FOCAL PERIPHERAL NEUROPATHIES

Geraint Fuller

ii20

J Neurol Neurosurg Psychiatry 2003;74(Suppl II):ii20–ii24

Focal peripheral neuropathies are not at the fashionable end of the neurological street. However they are important, as they are very common, sometimes disabling, and often treatable. They can also be a source of confusion when they occur in patients with other neurological diseases.

This article will not go over the detailed clinical features of the many focal peripheral neuropathies that occur, though these are briefly summarised in tables 1 and 2. These can be found in many neurology textbooks, though I would particularly recommend two short texts that include clear, copiously referenced descriptions of all focal neuropathies.^{1 2} *Aids to the examination of the peripheral nervous system*³ is a useful aide memoir, which you should carry in your bag.

This brief review will explore the general approach to focal neuropathies, including issues relating to management and clinical presentation.

GENERAL APPROACH

The management of focal peripheral neuropathies is based on certain general principles with a relatively limited backing from clinical trials. These principles relate to understanding the:

- ▶ types of peripheral nerve injury
- ▶ mechanisms of injury
- ▶ ability and limitations of neurophysiology to aid diagnosis
- ▶ peripheral nerve anatomy.

Types of peripheral nerve injury

Regardless of the cause, nerve injury can be classified according to severity. This directs management and acts as guide to rate of recovery. The types of injury are:

- ▶ a **neuropraxia**, where there is focal or segmental demyelination with preservation of the axon and recovery in 2–12 weeks
- ▶ an **axonotmesis**, where the axon is divided but the epineurium remains intact and regrows at 1 mm per day from the site of injury
- ▶ a **neurotmesis**, where the nerve is divided and no longer in continuity with no recovery.

At the site of focal nerve injury there may be a combination of these types of injury, most commonly a mixture of neuropraxia and axonotmesis. This can be observed clinically by the relatively rapid early recovery followed by a more protracted improvement thereafter.

Mechanisms of peripheral nerve injury

A focal neuropathy results from injury to a peripheral nerve at one site. For every nerve there are anatomical weaknesses making injury more likely at a particular location, typically where a nerve runs beside bone or across a joint. Nerve injury can occur:

- ▶ from **external insult**, such as direct trauma, including prolonged external compression as occurs in prolonged unconsciousness, repeated minor trauma, traction, injection, cold, burns, radiation
- ▶ from **internal entrapment or compression**; examples would include entrapment of the median in the carpal tunnel or the ulnar nerve in the cubital tunnel and compression by tumours/deposits or vascular malformations
- ▶ an **intrinsic lesion** to the nerve—for example, an infarct. This usually arises as a focal manifestation of a more generalised process—for example, a nerve infarct caused by vasculitis, an area of conduction block in multifocal motor neuropathy
- ▶ as a result of **increased susceptibility** to nerve injury—for example, in diabetes—combined with minor entrapment or compression.

Neurophysiology in the diagnosis of focal peripheral neuropathies

Investigation of a focal neuropathy aims to determine the site of focal involvement and its cause. The site of involvement may be determined neurophysiologically (this also screens for evidence of abnormalities in other nerves or a generalised neuropathy). However neurophysiology has limitations; indeed, one of the main reasons trainees in neurology can benefit from practical knowledge of neurophysiology is to appreciate these (table 3).

Correspondence to:
Dr GN Fuller, Department of
Neurology, Gloucester Royal
Hospital, Great Western Road,
Gloucester GL1 3NN, UK;
geraint@Fullerg.demon.co.uk

