NERVE CONDUCTION STUDIES: PRACTICAL PHYSIOLOGY AND PATTERNS OF ABNORMALITIES

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Introduction

Nerve conduction studies (NCS), together with the needle electrode examination (NEE), constitute the electrodiagnostic examination. For most neuromuscular diagnostic problems, the NCS are the initial probe into the peripheral nervous system. The findings from the NCS will dictate what muscles must be studied during the subsequent NEE. Usually a complete electrodiagnostic impression depends upon the findings of both the NCS and the NEE, but only the NCS can confirm the presence of entrapment mononeuropathies, demyelinating neuropathies, and defects of neuromuscular junction (NMJ) transmission.

Responses can be recorded along peripheral motor and sensory axons. Characteristics of the responses include the amplitude, duration, latency, and velocity of responses. From these parameters, patterns of nerve pathology can be identified, including axon loss, demyelination, and conduction block. Although there are no specific NCS features of myopathy, muscle fiber loss and muscle fiber inexcitability affect the amplitude of motor responses. With NMJ transmission defects, specific abnormalities on NCS are identified.

Generation of an Action Potential

An electrical stimulus applied to a sensory or motor nerve fiber opens voltage-gated sodium channels in the nerve fiber membrane, leading to sodium influx and local depolarization of the membrane. If the threshold of depolarization is reached, a self-sustaining electrical impulse is generated at that site, termed an "action potential". The action potential is propagated along the nerve fiber by sequentially depolarizing the membrane in both directions from the original point of stimulation.

The Sensory Nerve Action Potential (SNAP)

The electrical field generated around a propagated action potential can be measured at some distance from the nerve fiber itself, but the size of the recorded response drops off as a square of the distance between the generator and the recording electrodes. When a group of nerve fiber action potentials are being propagated simultaneously in a nerve trunk, the electrical fields of the potentials summate in the surrounding area, known as the volume conductor. The SNAP is recorded from tin disc electrodes placed on the skin over the nerve trunk, either proximal or distal to the stimulation point of the nerve. It represents the summation of action potentials from all recordable nerve fibers in the volume conductor. Measurable features of a SNAP include the amplitude, duration, latency, and configuration (figure 1). SNAP amplitudes range from 5 to over 200 microvolts, depending on the particular nerve trunk being studied. Normally the SNAP is a triphasic waveform with an initial positive deflection, because the propagated depolarization along the nerve trunk approaches the recording electrode from the stimulation site.

The Compound Muscle Action Potential (CMAP)

With motor NCS, stimulation is applied at distal and proximal sites along a nerve trunk. Recording of the resulting action potential occurs with surface electrodes overlying a muscle belly innervated by the stimulated nerve. Since the active recording electrode overlies a muscle belly, the recorded response is a compound muscle action potential (CMAP), not a nerve action potential. The CMAP represents a summation in the volume conductor of all the individual muscle fiber action potentials activated by the stimulus and within the pick up territory of the active recording electrode. Normally, the CMAP is a biphasic waveform with an initial negative deflection (figure 2). This configuration results from placement of the active recording electrode at the motor point of the muscle belly, where the muscle fibers are initially depolarized and their action potentials are generated. Displacement of the active recording electrode off the motor point will result in an initial positive deflection in the recorded CMAP due to volume conduction of the muscle fiber action potentials from the motor point to the

electrode. The CMAP is measured in millivolts, compared to microvolts for a sensory action potential, because the size of an action potential is proportional to the diameter of the excitable tissue from which it is derived.

Factors Influencing the Recorded Action Potential

A number of factors contribute to the size and shape of a normal SNAP and CMAP. These include the spatial relationship between the active and reference recording electrodes, the effect of recording distance on action potential size, the effect of filtering, and the effect of temperature.

Effects of Recording Electrode Placement

Manipulating the electrode placement in a differential amplifier recording system can affect the amplitude of the recorded potential. This is especially necessary when recording sensory nerve action potentials in the microvolt range. By maintaining a 2-4 cm distance between the active and reference electrodes, summation of the responses from each of the electrodes produces a higher amplitude potential than either response individually (figure 7).

Because the CMAP size is measured in millivolts, it is not necessary to space the active and reference recording electrodes so that the potential at the reference electrode site adds amplitude to the waveform. Rather, by minimizing the reference electrode's contribution to the CMAP response, variability in response size due to imprecise electrode placement can theoretically be minimized, and standardization of the technique improved. This has traditionally been accomplished by applying the reference electrode over the tendon distal to the muscle belly on which the active electrode is applied. Recent work has confirmed that the reference electrode may not be electrically silent in relation to the active electrode. This is especially true for the ulnar and tibial motor nerve conduction studies, where the traditional reference electrode position can contribute a greater amount toward the main negative peak of the CMAP than does the active electrode.[1, 2]

Effects of Distance from Point of Stimulation to Recording Site

The CMAP generated at a proximal site of stimulation differs modestly from the CMAP obtained with distal stimulation (figure 8). The measurable differences include reduced amplitude and area, increased duration, and shallower initial negative slope of the proximally generated CMAP. These changes result from temporal dispersion, or desynchronization, of the individual muscle fiber action potentials, due to different rates of conduction along motor nerve fibers.[3] The lesser degree of temporal dispersion seen in CMAPs compared to SNAPs is attributed to the narrower range of conduction velocities along motor nerve fibers in a nerve trunk, and the broader duration of CMAPs.[4] (figure 9) Based on a mathematical model of the CMAP as a sum of asynchronous single nerve fiber action potentials, it has been estimated that there is an 11 m/sec difference between fastest and slowest motor fibers in a motor nerve trunk, versus a 25 m/sec difference for sensory fibers.[5]

For a SNAP, the lower amplitude obtained after proximal stimulation is likely related to physiological phase cancellation due to the velocity-related temporal dispersion of sensory action potentials over a nerve segment and the short duration of sensory action potentials.[4] (figures 10,11) For motor NCS in normal subjects, most laboratories expect less than 20% decrease in the amplitude between the distal stimulation site and elbow or knee, with the exception of the tibial study, where up to a 50% decrease in amplitude with proximal stimulation can occur.

The degree of temporal dispersion in a CMAP is related to the length of the conducted segment and the range of conduction velocities in the nerve trunk. Therefore, the impact will be greater along nerves in the leg, especially the tibial nerve. Using clinical measurements and Fourier analysis from 86 subjects, Schulte-Mattler, et al. found that amplitude loss was most marked for the tibial (36%) and ulnar (21%) nerves, area loss for the median (12%) and ulnar (18%) nerves, and duration prolongation for the tibial (32%) and ulnar (17%) nerves.[3] None of these findings was age dependent. Their data showed that the dependence of these variables on length was approximately linear. In a disease state, the range between fastest and slowest motor fibers increases, and phase cancellation becomes more prominent along motor nerves.[6]

Effects of Filtering

Electrophysiological recordings obtained from a differential amplifier can be altered by manipulating the bandwidth of frequencies allowed to contribute to the recording. Filter settings are chosen to maximize the

contribution of frequencies close to the recording electrodes and minimize contamination of the recording by remote generators. Because amplitude, latency, and waveform configuration change as filter settings are altered, standard settings are required.

