Neurophysiologie Clinique / Clinical Neurophysiology 55 (2025) 103076

Contents lists available at ScienceDirect

Neurophysiologie Clinique

journal homepage: www.elsevier.com/locate/neucli

Original article

Characterizing repeater F waves using the compound muscle action potential scan and machine learning techniques

Xiaoyan Li [a,b,*], Maoqi Chen [c], Paul E. Barkhaus [b], Sanjeev D. Nandedkar [b,d], Marek Cierny [b], Caitlin Moore [b], Ping Zhou [c]

[a] Fischell Department of Bioengineering, University of Maryland at College Park, College Park, MD, USA
[b] Department of Neurology, Medical College of Wisconsin, Milwaukee, WI, USA
[c] School of Rehabilitation Science and Engineering, University of Health and Rehabilitation Sciences, Qingdao, PR China
[d] Natus Medical, Inc, Middleton, WI, USA

ARTICLE INFO

Key words:
Compound muscle action potential (CMAP) scan
Motoneuron (MN)
machine learning
hand muscles
electrophysiology
Repeater F-waves

ABSTRACT

Objectives: The purpose of this study is to introduce a new analytical technique on repeater F waves (RFws) using compound muscle action potential (CMAP) scan and new features to differentiate the nerves innervating hand muscles.
Methods: Twenty-four healthy subjects participated in the CMAP scan study. Tests were performed on the abductor pollicis brevis (APB) and abductor digit minimi (ADM) muscles. RFws were extracted using unsupervised machine learning and analyzed through conventional characteristics such as amplitude, latency, indices of F repeaters and total F repeaters, as well by new variables, including relative stimulus intensity (ReSI), relative F/M ratio (RF/MR), and range of stimulation intensity (RaSI).
Results: Significantly higher indices of F repeaters (APB: 18.42±4.92 %, ADM: 13.58±4.68 %, $p < 0.005$) and total F repeaters (APB: 34.75±7.8 %, ADM: 26.67±8.56 %, $p < 0.005$) were observed in the APB compared with the ADM muscles. The ReSI ($Z = 13.81$, $p < 0.001$) and RaSI (Z=-2.46, $p < 0.05$) showed significant differences between the two muscles.
Discussion and Conclusion: This study provides normative data for RFws based on the CMAP scan recording and identifies different characteristics of repeaters between APB and ADM muscles. Findings of the study improve understanding of motoneuron physiological properties in hand muscles. The CMAP scan-based F wave analysis can be combined with motor unit number estimation technique to provide insights into surviving motoneuron function in neurological disorders.

Introduction

Repeater F waves (RFws) represent the category of F waves produced by recurrent 'backfiring' (antidromic activation) of the same motoneuron (MN) or MNs with identical waveforms and latencies [1,2]. Although they are sensitive to abnormal physiological conditions in the peripheral and central nervous systems [3,4], the mechanisms underlying generation of RFws remain unclear [2,5]. This may limit the application of F waves in the neurophysiological examination. Current literature on RFws is generally obtained from conventional tests which evoke the responses at constant intensities [2,6–8]. There is a lack of information on RFws from a more dynamic physiological environment.

The compound muscle action potential (CMAP) scan is a technique used in motor unit number estimation (MUNE), which records muscle responses to finely graded declining electrical stimuli [9–14]. When the stimulus intensity changes from the supramaximal strength to the subthreshold of the lowest motor unit, it activates different subgroups of MNs and induces environmental changes that affect the generation of F waves. In a previous study [15], we developed a novel analytical technique to examine F wave characteristics based on the CMAP scan recording.

In this study, we aimed to assess RFws using the F wave data from the previous study [15]. An unsupervised machine learning technique was applied to cluster F waves collected from the CMAP scan. In contrast to conventional F wave tests, RFws from the same cluster were evoked at different intensities and the amplitude of associated CMAP (the muscle

* Corresponding author at: Fischell Department of Bioengineering, University of Maryland at College Park, College Park, MD, USA.
E-mail address: xli025@umd.edu (X. Li).

https://doi.org/10.1016/j.neucli.2025.103076
Received 3 March 2025; Accepted 27 April 2025
Available online 8 May 2025

response proceeding the F wave) varied in each trial. This allowed us to investigate new features of individual RFws and clusters of RFws for further understanding of RFw generation.

The abductor pollicis brevis (APB) and abductor digit minimi (ADM) are two hand muscles typically examined in neurophysiological tests. They show different progression of motor unit loss in the course of amyotrophic lateral sclerosis (ALS), with preferential wasting of APB and relative preservation of ADM [16–18]. As the mechanisms of the clinical phenomenon are unknown, we aimed to examine the nerves innervating the two muscles to help understand the differences in nerve properties that lead to different performance in pathological conditions. We compared RFws characteristics including amplitude, latency, and persistence to evaluate MN pool excitability and nerve conduction in the two muscles. We hypothesized that there were significant differences in RFws between the APB and ADM muscles.

Methods

The F waves and CMAP scan recordings used in this research were gathered from our previous study [15], which gives details of subject demographic information and experimental procedures. In brief, twenty-four healthy subjects, 13 females and 11 males with a mean age of 40 ± 12 years, participated in the CMAP scan study. The study was approved by the Institutional Review Board of the Medical College of Wisconsin (Milwaukee, WI, USA). All subjects gave signed informed consents before the experiment. Tests were performed on the dominant APB and ADM muscles. The CMAP scan protocol involved repetitive electrical stimuli, with the intensity declining linearly from the preset supramaximal strength to below the activating threshold of the lowest motor unit in 500 steps. Muscle responses were saved in 100 ms epochs at each stimulus intensity. This resulted in 500 trials recorded in each muscle.

Data analysis

CMAP scan data were exported and analyzed in Matlab (MathWorks Inc, Natick, MA, USA). For each trial, the stimulus intensity and amplitude of the corresponding CMAP waveform were measured in the program and the occurrence of F waves was checked. Details of F wave extraction and processing are given in our previous study [15]. We collected an average of 205 F waves per APB and 195 F waves per ADM. The quantity of F waves ensured RFws analysis in this study.

