Axonal excitability and motor propagation velocity of peripheral nerves in patients with acute vascular lesions of the brain

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SYNOPSIS From measurements of maximum and minimum motor nerve propagation velocity and neuronal excitability we conclude that there is a functional loss of motor units and distal nerve 'dying back' in persons affected with unilateral acute cerebral vascular lesions. The study also suggests that transynaptic degeneration affects the lower motor neurone function on both sides.

The aim of the work reported here was to study, by means of conventional electrophysiological techniques, the changes in axonal excitability and motor propagation velocity of the motor unit (MU) in patients with acute vascular lesions of brain.

Some investigations have been already carried out in patients with cerebrovascular lesions by McComas *et al.* (1971b) and in spinal cord vascular diseases by Gay and Silberberg (1964), Fenichel *et al.* (1964), and Hausmanova-Petrusewicz and Kopec (1971).

In some cases the histological changes in muscle have also been studied (Serratrice *et al.*, 1975; Scarlato *et al.*, in press). In our study we measured the dispersion of motor propagation velocity by the method previously used for the ulnar nerve by Namba *et al.* (1971).

METHODS

PATIENTS Nine patients (five men and four women) with a mean age ($\pm$ SD) of 63 ± 5 , all affected with an acute cerebral vascular lesion, were studied. The lesions included eight cases of stroke and one of left internal carotid thrombosis. Patients with a history of compressive neuropathies or of limb trauma were excluded.

Blood chemistry examinations for metabolic disorders, including kidney and liver function tests, were normal in all cases.

The patients had a first control examination 20 days after the onset of the stroke. All had motor disabilities, flaccid hemiplegia in seven cases and hemiparesis with upper-limb spasticity in two. In only two cases was epicritic and protopathic sensation affected on the side of motor impairment. In two cases the lesion, localized on the dominant side, had caused some 'parietal-type' impairment of speech. Six of the nine patients were examined again after six months. Two patients had died meanwhile and one patient refused a second examination.

TECHNIQUES In all patients the ulnar and the external popliteal nerves were studied on both the healthy and impaired side by means of stimulation and recording techniques with surface electrodes and the following were measured: (1) maximum motor propagation velocity; (2) dispersion of motor propagation velocity by the Hopf (1962) method of 'incomplete antidromic block', expressed in metres per second; (3) dispersion of motor conduction velocity by the method of desynchronization of the distal and proximal electrical response amplitudes (Pinelli, 1953); (4) proximal and distal latency of the electrical response; (5) proximal and distal amplitude of the electrical response; and (6) index of functioning motor units (McComas *et al.*, 1971a).

The stimulation and recording were performed by a Medelec MS6 four-trace electrophysiological unit. All physiological reactions were measured on Polaroid photographs taken from a Tektronix 603 storage oscilloscope. Temperature was also measured on the recording sites by a thermoelectric couple connected to a metering device; the temperature was kept constant at 37°C by a source of infrared rays.

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Stimulation was performed by Hopf's method with bipolar surface electrodes connected to a single and double delayed constant current stimulator, type Medelec NT6-NS6. Recordings were made with a pair of silver ribbon electrodes applied to the carefully cleaned skin of the hypothenar eminence (stigmatic electrode) and the fifth finger (reference electrode) for the ulnar nerve, and over the extensor digitorum brevis muscle of the foot (stigmatic electrode) and the medial sole (reference electrode) for the external popliteal nerve.

The significance of the data was statistically evaluated from the means, standard errors of means, and *P* (Student's *t* test) given in confidence limits of *P* as follows: NS=not significant; <0.05=low significance; <0.01=highly significant; <0.0051=very highly significant.

RESULTS

The maximum propagation velocity of the ulnar and external popliteal nerves did not show any significant difference at the first and second control examination when the healthy and impaired sides were compared (Table 1). Surprisingly, however, there was a significant decrease in maximum propagation velocity for both the impaired and the healthy limbs between the first and second examination.

The study of the dispersion of motor propagation velocity with Hopf's method showed a significant difference between the impaired (18 ± 2) and healthy limbs (12.7 ± 2) for the external popliteal nerve only

at the first examination. This difference was not seen at the second examination and the ulnar nerve results were unchanged. Comparison of the values for the external popliteal nerve in the healthy limbs at the two examinations shows that there was a significant increase in dispersion after six months. This did not occur in the impaired limbs. There was an increase in dispersion in the ulnar nerve on both the healthy and impaired sides at the second examination (Table 1).

The study of dispersion with the method of desynchronization of the amplitudes gave results similar to those with the method of antidromic block (Table 1).

The results of the study of proximal and distal motor latencies are shown in Table 2.

