Twitch Response of Intact Human Tibialis Anterior Muscle to Doublet Stimulation at Graded Strengths

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Abstract— **The purpose of this project was to determine if the properties of doublet force twitches change with recruitment level. Isometric, human tibialis anterior force twitches were measured in response to singlet and doublet stimulation at several recruitment levels for eight healthy subjects. All doublets showed nonlinear force summation. When normalized to singlet responses at the equivalent recruitment level, doublet peak force, torque-time integral, half pulse width and half decay time changed with recruitment while start time and contraction time did not. Although the number of subjects was small, the results suggest that caution must be exercised when extending doublet properties at full recruitment to partial recruitment conditions.**

I. Introduction

It is well known that skeletal muscle responds with nonlinear twitch force summation when excited by a double pulse with short spacing between pulses [1-11]. The force twitch from doublet stimulation has more than double the amplitude and more than double the area of the twitch resulting from a single pulse [5, 7, 8]. The pulse spacing that results in optimal force summation is about 5 ms [7]. It is known that the nonlinear force summation is an inherent property of the muscle fiber and not caused by additional motor unit recruitment from the second pulse in the doublet [12]. The most likely cause for increased force is a nonlinear increase in free calcium concentration caused by the double pulse, although this has yet to be proven definitively [1, 13, 14]. While the mechanics of muscle contraction are complex, a few mathematical models of nonlinear twitch summation have been developed [15-18]. Doublet stimulation has potential applications in function electrical stimulation (FES) because it can reduce muscle fatigue [2, 7, 10], and in diagnosing and monitoring muscle disease [19, 20].

Most studies in doublet stimulation have used fixed, supramaximal muscle activation. For FES and muscle monitoring applications, there are advantages to doublet stimulation over a range of activation levels that modulate motor unit recruitment. In FES motor unit recruitment is the method of choice for varying muscle activation level while in non-invasive muscle monitoring, lower activation levels are more comfortable for the patient. The objective of this study was to measure the properties of doublet stimulation in the intact human tibialis anterior muscle as a function of recruitment level. The study is part of a larger project to examine doublet twitch properties in several intact human muscles.

II. Methods

Eight healthy subjects (5 male, 3 female, age range 24-59, mean 30, SD 12) participated in the study, which was approved by the University of Minnesota IRB. Subjects sat with their left shank and foot rigidly coupled to a custom apparatus that held their foot at 90 deg with respect to the shank (Fig. 1). Subjects were trained how to actively relax their entire leg during an experiment run to eliminate contamination by voluntary contraction.

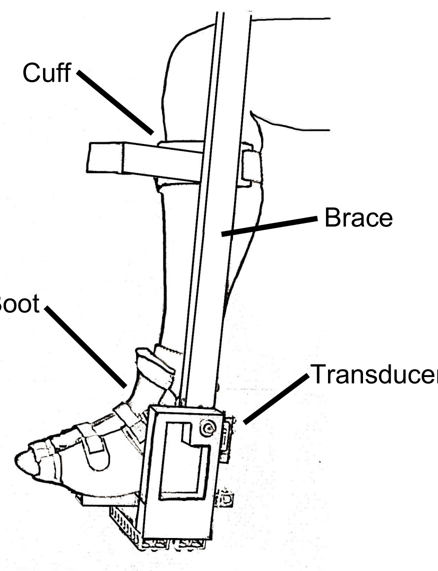

Fig. 1. Experiment apparatus.

A force transducer (Omega Engineering, LCEB-25) was configured to measure ankle dorsiflexion torque. The tibialis anterior was activated by stimulating the muscle belly at its motor point using 1.5 x 2 in. self stick surface electrodes (Re-Ply 650PK). A custom built stimulator delivered current-controlled, monophasic, rectangular current pulses to the electrode under computer control. Pulse amplitude

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was set manually to the maximal comfort level of the subject while pulse width and timing were varied by the computer application. Pulse width could range between 0 and 100% of the nominal 300 µs width.

Muscle was activated with a train of 105 twitches spaced at 1 s intervals according to the protocol shown in Fig. 2. Control singlets at the start and end of the run were averaged and compared to check for excess muscle fatigue. Records where the peak force had declined by more than 10% over the run were rejected, but this was a rare occurrence. One run was conducted for each subject.

Warm up singlets (5)	Control singlets (5)	Experiment twitches (90)	Control singlets (5)

Fig. 2. Protocol for train of 105 twitches at 1 s intervals.

