Electrophysiological study after surgical repair of sectioned human peripheral nerves

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SUMMARY Clinical and electrophysiological assessment of recovery of function are reported on 20 patients with median or ulnar nerve sections up to 53 months after surgical repair. Maximum improvement of sensory function was apparent by both methods of assessment at 15 months after suture, and thereafter conduction velocities in sensory fibres averaged 80% of normal in median nerves and 70% of normal in ulnar nerves. Similarly, the mean amplitude of the sensory action potential at the wrist remained depressed at 15% of control values. The clinical recovery of motor function pursued a similar time course with, however, some evidence to indicate a continuing improvement in the neurophysiological maturation of the motor nerve fibres up to 47 months after repair. The results are discussed in relation to previous electrophysiological studies on animals.

The recovery of function after traumatic peripheral nerve injury has been assessed clinically both in civilian practice (Nicholson and Seddon, 1957; Edshage, 1968) and in the war-injured (Seddon, 1954). Little information is, however, available concerning neurophysiological details of recovery or how these might correlate with the clinical findings. While there is also a considerable literature based on animal experimentation with a variety of peripheral nerve injuries (Berry *et al.*, 1944; Guth, 1956; Cragg and Thomas, 1964; Jacobson and Guth, 1965; Grabb, 1968), there remains a relative lack of information on the electrophysiological maturation of sectioned and resutured regenerating nerve fibres in humans.

The present investigation was planned to measure the degree of recovery in regenerated human nerves after traumatic section and surgical repair. Quantitative electrophysiological studies of motor and sensory conduction and of the recovery of nerve action potentials have been performed on the median and ulnar nerves in twenty subjects.

METHODS

The fastest motor conduction velocity in the median and ulnar nerves was measured using standard

techniques with recording of the evoked motor response in the abductor pollicis brevis or hypothenar muscles respectively (Hodes *et al.*, 1948). For the determination of terminal motor latency, the stimulating electrodes were placed distal to the site of the nerve lesions.

Sensory nerves were studied both orthodromically and antidromically. Orthodromic studies were made by surface stimulation of the digital nerves using silver strip ring electrodes (Dawson, 1956). The thumb, index, and middle fingers were studied in the case of the median nerve, and the little finger for the ulnar nerve. The sensory nerve action potentials (SNAP) were recorded from 0.5 cm diameter saline-padded silver electrodes situated 3 cm apart over the nerve at the wrist with the stigmatic electrode below the site of the lesion. A rectangular electrical stimulus 0.1 msec in duration and two to three times the threshold voltage was used. Antidromic studies were made simply by reversing the sites of stimulation and recording using the same electrodes. In these studies, stimuli were supramaximal for the motor response. The mixed nerve action potential (MNAP) evoked by stimulation of the nerve trunk at the wrist was recorded above the elbow using saline-padded silver surface electrodes as above. A similar electrode was used for stimulation, with the cathode distal to the site of the injury. Rectangular stimuli of 0.1 msec duration were delivered by an isolated constant current stimulator (Devices) triggered by an

external time signal (Digitimer). Stimuli were supra-maximal by 20% for the motor response; larger stimuli were not used to avoid stimulation of the nerve trunk proximal to the electrodes, and to reduce the possibility of concomitant stimulation of adjacent nerve trunks, especially that of the radial nerve in the case of sensory studies.

Potentials were amplified by a low noise amplifier, having a 2–3 μ V noise level with a 5 kHz filter, and displayed on a storage oscilloscope (Tektronix 564), together with an external time signal on a separate channel. For the nerve action potential studies (MNAP and SNAP) the peak to peak amplitude of the potential and the latency to the onset of the initial negative response were recorded. The velocity was calculated over the corresponding distance between electrodes.

All studies were repeated on the corresponding nerve of the contralateral normal limb so that each parameter could be matched with a control value obtained from the same subject. The results have been expressed as a percentage of these internal controls. Mean values have been expressed together with standard errors of the mean. The investigations were

conducted in a thermostatically controlled room and skin temperatures were recorded with a surface thermister. Where necessary the temperature was adjusted to $37 \pm 0.1^\circ$ C with an infra-red lamp.

