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The age dependent effect of partial denervation of rat fast muscles on their activity

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Abstract. In 3 or 18 day old Wistar rats the hindlimb muscles were partially denervated by cutting the L4 spinal nerve. Three months later, the effects of partial denervation of the fast extensor digitorum longus (EDL) muscle on the activity of its remaining motor units were studied using electromyographic (EMG) recordings in freely moving animals. In spite of a reduced number of motor units the amount of aggregate EMG activity was greater in the partially denervated EDL muscle in all experimental conditions. This increase was more obvious at rest than during exploratory behaviour, and was significantly greater in muscles that were partially denervated at 3 days than at 18 days of age. On the other hand, the effect of partial denervation on the EMG activity pattern during locomotion was similar in animals partially denervated at 3 or 18 days of age. Unlike in intact EDL, in the partially denervated EDL muscle the duration of the bursts was influenced by the step cycle duration. Thus, we conclude that although partial denervation of EDL muscle influences the amount and pattern of activity of the remaining undamaged motor units in all animals, some of the alterations of EMG activity were more pronounced in animals denervated at younger age.

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INTRODUCTION

After loss of a proportion of motor axons due to injury or disease the muscle is innervated by a reduced number of motoneurones and has to rely on the recruitment and activity of these remaining motor units (MUs) during any motor task (Gordon et al. 1993, Einsiedel and Luff 1994, Tyč and Vrbová 1995). It is, therefore, important to establish the effects of the removal of part of the muscle's innervation on the function of the remaining uninjured motor units. Previous results show that partial denervation of fast muscles in adult rats leads to a moderate but consistent increase of the activity of the remaining motor units and a change in the relationship between the EDL burst duration and step cycle duration during locomotion (Sławińska et al. 1998). More profound changes of activity were observed in conditions where following nerve injury in young animals a large proportion of motoneurones died and the surviving motoneurones that reinnervated the muscle were excessively active and remained so throughout the animals life (Navarrete and Vrbová 1983, Vejsada et al. 1991). These surviving motor units displayed extraordinary changes in their activity, and it is possible that these changes developed as a result of some altered properties of the motoneurone due to neonatal nerve injury. Recently it has been reported that partial denervation in neonatal rats leads to delayed maturation of the axons and motoneurones that were undamaged and supplied a partially denervated muscle (Harding et al. 1998). The possibility that such motoneurones became permanently influenced by this delayed maturation was suggested by results of Tyč and Vrbová (1995), where, after partial denervation in neonatal animals, the remaining motor units became more active and the characteristic properties of muscle fibres of these units were typical of continuously active muscles, i.e. they were fatigue resistant, had high levels of oxidative enzymes and a large number of muscle fibres expressed slow myosin heavy chain isoforms.

Here we examined the possibility that partial denervation in young animals may have permanent effects on the integration of the intact motoneurones into the central nervous system and their activity patterns during locomotor behaviour of the freely moving animals. We carried out experiments where the changes of activity of motor units during a variety of motor tasks of muscles partially denervated shortly after birth were compared to those injured later. Some preliminary results on the effects of partial denervation on muscles have been already published elsewhere (Sławińska et al. 1996).

METHODS

Surgical procedures

The experiments were performed on 2 groups of Wistar rats. In the first group of animals ($n = 8$) the partial denervation was carried out under ether anaesthesia at 3 days of age (the day of birth was taken as day zero) and in the second group ($n = 8$) under halothane (2% in O_2, ICI Pharmaceuticals) anaesthesia at 18 days of age. In both groups, the partial denervation of the left EDL muscle was achieved using sterile precautions by section of the L4 spinal nerve, which contributes 60-80% of the innervation of the EDL muscle (Albani et al. 1988). The L4 spinal nerve was carefully exposed at its exit from the vertebral column and cut with fine scissors. In order to prevent reinnervation about 2 to 4 mm of the spinal nerve was excised. Care was taken to avoid damage of the L5 spinal nerve, which contains the remaining 20-40% of the EDL's innervation. The incision was closed, and after recovery from the anaesthesia, the rats were returned to their mothers. In all experiments, the contralateral unoperated side was used as a control.