1. The proximal latency did not show any significant difference between the healthy and impaired sides for either the ulnar or the external popliteal nerve at either examination. However, the proximal latency increased significantly on both the impaired and healthy sides during the six months from the first control examination, as was seen in the maximum motor propagation velocity.

2. At the first examination there was a significant difference in distal motor latency for the external popliteal nerve between impaired (4.7 ± 0.1 ms) and healthy limbs (4.0 ± 0.3 ms), but this was not so for the ulnar nerve. However, at the second examination the ulnar nerve also showed a significant difference between the impaired (3.5 ± 0.0 ms), and healthy sides (3.0 ± 0.15 ms). Hence, the distal latency also increased significantly on both sides during the six months (Table 2).

TABLE 1

DIFFERENCES IN MEAN ($\pm$ SEM) MAXIMUM MOTOR PROPAGATION AND DISPERSION OF PROPAGATION VELOCITIES BETWEEN HEALTHY AND IMPAIRED SIDES AT FIRST AND SECOND CONTROL EXAMINATIONS (*P*: STUDENT'S *t* TEST)

First examination (9 cases)				Second examination (6 cases)			
Ulnar nerve		External popliteal nerve		Ulnar nerve		External popliteal nerve	
Healthy	Impaired	Healthy	Impaired	Healthy	Impaired	Healthy	Impaired
(1) Maximum velocity (m/s)							
59.6 ± 1.0	60.5 ± 2.0	56.6 ± 2.0	58.4 ± 2.0	50.0 ± 1.0	45.3 ± 2.0	48.0 ± 3.0	46.0 ± 5.0
(NS)		(NS)		(NS)		(NS)	
(2) Dispersion of velocity (%) (Hopf's method)							
14.6 ± 1.0	13.4 ± 2.0	12.7 ± 2.0	18.0 ± 2.0	17.1 ± 3.0	19.0 ± 4.0	17.0 ± 4.0	15.8 ± 1.0
(NS)		(<i>P</i> < 0.005)		(NS)		(NS)	
(3) Dispersion of velocity (%) (Desynchronization amplitude method)							
10.5 ± 1.0	10.0 ± 2.0	6.9 ± 1.0	18.5 ± 1.0	6.2 ± 1.0	8.5 ± 1.0	16.0 ± 1.0	10.0 ± 1.0
(NS)		(<i>P</i> < 0.01)		(NS)		(NS)	

NS = not significant.

TABLE 2

DIFFERENCES IN MEAN ($\pm$ SEM) PROXIMAL AND DISTAL LATENCIES BETWEEN HEALTHY AND IMPAIRED SIDES AT FIRST AND SECOND CONTROL EXAMINATIONS (P: STUDENT'S *t* TEST)

First examination (9 cases)				Second examination (6 cases)			
Ulnar nerve		External popliteal nerve		Ulnar nerve		External popliteal nerve	
Healthy	Impaired	Healthy	Impaired	Healthy	Impaired	Healthy	Impaired
(1) Proximal (m/s)							
8.5 $\pm$ 0.2 (NS)	8.7 $\pm$ 0.2	9.6 $\pm$ 0.2 (NS)	9.6 $\pm$ 0.4	10.3 $\pm$ 0.2 (NS)	11.2 $\pm$ 0.2	11.4 $\pm$ 0.5 (NS)	13.2 $\pm$ 0.5
(2) Distal (ms)							
2.3 $\pm$ 0.1 (NS)	2.5 $\pm$ 0.1	4.0 $\pm$ 0.3 (P < 0.005)	4.7 $\pm$ 0.1	3.0 $\pm$ 0.15 (P < 0.005)	3.5 $\pm$ 0.0	4.8 $\pm$ 0.3 (P < 0.01)	6.2 $\pm$ 1.0

NS = not significant.

The study of proximal and distal amplitudes of evoked muscle potentials (Table 3) showed:

1. The proximal amplitude at the first examination was significantly different for the ulnar nerve between the impaired (8.8 $\pm$ 0.8 mV) and healthy sides (12 $\pm$ 0.5 mV). Such a difference was present also in the external popliteal nerve 2.7 $\pm$ 0.5 mV (impaired side) and 4.4 $\pm$ 0.8 mV (healthy side). This difference was confirmed in the second examination for the ulnar nerve 8.6 $\pm$ 1.5 mV (impaired); 13 $\pm$ 1.0 mV (healthy), and for the external popliteal nerve 2.5 $\pm$ 0.7 mV (impaired); 4.1 $\pm$ 0.8 mV (healthy).