The 90 experiment twitches consisted of 6 instances of 15 cases randomly sequenced to eliminate fatigue order effects. The 15 cases were combinations of 3 pulse spacings (singlets S, doublets at 5 ms D5, doublets at 50 ms D50) and 5 pulse widths (L1, L2, L3, L4 and 100% of 300 µs). Pulse width percentages L1-L4 were chosen on a subject by subject basis to approximately evenly span the torque recruitment space between 0 and the torque generated by a 300 µs (100%) pulse. This was done prior to data collection using an interactive recruitment curve process.

Twitch torque was sampled at 1000 Hz for 500 ms starting at the stimulus pulse. The six replications of twitch torque for one combination of pulse type and recruitment level were averaged and the average used for subsequent data analysis. The metrics shown in Table 1 were computed for the average twitch torque records. Metrics for D5 twitches were normalized by the metric for S twitches at the same recruitment level and to enable analysis of doublet compared to singlet twitch properties. Metrics for D50 twitches were not included as doublets at 50 ms are not completely fused into a single twitch. One-factor, 5-level ANOVA were computed to determine if the normalized metrics varied with recruitment level.

TABLE 1
TWITCH FORCE METRICS

Metric	Definition
Peak Force (PF)	Highest force attained by the twitch.
Torque-Time Integral (TTI)	Area under the twitch torque curve from 10% of peak to 10% of peak
Start Time (ST)	Stim to 5% of peak
Contraction Time (CT)	Time from 5% of peak to 100% of peak
½ Peak Width (HPW)	Width of twitch at half peak amplitude
½ Decay Time (HDT)	Peak to 50% of peak

III. RESULTS

Fig. 3 shows the average twitch records for one subject with one panel for every recruitment level. Within the panel, the three twitches from smallest to largest amplitude are S, D50 and D5. All D5 and D50 twitches show nonlinear summation.

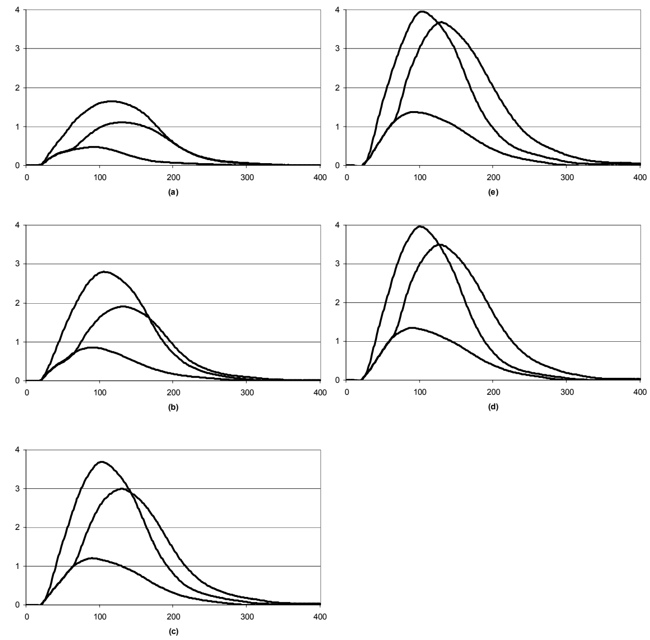

Fig. 3. Twitch traces from one subject. Panels (a)-(e) are recruitment levels L1, L2, L3, L4 and 100%. Twitches from large to small amplitudes are response to D5, D50 and S. Horizontal axis is time (ms), vertical axis is torque (Nm). Nonlinear doublet summation is present in all panels.

Fig. 4 shows the normalized metrics for D5 twitches as a function of recruitment level. For the PF and TTI metrics, normalized values greater than two occurred at all recruitment levels which means nonlinear summation occurred at all recruitment levels. For the four time-based metrics, deviations of the normalized values from 1.0 implies the shape of the D5 twitch differed from the shape of the S twitch. The results from the ANOVA calculations (Table 2) indicate there were significant variations with recruitment for PF, TTI, HPW and HDT metrics and no variations with recruitment for ST and CT metrics.

Fig. 5 shows the contraction time (CT) for S and D5 twitches, normalized to CT for S twitches at full recruitment. The purpose of this plot was to determine whether there was orderly recruitment of motor unit types in the muscle which would be reflected by a rising (fast-to-slow recruitment) or falling (slow-to-fast recruitment) CT curve. The ANOVA analysis showed there was no significant difference in normalized contraction between the recruitment levels for singlets ($F = 0.07$, $Fcrit(.05) = 2.71$, $p = 0.99$), but a significant difference for doublets ($F = 4.13$, $Fcrit(.05) = 2.71$, $p = .01$).

