

Original Research Article

F-wave records with submaximal stimulation: sustainability of the data and subject discomfort levels

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ABSTRACT

Background: F-wave studies are valuable electrodiagnostic tests with considerable roles in early diagnosis of diabetic neuropathy, detection of axonal neuropathies and focal proximal nerve dysfunctions. The recording of F-waves, however, requires recurrent supramaximal stimulation which entails subjects' discomfort during the procedure. The present study hence attempted to assess the validity of the F-wave data obtained after submaximal stimulation thereby lessening the subject discomfort levels.

Methods: The study was conducted on 64 healthy subjects in the age-group of 18-40 years with normal neurological examinations. F responses from median, ulnar, tibial and peroneal nerves by both supramaximal and submaximal stimulation were recorded. Subjects rated discomfort level on a visual analogue scale. Mean values of F-wave minimum latency, mean latency, mean duration, persistence, chronodispersion, F/M amplitude ratio and subject's discomfort level obtained by the two techniques were compared by paired t-test. P value <0.05 was considered as statistically significant.

Results: Mean values of F-wave mean latency, minimum latency, chronodispersion and stimulus duration were not found to be statistically significantly different in the groups ($p>0.05$). Mean persistence, mean F/M amplitude ratio and mean subject discomfort levels varied statistically significantly.

Conclusions: F-wave data can be attained by submaximal stimulation. F-wave mean and minimum latency, chronodispersion and duration remain relatively stable, but more stimuli may be needed for accurate values. For F/M amplitude ratio and F-wave persistence, submaximal reference range would be required. Nonetheless, diminution in subject discomfort with valid F-wave latency values, favours low intensity stimulation.

Keywords: F-wave, Latency, Stimulation, Submaximal, Supramaximal

INTRODUCTION

F-waves have been growingly used as paramount electrophysiological responses in the clinical neurophysiology. F-waves are recorded as late compound action potential evoked by supramaximal stimulation of a motor nerve. Antidromic activation of alpha motor neurons results in the formation of these small amplitude waves. Clinical applications of F-waves are widespread. They have been found to be most sensitive in acquired demyelinating neuropathies, where they may be quite

prolonged. In acute inflammatory demyelinating polyneuropathy (IDP), this may be the only conduction abnormality.¹ F-wave latency has been considered as most sensitive nerve conduction parameter in diabetes for detection of nerve pathology.² In early diagnosis of sub-clinical neuropathy in diabetes mellitus it has been found to be an important electrophysiological test.³ F-wave minimum latency has been suggested to be a better predictor than SNCS (sensory nerve conduction studies) and MNCS (motor nerve conduction studies) in detecting other peripheral neuropathies.⁴ F-wave

latencies have been reported to be the most stable and reliable measurement for sequential nerve conduction studies in the same subjects.⁵ Other conditions where F-wave studies provide useful information is true thoracic-outlet syndrome in which ulnar F-wave is found to be frequently prolonged as compared to the ipsilateral median.⁶ In various spastic conditions, increased mean F-wave amplitude/CMAP (compound muscle action potential) amplitude is a good indicator. F-wave has also been studied to demonstrate the response of drugs like baclofen in severe spastic syndromes.⁷ Also F-wave chronodispersion has been found to be valuable in some radiculopathies.⁸ Hence, F-wave responses have multiple clinical utilities. Recording of F-waves, however require supramaximal stimulation of peripheral nerves which yields increased amplitude and persistence. The conventional stimulus intensity is 25 percent above maximal for eliciting a direct response.⁹ However, F-waves are present at submaximal stimulation. This has the advantage of decreased patient discomfort. Adequate information regarding F-wave latencies can still be attained.⁹ Low-intensity stimulation hence could lessen patient discomfort without affecting F-wave latency or duration.¹⁰⁻¹²

All normative F-wave data are usually based on supramaximal stimulation. If submaximal stimulation can produce reliable and reproducible information for all F-wave parameters, and the number of stimuli required for such values has been determined then it could serve to minimize the discomfort or pain during the recording. Moreover, most of the previous similar studies have included F-wave responses from a single nerve. But as the response differs in different nerves owing to the different persistence values, the data should include the routinely studied nerves for the optimal clinical application. The present study, hence, attempts to evaluate the effect of submaximal stimulation on F-waves recorded for median, ulnar, tibial and peroneal nerves. The study plans to test the hypothesis that F-wave latency parameters did not vary significantly under submaximal and supramaximal stimulation. The study aims to test the reliability of the F-wave data so that it could be applied successfully while decreasing the subject discomfort level.