Table 1 Outline of focal neuropathies in the upper limb

Nerve	Site of lesion	Common causes	Motor deficit	Sensory deficit	Differential diagnosis
<i>Common</i>					
Median	Carpal tunnel	Entrapment, diabetes, hypothyroidism, connective tissue disease	Abductor pollicis brevis, opponens pollicis	Thumb, index and middle finger	C6 or C7 radiculopathy; local pathologies
Ulnar	Elbow (cubital tunnel)	External compression, trauma (recent or distant)	Long flexors of little and ring fingers, finger abductors and adductors and lumbricals	Little and ring fingers	More distal or proximal ulnar lesion; motor neurone disease; T1 lesions
<i>Uncommon</i>					
Radial	Upper arm	External compression, trauma	Finger and wrist extensors, some weakness of brachioradialis	Anatomical snuffbox	C7 radiculopathy
Axillary	Humeral head	Trauma, humeral head	Deltoid	Lateral shoulder	
Ulnar	Wrist (Guyon's canal) or hand	Compression (cycling), entrapment	Wrist: adductor pollicis, interosseous muscles and hypothenar muscles Hand: adductor pollicis, interosseous muscles	Wrist: little and half ring finger Lesions in the hand: none	Motor neurone disease, Syringomyelia, T1 radiculopathy
Long thoracic	Not clear	Usually unknown; trauma	Serratus anterior; winging of scapular	None	Neuralgic amyotrophy
<i>Rare</i>					
Anterior interosseous branch of median nerve	Just below the elbow	Fibrous bands, trauma	Flexor pollicis longus, flexor digitorum profundus of index finger (loss of pinch sign), pronator quadratus		
Posterior interosseous branch of radial nerve	As nerve enters supinator muscle	Entrapment, trauma	Finger extensors: finger drop without wrist drop	None	C7 radiculopathy, upper motor neurone lesions, neuralgic amyotrophy
Suprascapular	Suprascapular notch	Trauma, lifting (rucksack)	Supraspinatus and infraspinatus	None	Shoulder pathology, neuralgic amyotrophy
Musculocutaneous		Trauma, iatrogenic	Biceps	Lateral forearm	C6 radiculopathy

Nerve conduction studies can identify a focal neuropathy in several ways, depending on the nerve studied and the manner in which it is affected. The significance of different findings vary and provide more or less clear cut evidence of a focal neuropathy.

- ▶ Demonstrating a focal delay (slowing over a short segment of nerve) and conduction block (a reduction in the amplitude and dispersal of the response) in one segment of the nerve, with associated denervation changes in the muscles supplied by the nerve, would be the clearest indication of a focal neuropathy.
- ▶ Demonstrating a focal delay without either conduction block or denervation changes would also show the existence of a focal neuropathy and determine the level directly, though less clearly. Unfortunately this depends on having the segment of peripheral nerve involved accessible for the application of superficial electrodes, as with the median nerve at the wrist or the ulnar nerve at the elbow.
- ▶ Demonstrating denervation changes limited to muscles innervated by a specific nerve or a reduction in motor or sensory responses from the affected nerve not found in other nerves. These findings determine the lowest site a lesion could be to produce the clinical problem; the exact site of nerve dysfunction to be inferred from the clinical presentation and other studies.
- ▶ Finding a reduction in size of motor or sensory responses also indicate a lesion proximal to the site of recording, though do not determine its level.

The use of neurophysiological studies to explore prognosis will be discussed below.

Peripheral nerve anatomy

A knowledge of peripheral nerve anatomy allows clinical localisation. Making the diagnosis of a focal peripheral neuropathy depends on recognising that a patient's symptoms

and any physical signs fall within the distribution of a single peripheral nerve. For the more commonly affected nerves—the median, ulnar, and lateral cutaneous nerve of the thigh—this can often be considered on the basis of symptoms alone. For less commonly affected nerves the diagnosis is usually based on signs. Diagnosis is going to depend on an appropriate knowledge of anatomy to allow these rarer entities to be diagnosed. Tables 1 and 2 provide a brief summary of most focal peripheral neuropathies likely to be encountered.

The fascicular arrangement of peripheral nerves can lead to difficulties in localisation, as a proximal nerve lesion may mistakenly be thought to be peripheral. For example, a partial sciatic nerve lesion at the level of the hip can be mistaken clinically for a common peroneal nerve lesion at the fibular head.

PRESENTATIONS OF FOCAL NEUROPATHIES

These can be broadly divided into acute lesions and those of more insidious onset. The clinical approach to each differs.

Acute deficit

The cause of an acute lesion is often straightforward and identifiable from the history—for example trauma, laceration, surgery or injections. Sometimes it can be easily deduced—for example, a period of unconsciousness (anaesthetic or otherwise), a post-ictal state, and coma from drugs or alcohol intoxication. These raise the possibility of prolonged external nerve compression, the ulnar, sciatic, common peroneal, and gluteal nerves being especially vulnerable. In patients with acute focal neuropathies the clinical focus is on optimising recovery and assessing prognosis.

An acute spontaneous deficit that develops at a site that is not a common site of external compression strongly suggests an intrinsic nerve lesion—for example, infarction. Investigation for evidence of a multifocal, particularly vasculitic, neuropathy needs to be undertaken (see Willison and Winer⁴).