2. A significant difference was found between the distal amplitude of the ulnar nerve on the impaired (10 $\pm$ 0.8 mV) and the healthy side (13.9 $\pm$ 0.5 mV) at the first examination. The difference was also signifi-

cant for the external popliteal nerve between impaired (3 $\pm$ 0.6 mV) and healthy sides (4.8 $\pm$ 0.8 mV). A further, possibly insignificant, decrease of the evoked muscle potential amplitudes was confirmed at the second examination for both nerves: ulnar nerve (impaired, 9.1 $\pm$ 1.6 mV; healthy, 14.6 $\pm$ 1.5 mV) and external popliteal nerve (impaired, 2.8 $\pm$ 1.0 mV; healthy, 5.0 $\pm$ 1.0 mV) (Table 3).

The index of functioning motor units proved to be already significantly different at the first control examination between the healthy and impaired hypothenar eminence (impaired side 434 $\pm$ 71; healthy side 698 $\pm$ 120). A similar significant difference was present also for the extensor digitorum brevis muscle (impaired 105 $\pm$ 14; healthy 183 $\pm$ 34). At the second examination this change proved to be

TABLE 3

DIFFERENCES IN MEAN ($\pm$ SEM) PROXIMAL AND DISTAL AMPLITUDE OF ELECTRICAL RESPONSES BETWEEN HEALTHY AND IMPAIRED SIDES AT FIRST AND SECOND CONTROL EXAMINATIONS (P: STUDENT'S *t* TEST)

First examination (9 cases)				Second examination (6 cases)			
Ulnar nerve		External popliteal nerve		Ulnar nerve		External popliteal nerve	
Healthy	Impaired	Healthy	Impaired	Healthy	Impaired	Healthy	Impaired
(1) Proximal (mV)							
12.0 $\pm$ 0.5 (P < 0.01)	8.8 $\pm$ 0.8	4.4 $\pm$ 0.8 (P < 0.05)	2.7 $\pm$ 0.5	13.0 $\pm$ 1.0 (P < 0.005)	8.6 $\pm$ 1.5	4.1 $\pm$ 0.8 (P < 0.05)	2.5 $\pm$ 0.7
(2) Distal (mV)							
13.9 $\pm$ 0.5 (P < 0.01)	10.0 $\pm$ 0.8	4.8 $\pm$ 0.8 (P < 0.05)	3.0 $\pm$ 0.6	14.6 $\pm$ 1.5 (P < 0.01)	9.1 $\pm$ 1.6	5.0 $\pm$ 1.0 (P < 0.05)	2.8 $\pm$ 1.0

NS = not significant.

still significant for both muscles (hypothenar 366 ± 100 impaired, 602 ± 95 healthy; extensor digitorum brevis 110 ± 23 impaired, 216 ± 54 healthy) (Table 4).

The difference between the mean incremental amplitudes recruited by increasing the intensity of stimulus above threshold was not significantly different between the impaired and normal limbs for both the hypothenar eminences and extensor digitorum brevis muscles (Table 4).

DISCUSSION

From our analysis of the data for two different functions of the motor unit nerve excitability and motor propagation velocity we observed a different behaviour between the normal and impaired sides in that some parameters significantly changed during the follow-up period while others did not. Each must be considered separately because of their different functional significance.

The maximum motor conduction velocity of the peripheral nerve was unchanged proximally near the neurotrophic centres a short time after an acute brain stroke. Nevertheless, an increase in dispersion of conduction suggests partial involvement of the slowest motor fibres in the external popliteal nerve, which is further than the ulnar nerve from upper motor neurone control. On the other hand, small calibre and thin myelinated axons seem to be more exposed to damage due to impairment of trophic control (Namba *et al.*, 1971).

The predominant involvement of distal as compared with proximal motor latency further emphasizes the importance of a trophic control distance factor so far as the external popliteal nerve is concerned. An increase in the dispersion of motor conduction velocities of the ulnar nerve, but re-

quiring a longer period to elapse (six months), is also consistent with a trophic influence and with the presence of more synaptic junctions between the cortex and the spinal cord motoneurone biasing the nerve because of the higher capability of the efferent control on the upper arm muscles, which should limit an 'immediate' effect of the central lesion on the upper arm motor units. The changes in all the motor propagation velocity parameters seen six months after the brain stroke were of considerable interest.

Such a response illustrates an effect induced by central lesions on the subsegmental structures, possibly through crossed synaptic connections (Gay and Silberberg, 1964).

