Quantitative analysis of the features of fasciculation potentials and their relation with muscle strength in amyotrophic lateral sclerosis

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Running head: fasciculation potentials in ALS

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Acknowledgements: This study was supported by a Grant-in-Aid for ALS and Neuropathy Project from the Tokyo Metropolitan Institute of Medical Science.

Abstract

Objectives: This study aimed to quantitatively analyze fasciculation potentials (FPs) and to investigate their relationship with muscle strength in amyotrophic lateral sclerosis (ALS).

Methods: Fifty-one patients with sporadic ALS or progressive muscular atrophy (25 men, 26 women, mean age of 68 years) underwent needle EMG. We determined the duration, phase number, and amplitude of FPs from three muscles (upper trapezius, biceps brachii, and tibialis anterior) and examined their relations with muscle strength. *Results:* In total, 878 FPs were analyzed. FP duration displayed a significant negative relation with the strength of all three muscles; the weaker muscles showed longer durations of FPs than the muscles with normal strength. The amplitude and phase number were not related with muscle strength, but there were significant correlations between the duration and amplitude of FPs in the trapezius and tibialis anterior muscles. *Conclusion:* The longer duration of FPs in muscles with weak strength suggest that the morphological changes of FPs were caused by temporal dispersion through progressively degenerating and/or immature reinnervating motor branches, and were observed uniformly in different muscles along with disease progression.

Keywords: amyotrophic lateral sclerosis, fasciculation potential, electromyography, quantitative analysis, muscle strength

Introduction

Fasciculations, often emerging across a wide range of body regions, are a clinical and electromyographic hallmark of amyotrophic lateral sclerosis (ALS). The Awaji criteria proposed in 2008 re-evaluated electrophysiological findings in ALS and emphasized the diagnostic significance of fasciculation potentials (FPs) [1]. According to the Awaji criteria, in the case of chronic neurogenic changes, FPs are a clinically significant indication equivalent to "denervation potentials" (fibrillation potentials – positive sharp waves; fib-psw) and are a major manifestation of the progressive denervation of muscles in ALS [1].

The characteristic features of FPs in ALS are complexity and instability. The Awaji criteria defines complex FPs (CFPs) as having polyphasic features (>4 phases), increased duration, or increased amplitude compared with the normal values for motor unit potentials (MUPs) in the affected muscles [1]. CFPs are often unstable, showing an increased jitter and conduction block within the terminal branches of MUPs. De Carvalho et al. proposed that simple and stable FPs arise proximally in the motor neurons, whereas CFPs originate in distal motor axonal sprouts associated with the reinnervation process [2, 3]. De Calvalho and Swash also emphasized the importance of morphological analysis of FPs by showing that there are

increased amplitudes, durations, and phase numbers of FPs in mildly weak tibialis anterior (TA) muscles compared to muscles with normal strength [4]. They concluded that these morphological changes of FPs resulted from the reinnervation of motor units associated with degeneration of lower motor neurons.

The aim of this study was to investigate the quantitative changes of FPs in muscles other than the TA, including the cervical muscles, and to compare FP properties across muscles with normal, mildly weak, or severely weak strengths in Japanese ALS patients.

Patients and methods

Patients

We investigated consecutive 51 Japanese patients with sporadic motor neuron disease in total. Forty-four patients with sporadic ALS (21 men and 23 women) were recruited from the EMG laboratories of Tokyo Metropolitan Neurological Hospital from October 2013 to June 2014. All patients fulfilled the revised El Escorial criteria for ‘definite’ (n = 11), ‘probable’ (n = 7), ‘probable-laboratory supported’ (n = 15), or ‘possible’ (n = 11) ALS at the time of EMG examination [5]. We also included seven patients with progressive muscular atrophy (PMA)

without family history (4 men and 3 women), because PMA is considered to share a common pathophysiology with ALS [6–8], and electrophysiological studies on ALS have included PMA patients as well with a same diagnostic significance [9–11]. Among the 11 patients with possible ALS, the number who progressed to “definite”, “probable”, or “probable-laboratory supported ALS” during the follow-up period was 1, 2, and 4, respectively. Among patients with PMA, 4 of 7 progressed to “probable” or “probable-laboratory supported ALS” during the follow-up period. Diagnosis of PMA was consistent for the remaining 3 patients throughout the study. All patients displayed relentless progressive courses, and no other causative disorders other than ALS or PMA were found during follow-up.