Identification of repeater F waves

RFws were identified within each muscle. The procedure consisted of two steps. The first step was to apply unsupervised machine learning technique to automatically cluster F waves with identical waveforms and latency. F wave latency in each cluster should vary within 100 μs. This process involved calculation of the waveform similarity and application of the hierarchical method to stratify them. City block distance and Euclidean distance are among the most frequently used similarity measures, and both are easy to implement. Since the algorithm of this study was developed based on our previous F wave MUNE paper [19], we continued to use the Euclidean distance for similarity measures. The performance of clustering RFws also depends on selection of appropriate thresholds. The Euclidean distance between two small waveforms is more susceptible to noise than that between two larger F waves. Therefore, a normalized Euclidean distance was used to improve classification accuracy. Euclidean distance and normalized Euclidean distance were calculated between any two F waves in the same muscle to quantify waveform similarities. Assuming F_i and F_j represent two randomly selected F waves in the same muscle, the Euclidean distance between the two waveforms is defined as:

$$D_{i,j}{}^2 = \left(F_i - F_j\right)^T\left(F_i - F_j\right) \tag{1}$$

The normalized Euclidean distance is defined as the following [20]:

$$d_{i,j}{}^2 = \frac{D_{i,j}{}^2}{F_j{}^T F_j} \tag{2}$$

Next, a cluster tree was created based on the nearest Euclidean distance using the Ward method. By computing the inconsistent value of each non-leaf node in the cluster tree, the program determined an appropriate threshold to differentiate the clusters. Subsequently, the program stepped down through the tree to search for the node whose inconsistent value was below the threshold and grouped all leaves below the node into a cluster.

In the subsequent step, a human operator carefully inspected the waveforms of the clustered F waves based on the values of Euclidean distance and normalized Euclidean distance and partitioned the misclassified clusters. Next, the F waves within each confirmed cluster were averaged to create a new group of F waves and the above procedures were repeated on the new group of F waves to check if the clusters could be further merged. Although identification of RFws relies largely on the Matlab program we developed, we included the function to allow the operator to manually merge or delete the clusters to ensure that the clustered F waves presented identical shape, size and latency.

Analysis of repeater F waves

As RFws were evoked at different intensities, we analyzed the individual RFws and the clusters of RFws separately.

For individual RFws, we calculated the absolute stimulus intensity and the relative stimulus intensity (ReSI), which was defined as the ratio of F wave associated CMAP amplitude and the maximal CMAP of the muscle. For example, the absolute stimulus intensity of two RFws in Fig. 2a is 14.79 mA and 16.17 mA, and the CMAP amplitude associated with the two RFws is 16.76 mV and 17.22 mV, respectively; the maximal CMAP of the muscle is 17.43 mV. Therefore, ReSI for the two F waves is 96.17% (16.76 mV /17.43 mV × 100%) and 98.81% (17.22 mV /17.43 mV × 100%) of the maximal CMAP amplitude, respectively.

In addition, the relative F/M ratio (RF/MR) was calculated for individual RFws, defined as the ratio between the individual RFws amplitude and the associated CMAP amplitude. This variable measures the proportion of an individual F wave in the activated MN pool. For example, the amplitude of the two RFws in Fig. 2a is 642.18 μV. Since the F wave associated CMAP amplitudes are 16.76 mV and 17.22 mV, the RF/MR of the two RFws is 3.83% (642.18 μV / 16.76 mV x 100%) and 3.73% (642.18 μV / 17.22 mV x 100%) of the associated CMAP amplitude (Fig. 2b), respectively.

For each repeater cluster, we measured its amplitude and latency. The repeater cluster amplitude was defined as the difference between the negative peak and the baseline of the waveform. Repeater cluster latency (or F-M latency) was calculated as the interval between the onset of the waveform and distal motor latency [21,22]. In addition, the range of stimulation intensity (RaSI) was calculated, which was defined as the difference between the maximal and minimal relative stimulus intensities of the individual RFws in the same cluster. For example, the range of ReSI in Fig. 2a (the two RFws evoked at 14.79 mA and 16.17 mA) is 2.64% (98.81% - 96.17%) of the maximal CMAP.

For each muscle, the index of F repeaters (iFR) and index of total F repeaters (iTFR) [7] were examined. Specifically, the iFR quantifies the proportion of repeater motoneurons generating the RFws, and the iTFR assesses the proportion of all RFws. Variables including the number of repeater clusters, total number of RFws, number of non-RFws, and total number of F waves were measured. The iFR is defined as: number of repeater clusters / (number of repeater clusters + number of non-RFws) × 100%. The iTFR is defined as: total number of RFws / total number of F waves × 100% [7]. For example, a total of 208 F waves was detected in the APB muscle (Fig. 2). Among them, there were 37 repeater clusters (Fig. 1, in total of 89 RFws) and 119 non-RFws. The iFR was calculated as: 37/ (37+119) × 100% = 23.71%., and the iTFR was 89/208 × 100%

