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Characterization of the tendon vibration reflex response in hemi-spastic stroke individuals.

Nina L. Suresh, Inga Wang, C.J. Heckman and W. Zev Rymer, *Senior Member, IEEE*

Abstract—The objective of our study was to assess the role of persistent inward currents, or PICs, on the excitability of motoneurons innervating spastic muscle in hemi-spastic stroke individuals. This was accomplished by examining the effects of tonic vibration applied to the tendon of the biceps brachii muscle. The elicited TVR (tonic vibration reflex) provides a useful way to assess the degree of excitability of spinal neurons in spastic syndromes, and it has additional features that may signify the presence of PIC's in spastic motoneurons. We applied sinusoidal stretches of varied duration to the biceps tendon of two hemi-spastic stroke individuals and one neurologically intact individual. We recorded the resulting TVR response from electromyographic(EMG) signals obtained from the biceps as well as force recorded at the wrist. The results of our preliminary study show that the initial rise of the TVR force response as well as the force magnitude are generally greater in spastic muscle, perhaps a marker of motoneuron excitability. Additionally, a shorter vibration duration was sufficient to evoke a response on the spastic side of our tested stroke subjects. However, the key marker of PICs – the decay of the force response as well as sustained after-discharge did not exhibit clear differences. Our present data suggests that motoneurons innervating spastic muscle are more readily activated, and thus exhibit increased excitability, which could possibly be a function of greater depolarization, without a change in PIC magnitude. Our data does not rule out the possibility of subthreshold activation of the PIC resulting in enhanced motoneuron depolarization.

I. INTRODUCTION

Spasticity is characterized by exaggerated reflex responses to muscle stretch or tendon tap, perhaps as the result of increased motoneuron excitability, although this has not been definitively established. The objective of our study was to assess the role of persistent inward currents, or PICs, on motoneurons innervating spastic muscle in hemiparetic stroke individuals, by examining the effects of tonic vibration applied to the biceps tendon. The TVR (tonic vibration reflex) provides a useful way to assess the degree of excitability of spinal neurons in spastic syndromes, and it has additional features that may signify the presence of PIC's in spastic motoneurons. The TVR relies on the fact that small amplitude high frequency vibration applied to the muscle tendon generates a phase locked train of Ia afferent impulses at the frequency of the vibration signal (provided the frequency is not too high i.e., > 150cycles/second)[1]. These high frequency Ia afferent trains induce progressive excitation of the homonymous motoneurons, and appear to excite persistent inward currents in these motoneurons, as evidenced by the slow increase in isometric force during the vibration sequence, and, even more visibly, by the sustained force that persists after the vibration is turned off [1][2]. This sustained force is termed "hang up", and it is an excellent marker for the presence of monoamine dependent PIC's. If PIC's are increased in amplitude in motoneurons that innervate spastic muscle, we would expect to see enhanced TVR induced EMG and torque responses in such muscles, with prolongation of force and EMG well after vibration is terminated. In a similar study, McPherson et.al., reported significantly greater increases in elbow flexion torque and EMG activity in the spastic as compared with the non-spastic limbs of chronic hemi-spastic stroke survivors, both during biceps vibration and up to 5 s following vibration cessation. The vibration was applied on the belly of the biceps muscle for a duration of 8 seconds with a vibration frequency of 112 Hz.

In contrast, in our study, 80 Hz vibration of varying durations are applied to the tendon of the biceps brachii muscle while the subject is in a passive state. By varying vibration duration we are able to assess motoneuron excitability in addition to the ease of PIC activation, which often requires a prolonged input (calcium channel PICs). The results of our preliminary study show that the initial rise of the TVR as well as the force magnitude are generally greater in spastic muscle, perhaps a marker of increased motoneuron excitability. Also a shorter vibration duration is required to evoke a response on the spastic side of our tested stroke subjects . However, the key marker of PIC presence – the decay of the force response, does not exhibit clear differences. Our data suggests that motoneurons innervating spastic muscle are more readily activated, and thus exhibit increased excitability, which could possibly be a function of greater baseline depolarization, without a

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Nina L. Suresh is with the Rehabilitation Institute of Chicago (phone: 312-238-1273; fax: 312-238-2208; e-mail: n-suresh@northwestern.edu).

