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Factors influencing F-wave latency detection of lumbosacral root lesions using a detection theory based model

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Abstract

Objective: To evaluate the F-wave dilution hypothesis; which implies that absolute F-wave latencies obscure the much smaller delay associated with slow intra-lesion conduction, such is caused by nerve root compression in lumbosacral radiculopathy. A corollary objective is to determine how F-wave measurement and pathological factors influence diagnostic accuracy.

Methods: An analytical model is developed based on signal detection theory and a number of simplifying assumptions. Diagnostic accuracy, quantified by the area under the receiver operating characteristic (ROC) curve, is determined for various model realizations derived from the clinical and experimental neurophysiology literature. A preliminary experimental validation of model predictions is also performed.

Results: Absolute F-wave latency does not influence the accuracy of focal lesion detection. F-wave latency variance and lesion pathology are the determinant factors. F-wave latencies and distal latencies are estimated to have qualitatively similar detection characteristics, although distal latencies have quantitatively better diagnostic efficacy for comparable focal pathology. Preliminary experimental results support the modeled dependence of diagnostic accuracy on latency variance and lesion severity.

Conclusions: Absolute F-wave latency does not dilute slow conduction within focal lesions, such as in lumbosacral radiculopathy. The dominant measurement factor is F-wave latency variance.

Significance: To maximize the diagnostic utility of F-wave latencies, focus must be placed on reducing latency variance, such as through correction for demographic covariates. This model calls into question the F-wave dilution hypothesis.

Keywords: F-wave; Model; Radiculopathy; Detection theory; Root lesion; Diagnostic accuracy; Variance; ROC; Lumbosacral; Nerve conduction

1. Introduction

F-waves are distally recorded late responses evoked by antidromic activation of motor neurons. This 'back-firing' behavior is caused by somatic repolorization of the low threshold initial axon segment. If that region of membrane is not refractory then an action potential may be triggered and propagate orthodromically. Somatic re-excitation of the initial segment is dependent on many factors including structural and biophysical characteristics of the motor neurons, and the level of excitability of the soma, which is influenced by local excitatory and inhibitory interactions within the spinal cord. Since, the F-wave response propagates through the anterior nerve roots they should be delayed or blocked by lesions caused by compressive, inflammatory, and ischemic complications of disc herniation, exposure to nucleous pulposes, and spinal stenosis (Cornefjord et al., 1996; London and England, 1991; McCarron et al., 1987; Rydevik et al., 1984). These conduction abnormalities are likely caused by focal demeylination and biophysical changes within the root. The use of F-waves in detecting root lesions, or lumbosacral radiculopathy (LSR), was initially reported by Eisen and co-workers (1977). Reports on the sensitivity of F-waves for LSR have ranged from a low of 18% (Aminoff et al., 1985) to a high of 80–90% (Eisen et al., 1977; Weber and Albert, 2000).

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These studies, however, were performed using different F-wave methods and LSR case definitions, and cannot be directly compared. In the study with the lowest sensitivity (Aminoff et al., 1985), F-waves were only recorded from the extensor digitorum brevis, a predominately L5 innervated muscle (Young et al., 1983), whereas most patients had S1 root lesions. Consistently high sensitivity comparable to needle electromyography (nEMG) has been obtained in studies that controlled for height or limb length, utilized multiple F-wave parameters not limited to the minimum latency, and compared F-wave and nEMG methods at similar specificity (Fisher, 2002; Scelsa et al., 1995; Toyokura and Murakami, 1997; Voulgaris and Constantinidis, 1996; Weber and Albert, 2000).