Two to 3 months after partial denervation the EMG activity from the partially denervated and control EDL muscles was recorded in freely moving rats using the method of chronically implanted electrodes previously described (Navarrete and Vrbová 1983, 1984, Vejsada et al. 1991, Sławińska et al. 1995, 1998, Tyč and Vrbová 1995). The electrodes were made from multistranded, teflon-coated stainless steel wire (7SS-2t; Clark Electromedical Instruments, UK) enclosed in silicon tubing (0.5 x 0.25 mm diameter, Esco Rubber), provided with a multipin connector reinforced with dental cement (Austenal Dental Products Ltd) and covered with adhesive silicone (3140 RTV, Dow Corning). The electrodes were implanted into the partially denervated and contralateral control EDL muscles under chloralhydrate (4% solution, 1 ml/100 g body weight i.p.) anaesthesia using sterile precautions. The multipin connector was secured to the back of the animal. The loops of wire electrodes with about 100 μm of the insulation removed (as a recording surface) were led under the skin and sutured to the belly of the muscle. The distance between the tips of electrodes

was 1-2 mm. After surgery the animals were returned to their home cages and the experiments with the EMG recordings started after few days of recovery.

Electromyography

EMG activity was amplified using a Tectronix 2A61 differential amplifier, filtered (band pass 0.1-1.0 kHz), monitored on a storage oscilloscope (Tektronix 5113) and recorded on a tape recorder (Racal 4DS). The EMG activities of the partially denervated and contralateral control EDL muscles were simultaneously recorded in freely moving animals during several consecutive 5 min periods when the animals were exploring or resting in the cage. EMG activity was also recorded during regular locomotion when the animals were walking along the runway 1.5 m long and 5 cm wide (Sławińska et al. 1995, 1998).

EMG analysis

AGGREGATE ACTIVITY

In order to provide a quantitative estimate of overall muscle activity, the aggregate EMG activity of EDL muscles from both hindlimbs was analysed. The aggregate EMG activity, defined as a number of potentials higher than the threshold close to the noise level (usually < 50 μV), was measured during exploratory or resting behaviour at 5 min intervals. In all rats the exploratory behaviour was characterised by a vigorous locomotor movement around the experimental cage associated with sniffing, climbing, grooming. In contrast to the exploratory behaviour, the animals during rest were most of the time sitting motionless, lying on the ground or even sleeping. For further analysis of aggregate activity only those data with perfect EMG recordings without any single artefact were chosen. The detection of the EMG signal crossings the threshold was done using a spike trigger (NL 200; Neurolog system, Digitimer Ltd., UK). The triggered pulses and the analysed signal were monitored on an oscilloscope and counted by a computer using a software package (MRATE program; Cambridge Electronic Design, UK). The results were expressed as mean counts per second. The counts of aggregate EMG activity of partially denervated EDL muscle were then expressed in relation to the counts of aggregate EMG activity of the control EDL muscle recorded simultaneously.

SINGLE MOTOR UNIT ACTIVITY

The frequency of single MU activity in partially denervated EDL muscle was calculated from selected segments of EMG activity recorded in resting animals. In the analysed segments no more than two MUs were active, as estimated on the basis of relatively stable amplitude and shape of the MU activity potentials (MUAPs). The firing frequency of bigger MUAP was calculated using a spike trigger (NL 200; Neurolog system, Digitimer Ltd., UK) with the threshold individually set for each segment of single MU. The triggered pulses and the analysed signal were monitored on an oscilloscope and counted.

EMG PATTERN DURING LOCOMOTION

To analyse EMG activity recorded during regular locomotion the signals were played back from the magnetic tape, rectified and integrated (time constant 5 ms). After analogue-digital conversion at sampling frequency 400 Hz the portions of EMG activity recorded during locomotion at a relatively constant stepping rate were stored in the PC computer. Further analysis, using computer software developed in our laboratory (Sławińska et al. 1995, 1998), enabled us to assess semiautomatically the burst and step cycle duration of EMG signals from partially denervated as well as control EDL muscles. The burst duration (BD) was defined as the time between the beginning and the end of an EMG burst; the step cycle duration (CD) was defined as the time elapsed between consecutive EMG bursts of the same muscle (the insert in Fig. 3 shows how the BD and CD were defined). The relations between the burst duration and the step cycle duration were examined using the method of linear regression (least square method). The coefficients of the regression function were compared using the analysis of variance.

RESULTS

EMG activity during sitting and exploratory behaviour

PARTIAL DENERVATION AT 3 DAYS

In rats tested 2 to 3 months after partial denervation carried out at 3 days of age, the use of the hindlimb on the injured side was altered. During standing the partially