Table 2 Outline of focal neuropathies in the lower limb

Nerve	Site of lesion	Common causes	Motor deficit	Sensory deficit	Differential diagnosis
<i>Common</i>					
Lateral cutaneous nerve of the thigh	Inguinal ligament	Obesity, pregnancy, surgery	None	Lateral thigh	L2 radiculopathy
Common peroneal	Fibular head	External compression (leg crossing, iatrogenic), trauma	Foot dorsiflexion and eversion, toe extension	Lateral calf and dorsum of foot	L5 radiculopathies, proximal sciatic lesions. Also upper motor neurone weakness and motor neurone disease
Interdigital	Between heads of metatarsals	Entrapment	None	Web spaces between affected toes	
<i>Uncommon</i>					
Femoral		Psoas haematoma, iatrogenic injury, trauma	Hip flexion, knee extension	Anterior thigh, medial calf	L3, L4 radiculopathies, diabetic amyotrophy
Sciatic	Pelvis, buttock or thigh	Trauma, compression in buttock, tumour, injection	Hamstrings plus common peroneal and tibial nerve deficits	Posterior cutaneous nerve of thigh plus common peroneal plus posterior tibial	L5, S1 radiculopathies
Tibial, at ankle	Tarsal tunnel	Entrapment	Abductor hallucis (not reliably tested clinically)	Distal sole, sparing heel	Partial sciatic, S1 radiculopathy
Perineal	Alcock's canal	Cycling	None	Penis or labia majora	Conus lesions
Saphenous	Thigh or knee	Knee surgery or arthroscopy	None	Medial calf	
<i>Rare</i>					
Tibial, at knee		Trauma	Plantar flexion, inversion	Sole of foot, including heel	Partial sciatic, S1 radiculopathy
Posterior cutaneous nerve of the thigh		Compression, trauma	None	Posterior thigh	S3, S4 radiculopathy
Obturator	Obturator foramen	Obturator hernia, pelvic tumours, surgery	Adductors of the hip	Medial thigh	Lumbosacral plexopathy
Gluteal		Trauma	Hip extensors, abductors	None	
Sural		Trauma, surgery (especially biopsy!)	None	Lateral aspect of foot	

Table 3 Some difficulties in neurophysiological diagnosis of focal neuropathies

Anatomy, limitation of access. Nerve conduction studies can only routinely study nerves that run subcutaneously. Segments available for study may be long, limiting the precision in localising a focal neuropathy

Short segments. Focal slowing is most useful if demonstrated over a short segment as it most precisely localises the lesion. However, measuring distances of short segments is prone to large errors, increasing the risk of error

Subclinical involvement. Population studies have found high levels (up to 18% have median dysfunction at the wrist in one study³) of abnormalities in asymptomatic patients

Multiple pathologies. Denervation changes from coexistent cervical or lumbosacral radiculopathies limit EMG localisation

Absent or limited denervation changes: A demyelinating lesion does not lead to the development of fibrillations or fasciculations; the changes in motor units and interference pattern are more subtle and thus less reliable

Timing of denervation changes: Denervation changes take 2 weeks to develop; early studies may be misleading.

EMG, electromyogram.

If the lesion is traumatic, regardless of cause, anything that could continue or worsen nerve injury must be identified and removed. Examples would include local factors such as continued compression from local haematoma or compartment syndromes (this may require imaging of the site of compression with timely decompression) as well as systemic factors such as hypoxia and hyperglycaemia.

Subsequent management depends on the type of nerve injury. If the lesion is a neuropraxia or an axonotmesis and the cause of nerve damage is removed there will be spontaneous recovery. Sometimes this pattern can be recognised clinically, when a nerve lesion is incomplete and there is some power, no matter how little, to indicate the nerve is in continuity. The same phenomenon can be found neurophysiologically by demonstrating single units under voluntary control on electromyogram (EMG).

However, a nerve that has no clinical or neurophysiological evidence of active motor function can still have suffered a

severe neuropraxia or axonotmesis and acutely this is indistinguishable from a neurotmesis. This is a very important distinction, as a neurotmesis will not recover unless the nerves are sutured or grafted. The only way these can be reliably identified is by surgical exploration. The nature of injury and the likelihood of a neurotmesis need to be considered when contemplating exploration.

Physiotherapy to maintain joint mobility and occupational therapy to improve function and to direct the use of splints are both important during the recovery phase. Neuralgic pain is common and pain modulating drugs such as amitriptyline, carbamazepine or gabapentin are helpful.