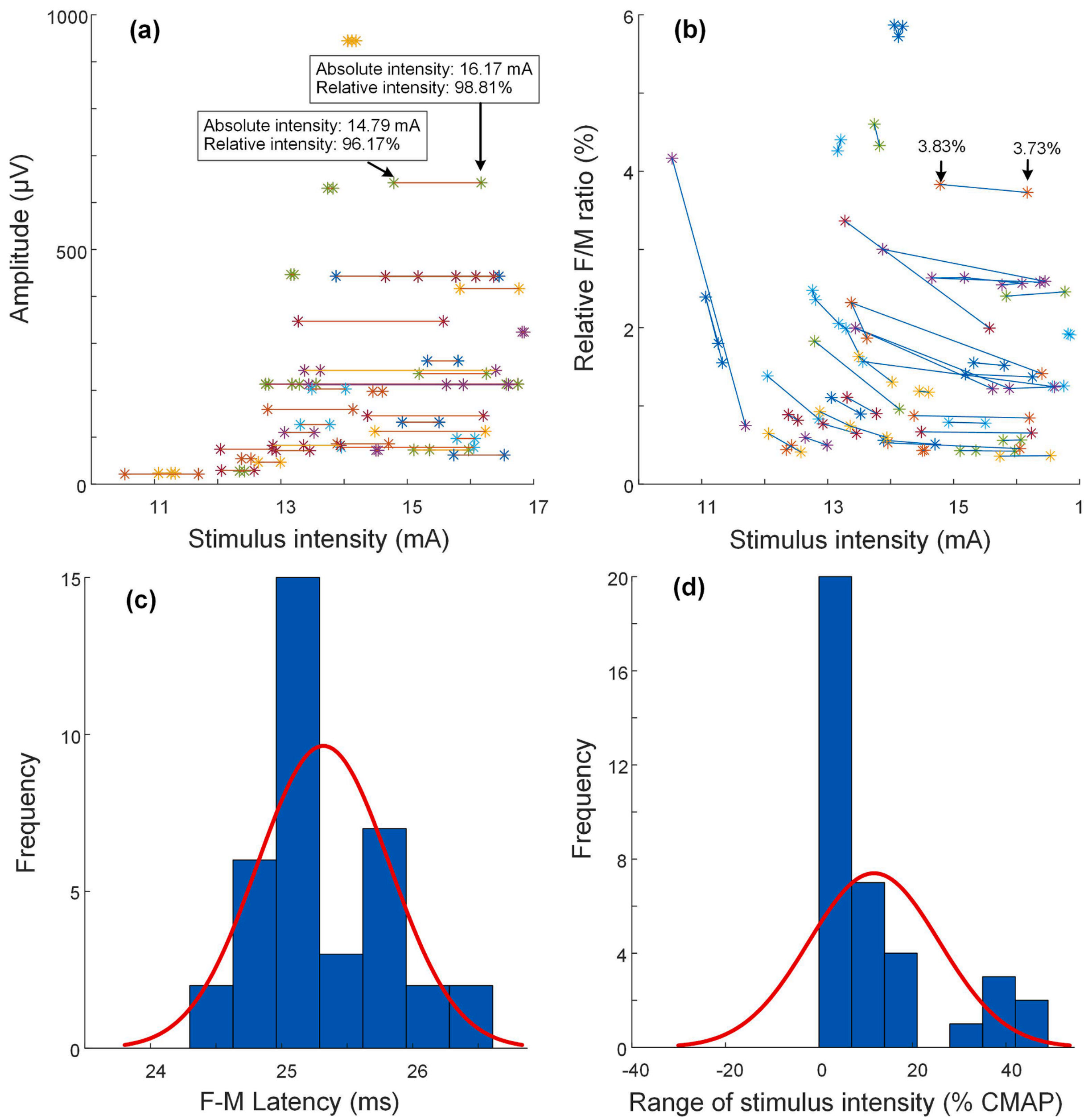

Fig. 2. Analysis of RFws on the same muscle as Fig. 1. (a) Repeater cluster amplitude with stimulus intensity. F waves belonging to the same cluster are displayed in the same color and connected by a solid line. Different clusters were randomly assigned a color in the plot. (b) RF/MR with stimulus intensity. (c) Histogram of repeater cluster latency. (d) Histogram of RaSI.

= 42.79%.

Statistical analysis

Statistical analysis was performed using the Statistics and Machine Learning Toolbox in Matlab. Shapiro-Wilk test was applied to assess normality of the indices of F repeaters and total F repeaters in the APB and ADM muscle groups, respectively. After the normality was confirmed, paired *t*-tests were applied to compare the differences of the indices between the two hand muscles.

Repeater cluster variables including amplitude, latency and RaSI, were pooled into the APB and ADM muscle groups. Similarly, individual RFws variables including RF/MR and ReSI were pooled into the two muscle groups. Kolmogorov-Smirnov test (sample size $>$ 100) was applied to assess normality of the distributions of the above variables. As the null hypothesis was rejected in all variables, the Box-Cox equation was applied to transform the skewed distribution to normal ones except the ReSI which is binomially distributed. Z-score was calculated to compare the differences of the transformed distributions between the APB and ADM muscle groups. The Mann–Whitney U test was used to compare the difference of ReSI between the two muscles.

Kendall rank correlation was applied to examine the linear relationship between the repeater cluster variables including the amplitude, latency, and RaSI in the APB and ADM muscles, respectively. Similarly, correlation analysis was performed between the RFw variable including RF/MR and ReSI in the two muscle groups. Statistical significance was defined as $p < 0.05$. Results were reported in the mean ± std format.