There were no patients with systemic diseases such as malignancy, diabetic complication, or collagen diseases The age of the enrolled patients was 34–88 (median 71) years at the EMG examination. Onset was defined as the time (month) when the first symptom related to ALS was noticed by the patients, and the duration from onset to the examination was 4–72 (median 24.5) months. The body regions affected at onset were bulbar (n = 13), upper limb (n = 19), lower limb (n = 16), respiratory (n = 2), and axial (n = 1). All patients were free from non-invasive or tracheostomy invasive ventilation. We did not examine known ALS-related gene variants for all the patients.

Electromyography

Needle EMG examinations using concentric needles were carried out by anyone of five authors (K.B., T.S., H.K., T.K., and T.Y.) with a Neuropack-2200 or Neuropack-2300 EMG system (Nihon Kohden, Co. Ltd., Tokyo). The standard filter setting was used (10 Hz –5 kHz). Although the number of examined muscles in each patient was determined by diagnostic indications and the patients' neurological findings, the upper trapezius (TPZ), biceps brachii (BB), and TA muscles of every patient were assessed. We examined the TPZ muscle instead of the tongue or other bulbar muscles according to previous reports on the high utility of TPZ for a diagnosis of ALS [9, 12].

The examination was performed unilaterally on the more affected side in individual patients. For each muscle, fib-psw was explored in at least 10 different sites within a muscle. The definition of fib-psw was the same as the description in the Awaji criteria [1]. Only regularly firing potentials that lasted more than 3 s were accepted as fib-psw. FPs were defined as motor unit potential-shaped potentials that repeatedly fired in a highly irregular pattern [9, 10]. We avoided any persistent voluntary EMG discharges, and performed observations for 60–90 s for each completely relaxed muscle to determine FPs after searching

for fib-psw [13]. We discarded spontaneous potentials that discharged only once during the observation period from the analysis, as these potentials could not be completely distinguished from potentials evoked by voluntary contractions or slight needle movements. FPs were defined as having an amplitude of more than 50 μV in peak-to-peak measurement [14]. Because the morphology of FPs varies depending on the needle position in the muscle, hand manipulation of the needle was avoided during the observation period in order to ensure the needle was immobilized.

Analysis

After the needle EMG examination, we quantitatively analyzed the morphology and firing frequency of all pooled FPs off-line. Analyses of the morphology included the peak-to-peak amplitude, duration, and phase numbers. Duration was measured as the time from initial negative or positive deflection of the potentials to a return to baseline at a gain scale of 200 μV/div and time scale of 10 ms/div. During the observation period for each muscle, we identified the same, repeatedly firing FPs, and for statistical analyses, we evaluated the data for each type of FP. The firing number over 60 s was measured for each type of FP as an

index of firing frequency. We also evaluated the rate (%) of occurrence of FPs and fib-psw for each muscle in the entire patient cohort.

To investigate the relationship between FPs or fib-psw and muscle strength, we evaluated the MRC (medical research council) grading scales for muscle strength of the TPZ (shoulder elevation), BB (elbow flexion), and TA (ankle dorsiflexion). To minimize the variability of these results, we classified muscle strength into three categories: 'Normal', 'moderate' and 'weak' represent MRC grades '5', '4', and '≤ 3', respectively. Potential correlations of muscle strength with amplitude, duration, phase number and firing frequency of FPs, and also the occurrence rate (%) for FPs or fib-psw were analyzed using Kruskal-Wallis and Man-Whitney U tests. In addition, we analyzed the correlations between the duration of FPs and the amplitude of FPs by Pearson's correlation test. $P < 0.05$ was considered significant. All statistical analyses were performed using JMP 9.0.0 for Macintosh (SAS Institute Inc. Cary, North Carolina, USA).

