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The relationship between sensory latency and amplitude

Elliot B. Bodofsky M.D. *, Stephen J. Cohen M.D., Rohini J. Kumar M.D., Adam Schindelheim M.D., John Gaughan PhD

Cooper Medical School of Rowan University, United States

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ABSTRACT

Purpose: To prove that the relationship between sensory latencies and amplitudes is useful in determining the severity of neuropathies. This is achieved by deriving a mathematical relationship between sensory distal latency and amplitude. Determine whether sensory amplitudes below predicted correlate with a worse pathology. Procedures: Patients seen for Nerve Conduction Studies by the Department of Physical Medicine and Rehabilitation at Cooper University Hospital between 12/1/12 and 12/31/14 were invited to participate in a prospective database. The median, ulnar and sural sensory latencies and amplitudes were analyzed with both linear and power regression. Patients with amplitudes above and below the regression curve were compared for latency, amplitude and velocity of other nerves. Carpal Tunnel Patients were analyzed to determine whether Median sensory amplitude below predicted correlated with more severe disease. Results: For the Median nerve, Power Regression Analysis showed a stronger correlation ($R^2 = 0.54$) than linear regression ($R^2 = 0.34$). Patients with Median sensory amplitude below the power correlation curve showed significantly longer ulnar sensory latency, and lower sensory amplitude than those above. Carpal Tunnel Syndrome patients with Median sensory amplitude well below predicted by the power relationship showed more advanced disease. For the ulnar and sural sensory nerve, the difference between power and linear regression was not significant. Conclusions: A power regression curve correlates sensory latency and amplitude better than linear regression. The latency amplitude relationship correlates with other parameters of nerve function and severity of Carpal Tunnel Syndrome. This implies that below predicted sensory amplitude may indicate worse disease, and could be a useful diagnostic tool.

1. Introduction

Nerve conduction studies are the key diagnostic technique for focal nerve compressions and diffuse neuropathies. These are both extremely common, with over 900,000 cases of Carpal Tunnel Syndrome (CTS) alone diagnosed each year in the US (Nordstrom et al., 1998; Gelfman et al., 2009).

For most peripheral neuropathies, the latency (or velocity) is considered much more important than the amplitude. Even when present, the amplitude is considered less important. On the other hand, an absent sensory response is indicative of more severe disease. For common focal neuropathies such as CTS and common diffuse peripheral neuropathies such as diabetic neuropathy, sensory studies are considered more sensitive than motor (Kuntzer, 1994). Overall, the speed of sensory conduction appears to be more accurate than amplitude, or the amount of response in determining severity (Kuntzer, 1994; Prakash et al., 2006; Joynt, 1989). However, a few authors consider Median Sensory Amplitude important in grading CTS, because it reflects the functional state of axons (Ogura et al., 2003).

Our hypothesis is that the relationship between sensory latency and amplitude is also useful in determining the severity of both focal and diffuse neuropathies. If sensory amplitude is unusually small relative to latency, either the disease is more severe than the latency alone would indicate, or there are multiple pathologies. Likewise, a larger than predicted amplitude would suggest that the process is not as advanced as the latency alone would indicate, and this would argue against coexisting conditions. Therefore, it is important to determine the relationship between sensory latency and amplitude, and whether deviations from this relationship do, in fact, correlate with other measures of peripheral nerve function.

Different focal and diffuse neuropathies cause demyelination and axonal degeneration to varying degrees. Nonetheless, as velocity decreases and latency increases, amplitude should decline.

* Corresponding author at: 1 Cooper Plaza Suite 550, Camden, NJ 08103, United States.

E-mail address: Bodofsky-elliot@cooperhealth.edu (E.B. Bodofsky).

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There is evidence of an inverse relationship between sensory latency and amplitude in normal subjects (Stetson et al., 1992; Rivner et al., 2001), and between sensory and motor latencies and amplitudes (Moses et al., 2007). A strong correlation (R-square = 0.70) between Median sensory amplitude and latency was found in moderate to severe CTS (Plaja, 1971). A similar correlation of 0.70 between palmar nerve conduction velocity (NCV) in moderate to severe CTS and amplitude was observed (Kimura and Ayyar, 1985). A strong (0.58) correlation between Median Motor Latency and Amplitude in CTS of all severities was seen in one study (Shibuya et al., 2009). By contrast, correlation between median sensory palmar conduction and sensory amplitude in patients with CTS of all severities was much lower (0.26) (Joynt, 1989).

All of these studies looked for a linear relationship between velocity (or latency) and amplitude. While there are many linear relationships in neurophysiology, interestingly, there are many that are nonlinear. For example, the relationship between age and both nerve conduction velocity and amplitude is nonlinear (Taylor, 1984). The relationship between sensory amplitude and conduction velocity in Chronic Acquired Demyelinating Neuropathy is also clearly nonlinear (Krarup and Trojaborg, 1996). In fact, it showed a much more rapid decline in amplitude than velocity, supporting our theory (Krarup and Trojaborg, 1996). There is also a nonlinear relationship between motor conduction velocity and amplitude in diabetic neuropathy and Amyotrophic Lateral Sclerosis (Feinberg et al., 1999 and Herrman et al., 2002). This suggests a nonlinear relationship is not only quite possible, but extremely likely.

