Muscle fiber conduction velocity (MFCV) in biceps brachii was studied in traumatic brachial plexus lesions (16 patients) and ALS (22 patients) by means of an invasive (I-MFCV) and a surface (S-MFCV) method. In traumatic brachial plexus lesions after complete denervation an exponential decrease of the mean I-MFCV was found, \( T_{1/2} = 1.1 \) month. After 4 to 5 months this resulted in severely reduced conduction velocities (mean 1.4 m.s\(^{-1}\), range from 0.5 to 2 m.s\(^{-1}\)). Simultaneous with signs of reinnervation, fibers with faster conduction velocities were seen. In ALS, a decrease of the mean I-MFCV was found, and slow conducting fibers were found in every patient in at least one side. At the same time muscle fibers with increased I-MFCVs were found. This increased range of velocities seems based on a combination of slow conducting, atrophic fibers, with fast conducting, hypertrophic fibers, compensating the force loss. In some patients we found these disturbances without clear abnormalities with concentric needle EMG, and with unimpaired muscle force. The surface-EMG measurements in the ALS patients revealed increased S-MFCV values in combination with a decrease of the median frequency (F\(_{\text{med}}\)). We suggest that the opposite finding of an increased S-MFCV is a consequence of the muscle fiber hypertrophy in the surviving, voluntarily recruited motor units. The simultaneous decrease of the F\(_{\text{med}}\) seems to be caused mainly by the change in shape of the motor unit potential.
INTRODUCTION

Studies of muscle fiber conduction velocity (MFCV) in neurogenic lesions are relatively scarce. Buchthal and Rosenfalck (1958) studied impulse conduction both in partially and completely denervated human muscle after severe lesions of the brachial plexus. They found that the majority of paretic muscles contained fibers which conducted at a markedly reduced rate. Troni et al. (1983a) also showed a slowing of the MFCV in a completely denervated biceps muscle. In a single fiber EMG (SFEMG) study Stålberg et al. (1975) found a progressive slowing of the MFCV in the late single fiber potential components in a case of progressive spinal muscular atrophy. They suggested that this is the case in almost all 'late' components found with SFEMG recordings in motor neuron diseases, including amyotrophic lateral sclerosis (ALS).

However, although it is likely that changes in MFCV in neurogenic lesions take place, little is known about the the extent and time course of such changes. Additionally, it is not clear in how far MFCV changes are related with total or partial denervation and reinnervation. In order to get a better idea of the changes in MFCV induced by acute and chronic neurogenic lesions, we used an invasive method to study the MFCV in patients with traumatic lesions of the plexus brachialis during complete denervation and at different stages of reinnervation. Additionally, we studied the MFCV in a group of ALS patients by means of an invasive and a surface EMG method.

PATIENTS AND METHODS

Lesions of the plexus brachialis

We studied 16 patients with acute, complete traumatic lesions of the plexus brachialis. The group consisted solely of men, aged 16 to 32, mean 21.9 years. The patients were tested either in the phase of complete denervation (10 measurements) or during reinnervation after complete denervation (14 measurements), 1 to 28 months after the trauma. 5 patients were tested 2 or 3 times successively during various stages of recovery. As the EMG criterium for reinnervation was used any appearance of volitionally recruited, (polyphasic, low amplitude) potentials.

ALS patients

The investigations were carried out on 22 patients with a definite diagnosis of ALS, 14 men and 8 women, aged 33 to 78, mean disease duration 10.9 months. All had a progressive neuromuscular disorder that clinically involved both the upper and lower motor neuron. Six patients showed mainly bulbar symptomatology, five patients showed primary involvement of the legs, and the remaining eleven patients had predominantly arm involvement. Other possible diagnoses were excluded by appropriate laboratory tests including serum protein and immunoelectrophoresis, lumbar puncture, and screens for intoxications. In the cases without bulbar involvement, either CT or MR imaging of the cervical spinal cord was performed, to exclude a local lesion. In most cases electromyography supported the diagnosis of ALS at first investigation, and in the remaining cases at follow up. The EMG showed signs of acute and chronic denervation with evidence of reinnervation in 3 or more limbs. Motor and sensory nerve conduction studies were normal, except
Muscle Fiber Conduction Velocity in Neurogenic Lesions

TABLE 1. Results of invasive MFCV measurements and standard deviation (SD) in traumatic lesions of the plexus brachialis.