Results

In total, 878 FPs from the three muscles were analyzed. Of 878 FPs, 261, 408, and 209 were

detected from the TPZ, BB, and TA muscles, respectively. Thereafter, we identified 67, 127, and 77 types of FPs from the TPZ, BB, and TA muscles, respectively, by counting the same, repeatedly firing FPs as one FP. The median values (IQR; interquartile range) of the duration, amplitude, phase number and firing frequency are shown in Table 1. The durations of FPs increased significantly as muscle strength decreased in all the three muscles (Kruskal-Wallis test). In particular, muscles with weak strength (MRC $\leq$ 3) consistently showed significantly prolonged durations of FPs when compared with the FP durations in muscles with normal (MRC 5) or moderate (MRC 4) strength (Mann-Whitney test). By contrast, the amplitudes of FPs showed no significant changes across different strengths of all three muscles (Kruskal-Wallis test). Analyses of the phase number of FPs revealed that only the BB muscle showed significantly increased phase numbers in muscles with weak strength (MRC $\leq$ 3, Kruskal-Wallis and Mann-Whitney U test), while the TPZ and TA muscles showed no significant alterations between muscles with different strengths. Analyses of the firing frequency of FPs showed that only the TA muscles with weak strength (MRC $\leq$ 3) exhibited significantly increased firing frequency (Kruskal-Wallis and Mann-Whitney U test).

Analyses of the correlations between the durations and amplitudes of FPs demonstrated significantly positive correlations in the TPZ and TA muscles (Fig. 1), although the

correlation coefficients were low in both muscles (R^2 = 0.0814 for TPZ and 0.1152 for TA). The BB muscle showed no significant correlation. There were no significant correlations between each parameter of FP and the onset region or disease duration for each muscle.

Table 2 shows the occurrence rate of FPs and fib-psw for each muscle in a total patient cohort. The occurrence rate of fib-psw was related with the severity of muscle weakness: muscles with an MRC ≤ 3 showed the highest occurrence of fib-psw for all muscles. On the other hand, the occurrence rate of FPs showed a significant difference only in the TA muscle, in which FP occurrence was lowest in weak muscles (MRC ≤ 3) (Kruskal-Wallis test). For all three muscles, FP occurrence was highest in muscles with moderate strength (MRC = 4).

Discussion

We evaluated morphological changes and firing frequencies of FPs of three different muscles in patients with ALS across a range of muscle strengths. The study showed that abnormally prolonged durations of FPs were associated with muscle weakness, whereas the amplitudes of FPs did not significantly change across muscles with different strength. Association analyses between the duration and amplitude, however, showed significant correlations in two muscles,

suggesting that the prolongation of FPs might originate from the temporal dispersion through degenerating and/or immature reinnervating motor branches with conduction slowing.

Fasciculation and FP are hallmarks of ALS [15, 16], and detection of FPs is important not only for making a diagnosis but also predicting a prognosis in ALS [10, 17], indicating that FPs are strongly related with the pathogenesis of ALS. Although FPs in ALS can originate from multiple sites of lower and upper motor neurons [2, 18–20], the most frequent origin is considered to be the most distal site of the axonal arborization of the lower motor neurons [20–22]. The complexity of FPs might be explained by the following mechanism [23]: (1) temporal dispersion caused by retrograde transmission of potentials which fire at distal sites in axon sprouts, thereby leading to conduction through neighboring branches; (2) temporal dispersion due to distal degenerating branches with conduction slowing; (3) double or triple firing at identical or nearly identical axonal terminal sites; (4) temporal dispersion through immature reinnervating motor branches with conduction slowing; (5) firing of double motor units due to ephatic axonal transmission [24]. Firing sites of FPs may vary with disease stages [2, 3]. Although our results showed a discrepancy between the duration and amplitude of FPs, the weak, but significant correlations between the duration and amplitude in the TPZ and TA muscles suggest that the temporal dispersion was accompanied by reinnervation

process. This study showed no correlation between the disease duration and FP parameters. That would be because the FP occurs from early disease stages and continues to be found through the disease course, and because the reinnervating branches would always show a simultaneous denervation process.

