Involvement of peripheral vasomotor fibres in carpal tunnel syndrome

MICHAEL J. AMINOFF

From the Department of Neurology, School of Medicine, University of California, San Francisco, California, USA

SUMMARY It is often assumed that large diameter nerve fibres are affected selectively in patients with compressive peripheral nerve lesions. However, in five of 13 patients with the carpal tunnel syndrome, plethysmography revealed that the normal digital vasoconstrictor response to inspiration was abolished in the index finger but preserved in the little finger of the affected hand. This indicates that the function of sympathetic efferent fibres destined for a median-innervated digit is sometimes disturbed also in patients with median nerve entrapment at the wrist.

Most of the published accounts of the peripheral nerve entrapment syndromes have been concerned with their motor and sensory manifestations, and it is similarly the functional integrity of motor and sensory nerve fibres that is evaluated by nerve conduction studies in the clinical EMG laboratory. Sympathetic nerve fibres are also an important component of the peripheral nerves, however, and conspicuous changes result if their function is deranged. These changes have been reviewed in detail by Sunderland (1968) who stressed that some peripheral nerves, and in particular those which supply the hand and foot, contain more sympathetic fibres than others. The present study was, therefore, designed to ascertain whether the function of sympathetic vasomotor fibres was disturbed in patients with a common entrapment neuropathy, and to determine whether the laboratory demonstration of any such disturbance could be of practical significance with regard to the diagnosis of the underlying peripheral nerve lesion.

The functional integrity of vasomotor fibres was assessed by studying the effect of a sudden deep inspiration on digital blood flow as measured by venous occlusion plethysmography. This is a well-established method of measuring digital blood flow, and depends on the sudden and complete arrest of the venous return from the finger without any direct interference with arterial inflow.

In such circumstances, the initial increase in volume of the digit beyond the site of venous occlusion can be taken to represent the rate of arterial inflow. It has been shown by a number of independent workers that reflex vasoconstriction occurs in the digits after a deep inspiration (Bolton *et al.*, 1936; Wilkins *et al.*, 1938; Hertzman and Dillon, 1939; Mulinos and Shulman, 1939; Gilliatt, 1948), and studies in paraplegic patients with a complete break in functional continuity of the spinal cord above the level of sympathetic outflow to the hands led Gilliatt *et al.* (1948) to conclude that this reflex may be mediated by a purely spinal mechanism. The afferent pathways subserving the reflex remain unknown, but the efferent fibres mediating it are sympathetic. Sympathetic nerve fibres have the same peripheral distribution as the somatic branch of the peripheral nerve which contains them (Sunderland, 1968), and there is a correspondence of cutaneous areas of sensory and sympathetic loss after severe nerve injuries (Herz *et al.*, 1946). In the present study, therefore, the integrity of the inspiratory digital vasoconstrictor reflex has been studied in a median- and an ulnar-innervated finger in patients with the carpal tunnel syndrome.

Methods

The study was performed on seven healthy volunteers and on one male and 15 female patients, ranging in age between 24 and 84 years, who were attending the University of California Medical

Address for reprint requests: Dr M. J. Aminoff, Department of Neurology, University of California, San Francisco, CA 94143, USA.

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Center in San Francisco and who had been referred for investigation to the EMG laboratory. Patients on drugs known to affect the function of the autonomic nervous system were excluded. The study was undertaken only with the informed consent of each subject and with the approval of the Committee on Human Research of the University of California.

The subject under investigation lay back in a reclining chair in a darkened room, with the arm abducted, extended, and supported on an arm rest. Since vessels that are already distended will probably fail to accommodate blood at the normal rate (Hyman and Winsor, 1961), care was taken to ensure that the veins of the hand were not congested, in particular by maintaining the hand and arm at the level of the heart. The ambient temperature in the examination room was kept high so that the patient was warm and therefore had a good arterial inflow to the digit. This was essential to reduce background vasomotor tone and prevent it from obscuring any vasoconstrictor response to inspiration. Absolute quiet was maintained during the study, save for the rather monotonous noise made by the apparatus itself. Each subject was allowed to rest in the examination room for up to an hour before the study began. The experimental procedure itself usually took about 30 minutes, during which each subject was asked to breathe normally except when instructed to take a sudden deep inspiration, while digital blood flow was measured. Digital vasoconstriction of psychological origin often occurred in response to the voice of the examiner in normal subjects, but interference of this sort did not occur once the subjects had gained familiarity with the technique.