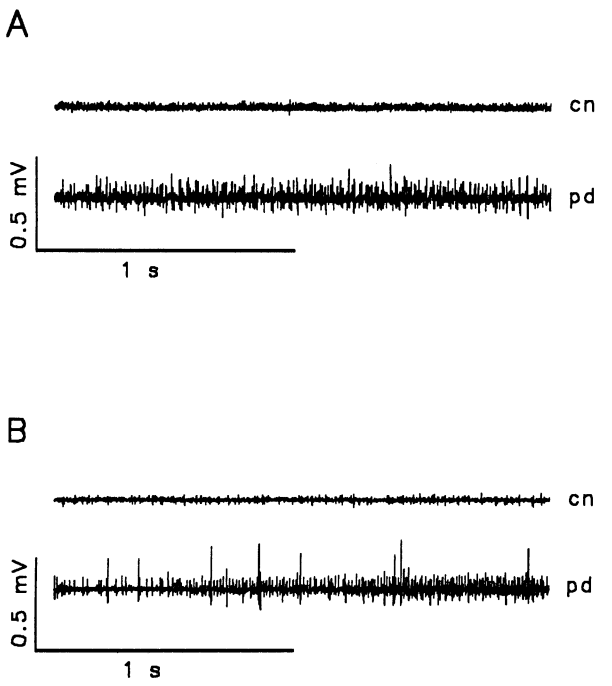

Fig. 1. Examples of EMG activity recorded from control (cn) and partially denervated (pd) EDL muscles of two adult rats during sitting: (A) partially denervated at 3 days of age and (B) at 18 days of age.

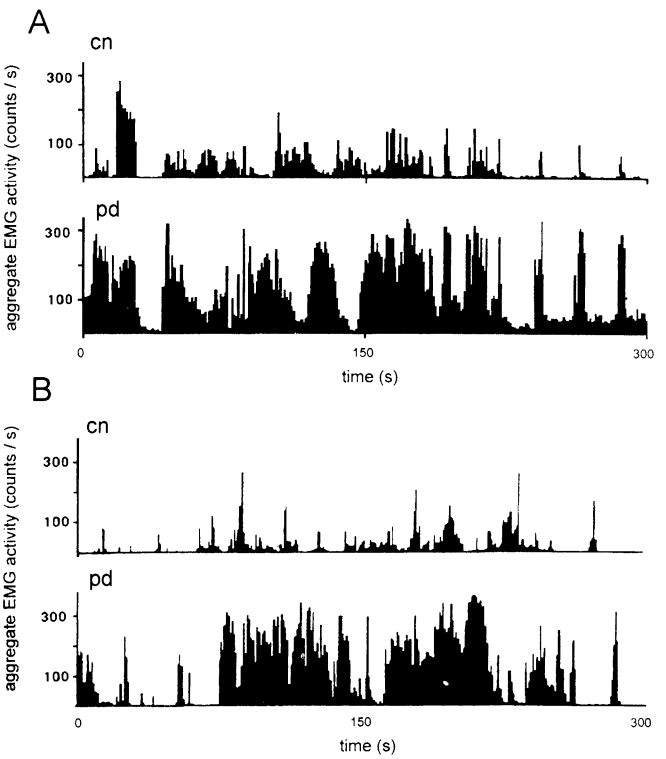

Fig. 2. Examples of aggregate EMG activity (counts/s) recorded from control (cn) and partially denervated (pd) EDL muscles of two adult rats during exploratory behaviour in the experimental cage: (A) partially denervated at 3 days of age and (B) at 18 days of age.

denervated hindlimb was sometimes extended with its toes flexed. However, during exploratory behaviour in the experimental cage, hardly any changes could be noticed in the use of the partially denervated hindlimb. Both hindlimbs, the partially denervated and the control, were used in the same way during sitting, scratching, climbing, walking. Only occasionally, during changes of the direction of locomotion, the partially denervated hindlimb was held extended, and did not participate in the movement.

The pattern of EMG activity in the partially denervated EDL muscle was different from that of the control EDL. Fig. 1A shows examples of EMG activity recorded from control (top trace) and partially denervated (bottom trace) EDL muscles when the animal was sitting. It is clear that in the control EDL muscle only little EMG activity could be seen, whereas in the partially denervated muscle continuous, long lasting activity was present. The amount of aggregate EMG activity, calculated during 5 min recording sessions, was much greater in the partially denervated EDL muscle than in the control EDL. In 4 rats tested during rest when they were mainly sitting motionless in the experimental cage, the overall aggregate EMG activity obtained in the partially denervated muscles was 4.1 ± 0.4 (mean ± SEM) times greater than that of the control side.