PATIENTS Twenty patients were investigated aged 15 to 53 (30.9 ± 3.0) years. Fourteen patients had sustained complete section of the median nerve at the wrist four to 47 (mean 26 ± 4.2) months before. Eight patients had sustained complete ulnar nerve section 13 to 53 (31 ± 4.4) months before. All patients had undergone surgical exploration and repair. In the median nerve group 12 repairs were by primary and two by delayed secondary suture, while in the ulnar group six primary and two secondary sutures had been performed.

Muscle power in the abductor digiti minimi (ADM) or abductor pollicis brevis (APB) was graded clinically 0 to 5 according to the MRC scale (Seddon, 1954), while sensory loss was estimated in terms of the area of loss to pinprick and light touch, and its intensity noted as mild, moderate, or severe, depending on the patient's subjective response. Tests of two-point discrimination were made with the calipers

TABLE
MEAN VALUES $\pm$ SEM

	Controls	Sutured nerves	<i>t</i> (paired test)	<i>P</i>
<i>Median nerves (14 subjects)</i>				
Motor latency				
(wrist to abductor pollicis brevis) (msec)	2.90 $\pm$ 0.23	4.00 $\pm$ 0.33	3.9542	< 0.01
Motor conduction velocity				
(elbow to wrist segment) (m/sec)	56.38 $\pm$ 1.80	56.70 $\pm$ 4.14	0.1847	NS
Antidromic sensory conduction velocity:				
Thumb–wrist (m/sec)	44.70 $\pm$ 1.93	56.70 $\pm$ 4.14	0.1847	< 0.02
Index–wrist (m/sec)	52.85 $\pm$ 1.32	40.87 $\pm$ 3.21	3.7981	< 0.01
Middle–wrist (m/sec)	51.09 $\pm$ 1.41	42.84 $\pm$ 2.30	3.2943	< 0.01
Orthodromic sensory nerve action potential amplitude:				
Thumb–wrist (μ V)	33.5 $\pm$ 2.56	3.09 $\pm$ 0.86	10.1593	< 0.001
Index–wrist (μ V)	18.75 $\pm$ 1.74	2.10 $\pm$ 0.90	8.3397	< 0.001
Middle–wrist (μ V)	23.31 $\pm$ 3.92	2.04 $\pm$ 0.86	5.0450	< 0.001
Mixed nerve action potential conduction velocity				
(wrist to above elbow) (10 subjects) (m/sec)	63.84 $\pm$ 2.45	57.54 $\pm$ 2.04	3.1281	< 0.05
Mixed nerve action potential amplitude				
(wrist to above elbow) (μ V)	47.28 $\pm$ 7.46	13.86 $\pm$ 2.41	5.0291	< 0.01
<i>Ulnar nerves (8 subjects)</i>				
Motor latency				
(wrist to abductor digiti minimi) (msec)	2.44 $\pm$ 0.13	3.73 $\pm$ 0.24	4.8984	< 0.01
Motor conduction velocity				
(below elbow to wrist segment) (m/sec)	57.33 $\pm$ 2.43	59.36 $\pm$ 6.63	0.2885	NS
Antidromic sensory conduction velocity				
(wrist to 5th digit) (m/sec)	54.20 $\pm$ 2.31	37.6 $\pm$ 5.03	4.0079	< 0.01
Orthodromic sensory nerve action potential amplitude (5th digit) (μ V)	12.63 $\pm$ 1.93	1.65 $\pm$ 0.62	5.3140	< 0.01
Mixed nerve conduction velocity				
(wrist to below elbow) (6 subjects) (m/sec)	59.97 $\pm$ 3.32	60.37 $\pm$ 6.65	0.0457	NS
Mixed nerve action potential amplitude				
(wrist to below elbow) (μ V)	57.00 $\pm$ 13.47	22.50 $\pm$ 5.45	3.1034	< 0.05

FIG. 1. (a) Peripheral motor latencies as percentage of control values. (b) Fastest motor conduction velocities as percentage of control. ● Median nerves. × Ulnar nerves.

separated by 4 mm on the thumb, index, and middle fingers in the case of a median nerve lesion, and on the fifth digit only for the ulnar nerve. Each finger was tested on five occasions and the number of correct scores recorded. The contralateral normal limb was used as control.