Inga Wang is with the Department of Occupational Science and Technology, University of Wisconsin-Milwaukee and with the Feinberg School of Medicine, Northwestern University, Department of Physical Medicine and Rehabilitation (e-mail: inga.wang.melnychuk@gmail.com).

C.J. Heckman is with the Department of Physiology, The Feinberg School of Medicine, Northwestern University (email: c-heckman@northwestern.edu).

W.Zev Rymer is with the Rehabilitation Institute of Chicago and Northwestern University, Department of Biomedical Engineering and The Feinberg School of Medicine, Northwestern University, Department of Physical Medicine and Rehabilitation (e-mail: w-rymer@northwestern.edu).

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change in PIC magnitude. Our data does not rule out the possibility that there is subthreshold PIC activation resulting in enhanced motoneuron depolarization.

II. METHODS

A. Study Participants

We recorded the TVR responses of the biceps brachii on both sides of 2 hemi-spastic stroke individuals as well as in one neurologically intact individual. A clinical assessment was performed by an occupational therapist. Upper extremity impairment was assessed using the Fugl-Meyer test and spasticity was assessed using the Modified Ashworth score. All participants gave informed consent via protocols approved by the Institutional Review Board under the Office for the Protection of Human Subjects at Northwestern University. Stroke participants were adults who had sustained a hemiparetic stroke at least six months prior to experimental testing. Table 1 shows the clinical information for the tested stroke subjects.

Table 1. Demographic information of stroke subjects

ID	G	Age	A	FT	C	Duration (years)	Paretic side
1	F	58	4	29/66	3h	12	L
2	M	48	5	24/66	4h	18	L

G: gender, A: Ashworth test (biceps (Scale: 0-5)), FT: Fugl-Meyer test, C: Chedoke-McMaster test, h: hand only,

B. Experimental set-up

Participants were seated upright in a mobile Biodex Chair with their shoulder placed in 45° of abduction and neutral rotation, with the elbow in 60° of flexion, and the wrist in 45° of supination and 0° of flexion/extension. The forearm was cast from just below the elbow to the most distal point of the finger and fixated to a ring-mount interface attached to a six degrees-of-freedom load cell (ATI, Inc.) to standardize position and minimize activity of unmeasured muscles. Force was measured using a 6 degree of freedom load cell during isometric conditions (ATI FT-4007) (**Figure 1**). Tendon vibration was applied to the bicipital tendon using a LinMot Inc, position-controlled motor which has a plastic attachment shaped to accommodate the human tendon at the tapping end. The LinMot was driven by a sinusoidal signal (80 Hz, amplitude of 1 mm) of varying durations of vibration: 0.5, 1, 5, 10 and 25 seconds, 5 times each. A computer program randomized the vibration sequence. Electromyographic signals were recorded from surface electrodes (Delsys, Inc) placed over the medial and lateral biceps brachii, brachioradialis and triceps muscles.

In **Figure 2** are two examples of the tendon vibration reflex response. In Figure 2a (top) is an example of a TVR response to a 10 second tendon vibration derived from the contralateral side of a stroke survivor and in figure 2b (bottom) is an example of a TVR response from the affected side of a different stroke subject. The TVR response on the affected side starts earlier with a much quicker rise to the peak force magnitude and often reaches a higher force magnitude than that obtained on the contralateral side of the same subject (which is not clearly evident in the raw data shown due to the variability among stroke subjects in force generation capacity). Both subjects show an exponential decay upon vibration cessation, with a slightly longer (force) response decay time in the spastic muscle.