During exploratory behaviour, when the rat was moving freely in the cage, the extent of EMG activity of both, the control and partially denervated EDL muscles, depended on the rats behaviour. An example of the aggregate EMG activity in control (top trace) and partially denervated (bottom trace) EDL muscles during exploratory behaviour is illustrated in Fig. 2A. The control EDL muscles were active mainly during movement where the bursts of EMG activity were related to the swing phase of the step cycle, while the periods of silence were related to the stance phase. Thus, the periods of peak in the aggregate EMG activity were separated by periods of silence. In the partially denervated EDL muscles the episodes of peak activity were followed by continuous activity of some MUs which was absent in control EDL muscles. During exploratory behaviour of 4 tested rats, the total aggregate EMG activity of the partially denervated EDL was 2.3 ± 0.4 (mean ±

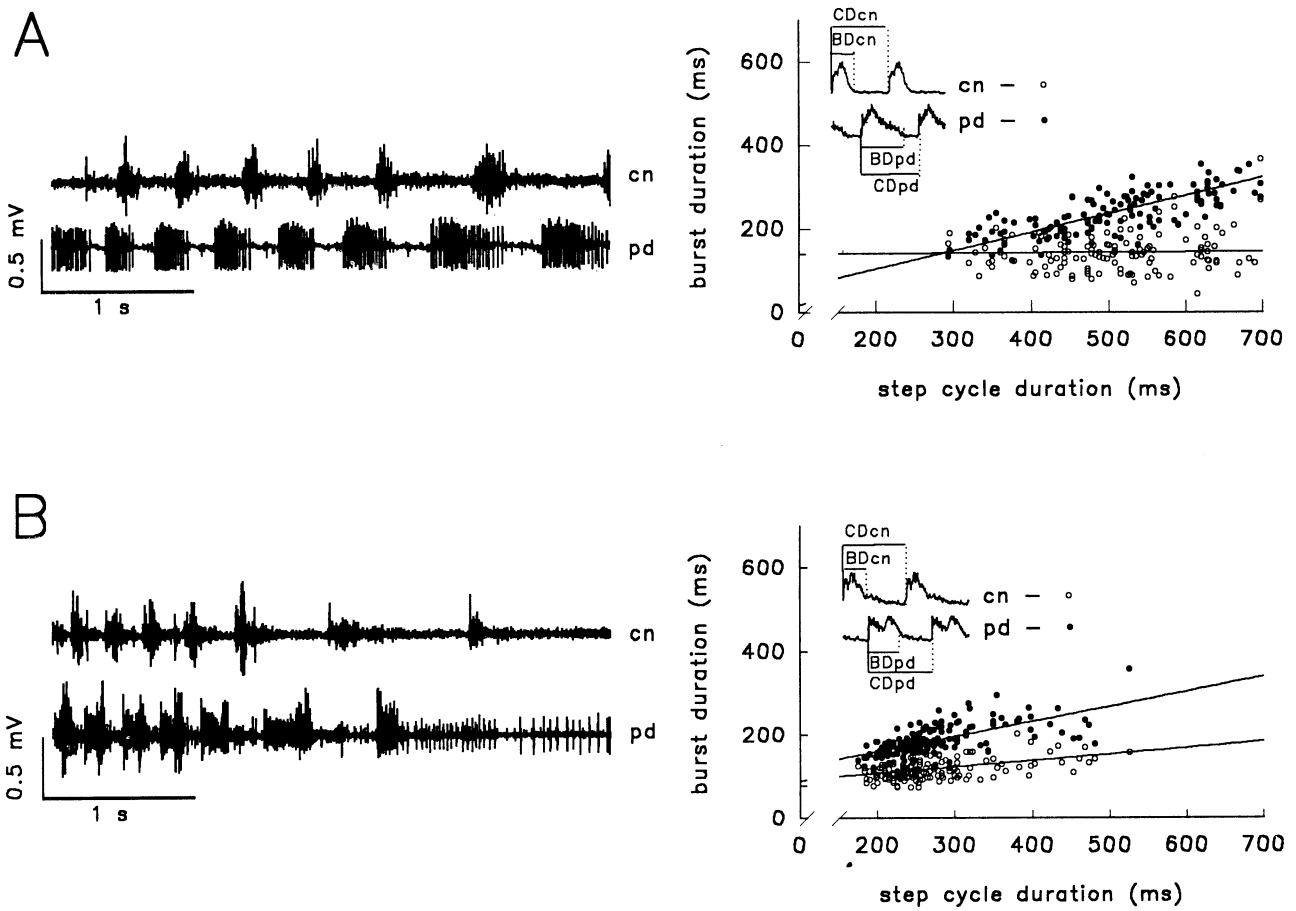

Fig. 3. Left side: examples of EMG activity recorded from control (cn) and partially denervated EDL (pd) muscles operated at 3 days (A) or 18 days of age (B) of two adult rats during locomotion. Right side: the relationship between the burst duration and step cycle duration which was established for the control and partially denervated EDL muscles in two animals: partially denervated at 3 days (A) and at 18 days of age (B). The inserts show records of averaged, rectified and integrated EMG activity from both EDL muscles and illustrate how the step cycle duration (CD) and burst duration (BD) were estimated.

