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Motor Unit Number Index Examination in Dominant and Non-Dominant Hand Muscles

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Abstract

This study investigated the effect of handedness on motor unit number index (MUNIX). Maximal hand strength, compound muscle action potential (CMAP), and voluntary surface electromyography (EMG) signals were measured bilaterally for the first dorsal interosseous (FDI) and thenar muscles in 24 right-handed and 2 left handed healthy subjects. Mean ($\pm$ standard error) grip and pinch forces in the dominant hand were 43.99 ± 2.36 kg and 9.36 ± 0.52 kg respectively, significantly larger than those in the non-dominant hand (grip: 41.37 ± 2.29 kg, $p < 0.001$; pinch: 8.79 ± 0.46 kg, $p < 0.01$). Examination of myoelectric parameters did not show a significant difference among the CMAP area, the MUNIX or motor unit size index (MUSIX) between the two sides in the FDI and thenar muscles. In addition, there was a lack of correlation between the strength and myoelectric parameters in regression analysis. However, strong correlations were observed between dominant and non-dominant hand muscles in both strength and myoelectric measures. Our results indicate that the population of motor units or spinal motor neurons as estimated from MUNIX may not be associated with handedness. Such findings help understand and interpret the MUNIX during its application for clinical or laboratory investigations.

Keywords

compound muscle action potential (CMAP); electromyography (EMG); hand dominance; motor unit number index (MUNIX)

INTRODUCTION

The motor unit number index (MUNIX) technique was introduced by Nandedkar and colleagues to provide a convenient and easy-to-apply approach for an estimation of functioning motor units in a muscle (Nandedkar, Barkhaus, & Stalberg, 2010; Nandedkar, Nandedkar, Barkhaus, & Stalberg, 2003, 2004; Neuwirth, Nandedkar, Stalberg, Barkhaus, Carvalho, Furtula, Dijk, et al., 2011a). Conventional motor unit number estimation (MUNE) and its various forms are laborious, time-consuming, and thus have limited clinical utility. They require hundreds of nerve stimuli, or decomposition of electromyography (EMG) signals to estimate the average motor unit size (Bromberg, 2007; Bromberg & Brownell, 2008; Daube, 1995; McComas, Fawcett, Campbell, & Sica, 1971). Compared with the MUNE techniques, MUNIX estimation relies on measurements of compound muscle action potential (CMAP) as well as voluntary surface EMG interference patterns of the muscle. The involved experiment and data analysis procedures are simple and straightforward to implement. Discomfort of subjects, which may be induced by a large number of repetitive electrical nerve stimulations, can also be greatly alleviated.

The MUNIX technique has been used to examine motor unit loss in amyotrophic lateral sclerosis (ALS), aging, sarcopenia, and other neuromuscular disorders (Drey, Grosch, Neuwirth, Bauer, & Sieber, 2013; Furtula et al., 2013; Kaya, Nakazawa, Hoffman, & Clark, 2013; Li, Jahanmiri-Nezhad, Rymer, & Zhou, 2012; Li, Wang, Suresh, Rymer, & Zhou, 2011; Nandedkar et al., 2010; Neuwirth, Nandedkar, Stalberg, & Weber, 2010). Differences of MUNIX estimations were assessed between healthy control subjects and subjects with neuromuscular disorders. So far, however, a fundamental question remains unclear is whether handedness can be a factor that affects MUNIX estimation. Handedness is often observed as one side is more frequently used than the other side in daily activities. Long-term preferential use of one side might lead to physiological and mechanical modifications to muscle structure and composition (Fugl-Meyer, Eriksson, Sjostrom, & Soderstrom, 1982; Tanaka, McDonagh, & Davies, 1984; Williams, Sharma, & Bilodeau, 2002; Zijdwind, Bosch, Goessens, Kandou, & Kernell, 1990). The lateral differences also manifest in the control property changes of muscle contraction, demonstrated by compression of the motor unit recruitment threshold, decreased motor unit firing rates, and increased levels of synchronization in the dominant hand muscles (Adam, De Luca, & Erim, 1998; Semmler & Nordstrom, 1995). Such lateral asymmetry could be related to the physiological asymmetries of the brain, as asymmetrical excitability of the corticospinal pathway and of motoneurons was observed in transcranial magnetic stimulation and H-reflex studies (De Gennaro et al., 2004; Tan, 1989; Triggs, Calvanio, Macdonell, Cros, & Chiappa, 1994).