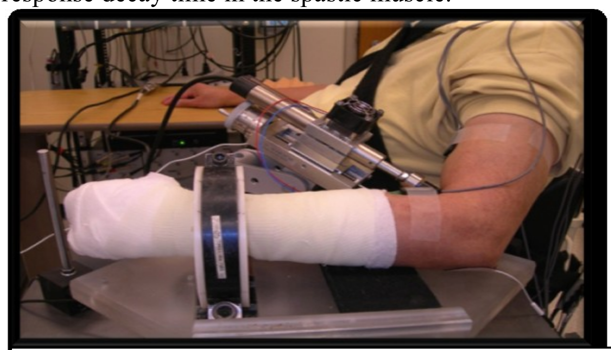


Figure 1: Experimental set up: a position-controlled linear actuator (Linmot, Inc.) was placed perpendicular to the tendon of the biceps brachii. The actuator was lowered onto the tendon and then used to sinusoidally vibration the tendon. Both surface EMG from the biceps brachii and the force generated at the wrist were measured.

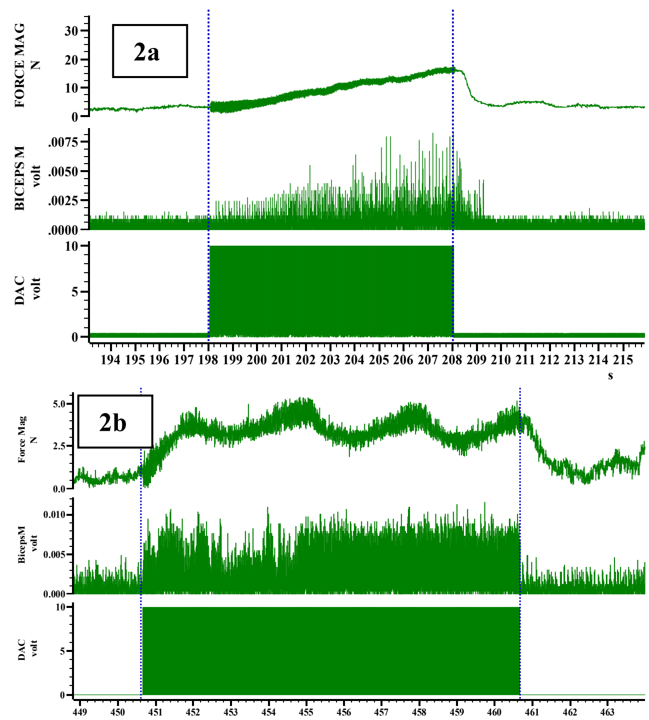


Figure 2: Representative TVR responses from the contralateral side of stroke subject#1 (2a) and from the affected side of stroke subject#2 (2b). For each data set: **Top:** Force magnitude (recorded at the wrist); **Middle:** Biceps brachii EMG; **Bottom:** Digital control signal