Increasing the low frequency filter setting tends to reduce SNAP and CMAP amplitude, peak latency, and total waveform duration (figure 12). These effects are related to the filtering out of important low frequency components contributing to the overall size of the waveform. There is no effect on the onset latency of the waveform.[7] Decreasing the high frequency filter tends to increase peak and onset latencies, and increase the negative spike component of the SNAP and CMAP (figure 13). Onset latency becomes delayed because high frequency components over a short duration at the onset of the waveform are filtered out, causing a "drop out" of the first part of the potential. There is little effect on the amplitude down to a frequency of 500 Hz for the CMAP, but the SNAP amplitude drops significantly.

Because SNAP amplitudes are low, their waveforms can be easily corrupted by extraneous low frequency components distant to the sensory nerve generators being recorded. This occurs because physiological tissue acts as a "low-pass" filter, a tendency that can be minimized by increasing the low filter setting for sensory NCS. Therefore, for routine sensory NCS, the low filter setting is set at 20 Hz and the high filter setting is at 2 KHz.

Filter settings for motor NCS should allow a wider recording bandwidth. The low filter setting is usually set at 2 Hz, and the high filter setting is 10 KHz. Because the CMAP response is large (measured in millivolts), the effect of contamination from CMAPs of neighboring muscle bellies is less important. Thus, the objective is to include as many of muscle fiber action potentials as possible in the summated CMAP of the recorded muscle.

Effects of Temperature

As muscle temperature decreases, SNAP and CMAP amplitude, duration, rise time, area, and latency all increase (figure 14). Local cooling leads to increased voltage of nerve fiber and muscle fiber action potentials.[8] This is the result of delayed voltage gated sodium channel inactivation, leading to excess depolarization of the fiber membrane and subsequently increased propagated action potential duration, spike height, and area.[9]

Late Responses

Late responses are electrical stimulus-evoked motor potentials that can be used to measure the travel time of propagated nerve action potentials from a distal point of electrical stimulation along a peripheral nerve trunk, proximally to the spinal cord, and then back down the limb to a muscle belly innervated by the same peripheral nerve trunk. Theoretically, they make possible the assessment of conduction through segments of peripheral nerve proximal to the segment evaluated with standard NCS.

F Waves

The F wave is a motor response recorded from a muscle belly after stimulation of the peripheral nerve trunk innervating the muscle. It is thought to arise from the "backfiring" of motor neurons as impulses arrive antidromically from a peripheral site of motor nerve trunk stimulation. The F wave occurs after the orthodromic CMAP, but as the point of nerve trunk stimulation is moved more proximally, the CMAP latency lengthens and the F wave latency shortens, indicating that the impulse eliciting the F wave travels away from the recording electrodes toward the spinal cord before returning to activate distal muscles. Traditionally the shortest latency of at least 8 consecutive discharges is measured (figure 15). The absence of an F wave response from stimulation of the median, ulnar, or tibial nerve in the presence of normal evoked CMAPs from the same muscle suggests conduction block or very recent (less than 5-8 days) axon loss somewhere along the nerve trunk proximal to the point of nerve stimulation. The usual measurement is latency, as the amplitude of the F wave (usually 100-500 microvolts) is variable. Other measurement parameters may be more sensitive, such as F wave duration, mean F latency, and chronodispersion. Peroneal F responses are not reliably recorded in normal individuals.

The H-reflex

The H-reflex has been considered the electrophysiological equivalent of the Achilles tendon (ankle) muscle stretch reflex, when elicited from the soleus/gastrocnemius muscle complex after tibial nerve stimulation at the popliteal fossa (figures 16,17). While the contention that the H reflex represents conduction through a monosynaptic pathway is likely to be overly simplistic, it is clear that the electrical stimulus travels orthodromically

along Ia afferents to the spinal cord, where the motor neuron in the same segment is activated, producing a motor response peripherally. Under normal circumstances, aside from the H reflex elicited from tibial nerve stimulation at the popliteal fossa, an H reflex can be elicited reliably only from the median nerve, recording over the flexor carpi radialis. In the presence of corticospinal tract disease, it can be elicited from many nerve trunks, as a result of loss of the normal central inhibitory influences on motor neuron pools. Only the tibial H reflex is routinely used in clinical practice, where it is an extremely sensitive test for the assessment of the integrity of the tibial/S1 sensory pathway, including the intraspinal course of the S1 root. Abnormalities anywhere along the tibial/S1 sensory or motor pathway will alter the H response, including posterior tibial mononeuropathies proximal to the branch point of the nerve to the soleus and gastrocnemius muscles. Thus, an H reflex abnormality is insufficient by itself to confirm the presence of an S1 radiculopathy.

Basic Patterns of Abnormality

Electrodiagnostic Correlates of Weakness

Although a number of symptoms bring patients to the electrodiagnostic laboratory, weakness is the primary symptom being explored with motor NCS. Among all the motor parameters examined, CMAP amplitude is the only one that correlates closely with weakness. While changes in conduction velocity and latency may be seen in patients who are weak, weakness is directly related to interruption of impulses along motor nerves, leading to failure to depolarize muscle fibers. Established axon loss of motor nerve fibers produces CMAPs of reduced amplitude at all points of stimulation along the nerve, irrespective of the location of initial injury to the nerve fibers. Conduction block is the result of demyelination along motor nerve fibers to the extent that essentially all action potential propagation across the demyelinated segment ceases, even though the underlying motor axons remain intact. The result of either axon loss or conduction block along a nerve fiber is the failure of action potential arrival at the nerve terminal, and ultimately failure of muscle fiber contraction. Less complete demyelination along a nerve fiber may cause disruption of saltatory conduction without complete interruption of action potential transmission. The result is slowing of conduction, but the action potential reaches the nerve terminal, and ultimately its muscle fiber contracts. Thus, slowing of conduction velocity and prolongation of latency do not by themselves cause weakness.

Evolution of CMAP and SNAP Loss in an Acute Axon Loss Process

After nerve transection, a series of pathological events take place culminating in Wallerian degeneration of the nerve fibers. In spite of complete disconnection of the distal nerve fibers from their proximal portions and their anterior horn cells, and in spite of cessation of axonal transport, the distal nerve fiber membranes can still be depolarized and action potential propagation continues for some days. Progressively, nerve fiber disintegration and neuromuscular junction transmission failure result in loss of nerve excitability and loss of muscle fiber depolarization.