SEM) times greater than that of the control muscle. Thus, in spite of the much reduced number of MUs in the partially denervated EDL muscles the aggregate activity was higher than that in control EDL muscles.

PARTIAL DENERVATION AT 18 DAYS

In animals, partially denervated at 18 days of age, changes in the posture or locomotion were less pronounced compared to those seen in animals partially denervated at 3 days. Only rarely, when the rat was changing the direction of locomotion, a slight extension of the partially denervated hindlimb was observed. During standing or exploratory behaviour both hindlimbs were used in the appropriate way without any visible difference between the control and partially denervated hindlimbs.

In rats operated at 18 days the pattern of EMG activity recorded from the partially denervated EDL muscles was also different from that of the control EDL muscle. When the animals were sitting there was more EMG activity in the partially denervated EDL than in the control muscle (Fig. 1B). During 5 min periods of recordings from muscles of resting animals the background EMG activity was less regular and rarely continuous compared to the activity of partially denervated EDL muscles from animals operated at 3 days. The total aggregate EMG activity of the partially denervated EDL obtained in 4 animals was 2.0 ± 0.1 (mean $\pm$ SEM) times higher than that of the control muscle.

During exploratory behaviour bursts of EMG activity were present in both partially denervated and control EDL muscles. In addition, partially denervated EDL muscles showed continuous activity between the bursts. Figure 2B illustrates examples of the aggregate EMG activity recorded from control and partially denervated EDL muscles during exploratory behaviour. The amount of the aggregate EMG activity in the partially denervated EDL muscle of 4 tested animals was 1.8 ± 0.2 (mean ± SEM) times higher than in the control muscle.

EMG during locomotion

PARTIAL DENERVATION AT 3 DAYS

EMG activity of both partially denervated and control EDL muscles was recorded simultaneously during locomotion along a runway. The EMG recordings during locomotion showed bursts of activity in both the partially denervated and control EDL muscles (Fig. 3A). These bursts alternated with periods of silence related to the stance phase of the step cycle. However, unlike in the control EDL, in the partially denervated EDL muscles additional long lasting activity prolonged the duration of the bursts usually related to the swing phase of the step cycle. Thus, in the partially denervated EDL muscles the duration of the burst was always longer than that in the control EDL (Table I).

In adult normal rats during locomotion, the burst duration of EDL muscle is not related to the step cycle duration (Sławińska et al. 1998). Quantitative analysis of the relationship between the duration of the burst and the duration of the step cycle confirmed that in the control EDL muscle the EMG burst duration remained constant and was not influenced by the step cycle duration. The correlation coefficient of the relationship between the duration of the burst and the duration of the step cycle ranged in different animals (n = 5) from 0.04 to 0.41, while the slopes of established regression lines ranged from 0.01 to 0.15. In contrast, in the partially denervated EDL the duration of the burst was strongly correlated with the duration of the step cycle. In 5 tested animals the correlation coefficients between the duration of the burst and the step cycle duration ranged from 0.63 to 0.90 and the slopes from 0.20 to 0.50. Analysis of variance performed for slopes of linear regression showed a significant difference (P<0.001) between the relationship of the burst duration *versus* step cycle duration obtained in the partially denervated and control EDL muscles. Figure 3A (right side) illustrates the relationship between

TABLE I

Changes in EDL burst duration after partial denervation

Age of partial denervation	Number of steps	Burst duration of EDL muscle (ms)		Step cycle duration (ms)
		Partially denervated (ms)	Contralateral (ms)	
3 days	241	219.35 ± 5.32	161.23 ± 2.82	415.24 ± 9.68
	121	194.11 ± 4.40	101.57 ± 2.79	386.46 ± 14.84
	70	232.67 ± 8.20	129.47 ± 3.91	420.77 ± 19.27
	280	263.65 ± 5.26	157.14 ± 3.66	574.07 ± 10.98
	159	163.45 ± 6.27	80.36 ± 2.43	342.16 ± 12.42
18 days	40	179.55 ± 3.74	101.07 ± 2.41	380.05 ± 11.13
	158	178.45 ± 2.34	120.79 ± 2.09	282.84 ± 6.13
	34	125.88 ± 6.28	81.47 ± 4.49	383.45 ± 18.37
	32	162.69 ± 8.60	129.09 ± 3.97	329.12 ± 13.12
	38	245.32 ± 9.88	108.68 ± 6.74	347.31 ± 15.00

Values are means ± SEM. The difference between the burst duration of partially denervated and contralateral EDL muscles is significant (Students t-test, P<0.001) in both groups of animals (age of injury: 3 days, 18 days).

burst and step cycle duration observed in one of the animals.

