Principles and pitfalls of nerve conduction studies

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The essential function of a nerve fiber centers on the transmission of impulses. Saltatory conduction is made possible by the myelin, which normally provides high impedance and low capacitance preventing leakage current through the internodal membrane. Action current through sodium channels at the activated node of Ranvier produces "inward ionic current", which subsequently causes "outward capacitative current" at the next node to be excited. This in turn depolarizes the nodal membrane to threshold, thus opening the sodium channels and initiating another cycle of "inward ionic current". The safety factor of transmission is defined as a ratio of action current available at a node to threshold current. For conduction through a node to be successful, it has to be more than unity. Slowing of conduction velocities merely delays conveyance of information but failure of conduction abolishes the function. Rate-dependent block may falsify input by disturbing the neural coding.

Optimal application of the nerve conduction study depends on an understanding of the principles and recognition of the pitfalls of the technique. The conventional methods deal primarily with distal nerve segments in extremity. Other techniques allow one to assess nerve segments in less accessible anatomical regions, to improve the accuracy in precisely localizing a focal lesion, and to increase sensitivity in detecting subclinical abnormalities. The diagnosis of conduction block is complicated by phase cancellation and many other physiologic and technical factors, which may mimic the condition. Despite certain limitations, nerve conduction studies can provide diagnostically pertinent information if they are used judiciously in appropriate clinical contexts.

Motor Nerve Conduction Study. The nerve is stimulated at 2 or more points along its course with the pulses of moderate intensity to adjust the position of the cathode at the best stimulating site. Stimulation with maximal intensity excites all nerve fibers resulting in a full size of the muscle potential. It is customary to use a 20-30% supramaximal intensity to guarantee the activation of all the nerve axons. A pair of recording electrodes consists of an active lead (G1) placed on the belly of the muscle and an indifferent lead (G2) on the tendon (belly-tendon recording). The propagating muscle action potential, originating under G1 located near the motor point, gives rise to a simple biphasic waveform with initial negativity (Kincaid, Brashear and Markand, 1993). The presence of an initial positivity suggests incorrect positioning of the active electrode or represents a volume conducted potential from distant muscles, activated by anomalous innervation or by accidental spread of stimulation to other nerves.

The usual measurements include amplitude from the baseline to the negative peak, duration from the onset to the positive peak or to the final return to the baseline, and latency from the stimulus artifact to the onset of the negative response. Electronic integration can provide the area under the waveform, which shows linear correlation to the product of the amplitude and duration measured by the conventional means (Gans and Kraft, 1981). The onset latency, as a measure of the fastest conducting motor fibers, consists of 3 elements: 1) nerve conduction time 2) neuromuscular transmission time and 3) propagation time along the muscle membrane. Of these, the last 2 are common to any stimulus site. Thus, the latency difference between the 2 separate points represents the time necessary for the nerve impulse to travel from one stimulus point to the other.

Sensory Nerve Conduction Study. For sensory conduction studies in the upper extremities, stimulation of the digital nerves elicits an orthodromic sensory potential at a more proximal site, or stimulation of the nerve trunk evokes an antidromic digital potential (Winkler, Stälberg and Haas, 1991). Shocks applied to the ulnar or median nerve at the wrist give rise to a mixed nerve potential along the nerve trunk at the elbow. Some motor axons have thresholds similar to those of large myelinated sensory axons (Gilliatt, Melville, Velate et al, 1965). In studying a mixed nerve, therefore, superimposition of action potentials from distal muscles may obscure antidromically recorded sensory potentials. Fortunately, the onset latency can still be measured accurately because the large diameter sensory fibers conduct faster than motor fibers by approximately 5-10% (Dawson, 1956). Thus, stimulation of a mixed nerve allows determination of the fastest sensory nerve conduction velocity in the face of co-activated muscle action potentials. This relationship between sensory and motor impulses, however, may not hold in disease states that affect different fibers selectively. Such circumstances would preclude differentiation between the sensory and muscle action potentials.