In one sense we can suppose that the lesion has not only an inter-hemispheric but also a subcortical or even a spinal effect through long polysynaptic pathways (Hausmanowa-Petrusewicz and Kopec, 1971; Scarlato *et al.*, in press). But this hypothesis does not exclude the presence of a 'dying-back' type of involvement of the distal nerve fibres leading to an increase in the distal motor latency. Finally, the decrease seen in the electrical response amplitude has also to be taken into account as an excitability parameter of the whole muscle motoneuronal population. Following the work of Serratrice *et al.* (1975), we can postulate the existence of a considerable amount of 'motoneuronal depopulation' (from 20% to 40%) in both extensor digitorum brevis and hypothenar muscle, but greater in the former. Motor unit blocking did not change with time in the extensor digitorum brevis, whereas it seems to increase in the hypothenar muscles six months after the brain stroke. At this point some disuse effects also have to be taken into account. However, with the term 'depopulation' we can (according to the 'sick motoneurons' hypothesis of McComas *et al.* (1971b))

TABLE 4

DIFFERENCE IN MEAN ($\pm$ SEM) FUNCTIONING MOTOR INDEX BETWEEN HEALTHY AND IMPAIRED SIDES AT FIRST AND SECOND CONTROL EXAMINATIONS (P: STUDENT'S *t* TEST)

First examination (9 cases)				Second examination (6 cases)			
Hypothenar		Extensor digitorum brevis		Hypothenar		Extensor digitorum brevis	
Healthy	Impaired	Healthy	Impaired	Healthy	Impaired	Healthy	Impaired
698 ± 120	434 ± 71	183 ± 34	105 ± 14	602 ± 95	366 ± 100	216 ± 54	110 ± 23
(P < 0.05)		(P < 0.01)		(P < 0.05)		(P < 0.05)	
Mean amplitude of first incremental responses							
28 ± 6.9	27.3 ± 3.9	28 ± 3.0	35.1 ± 5.2	28.4 ± 4.0	28.3 ± 2.2	37.4 ± 13	31.4 ± 3.8
(NS)		(NS)		(NS)		(NS)	

NS = not significant.

propose a functional block of nerve excitability without necessarily including anatomical damage. Such a term therefore involves a concept of damage reversal. But we are not yet in a position to establish the level at which the block occurs or to talk about the involvement in relation to the functional properties of the affected motor units—that is, low or high threshold motor units—or about collateral sprouting of nerve endings. In fact, the data obtained with the index of functioning motor unit technique of McComas *et al.* (1971a, b) show a global decrease in motor units as far as the total electric response is concerned, but they do not show significant changes in the amplitudes of the first recruited increments.

The maximum electrical response seems, therefore, the only parameter of any value in showing a motor unit functional block after an acute vascular lesion of the CNS.

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REFERENCES

- Fenichel, G. M., Daroff, R. B., and Glaser, G. H. (1964). Hemiplegic atrophy. *Neurology (Minneapolis)*, **14**, 883–890.
- Gay, A. J., and Silberberger, D. H. (1964). Histochemical correlates of transynaptic degeneration. *Archives of Neurology (Chicago)*, **10**, 85–90.
- Hausmanova-Petrusewicz, I., and Kopec, J. (1971). Motor nerve conduction velocity in anterior horn lesions. *Fourth International Congress of Electromyography*, 63–64.
- Hopf, H. C. (1962). Untersuchungen über die Unterseide in der Leitungsgeschwindigkeit motorischer Nervenfasern beim Menschen. *Deutsche Zeitschrift für Nervenheilkunde*, **183**, 579–590.
- McComas, A. J., Fawcett, P. R. W., Campbell, M. J., and Sica, R. E. P. (1971a). Electrophysiological estimation of the number of motor units within a human muscle. *Journal of Neurology, Neurosurgery, and Psychiatry*, **34**, 121–131.
- McComas, A. J., Sica, R. E. P., Upton, A. R. M., Aguilera, N., and Currie, S. (1971b). Motoneuron dysfunction in patients with hemiplegic atrophy. *Nature New Biology*, **233**, 21–23.
- Namba, T., Schuman, M. H., and Grob, D. (1971). Conduction velocity in the ulnar nerve in hemiplegic patients. *Journal of the Neurological Sciences*, **12**, 177–186.
- Pinelli, P. (1953). Ricerche sul reclutamento delle unità motorie del muscolo dell'uomo in condizioni normali e patologiche (con particolare riguardo all'adduttore del pollice). *Rivista di Patologia Nervosa Mentale*, **74**, 607–620.
- Scarlato, G., Pagni, F., Valli, G., and Savanone, C. L'amiotrofia spinale midollare nelle sindromi apalliche. *Acta Neurologica* (in press).
- Serratrice, G., Gastaut, J. L., Pellissier, J. F., Baret, J., Roux, H., and Cartouzou, G. (1975). Amiotrophies et depopulation neuronales d'origine encephalique. *Revue Neurologique*, **131**, 185–192.