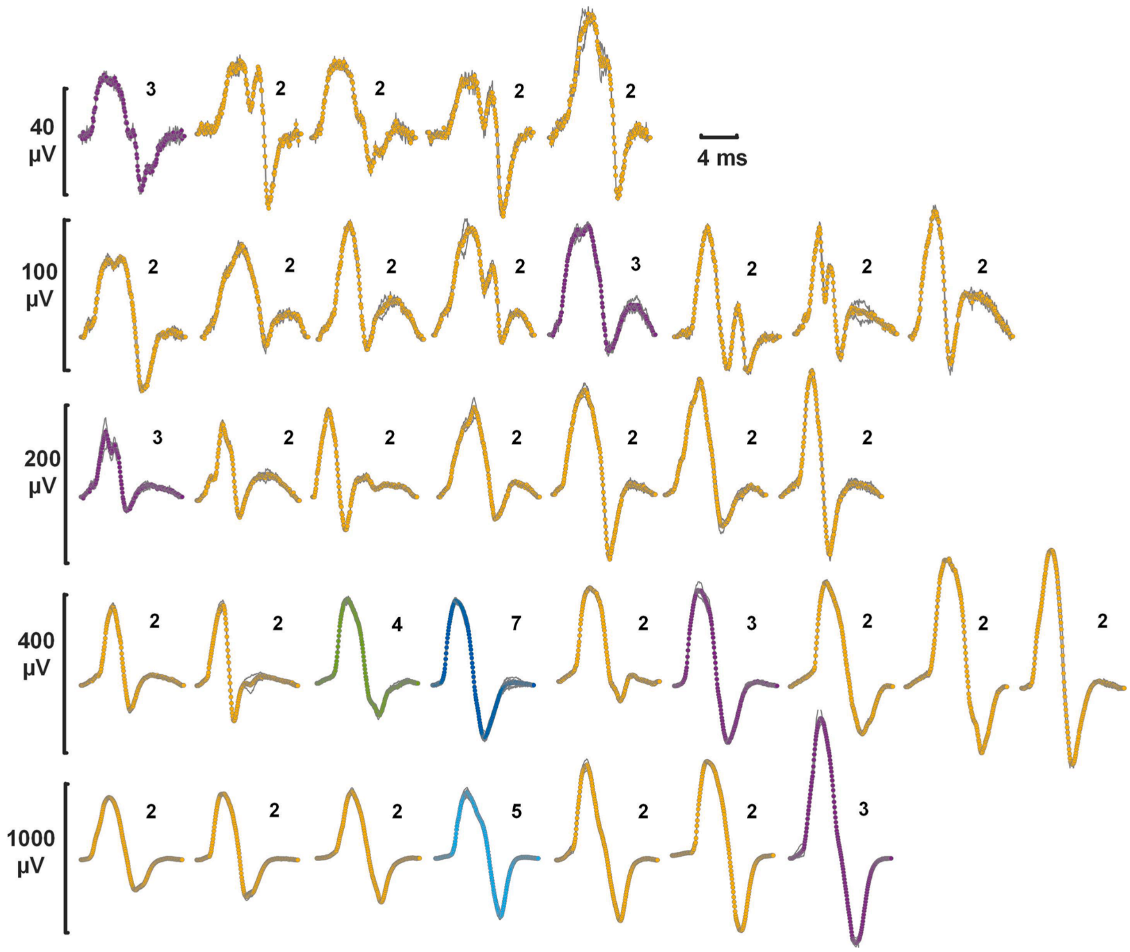

Fig. 1. Examples of identified RFws from a representative APB muscle. RFws were arranged in different rows according to the amplitude. Repeater clusters consist of a different number of waveforms. Repeater clusters with the same occurrence frequency are displayed in the same color with the frequency displayed. Individual RFws from the same repeater clusters are overlapped. The dotted line indicates averaged waveforms.

Results

Analysis of repeater F waves in a representative muscle

Figs. 1 and 2 illustrate characteristics of individual RFws and repeater cluster in the APB muscle from a representative subject. Eighty-nine RFws were identified from a total of 208 F waves in the muscle and classified into 37 clusters (Fig. 1). Individual RFws belonging to the same cluster are superimposed and displayed in Fig. 1. The iFR and iTFR in the muscle are 23.71% and 42.79%, respectively. The recurrence frequency of the 37 clusters is displayed in Fig. 1. There are 29 repeater clusters (78.38%) occurring twice. The amplitude of repeater clusters ranges from 21.37 μV to 944.65 μV. There are 15 (40.54%) repeater clusters with amplitudes smaller than 100 μV.

Fig. 2a illustrates the RFws amplitude distribution with stimulus intensities. The ReSI of individual RFws ranges from 2.94% to 99.8% of maximal CMAP amplitude. Among them, 52 RFws evoked at >80% CMAP amplitude. The relationship of the RF/MR with the stimulating intensity is displayed in Fig. 2b. RFws belonging to the same repeater cluster are connected by a line. The RF/MR of RFws ranges between 0.36% and 5.87% of the associated CMAP amplitude in the muscle (Fig. 2b).

The range of repeater cluster latency (F-M latency) varies between 24.38 ms and 26.56 ms in the APB muscle. The frequency distribution of the latency from 37 repeater clusters is displayed in Fig. 2c. The mean and median of the latency are 25.32 ms and 25.01 ms, respectively. The RaSI of the repeater clusters is illustrated as the length of the lines connecting the RFws in Fig. 2a. The distribution of the RaSI from 37 repeater clusters is presented in Fig. 2d. For this APB muscle, the RaSI varies from 0.63% to 48.55% of the maximal CMAP amplitude. There are 22 repeater clusters (59.46%) showing a RaSI <10% of the maximal CMAP amplitude.

Group analysis of repeater F waves

Recurrence frequency of repeater cluster

In our previous report, a total of 9613 F waves were collected from the CMAP scan recording, with 4925 F waves in the APB and 4688 in the ADM muscles [15]. We identified 1666 RFws (from 698 repeater clusters) in the APB and 1231 RFws (from 518 repeater clusters) in the ADM muscles. The frequency of repeater cluster recurrence in the APB and ADM groups is summarized in Table 1. Recurrence of these repeater clusters varies from two to eight in the APB and from two to nine in the ADM muscle groups. Most of the repeater clusters (>75%) recurred twice and less than 3% of the clusters recurred more than five times.

Indices of F repeaters and total F repeaters

Comparison between the APB and ADM muscle groups showed significant differences in the iFR (APB: 18.42 ± 4.92 %, ADM: 13.58 ± 4.68 %, $p < 0.005$) and iTFR (APB: 34.75 ± 7.8 %, ADM: 26.67 ± 8.56 %, $p < 0.005$).

Characteristics of individual repeater F waves and repeater clusters

The distributions in the range of repeater cluster stimulation

Table 1
Summary of recurrence of repeater F waves in the APB and ADM muscles.