There are some differences between our findings and previous reports on quantitative analyses of FPs in ALS. The FP amplitudes in the tibialis anterior muscle reported by de Carvalho and Swash (719 μV in average in muscles with MRC = 5, and 1,115 μV in muscles with MRC = 4) were much greater than our results [4]. They discussed that the prolonged duration and increased amplitude of FPs were associated with partial denervation and reinnervation of motor units. On the other hand, Mills reported that there were no changes of FP amplitude between muscles with normal (410 μV) and weak strength (380 μV) [14]. Mills investigated several muscles inclusively, and our results were similar to his report.

Although exact reasons of these differences are unknown, we speculate following reasons: (1) The cut-off values for defining FP were different (100 μV by de Carvalho and Swash, and ± 25 μV by Mills). Our method (50 μV) followed the criteria by Mills. If the cut-off value is low, the mean FP amplitude will be lowered. This difference, however, cannot explain the changes between muscles of different strength. Actually, we could not find FPs

with a very large amplitude such as > 3,000 μV in contrast with the cases by de Carvalho and Swash [4]. (2) There might be some differences of a focusing technique in recording FPs. Focusing for all FPs in every muscle, however, is practically difficult in a limited examination time. Instead, we lowered the cut-off value for amplitude, which enabled us to detect many FPs as possible during 60 to 90 ms without needle manipulation [13]. (3) There might be differences in the ethnicity and/or genetic background of patients in each cohort, such as a difference in frequency of C9orf72 gene abnormalities between Caucasian and Japanese patients with sporadic ALS [25, 26]. Since we did not examine known ALS-gene variants for all the patients, there is a possibility of including gene-related sporadic ALS cases. However, only 3.0% of sporadic Japanese ALS patients have any of known ALS-related gene variants [27], suggesting that major ALS-related genes gave no significant influences on the results.

The relationship between the occurrence rates of FPs and fib-psw was almost the same as in previous reports [10]. Fib-psw appeared in weak muscles, whereas FPs were detected in moderate to strong muscles. This also supports the idea that the reinnervation process in progressively weaker muscles fails to produce a full synchronization of MUPs and an increase in FP amplitude. The exact reason why some patients did not show fib-psw in weak muscles is unknown (Table 2), but we speculate that upper motor neuron involvement might have

affected the results.

One of the limitations of this study is that individual patients were not evaluated chronologically over the disease course. Since needle EMG is an invasive examination, however, it is difficult to repeat examinations. Furthermore, it is actually impossible to evaluate identical FPs at different times. The other limitation is that we did not investigate a correlation of morphological values of FPs with those of MUPs, which would elucidate the pathophysiology of FPs in more detail [28]. It is, however, also difficult to define MUPs and FPs with identical axonal origins.

In conclusion, the duration of FPs in ALS was prolonged in weak muscles. This change of FPs associated with disease severity might be caused by temporal dispersion through progressively degenerating and/or immature reinnervating motor branches, and observed uniformly in different muscles along with disease progression.

Conflict of interests: The authors report that they have no conflicts of interest.

Ethical standard: This study was approved by the Ethics Committee of Tokyo Metropolitan Neurological Hospital.

Informed consent: All patients provided their informed consent prior to the examination.

References

1. de Carvalho M, Dengler R, Eisen A, England JD, Kaji R, Kimura J, Mills K, Mitsumoto H, Nodera H, Shefner J, Swash M (2008) Electrodiagnostic criteria for diagnosis of ALS. Clin Neurophysiol 119:497-503. doi: 10.1016/j.clinph.2007.09.143

2. de Carvalho M (2000) Pathophysiological significance of fasciculations in the early diagnosis of ALS. Amyotroph Lateral Scler Other Motor Neuron Disord 1 Suppl 1:S43-46.

3. de Carvalho M, Swash M (1998) Fasciculation potentials: a study of amyotrophic lateral sclerosis and other neurogenic disorders. Muscle Nerve 21:336-344.

4. de Carvalho M, Swash M (2013) Fasciculation potentials and earliest changes in motor unit physiology in ALS. J Neurol Neurosurg Psychiatry 84:963-968. doi: 10.1136/jnnp-2012-304545

5. Brooks BR, Miller RG, Swash M, Munsat TL (2000) El Escorial revisited: revised criteria for the diagnosis of amyotrophic lateral sclerosis. Amyotroph Lateral Scler Other Motor Neuron Disord 1:293-299.