In contrast to investigations on the lateral asymmetry in the central nervous system, aspects related to lateral asymmetry of the peripheral nervous system have been relatively less studied. By applying the MUNE technique, a previous study observed that the number of motor units of the abductor pollicis brevis (APB) muscle was higher for the non-dominant hand than the dominant hand muscles (Cuturic, Shamsnia, & Palliyath, 2005). It remains unclear how the effect of handedness might influence the MUNIX estimation. In this study, MUNIX estimates were compared between dominant and non-dominant hand muscles of healthy individuals and demonstrated that there was no significant difference between the

two sides. The findings indicate that the aspects of lateral asymmetry in the central nervous system and muscle differences associated with hand dominance did not have a significant effect on the MUNIX estimates. The examinations presented in this study may provide a better understanding and interpretation of the MUNIX when it is used in clinical trials or laboratory investigations.

METHODS

Experiment

Subject information—We recruited 24 right-handed and 2 left-handed healthy volunteers (9 female and 17 male), without any known neurological or neuromuscular disorders, aged 19 to 58 years (mean $\pm$ standard deviation: 33 ± 12 years). Subjects were pre-screened by taking the Edinburgh Handedness Inventory (Oldfield, 1971) and were identified as right-handed with a score higher than 40 or as left-handed with a score lower than -30 . All subjects submitted the written consent approved by the Institutional Review Board of Northwestern University (Chicago, IL, USA) and University of Texas Health Science Center at Houston (Houston, TX, USA). Subjects were tested during a one-day session with both hands examined. The order for testing the dominant and non-dominant hands was randomized for each subject.

Strength test—Subjects were seated in an upright posture with their shoulder adducted and neutrally rotated, their elbow flexed between 80° to 100° , and their forearm in the neutral position. This posture can minimize the influence of the upper extremity, which was recommended by the American Society of Hand Therapists (Fess & Moran, 1981). A portable Jamar Plus digital hand dynamometer (Jamar, Los Angeles, CA, US) was used to measure the grip force. The key pinch force was measured as the thumb padded to the lateral part of middle phalanx of index finger (Mathiowetz et al., 1985). Subjects were encouraged to squeeze both the dynamometer and pinch gauge (B&L Engineering, Santa Fe Springs, CA, US) using their maximum strength. Each measurement was repeated for three trials with sufficient relaxation time between the two trials. The highest value of the three trials was determined as the final measurement.

EMG recordings—Subsequent to the strength tests, electrical stimulation was performed to elicit muscle responses from the first dorsal interosseous (FDI) and thenar muscles. The active electrode (Ag-AgCl electrode, 1.0 cm diameter) was placed on the FDI or thenar muscles over the motor points. The location of the reference electrode and the ground electrode were the same for both the FDI and the thenar muscles. The reference electrode was positioned at the metacarpophalangeal (MCP) joint of the thumb and the ground electrode was placed at the dorsal side of the hand. Electrical stimuli were applied to the ulnar nerve (for FDI muscle) or median nerve (for thenar muscle) via a standard bar electrode positioned 2 cm proximal to the wrist crease. The cathode of the electrode was oriented towards the recording electrodes. After placement of the electrodes, a single stimulus with a pulse width of 200 μ s was delivered. The stimulation began with a relatively low intensity of approximately 10 mA and increased at 2 mA per step, until the maximal compound muscle action potential (CMAP) was acquired. Supramaximal electrical

stimulation was then applied, at 20% higher than the final intensity, to guarantee activation of all the motor axons innervating the muscle.

After the stimulation test, voluntary surface EMG interference patterns (SIPs) were collected from the FDI and thenar muscles with all recording electrodes remaining at the same position. Subjects were instructed to gradually increase their strength from minimal effort to maximum strength over approximately 20 s. Brief rests were given between trials or upon the request of subjects, to avoid fatigue. At least four trials of voluntary contractions were recorded for each muscle.

Muscle electrical activities were recorded via the Sierra Wave EMG system (Cadwell Lab Inc, Kennewick, WA, USA). The CMAP signals and SIPs were sampled at 12.8 kHz and 32 kHz respectively with band-pass filter setting as 1 Hz – 3 kHz for CMAP signals and 10 Hz – 10k Hz for SIPs respectively.