<table>
<thead>
<tr>
<th></th>
<th>no reinnervation mean</th>
<th>SD</th>
<th>reinnervation mean</th>
<th>SD</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>mean (m.s⁻¹)</td>
<td>1.83</td>
<td>0.52</td>
<td>1.96</td>
<td>0.32</td>
<td>N.S.</td>
</tr>
<tr>
<td>slow (m.s⁻¹)</td>
<td>1.24</td>
<td>0.64</td>
<td>0.93</td>
<td>0.26</td>
<td>N.S.</td>
</tr>
<tr>
<td>fast (m.s⁻¹)</td>
<td>2.50</td>
<td>0.49</td>
<td>3.76</td>
<td>0.62</td>
<td>&lt;.0005</td>
</tr>
<tr>
<td>ratio</td>
<td>2.32</td>
<td>0.76</td>
<td>4.36</td>
<td>1.36</td>
<td>&lt;.0008</td>
</tr>
<tr>
<td>spikes pro ins</td>
<td>20.2</td>
<td>6.7</td>
<td>33.4</td>
<td>11.3</td>
<td>&lt;.0032</td>
</tr>
<tr>
<td>n</td>
<td>10</td>
<td></td>
<td>14</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Statistical analysis: Mann-Whitney test, unpaired samples, 2-tailed
Abbreviations: mean: mean I-MFCV, slow: mean of slowest measured fibers, fast: mean fastest fibers measured, ratio: mean ratio between fastest and slowest fibers measured, spikes pro ins: number of spikes pro insertion, n = number of investigations, N.S. = not significant

for reduced compound muscle action potentials in the more atrophic muscles. Special attention had been given to exclude patients with nerve conduction blocks.

Controls
Normal values were derived from a group of 28 healthy individuals, 18 men and 10 women, without complaints about their neuromuscular system. Age 34 to 74, mean 47.0 years. The control group had been age matched with the ALS patient group to allow a direct comparison between them. All measurements, both in controls and patients, were performed after obtaining informed consent.

MFCV estimation

1. Invasive Method
Experiments were performed in the brachial biceps (short head) muscle at rest. We used a modified method of Troni et al. (1983a) on a Nicolet EMG apparatus (Viking I). A stimulation needle electrode (Dantec 13L64, area of uninsulated tip: 2 mm²), was placed in the distal part of the muscle. A silver surface electrode was used as anode 10 to 15 mm distally. The muscle was stimulated with gradually increasing strength (suprathreshold), until a clear twitch was palpable (1 - 2 mA, 0.2 msec, 1 Hz). Guided by the twitch, a small concentric needle electrode (Dantec 13L58) was placed 50 - 60 mm proximal and manipulated until reproducible polyphasic action potentials were seen, amplitudes 20 - 500 µV. The signals were amplified and bandpass filtered, 500 Hz - 10 kHz; the time base varied between 5 - 10 msec per division. Care was taken to place the electrodes perpendicular to the skin. A 4-trace storage was used to ensure the exact reproducibility of the action potentials. Only spikes larger than 20 µV of a representative sample were used for
calculations. All latencies were measured at the positive turning points and resulting invasive MFCV (I-MFCV) was calculated. As parameters were used mean I-MFCV, fastest and slowest I-MFCV, and ratio fastest / slowest I-MFCV (F/S ratio), indicating the scatter in conduction velocities.

