Electrodiagnosis in Diabetic Neuropathy

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What is Electrodiagnosis (EDx)?

EDx a diagnostic procedure which consists of a series of tests employed for the diagnosis of neuromuscular diseases. These tests must be conducted by a physician trained in electrodiagnostic medicine as they are customised according to the presenting clinical problem, sequentially done, collectively interpreted and then correlated with the clinical features to arrive at a diagnosis that explains the neuromuscular disease. It is the only procedure that evaluates the function of the lower motor & sensory neuron. Multiple tests can be performed depending on the disease, but below given are a few with relation to the diagnosis of diabetic neuropathies.

EDx tests

- Nerve conduction studies: sensory and motor
- F wave studies
- H reflex studies
- Needle electromyographic examination (NEE or EMG)
- Heart rate variability test
- Sympathetic skin response

Terminology in Electrodiagnosis

- Clinical neurophysiology includes EDx, EEG and Evoked potential testing
- Electrodiagnosis (EDx) aka neuro-electrodiagnosis
- Electroneuromyography (ENMG) is synonymous with EDx and is the preferred term (as there cardio-electrodiagnosis as well)
- NCS is nerve conduction studies
- EMG is electromyography also known as needle electromyography
- An Electromyographer is the physician conducting the procedure: - the Electrodiagnostician
- An Electromyograph is the equipment Fig. 1

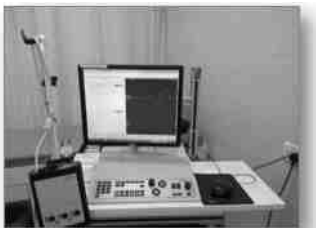

Fig. 1: The Electromyograph. The equipment used in EDx essentially consists of a computer with a stimulating apparatus a head-box to collect the biological signals from the patient and a loud speaker to listen to the EMG signal

Utility of EDx

Electrodiagnosis is considered to be an extension of the clinical examination and its uses include:

- Objective record: important for documentation and comparison on follow-up
- Localisation
- Detecting the predominant pathology: axonal vs demyelinating
- Judging the extent
- Defining the distribution
- Determining the predominant fibre involvement: sensory/ motor or autonomic

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- Knowing the temporal profile: whether acute/ chronic/ ongoing /old /acute on chronic
- Documenting the severity
- Assessing progress
- Post-operative evaluation after nerve repair
- Intra-operative monitoring
- Intra-operative evaluation of nerve continuity in trauma

Localisation

The site of the lesion could be localised to

- Anterior horn Cell
- Root
- Plexus
- Peripheral nerve
- Neuromuscular junction
- Muscle

Principles of localisation

1. Axons degenerate when disconnected from their parent neuron
2. Degeneration starts distally-takes time to complete

The parent neuron of the sensory fibres (afferent) is the dorsal root ganglion (DRG) which lies outside the spinal canal. That of the motor fibres (efferent) is the anterior horn cell which is within the spinal cord. When there is a lesion proximal to the DRG, i.e. in the level of the anatomical roots the sensory fibres of the peripheral nerve do not lose continuity with their parent neuron and hence do not degenerate. As a result, the sensory conduction in the nerve remains normal in-spite of clinical sensory signs and symptoms (which are due to involvement of the sensory pre-ganglionic fibres) (Fig. 2.)

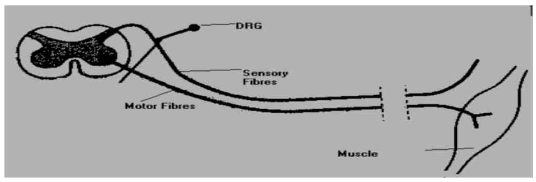


Fig. 2: The line diagram shows the motor unit. A lesion in the peripheral nerve will affect the SNAP, while a lesion above the DRG will not

In peripheral neuropathies the sensory fibres degenerate and the sensory conduction studies become abnormal. Hence sensory symptoms with normal sensory conduction place the lesion at the root level; e.g. compressive or non-compressive radiculopathies, but sensory symptoms with abnormal sensory conductions place the lesion within the nerves e.g. peripheral neuropathy. Motor fibres however degenerate in either case as their neuron lies in the spinal cord.

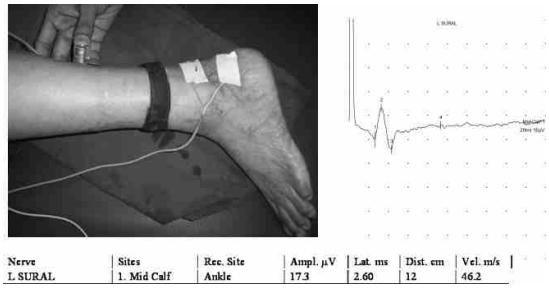
Now, by doing bilateral studies and sampling multiple nerves the symmetry and length dependent process can be identified. Similarly, other disease processes have their typical findings and distribution in the various EDx tests which are outside the scope of this article to describe.

