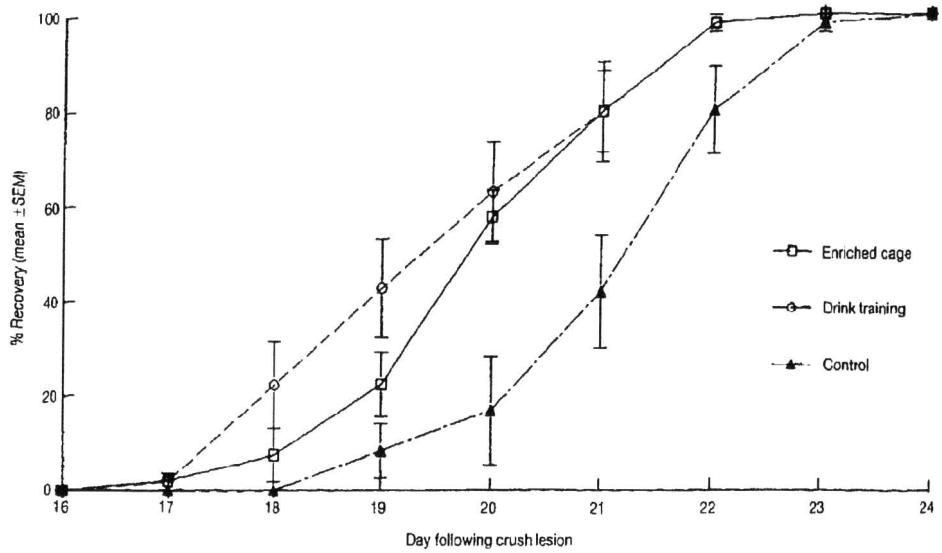

Fig. 6 Recovery of sensory function following crush lesion of the n. ischiadicus measured by local electrical stimulation of the foot sole (footshock).

Table 2
Mean (±SEM) percent recovery of sensitivity measured using footshock

Day following crush lesion	Group		
	Control (n=10)	Enriched cage (n=9)	Drink-training (n=9)
16	0±0	0±0	0±0
17	0±0	2.0±0.1	1.8±1.8
18	0±0	7.4±5.6	22.2±9.2
19	8.3±5.7	22.3±6.8	42.6±10.4
20	16.7±11.4	57.4±5.7	62.7±10.5
21	41.7±11.8	79.7±8.6	79.6±10.6
22	79.8±9.2	98.1±1.8	98.1±1.8
23	98.1±1.8	100.0±0	100.0±0
24	100.0±0	100.0±0	100.0±0

meters), it was shown that two different kinds of treatment, namely heightened functional activity (the enriched cage group) and training (the drink-training group), facilitated recovery of the walking pattern and (noci)sensory sensation following crush lesion of the n. ischiadicus in the rat. The accelerated recovery suggests that these two kinds of physical exercise have a neurotrophic effect. It may be concluded that both motor function and (noci)sensory function of the rats in the enriched cage group and those in the drink-training group recovered significantly earlier than did the control rats who received less training stimulation. It seems justifiable to conclude that the heightened activity of the enriched cage and training groups as against the control group is responsible for the recovery of function after a crush lesion.

The SFI of the trained rats suggests that their motor axons make functional contact with the effector muscles sooner than do the motor axons in the untrained group. An alternative explanation, namely that training improved the condition of the undenervated muscles, causing a significant difference in the walking test, is unlikely. Bain's SFI only indexes the recovery of the denervated muscle function of the hindfoot in relation to that of the contralateral hindfoot. In calculations using the SFI described by De Medinacelli, Freed and Watt (1982), step-length

was also taken. Step-length is, however, not only determined by the deinnervated n. ischiadicus musculatue. It is, of course, not only the two hindfeet that are exercised in the enriched cage and drink-training groups. The effect of exercise on muscles other than the denervated muscles could also be seen in De Medinacelli and co-workers' SFI. The decision to use Bain's method of analysis was partially based on the fact that injury to a peripheral nerve has a trans-spinal effect on the heterolateral, intact nerve (Souyri and Bourre, 1989); functional changes in the non-operated side are, thus, incorporated.