PARTIAL DENERVATION AT 18 DAYS

The EMG activity recorded during locomotion in animals partially denervated at 18 days revealed also an alternating pattern of activity in both control and partially denervated EDL muscles (Fig. 3B), similar to the pattern of activity observed in normal, unoperated animals. However, unlike in the control side (but similar to EDL muscles partially denervated at 3 days of age), in EDL muscles partially denervated at 18 days the burst of activity was followed by continuous activity of some MUs, which resulted in an increase of duration of the EMG burst when compared to the control EDL muscle (Table I). The means of duration of EMG burst of EDL muscles partially denervated at 3 and 18 days were not significantly different ($P>0.05$ Students t-test; $P>0.05$ nonparametric Kolmogorov-Smirnov test).

Similar to normal rats (Sławińska et al. 1998), the burst duration of the control EDL muscle was not correlated with the step cycle duration (the correlation coefficient ranged from 0.05 to 0.41 and the slopes from 0.03 to 0.16 for different animals (n = 5)). In contrast, the burst duration of the partially denervated EDL muscle was strongly correlated with the step cycle duration (Fig. 3B) as in rats partially denervated at 3 days of age. The correlation coefficients ranged from 0.54 to 0.91 and the slopes from 0.18 to 0.60 for different animals (n = 5). Analysis of variance for coefficients of linear regression showed a significant difference ($P<0.001$) between the