	APB	ADM
Total F waves	4925	4688
Total repeater F waves	1666	1231
Total repeater clusters	698	518
Recurrence: 2	534 (76.5%)	412 (79.54%)
Recurrence: 3	99 (14.18)	64 (12.36%)
Recurrence: 4	38 (5.44%)	19 (3.67%)
Recurrence: 5	19 (2.72%)	8 (1.54%)
Recurrence: 6	4 (0.57%)	11 (2.12%)
Recurrence: 7	2 (0.29%)	0 (0%)
Recurrence: 8	2 (0.29%)	3 (0.58%)
Recurrence: 9	0 (0%)	1 (0.19%)

(): percentile in the total population.

intensity of the APB and ADM muscle groups are presented in Fig. 3a. Fig. 3b illustrates the distributions after the Box-Cox transformation. Z-test was performed on the transformed data and the score was −2.46. Given that the significance level of 0.05 was reached at a Z score of either >1.96 or <−1.96, a significantly smaller RaSI was observed in the APB muscle. Similarly, the distributions of repeater cluster amplitude and latency were transformed. The Z scores were calculated as 41.89 and −6.58, respectively. The tests confirmed significant larger repeater cluster amplitude in the APB muscle and longer repeater cluster latency in the ADM muscle group.

Distributions of the RF/MR of individual RFws in the two muscle groups are displayed in Fig. 4a and the transformed distributions are plotted in Fig. 4b. The Z test ($Z = -9.62$) indicates a significantly larger RF/MR in the ADM compared to the APB muscle. The ReSI of individual RFws is binomially distributed in both the APB and ADM muscles (Fig. 4c and 4d). The first (or main) peak of the ReSI appears between 90–100% of maximal CMAP amplitude, which represents approximately 62.73% of the total RFws in the APB and 38.34% of RFws in the ADM muscles. The second peak appears between 10–20% of the maximal CMAP amplitude in the APB muscle which represents 4.86% of total RFws. For the ADM muscle, the second peak appears below 10% of the maximal CMAP with 12.19% of the whole waves. Given that the sample size of ReSI was large (>500), the Mann–Whitney U test in Matlab applied the normal distribution approximation to compare the difference of ReSI between the two distributions. The Z score was 13.81, indicating RFws in the APB muscle were activated by higher ReSI compared with those in the ADM muscle.

Correlation analysis

Correlation analysis on repeater cluster characteristics in terms of amplitude, latency, and RaSI, did not show any significance between pairs of the variables in either APB or ADM muscle group. In contrast, significant correlations were observed in individual RFws, between the RF/MR and relative F wave stimulus intensity, in both muscles (APB: $\tau=-0.28$, $p < 0.001$; ADM: $\tau=-0.16$, $p < 0.001$).

Discussion

The index of F repeaters (iFR) and index of total F repeaters (iTFR) in the APB muscle are significantly higher than those in the ADM muscle. Repeater clusters in the APB muscle show significantly larger amplitude, shorter latency and narrower RaSI than those in the ADM muscle. Analysis of the distributions of individual RFws indicates higher ReSI and lower RF/MR in the APB muscle compared with the ADM muscle.

Indices of F repeaters and total F repeaters

The iFR and iTFR are one of the most reported parameters in F wave studies [8]. The values of these indices in this study based on the CMAP scan recordings are larger than those from the conventional studies using supramaximal electrical stimulations [1,7,23]. The iFR and iTFR are found to increase significantly at submaximal stimulation compared with the supramaximal condition, and correlate negatively with the quantity of F waves [1]. The differences in the index values between our study and conventional studies may result from the different electrical stimulation intensities and the number of electrical stimuli to evoke F waves.

The iFR and iTFR are considered sensitive parameters to differentiate muscles with MN dysfunction from intact ones. Researchers have reported a significant change in these indices in ALS, carpal tunnel syndrome, and other neuropathies [4,18,23–25]. These indices are negatively correlated with MUNE and neurological index [18,26]. It is suggested that increases of the iFR and iTFR in the neurogenic atrophied muscles are likely associated with loss of functioning MNs [26,27].

Similar to the results in our study, higher iFR and iTFR were observed in the intact APB compared with the ADM muscles in previous F wave studies using supramaximal stimulus intensity [18,23]. The iFR and iTFR have also been compared between control and ALS groups. It has been shown that ALS patients had significant increases of these indices in the APB muscle despite of the inconsistent results in the ADM muscle [18,23]. In a longitudinal study of lower MN degeneration, the APB

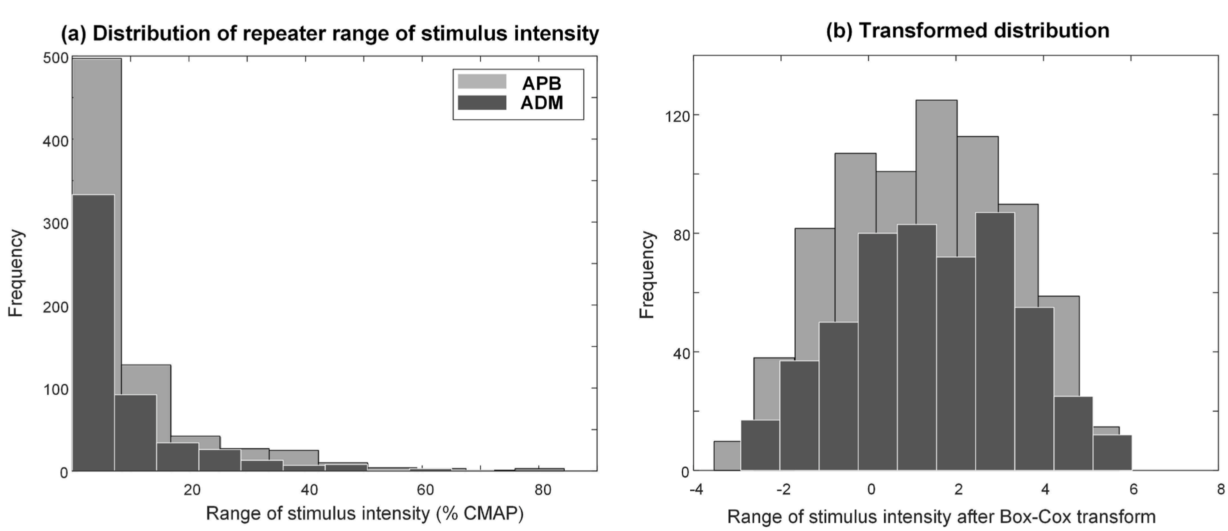

Fig. 3. Analysis of range of stimulation based on the pooled data. A total of 698 repeater clusters in the APB and 518 repeater clusters in the ADM. (a) Distribution of range of stimulation in the APB and ADM muscles. (b) Transformed distribution of range of stimulation using the Box-Cox transformation.