After a severe proximal motor nerve trunk transection, with stimulation of the nerve distal to the point of transection, the evoked CMAP amplitude remains normal until day 3 after transection (figure 18). From that point, until day 5-8, there is a nearly linear decline in the evoked CMAP amplitude until the lowest amplitude is obtained, determined by the proportion of motor nerve fibers transected. [10] During this process there is no significant change in the motor latencies or conduction velocities. In studies of progressive motor neuron disease of the ALS type (amyotrophic lateral sclerosis), Lambert demonstrated that the mean ulnar motor conduction velocity of 322 patients did not fall below 50 m/s until >75% of CMAP amplitude had been lost, corresponding to loss of the last fastest-conducting motor nerve fibers. [11]

In comparison, the SNAP amplitude falls at a different rate after nerve fiber transection. With stimulation and recording distal to the point of nerve transection, the sensory nerve action potential amplitude remains normal until day 5. From that point, until day 8-10, there is a nearly linear decline in the evoked sensory nerve action potential amplitude until the lowest amplitude is obtained, determined by the proportion of sensory nerve fibers transected (Wilbourn, 1986). Decline of the sensory nerve action potential amplitude reflects failure of nerve fiber action potential propagation alone, since the response is recorded from the nerve fibers themselves. The faster failure of motor conduction as measured from the CMAP likely reflects earlier failure of neuromuscular junction transmission.

Patterns of Abnormality on Routine Nerve Conduction Studies

Disorders affecting peripheral nerves may be primarily axon loss in etiology, primarily demyelinating, or mixed. The following discussion focuses on the effects of axon loss and depolarization along motor nerve fibers.

With axon loss processes, the NCS pattern differs for acute and subacute/chronic lesions. With an acute complete transection of the median nerve trunk in the forearm of 3 days duration or less, stimulation of the median nerve at the elbow, recording over the thenar eminence will yield no CMAP response. With stimulation anywhere below the site of transection, the CMAP will have normal amplitude. After 8 days from the time of transection, stimulation of the nerve anywhere along its course will yield no CMAP response (figure 19).

With predominantly demyelinating processes, the NCS pattern varies according to the nature and severity of the demyelinating lesion (figure 20). A diffusely and homogeneously demyelinating process (such as Charcot Marie Tooth Disease Type 1a) will demonstrate relatively preserved CMAP configurations with prolonged latencies and slowed conduction velocities. A non-uniform, segmental demyelinating process (such as acute inflammatory demyelinating polyneuropathy; i.e., Guillain Barré Syndrome) may demonstrate conduction block and variable slowing within the same nerve trunk, resulting in CMAPs with reduced amplitude and dispersed configuration at proximal sites of stimulation. Focal or generalized slowing of conduction as the sole manifestation of a peripheral nerve disorder is uncommon. Median neuropathy at or distal to the wrist (carpal tunnel syndrome) of mild-moderate severity may be the only common example of this pattern. A focal conduction block (such as is seen with compressive radial neuropathy at the spiral groove) will resemble the pattern noted in the acute stage of a partial or complete nerve trunk transection.

Mixed patterns of demyelination and axon loss are common (figure 21). This is because, (1) progressive demyelination is often associated with damage to the underlying axons, and (2) axon loss processes develop electrophysiological features of demyelination along regenerating nerve fibers. Some axon loss disorders, such as diabetic polyneuropathy, have an electrophysiological signature that includes mild features of demyelination. Focal entrapment of the peroneal nerve at the fibular head is an example of a focal nerve disorder that is characterized most commonly by the presence of focal demyelinating conduction block across the fibular head, with associated features of axon loss. With NCS, peroneal motor CMAPs are reduced in amplitude at all sites of stimulation, but there is superimposed additional loss of amplitude with stimulation proximal to the fibular head.

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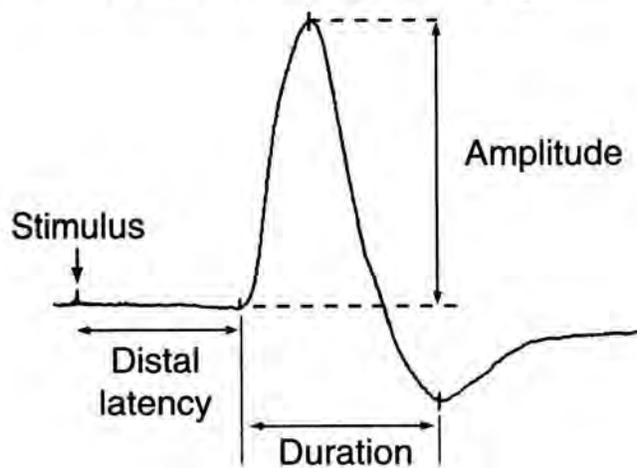
Figure 1

Sensory nerve conduction study
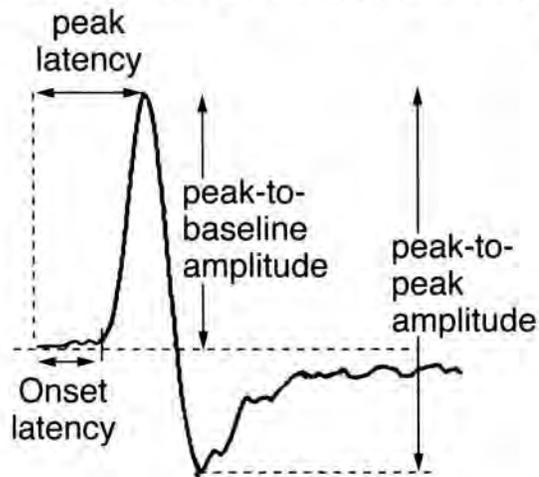
peak latency