2. Surface method
The experiments were performed on the biceps brachii muscle. The arm was fixed in a horizontal semiflexed position with an angle of 120 degrees, supported at the elbow and the wrist. The isometric force of the elbow flexion was measured at the wrist. The exerted force was displayed in front of the subject on a voltmeter and simultaneously recorded on paper. Three silver electrodes (diameter 2 mm) were placed in a rigid bipolar array with a common centre electrode, interelectrode distance 10 mm. The localization of the electrodes was parallel to the fiber direction, nearly half way between the innervation zone and the distal tendon. The two EMG signals were differentially amplified (Disa EMG amplifier type 14C13) and bandpass filtered (20 - 500 Hz). The EMG signals were synchronously digitized by a 12-bit A/D converter with two different sample rates: 6024 Hz (velocity estimation) and 2048 Hz (power spectra) over two connected signal periods of 0.34 and 1.025 sec respectively. The surface MFCV (S-MFCV) was calculated from the delay of the two signals by the cross correlation method (Naeije and Zorn, 1983). Only correlation coefficients higher than 0.85 were accepted. The power spectrum was computed over the

![Figure 1. Relation between mean muscle fiber conduction velocity, invasive method (mean I-MFCV) and time after denervation (months). Squares: no signs of reinnervation (concentric needle EMG), triangles: with signs of reinnervation. Solid line: exponential decrease, T½=1.1 month, R²=0.95.](image-url)
Muscle Fiber Conduction Velocity in Neurogenic Lesions

frequency range of 5-250 Hz by application of the fast fourier transform over the digitized signal. The median frequency (Fmed) was calculated. All measurements were performed on different force levels in duplo: 20-30-50-75 and 100% MVC. The mean S-MFCV and the mean Fmed were calculated from the summarized data at the different force levels.

**Procedure**
All patients were examined with standard EMG techniques. Additionally, in the ALS patients the muscle force of the biceps brachii muscle was measured by a hand-held dynamometer according to a standardized procedure (Van der Ploeg *et al*. 1991). MFCV estimation was performed on the side with the lowest muscle force at elbow flexion. If the elbow flexion force was symmetrical, we tested the left side. If possible, we performed surface EMG on the same side.

**Statistics**
Differences between groups were analyzed by means of the Mann-Whitney non-parametric test, unpaired samples, 2-tailed (plexus lesions) and the Students t-test, unpaired samples, 2-tailed (ALS vs controls). Linear and non-linear regression analysis were used to test changes in time. Statistical significance was accepted at a level of 5%.

---

**TABLE 2.** Results of invasive (*I-MFCV*) and surface (*S-MFCV*) MFCV measurements in ALS patients and controls.

<table>
<thead>
<tr>
<th></th>
<th>ALS</th>
<th>SD</th>
<th>Contr</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>I-MFCV</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean (m.s⁻¹)</td>
<td>2.84</td>
<td>0.38</td>
<td>3.23</td>
<td>0.21</td>
</tr>
<tr>
<td>slow (m.s⁻¹)</td>
<td>1.38</td>
<td>0.32</td>
<td>2.77</td>
<td>0.29</td>
</tr>
<tr>
<td>fast (m.s⁻¹)</td>
<td>4.22</td>
<td>0.33</td>
<td>3.77</td>
<td>0.27</td>
</tr>
<tr>
<td>ratio</td>
<td>3.26</td>
<td>0.92</td>
<td>1.38</td>
<td>0.17</td>
</tr>
<tr>
<td>spikes pro ins</td>
<td>16.2</td>
<td>5.5</td>
<td>7.3</td>
<td>2.3</td>
</tr>
<tr>
<td><strong>S-MFCV</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S-MFCV</td>
<td>4.90</td>
<td>0.50</td>
<td>4.21</td>
<td>0.38</td>
</tr>
<tr>
<td>Fmed (Hz)</td>
<td>72.6</td>
<td>8.2</td>
<td>80.3</td>
<td>12.1</td>
</tr>
</tbody>
</table>

*Statistical analysis students t-test, unpaired samples, 2-tailed* *<0.0001, p=0.05. Abbrevations: Fmed: median frequency, see further table 1.*
RESULTS