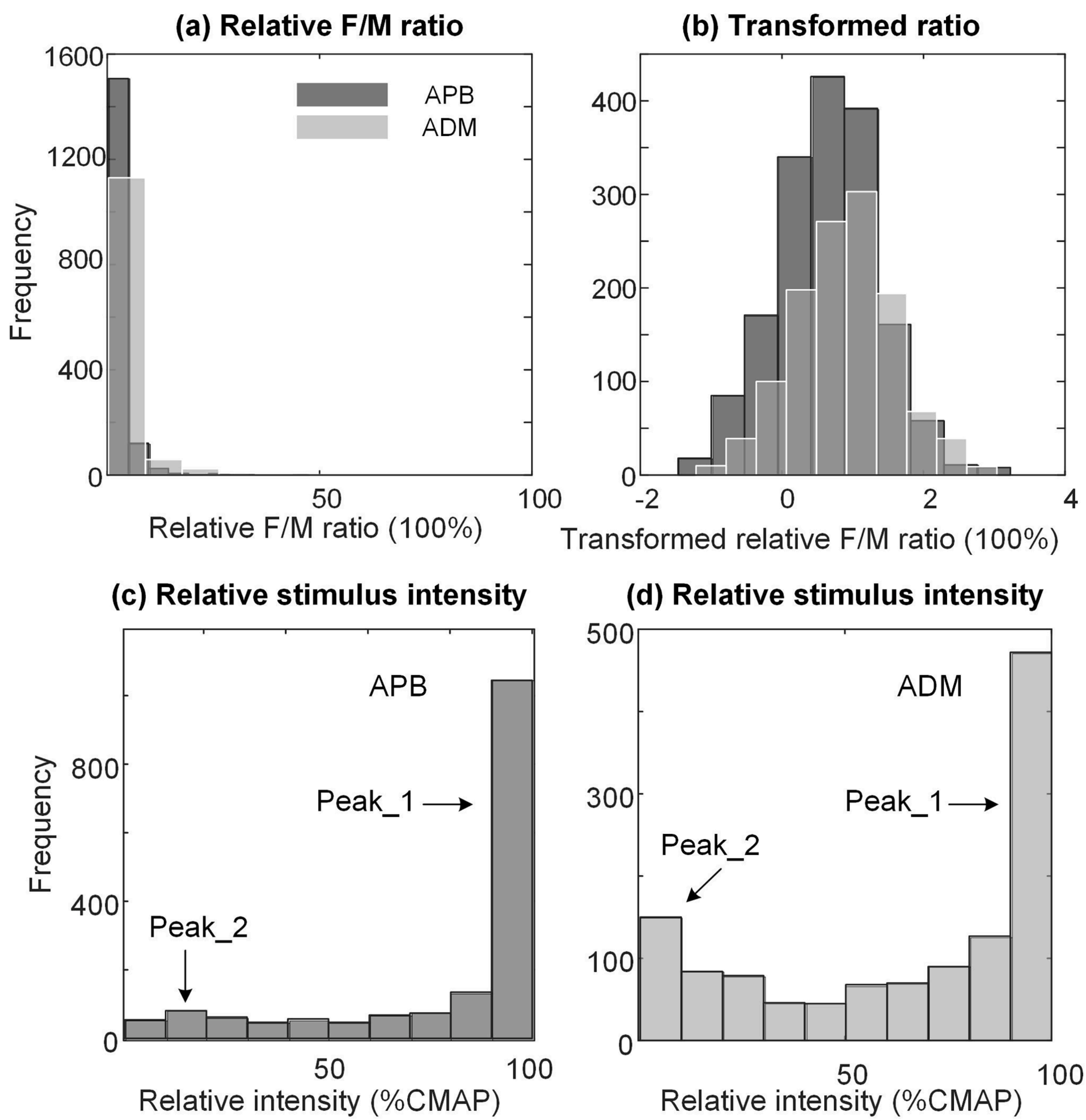

Fig. 4. Analysis of RF/MR and ReSI based on the pooled data. A total of 1666 RFws in the APB and 1231 RFws in the ADM. (a) Distribution of RF/MR in the APB and ADM muscles. (b) Transformed distribution of RF/MR in the APB and ADM muscles. (c) Distribution of ReSI in the APB muscle. (d) Distribution of ReSI in the ADM muscle.

muscle showed more severe and greater rate of motor unit loss than the ADM [28]. As the occurrence of RFws is associated with MN excitability [26,29], the differences in indices of RFws may reflect different cortical and axonal excitability in the nerves innervating the APB and ADM muscles [30,31]. It is unclear whether the differences in MN degeneration between the two muscles are associated with variations in MN excitability. Future studies tracking MUNE and the combination of F wave parameters including the iFR and iTFR, F wave persistence, latency, and amplitude with the CMAP scan technique may provide new information about MN degeneration .

Amplitude and relative F/M ratio

In F wave analysis, our previous study [15] and studies using conventional tests [7,23,32] reported non-significant differences of amplitude and F/M ratio between APB and ADM muscles in healthy subjects. In contrast, this study found a significantly higher RFws amplitude and lower RF/MR in the APB muscle compared with the ADM. The differences of RFws amplitude in the hand muscles may be attributed to the fact that there are more RFws evoked between 90–100% of maximal CMAP in the APB (62.73%) than in the ADM (38%) (Fig. 4). RFws amplitude tends to be larger at maximal stimulus intensity than that at submaximal intensities.