METHODS

The study was conducted on 64 healthy volunteers in the age-group of 18-40 years with normal neurological examinations. The study was carried out in Neurophysiology laboratory, AIIMS, Patna between October 2018 and April 2019. Approval from Institutional Ethics committee was obtained to perform the study. The exclusion criteria for the study group were the subjects with peripheral neuropathies, radiculopathies and spastic syndromes. It was a cross-sectional analytical study with a study duration of six months (sample size calculation was done on the basis of a previous similar study taking the reference of pain scores.¹¹ Unilateral F

responses from median, ulnar, tibial and peroneal nerves by both supramaximal and submaximal stimulation were recorded in each volunteer.

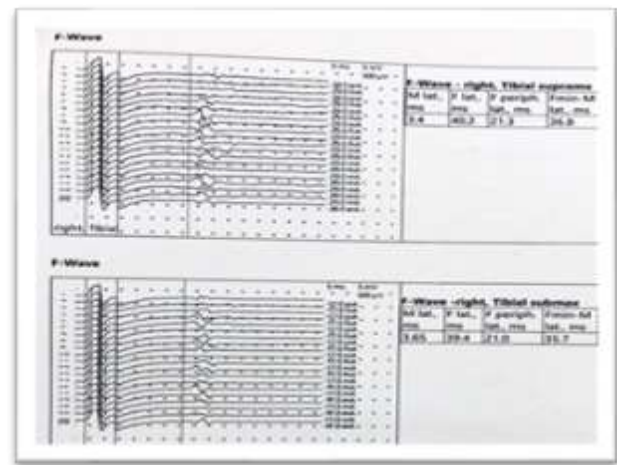


Figure 1: F-wave record of a subject showing tibial nerve stimulation with supramaximal and submaximal strength (20 stimuli).

(Stimulus frequency: 0.5 Hz, duration: 0.2 ms, amplifier gain: 500 μ v, sweep speed: 5 ms/div).

F-waves were recorded on Neuro-MEP ω EMG and EP digital neurophysiological system software in Neurophysiology laboratory, AIIMS, Patna. A written informed consent was obtained prior to the study. The temperature in the laboratory was maintained at 26°C. F-waves recordings were performed from the abductor pollicis brevis (APB) muscle, abductor digiti minimi muscle (ADM), abductor hallucis (AH) and extensor digitorum brevis (EDB) for median, ulnar, tibial and peroneal nerves respectively by surface electrodes (Figure 1). The recordings were performed with muscles fully relaxed. The occurrence of A-waves is usually infrequent in normal subjects, yet as submaximal stimulation increases the probability of contamination with A-wave, axon reflexes and H-reflexes, a computer algorithm was employed to detect them, if present, and those F-wave data were excluded which had these activities obscuring the F wave responses. Stimulus was given at the rate of 0.5 Hz with stimulus duration of 0.2 milliseconds. Amplifier gain was 500 μ V per division and sweep speed was 5 ms per division. Supramaximal stimulation was that level of stimulus intensity at which the M-wave amplitude did not further increase. Stimulus intensity employed for eliciting responses was 25 percent above maximal. Based on the associated M-wave amplitudes, measured from peak-to-peak, submaximal stimuli was given at intensities that produced 50% of the supramaximal compound muscle action potential amplitudes. 20 stimuli were provided at supramaximal stimulation. The number of stimuli for the submaximal stimulation for each nerve was decided depending upon the persistence at supramaximal stimulation and the drop of persistence as noted by previous similar studies so that

at least 10 F-waves should be obtained (the drop of persistence has been found to be about 20% under submaximal stimulation).^{10,11} The order of the application of submaximal and supramaximal stimulation while recording was randomized and subjects were blinded to the intensity. Subjects were instructed to rate discomfort level on a visual analogue scale (VAS) (0 to 10 cm) (designated as no pain to unbearable pain). The VAS employed was a straight horizontal line of 100 mm. The ends were defined as the extreme limits of the pain/discomfort.¹³