A point to be noted is that the process of degeneration starts distal most & takes time to start and complete. Hence in acute conditions it takes time for the neurophysiological tests to localise the site of the abnormality. For example, for lesion at brachial plexus level, motor fibres take 4-7 days to degenerate, sensory fibres take 7-11 days and abnormality in the needle EMG can take up to 21 days to be fully established. This is a limitation due to the time taken for the degenerative pathological process.

Tests done

Nerve conduction studies are the building blocks of the entire study and must be performed carefully by trained physicians. Technicians, when doing it should be supervised throughout the test - else the incorrect recording could lead to incorrect interpretation. These tests examine the fastest conducting fibres and hence give information regarding the large fibres in the peripheral nerves

Sensory study (Fig. 3)

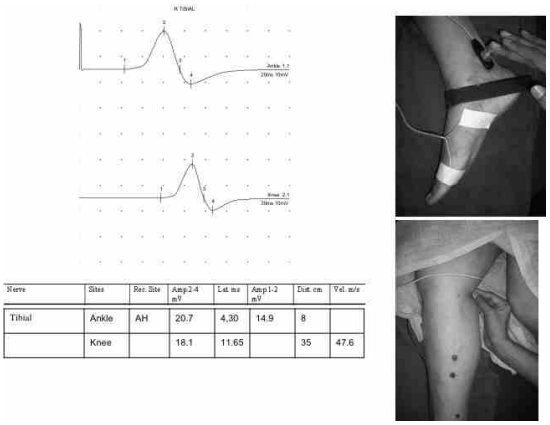


Nerve	Sites	Rec. Site	Ampl. µV	Lat. ms	Dist. cm	Vel. m/s
L SURAL	1. Mid Calf	Ankle	17.3	2.60	12	46.2

Fig. 3: Sensory conduction study in the Left sural nerve. Top left shows the technique. Top right is the SNAP and bottom is the data obtained

In this study the sensory nerve is electrically stimulated with a mild impulse at one site and the response is recorded along the nerve from another. The response obtained is called the sensory nerve action potential (SNAP) and the latency and amplitude of the response is measured and compared with reference data for the same age group and also with the other side. In axon loss lesions the amplitude of the response is attenuated and when severe the response maybe absent. In demyelinating lesions, the response is slowed beyond a certain critical limit which is defined by well-established criteria. The abnormal SNAP places the lesion at a post ganglionic level: either in the plexus or the relevant nerve. Symmetrically absent/ low amplitude SNAPs in nerves of lower limbs suggest a generalised peripheral neuropathy

Motor study (Fig. 4)



Nerve	Sites	Rec. Site	Ampl 2-4 mV	Lat. ms	Ampl 1-2 mV	Dist. cm	Vel. m/s
Tibial	Ankle	AH	20.7	4.30	14.9	8	
	Knee		18.1	11.65		35	47.6

Fig. 4: Motor conduction study in the Tibial nerve. Pictures to the right show the technique with stimulation at the ankle and in the popliteal fossa. Top left are the traces and the at bottom is the data obtained

In this study the response is recorded from a muscle when its nerve is stimulated at 2 sites along its course. The response is called a compound motor action potential (CMAP). The onset latency is measured at both sites and the amplitude of the response is also recorded. Measuring the distance between the stimulus sites and dividing it by the time taken for the response to travel that distance gives the motor nerve conduction velocity. The amplitude is a measure of axon numbers and drops in axonal neuropathies. In demyelinating neuropathies there is slowing of the conduction velocity and /or onset latency with conduction blocks and dispersion of the response. Criteria have been defined to recognise demyelination

Needle electromyography (Fig. 5)

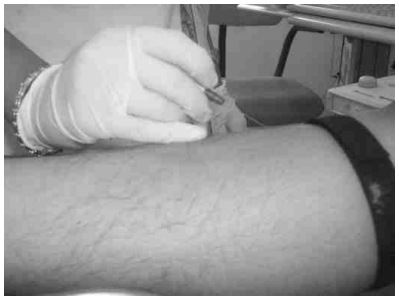


Fig. 5: Needle electromyography technique

This is an audio-visual, on-line study done with a needle electrode, which is introduced into a muscle and the activity from that muscle is recorded in 4 steps. The configuration of the potentials and sound they produce are both studied.