Logically, sensory amplitude should decrease sharply when the amplitude is large, and the latency is becoming mildly prolonged. When latency is quite prolonged and the amplitude is already small it should not decline as rapidly. Stated another way, as latency increases, loss of amplitude should be large in the normal range, and gradually decrease. It has been previously proposed that there is a strong nonlinear relationship between nerve length, velocity and amplitude (Bodofsky et al., 2009). This should be a power relationship,

$$A = KT^{N} \quad (1)$$

where A is sensory amplitude, K is a constant, and T is time (or latency) and N is between -1 and -3. We propose that this relationship holds for normal sensory nerve conduction, focal nerve compression, and diffuse neuropathies.

2. Methods

2.1. Subjects

All patients seen for Nerve Conduction Studies by the Department of Physical Medicine and Rehabilitation at Cooper University Hospital, a 530 bed academic hospital in Camden, NJ, starting on 12/1/12 were invited to participate in the Registry of Nerve Conduction Data, a prospective database. All consenting patients seen between 12/1/12 and 12/31/14 were reviewed for this study. The Hospital Institutional Review Board approved both the Registry of Nerve Conduction Data and this study.

2.2. Inclusion and exclusion

Inclusion Criteria for this study were i. Age 18 or above (no age limit). ii. At least 4 nerves in the Upper or Lower Extremities tested. iii. Unilateral and Bilateral Studies. iv. Normal and abnormal studies, including patients with multiple pathologies.

Exclusion criteria for the study were i. Age less than 18. ii. Pregnancy. iii. Facial studies (without Upper or Lower Extremity testing). Nerves with absent motor and/or sensory responses were completely excluded from analysis because there is no accurate way of analyzing such data.

Inclusion criteria for the diagnosis of Carpal Tunnel Syndrome were: i. Hand pain, tingling or numbness (unilateral or bilateral) and ii. (Median-Ulnar) motor latency difference >1.0 ms or (Median-Ulnar) sensory latency difference >0.4 ms.

2.3. Patient characteristics

There were 394 upper extremity sensory nerve responses from 213 patients. Mean age was 54.4, range was 22–93. There were 132 Female and 81 Male patients. Median height was 166.1 cm. Median weight was 84.7 kg (Table 1), which is a bit higher than the overall US median adult weight of 81 kg. This may be due to significant numbers of patients with Carpal Tunnel Syndrome, who tend to be heavier than average.

There were 88 lower extremities with sensory results from 52 patients. Mean age was 51.1, range was 26–79. There were 30 Female and 22 Male patients. Median height was 169.4 cm. Median weight was 93.2 kg (Table 1), which is well above average, and may be due to patients being referred for evaluation of low back pain, which is more common in obese patients.

2.4. Nerve conduction testing

All studies were performed on either XLTEK Neuromax, or Dantec systems. Previous testing had shown no significant differences between the machines when testing normal subjects. Motor studies included the Median, Ulnar, and Peroneal nerves using bar electrodes. Stimulus duration was 100 µs, starting with a 5 mA stimulus, increasing by 5–10 mA per stimulation until a maximal response was achieved. Motor Latency was measured to the onset of the Compound Motor Action Potential (CMAP), and amplitude was measured onset to peak. All studies were performed at a skin temperature of at least 32 °C (using warming techniques if needed).

For the Median Nerve, the active electrode was placed midway between the distal wrist crease and the first metacarpal phalangeal (MCP) joint, reference distal to the MCP joint, and ground electrode was placed on the dorsum of the hand. Distal stimulation was 8 cm proximal to the active electrode (proximal to the distal wrist crease), and proximal stimulation was just medial to the Brachial Artery in the antecubital region (Buschbacher, 1999).

The Ulnar motor nerve test was performed with the active electrode midway between the pisiform bone and 5th MCP joint, reference distal, and ground on the hand dorsum. Distal stimulation was 6.5 cm proximal to the active electrode, and proximal stimulation was 4 cm distal and proximal to the medial epicondyle (Buschbacher, 1999; Falco et al., 1992). For the Peroneal Motor study, the active electrode was placed over the middle of the extensor digitorum brevis muscle, reference distal, and ground

Table 1
Demographics.

	UEs	LEs
Total patients	213	52
Limbs tested	394	88
Mean age (Range)	54.4 (22–93)	51.1 (26–79)
# Female patients	132 (62%)	30 (58%)
# Male patients	81 (38%)	22 (42%)
Mean height in cm (range)	166.1 (147–193)	169.4 (157–191)
Mean weight in kg (range)	84.7 (39–155)	93.2 (56–136)