The latency of the orthodromic sensory potentials is measured to the initial positive peak or to the subsequent negative peak (Joynt, 1983). Sensory potentials elicited by stimulation at different sites along the nerve vary in waveform. Because of temporal dispersion between fast and slow fibers, the interval
between the positive and negative peaks increases in proportion to the distance. Therefore, the conduction velocity calculated using the latency to the negative peak does not necessarily correspond to the fastest conducting sensory fibers (Dawson, 1956). With the biphasic digital potential recorded antidromically, the onset latency measured to the initial take-off of the negative peak corresponds to the conduction time of the fastest fibers from the cathode to G1. The use of the peak latency has little, if any, justification for antidromically recorded digital potentials, which considerably exceed orthodromic potentials in amplitude.

**Segmental Stimulation in Short Increments.** Ordinary conduction studies are sufficient to approximate the site of involvement in entrapment neuropathies (Daube 1980; Kimura 1989). More precise localization requires inching the stimulus in short increments along the course of the nerve in order to isolate the affected segment (Kimura 1979; Miller 1979). In the evaluation of a focal lesion such as compressive neuropathy, inclusion of the unaffected segments in calculation dilutes the effect of slowing at the site of lesion and lowers the sensitivity of the test. Therefore, incremental stimulation across the shorter segment helps isolate a localized abnormality that may otherwise escape detection. Thus, the study of short segments provides better resolution of restricted lesions. Assume a nerve impulse conducting at a rate of 0.2 msec/cm (50 m/sec) except for a 1-cm segment where demyelination has doubled the conduction time to 0.4 msec/cm. In a 10-cm segment, normally covered in 2.0 msec, a 0.2 msec increase would constitute a 10% change, or approximately one standard deviation, well within the normal range of variability. The same 0.2-msec increase, however, would represent a 100% change in latency if measured over a 1-cm segment. The large per unit increase in latency more than compensates for the inherent measurement error associated with stimulating multiple times in short increments.

This technique is particularly useful in assessing a patient with possible compressive lesions such as the carpal tunnel syndrome (Kimura 1979; Ross and Kimura, 1995). With stimulation of a normal median nerve in 1-cm increments across the wrist, the latency changes approximately 0.16 to 0.21 msec/cm from mid-palm to distal forearm. A sharply localized latency increase across a 1-cm segment indicates a focal abnormality of the median nerve. An abrupt change in waveform nearly always accompanies a latency increase across the site of compression (Kimura 1979). In fact, waveform analysis often localizes a focal lesion more precisely and unequivocally than excessive latency jumps, which may be induced by inaccurate advances of the stimulating electrodes. If technical difficulties preclude incremental activation across the segment in question, wave-form changes identified by a series of shocks above and below the segment still uncover a conduction abnormality within that short range. In these cases, 2 parallel lines are formed if one connects the onset (or peak) of successive responses above and below the affected zone, confirming a non-linear latency change caused by a focal lesion.

**Evaluation of Long Pathways.** Nerve stimulation studies commonly used in an electromyographic laboratory apply mainly to the distal, relatively short segments of the peripheral nerves. In assessing a more diffuse or multi-segmental process as might be seen in polynuropathies, the longer the segment under study, the more evident the conduction delay. In another word, this approach has an advantage in accumulating all the segmental abnormalities, which individually might not show a clear deviation from the normal range. If a nerve impulse conducts at a rate of 0.2 msec/cm (50m/s), for example, a 20% delay for a 10 cm segment is only 0.4 msec, whereas the same abnormality for a 100cm segment amount to 4.0 msec, an obvious increase which is easily detectable. Evaluating a longer segment improves the accuracy for the same absolute error in measurement because it constitutes a smaller percentage. Consequently, the study of a longer path offers a better sensitivity and reproducibility in serial studies. A number of neurophysiological methods supplement the conventional techniques for the assessment of longer pathways (Fraser and Olney, 1992). The selection of such techniques necessarily reflects the special orientation of each laboratory. Of general interest, however, are the F wave and the H reflex.