Despite these observations, the diagnostic utility of F-wave latencies in root lesions continues to be questioned on theoretical grounds. A core argument is that the conduction time resulting from propagation over the entire nerve segment 'dilutes' the lesion-associated delay (Wilbourn and Aminoff, 1998). Since, the diagnostic application of F-wave latencies is generally framed as a binary decision between normal and abnormal based on a threshold value, their accuracy is appropriately characterized using signal detection theory (Stanislaw and Todorov, 1999; Swets, 1988). If the F-wave dilution argument is to be valid and consistent with signal detection theory, then the coefficient of variation of nerve conduction latencies must be constant. For example, if the deep peroneal distal motor latency (DML) in control subjects is 3.77 ms with a standard deviation of 0.86 ms (Kimura, 2001), then a peroneal F-wave latency distribution with a mean of 48.4 ms (Kimura, 2001) should have a standard deviation of 11.0 ms. However, methodological factors that impact variance in distal latencies, which include distance measurement errors and cursor setting uncertainty, are much less relevant to F-wave latencies. Hence the comparable reported F-wave latency standard deviation is only 4 ms (Kimura, 2001). In fact, because F-wave latencies have a disproportionately low coefficient of variation (Andersen et al., 1997) and are the most reproducible measurement in nerve conduction studies (Kohara et al., 2000), the validity of the F-wave dilution argument is questionable and requires scrutiny. In this report, a model relating F-wave latency parameters to lesion characteristics is developed based on common pathological assumptions and signal detection theory. This model is used to explore factors influencing the diagnostic utility of F-wave latencies in root lesions causing conduction slowing.

2. Methods

2.1. Model derivation

An F-wave response may not occur following every stimulus and is characterized by stimulus-to-stimulus variation in latency and morphology. This variation requires the use of statistical parameters, such as the minimum or mean, that represent characteristics of the latency distribution. This model uses a generic F-wave latency parameter (hereafter referred to as a F-wave latency, but implying a statistical measure of multiple F-wave response latencies) and a sufficient number of responses is always assumed to be available for latency parameter determination. The model assumes that F-wave latencies are normally distributed (Fisher et al., 1994) and that the control and disease groups differ exclusively due to slowed impulse conduction through a root lesion. The presence of other pathology, such as polyneuropathy, is not addressed. The control population distribution of F-wave latencies is parametrically represented by a mean value, μ, and a standard deviation, σ. The F-wave latency variance (σ^2) includes intra-subject, inter-subject, and technical variance. Intra-subject variance is primarily caused by temporal (e.g. circadian) and random physiological fluctuation. Inter-subject variance is related to individualized factors that regulate F-wave parameters. Some of these factors, such as demographic variables (e.g. age, height, gender) are measurable and can be corrected. Others are genetic or acquired and are not readily normalized. Technical variance is associated with F-wave latency measurement variability, such as how different observers assign latencies to F-wave responses. Strategies for reducing F-wave latency variance focus on reducing measurable components of inter-subject variance (i.e. age, height correction) and standardizing F-wave latency measurement technique.

An individual with an F-wave latency exceeding the threshold, t, given in Eq. (1) is detected as abnormal

$$t = \mu + \Phi^{-1}(x)\sigma \tag{1}$$

Φ^{-1} is the inverse of the standard normal cumulative distribution function Φ. The standard normal cumulative distribution function converts a z-score (i.e. normal deviate) into a probability, e.g. $\Phi(1.96) = 0.975$ and $\Phi^{-1}(0.975) = 1.96$. As applied to signal detection, the standard cumulative distribution function converts abnormality thresholds (e.g. 'two-standard deviations from the mean') into probabilities (e.g. 97.5% specificity). The specificity of the abnormality threshold, t, in Eq. (1) is given by x. Specificity is defined in the classical way as the probability of normal nerves being classified as negative (i.e. F-wave latency less than threshold t). By convention, the specificity of F-wave latencies is typically set to 0.975 (i.e. z-score approximately 2).

The disease population is differentiated from the control population by the presence of a root lesion causing incremental delay Δ in each direction of propagation. The distribution of F-wave latencies in the disease group is parametrically represented by mean μ', and standard deviation σ, where the mean is given by Eq. (2)

$$\mu' = \mu + 2\Delta \tag{2}$$