peak-to-baseline amplitude

peak-to-peak amplitude

Onset latency

Lederman RJ. Nerve conduction studies. In: Comprehensive Clinical Neurophysiology (Levin KH, Lüders HO, eds). WB Saunders, 2000, p99, with permission.
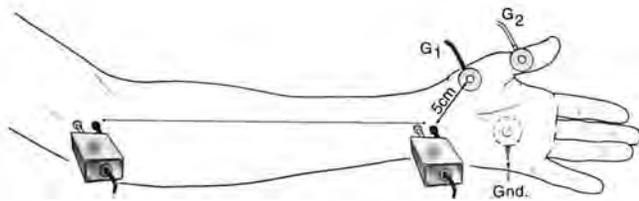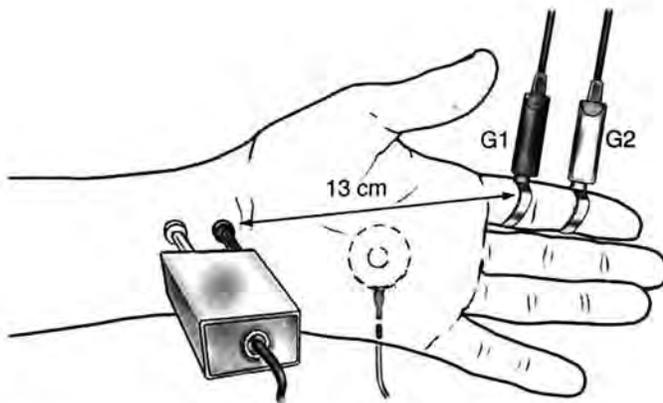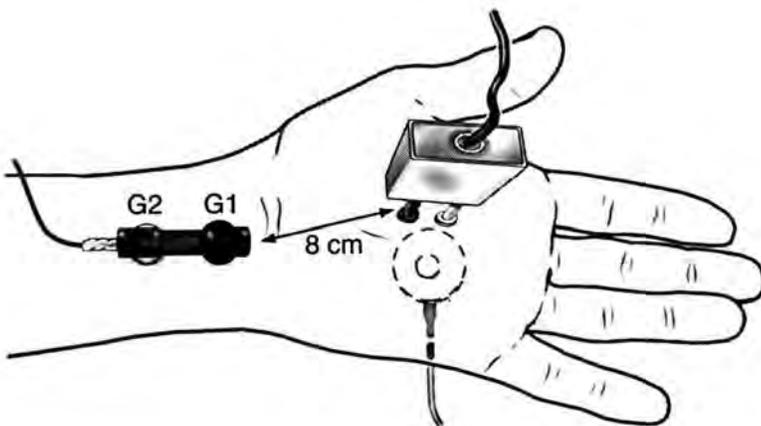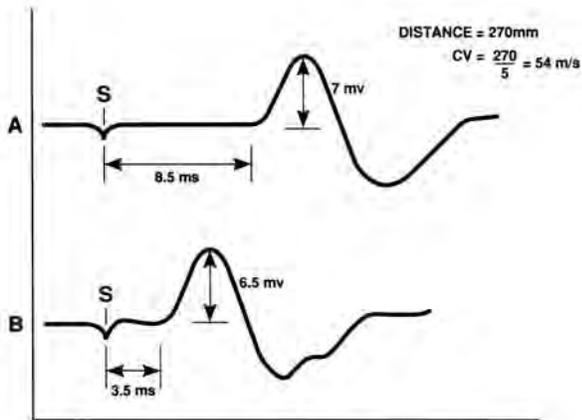
Figure 2
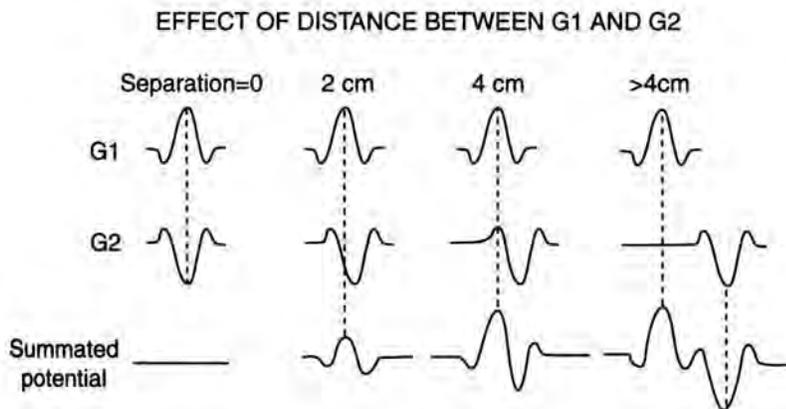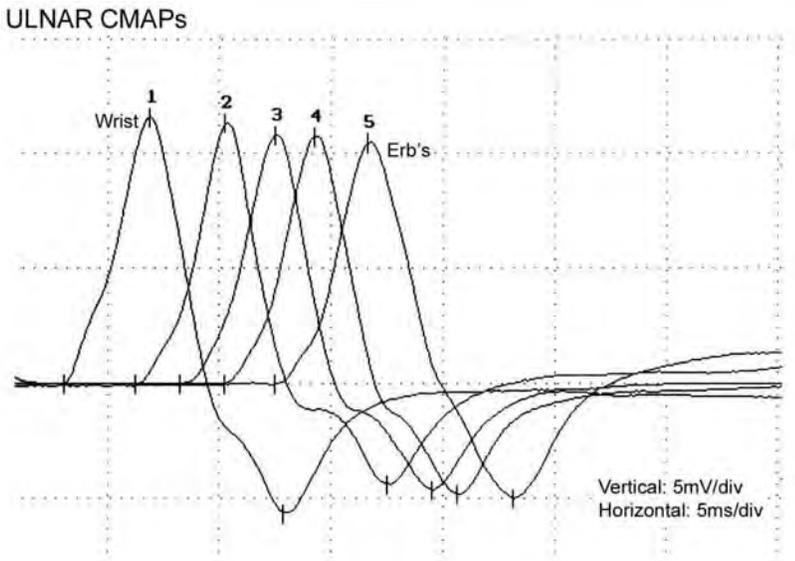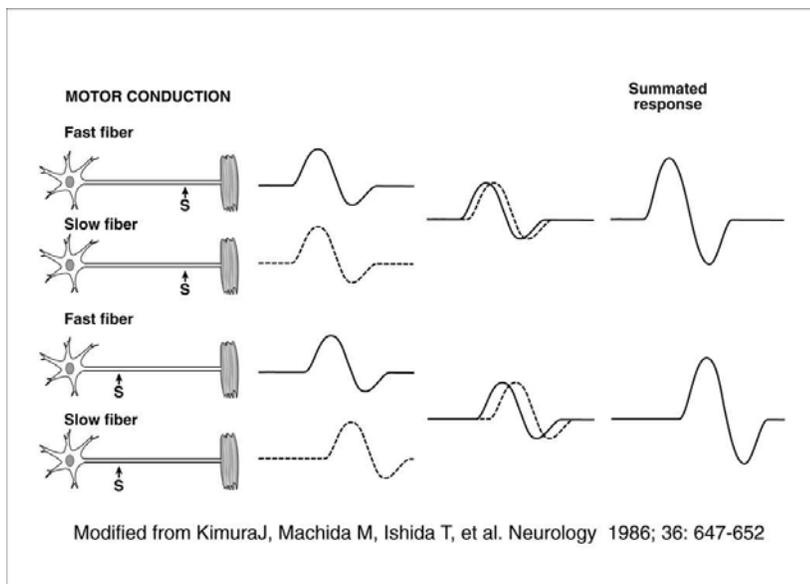

Motor nerve conduction study

Amplitude

Stimulus

Distal latency

Duration

Lederman RJ. Nerve conduction studies. In: Comprehensive Clinical Neurophysiology (Levin KH, Lüders HO, eds). WB Saunders, 2000, p97, with permission.

Figure 3

Reproduced with permission.

Figure 4

Lederman RJ. Nerve conduction studies. In: Comprehensive Clinical Neurophysiology (Levin KH, Lüders HO, eds). WB Saunders, 2000, p99, with permission.

Figure 5

Lederman RJ. Nerve conduction studies. In: Comprehensive Clinical Neurophysiology (Levin KH, Lüders HO, eds). WB Saunders, 2000, p101, with permission.

Figure 6

DISTANCE = 270mm

$$CV = \frac{270}{5} = 54 \text{ m/s}$$

Levin KH. Common focal mononeuropathies and electrodiagnosis. J Clin Neurophysiology 1993; 10:181-189, with permission.

Figure 7

EFFECT OF DISTANCE BETWEEN G1 AND G2

Lederman RJ. Nerve conduction studies. In: Comprehensive Clinical Neurophysiology (Levin KH, Lüders HO, eds). WB Saunders, 2000, p105, with permission.