RESULTS

MOTOR NERVE STUDIES *Distal motor latencies* (Table, Fig. 1) In the case of two patients examined four and six months after median nerve lesions, no muscle response in the hand could be obtained to indirect stimulation of the nerve. The latencies in patients at 10 to 20 months after median nerve injury remained in excess of normal, decreasing from 233% to 118% of control values over this period, while even after 40 months only two of five patients had a distal latency equivalent to control values. A progressive decrease in the ulnar distal motor

latencies was found from a high of 204% at 13 months to a low of 115% at 36 months, but nevertheless normal values were not found even at 53 months.

Conduction velocity in the fastest motor fibres (Table, Fig. 1) The forearm conduction velocity could first be measured at 10 months and thereafter the values obtained were comparable with those of the controls. Abnormally fast conduction proximal to the site of injury was estimated in three patients at 30, 42, and 45 months respectively, probably as a result of technical difficulties in stimulating the nerve at the site of injury or due to aberrant innervation from cross-anastomosis between the ulnar and median nerves.

CLINICAL ASSESSMENT OF POWER (Fig. 2) In only two of the median nerve group, at 42 and 47

FIG. 2. Clinical assessment of power. (Top) Muscle power (MRC grading). (Bottom) TPD objective sensory testing. Score as percentage control side. ● APB. ✕ ADM.

months, was power in the APB thought to be in the normal range (grade 5). After 30 months two patients had obtained only grade 3 power or less, while, conversely, four patients studied between 10 and 15 months after injury had regained power of grade 4–4+. In the patients with ulnar nerve lesions, power in the ADM muscle remained subnormal in all patients, grade 4 being the best obtained.

SENSORY STUDIES Median nerve sensory conduction velocities (Table, Fig. 3) We were unable to demonstrate a sensory response to stimulation before 10 months in any digit, while at 10 months a small antidromic response only was obtained from the thumb and middle fingers alone of one patient. The conduction velocities in the regenerated fibres lie mainly between 60 and 95% (mean $80.8 \pm 2.9\%$) of controls, with little evidence that further improvement occurred with the passage of time. The antidromic method was

adopted for the assessment of sensory conduction velocity, since a potential could often be detected by this technique when no recordable response to orthodromic sensory stimulation was obtained. In all patients the antidromically-evoked action potential (SNAP) was of shorter latency than the muscle response. However, since the deflection due to the onset of the muscle action potential at times occurred within the duration of the SNAP, only SNAP amplitudes obtained from the orthodromic studies have been considered in the statistical analysis. These values have been used for the purpose of estimating the number of regenerated large diameter myelinated fibres. In these studies (Table, Fig. 4), a SNAP was not obtained before a lapse of 10 months, but later studies gave values up to 30% of control amplitude with no tendency to larger potentials with prolonged follow-up. Only three patients had a median SNAP above 30% of control value in a single digit each. There was no

FIG. 3. Antidromic sensory conduction velocities as percentage of control values. ● Thumb. ○ Index finger. □ Middle finger. × Fifth finger.

FIG. 4. Orthodromic sensory action potential amplitudes as percentage of control values. ● Thumb. ○ Index finger. □ Middle finger. × Fifth finger.

consistent trend for a better recovery in one digit rather than another.

Ulnar nerves Six of the eight subjects had sensory conduction velocities below 70% of normal (mean $67.5 \pm 8.5\%$) with no consistent improvement in the values over the 53 months. The amplitudes of orthodromically evoked SNAP were below 40% in all patients, and in three patients at 30, 36, and 42 months were still unobtainable.