The terminal phalanx of the index or little finger was inserted into a rigid, nondistensible cylindrical metal or plastic cup that contained air at atmospheric pressure. The size of the container was suited as far as possible to each subject, but was always sufficiently large that there was a slight space between its inner wall and the skin. The proximal end of the container was sealed with zinc oxide paste to make an air-tight seal without causing venous engorgement. The distal end was connected by means of polythene tubing to a Grass volumetric pressure transducer (PT-5-A), and this in turn was connected to one channel of a Grass polygraph so that a continuous record was obtained of changes in finger volume. The accumulation of sweat in the container did not produce any significant change in the records obtained during the period of study, but the high thermal expansion coefficient of air led occasionally to a problem with baseline drift

(cf Hyman and Winsor, 1961).

An inflatable plastic cuff was wound loosely around the base of the finger, and lightly secured with nondistensible adhesive bandage so that it did not exert any pressure when deflated. It was connected through a pressure transducer to a solenoid valve controlled by a timing device, and from this to a pressure regulator and then to an air pressure pump. This permitted rapid inflation and deflation of the cuff to be performed automatically about five times per minute, the cuff remaining inflated for five seconds at a time and deflated for six seconds. The pressure transducer was connected to a second channel on the polygraph so that a record was obtained of the times at which the cuff was inflated and deflated. The inflation pressure was sufficient to arrest the venous return from the finger but was always below the diastolic level; it was individually selected for each subject so that it gave the highest apparent rate of arterial inflow when digital blood flow was measured. Inflation of the cuff inevitably led to compression and some distortion of the subjacent finger, and this sometimes caused an initial "jump" artefact on the trace of finger volume. Preliminary experiments confirmed that the extent of the artefact varied with the applied pressure and also with the distance of the cuff from the plethysmograph. Although the artefact could, therefore, have been eliminated by placing the cuff more proximally (for example, at the wrist) this would have allowed blood to accumulate between it and the digital container, and the measurement obtained with the plethysmograph would not then have necessarily reflected the arterial inflow to the finger. Accordingly, the cuff was always placed on the finger under examination and as close to the plethysmograph as possible; its final position was generally a matter of compromise, but was usually within 10 mm of the digital container.

It was not intended to obtain absolute values for the rate of arterial inflow to the fingers, but rather to observe any qualitative changes in blood flow to the digits in response to a deep inspiration. Accordingly, since the volume of the dead space in the recording system varied slightly in different subjects, no attempt was made to calibrate the plethysmograph to obtain a quantitative estimate of digital blood flow.

Results

In analysing the records obtained with the plethysmograph, attention was directed only to the initial slope of the traces. This portion of the record, which reflects the rate at which the volume

Fig. 1 Different types of plethysmographic record. The interpretation of these records is considered in the text. Time in seconds.

of the finger first increases after venous occlusion, can be related most clearly to the actual rate of arterial inflow immediately before the venous return is arrested. Later portions of the traces are unreliable in this respect because of the effect that increasing venous pressure has on blood flow to the finger.

Considerable care must be taken in interpreting plethysmographic records if valid conclusions are to be reached from them. In records of the type shown in Fig. 1A, there is no difficulty in constructing a line that corresponds to the initial slope of the record. The appearance of records such as the one shown in Fig. 1B is suggestive of a jump artefact due to inflation of the cuff. Such artefacts were always complete in less than one second, and the true slope of the record was never in doubt. Records of the type shown in Fig. 1C, where the trace exhibits a convex deflection facing upward, were encountered not uncommonly, and in interpreting them a line was constructed to correspond to the slope of the first two or three pulse waves, allowance being made for any jump artefact. This permitted relative changes in blood flow to be followed with some confidence (Greenfield, 1960). Finally, if records were obtained that

showed a concave upward deflection (Fig. 1D), the position of the occluding cuff was adjusted and the study repeated, because such records imply that blood is collecting initially in that part of the finger which is outside the plethysmograph, and do not, therefore, reflect the true rate of arterial blood flow to the digit. Artefacts were sometimes caused by movement of the subject, but these were usually recognised easily and were discounted.