Figure 8

ULNAR CMAPs

Vertical: 5mV/div
Horizontal: 5ms/div

Figure 9

Modified from KimuraJ, Machida M, Ishida T, et al. Neurology 1986; 36: 647-652

A model of phase cancellation among muscle fiber action potentials from fast and slow conducting motor nerve fibers. In the volume conductor, with distal stimulation two motor unit action potentials summate to produce a motor action potential that is twice as large. With proximal stimulation the long duration motor unit action potentials still superimpose nearly in phase despite the latency shift of the slow motor fibers.

Figure 10

MEDIAN SNAPs

Vertical: 20 mcV/div
Horizontal: 2 ms/div

Figure 11

Modified from KimuraJ, Machida M, Ishida T, et al. Neurology 1986; 36: 647-652
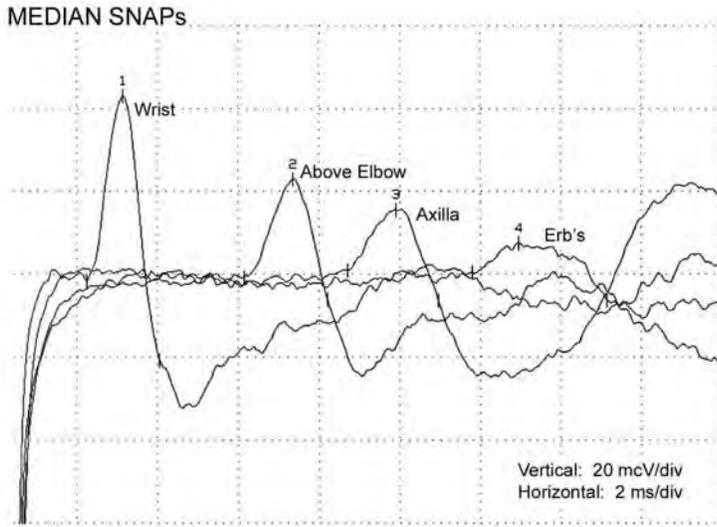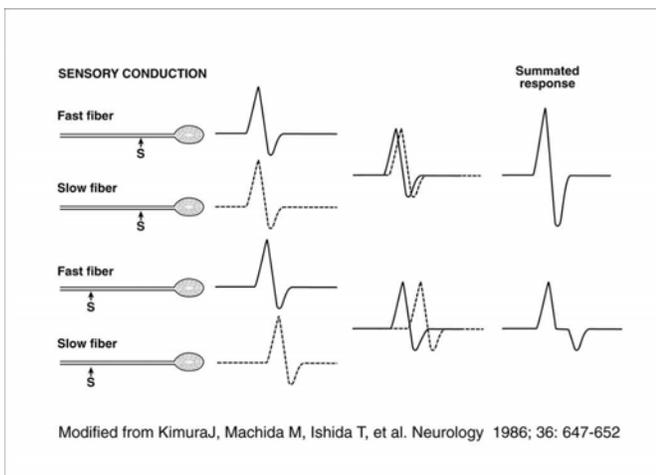
A model of phase cancellation among action potentials from fast and slow conducting sensory nerve fibers. In the volume conductor, with distal stimulation the sensory action potentials summate to produce an action potential that is twice as large. With proximal stimulation the latency shift of the slow SNAPs causes phase cancellation when summated with the faster SNAPs.

Figure 12

MEDIAN SNAP

3.4 msec

10 μV

1 msec

3 Hz - 2k Hz

10 Hz - 2k Hz

100 Hz - 2k Hz

3.1 msec

500 Hz - 2k Hz

Gitter AJ, Stolov WC. Muscle Nerve 1995; 18: 799-811
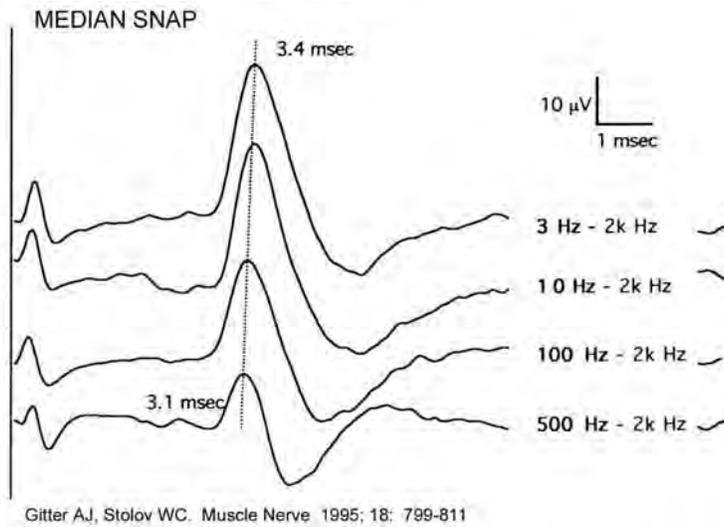
The effect of the low frequency response on the SNAP. Increasing the low frequency filter decreases amplitude and peak latency. Reproduced with permission.

Figure 13

MEDIAN SNAP

10Hz - 10k Hz

10Hz - 2k Hz

10Hz - 500 Hz

10 μV

1 msec

42 μV

26 μV

Gitter AJ, Stolov WC, Muscle Nerve 1995; 18: 799-811
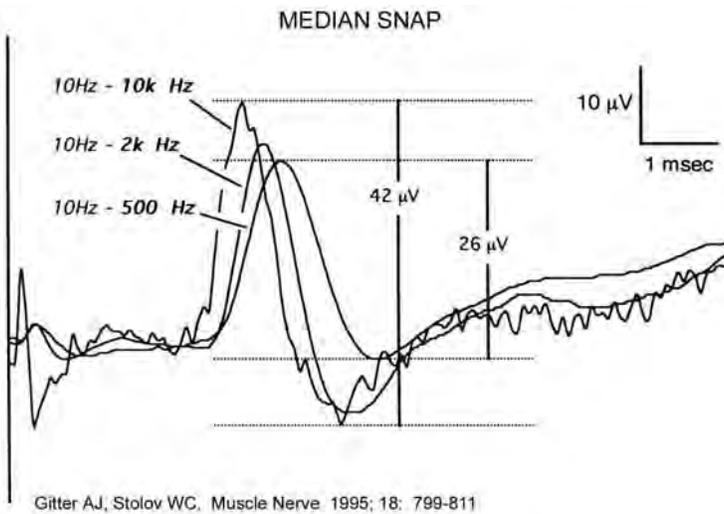
Changes in the median SNAP recorded with high frequency filter settings ranging from 10 KHz to 500 Hz. Decreasing the high frequency filter decreases amplitude and increases peak latency. Reproduced with permission.