The studies by Herbison and colleagues mentioned in the Introduction showed that overwork during the early recovery phase has a negative influence and that this can be quantified using muscle weight, types of muscle fibre and protein concentrations in the muscles. The training had *no* influence on reinnervation, making it difficult to understand *how* this is quantified (Herbison et al, 1980a). Our experiment differs somewhat from the experimental design used by Herbison. Hebison and co-workers performed a double-sided crush lesion in female Wistar rats, used swimming or walking on a sloping walkway for exercise stimulation and started training only in the second, third or sixth post-operative week (Herbison et al, 1973, 1974). It is possible that the reinnervation effect was 'missed' because of the late commencement of exercise training. Gutmann and Jakoubek (1963) found that with 3 days of training (swimming) following crush, the length of the outgrown axons was significantly greater as compared to untrained rats, and concluded that the latent period (from the time of damage to the start of axonal outgrowth) was shortened by training. The training of the enriched cage and the drink-training groups commenced the day following the crush operation and possibly shortened the latent period. Repeat experiments, with training starting only several days after crush, should indicate the 'critical period' for stimulation by training. Interestingly enough, with alpha-MSH the critical sensitive period showing neurotrophic effect was during the first 8 days following crush (Edwards et al, 1984).

The neurotrophic effect can be explained as follows. Lesioned n. ischiadicus motor neurons generate action potentials during physical activity that are measurable at the point of injury and cause an increase in endoneural blood flow (Davis et al, 1978; Gordon, Hoffer, Jhamandas and Stein, 1980; Gordon and Davis, 1986; Sugimoto, Monafo and Shimazaki, 1987; Zochodne and Ho, 1991). Axonal transport and impulse traffic in the axons are also dependent on local uninterrupted metabolic supply; a rich intraneural microvascular supply ensures the optimal nutritional status of the nerve under varying conditions (Davis et al, 1978; Heumann et al, 1987; McMahon and Gibson, 1987; Lundborg, 1988a, 1988b). Axonal transport of structural components makes outgrowth of axons possible (Grafstein and Forman, 1980). Taken together, this suggests that the physical activity performed by the drink-training and enriched cage rats possibly resulted in improved neurotrophy, thereby stimulating recovery of the nerve.

Denervated mouse and rat muscles exhibit spontaneous, irregular contractions and fibrillation potentials that are measurable electrophysiologically. Catecholamines, epinephrine and norepinephrine see to the regular and increased frequency of these spontaneous contractions and effect an increase in muscle tension (Evans and Smith, 1973; Smith and Thesleff, 1976; Thesleff and Ward, 1978). In cats and mice, the number of sympathetic efferents in denervated muscles increases and it is presumed that this phenomenon forms an intrinsic protective mechanism for the maintenance of musculature morphology (Nomoto, Yoshihara, Kanda and Kaneko, 1991). That is, orthosympathetic post-ganglionic norepinephrinergic efferent activity and epinephrine production by the adrenal gland, both of which increase temporarily during exercise (Guyton, 1991), seem to restrict muscular atrophy following denervation. Two recent articles concerning electrostimulation of denervated muscles also cover the prevention of muscular atrophy. Both articles point to the lack of satisfactory results and a scientific basis for the effects of physiotherapeutically adapted electrostimulation to denervated muscles (Bélanger, 1990; Van Sambeek, 1990). Training/physical exercise is a possible solution to muscular denervation atrophy.

However, the results of the experiment pre-

sented here require further investigation and reproduction before conclusions and/or generalisations can be made. Research in this direction including humans would be beneficial for the rationale of physiotherapy. Physiotherapeutic applications, in particular physical exercise, are primarily directed towards functional recovery *after* contact between the nervous system and target organ has been made, that is, when the transfer of efferent and afferent somatic information has been effected. By this we mean the training of force, coordination and endurance. Research that is taking place at present will contribute to the scientific basis of possible neurotrophic effects of physiotherapy in peripheral neuropathy. Ongoing research is directed towards the optimalization of the parameters (type, duration, frequency and intensity and the abovementioned 'critical period') of training stimulation. Furthermore, training stimulation that could lead to the recovery of nerve conduction velocity following crush lesion is being studied. Next, pharmacotherapy and training will be combined for the realization of complementary effects if present. Research into the working mechanisms of the effects of training and the influence of stressors on nerve recovery are possible targets of future study.