6. Ince PG, Evans J, Knopp M, Forster G, Hamdalla HH, Wharton SB, Shaw PJ (2003)

Corticospinal tract degeneration in the progressive muscular atrophy variant of ALS. Neurology 60:1252-1258.

7. Kim WK, Liu X, Sandner J, Pasmantier M, Andrews J, Rowland LP, Mitsumoto H (2009) Study of 962 patients indicates progressive muscular atrophy is a form of ALS. Neurology 73:1686-1692. doi: 10.1212/WNL.0b013e3181c1dea3

8. Geser F, Stein B, Partain M, Elman LB, McCluskey LF, Xie SX, Van Deerlin VM, Lee VM, Trojanowski JQ (2011) Motor neuron disease clinically limited to the lower motor neuron is a diffuse TDP-43 proteinopathy. Acta Neuropathol 121:509-517. doi: 10.1007/s00401-011-0797-z

9. Sonoo M, Kuwabara S, Shimizu T, Komori T, Hirashima F, Inaba A, Hatanaka Y, Misawa S, Kugio Y; Tokyo Metropolitan Neuromuscular Electrodiagnosis Study Group (2009) Utility of trapezius EMG for diagnosis of amyotrophic lateral sclerosis. Muscle Nerve 39:63-70. doi: 10.1002/mus.21196

10. Shimizu T, Fujimaki Y, Nakatani-Enomoto S, Matsubara S, Watabe K, Rossini PM, Ugawa Y (2014) Complex fasciculation potentials and survival in amyotrophic lateral sclerosis. Clin Neurophysiol 125:1059-1064. doi: 10.1016/j.clinph.2013.10.052

11. Sleutjes BT, Montfoort I, van Doorn PA, Visser GH, Blok JH (2015) Diagnostic

accuracy of electrically elicited multiplet discharges in patients with motor neuron disease. J Neurol Neurosurg Psychiatry 86:1234-1239. doi: 10.1136/jnnp-2014-308589

12. Xu YS, Zheng JY, Zhang S, Fan DS (2011) Upper trapezius electromyography aids in the early diagnosis of bulbar involvement in amyotrophic lateral sclerosis. Amyotroph Lateral Scler 12:345-348. doi: 10.3109/17482968.2011.582647

13. Mills KR (2011) Detecting fasciculations in amyotrophic lateral sclerosis: duration of observation required. J Neurol Neurosurg Psychiatry 82:549-551. doi: 10.1136/jnnp.2009.186833

14. Mills KR (2010) Characteristics of fasciculations in amyotrophic lateral sclerosis and the benign fasciculation syndrome. Brain 133:3458-3469. doi: 10.1093/brain/awq290

15. Eisen A, Vucic S (2013) Fasciculation potentials: a diagnostic biomarker of early ALS? J Neurol Neurosurg Psychiatry 84:948. doi: 10.1136/jnnp-2013-305036

16. Kuwabara S, Shibuya K, Misawa S (2014) Fasciculations, axonal hyperecitability, and motoneuronal death in amyotrophic lateral sclerosis. Clin Neurophysiol 125:872-873. doi: 10.1016/j.clinph.2013.11.014

17. Krarup C (2011) Lower motor neuron involvement examined by quantitative electromyography in amyotrophic lateral sclerosis. Clin Neurophysiol 122:414-422. doi:

10.1016/j.clinph.2010.06.027

18. de Carvalho M, Miranda PC, Lourdes Sales Luis M, Ducla-Soares E (2000) Neurophysiological features of fasciculation potentials evoked by transcranial magnetic stimulation in amyotrophic lateral sclerosis. J Neurol 247:189-194.

19. Hirota N, Eisen A, Weber M (2000) Complex fasciculations and their origin in amyotrophic lateral sclerosis and Kennedy's disease. Muscle Nerve 23:1872-1875.

20. Kleine BU, Stegeman DF, Schelhaas HJ, Zwarts MJ (2008) Firing pattern of fasciculations in ALS: evidence for axonal and neuronal origin. Neurology 70:353-359. doi: 10.1212/01.wnl.0000300559.14806.2a

21. Janko M, Trontelj JV, Gersak K (1989) Fasciculations in motor neuron disease: discharge rate reflects extent and recency of collateral sprouting. J Neurol Neurosurg Psychiatry 52:1375-1381.