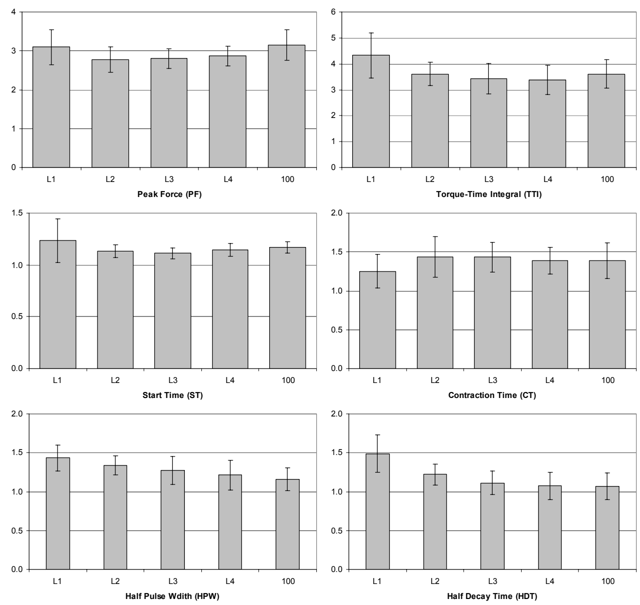

Fig. 4. Doublet twitch metrics, normalized to metric for singlet at same recruitment level. Metrics are described in Table 1.

TABLE 2
ANOVA FOR TWITCH METRICS WITH RECRUITMENT LEVEL FACTOR

Metric	F	Fcrit	p	sig
PF	3.44	2.71	.02	*
TTI	7.80	2.71	.00	*
ST	1.55	2.71	.21	
CT	1.98	2.71	.13	
HPW	13.6	2.71	.00	*
HDT	14.5	2.71	.00	*

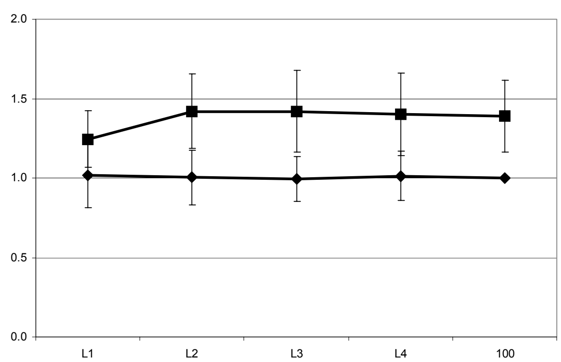

Fig. 5. Contraction time (CT) metric for several recruitment levels, normalized to CT for singlet at 100%. Singlet (diamond) and doublet (square) twitches.

IV. DISCUSSION

Stimulating the tibialis anterior with doublets resulted in nonlinear summation for all recruitment levels for all subjects with the peak force of the doublet averaging around three times the peak force of the corresponding singlet. As shown in Fig. 6, the shape of the doublet twitch was different than the scaled singlet shape indicating that the underlying process is more than simple nonlinear summation. Additional evidence that more than simple summation underlies doublet twitch response comes from the contraction time results with doublets reaching their peak force an average of 1.4 times later than singlets as can be seen in Figs. 3 and 6.

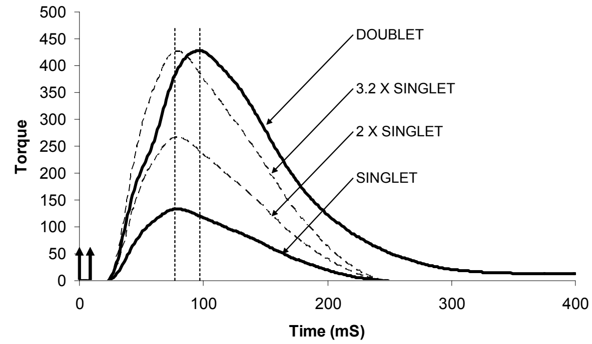

Fig. 6. Demonstration that doublet twitch has more than twice the amplitude of singlet and that doublet has a different shape than the singlet. Dotted traces are scaled singlet. Solid traces are experiment data. 100% recruitment level.

The normalized peak force, torque-time integral, half pulse width and half decay time all varied with recruitment which means one must be cautious in using these metrics for less than full recruitment. The variation, however, was not large. There was no difference with recruitment in normalized start time or contraction time. The contraction time of singlets did not vary with recruitment indicating there was no uniform change in motor unit size with recruitment. CT for doublets did vary, but only because of the value at the lowest recruitment level.

The significance of these findings is that doublet nonlinear summation occurs at all recruitment levels, but there is some variation in the details of doublet twitch summation, particularly at low recruitment. The findings are limited to tibialis anterior.

