Acute nerve compression at low pressures has a conditioning lesion effect on rat sciatic nerves

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Effects of acute compression for 2 hours around the sciatic nerve trunk at 30 or 80 mmHg on the regeneration potential in rat sciatic nerves were studied. Sham compression or mobilization was performed contralaterally. A week later a crush injury was inflicted proximal to the compressed segment. After another 3 or 6 days the length of axonal outgrowth was measured, using the pinch test technique. We found that compression at either level caused an increased length of axonal outgrowth compared to the mobilized or sham-compressed nerves. The results show that an acute compression at low pressures does have a conditioning lesion effect on peripheral nerves.

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McQuarrie and Grafstein (1973) described an increased regeneration potential in a transected nerve when the lesion was preceded by a crush injury which thus seemed to potentiate the regeneration capacity. Different types of induced injuries have been tried and the results of the investigations all point in one direction: the nerve is easily irritated or stimulated and has an increased regeneration potential after a subsequent crush (test) lesion (Bisby and Pollock 1983, Arntz et al. 1989, Sisken et al. 1989, Dahlin and Kanje 1992, Dahlin et al. 1992a).

We report the impact of a short-time/low pressure compression on the sciatic nerve of rats upon the regeneration potential, i.e., functional changes in the nerve.

Material and methods

Female Wistar rats weighing 200–210 g were divided into 4 groups. The rats were anesthetized with an 0.3 mL intraperitoneal injection consisting of pentobarbital (60 mg/mL), 0.9% saline and diazepam (5 mg/mL) in a 1/1/2 volume proportion.

By lateral incisions in the midthigh, the sciatic nerves were exposed and mobilized. A 2-piece perspex chamber (Dahlin et al. 1986, Powell and Myers 1986), with thin rubber membranes, was applied around the nerve trunk and secured with screws, leaving a compressed segment of the nerve of approximately 6 mm. Each chamber half was connected to a compressed air system and inflated to 30 mmHg (n 10) or 80 mmHg (n 8) for 2 hours while the rat was kept asleep and the wound was temporarily closed. The contralateral sciatic nerve was identically mobilized and equipped with an uninflated twin chamber (n 18) serving as a sham compression or just mobilized (no chamber applied; n 9). After 2 hours the chambers were removed and the wounds were closed with single silk stitches in the skin.

7 days later the nerves were re-exposed bilaterally and subjected to a crush injury proximal to the previously compressed segment, using special pliers (Kanje et al. 1988). The crush site was labeled with a 9–0 epineurial Ethilon® suture. Again the wounds were closed and the rat was allowed to recover.

3 and 6 days later the rats were lightly re-anesthetized (same mixture as above, but a smaller dose), the nerves exposed and the leading regenerating sensory axons were localized and labeled by pinching the nerve in a distoproximal direction until a withdrawal reflex was elicited (Young and Medawar 1940, Gutmann et al. 1942, Kanje et al. 1988). The distance between this point and the previous crush mark was then measured.

The Kruskal-Wallis and Mann-Whitney *U*-tests were used to compare the regeneration distances of the experimental groups. A *P*-value less than 0.05 was considered statistically significant.

Table 1. Effects of acute, graded 2-hour compression on axonal outgrowth length after a crush injury. Mean *SD* [number of nerves]

Compression	Outgrowth length (mm) after					
	3 days			6 days		
Control	5.4	*0.1*	[5]	15.6	*0.3*	[4]
Sham (0 mmHg)	6.1	*0.6*	[8]	16.3	*0.6*	[10]
30 mmHg	7.3	*0.2*	[4]	17.9	*0.3*	[6]
80 mmHg	7.0	*0.6*	[4]	18.0	*0.7*	[4]
P-value						
Control vs Sham	0.03			0.03		
Sham vs 30 mmHg	0.007			0.001		
30 mmHg vs 80 mmHg	ns			ns		
Sham vs 80 mmHg	ns			0.008		

ns not significant.