All F-wave parameters were determined by automated computer algorithms. F-wave amplitude was the largest consecutive peak-to-peak amplitude. F/M amplitude ratio was obtained as the ratio of mean F wave amplitude to the maximum CMAP amplitude (F-wave/CMAP×100). F-wave persistence was the percentage of F-wave traces with amplitude of $\geq 0.5\%$ of the corresponding CMAP amplitude. As data from such 8 to 10 identifiable sequential F-waves have been suggested to provide a reasonable estimate of persistence, records with less than 10 traces (with identifiable peak-peak amplitude) were not included.⁹ Chronodispersion was the difference between the minimum and maximum F-wave latency. Individual F-wave duration is the total time span between F-wave latency onset and final return of F-wave to

baseline in each trace.^{14,15} Mean value of all the recorded F-wave duration in the set was obtained.

Statistical analysis

F-wave minimum latency, F-wave mean latency, F-wave mean duration, persistence, chronodispersion, F/M amplitude ratio and subject's discomfort level obtained by the two techniques were expressed as mean±standard deviations (SD). Means were compared by paired t-test considering the null hypothesis that the parameters under the two stimulation conditions do not have the same mean. P value <0.05 was considered as statistically significant.

RESULTS

64 subjects (39 males 25 females) participated in the study. Mean age of the participants was 27.5 years (SD=8.49). Mean height of the subjects was 164.5 cm (SD=6.58). Unilateral F-wave records (left limb) of total 251 (64 median, 64 ulnar, 63 tibial and 60 peroneal) nerves were obtained. Four peroneal nerve records with fewer than 10 F-wave latencies at both sub- and supramaximal levels while one tibial nerve record with fewer than 10 latencies (at the submaximal level) were not included in the analysis.

Table 1: Comparison of F-wave study outcome between supramaximal and submaximal stimulation (recorded from median nerve) (n=64).

Study variables	Results in mean±SD		Paired t-test value
	Supramaximal	Submaximal	
Stimulus magnitude (mA)	19.45±4.92	10.52±3.58	p<0.0001
Subjects' discomfort level	10.52±0.86	5.20±1.05	p<0.0001
Mean duration (ms)	6.6±1.04	6.48±1.27	0.3215
Mean latency (ms)	25.49±1.4	25.62±1.22	0.4286
Minimum latency (ms)	24.26±1.33	24.6±1.22	0.1491
F/M amplitude (%)	2.43±1.03	2.64±1.33	0.0042
Chronodispersion (ms)	1.5±0.96	1.22±0.7	0.0714
Persistence (%)	89.33±8.55	82.29±9.99	p<0.0001

Table 2: Comparison of F-wave study outcome between supramaximal and submaximal stimulation (recorded from ulnar nerve) (n=64).

Study variables	Results in mean±SD		Paired t-test value
	Supramaximal	Submaximal	
Stimulus magnitude (mA)	18±2.27	10±1.58	p<0.0001
Subjects' discomfort level	8.2±1.16	5.2±1.08	p<0.0001
Mean duration (ms)	6.24±0.78	6.15±0.99	0.4236
Mean latency (ms)	26.87±1.22	26.64±1.24	0.1680
Minimum latency (ms)	25.34±0.93	25.39±1.2	0.8058
F/M amplitude (%)	1.5±0.83	1.59±0.76	0.0157
Chronodispersion (ms)	2.52±0.97	2.480±1.021	0.6807
Persistence (%)	90.01±7.38	86.02±9.16	0.0014

Table 3: Comparison of F-wave study outcome between supramaximal and submaximal stimulation (recorded from tibial nerve) (n=63).