The preliminary experiments in normal subjects confirmed that digital vasoconstriction occurred in response to a sudden deep inspiration in every case (Fig. 2). In other words, the initial slope of the plethysmographic record, which represents arterial inflow to the finger, was reduced after the deep inspiration. The latency of this reflex response was about three seconds, and the vasoconstriction itself lasted for a variable period up to about one minute. Accordingly, when recording the responses in patients with the carpal tunnel syndrome, digital blood flow was evaluated some two to seven seconds after a preceding deep inspiration, as well as when the patient was breathing quietly at his normal rate and rhythm. The traces so obtained from all the patients were subsequently

Fig. 2 Effect of a sudden deep breath (at the time indicated by the marker) on blood flow to the index finger of a normal subject, as shown plethysmographically. Time in seconds.

analysed without knowledge or reference to the individual electrophysiological findings.

In three of the 16 patients suspected of having a carpal tunnel syndrome, electromyography and nerve conduction studies revealed no abnormality whatsoever, and the peripheral vasoconstrictor reflex was similarly preserved in both the index and the little fingers of the affected hand. In the remaining 13 patients, the results of nerve conduction studies were clearly abnormal, being consistent with or confirmatory of the clinical diagnosis, while in two there was also electromyographic evidence of chronic partial denervation in the abductor pollicis brevis muscle. Thus, in nine patients the terminal motor latency of the median nerve was prolonged. In six of these nine patients, median nerve sensory action potentials recorded orthodromically at the wrist after stimulation of the index finger, or antidromically in the finger after stimulation at the wrist, were either unrecordable or of reduced amplitude and prolonged latency; in one they were small but of normal latency, and in two the function of sensory

fibres was not evaluated. In four patients the terminal motor latency of the median nerve was within normal limits, but in each case the median nerve sensory action potential was of low amplitude and prolonged latency. In no case did the electrophysiological investigations reveal evidence of any more generalised peripheral nerve involvement.

The inspiratory vasoconstrictor reflex was absent in the index finger (Fig. 3) but preserved in the little finger in five of these 13 patients, one of whom had a bilateral carpal tunnel syndrome and bilateral impairment of vasomotor function in the median-innervated digit. In the remaining eight patients a normal digital vasoconstrictor response to inspiration was found. The functional integrity of this reflex response could not be related to the degree of impairment of motor and sensory conduction as judged by the results of the nerve conduction studies. Thus, in two of the eight patients with normal digital vasoconstrictor responses the values obtained for terminal motor latency of the median nerve were particularly long, and the

Fig. 3 Effect of a sudden deep inspiration (at the time shown by the marker) on blood flow to the index (A) and little (B) fingers of a patient with the carpal tunnel syndrome, as recorded plethysmographically. Time in seconds.

median nerve sensory action potential could not be identified at the wrist. One of these two patients had electromyographic evidence of chronic partial denervation in the abductor pollicis brevis muscle, and another patient with similar findings on needle electromyography also had preserved vasoconstrictor responses in the fingers. Conversely, in one of the five patients in whom the function of vasomotor fibres was clearly impaired as judged by the loss of this reflex vasoconstrictor response, motor conduction velocity and terminal latency of the median nerve were normal, and the only electrophysiological evidence to support the diagnosis of carpal tunnel syndrome was a mild reduction in amplitude and prolongation in latency of the median nerve sensory action potential recorded at the wrist.

Review of the medical history and physical findings among the two groups of patients revealed no consistent differences save with regard to the presence of pain. All of the patients in whom the peripheral inspiratory reflex was lost complained of at least some pain in the hand, although in three of them it was inconspicuous and restricted to a small region. In contrast, only four of the eight patients with a normal vasoconstrictor response complained of pain, although in two it was severe and troublesome.

Discussion

In this study the integrity of postganglionic autonomic nerve fibres was evaluated by examining the effect of a sudden deep inspiration on digital blood flow, using the method of venous occlusion plethysmography. Although there are other methods for measuring peripheral blood flow and vasoconstrictor reflexes, or evaluating peripheral autonomic function, the present method has given reliable and consistent results in the hands of the author, and other workers have also commented on its value in this respect (eg Greenfield *et al.*, 1963). Nevertheless, the electrodermal or galvanic skin reflex—a change in skin potential that is evoked by a number of different stimuli—may be complementary to the technique used in this study, since the galvanic skin and peripheral vasoconstrictor reflexes appear to use independent postganglionic pathways and are behaviourally distinct (Prout, 1967; Furedy and Gagnon, 1969).