C. Data Analysis

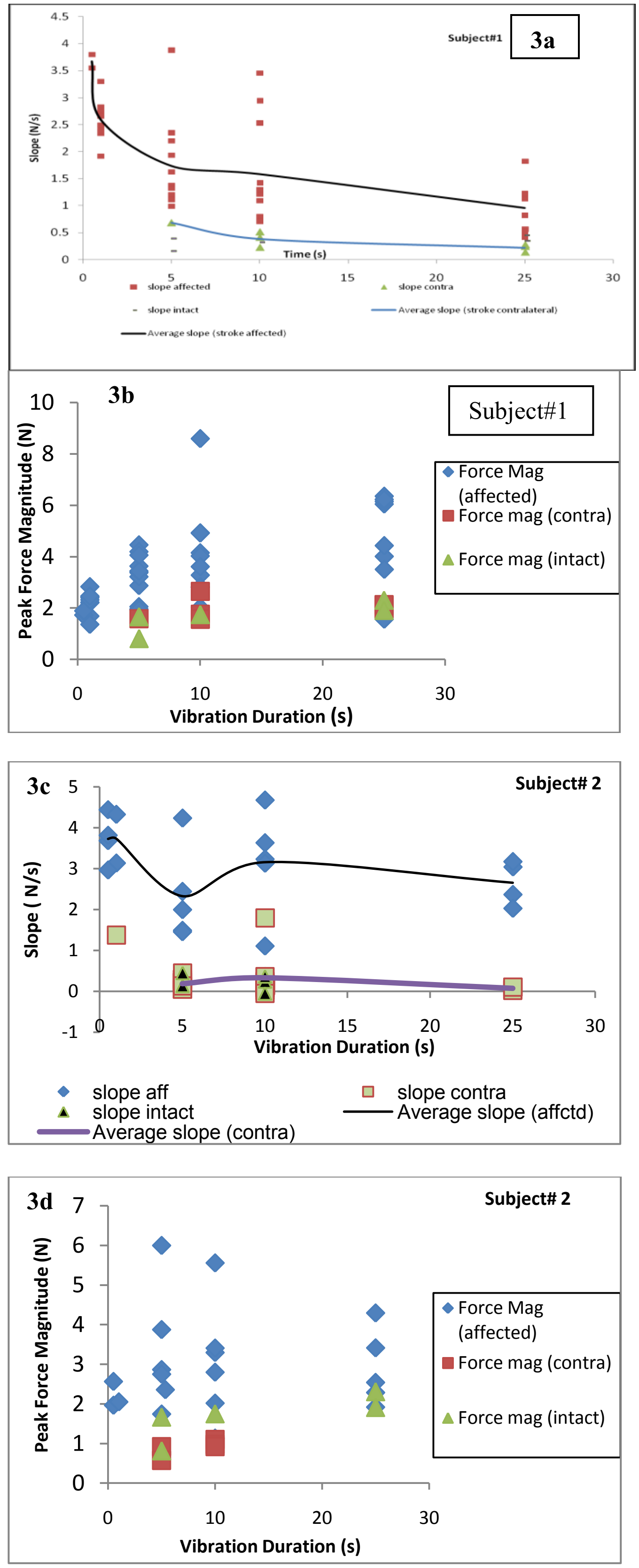
TVR Analysis: Response characteristics derived from our recorded data were: 1) time for the force to reach plateau (rise time and slope are calculated 2) peak reflex force magnitude 3) peak half decay time (time it takes for the force magnitude to decay to half the peak magnitude upon cessation of vibration) 4) the after discharge time, which is the time it takes for either or both the force and EMG signals to return to within 10% of the pre-vibration levels. All of these experimental measures are markers of motoneuron excitability, the after discharge and decay time are considered to be the result of activation of persistent inward currents (PICs) [4].

III. RESULTS

We have tested both sides of two hemiparetic stroke subjects as well as one age matched control subject using varying durations of vibration input. The relevant features of the TVR response are the peak force magnitude, the decay time and the persistent response upon cessation of vibration input. In addition, we have found that the rise to peak force magnitude is markedly different between the affected and contralateral sides of the stroke subjects.

In Figure 3 we show the key features of the TVR that exhibit significant differences between the two sides of our two tested stroke subjects. These are the slope of the rise to peak force and the peak force TVR response magnitude. In Figures 3a and 3b are the slope of the initial force response rise and the peak force response magnitude. The affected side of our stroke subject exhibits a much larger slope (3a) (quick rise to peak force) as well as a much larger peak force magnitude(3b). The 'trend' lines in the slope plots are drawn across the average response value for each vibration duration. For each side each vibration duration was applied 5 times. However, as can be seen from the plots, the number of evoked responses, at each vibration duration, was significantly larger on the affected side. Finally, on average the vibration durations of 0.5 and 1 second did not evoke a response on the contralateral side of our stroke subjects. A minimum of 5 seconds was required to elicit a TVR response on the contralateral side, this was not the case on the affected side. In Figures 3c and 3d, the (initial) slope of the force response as well as the peak force magnitude are plotted as a function of tendon vibration duration in stroke subject #2.

We found no consistent or significant differences between the affected and contralateral limbs neither in the measured TVR half decay time nor in the duration of the persistent TVR after discharge.



IV. DISCUSSION

The results of our preliminary study show that the initial rise of the TVR as well as the steady state force magnitude are generally greater in spastic muscle, perhaps a marker of increased motoneuron excitability. Additionally, a shorter vibration duration is required to evoke a response on the affected side. However, the key marker of PICs – the decay of the force response, does not exhibit clear differences. Perhaps with more tested subjects, there will be a range of responses with some spastic muscle showing greater 'hang-up'. Our present data suggests that there is greater motoneuron excitability possibly as a function of increased depolarization, without a change in PIC magnitude, that is , assuming PIC magnitude is assumed to be correlated with decay time and persistent discharge.