Lesions of the plexus brachialis

All measurements were performed with the invasive method, due to the complete or nearly complete paralysis of the muscles investigated. The data are summarized in table I. In the non-reinnervation group we found a mean I-MFCV value of 1.83 (SD 0.52) m.s\(^{-1}\), in the group with reinnervation a mean I-MFCV value of 1.96 (SD 0.32) m.s\(^{-1}\). In the non-reinnervation group the mean I-MFCV showed an exponential decrease, T\(1/2\)=1.1 month, R\(^2\)=0.95 (fig. 1). Remarkable was the presence of very slow conducting fibers, 0.5 - 1.0 m.s\(^{-1}\), 5-6 months after denervation, without significant difference between the reinnervation and non-reinnervation group (fig. 2). In contrast, simultaneous with signs of reinnervation at concentric needle EMG, a group of faster conducting fibers was observed (fig. 3 and 4). This resulted in a significant rise in F/S ratio in the reinnervation group, mean 4.36 (SD 1.36) vs mean 2.32 (SD 0.76) in the non-reinnervation group. Both patient groups showed a clearly higher number of spikes pro insertion than the controls (fig. 5). This effect was most pronounced in the reinnervation group, see table I.
Invasive method

The data are summarized in table II. The patient group showed a significantly reduced mean I-MFCV. All patients showed the presence of slow conducting fibers in biceps brachii muscle. This resulted in a mean slowest I-MFCV value of 1.38 (SD 0.32) m.s\(^{-1}\), controls 2.77 (SD 0.29) m.s\(^{-1}\). At the same time the patient group showed also increased MFCV values in the fastest fibers measured. Mean fastest I-MFCV value 4.22 (SD 0.33) m.s\(^{-1}\), controls 3.77 (SD 0.27)m.s\(^{-1}\). This resulted in an increase of the mean F/S-ratio: 3.26 (SD 0.92) in the ALS patients vs 1.38 (SD 0.17) in the controls. A clear distinction between the ALS patients and controls can be seen when we plot fastest vs slowest I-MFCV results (fig. 6). In five subjects, we found an increased F/S ratio of the biceps in combination with unimpaired muscle force as measured with dynamometry (fig. 7) and without clear abnormalities with concentric needle EMG at visual examination. These patients had all a predominant bulbar or distal involvement. We found a slight, but not significant correlation between F/S ratio and disease duration (linear regression analysis). The patient group showed a significantly higher number of spikes pro insertion, patients 16.2 (SD 5.5), controls 7.3 (SD 2.3) (fig. 5). In 6 patients we measured both sides during the same investigation. All 6 patients showed the highest F/S ratio on the side with the lowest muscle force.
Chapter 5

Surface method
Data are summarized in table II. The patient group showed significantly higher S-MFCV values than the controls. This difference was most pronounced in men. In contrast the Fmed showed lower values mostly, but this difference was only marginally significant p=0.05).

Figure 4. Examples of muscle fiber conduction velocity determination, invasive method, biceps brachii muscle. Two traces superimposed. A. Normal control. Note a 'late', not reproducible potential. B. ALS. Note the combination of shorter and longer latencies compared to the normal control. C. Plexus lesion, no signs of reinnervation, 22 months after denervation. D. Plexus lesion during reinnervation, 28 months after denervation.
DISCUSSION

We measured the conduction velocity along human muscle fibers with both an invasive and a noninvasive method. Previous studies have shown its applications in myopathies characterised by a disturbed membrane function (Troni et al. 1983b; Zwarts et al. 1988). In this study it was our aim to describe the changes in neurogenic lesions. The invasive method has the advantage of non-volitional, direct muscle activation. The fact that measured action potentials are the consequence of direct muscle fiber stimulation is supported by the following arguments: (1) Anatomical experiments (Aquilonius et al. 1984) and multi-electrode surface EMG registrations (Masuda et al. 1983), show a well defined end-plate zone in biceps brachii muscle of 5-10 mm width nearly half way the muscle. The end plate broadening during neurogenic lesions is supposed to be delimited to maximally 20-25 mm. (2) During stimulation with decreasing strength a gradual disappearance of the spikes is found, which argues against indirect neural excitation ('all or nothing' effect). (3) Troni et al. (1983) have shown that curarization did not influence the results. (4) Measured MFCVs are well within the range as found by others, who use different techniques (Arendt-Nielsen and Zwarts 1989).

After complete traumatic lesions of the brachial plexus we found an exponential decrease of the mean I-MFCV, \( T_{1/2} = 1.1 \) month, with only a moderate increase in F/S ratio. Slowest I-MFCV values measured were around 0.5-0.6 m.s\(^{-1}\). During reinnervation the mean I-MFCV increases (fig. 1). A remarkable observation is a clear increase in F/S ratio, on the basis of the return to faster conduction velocities in combination with the continued presence of slow conducting fibers (fig. 4).