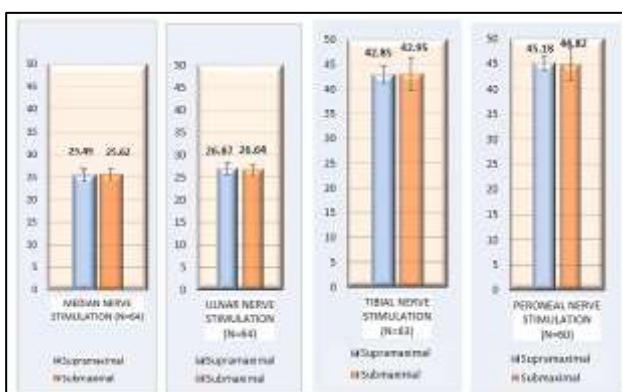
Study variables	Results in mean±SD		Paired t-test value
	Supramaximal	Submaximal	
Stimulus magnitude (mA)	29±4.96	16±1.77	p<0.0001
Subjects' discomfort level	8±0.97	5±0.87	p<0.0001
Mean duration (ms)	5.8±0.5	5.6±0.64	0.035
Mean latency (ms)	42.85±1.66	42.95±3.32	0.7655
Minimum latency (ms)	41.24±2.86	40.85±2.61	0.2056
F/M amplitude (%)	2.4±0.97	2.59±0.91	0.028
Chronodispersion (ms)	3.6±1.06	3.88±0.7	0.05
Persistence (%)	96.20±4.71	91.27±2.28	p<0.0001

Table 4: Comparison of F-wave study outcome between supramaximal and submaximal stimulation (recorded from peroneal nerve) (n=60).

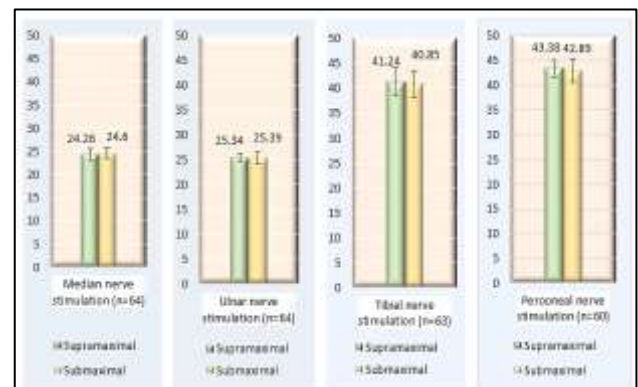
Study variables	Results in mean±SD		Paired t-test value
	Supramaximal	Submaximal	
Stimulus magnitude (mA)	25.7±6.27	19.04±3.14	p<0.0001
Subjects' discomfort level	8±0.64	4.73±0.59	p<0.0001
Mean duration (ms)	5.23±1.08	5.26±0.84	0.62
Mean latency (ms)	45.18±1.37	44.82±3.24	0.4
Minimum latency (ms)	43.38±1.69	42.89±2.3	0.015
F/M amplitude (%)	2.18±0.06	2.37±0.66	0.026
Chronodispersion (ms)	5.34±1.57	5.3±1.8	0.73
Persistence (%)	84.32±10.99	76.20±10.59	p<0.0001

Mean value for the stimulus magnitude required for supramaximal stimulation varied (with statistical significance) from that required for submaximal stimulation in recordings obtained from all four nerves studied (p<0.0001). Mean score for subjects' discomfort/pain level was found to be extremely significant (p<0.0001) (paired t test) in recordings from all four nerves (Tables 1-4).

tibial and 8±0.64 and 4.73±0.59 for peroneal nerve F-wave study.

**Figure 2: Comparison of mean F-wave latency after supramaximal and submaximal stimulation.**

VAS scores (supramaximal versus submaximal) were 10.52±0.86 and 5.20±1.05 for median nerve study, 8.2±1.16 and 5.2±1.08 for ulnar, 8±0.97 and 5±0.87 for

**Figure 3: Comparison of minimum F-wave latency after supramaximal and submaximal stimulation.**

Latency analysis revealed that both the important latency parameters, mean and minimum F wave latencies were not found to be statistically significant (p>0.05) (paired t test) when compared between the two modes of stimulation in F-wave recordings of all the four nerves (Figure 2 and 3 respectively). Mean F-wave duration and chronodispersion also did not vary significantly among the two techniques (Tables 1-4). However, F/M amplitude ratio and persistence were found to reveal significant differences in the mean values when

compared between the two techniques (Tables 1-4) with greater statistical significance in persistence value differences.