A. *Vibration Duration*

The averaged response force magnitude as well as the averaged force slope did not increase significantly with vibration duration on the affected side. In addition, in spastic muscle, TVR responses were often obtained for the smallest tested duration of .5 secs. In combination, these results would seem to suggest that the motoneuron pool on the spastic side of our tested stroke subjects is largely activated in response to a short duration input, one that would not normally evoke a strong TVR response in non-spastic muscle. Given that the TVR response develops with a relatively short duration input, it is possible that NaPICs are enhanced on the affected side of our stroke subjects. NaPICs are short lived PICs that do not require the prolonged input duration that CaPICs require. However, it is difficult to explain this phenomenon within the context of increased monoaminergic activity in the post-stroke spinal cord, as both types of PICs would be affected by such increases. The tendon vibration reflex has a slow developing response due to the fact that each period of the input sinusoidal signal consists of a small amplitude stretch. It is the summation of Ia activity from progressive stretches (cycles) that eventually results in the observed reflex responses[1]. It is possible that the motoneurons on the spastic side are sufficiently depolarized such that less Ia input summation (fewer sinusoidal cycles) is required to elicit a response; thus a shorter vibration duration is sufficient to activate a large portion of the motoneuron pool. Data from more subjects, as well as variations in frequency as well as amplitude of tendon vibration are required for definitive confirmation.

B. *Rise to peak force magnitude.*

The quick rise to peak force magnitude on the affected side as compared to the slowly increasing peak force on the contralateral side (slope of force rise), again seems to indicate that a large portion of the motoneuron pool is activated rather easily, thus resulting in a relatively large response force magnitude over a short time period. This would suggest that the motoneuron pool on the spastic side is readily activated or hyperexcitable.

It is also possible that the afferent activity from each sinusoidal stretch is larger on the affected side, thus resulting in a quickly activated motoneuron pool, however, there is no clear evidence suggesting this is the case in spastic muscle. Further studies that vary experimental parameters, such as the vibration amplitude would provide us with a more definitive answer.

V. CONCLUSION

In summary, the objective of this study was to investigate the role of persistent inward currents in post-stroke spasticity by applying sinusoidal stretches to the biceps tendon in order to elicit and characterize the tendon vibration reflex response. We expected that upon cessation of the vibrational input to the tendon, that there would be a relatively slow decay of the TVR response with a longer sustained discharge on the spastic side of our tested stroke subjects. These are two markers of PIC activation in spinal motoneurons.

However, data collected from two hemi-spastic stroke subjects exhibited no significant differences in the sustained discharge and half decay time of the TVR response. Instead, we observed much larger peak (steady state) force response magnitudes as well as much larger initial slope values during the rising phase of the force response. These observations seems to suggest that PIC activation or magnitude may not be augmented in stroke, instead the motoneuron pool may be in a hyper-excitable state. The results of our study can not rule out the possibility of sub-threshold PIC activation leading to increased motoneuron excitability.

REFERENCES

[1] Heckman CJ and Binder MD Analysis of effective synaptic currents generated by homonymous Ia afferent fibers in motoneurons of the cat. Journal of Neurophysiology, 60:6, 1946-1966, 1988.

[2] Carp JS, Rymer WZ. Enhancement by serotonin of tonic vibration and stretch reflexes in the decerebrate cat. Exp Brain Res. 62(1): 111-22, 1986.

[3] McPherson JG, Ellis MD, Heckman CJ, Dewald JP Evidence for increased activation of persistent inward currents in individuals with chronic hemiparetic stroke. Journal of Neurophysiology, 100(6): 3236-43, 2008.

[4] Heckman CJ, Mottram C, Quinlan K, Theiss R, Schuster J Motoneuron excitability: the importance of neuromodulatory inputs. Clin Neurophysiol, 120(12): 2040-54, 2009.