22. Layzer RB (1994) The origin of muscle fasciculations and cramps. Muscle Nerve 17:1243-1249.

23. Shimizu T, Bokuda K (2015) Complex fasciculation potentials in amyiotrophic lateral sclerosis. US Neurology 11:53-56.

24. de Carvalho M, Swash M (2013) Origin of fasciculations in amyotrophic lateral

sclerosis and benign fasciculation syndrome. JAMA Neurol 70:1562-1565. doi: 10.1001/jamaneurol.2013.4437

25. Majounie E, Renton AE, Mok K, Dopper EG, Waite A, Rollinson S, et al (2012) Frequency of the C9orf72 hexanucleotide repeat expansion in patients with amyotrophic lateral sclerosis and frontotemporal dementia: a cross-sectional study. Lancet Neurol 11:323-330. doi: 10.1016/S1474-4422(12)70043-1

26. Konno T, Shiga A, Tsujino A, Sugai A, Kato T, Kanai K, Yokoseki A, Eguchi H, Kuwabara S, Nishizawa M, Takahashi H, Onodera O (2013) Japanese amyotrophic lateral sclerosis patients with GGGGCC hexanucleotide repeat expansion in C9ORF72. J Neurol Neurosurg Psychiatry 84:398-401. doi: 10.1136/jnnp-2012-302272

27. Nakamura R, Sone J, Atsuta N, Tohnai G, Watanabe H, Yokoi D, et al (2016) Next-generation sequencing of 28 ALS-related genes in a Japanese ALS cohort. Neurobiol Aging 39:219.e1-8. doi: 10.1016/j.neurobiolaging.2015.11.030

28. de Carvalho M, Turkman A, Swash M (2014) Sensitivity of MUP parameters in detecting change in early ALS. Clin Neurophysiol 125:166-169. doi: 10.1016/j.clinph.2013.06.014

Figure legends

Figure 1. Relationships between the duration and amplitudes of FPs in the upper trapezius (A), biceps brachii (B), and tibialis anterior (C) muscles.

Table 1. Analyses of fasciculatipn potentials in three muscles compared with muscle strength

	Muscle strength				*p*-value			
	All	Normal (MRC 5)	Moderate (MRC 4)	Weak (MRC ≤ 3)	For all groups	Normal vs. Moderate	Normal vs. Weak	Moderate vs. Weak
Upper trapezius								
Number of FP types	67	14	36	17				
Duration (ms)	17.6	15.2	15.2	18.6	**0.0161**	0.5097	**0.0122**	**0.0092**
(IQR)	(14.0–19.0)	(14.1–18.5)	(10.5–19.5)	(17.9–19.6)				
Amplitude (μV)	330	296	357	330	0.6978	0.4366	0.4749	1.0000
(IQR)	(160–572)	(137–443)	(160–675)	(205–594)				
Phase number	4	3.5	4	5	0.3521	0.7648	0.2274	0.2045
(IQR)	(3–6)	(3–5.25)	(3–5)	(3–8)				
Firing frequency (/min)	2	2	2	1	0.6601	0.9727	0.5121	0.3820
(IQR)	(1–4)	(1–4)	(1–10)	(1–3.5)				
Biceps brachii								
Number of FP types	127	30	50	47				
Duration (ms)	17.3	13.8	17.3	18.6	**0.0002**	**0.0280**	**<0.0001**	**0.0310**
(IQR)	(13.5–20.2)	(10.6–17.2)	(12.6–20.3)	(16.6–21.0)				
Amplitude (μV)	222	174	210	261	0.1779	0.3252	0.0857	0.2452
(IQR)	(141-531)	(101–546)	(140–480)	(163–593)				
Phase number	3	3	3	4	**0.0020**	0.1030	**0.0009**	**0.0221**
(IQR)	(3–5)	(2–3.25)	(2.75–4)	(3–6)				
Firing frequency (/min)	2	2	2	2	0.5166	0.8428	0.4757	0.2587
(IQR)	(1–4)	(1–4.25)	(1–4)	(1–2)				
Tibialis anterior								
Number of FP types	77	37	27	13				
Duration (ms)	16.4	15.6	14.7	18.4	**0.0146**	0.3732	**0.0036**	**0.0417**
(IQR)	(12.2–18.4)	(11.4–16.8)	(11.2–19.4)	(16.4–21.1)				
Amplitude (μV)	331	338	384	189	0.1347	0.3732	0.1919	**0.0418**
(IQR)	(158–727)	(161–716)	(212–762)	(124–515)				
Phase number	3	3	3	3	0.1155	**0.0416**	0.2487	0.8088
(IQR)	(3–4)	(2.5–3)	(3–5)	(2.5–5)				
Firing frequency (/min)	2	2	1	4	**0.0183**	0.7374	**0.0104**	**0.0117**
(IQR)	(1–2)	(1–2)	(1–2)	(1.5–10)				