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References

Bain JR, Mackinnon SE, Hunter RT 1989 Functional evaluation of complete sciatic, peroneal, and posterior tibial nerve lesions in the rat. Plastic and Reconstructive Surgery 83: 129–136

Bélanger AY 1990 Neuromusculaire elektrostimulatie in de fysiotherapie. Een kritische blik op controversiële vragen. Nederlands Tijdschrift voor Fysiotherapie 100: 189–192

Bernards ATM 1988 Relaties tussen belasting en belastbaarheid. Issue 5: 1–5

Brakkee JH, De Koning P, Gispen WH 1987 Methode voor het maken van een reproduceerbare afklemleasie in de nervus ischiadicus en nervus tibialis van de rat en voor een snelle en nauwkeurige meting van het herstel van de sensibele functie. Biotechniek 26: 5–7

Davis LA, Gordon T, Hoffer JA, Jhamandas J, Stein RB 1978 Compound action potentials recorded from mammalian peripheral nerves following ligation or resuturing. Journal of Physiology 285: 543–559

De Medinaceli L, Freed WJ, Watt RJ 1982 An index of the functional condition of the sciatic nerve based on measurements made from walking tracks. Experimental Neurology 77: 634–643

De Witte J, Van der Werken C 1983 Gecompliceerde fracturen van het onderbeen met ernstig wekedelen letsel. Fysiotherapeutoische aspecten Deel II. Nederlands Tijdschrift voor Fysiotherapie 93: 248–251

Edwards PM, Van der Zee CEEM, Verhaagen J, Schotman P, Jennekens FGI, Gispen WH 1984 Evidence that the neurotrophic actions of α-MSH may derive from its ability to mimic the actions of a peptide formed in degenerating nerve stumps. Journal of Neurological Science 64: 334–340

Evans RH, Smith JW 1973 Mode of action of catecholamines on skeletal muscle. Journal of Physiology 232: 81pp

Gispen WH 1990 Therapeutic potential for melanocortins in peripheral nerve disease. Trends in Pharmacological Science 11: 221–222

Gispen WH, Sporel-Özakat RE, Duckers E, Edwards PM 1990 The Ca^{2+} antagonist nimodipine and recovery of function following peripheral nerve damage in the rat. Neuroscience Research Communications 8: 175–184

Gordon T, Davis LA 1986 Electrical activity in injured peripheral nerves. In: Nix WA, Vrbová G (eds) Electrical stimulation and neuromuscular disorders, pp 64–74. Springer-Verlag, Berlin

Gordon T, Hoffer JA, Jhamandas J, Stein RB 1980 Long-term effects of axotomy on neural activity during cat locomotion. Journal of Physiology 303: 243–263

Grafstein B, Forman DS 1980 Intracellular transport in neurons. Physiology Reviews 4: 1167–1283

Gutmann E, Jakoubek B 1963 Effect of increased motor activity on regeneration of the peripheral nerve in young rats. Physiologia Bohemoslovenica 12: 463–468

Guyton AC 1991 Textbook of medical physiology, 8th edn. WB Saunders, London

Herbison GJ, Jaweed MM, Ditunno JF, Scott CM 1973 Effect of overwork during reinnervation of rat muscle. Experimental Neurology 41: 1–14

Herbison GJ, Jaweed MM, Ditunno JF 1974 Effect of swimming on reinnervation of rat skeletal muscle. Journal of Neurology, Neurosurgery and Psychiatry 37: 1247–1251

Herbison GJ, Jaweed MM, Ditunno JF 1980a Effect of activity and inactivity on reinnervating rat skeletal muscle contractility. Experimental Neurology 70: 498–506