Insidious onset

Here you need to understand fully the aetiology before contemplating treatment. Insidious lesions tend to arise from internal entrapment or compression, sometimes combined with factors that increase nerve susceptibility or from repeated external

compression. The history needs to be reviewed for clues, asking directly about previous trauma, postures, habits, and hobbies. Are there any symptoms outside the distribution of this nerve, suggesting a multifocal or generalised process? Are there any factors in the history that might make the nerves more vulnerable to injury—for example, excess alcohol intake, diabetes? Have there been any previous focal neuropathies suggesting a liability to pressure palsies?

A careful neurological examination should look particularly for evidence of other focal neuropathies or a more generalised neuropathy. Neurophysiology may confirm the site or simply support the diagnosis of focal neuropathy and may provide evidence of multifocal involvement.

Further investigation

If the history provides an appropriate explanation (for example, trauma, repeated external compression) or if the nerve is involved at a common site of entrapment then no further investigations may be needed. If no explanation is found, particularly if the nerve is involved at an unusual site, then further investigation is indicated. These aim to identify unusual causes of internal entrapment or compression such as nerve tumours, or vascular malformations. Magnetic resonance imaging of the site of involvement should be considered initially. At the same time evidence of any factors that could make the nerves more vulnerable should be addressed, including the investigation of multifocal neuropathies as described elsewhere in this supplement.⁴ If all this proves unhelpful, exploration of the nerve could be considered, depending on the site and the severity of the focal neuropathy. Some internal entrapments—for example, fibrous bands—will only be found on exploration.

If neurophysiological studies have not identified direct evidence of a focal neuropathy you should consider other sites/conditions, such as radiculopathies, within the differential diagnosis. These will then require their own appropriate investigations. It is always worth considering whether the focal neuropathy demonstrated neurophysiologically is an adequate explanation of the clinical picture

Management of focal neuropathies at common sites of entrapment

Despite these problems being very common—for example, carpal tunnel syndrome has a prevalence of 3–5%⁵—there is still limited evidence as to the best approach to diagnosis and management. The difficulties arise, at least in part, because of case definition. These focal neuropathies are not present or absent but constitute a spectrum. This can be recognised clinically and neurophysiologically. A patient with minor intermittent ulnar sensory symptoms with minor reduction in ulnar sensory action potential (SAP), and a patient with a wasted claw hand and dense ulnar sensory loss and no motor and sensory responses from the ulnar nerve with denervation, both have focal ulnar neuropathies but can scarcely be considered as having the same extent of problem. In addition, the natural history of the common focal neuropathies is poorly understood. Such factors lead to difficulties in studies considering both diagnosis and treatment.

Carpal tunnel syndrome

Identifying a patient with a severe carpal tunnel syndrome is relatively straightforward, recognising lesser degrees is less so. There are a wide range of clinical signs taken to support the diagnosis. The specificity and sensitivity of the clinical signs have recently been reviewed,⁶ as have the specificity and sensitivity for different neurophysiological methods of

assessment.⁷ This approach is inherently difficult when there is no “gold standard” method of diagnosis. Interestingly, clinical tests such as Tinel’s and Phalen’s signs were not found to be helpful predictors of neurophysiological abnormality; however, hand diagrams, where the patient draws and marks the location of their symptoms of numbness and tingling (likelihood ratio of positive (LR+) = 2.4, 95% confidence interval (CI) 1.6 to 3.5; LR of negative (LR–) = 0.5, 95% CI 0.3 to 0.7), square wrist sign* (LR+ 2.7, 95% CI 2.2 to 3.4; LR– 0.5, 95% CI 0.4 to 0.8), and weak thumb abduction (LR+ 1.8, 95% CI 1.4 to 2.3; LR– 0.5, 95% CI 0.4 to 0.7) all achieved statistical significance. The flick sign, where the patient flicks their hand to improve symptoms, is promising but has only been the subject of a single study (LR+ 21.4, 95% CI 10.8 to 42.1; LR– 0.1, 95% CI 0 to 0.1).⁶

The Cochrane reviews of carpal tunnel support the use of oral steroids, splinting, ultrasound, yoga, and carpal bone mobilisation to provide short term benefit in mild cases.⁸ Local corticosteroid injections improve outcome at one month compared to placebo, and at three months when compared to oral steroids, but no benefit was demonstrated over non-steroidal anti-inflammatories and splinting at two months.⁹ Surgery improved outcome compared to splinting,¹⁰ a finding supported by a recent randomised study.¹¹ No one technique is clearly superior to another.¹²

Thus, patients with mild carpal tunnel should try non-invasive treatment initially, particularly if there is another factor such as pregnancy or hypothyroidism, and then proceed to decompression if symptoms persist. Patients with moderate carpal tunnel syndrome should probably proceed directly to decompression, though a trial of splinting while awaiting surgery might spare some surgery. It is not clear whether patients with severe compression, atrophy, and dense sensory loss benefit from surgical interventions. A large pragmatic trial is therefore strongly needed.