Figure 14

EFFECTS OF TEMPERATURE ON SNAP

----- 22°C
——— 31°C
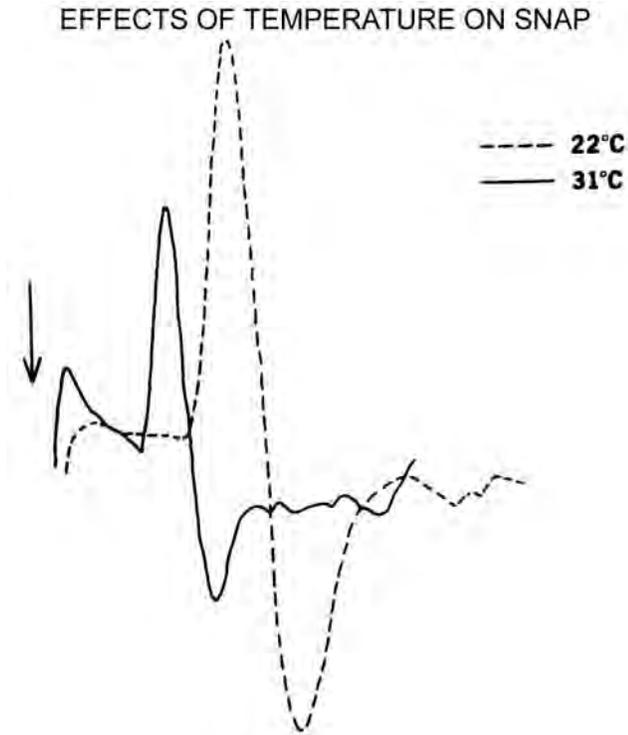
Bolton CF. AAEM Minimonograph #17. American Association of Electromyography and Electrodiagnosis 1981, reproduced with permission.

Figure 15

F wave

1 mV

10 msec
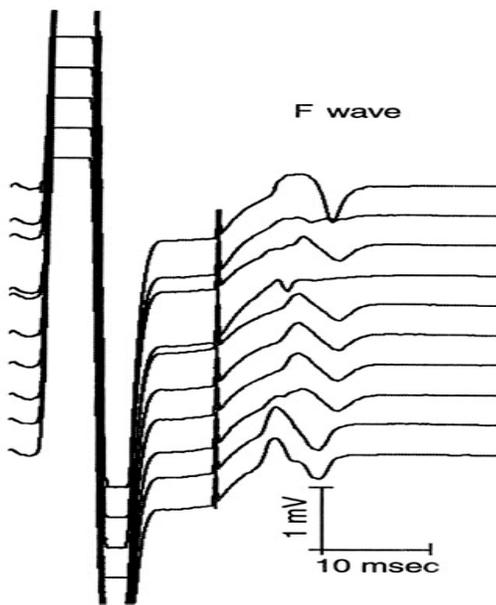
F waves. Lederman RJ. Nerve conduction studies. In: Comprehensive Clinical Neurophysiology (Levin KH, Lüders HO, eds). WB Saunders, 2000, p103, with permission.

Figure 16
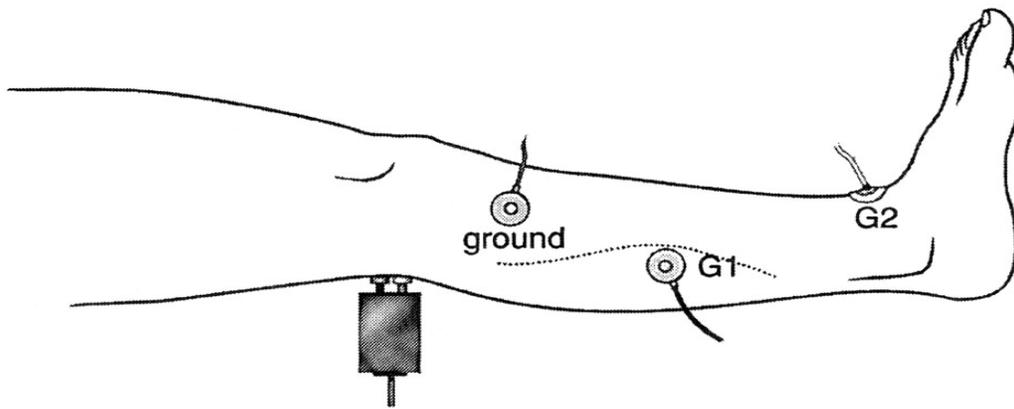
Set up for performing an H-reflex. Lederman RJ. Nerve conduction studies. In: Comprehensive Clinical Neurophysiology (Levin KH, Lüders HO, eds). WB Saunders, 2000, p101, with permission.

Figure 17
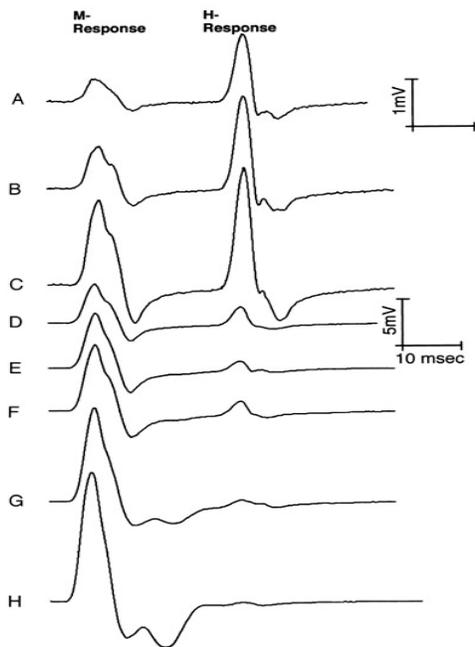
The H-reflex. Lederman RJ. Nerve conduction studies. In: Comprehensive Clinical Neurophysiology (Levin KH, Lüders HO, eds). WB Saunders, 2000, p102, with permission.

Figure 18
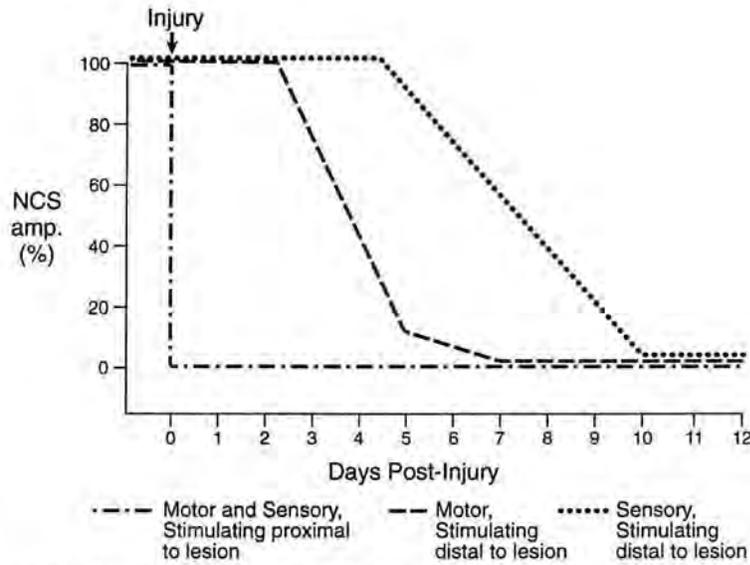
Wilbourn AJ. Muscle Nerve 1986; 9: 825-836.