Herbison GJ, Jaweed MM, Ditunno JF 1980b Histochemical fiber type alterations secondary to exercise training of reinnervating adult rat muscle. Archives of Physical Medicine and Rehabilitation 61: 355–357

Herbison GJ, Jaweed MM, Ditunno JF 1981 Contractile properties of reinnervating skeletal muscle in the rat. Archives of Physical Medicine and Rehabilitation 62: 35–39

Heumann R, Lindholm D, Brandtlow C, Meyer M, Radeke MJ, Misko TP, Shooter E, Thoenen S 1987 Differential regulation of mRNA encoding nerve growth factor and its receptor in the rat sciatic nerve during

development, degeneration, and regeneration: Role of macrophages. Proceedings of the National Academy of Science USA 84: 8735–8739

Kooiker-Swart T 1989 De obstetrische Erbse parese. Nederlands Tijdschrift voor Fysiotherapie 99: 96–99

Kuiters RRF, Brakkee JH, Van der Zee CEEM, Gerritsen van der Hoop R 1998 Factors promoting peripheral nerve repair. I. Recovery from peripheral nerve transection in the rat is accelerated by subcutaneous application of α-MSH. Neuro-Orthpedics 6: 87–90

Lundborg G 1988a Nerve and repair. Churchill Livingstone, London

Lundborg G 1988b Intraneural microcirculation. Orthopedic Clinics of North America 19: 1–12

McMahon SB, Gibson S 1987 Peptide expression is altered when afferent nerves reinnervate inappropriate tissue. Neuroscience Letters 73: 9–15

Nomoto M, Yoshihara T, Kanda T, Kaneko T 1991 Synapse formation by autonomic nerves in the previously denervated neuromuscular junctions of the feline intrinsic laryngeal muscles. Brain Research 539: 276–286

Smith W, Thesleff MR 1976 Spontaneous activity in denervated mouse diaphragm muscle. Journal of Physiology 257: 171–186

Souyri F, Bourre JM 1989 Altered metabolism of rat sciatic nerve after microinjection into the endoneurium of the ipsilateral sciatic nerve. Neuroscience Letters 96: 351–355

Sugimoto H, Monafo WW, Shimazaki S 1987 Regional nerve blood flow response to limb movement. American Journal of Physiology 252: H439–H441

Taniuchi M, Brent Clark H, Schweitzer JB, Johnson EM 1988 Expression of nerve growth factor receptors by Schwann cells of axotomized peripheral nerves: Ultrastructural location, suppression by axonal contact, and binding properties. Journal of Neuroscience 8: 661–664

Thesleff S, Ward MR 1978 Studies on the mechanism of fibrillation potentials in denervated muscle. Journal of Physiology 244: 313–323

Van der Linden A 1982 Het carpaal tunnel syndroon. Nederlands Tijdschrift voor Fysiotherapie 92: 104–106

Van der Zee CEEM, Gerritsen van der Hoop R, Gispen WH 1989 Beneficial effect of Org 2766 in treatment of peripheral neuropathy in streptocin-induced diabetic rats. Diabetes 38: 225–230

Van Gelder RS, Zegers JG, Kobus MH, Van Wieringen PCW, Devriese PP, Whiting HTA 1985 Perifere aangezichtsverlamming en aspecten van de behandeling. Nederlands Tijdschrift voor Fysiotherapie 95: 236–249

Van Sambeek HWR 1990 Effecten van elektrostimulatie bij spierdenervatie. Nederlands Tijdschrift voor Fysiotherapie 100: 184–188

Vitadello M, Triban C, Marini, P, Zanoni R, Fabris M, Gorio A 1986 Assessment of the regenerative capacity of peripheral nervous system: Enhancement of sprouting capacity by exogenous gangliosides. In: Nix WA, Vrbová G (eds) Electrical stimulation and neuromuscular disorders, pp 75–79. Springer–Verlag, Berlin

Zochodne DW, Ho LT 1991 Stimulation-induced peripheral nerve hyperemia: Mediation by fibers innervating vasa nervorum? Brain Research 546: 113–118

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