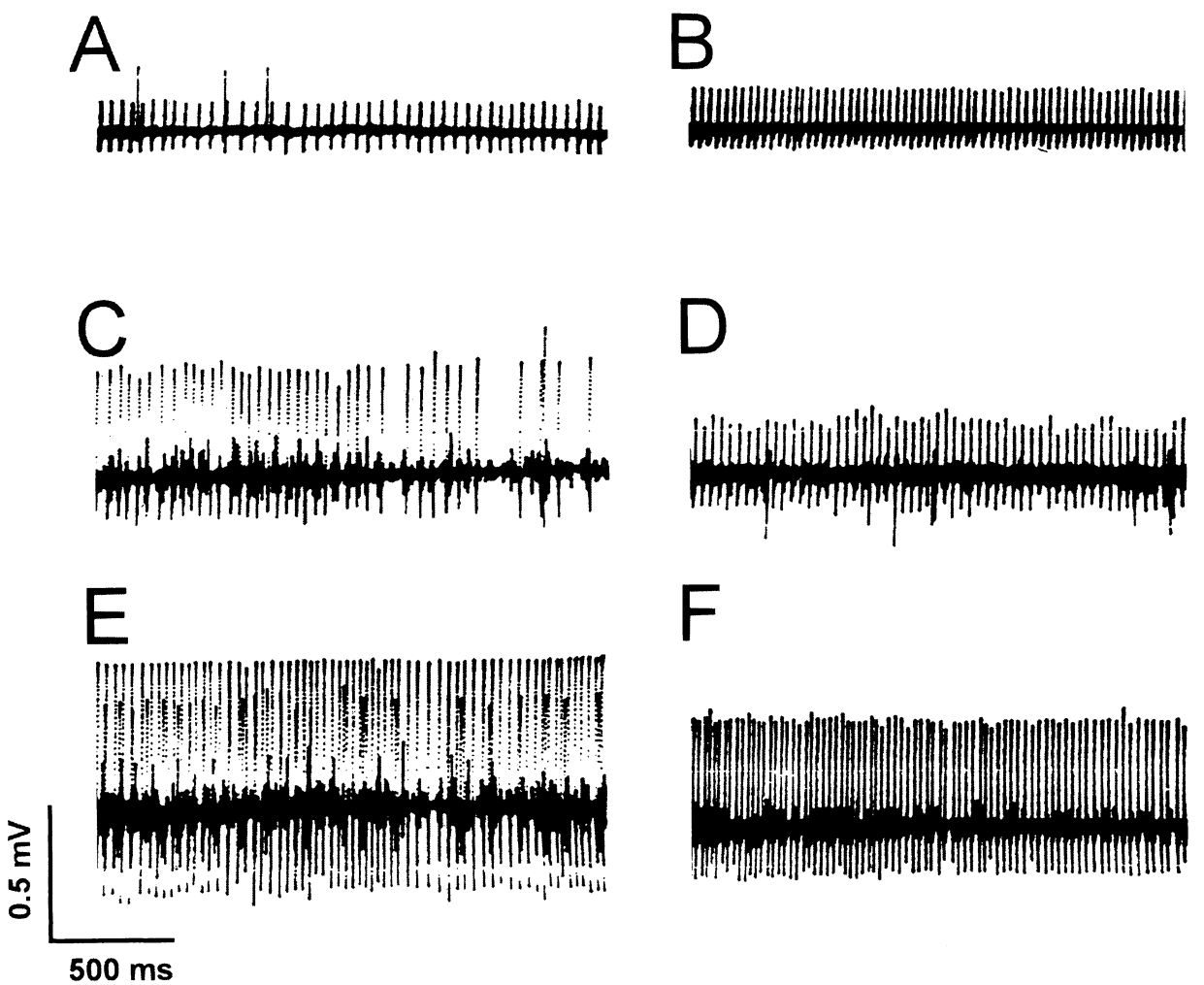

Fig. 4. Examples of EMG activity of several single MUs (A, B, C, D, E, F) recorded in resting animals from EDL muscles partially denervated at 3 days of age. No activity was seen in the control EDL muscles (control traces not shown).

relationship of the burst duration *versus* step cycle duration of partially denervated EDL muscles and that of the control side. Thus, the partial denervation at 18 days induced similar changes in the relationships of burst duration and step cycle duration during regular locomotion as that seen in EDL muscles partially denervated at 3 days. Moreover, the statistical analysis did not show significant differences between the coefficients of linear regression established for partially denervated EDL muscles in either of the experimental groups ($P>0.05$ Students t-test; $P>0.05$ nonparametric Kolmogorov- -Smirnov test).

Changes of Motor Unit activity after partial denervation

The small number of MUs in the partially denervated EDL muscles (Tyč and Vrbová 1995) enabled us to distinguish the activity of individual MUs, and determine their characteristic firing patterns. After partial denervation at 3 days, many MUs fired continuously for long periods of time in resting animals. Examples of continuous EMG activity of several single MUs recorded from different animals partially denervated at 3 days are shown in Fig. 4. The firing frequency of these different MUs ranges from 20 to 45 Hz. After partial denervation at 18 days such continuous MU activity of EDL muscles was not so often observed. However, the obtained firing frequency was at the same level as in animals operated at 3 days. Simultaneous recordings from control EDL muscles revealed that there was no EMG activity present at this time (not shown in the Figure) in the contralateral control EDL muscles.

DISCUSSION

The present results show considerable changes of EMG activity 2-3 months after partial denervation of the fast EDL muscle. Although such changes were observed in animals that were partially denervated at 3 days as well as at 18 days of age, some of the changes of EMG activity were more pronounced in animals that were partially denervated at a younger age.

In spite of much reduced number of MUs in the partially denervated EDL muscle (Tyč and Vrbová 1995), there was an increase in the aggregate EMG activity in these muscles in all the experimental conditions examined. It was most obvious in resting animals, when there was hardly any activity in the contralateral EDL muscle, while the few remaining MUs in the partially denervated muscles were almost continuously active. This increase of muscle activity, though present in both groups of animals, was greater in rats that were partially denervated at 3 days of age.

It is known that in 3 day old rats the neuromuscular system is immature: the neonatal motoneurones occupy a large territory in the particular muscle (Brown et al. 1976, Balice-Gordon and Thompson 1988) and the appropriate activity pattern of the skeletal muscles is not yet developed (Navarrete and Vrbová 1983). The developmental changes which lead to the reduction of MU territory continues until 18 days of age when the EDL MUs reach their adult size (Balice-Gordon and Thompson 1988) and their activity pattern typical for the flexor function of this muscle is finally established (Navarrete and Vrbová 1983). Our results indicate that partial denervation performed at the age before reduction of the neonatal MU territory results in the greater alteration of the MUs activity pattern in flexor EDL muscle. This is particularly seen as an atypical continuous MUs activity of this muscle in resting animals. The continuous MUs activity was probably the main cause of the complete transformation of fast to slow muscle fibres induced by partial denervation which was more obvious in the group operated on at 3 days of age (Tyč and Vrbová 1995). In the group of animals partially denervated at 18 days of age a transformation from fast type II to type I fibres also occurred, but the extent of the change was smaller as was the increase of the aggregate EDL activity (Tyč and Vrbová 1995). This incomplete fast to slow transformation of muscle fibres seen in animals injured at 18 days is consistent with previous studies that show that in adult rats transformation from fast to slow type of muscles fibres is difficult to achieve (Pette and Vrbová 1992), while increased activity in neonatal animals can transform rat muscle fibres quite effectively (Tyč and Vrbová 1995).