DISCUSSION

F-waves have been indicated as sensitive and reliable electrodiagnostic tool. Minimum F-wave latency and mean F latency have been reported to be the most useful F-wave measurement.^{6,9} However, F-wave parameters other than latency can also provide additional valuable electrophysiological information. With regard to the technique, although the conventional stimulus intensity is 25 percent above maximal for eliciting a direct response, F-waves are found to be present at submaximal stimulation. Increased patient comfort at this stimulus condition may provide adequate information in certain crucial situations.

F-wave latency and duration are reported to be unaffected by submaximal stimulation, yet the studies investigating the same, so far, are limited and the data remains confined to single nerve studies. The present research involved all routinely tested nerves for F-wave parameters to appraise the validity of the data with low intensity stimulation to lessen patient discomfort.

Mean values obtained by supramaximal stimulation for all the F wave parameters conform to the similar studies in the past.¹⁶⁻¹⁹ Stimulus magnitude for submaximal stimulation in the present study (for median nerve F-wave study) was 10.52 ± 3.58 (mA \pm SD) (Table 1) which is in accordance with the similar study by DiBenedetto et al.¹² This study reported no statistically significant difference between F-wave latencies, chronodispersion, and persistence elicited with maximal and low-current stimulation. Only amplitudes were found to be larger when using supramaximal current stimulation.¹² In a similar alignment, present study reports F-wave mean latency, F wave minimum latency, F-wave duration and chronodispersion values with no significant differences ($p > 0.05$) with that under supramaximal stimulation for all nerves studied (Table 1-4). This relative stability in F-wave latency and duration values irrespective of stimulus intensity supports the absence of bias in the selection of motor units in the generation of F-waves and that these are not preferentially generated in a select group of motoneurons with certain physiologic characteristics. It was suggested that recurrent discharges in the form of F-waves occur in approximately 1% of antidromically activated motoneurons irrespective of their peripheral excitability or conduction characteristics.²⁰

Amplitude analysis included mean F/M amplitude ratio which was found to be reduced under supramaximal stimulation for all the nerves (Tables 1-4). The finding conforms to that by Fisher et al. This in turn reflects an increase in M-wave amplitudes with increasing stimulus intensity without a comparable increase in F-wave amplitudes.¹⁰

Submaximal stimulation resulted in a statistically significant reduction of persistence also (Tables 1-4). This finding suggests that clinical interpretation of submaximal stimulation persistence must be made in the context of a submaximal reference range. Also, lower persistence implies that a higher number of submaximal stimuli must be delivered in order to attain adequate number of F-waves for F-wave parameter estimation.¹¹ Chroni et al suggested that minimum F-wave latency and chronodispersion require a higher number of stimuli that would yield about 40 F-waves.²¹ Reduction of the persistence from 65% to 48% in the study by Kong et al was inferred as the requirement of additional 11 stimuli to accumulate adequate F-wave latencies under submaximal stimulation condition.¹¹ A similar requirement of additional number of stimuli in the present study was computed (for adequate F-wave parameters) based on the reduction in the persistence values (Tables 1-4) which revealed that median nerve F-wave study may require ≥ 22 stimuli based on the drop in the persistence. Similarly, adequate number of stimuli required for ulnar and tibial were ≥ 21 , while for peroneal ≥ 22 stimuli will be required for adequate estimation of F-wave parameters under submaximal stimulation. Data from various researches have also reported that 20 or more stimuli providing 16-20 F-waves may be needed for accurate measurements.²²⁻²⁴ It is hence, evident that owing to the differences in the persistence values, accurate measurement can be attained and application of the F-wave values under submaximal stimulation will be valid, if adequate number of stimuli are applied. The present study hereby provides an estimate of the required number of stimuli for the submaximal F-wave data to be comparable with the supramaximal values. It also yields the reference range for stimulus magnitude and other F-wave parameters for its feasibility and the clinical application.

CONCLUSION

F-waves can be obtained at submaximal stimulation. F-wave mean and minimum latency, chronodispersion and duration values remain consistent, but more stimuli may be needed for accurate values. The present study provides the estimates of the number of stimuli required for the accurate measurements and the applicability of the same. For other parameters including mean F/M amplitude ratio and F-wave persistence, submaximal reference range would be needed.

An evident decline in the subjects' discomfort during the procedure stipulates for the utilization of the technique, as the most useful F-wave parameters seem to be interpreted with considerable validity as supramaximal values.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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