A supramaximal stimulus applied at virtually any point along the course of a motor nerve elicits a small late response following the regular compound muscle action potential (CMAP). This long latency response, designated the F wave, results from backfiring of antidromically activated motor neurons. The F-wave latencies measured from the stimulus artifact to the beginning of the evoked potential vary by a few milliseconds from one stimulus to the next (Daube 1979; Dengler, Kossev, Wohlfahrt et al, 1992; Kimura 1974). Hence, an adequate study requires more than 10 F waves clearly identified among 15 to 20 trials. The most sensitive criterion of abnormality is a latency difference between the 2 sides, or between 2 nerves in the same limb in a unilateral disorder affecting single nerves. Absolute latencies are also useful for assessing the entire course of the nerve sequentially (London and England, 1991; Young and Shahani, 1976). The F wave conduction velocity and the F ratio provide a better comparison between proximal and distal segments (Kimura, 1989). The difference between the minimal and maximal F wave latencies determines the degree of scatter among consecutive F waves as an estimate of the range of motor conduction velocities in the nerve (Kimura, Yanagisawa, Yamada et al, 1984; Panayiotopoulos, 1979).
The electrically elicited stretch reflex, called the H reflex after Hoffmann for his original description, greatly resembles in many respects the stretch reflex elicited by a mechanical tap to the tendon. The group 1A sensory fibers and alpha motor neurons form the afferent and efferent arcs of this predominantly monosynaptic reflex (Burke, Adams and Skuse, 1989). In contrast, one can elicit the F wave in any distal limb muscle. The effect of increasing stimulus intensity also distinguishes the H reflex from the F wave. A long duration (Panizza, Nilsson and Hallett, 1989) stimulus submaximal for CMAPs best elicits the H reflex, whereas the F wave requires supramaximal shock intensity.

Reproducibility of various measures. Nerve conduction study is widely used for the assessment of polyneuropathy not only to evaluate the degree of abnormality but also to document serial changes in general and for drug trials in particular (Kimura, Yamada and Stevland, 1979). Although the method serves as a sensitive and objective indicator, its accuracy primarily depends on the adherence to technical details (Chaudhry, Corse, Freimer et al, 1994). Any deviations from the standards result in inconsistencies of the results. The awareness of this possibility is especially important in designing a multicenter clinical trial, which involves many investigators of different backgrounds and training. Nonetheless, few studies have dealt with technical factors influencing the reproducibility of nerve conduction measurements in the evaluation of polyneuropathy (Valensi, Attali and Gagant, 1993).

Several investigators (Honet, Jebson and Perrin, 1968; Bergman, 1971; Bleasel and Tuck, 1991) reported on the reliability of nerve conduction velocity (NCV) in normal subjects and patients with diabetic polyneuropathy (Claus, Mustafa, Vogel et al, 1993; Dyck, Kratz, Lehman et al, 1991; Valensi, Attali and Gagant, 1993). Of a few reported studies on F waves, all but one (Valensi, Attali and Gagant, 1993) dealt with the experience at a single laboratory, showing variation of NCV up to 10 m/sec (Honet, Jebson and Perrin, 1968; Bleasel and Tuck, 1991). A study in patients with diabetic polyneuropathy (Claus, Mustafa, Vogel et al, 1993; Dyck, Kratz, Lehman et al, 1991) revealed good reproducibility of median and peroneal NCV but not of amplitude. Dyck and colleagues (Dyck, Kratz, Lehman et al, 1991) described that F wave values were generally stable. A French multicenter study (Valensi, Attali and Gagant, 1993) of diabetic polyneuropathy also yielded an excellent reproducibility of the median and peroneal F wave latencies. In contrast, amplitude was considered unreliable for both the motor and sensory nerves.

We also conducted a multicenter analysis (Kohara, Kimura Kaji et al, 1994; Kohara, Kimura Kaji et al, 1995; Kohara, Kimura, Kaji et al, 1996) on inter-trial variability of nerve conduction studies to determine the confidence limits of the variations for use in future drug assessments for diabetic polyneuropathy. All measurements were repeated twice at a time interval of 1 to 4 weeks in 132 healthy subjects (63 men) and 172 patients with diabetic polyneuropathy (99 men). Using a standardized method, 32 and 65 centers participated in the study of healthy subjects, and patients with diabetic polyneuropathy, respectively. Motor nerve conduction studies consisted of stimulating the left median and tibial nerves and measuring amplitude, terminal latency (TL), and minimal F wave latency (FWL). We also calculated motor conduction velocity (MCV) and F wave conduction velocity (FCV). For sensory nerve conduction studies, amplitude was recorded antidromically after distal stimulation of the left median and sural nerves and measuring amplitude, conduction velocity (SCV) was calculated.