Table 2. Effects on regeneration rate of acute nerve compression

Compression	Regeneration rate (mm/day)
Control	3.4
Sham (0 mmHg)	3.4
30 mmHg	3.5
80 mmHg	3.7

Values calculated from data in Table 1.

Results

The length of axonal outgrowth, expressed as mm at the specific time-point, was increased ($P < 0.05$) in all the compressed nerves compared to the control nerves (Table 1). The values after compression at 30 and 80 mmHg were higher than those for sham-compressed nerves, when examined at 6 days. Sham-compressed nerves had higher values of outgrowth length as compared to controls (mobilization but no compression). Compression at 30 and 80 mmHg did not show any difference.

By subtracting the lengths of axonal outgrowth, obtained 6 days after the crush (test) lesion, by those found after 3 days and then dividing the obtained value by 3 days, the regeneration rate (mm/day) could be evaluated at that specific time interval (Table 2). The regeneration rates after compression at 80 and 30 mmHg were increased by 9 and 3 percent, respectively.

Discussion

Several studies using different experimental techniques have already pointed out this conditioning ability of the nerve, since McQuarrie and Grafstein (1973) and McQuarrie et al. (1977) showed an increased regeneration potential after a previous nerve injury. Pulsed electromagnetic fields of varying durations also have been reported to increase the regeneration rate markedly when given prior to a crush lesion (Sisken et al. 1989) and chronic nerve compression, which does not induce axonal degeneration, can also potentiate axonal regeneration (Dahlin and Kanje 1992). The amount of irritation applied to the nerve trunk above a specific level seems to be of minor importance, as is shown in the present study. Such a slight trauma as exposure of the hind limb of rats to defined vibrations can also act as a conditioning lesion (Dahlin et al. 1992a). In the present study a slight trauma to the nerve, that is sham-compression, also increased the outgrowth length but not to as large extent as pressures of 30 and 80 mmHg. The conditioning lesion of the sham-compressed nerves can be explained by some demyelination observed in the superficial parts of the fascicles after sham compression (Powell and Myers 1986). The evaluation method used in the study—pinch reflex test—is considered to be a very sensitive and appropriate method of determining tips of outgrowing sensory axons (Bisby and Pollock 1983, Danielsen et al. 1986, Redshaw and Bisby 1987, Kanje et al. 1988, Kerns et al. 1993, Rusovan Johnsson 1993).

The nature of the increased regeneration response in the present study is still poorly understood. Local damage like Schwann cell necrosis, edema, demyelination and axonal degeneration have been demonstrated in this model which was used in the present study after compression at 30 and 80 mmHg (Lundborg et al. 1983, Powell and Myers 1986). Compression at the pressures used in the present study, observed in clinical cases (Gelberman et al. 1981), can jeopardize the microcirculation of the nerve. Compression at 30 mmHg can impair the local venular blood flow and by 80 mmHg the arterial blood flow is cut off (Rydevik et al. 1981).These changes will lead to an endoneurial edema, which will increase the endoneurial fluid pressure, thereby further impairing the intraneural microcirculation (Lundborg et al. 1983, Powell and Myers 1986). The observed necrosis of Schwann cells in the present model (Powell and Myers 1986) may stimulate the remainder of the Schwann cells to proliferate or to increase their production and/or secre-

tion of neuronotropic factors. This may produce a perfect mileu for the advancing nerve fibers from a crush lesion proximal to the compressed segment. It is also possible that the observed effects on the regeneration potential may be caused by biochemical and morphological changes in the nerve cell bodies (Lieberman 1971, 1974, Barron 1983, Archer 1987), which also are seen after acute, graded compression, ranging from 30 to 400 mmHg (Dahlin et al. 1987, Dahlin et al. 1992b), and caused by inhibition of axonal transport (Dahlin 1986).

An interesting finding in our study was that peripheral nerve regeneration can be stimulated by compression at low pressure and of short duration. This has interesting possible implications for preoperative treatment of patients, scheduled for elective nerve surgery with the aim of increasing the regeneration potential in the reconstructed nerve.

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