The decrease in RF/MR of RFws in APB indicates a smaller proportion of F waves in the associated CMAP. As a majority of RFws were evoked at intensities close to maximal strength in APB, the amplitude of associated CMAP approximated the maximum or full activation of the MN pool. The increase of associated CMAP exceeds the increase of RFw amplitude, which causes the lower RF/MR in the APB. As illustrated in Fig. 3b, higher RF/MR generally appears in submaximal stimulations where the associated CMAP amplitude is low.

Relative stimulus intensity and range of stimulation intensity

Significantly larger ReSI was found in the APB muscles, which conforms to our previous finding of higher F wave activating threshold in the APB muscle in comparison to the ADM [15]. The difference of relative stimulation intensity between APB and ADM muscles may reflect the excitatory state of the MNs innervating the two muscles [30].

Occurrence of RFws is not evenly distributed throughout the range of stimulation in the CMAP scan data. There is a binomial distribution of the ReSI, and the secondary peak appears below 20% of CMAP intensity (Fig. 4c and 4d). Similarly, a previous study reported more repeaters were generated at 30% of maximal intensity than 60% of the maximal and supramaximal intensities [1]. In addition, the occurrence intervals between RFws were collected and there were four distinct peaks in the interval distribution [2]. These studies suggested that RFws were generated by neurons of a different functional group.

Repeater clusters present at a wide RaSI in both muscles in this study. The distribution of RaSI is right skewed and more than 70% of the repeater clusters are evoked at least twice with the range below 10% of the CMAP (Fig. 3a). In addition, the RaSI of repeater clusters is not correlated with amplitude or latency of the neuron. The results confirm that the repeaters are heterogenous anatomical groups [2,5].

This study and our previous study [15] proposed a new F wave analysis based on the CMAP scan. The technique can be potentially combined with the CMAP scan based MUNE technique to assess motor unit loss and survival MN excitability and conductivity in neurological disorders. Compared with other MUNE and conventional F wave tests, which usually involve two different protocols, the CMAP scan test can reduce testing time and cause less discomfort to the subjects. This study may expand the application of the CMAP scan technique in neurophysiological examination. There is a growing application of artificial intelligence (AI) and machine learning in neurophysiology [33]. This study used unsupervised machine learning to classify repeater F waves which reduced the intra-observer variability and time for cluster analysis, providing higher efficiency and accuracy in electrophysiological data analysis.

Limitations

We did not examine the effects of gender on RFws in this study. This may limit generalizability of our research findings. Previous studies based on conventional F wave analysis reported non-significant changes of F wave duration, amplitude (absolute and F/M ratio) and chronodispersion between sexes [34] or no relationship between F wave characteristics and sex [35]. The F wave minimal latency is found to be shorter in females [36], which is likely associated with the differences of height between men and women [21,34]. Given the minimal systematic effect of gender on F waves [21], a much larger sample size would be needed to investigate the effect of gender on RFws in future studies.

A general limitation in RFws analysis lies in the inherent variations in latency of F waves. The latency of RFws varies from <0.070 ms (in hand muscle) using single fiber electrode recordings [37] to < 2 ms (in foot muscle) using surface electrode recordings [3,4]. There is a slight possibility that the temporal variations may cause phase cancellation and potentially affect the morphology of F waves. Future studies examining the inter-operator variability in identification of RFws may confirm the reproducibility of the method.

Conclusion

To summarize, this study examined new features of RFws using the CMAP scan technique and identified differences in RFws characteristics between the APB and ADM muscles. Findings of this study may improve understanding of generation of RFws.

Conflict of Interest Statement

Dr. Nandedkar is an employee of Natus Medical Inc and has no conflicts to report. None of the other authors has any conflict of interest to disclose.

Acknowledgement

This work was supported by NIH [7 R21 NS113716–02]; Advancing a Healthier Wisconsin Endowment (AHW); NIDILRR RERC [90REMM0001–01–00]; and by Taishan Scholar Project of Shandong Province.