It is important to note that in the partially denervated EDL muscle its activity was generated by only about 5-12 MUs, as opposed to the 40 MUs in control muscles (Close 1967, Albani et al. 1988, Balice-Gordon and Thompson 1988, Tyč and Vrbová 1995). Despite this, the aggregate activity of the whole partially denervated muscle was much higher than on the control side. This suggests that each of the remaining MU increased its activity several fold. This is consistent with the results described in our previous paper concerning the partially denervated slow soleus muscle (Sławińska et al. 1995), where, although there was no increase in activity re-

corded from the whole muscle, the activity calculated per MU was also significantly higher. Thus, the changes in the activity of EDL motoneurones after partial denervation are similar to those seen in soleus muscle. It is possible, therefore, that in order to compensate for the loss of innervation following extensive (more than 65%) partial denervation, the remaining MUs of both extensor and flexor skeletal muscles increased their EMG activity.

The present results show that the increase in aggregate activity of partially denervated EDL muscle was most obvious in resting animals. We cannot exclude that the differences in the total amount of EMG activity recorded during various motor behaviours (resting vs. exploratory) might be due to a different involvement of EDL muscles in various motor tasks. On the other hand, because the normal EDL muscle contains about 5% of slow muscle fibres (Albani et al. 1988, Balice-Gordon and Thompson 1988), it could be argued that after section of the L4 spinal nerve the remaining axons in the L5 spinal nerve belong to tonic MUs and that this could explain the increased activity in the partially denervated muscles. However, this seems unlikely, since: (1) our results show that in normal EDL muscles that are also innervated by axons in the L5 spinal nerve, no continuous activity can be recorded in resting rats (see also Cohen and Gans 1975, Navarrete and Vrbová 1983, Sławińska et al. 1998); and (2) in spite of the greatly reduced number of MUs in the partially denervated muscle, the aggregate EMG activity was much higher than that recorded from the fully innervated EDL muscle, not only in resting rats, but also during spontaneous exploratory movement as well as during locomotion.

As expected, the activity of the partially denervated EDL muscle was increased also during locomotion. In partially denervated muscles the burst of EMG activity were, unlike in normal muscles, followed by prolonged activity of some MUs that prolonged the burst duration. Unlike in control EDL muscles where there is no correlation between the burst duration and the step cycle duration (Cohen and Gans 1975, Hruska et al. 1979, Nicolopoulos-Stournaras and Iles 1984, Goudard et al. 1992, Sławińska et al. 1998), in the partially denervated EDL muscles the burst duration was highly correlated with the step cycle duration. From the present results it is not possible to propose a reason for the burst prolongation in the partially denervated flexor muscles obtained during locomotion in freely moving rats. The longer burst of flexor muscle activity might have been caused by changes in the properties of remaining motoneurones themselves (Huizar et al. 1977). Moreover, the method of partial denervation used by us, in addition to the reduction of efferent signal, decreased also the afferent segmental input from the same, and partly from other muscles. Therefore, we cannot exclude that the partial denervation causes the reduction of the inhibitory inputs from antagonistic muscles that normally stop flexor muscles activity to switch from the swing to the stance phase during locomotion in intact animals.

In contrast to the differences in the total amount of EMG activity between animals partially denervated at 3 and 18 days of age seen during resting and exploratory behaviour, the changes in EMG pattern during locomotion were comparable in both groups of animals. These changes do not seem to be influenced either by the age at which the partial denervation has been carried out, or by the number of remaining motor units in the partially denervated muscle, which is more reduced in rats operated at younger age: 6 ± 0.32 (mean ± SEM) - in animals partially denervated at 3 days of age vs. 12 ± 0.83 (mean ± SEM) - in animals partially denervated at 18 days of age (Tyč and Vrbová 1995). A similar picture of EMG changes during locomotion was obtained in rats partially denervated as adults (Sławińska et al. 1998). The reason for this lack of age dependent differences of the EDL activity during locomotion requires further investigation.

Taken together, the results of the present paper show that in all situations tested the motoneurones to the partially denervated EDL muscles seem to be activated more readily and for longer periods of time than those to control EDL muscles. This change that reflected final outcome of motor function might not necessarily be caused by changes in the motoneurone itself. However, when considering the reasons for this result the following possibilities have to be taken into account: (1) the excitability of the remaining motoneurones is modified as a result of partial denervation, (2) motoneurones that supply partially denervated muscles receive an increase of synaptic inputs and therefore a greater excitatory drive, and (3) there is a decrease of inhibitory inputs that normally prevent activity during rest, or the stance phase of locomotor activity. Therefore, further experiments are needed to decide on any of these mechanisms.

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