CLINICAL ASSESSMENT OF SENSORY FUNCTION (Fig. 2) All patients complained of a sensory deficit to pinprick and cotton wool which varied from mild to severe, but no further attempt was made to quantitate this aspect of sensory loss more accurately. However, since two-point discrimination (TPD) is a more accurate method of quantitating sensory loss in peripheral nerve lesions (Seddon, 1954), this objective assessment was used. The correct scores out of five attempts for each digit have been expressed as a percentage of the control hand; in the case of the

median nerve results from thumb, index, and middle fingers were pooled. In the median nerve territory it is apparent that, apart from a severe loss of TPD below 10 months, the score there after remains below 70% of normal and does not improve over subsequent months. In the ulnar nerve territory there may be some improvement with the passage of time, but the value still did not exceed 50% of the control.

EVOKED MIXED NERVE ACTION POTENTIALS (Fig. 5) The conduction velocity in the median nerves showed a moderate reduction compared with the control values ($91 \pm 2.6\%$). There was no tendency to significant improvement with the passage of time. The values in the ulnar nerves were comparable with those of the controls.

In contradistinction to the sensory studies, the amplitude of the mixed NAP showed a progressive rise over the period of follow-up. This was more apparent in the median nerve group where a value of 87% of normal was reached at 47 months. The change was less distinct in the recovering ulnar nerves where one exceptionally

FIG. 5. (a) Evoked nerve action potential conduction velocity as percentage of control side. (b) Evoked mixed nerve action potential amplitudes as percentage of control side. ● Median. × Ulnar.

high value (122%) linked with a low normal response distorts the results.

DISCUSSION

Nicholson and Seddon (1957), in a report of their extensive experience of the results of surgical repair of the median and ulnar nerves in civil practice, found that good recovery of power (grade 4 or better on the MRC scale) had occurred in approximately 30% of subjects by three years. The recovery had been progressive over this period, and further but much slower improvement was present up to five years after suture. The recovery of sensory function followed a similar pattern. We have not found this pattern of recovery in our patients, where a plateau of improvement in power and sensation (as measured with two-point discrimination) was found by 15 months after injury, with no subsequent improvement of note. In the additional light of our electrophysiological studies we feel that a full clinical assessment of recovery from nerve injury at the wrist can be made by 15 to 18 months. While the numbers in the present study are small, we found no indication that age or method of surgical repair (primary or secondary suture) was of importance in the eventual outcome. This is in agreement with Nicholson and Seddon (1957).

Terminal motor conduction, as measured by distal motor latency to nerve stimulation, is determined by the conduction in the largest motor fibres and the delay at the neuromuscular junction. Impairment in either or both of these parameters may be responsible for the distal delay in conduction in regenerated nerves. Berry *et al.* (1944), in studies on cats after nerve section and suture, found progressive recovery of conduction velocity with time, corresponding to progressive increase in fibre diameters, but at 466 days the fastest conduction velocity remained at only 80% of normal. Hodes and others (1948) similarly found reduced conduction velocity at 60% of normal after regeneration in humans. Cragg and Thomas (1964), in studies of regeneration after crush injury to the peroneal nerve of the rabbit, found that the conduction velocity distal to the site of injury was only 75% of that in the contralateral control nerve at 12 months, and showed no further improvement in animals at 16