Reference

[1] Chroni E, Veltsista D, Papapaulou C, Trachani E. Generation of Repeater F Waves in Healthy Subjects. J Clin Neurophysiol 2017;34(3):236–42.
[2] Guiloff RJ, Modarres-Sadeghi H. Preferential generation of recurrent responses by groups of motor neurons in man. Conventional and single unit F wave studies. Brain 1991;114(Pt 4):1771–801.
[3] Fisher MA. F-waves–physiology and clinical uses. ScientificWorldJournal 2007;7:144–60.
[4] Petajan JH. F-waves in neurogenic atrophy. Muscle Nerve 1985;8(8):690–6.
[5] Kimura J, Yanagisawa H, Yamada T, Mitsudome A, Sasaki H, Kimura A. Is the F wave elicited in a select group of motoneurons? Muscle Nerve 1984;7(5):392–9.
[6] Yates SK, Brown WF. Characteristics of the F response: a single motor unit study. J Neurol Neurosurg Psychiatry 1979;42(2):161–70.
[7] Chroni E, Tendero IS, Punga AR, Stalberg E. Usefulness of assessing repeater F-waves in routine studies. Muscle Nerve 2012;45(4):477–85.
[8] Liampas I, Veltsista D, Germeni A, Batzikosta P, Michou E, Kefalopoulou Z, et al. F waves in amyotrophic lateral sclerosis: a systematic review and meta-analysis. Neurophysiol Clin 2025;55(4):103061.
[9] Li X, Zong Y, Klein CS, Zhou P. Motor unit number estimation of human abductor hallucis from a compound muscle action potential scan. Muscle Nerve 2018;58(5):735–7.
[10] Henderson RD, Ridall PG, Hutchinson NM, Pettitt AN, McCombe PA. Bayesian statistical MUNE method. Muscle Nerve 2007;36(2):206–13.
[11] Bostock H. Estimating motor unit numbers from a CMAP scan. Muscle Nerve 2016;53(6):889–96.
[12] Jacobsen AB, Bostock H, Tankisi H. CMAP Scan MUNE (MScan) - A Novel Motor Unit Number Estimation (MUNE) Method. J Vis Exp 2018;(136).
[13] Sorensen DM, Bostock H, Abrahao A, Alaamel A, Alaydin HC, Ballegaard M, et al. Estimating motor unit numbers from a CMAP scan: repeatability study on three muscles at 15 centres. Clin Neurophysiol 2023;151:92–9.
[14] Sorensen DM, Bostock H, Ballegaard M, Fuglsang-Frederiksen A, Graffe CC, Grotting A, et al. Assessing inter-rater reproducibility in MScanFit MUNE in a 6-subject, 12-rater "Round Robin" setup. Neurophysiol Clin 2022;52(2):157–69.
[15] Li X, Chen M, Barkhaus PE, Nandedkar SD, Schmit B, Zhou P. F wave analysis based on the compound muscle action potential scan. Muscle Nerve 2024;70(3):395–401.
[16] Corcia P, Bede P, Pradat PF, Couratier P, Vucic S, de Carvalho M. Split-hand and split-limb phenomena in amyotrophic lateral sclerosis: pathophysiology, electrophysiology and clinical manifestations. J Neurol Neurosurg Psychiatry 2021;92(10):1126–30.
[17] Eisen A, Kuwabara S. The split hand syndrome in amyotrophic lateral sclerosis. J Neurol Neurosurg Psychiatry 2012;83(4):399–403.
[18] Oguz Akarsu E, Sirin NG, Kocasoy Orhan E, Erbas B, Dede HO, Baslo MB, et al. Repeater F-waves in amyotrophic lateral sclerosis: electrophysiologic indicators of upper or lower motor neuron involvement? Clin Neurophysiol 2020;131(1):96–105.
[19] Li X, Fisher M, Rymer WZ, Zhou P. Application of the F-Response for Estimating Motor Unit Number and Amplitude Distribution in Hand Muscles of Stroke Survivors. IEEE Trans Neural Syst Rehabil Eng 2016;24(6):674–81.
[20] Stashuk D, Qu Y. Adaptive motor unit action potential clustering using shape and temporal information. Medical and Biological Engineering and Computing 1996;34(1):41–9.
[21] Puksa L, Stalberg E, Falck B. Reference values of F wave parameters in healthy subjects. Clin Neurophysiol 2003;114(6):1079–90.
[22] Puksa L, Eeg-Olofsson KE, Stalberg E, Falck B. Reference values for F wave parameters in healthy 3-20 year old subjects. Clin Neurophysiol 2011;122(1):199–204.
[23] Fang J, Cui L, Liu M, Guan Y, Li X, Li D, et al. Differences in Dysfunction of Thenar and Hypothenar Motoneurons in Amyotrophic Lateral Sclerosis. Front Hum Neurosci 2016;10:99.
[24] Macleod WN. Repeater F waves: a comparison of sensitivity with sensory antidromic wrist-to-palm latency and distal motor latency in the diagnosis of carpal tunnel syndrome. Neurology 1987;37(5):773–8.
[25] Fisher MA. AAEM Minimonograph #13: h reflexes and F waves: physiology and clinical indications. Muscle Nerve 1992;15(11):1223–33.
[26] Hachisuka A, Komori T, Abe T, Hachisuka K. Repeater F-waves are signs of motor unit pathology in polio survivors. Muscle Nerve 2015;51(5):680–5.

[27] Peioglou-Harmoussi S, Fawcett PR, Howel D, Barwick DD. F-response frequency in motor neuron disease and cervical spondylosis. J Neurol Neurosurg Psychiatry 1987;50(5):593–9.

[28] Baumann F, Henderson RD, Gareth Ridall P, Pettitt AN, McCombe PA. Quantitative studies of lower motor neuron degeneration in amyotrophic lateral sclerosis: evidence for exponential decay of motor unit numbers and greatest rate of loss at the site of onset. Clin Neurophysiol 2012;123(10):2092–8.

[29] Wang FC, de Pasqua V, Delwaide PJ. Age-related changes in fastest and slowest conducting axons of thenar motor units. Muscle Nerve 1999;22(8):1022–9.

[30] Murray JE, Jankelowitz SK. A comparison of the excitability of motor axons innervating the APB and ADM muscles. Clin Neurophysiol 2011;122(11):2290–3.

[31] Menon P, Kiernan MC, Vucic S. Cortical excitability differences in hand muscles follow a split-hand pattern in healthy controls. Muscle Nerve 2014;49(6):836–44.

[32] Ibrahim IK, el-Abd MA. Giant repeater F-wave in patients with anterior horn cell disorders. Role of motor unit size. Am J Phys Med Rehabil 1997;76(4):281–7.

[33] McGonigal A, Tankisi H. Artificial Intelligence (AI): why does it matter for clinical neurophysiology? Neurophysiol Clin 2024;54(4):102993.

[34] Fierro B, Raimondo D, Modica A. F-response assessment in healthy control subjects. Electromyogr Clin Neurophysiol 1990;30(8):501–8.

[35] Peioglou-Harmoussi S, Howel D, Fawcett PR, Barwick DD. F-response behaviour in a control population. J Neurol Neurosurg Psychiatry 1985;48(11):1152–8.

[36] Nelson C, White JA, Mitchell RU, Hall CD. Median nerve F wave conduction in healthy subjects over age sixty-five. Electromyogr Clin Neurophysiol 1990;30(5):269–76.

[37] Schiller HH, Stalberg E. F responses studied with single fibre EMG in normal subjects and spastic patients. J Neurol Neurosurg Psychiatry 1978;41(1):45–53.