The time course of changes in the CMAP and SNAP amplitudes following a severe axon loss lesion of the common peroneal nerve. Wilbourn AJ. AAEE Case Report #12: common peroneal mononeuropathy at the fibular head. Muscle Nerve 1986; 9: 825-836, reproduced with permission.
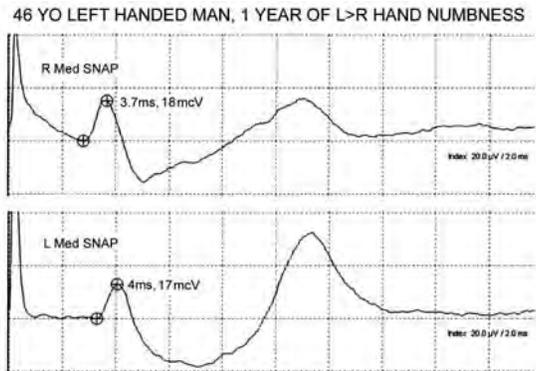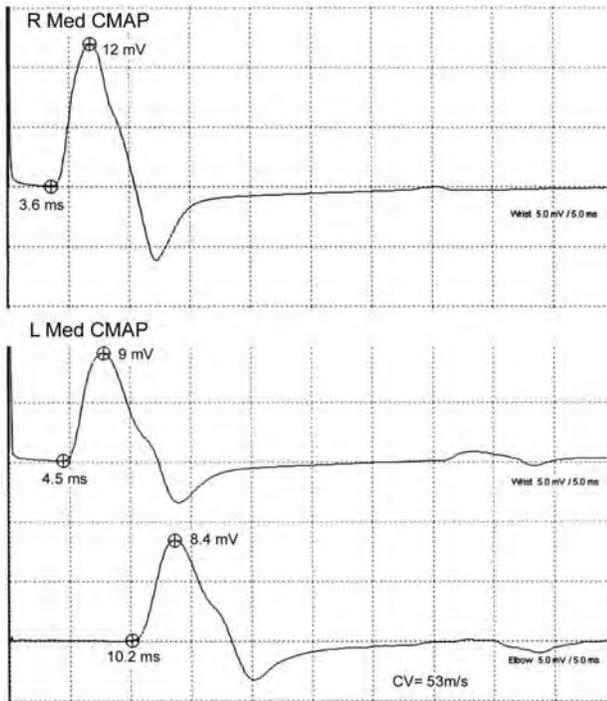
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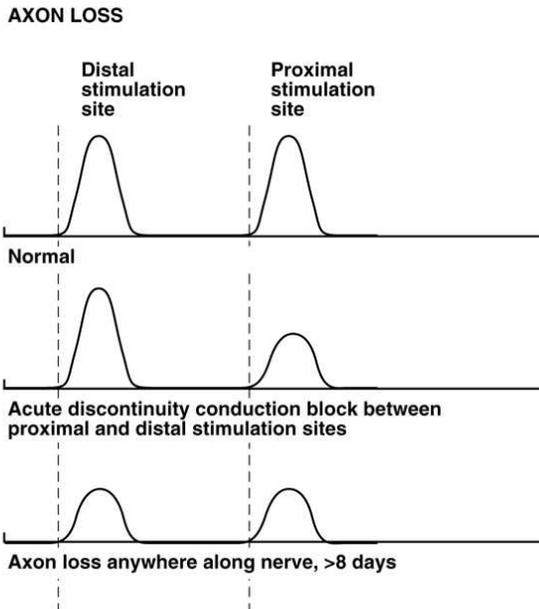
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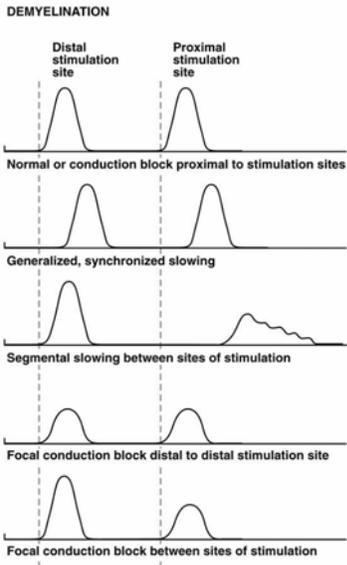
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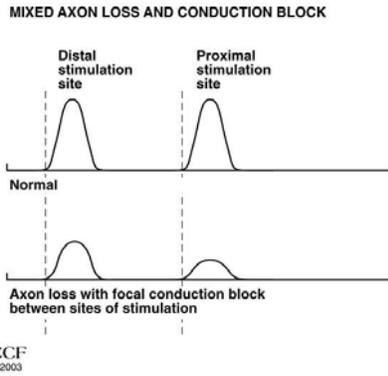
Figure 22