In both the controls and patients, amplitude varied most followed by TL, MCV and SCV. In contrast, FWL showed the least change, with the range of variability (Variation Range) of only 10% for the study of the median nerve and 11% for the tibial nerve in normal and 12% and 14% in patients with diabetic polyneuropathy. We conclude that FWL serves as the most stable and consequently reliable measure for a sequential nerve conduction study of the same subjects.

Conduction block. In demyelinating polyneuropathy, slowing of nerve conduction often accompanies a reduction of amplitude, which localizes a partial conduction block (Brown and Snow, 1991; Feasby, Brown, Gilbert et al, 1985; Jamieson, Giuliani and Martinez, 1991; Triggs, Cros, Gominak et al, 1992). Reversible conduction block is also seen in other conditions such as ischemic neuropathy (Hömberg, Reiners and Toyka, 1992). Electrophysiologic evidence of conduction block usually, though not always, implies the presence of focal demyelination (Sedal, Ghabriel, HE et al, 1983). The range of conduction velocities may be increased if certain fibers are selectively involved. In this instance, the evoked action potential broadens because of increased temporal dispersion. Desynchronization of the nerve volley may also result from repetitive discharges at the site of axonal injury after the passage of a single impulse. Unless secondary axonal degeneration is induced by damage of the myelin sheath, electromyography reveals little or no evidence of denervation. The motor unit potentials, though normal in amplitude and waveform, are recruited poorly, indicating a conduction block in severely demyelinated fibers.

The usual criteria for conduction block in motor fibers evolves around the comparison of CMAPs following proximal versus distal stimulation, expressed in the ratio of their amplitudes or areas (Uncini, Di Muzio, Sabatelli et al, 1993). This ratio remains normal with evenly reduced amplitudes or areas of CMAPs in axonal degeneration or neuromyopathy. A reduction in amplitude ratio greater than 20-40% has been...
generally accepted as a criterion for conduction block. Other diagnostic clues for motor conduction block or focal demyelinating lesions include more than 20% increase in duration of CMAP elicited by proximal stimulation (Kimura, Sakimura, Machida et al, 1988), slight conduction delay, abnormal F waves, and large distal CMAP amplitudes despite disproportionately severe clinical weakness (Kimura, 1989) or paucity of voluntarily activated motor unit potentials (Cornblath, Sumner, Daube et al, 1991).

Several factors are important in clinical assessment of conduction block. Insufficient stimulus intensities at the proximal site erroneously reduce the proximal CMAP amplitude. Likewise increased threshold for excitation in regenerated or chronically demyelinated nerves may account for a reduced proximal response. In some cases of multifocal motor neuropathy, this type of failure to maximally excite the involved segment precludes accurate assessment of conduction block. To circumvent this difficulty, we have resorted to in-situ stimulation using a needle electrode placed within the nerve at the time of exploration. During the course of wallerian degeneration, the distal stump of the nerve remains viable for several days at a time when its proximal part fails to transmit the signal across the injury site. In this situation, conduction studies performed soon after nerve severance show a decreased proximal-distal CMAP amplitude ratio. Unexpected excitation of anomalous branches such as Martin-Gruber anastomosis may lead to a false diagnosis of conduction block, as does current spread to a neighboring nerve at a proximal site of stimulation (Kimura, 1976). In either case, studies would show apparent discrepancy in amplitude between proximally and distally elicited responses.

A physiological temporal dispersion affects short duration sensory action potentials much more than long duration muscle action potentials, as implied by the term, duration-dependent phase cancellation (Kimura, Machida Ishida et al, 1986). According to computer simulation (Kimura, Sakimura, Machida et al, 1988; Rhee, England, Sumner, 1990), this phenomenon alone can reduce the normal sensory nerve action potential (SNAP) to below 50% in area as well as in amplitude, making the recognition of conduction block difficult. These are conservative figures, based on computation of a limited number of nerve fibers for analysis. Unlike the physiologic temporal dispersion, which is inherently limited for long duration muscle action potentials, phase cancellation alone could play a major role in the diminution of CMAP in demyelinated nerves. As shown in the simulation with concurrent stimulation of the median and ulnar nerves, pathological desynchronization of impulses across a focal demyelinating lesion can cause mutual subtraction of negative and positive phases among temporally dispersed sensory as well as muscle action potentials. This type of phase cancellation reduces the amplitude of CMAP well beyond the usual physiologic limits in the absence of conduction block. A triple stimulation method with double collisions allows identification of motor conduction block in the face of desynchronization (Roth and Magistris, 1989). The technique, however, fails if the nerve excitability is compromised at stimulus sites as the consequence of demyelination or degeneration.