Other nerves

While ulnar nerve lesions at the elbow are the second most common focal neuropathy, advice on treatment is not currently based on the results of trials. Conservative management to avoid repeated trauma may lead to resolution, particularly if a history of recent trauma or external compression has been established. More distant trauma, leading to the “tardy” ulnar palsy, tends not to improve with conservative management. If conservative management fails then surgical decompression could be considered. Two procedures are commonly used: simple decompression within the cubital tunnel or alternatively combining this with anterior transposition. There are no randomised studies comparing these procedures. Occasionally an unusual cause of internal entrapment, such as a ganglia or cyst, is found at operation. Again a large pragmatic trial is needed.

The lateral cutaneous nerve of the thigh is commonly entrapped in the inguinal ligament. As the symptoms are sensory and usually tolerable no specific treatment is needed. Identification and reversal of any potential cause, particularly recent weight gain, seems prudent.

*Square wrist sign present when anteroposterior dimension of wrist divided by mediolateral dimension, measured at the distal wrist crease, is greater than 0.7.

Management of focal neuropathies at uncommon sites of entrapment

Once again this advice reflects the experience derived from case reports and clinical series. If no repeated external compression is identified these are patients in whom unusual causes of internal entrapment need to be considered and investigated as outlined above. In the absence of a systemic cause, where there is no improvement or progression, exploration should be considered.

ii24

REFERENCES

- 1 **Staal A**, van Gijn J, Spaans F. *Mononeuropathies; examination, diagnosis and treatment*. London: WB Saunders, 1999.
- 2 **Stewart JD**. *Focal peripheral neuropathies*, 3rd ed. Lippincott, Williams, Wilkins, 2000.
- 3 **O'Brien MD**. *Aids to the examination of the peripheral nervous system*, 4th ed. London: WB Saunders, 2000.
- 4 **Willison HJ**, Winer J. Clinical evaluation and investigation of neuropathies. *J Neurol Neurosurg Psychiatry* 2003;**74**(suppl II):ii3–8.
- 5 **Atoshi I**, Gummesson C, Johnsson R, *et al*. Prevalence of carpal tunnel syndrome in a general population. *JAMA* 1999;**282**:153–8.
- 6 **D'Arcy CA**, McGee S. Does this patient have carpal tunnel syndrome? *JAMA* 2000;**283**:3110–17.
- 7 **Jablecki CK**, Andery MT, Floeter MK, *et al*. Practice parameter: electrodiagnostic studies in carpal tunnel syndrome. *Neurology* 2002;**58**:1589–92.
- 8 **O'Connor D**, Marshall S, Massy-Westropp N. Non-surgical treatment (other than steroid injection) for carpal tunnel syndrome (Cochrane Review). *The Cochrane Library*, Issue 1, 2003. Oxford: Update Software.
- 9 **Marshall S**, Tardif G, Ashworth N. Local corticosteroid injection for carpal tunnel syndrome (Cochrane Review). *The Cochrane Library*, Issue 1, 2003. Oxford: Update Software.
- 10 **Verdugo RJ**, Salinas RS, Castillo J, *et al*. Surgical versus non-surgical treatment for carpal tunnel syndrome (Cochrane Review). *The Cochrane Library*, Issue 1, 2003. Oxford: Update Software.
- 11 **Gerritsen AA**, deVet HC, Scholten RJ, *et al*. Splinting vs surgery in the treatment of carpal tunnel syndrome; a randomised controlled trial. *JAMA* 2002;**288**:1245–51.
- 12 **Scholten RJPM**, Gerritsen AAM, Uitdehaag BMJ, *et al*. Surgical treatment options for carpal tunnel syndrome (Cochrane Review). *The Cochrane Library*, Issue 1, 2003. Oxford: Update Software.

What's in the next issue

Future content

See which articles have just been accepted for publication and preview the table of contents for the next issue a month before it is published

www.jnnp.com