REFERENCES

[1] F. Abbate, J. D. Bruton, A. De Haan, and H. Westerblad, "Prolonged force increase following a high-frequency burst is not due to a sustained elevation of [Ca2+]i," *Am J Physiol Cell Physiol*, vol. 283, pp. C42-7, 2002.

[2] B. Bigland-Ritchie, I. Zijdewind, and C. K. Thomas, "Muscle fatigue induced by stimulation with and without doublets," *Muscle Nerve*, vol. 23, pp. 1348-55, 2000.

[3] R. E. Burke, P. Rudomin, and F. E. Zajac, 3rd, "Catch property in single mammalian motor units," *Science*, vol. 168, pp. 122-4, 1970.

[4] R. E. Burke, P. Rudomin, and F. E. Zajac, 3rd, "The effect of activation history on tension production by individual muscle units," *Brain Res*, vol. 109, pp. 515-29, 1976.

[5] S. Cooper and J. Eccles, "The isometric responses of mammamlian muscles," *J. Physiol. (Lon)*, vol. 69, pp. 377-385, 1930.

[6] J. S. Denslow, "Double discharges in human motor units," *J Physiol*, vol. 11, pp. 209-215, 1948.

[7] Z. Z. Karu, W. K. Durfee, and A. M. Barzilai, "Reducing muscle fatigue in FES applications by stimulating with N-let pulse trains," *IEEE Trans Biomed Eng*, vol. 42, pp. 809-17, 1995.

[8] F. Parmiggiani and R. B. Stein, "Nonlinear summation of contractions in cat muscles. II. Later facilitation and stiffness changes," *J Gen Physiol*, vol. 78, pp. 295-311, 1981.

[9] R. B. Stein and F. Parmiggiani, "Nonlinear summation of contractions in cat muscles. I. Early depression," *J Gen Physiol*, vol. 78, pp. 277-93, 1981.

[10] C. K. Thomas, R. S. Johansson, and B. Bigland-Ritchie, "Pattern of pulses that maximize force output from single human thenar motor units," *J Neurophysiol*, vol. 82, pp. 3188-95, 1999.

[11] F. E. Zajac and J. L. Young, "Properties of stimulus trains producing maximum tension-time area per pulse from single motor units in medial gastrocnemiu muscle of the cat," *J Neurophysiol*, vol. 43, pp. 1206-20, 1980.

[12] J. M. Elek, R. Dengler, A. Konstanzer, S. Hesse, and W. Wolf, "Mechanical implications of paired motor unit discharges in pathological and voluntary tremor," *Electroencephalogr Clin Neurophysiol*, vol. 81, pp. 279-83, 1991.

[13] M. W. Berchtold, H. Brinkmeier, and M. Muntener, "Calcium ion in skeletal muscle: its crucial role for muscle function, plasticity, and disease," *Physiol Rev*, vol. 80, pp. 1215-65, 2000.

[14] J. Duchateau and K. Hainaut, "Nonlinear summation of contractions in striated muscle. I. Twitch potentiation in human muscle," *J Muscle Res Cell Motil*, vol. 7, pp. 11-7, 1986.

[15] J. Bobet, E. R. Gossen, and R. B. Stein, "A comparison of models of force production during stimulated isometric ankle dorsiflexion in humans," *IEEE Trans Neural Syst Rehabil Eng*, vol. 13, pp. 444-51, 2005.

[16] J. Bobet and R. B. Stein, "A simple model of force generation by skeletal muscle during dynamic isometric contractions," *IEEE Trans Biomed Eng*, vol. 45, pp. 1010-6, 1998.

[17] J. Ding, A. S. Wexler, and S. A. Binder-Macleod, "Development of a mathematical model that predicts optimal muscle activation patterns by using brief trains," *J Appl Physiol*, vol. 88, pp. 917-25, 2000.

[18] A. S. Wexler, J. Ding, and S. A. Binder-Macleod, "A mathematical model that predicts skeletal muscle force," *IEEE Trans Biomed Eng*, vol. 44, pp. 337-48, 1997.

[19] W. K. Durfee and P. A. Iaizzo, "Rehabilitation and Muscle Tesing," in *Encyclopedia of Medical Devices and Instrumentation*, vol. 6, J. G. Webster, Ed., 2nd ed. Hoboken: Wiley, 2006, pp. 62-71.

[20] J. G. Quinlan, P. A. Iaizzo, E. H. Lambert, and G. A. Gronert, "Ankle dorsiflexor twitch properties in malignant hyperthermia," *Muscle Nerve*, vol. 12, pp. 119-25, 1989.