The observations reported in this paper show clearly that there is a disturbance of function of sympathetic efferent fibres destined for a median-innervated digit in some patients with carpal tunnel syndrome. The presence of an apparently normal digital vasoconstrictor reflex in the little

finger of these patients implies that its absence in the index finger was not part of a more generalised disturbance of sympathetic function, or the result of technical factors. Although it is not possible to localise the lesion responsible for loss of the reflex response, it seems reasonable to assume that it was also at the carpal tunnel rather than elsewhere.

It is of some interest that the function of sympathetic fibres is disturbed in some patients with the carpal tunnel syndrome, since it is often assumed that large diameter nerve fibres are selectively affected in compressive peripheral nerve lesions. In fact, relatively little attention has been directed at sympathetic function in patients with entrapment or compressive neuropathies. This is surprising since Seddon (1943), in his study of different types of nerve injury, found disturbances of sweating in seven of 26 cases of neurapraxia, and vasomotor abnormalities in one of the three cases evaluated with this in mind. In many of his cases, the affected peripheral nerves were ones that do not contain a large sympathetic component, and it is, therefore, not surprising that disturbances of peripheral autonomic function were not encountered more frequently. One of his patients, in whom there was a remarkable loss of postural and vibration appreciation in the arm after compressive nerve injury, is of particular interest because the nature of the sensory change was originally in some doubt, and the presence of an autonomic disturbance in the affected limb was one of the factors that led to the recognition of its organic basis. More recently, Bolton and McFarlane (1978) have described a patient in whom a motor and sensory deficit, and loss of the ability to sweat, occurred distal to a pneumatic tourniquet applied to her upper arm during an operation for Dupuytren's contracture. Tests of vasomotor function were not performed, but initial dysfunction of sudomotor fibres was followed by subsequent recovery. The tourniquet paralysis syndrome has also been studied in some detail by Moldaver (1954) who reported his findings in two patients and referred to five others whom he had evaluated. Electrical skin resistance was normal in one of these two cases, but initially abnormal in a small region of the hand in the other. Plethysmographic studies were undertaken in at least some of his patients, and no difference was found between the affected and unaffected sides. It would appear from the published account, however, that such studies did not assess adequately the integrity of vasomotor fibres, since only the resting blood flow was examined, and then while the hand was warm.

There is some histological evidence to support the belief that autonomic nerve fibres may be in-

volved in patients with compressive peripheral nerve lesions. Thus, in their quantitative electron microscopic study of unmyelinated fibres in normal and compressed nerves of the baboon, Fowler and Ochoa (1975) found that prolonged local compression resulted in damage to unmyelinated fibres, although this only occurred if the compression was severe enough to cause Wallerian degeneration in at least some of the myelinated fibres.

It is generally recognised that unmyelinated and small myelinated fibres are essential for the appreciation of painful stimuli. Since peripheral (post-ganglionic) vasomotor fibres are also unmyelinated, it was of some interest to determine whether any relationship existed between the presence of pain as a symptom of the carpal tunnel syndrome and the functional integrity of vasomotor fibres. Although pain was a feature of the history in all of the patients in whom the vasomotor reflex was impaired, no clear relationship could be identified. Thus, the digital vasoconstrictor response to inspiration was intact in the index finger of some of the patients who complained of severe pain in the hand, and also in others with little or no pain attributable to the carpal tunnel syndrome. Similarly, pain was a conspicuous feature of the history in some but not other patients in whom the reflex response was lost. The lack of any clear relationship is not, however, surprising. It is similarly not possible to explain the painful forms of polyneuropathy in terms of the types of nerve fibres that are involved (Nathan, 1976).