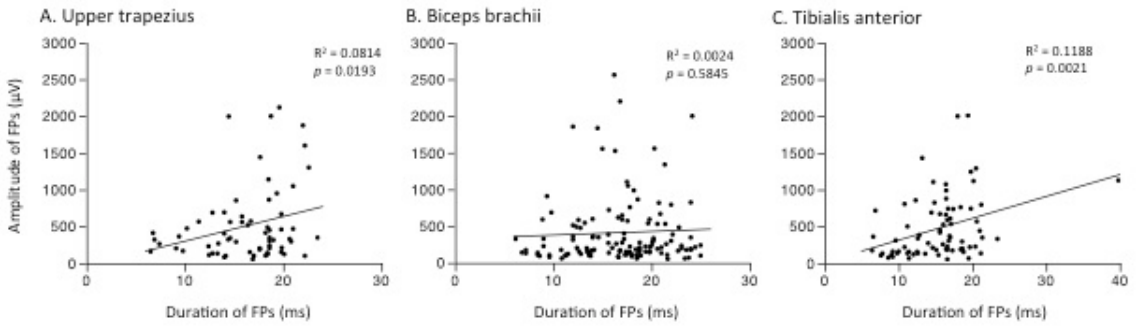
Variables are shown as median. FP, fasciculation potential; IQR, interquatile range; MRC, medical research council. Kruskal Wallis test was used for comparison across all subgroups, and Mann-Whitney U test was used for comparisons between two groups.

Table 2. Occurrence rate of fasciculation potentials and fibrillation potentials-positive sharp waves

	Muscle strength				*p*-value			
	All	Normal (MRC 5)	Moderate (MRC 4)	Weak (MRC ≤ 3)	For all groups	Normal vs. Moderate	Normal vs. Weak	Moderate vs. Weak
Upper trapezius								
Fib-psw occurrence (%)	62.8	17.7	76.5	94.1	**0.0008**	0.1635	**0.0002**	**0.0122**
FP occurrence (%)	47.1	29.4	64.7	47.1	0.1245	**0.0443**	0.3065	0.3169
Biceps brachii								
Fib-psw occurrence (%)	51.0	38.5	76.2	88.2	**0.0103**	**0.0318**	**0.0052**	0.3587
FP occurrence (%)	66.7	76.9	82.3	58.8	0.3911	0.5466	0.1926	0.4054
Tibialis anterior								
Fib-psw occurrence (%)	70.6	38.5	76.2	85.2	**0.0005**	**0.0294**	**0.0003**	0.2593
FP occurrence (%)	51.0	60.0	72.7	30.0	**0.0466**	0.5015	0.0619	**0.0260**

Fib-psw, fibrillation potential-positive sharp wave; FP, fasciculation potential; MRC, medical research council. Kruskal Wallis test was used for comparison across all subgroups, and Mann-Whitney U test was used for comparisons between two subgroups.

Figure 1


A. Upper trapezius
B. Biceps brachii
C. Tibialis anterior
Amplitude of FPs (μV)
Duration of FPs (ms)
R² = 0.0814
p = 0.0193
R² = 0.0024
p = 0.5845
R² = 0.1188
p = 0.0021