months after injury. The largest fibre diameters of the regenerated nerves were similar at both 12 and 16 months, at nearly 90% normal, but the internodal length of the regenerated nerves was less than 50% of control values for the corresponding fibre diameters. They estimated that the myelin thickness in relation to axon diameter was very nearly normal by 16 months. However, Schröder (1972) in morphological studies on dogs of sciatic nerve regeneration after suture and nerve grafting, found that, whereas the mean diameter of regenerated axons reached 79% of normal by 12 months, that of the myelin sheaths was only 57%. No further significant increase in the average maximum fibre diameter or in the thickness of the myelin sheath occurred between 12 and 24 months after grafting. This striking reduction of the thickness of the myelin sheath was present on the largest regenerated nerve fibres as well as the latter being reduced from normal diameter. Rushton (1951) had calculated on theoretical grounds that a decrease in the thickness of the myelin sheath would reduce conduction velocity to a greater extent than a similar decrease in the axon diameter. Hence Schröder suggested that the reduced conduction in regenerated nerve fibres was mainly due to the decreased thickness of the myelin sheath. Defects in neuromuscular transmission have also been reported after human nerve regeneration (Hodes, 1948) and intermittent failure of transmission in experimental regeneration was found by Dennis and Miledi (1971). It thus appears that several factors may play a part in the incomplete motor recovery, as shown by the prolonged distal motor latency in our studies, but we have no information of the effect of repetitive nerve stimulation in our patients.

The mean sensory conduction velocity in the regenerated nerves of this study was 80% of normal in the median nerve and 70% in the ulnar, comparing closely with values of 80% by Berry *et al.* (1944), and 75% obtained by Cragg and Thomas (1964). Furthermore, the velocity in our studies showed no significant improvement after 10 months from the time of suture. The fastest motor conduction velocities of the main nerve trunks were all within the normal range, indicating no block in conduction at the level of the lesion and no gross slowing over the small segment of regenerating fibres. Unusually fast

conduction was estimated in two median nerves compared with controls, but this was almost certainly due either to branching between the main motor nerves in the forearm or incomplete stimulation of the distal motor fibres within the scar tissue. The fastest velocity in the combined motor and sensory fibres, as measured in the MNAP studies, was similarly close to normal, but surprisingly a progressive increase in the amplitude of the response was found.

In a normal nerve, the amplitude of the evoked action potential is an indication of the number and size of the nerve fibres (Jacobson and Guth, 1965). In a regenerated nerve, the full normal fibre diameters are not attained, and the distribution of fibre size after experimental nerve section and suture remains defective (Gutmann and Sanders, 1943; Cragg and Thomas, 1964). However, in the absence of marked slowing of conduction and temporal dispersion of the NAP, the amplitude of the response evoked by stimulation of the regenerated nerve segment is an index of the number of functional regenerated fibres. The sensory nerve action potentials were all significantly reduced in amplitude and were mainly below 40% of the contralateral control values, with an overall mean of 15% after 15 months. These results compare with the 20% of normal values found by Jacobson and Guth (1965) in the sciatic nerves of the rat. The mixed nerve action potentials, although less reliable because of possible stimulation of proximal nerve fibre stumps at the wrist, similarly showed a reduced amplitude response at a mean of $42 \pm 8\%$ of normal after 12 months. In contrast with the SNAP studies, however, there was evidence of a progressive increase in the MNAP amplitude with time. We are uncertain of the explanation for this finding in view of the absence of such a change in the sensory nerves alone. The terminal motor fibres did, however, show a progressive maturation with a progressive decrease in the distal motor latency, and we assume that the sequential improvement in the amplitude of the MNAP must be related to this. Also, narrowing of nerve fibres for a distance proximal to a chronic constrictive lesion has been reported in animals (Anderson *et al.*, 1970). The slow recovery of the mixed NAP may be related to recovery in these fibres and subsequent synchronization of the evoked responses. However,

it would appear that with sensory reinnervation after nerve section and regeneration there is a permanent reduction both in the number of functional large diameter fibres and in the fibre diameter. The maximum recovery in nerve lesions at the wrist occurred by 15 months, and we were unable to detect electrophysiological evidence of sensory recovery in the digits before 10 months after injury. This interval is comparable with findings in the radial nerve in which Downie and Scott (1964) were unable to detect a sensory response 6 to 11 months after a traumatic lesion in continuity. A corollary of these findings is that where there is total absence of electrophysiological evidence of nerve regeneration with traumatic lesions of nerves at the wrist by 12 to 15 months, the site of the lesion should be explored and nerve grafting considered.

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