Before the introduction of modern electrodiagnostic techniques for the study of nerve conduction velocity, a number of studies were undertaken on sudomotor and vasomotor function in patients with peripheral nerve injuries sustained usually while on military service (Doupe, 1943; Jasper and Robb, 1945; Herz *et al.*, 1946). The information obtained indicated that studies of peripheral autonomic function had a definite place in the objective, clinical evaluation of patients in whom the lesion was complete. In patients with incomplete peripheral nerve lesions, however, such studies were found to be of much more limited practical value, at least when attention was confined to the integrity of sudomotor fibres (Herz *et al.*, 1946). The experience gained in the present work on vasomotor function might be taken to substantiate this belief. Thus, in only five of the 13 patients with clinical and electrophysiological evidence of median nerve compression at the wrist was there loss of the digital inspiratory vasoconstrictor reflex in the index finger, suggesting

that evaluation of the integrity of this reflex is of limited diagnostic value. However, in one of these five patients, the electrophysiological findings were mild, the only abnormality being a mild reduction in amplitude and prolongation in latency of the median nerve sensory action potential recorded at the wrist after digital stimulation. The possibility, therefore, remains that loss of this autonomic reflex response may be of some practical significance in the evaluation of patients with clinical features suggestive of carpal tunnel syndrome but in whom nerve conduction studies have yielded somewhat equivocal findings, and further studies are being undertaken with this in mind.

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References

- Bolton, B., Carmichael, E. A., and Stürup, G. (1936). Vasoconstriction following deep inspiration. *Journal of Physiology*, **86**, 83–94.
- Bolton, C. F., and McFarlane, R. M. (1978). Human pneumatic tourniquet paralysis. *Neurology (Minneapolis)*, **28**, 787–793.
- Doupe, J. (1943). Studies in denervation. B. The circulation in denervated digits. *Journal of Neurology and Psychiatry*, **6**, 97–111.
- Fowler, T. J., and Ochoa, J. (1975). Unmyelinated fibres in normal and compressed peripheral nerves of the baboon: a quantitative electron microscopic study. *Neuropathology and Applied Neurobiology*, **1**, 247–265.
- Furedy, J. J., and Gagnon, Y. (1969). Relationships between and sensitivities of the galvanic skin reflex and two indices of peripheral vasoconstriction in man. *Journal of Neurology, Neurosurgery, and Psychiatry*, **32**, 197–201.
- Gilliatt, R. W. (1948). Vaso-constriction in the finger after deep inspiration. *Journal of Physiology*, **107**, 76–88.
- Gilliatt, R. W., Guttman, L., and Whitteridge, D. (1948). Inspiratory vaso-constriction in patients after spinal injuries. *Journal of Physiology*, **107**, 67–75.
- Greenfield, A. D. M. (1960). Venous occlusion plethysmography. *Methods in Medical Research*, **8**, 293–301.
- Greenfield, A. D. M., Whitney, R. J., and Mowbray, J. F. (1963). Methods for the investigation of peripheral blood flow. *British Medical Bulletin*, **19**, 101–109.
- Hertzman, A. B., and Dillon, J. B. (1939). Selective vascular reaction patterns in the nasal septum and skin of the extremities and head. *American Journal of Physiology*, **12**, 671–684.

- Herz, E., Glaser, G. H., and Moldaver, J. (1946). Electrical skin resistance test in evaluation of peripheral nerve injuries. *Archives of Neurology and Psychiatry (Chicago)*, **56**, 365–380.
- Hyman, C., and Winsor, T. (1961). History of plethysmography. *Journal of Cardiovascular Surgery*, **2**, 506–518.
- Jasper, H., and Robb, P. (1945). Studies of electrical skin resistance in peripheral nerve lesions. *Journal of Neurosurgery*, **2**, 261–268.
- Moldaver, J. (1954). Tourniquet paralysis syndrome. *Archives of Surgery*, **68**, 136–144.
- Mulinos, M. G., and Shulman, I. (1939). Vasoconstriction in the hand from a deep inspiration. *American Journal of Physiology*, **125**, 310–322.
- Nathan, P. W. (1976). The gate-control theory of pain. A critical review. *Brain*, **99**, 123–158.
- Prout, B. J. (1967). Independence of the galvanic skin reflex from the vasoconstrictor reflex in man. *Journal of Neurology, Neurosurgery, and Psychiatry*, **30**, 319–324.
- Seddon, H. J. (1943). Three types of nerve injury. *Brain*, **66**, 237–288.
- Sunderland, S. (1968). *Nerves and Nerve Injuries*. Churchill Livingstone: Edinburgh.
- Wilkins, R. W., Doupe, J., and Newman, H. W. (1938). The rate of blood flow in normal fingers. *Clinical Science*, **3**, 403–411.