Insertional activity: This is the activity seen when the needle is gently moved in the muscle and consists of a burst of few tiny potentials. This activity is increased in early denervation and reduced when the muscle tissue is lost and replaced by fat or fibrous tissue

Muscle at rest: At rest there is no activity seen in a normal muscle, except at the end plate zone. In a denervated muscle spontaneous activity is seen in the form of fibrillation potentials - which are the hall mark of axon loss. (other forms of spontaneous activity are not described here)

Mild voluntary contraction of the muscle: When the patient is asked to give a mild voluntary contraction of the muscle being studied motor unit action potentials are seen. (MUAP or MUP). A motor unit action potential is generated by a motor unit which is the basis of all function. A motor unit- consists of the afferent fibres (peripheral sensory nerve and sensory roots) the motor neuron, (anterior horn cell) the efferent fibres (motor roots & peripheral motor nerve), the neuromuscular junction and the muscle fibres innervated by this motor neuron. The normal triphasic configuration of the motor unit gets altered in disease states and is useful to identify whether the lesion is "neuropathic" or "myopathic". In chronic neurogenic lesions the MUAP becomes larger and has a wider duration while in myopathic lesions the MUAP is small and short. (Fig. 6)

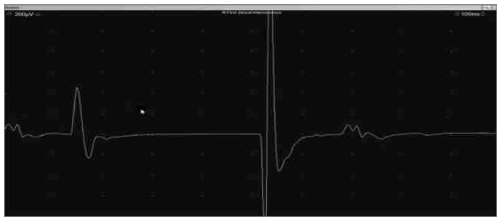


Fig. 6: Motor unit potentials from a chronic denervated muscle Note that they are of large amplitude and wide duration

Maximum voluntary contraction: In a normal muscle, maximum contraction yields a "full" interference pattern where individual motor unit action potentials are not discernible. Interference pattern correlates with the power of the muscle and hence is useful to document. When reduced it indicates that the muscle is weak.

F wave (Fig. 7)

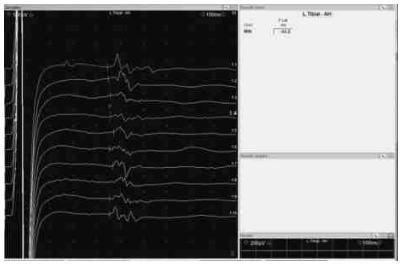


Fig. 7: Normal F waves from Tibial nerve stimulation

- Study done as for the motor nerve

- F wave is a late response and is recorded over the distal muscles
- Produced by back-firing of the motor neuron to the electrical stimulus
- Assesses the proximal segment of the motor nerve
- Utility: Demyelinating peripheral neuropathies, when it is always prolonged

NB: In early Diabetic peripheral neuropathy the only abnormality maybe a prolonged Tibial nerve F wave and hence it becomes a sensitive indicator

H reflex from gastrocnemius muscle (Fig. 8)

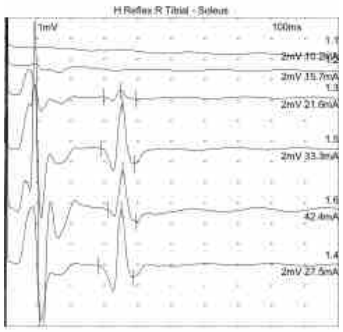


Fig. 8: Normal H reflex

This is a correlate of the ankle jerk and is a sensitive indicator of an early peripheral neuropathy

Autonomic tests

Sympathetic skin response (SSR) (Fig. 9)

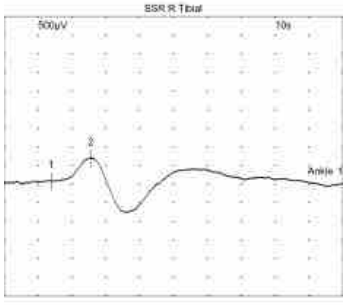


Fig. 9: Normal SSR

SSR is used for small fibre function testing and evaluated the sympathetic fibres

Heart rate variability (Fig. 10)

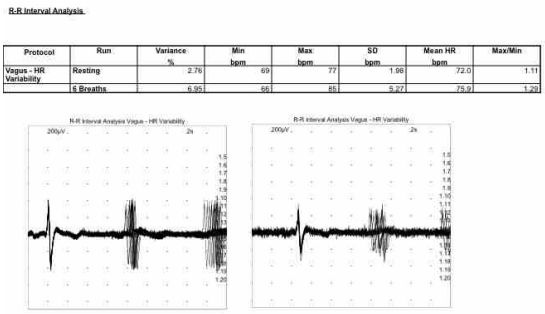


Fig. 10 Normal heart rate variability test

This is studied with deep breathing and is a study for the parasympathetic fibres

What should the patient expect?