Figure 23

Figure 24

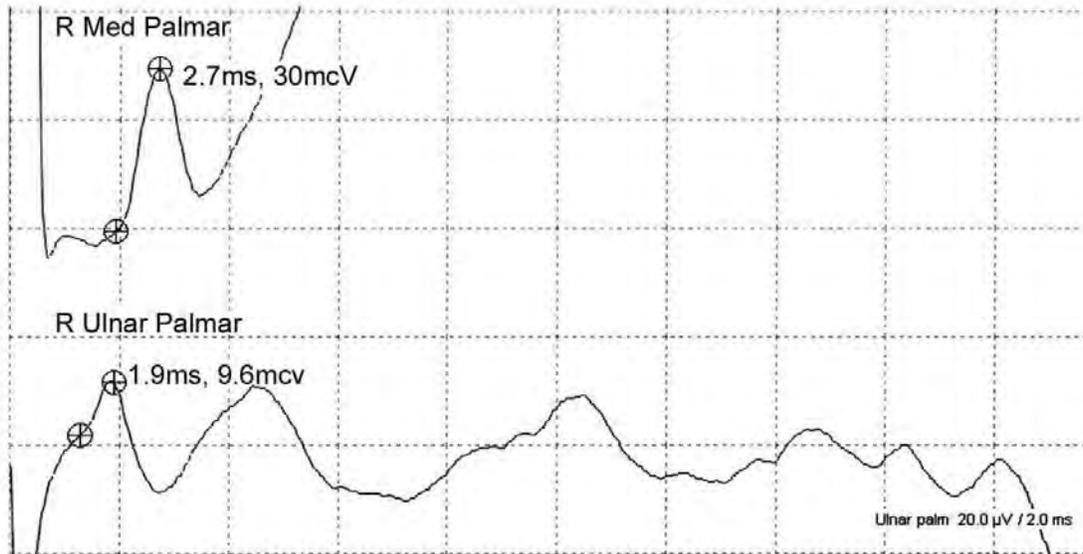## Figure 25

30 YO FELL ASLEEP IN CAR 4 WEEKS AGO AFTER ETOH AND
AWOKE WITH RIGHT WRIST DROP

R Radial CMAP — L Radial CMAP

Figure 26

RIGHT SNAPs — LEFT SNAPs
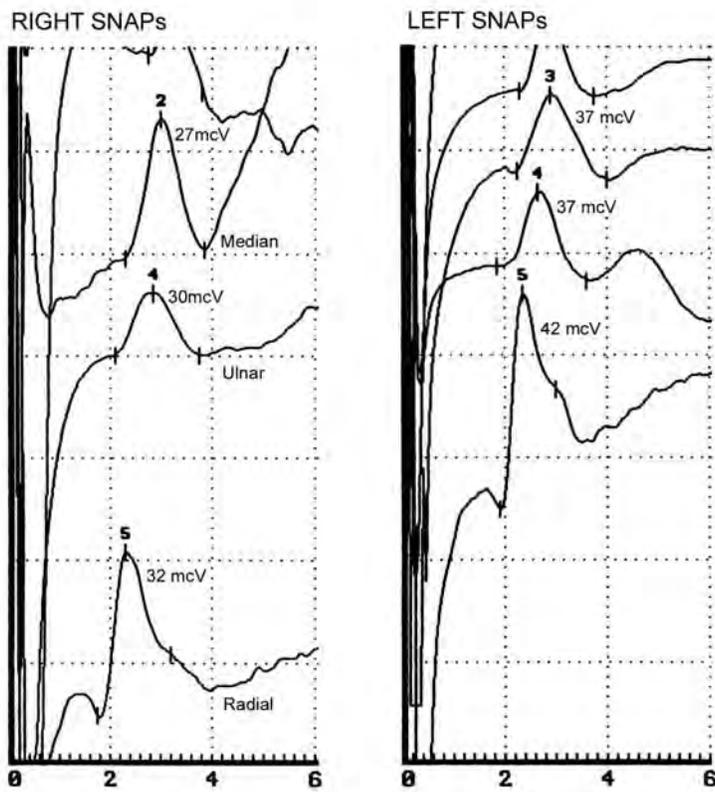
Figure 27

63 YO WITH 1 MONTH OF LEFT FOOT DROP
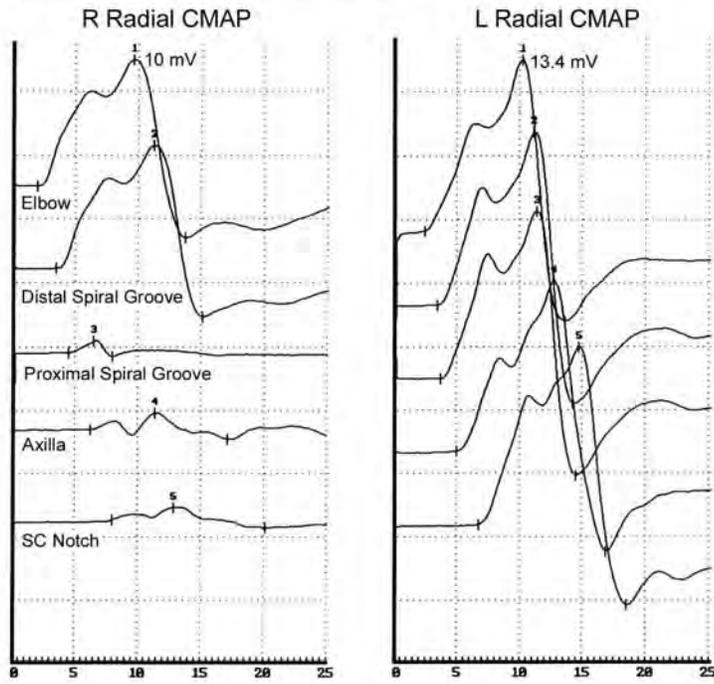
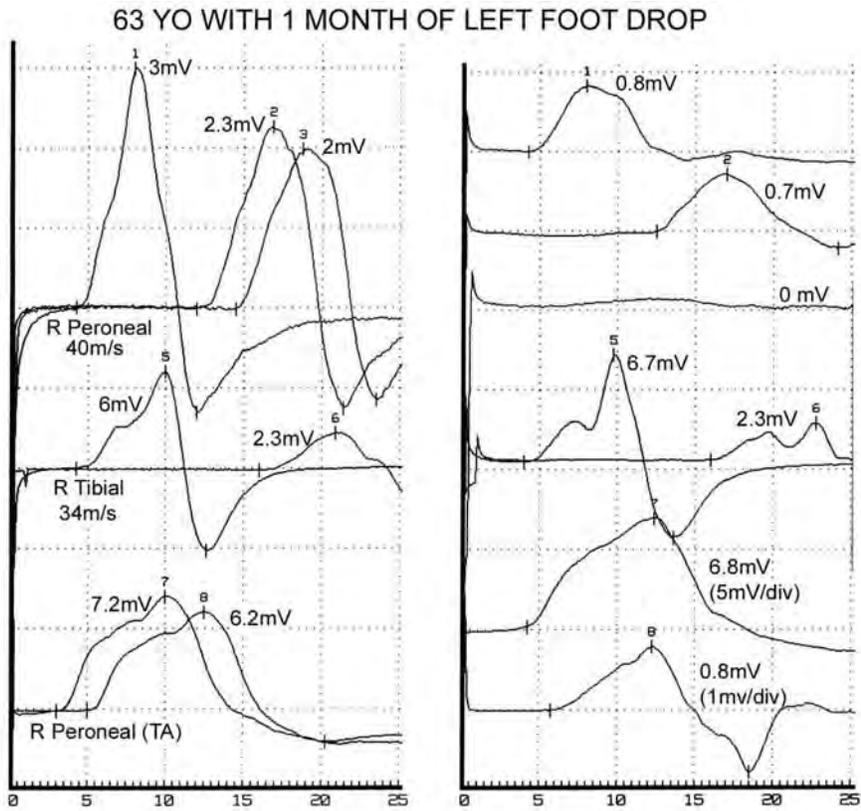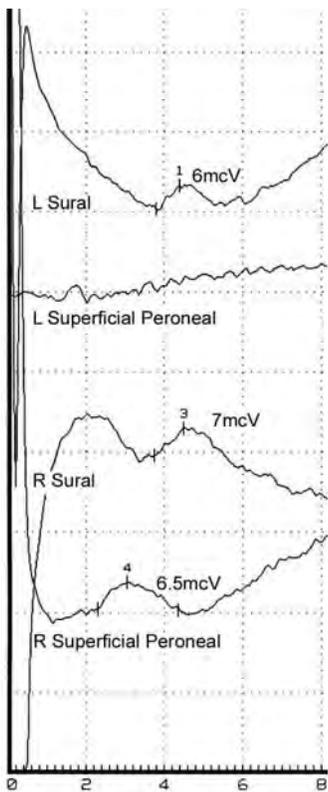Figure 28

Figure 29

56 YO MAN WITH 2 YEAR HISTORY OF NUMB, BURNING FEET

Nerve	Recording site	Amplitude		Latency	Velocity	F-wave
		Distal	Proximal			
Sural	Ankle	NR				
Superficial Peroneal	Ankle	NR				
Peroneal	EDB	.7	0.6	4.5	36	
Post Tibial	AH	.2	0.2	6.3	35	
Peroneal	TA	4.0	4.0	3.5	56	
Post Tib M	Soleus	11.0		4.4		
H-reflex	Soleus	NR				
Median (S)	D2	5.0		4.2		
Ulnar (S)	D5	7.0		3.3		
Radial (S)	Thumb base	12.0		2.7		
Median (M)	Thenar	14.0		4.0	50	34
Ulnar (M)	Hypothenar	8.0		2.3	47	38