Buchthal and Rosenfalck (1958) studied impulse conduction in partially and completely denervated human muscle, after brachial plexus lesions. The minimum rate of conduction decreased until 5 months after the lesion, from one half to one fifth of the normal value. Troni et al. (1983a), also showed a slowing down of conduction in a completely denervated biceps muscle.

Several factors can be responsible for the decay of the MFCV. After denervation of muscle fibers a rapid decrease of the resting membrane potential is found, within some days (Sellin and Thesleff 1980; Stanley and Drachmann 1980). This partial depolarization is accompanied by a slowing down of conduction velocity (Gruener et al. 1979). Moreover, muscle fiber atrophy will result in a decrease of the MFCV (Håkansson 1956). In their study of rats, Stonnington and Engel (1973) found a rapid decrease in mean fiber area during the first three weeks after denervation, followed by a further slow decrease afterwards. This time course suggests, that the fiber atrophy is the most important of these two factors. Additionally, changes in depolarization rate and capacitance probably add to the decline of the MFCV after denervation (Gruener et al. 1979; Sellin and Thesleff 1980).

In the group of ALS patients we found an increased range of velocities, consisting of a combination of 'slow' potentials, with a reduced MFCV and relatively 'fast' potentials with a higher MFCV than an age-matched group of normal subjects. This resulted in an increased F/S ratio. In some subjects we found an increased F/S ratio without clear abnormalities with concentric needle EMG at visual examination, and unimpaired muscle force when measured with dynamometry, which suggests subclinical involvement of the biceps muscle. It is well known that in ALS the process of denervation and reinnervation results in a large muscle fiber diameter variation. Patten et
al. (1979) found a reduced mean diameter of both type I and type II fibers, in combination with excessive variation of fiber diameters. Hansen and Ballantyne (1978) showed that reinnervation is sufficient to compensate completely for the loss of up to 50% of the motor neuron pool supplying the muscle. Stålberg et al. (1975) performed a SFEMG study in anterior horn cell diseases, including ALS. In 5-10% of the potentials they found a 'late' component following the initial fiber component of the complex. With a multi-electrode they showed a progressive slowing down of the propagation velocity in these later components, to approximately 1 m.s⁻¹. They suggested that these values were caused by atrophic fibers. Our findings are well matching these values.

Application of the above mentioned mechanism to the ALS patients suggests the following explanation of the I-MFCV findings. The loss of motor neurons results in denervated, and consequently slower conducting muscle fibers, thus increasing the F/S ratio. The neuropathic changes by concentric needle EMG during voluntary activity are the result of reinnervation. The early neurogenic changes in the motor units (MUs) are often difficult to detect at visual examination (Partanen and Nousiainen 1990). Additionally, spontaneous activity found after denervation is not always present. Its occurrence depends on different factors, among others, the temperature (Purves and Sakmann 1974; Buchthal 1982). This contrasts with changes in MFCV which can be measured easily, independent of voluntary activation and spontaneous activity of the muscle fibers.

Remarkable was the clearly increased number of spikes pro insertion in both patient groups (fig. 4 and 5). We suggest two explanations. In the controls the F/S ratio is low, based on relatively small differences in the conduction velocity of the muscle fibers, which results in superposition of

![Figure 5. Number of spikes pro insertion in the controls (contr) vs the 3 patient groups; ALS patients, traumatic plexus lesions without (Denerv) and with signs of reinnervation (Reinnerv) by concentric needle EMG. Horizontal bars indicate the mean value.](image)
single fiber potentials. This can be shown by reducing the stimulus strength, which results in a changed potential amplitude and shape, but with a constant latency. An increased range of conduction velocities will result in an increased number of visible potentials. This effect will be enhanced when the distance between stimulation and recording electrode is increased. An alternative explanation is found in the electrical properties of denervated muscle fibers. After denervation, the membrane potential is lowered, and, in addition, the critical level for action potential generation is increased (Thesleff and Ward 1975). These phenomena will result in an increased number of activated fibers.