NCS is done with surface electrodes and the stimulus is mild - in milli amperes and given locally. It is done safely even in new born babies. Only contraindication is in patients with older pacemakers. The patient feels the stimulus like a sharp tingle or a tap - initially it is a bit startling but the body gets used to it and most patients are fairly comfortable.

Needle EMG examination (NEE) is done using a thin gauge solid disposable needle electrode. Only the tip of the needle is inserted into the muscle. After recording the activity at rest (spontaneous activity, if any) the patient is made to contract the muscle. No stimulus is given and most people tolerate it well. NEE is avoided when there is local infection or patient has a bleeding disorder or is on anticoagulants

Diabetic neuropathies have multiple presentations

- Distal symmetrical sensory-motor peripheral neuropathy
- Small fibre peripheral neuropathy
- Painful distal sensory symmetrical neuropathy
- Radicular-plexo neuropathy
- Cranial neuropathies
- Focal neuropathies: Truncal, Femoral
- Autonomic neuropathy
- Predilection for entrapment neuropathies (carpal tunnel syndrome) & pressure palsies (Ulnar neuropathy & Fibula neuropathy)
- Acute painful neuropathy associated with rapid control of blood sugar
- Acute painful neuropathy associated with poor blood sugar control
- Chronic Inflammatory demyelinating polyradiculopathy in a diabetic patient

Distal symmetrical sensory-motor peripheral neuropathy

The commonest encountered in the EDx laboratory is the length dependent sensory-motor peripheral neuropathy. A case study would help to understand an EDx study report (Fig. 11)

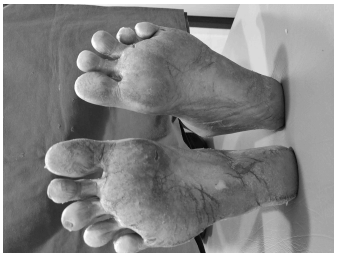


Fig. 11: Feet of a patient with severe, longstanding diabetic peripheral neuropathy. Note the wasted AH muscles, the scars of the healed ulcers and yet the lack of care for the feet

A 73 -year- old gentleman with a 33 -year- old history of diabetes mellitus is now seeking medical help for unsteady gait. On inquiry he has noticed that he has numbness in the feet since "many" years but was told by his doctor to expect this as he has diabetes. His slippers fall off his feet without his knowledge since at least 5-6 years and he has had injuries in the feet he is not aware of. His blood sugar levels fluctuate and have never really been well controlled.

ENMG study

Sensory nerve conduction study

Nerve	Sites	Rec. Site	Ampl. µV	Lat. ms	Dist. cm	Vel. m/s
R MEDIAN	1. Index finger	Wrist	2.7	2.95	14	47.5
R RADIAL	1. MFA	Snuff box	17.2	2.10	12	57.1

Comments

- R Median : Low amplitude
- R Radial : Normal for age
- L & R Sural: No Response
- L & R Sup peroneal: No Response

From the above it can be ascertained that there is significant symmetrical sensory involvement in lower limb > upper limb nerves

Motor nerve conduction

Comments

- No motor response from the Tibial nerves bilaterally
- Significantly attenuated motor response from the EDB muscle
- Tibialis anterior motor response is also mildly low amplitude
- Gastrocnemius motor amplitudes are normal
- Median motor is mildly slowed across the wrist but normal in amplitude

From the above it can be judged that there is a length dependent, lower limb, distal > semi-distal axonal peripheral neuropathy.

Muscle	Spontaneous	Voluntary	IP	Remarks
R Tibialis Anterior Deep Peroneal L45	Nil	Large wide tri & polyphasic motor unit potentials	Mildly Reduced	Chronic partial denervation
Left Abductor Hallucis Tibial Nr S12	Fibrillation potential +++	No motor units	Nil	Severe active denervation
R Vastus Medialis Femoral L34	Nil	Normal	Full	Normal
R First DIO Ulnar C8T1	Nil	Large wide triphasic motor unit potentials	Mildly Reduced	Mild Chronic partial denervation
R Gluteus Medius Sup Gluteal Nr L5	Nil	Normal	Full	Normal

Sympathetic Skin Response: Present from the palm, Absent from the sole

Needle EMG

EMG examination shows denervation in the distal >> semi-distal lower limb muscles >> distal upper limb muscles as listed below

IMPRESSION

There is EDx e/o a peripheral neuropathy

Type: Generalised, symmetrical, length dependent, axonal, distal, sensory -motor, affecting lower > upper limbs, large & small fibres -possibly related to Diabetes mellitus