Data Analysis

MUNIX computations—MUNIX analysis was performed using Matlab (MathWorks Inc, Natick, MA, USA). Surface EMG signals were down-sampled to 2 kHz and filtered to 10 Hz – 500 Hz prior to rectification. The individual SIP trial was segmented to 4–5 portions that represented different levels of voluntary contractions. For each SIP segment, the area and power were calculated over a 1 s epoch. In total, there were at least 12 pairs of SIP area and power values obtained per muscle. To obtain the MUNIX estimates, the CMAP parameters from the same muscles were also computed, which include: peak-to-baseline amplitude, area and power of the first negative phase of the CMAP curve. Next, these parameters and the SIP values were used to calculate the ideal case motor unit count (ICMUC) (Nandedkar et al., 2003, 2004)

$$ICMUC = \frac{M_p S_{area}}{M_{area} S_p} \quad (1)$$

where M_p and M_{area} represent the power and area of the negative phase of the CMAP, and S_p and S_{area} represent the power and area of the SIP.

The relationship between the ICMUC and SIP areas was estimated as

$$ICMUC = \beta * (S_{area})^\tau \quad (2)$$

where β and τ are constant coefficients determined by the SIP-ICMUC curve. From the SIP-ICMUC curve, the MUNIX is defined as the ICMUC value where the SIP area is equal to 20 mV·ms. Criteria for the validation of ICMUC and SIP values are established (Nandedkar et al., 2010). The average motor unit size index (MUSIX) was calculated by dividing the CMAP amplitude by the MUNIX value. Due to the small percentage of left-handed subjects, their data were combined with right-handed subjects for handedness analysis.

Statistical analysis—Repeated measures analysis using ANOVA implemented with linear mixed models was carried out to compare the differences (handedness x muscle) for parameters including CMAP area, MUNIX, and MUNSIX values (SPSS Inc., Chicago, IL, USA). Covariates included grip and pinch forces. Pairwise comparison using the Bonferroni correction with a family confidence coefficient of 0.95 was calculated for the significant effects in post-hoc tests. Additionally, a comparison of grip and pinch forces between the dominant and non-dominant hands was performed by means of paired t-tests. Results were reported as mean $\pm$ standard error.

RESULTS

Strength and electrophysiological measurement were taken for all subjects. An example of data collected from two left-handed subjects were presented in Table 1. Due to the small percentile of left-handed subject in the whole subject-pool, data from the dominant and non-dominant hands was averaged and compared between two sides. Muscle strength of the dominant side was stronger than the non-dominant side (Grip force, non-dominant: 41.37 ± 2.29 kg; dominant: 43.99 ± 2.36 kg; $p < 0.001$. Pinch force: non-dominant: 8.79 ± 0.46 kg; dominant: 9.36 ± 0.52 kg; $p < 0.01$; Figure 1a.). In contrast, myoelectric measures did not reveal any significant difference between the dominant and non-dominant sides. For example, comparison of the CMAP area between two hand muscles showed no effect of handedness. Specifically, the CMAP area of the non-dominant and dominant FDI muscles were 30.19 ± 1.68 mV·ms and 31.7 ± 1.5 mV·ms ($F(1,25)=1.16$, $p=0.29$) respectively (Figure 1b). The CMAP area of the non-dominant and dominant thenar muscles was observed as 36.35 ± 2.03 mV·ms and 35.76 ± 2 mV·ms ($F(1,25)=0.12$, $p=0.73$), respectively. Likewise, MUNIX for the two muscles indicated no significant difference between the two sides (FDI, non-dominant: 246 ± 8 ; dominant: 251 ± 8 ; $F(1,25)=0.18$, $p=0.68$. Thenar: non-dominant: 219 ± 9 ; right: 213 ± 11 ; $F(1,25)=0.24$, $p=0.63$. Figure 1c). In addition, an evaluation of MUSIX in the FDI and thenar muscles indicated that neither muscle had a significant difference between dominant and non-dominant hands (Figure 1d. FDI: non-dominant: 52.75 ± 2.97 μ V; dominant: 57.98 ± 2.44 μ V; $F(1,25)=3.61$, $p=0.07$. Thenar: non-dominant: 53.72 ± 3.18 μ V; dominant: 55.26 ± 1.5 μ V; $F(1,25)=0.23$, $p=0.64$).