In documenting conduction block, one should depend more on the combination of clinical and electrophysiologic finding, which usually circumvents the ambiguity of the electrophysiologic criteria based purely on waveform analysis. The presence of conduction block is confirmed if a shock applied distally to the nerve lesion in question elicits a normal or near normal CMAP and a vigorous twitch of the clinically weak muscle. As an exception, it must be noted that the same finding also characterizes any weakness attributable to upper motor neuron involvement or hysteria. In equivocal cases, inability to distinguish focal temporal dispersion from conduction block poses no major practical problem because either finding suggests demyelination, leading to an appropriate treatment.

**Consequence of demyelination.** The pathophysiology of demyelination and its clinical consequences (Gilliatt, 1982; Kaji, Suzumura, Sumner, 1988; Smith and McDonald, 1982) include 1) elevated thresholds and conduction block resulting in clinical weakness and sensory loss 2) increased desynchronization of volleys causing temporal dispersion of waveforms, loss of reflexes and reduced sensation 3) prolonged refractory periods with frequency dependent conduction block especially at very high firing rates, accounting for reduced strength during maximal voluntary effort 4) exaggerated hyperpolarization after the passage of impulse inducing conduction block even at low firing frequencies, possibly as the cause of fatigue after sustained effort, and 5) steady or bursts of ectopic discharges at sites of focal demyelination considered responsible for facial myokymia and spontaneous or mechanically-induced paresthesia.

Slowing of conduction by itself leads to little, if any, clinical symptoms, as long as all the impulses arrive at the target organ. As well a prolonged refractory period for transmission, though helpful as a diagnostic indicator (Gilliatt and Meer, 1990), causes no symptoms because the time intervals between voluntarily induced repetitive discharges in motor axons substantially exceed the refractory periods under physiologic condition. The identification of demyelination by these means, offer potentially important clues to conditions, which are reversible by pharmacologic, immunologic or surgical measures. In contrast to reduced conduction velocity and increased refractoriness, conduction block, assessed quantitatively,
correlates best with the degree of weakness in patients with demyelinating diseases. Thus, a complete or intermittent conduction block often accompanies major loss of strength.

In some hereditary neuropathies, the demyelinating disorder uniformly affects the nerve throughout its length. The saltatory conduction is affected more or less at all the nodes of Ranvier rather than segmentally. By contrast, conduction block in certain parts of the nerve characterizes acquired demyelinating neuropathies with non-uniform involvement. Among them, multifocal motor neuropathies (MMN) with persistent conduction block (Parry, Clarke, 1985; Pestronk, Cornblath, Ilyas et al, 1988) deserves special mention to distinguish this potentially treatable condition from amyotrophic lateral sclerosis (ALS) and other motor neuron syndromes. Similar to earlier reported cases with sensory and motor involvements (Lewis, Sumner, Brown et al, 1982) the long-lasting conduction block suggests chronic demyelination as the pathological basis. Although generally considered as a variant of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), the patient may have normal or even increased stretch reflexes with a normal or only slightly elevated CSP protein.

These features often make it difficult to diagnose the condition solely on the basis of clinical examination. Thus, electrophysiologic studies are required for confirmation before initiating therapeutic trials using, for example, immunosuppressants such as cyclophosphamide, which is often effective. Demonstration of motor conduction block at multiple sites differentiates this potentially treatable clinical entity from the small subgroup of amyotrophic lateral sclerosis (ALS) patients with only lower motor neuron involvement. Most patients have normal sensory conduction through the sites of motor conduction block, which suggests that motor fibers are selectively involved. Motor conduction block probably reflects a chronic focal demyelinating lesion, which for yet undetermined reason becomes persistent without relapses.

Further Reading


* Please note that references are textbook style rather than Vancouver style.