Hence EDx in a peripheral neuropathy helps to classify as below

- Generalised / focal / widespread
- symmetric / asymmetric / multifocal
- length dependent (LL>UL)
- Axonal or demyelinating
- distal / distal + proximal
- acute / acute on chronic / chronic
- severity
- large fibre / small fibre / both
- probable aetiology if possible

Nerve	Sites	Amp. 2-4 mV	Lat. ms	Amp. 1-2 mV	Area %	Dur. %	Dur. ms	Dist. cm	Vel. m/s
R MEDIAN -	1.Wrist	8.3	4.45	5.8	100	100	8.60	6	
APB	2.Elbow	8.1	9.05	5.8	84.1	98.3	8.45	26	56.5
L COMM	1. Ankle	0.3	6.35	0.2	100	100	7.20	8	
PERONEAL -EDB	2. Fib head	0.2	16.25	0.2	68	91.7	6.60	31	31.3
L TIBIAL - AH	1. Ankle		NR						
R TIBIAL_ AH	1. Ankle		NR						
L COMM PERONEAL - TA	1. Fib Head	5.4	3.2	2.4					
R TIBIAL - Gastroc	1. Knee	12.2	3.5	8.5					
L TIBIAL - Gastroc	1. Knee	14.6	3.7	9.2					

The above is an example of a severe peripheral neuropathy but the main forte of EDx is in diagnosing a sub-clinical peripheral neuropathy which could aid in preventing the development of such a severe condition as above. We are surprised by the number of diabetic patients who accept that they will develop a peripheral neuropathy and hence do not seek medical attention till it reaches the above state.

Early or subclinical peripheral neuropathy can be diagnosed using sensitive tests as listed below

- Distal sensory nerve action potentials of the medial plantar and dorsal sural nerve
- Tibial F wave minimal latencies
- Needle EMG of the feet muscles
- Sural: Radial amplitude ratio

Small fibre neuropathies are difficult

to diagnose and often the SSR is not sensitive enough to detect the small fibre involvement. However, if the SSR is absent, it suggests small fibre involvement. Though routine NCS only examine the large fibres, there is a recent study to show that distal foot muscles may show denervation in small fibre peripheral neuropathy

Diabetic radicular-plexopathies (earlier called Diabetic amyotrophy) have a typical clinical presentation with asymmetric painful weakness accompanied by weight loss. On EDx they show localised motor or motor > sensory axonal loss involving the plexus or roots. They need to be differentiated from compressive radiculopathies, which EDx can.

Truncal neuropathies (Fig. 12)

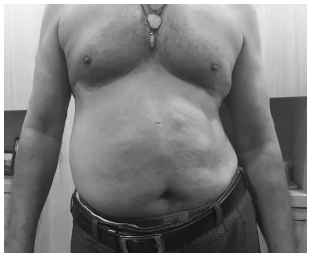


Fig. 12: Truncal neuropathy with an apparent swelling of the abdomen

They present as localised pain in the abdominal region and can be mis-diagnosed, leading to surgeries for a "painful abdominal swelling". EDx helps in the diagnosis as it shows denervation in the relevant abdominal/intercostal muscles

CIDP in a diabetic patient: Some patients develop rapidly progressive proximal weakness which should be diagnosed on EDx studies by the evidence of demyelination in the motor nerves. However, the presence of an underlying diabetic peripheral neuropathy makes the diagnosis of this treatable condition difficult, especially if the diabetic neuropathy has not been previously documented on EDx. Presence of significant demyelination on nerve conduction should raise the possibility of this condition

Carpal Tunnel Syndrome, Ulnar & Fibular pressure palsies can present as focal painless chronic / acute sensory-motor deficits on an underlying diabetic peripheral neuropathy. They can be diagnosed on nerve conduction studies

Painful mononeuropathies probably ischaemic, are known to occur in patients with diabetes and are usually monophasic. Recovery depends on the extent of axon loss among other factors and EDx should help to localise the site and prognosticate the severity

Autonomic neuropathies need more extensive diagnostic procedures. The heart rate variability test may help to document the parasympathetic dysfunction

To summarize, Electrodiagnosis is one of the essential tools in the treatment and care of the patient with diabetes mellitus. Even though peripheral neuropathies of various types as listed above may not be totally preventable, diagnosis of the sub-clinical length dependent peripheral neuropathy may make the patient aware that his nerves are being compromised and provoke him to take better care-preventing serious complications of ulceration and gangrene. In other neuropathies it is essential for the diagnosis and prognosis.