Correlation analysis was performed to examine the relationships between strength measures (grip, pinch force) and electrophysiological measures (CMAP amplitude, MUNIX and MUSIX values). No significant relations between the strength measures and the electrophysiological parameters were found ($p > 0.3$ for all). However, strong correlations between the dominant and non-dominant hands were observed in most of the analyzed parameters (Table 2). In particular, there was a linear relation in strength measures between the left and right sides (grip force: $r=0.96$, $p < 0.001$; pinch force: $r=0.93$, $p < 0.001$). Similar findings were found in the CMAP area of the FDI muscle ($r=0.62$, $p < 0.001$) and the thenar muscle group ($r=0.64$, $p < 0.001$) between the dominant and non-dominant hands. Estimation of MUNIX in the FDI and thenar muscles also indicated strong correlations between the left and right sides (FDI: $r=0.67$, $p < 0.001$; thenar: $r=0.72$, $p < 0.001$).

DISCUSSION

The objective of this study was to investigate whether MUNIX estimates of the FDI and thenar muscles are affected by handedness or associated with strength measures. From examination of 24 right-handed and 2 left-handed healthy individuals, we found no significant difference of MUNIX values in hand muscles between dominant and non-dominant sides. Consistent with previous findings (Armstrong & Oldham, 1999; Crosby, Wehbe, & Mawr, 1994), the dominant hand showed slightly stronger grip and key pinch strength. There was a lack of correlation between the MUNIX estimation and the strength measures in hand muscles. Strong correlations between the dominant and non-dominant hand were observed for both strength and the MUNIX measures.

Handedness is often associated with brain lateralization. Asymmetrical excitability in the corticospinal system has been observed in the studies with transcranial magnetic stimulation (De Gennaro et al., 2004; Triggs et al., 1994). Conflicting evidence was also reported showing no significant influence of handedness on motor evoked potentials (Livingston, Goodkin, & Ingersoll, 2010). The neural mechanisms underlying handedness is not fully understood. Regardless of neural origins of handedness, this study examined the MUNIX estimations in dominant and non-dominant hand muscles. The MUNIX estimations from bilateral hand muscles are in the range of previously reported reference values (Li et al., 2012; Neuwirth, Nandedkar, Stalberg, Barkhaus, Carvalho, Furtula, van Dijk, et al., 2011b; Zhou, Li, & Rymer, 2012). No significant difference in MUNIX or CMAP parameters was observed between the dominant and non-dominant hands for the FDI and thenar muscles, implying that the population of motor units or spinal motor neurons may not be associated with handedness.

Long-term preferential use of muscles from one side with respect to the other side can be viewed as a means of moderate exercise that leads to modifications of the muscle structure and function (Adam et al., 1998; Merletti, De Luca, & Sathyan, 1994). For example, Fugl-Meyer reported a higher proportion of type I muscle fibers in the dominant arm of the extensor carpi radialis brevis muscle (Fugl-Meyer et al., 1982). Subsequent studies measuring twitch force or fatigue indexes based on the spectral variables of surface EMG interference patterns have provided extra indirect evidence of the asymmetric composition in dominant muscles (Merletti et al., 1994; Tanaka et al., 1984; Williams et al., 2002; Zijdwind et al., 1990). However, with intramuscular needle EMG recordings a previous study reported no significant differences in motor unit action potential characteristics (such as amplitude, duration and rate of amplitude increment, etc.) between the two sides of the thenar and hypothenar muscles (Nelson, Cauley, Fink, Lauretani, & Simonson, 2003). In the current study, we found that the asymmetry of dominant and non-dominant muscles did not result in a significant difference in CMAP or MUNIX measurements of the FDI and thenar muscles. In addition, we found similar MUSIX values in the FDI and thenar muscles of dominant and non-dominant hands. The insignificantly higher MUSIX values for the dominant FDI muscles could be associated with the larger cross sectional area or muscle fiber size of the muscle measured in the dominant side (Triandafilou & Kamper, 2012).