We have interpreted the 'late' potentials as evidence for the presence of slow conducting fibers. This interpretation is, however, debatable. Trontelj and Stålberg (1983) studied responses of denervated human muscle fibers to electrical stimulation with single fiber EMG. Besides slow conducting fibers, they suggested some other causes of 'late' responses. One type was considered to be an extra-discharge of the same fiber. The jitters of these extra-discharges were quite large, varying from 0.5 to 10 ms. In our investigation, we excluded potentials with such jitter values by routinely superimposing four consecutive traces. Additionally, sometimes they found late potentials, which at threshold stimulation appeared and disappeared together (linked potentials). They suggested as most likely explanations recording from two branches of a split muscle fiber or ephaptic transmission between different muscle fibers at 'low threshold' sites. An increase in stimulus strength brought about a shortening of latency, explained as a direct activation of the second fiber. Although we checked carefully for the existence of linked potentials by varying stimulus strength, this phenomenon cannot be excluded completely in a multi-spike recording. The

**Figure 6.** Plot of fastest conducting fibers (fastest I-MFCV) vs slowest conducting fibers (slowest I-MFCV) of ALS patients and controls.
phenomenon of fiber splitting is supposed to be uncommon in neurogenic lesions (Dubowitz and Brooke 1973).

In our surface EMG experiment, we found an increased mean S-MFCV in the group of ALS patients. The mean Fmed showed decreased values. The opposite findings in invasive (reduced I-MFCV) and surface (increased S-MFCV) measurements can be explained as follows. With the invasive technique both denervated and innervated fibers are measured as a consequence of the electrical stimulation. This is supported by the I-MFCV findings: a combination of slow and fast conducting fibers, which seems to be the result of a combination of MU loss (atrophy) and adaptation of the surviving units (hypertrophy). With the surface method only the voluntarily recruited fibers can be measured. Additionally, the S-MFCV values are biased by the fastest conducting fibers (Zwarts 1989). This suggests that the increase in S-MFCV is a manifestation of the fiber hypertrophy. Remarkable is the simultaneous decrease of the Fmed in the ALS patients group. This seems contradictory, since most studies clearly show a positive correlation between S-MFCV and Fmed (Arendt-Nielsen and Mills 1985; Zwarts et al. 1987; Yaar and Niles 1992). This discrepancy between change in S-MFCV and Fmed can have different reasons. First, effective reinnervation will lead to an increase of MU potential duration and amplitude causing a decrease of the Fmed (Hermens et al. 1992). Secondly, alterations in MU firing patterns can change the Fmed. Reiners et al. (1989) showed selective impairment of rate modulation in lower motor neuron disease. The onset firing rates as well as the highest firing rates were decreased. This will result in a

Figure 7. Relation between muscle force of elbow flexors as measured with dynamometry and ratio between fastest and slowest conducting fiber (F/S ratio) in biceps brachii. The muscle force is normalized at the fifth percentile value of normal controls (males 216 N, females 146 N, according Van der Ploeg et al. 1991). Horizontal dotted line: 5 percentile value of normal controls. Vertical dotted line: F/S ratio + 2 SD. Note the cases with (near) normal muscle force in combination with increased F/S ratio.
Muscle Fiber Conduction Velocity in Neurogenic Lesions

decrease in Fmed. Thirdly, an (hypothetical) increased tendency to synchronisation of the remaining MUs can also play a role.

In conclusion we found clear MFCV abnormalities after neurogenic lesions. After complete lesions of the plexus brachialis the mean I-MFCV decreases exponentially (T½=1.1 month). During reinnervation fibers with increased conduction velocities in combination with slow-conducting fibers were found. When the ALS patients were studied with the invasive method an increased range of velocities had been demonstrated as well: slow-conducting, probably atrophic fibers after denervation, in combination with increased velocities, suggesting muscle fiber hypertrophy as a compensation for the loss of muscle force. With the surface method we found increased MFCV values in combination with a decrease of the Fmed. The increased S-MFCV values seem to be dependent on the muscle fiber hypertrophy. The simultaneous decrease of the Fmed could be explained on the basis of shape changes of the MU potentials, in combination with central factors such as a decreased MU firing frequency and (possibly) an increased tendency towards synchronisation.

REFERENCES