Thus, as expected, no correlation was observed between the MUNIX estimation and the strength measures in hand muscles. Although contraction of the FDI and thenar muscles can position and stabilize the thumb during grip and pinch force, it only provides partial tension in the pinch force and even less in the grip force. Another important factor is that exertion of voluntary grip and pinch forces involve interactions between the intrinsic and extrinsic hand muscles. For instance, co-contraction of the forearm flexors and extensors, together with co-contraction of the biceps brachii muscle group, can stabilize the wrist and elbow and contribute to pinch and grip forces (Bromberg & Larson, 1996; Kozin, Porter, Clark, & Thoder, 1999). Thus, electrophysiological measurements on one or two muscles of the hand may not disclose sufficient information on all muscle activities during grip or pinch force. In fact, weak or no correlations were found in MUNE studies examining the relationship between isometric hand strength and motor unit counts in thenar and hypothenar muscles (Aggarwal, 2012; Bromberg & Larson, 1996).

MUNIX has been used for the assessment of paretic muscles of stroke survivors by comparing values with those of the contralateral side. In this study, we observed that the MUNIX variability was more significant among different subjects (inter-subject variability) compared with the same subjects (intra-subject variability). This could have arisen from variability among different subjects in muscle bulk, skin resistance, and electrical properties of intervening soft tissue, etc., whereas these effects are relatively small in data collected from both hands of the same subject. In a previous study, it has been found that MUNIX estimates of paretic muscles are significantly lower than contralateral muscles in stroke (Li et al., 2011). The findings from the current study suggest that handedness does not affect MUNIX estimation, which provide additional evidence of the pathophysiological origins of altered MUNIX observed from affected muscles compared with unaffected or neurologically intact muscles. This implies that the majority of the MUNIX decrease observed in paretic muscles could be a result of stroke induced neuromuscular changes (e.g., motor unit loss, muscle fiber atrophy etc.), rather than induced from hand asymmetry.

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Figure 1.

Comparisons of strength and myoelectric data between the dominant and non-dominant hands. (a) Comparisons of grip force and pinch force between the dominant and non-dominant hands. Grip force: non-dominant: 41.37 ± 2.29 kg; dominant: 43.99 ± 2.36 kg; $p < 0.001$. Pinch force: non-dominant: 8.79 ± 0.46 kg; dominant: 9.36 ± 0.52 kg; $p < 0.01$. (b) Comparisons of the CMAP area between two sides for the FDI and thenar muscles. FDI muscle: non-dominant: 30.19 ± 1.68 mV·ms; dominant: 31.7 ± 1.5 mV·ms; $F(1,25)=1.16$, $p=0.29$. Thenar muscle: non-dominant: 36.35 ± 2.03 mV·ms; dominant: 35.76 ± 2 mV·ms; $F(1,25)=0.12$, $p=0.73$. (c) Comparisons of the MUNEX estimation between two sides for the FDI and thenar muscles. FDI muscle: non-dominant: 246 ± 8 ; dominant: 251 ± 8 ; $F(1,25)=0.18$, $p=0.68$. Thenar muscle: non-dominant: 219 ± 9 ; dominant: 213 ± 11 ; $F(1,25)=0.24$, $p=0.63$. (d) Comparisons of the MUSIX values between two sides for the FDI and thenar muscles. FDI muscle: non-dominant: 52.75 ± 2.97 μ V; dominant: 57.98 ± 2.44 μ V; $F(1,25)=3.61$, $p=0.07$. Thenar muscle: non-dominant: 53.72 ± 3.18 μ V; dominant: 55.26 ± 1.5 μ V; $F(1,25)=0.23$, $p=0.64$.

Table 1
Strength and electrophysiological measurement (CMAP amplitude, area, MUNIX and MUSIX) of the two left-handed subjects

ID	Age(y)	Sex	Grip (kg)		Pinch (kg)	
			D	ND	D	ND
1	42	F	33.5	30.1	8	8
2	41	M	46.1	39	10	8.5

<i>FDI muscle</i>							
Amplitude (mV)		Area (mV·ms)		MUNIX		MUSIX (μV)	
D	ND	D	ND	D	ND	D	ND
1	14.15	14.00	31.50	26.98	262	331	53.99
2	17.34	13.24	38.12	30.44	270	236	64.21

<i>Thenar muscle group</i>							
Amplitude (mV)		Area (mV·ms)		MUNIX		MUSIX (μV)	
D	ND	D	ND	D	ND	D	ND
1	11.57	13.15	33.19	33.70	187	228	61.88
2	11.76	12.92	36.16	39.52	195	209	60.31

D: dominant hand; ND: non-dominant hand

Table 2

Correlation coefficients among the strength and the electrophysiological parameters between dominant and non-dominant sides.

Measures	Correlation coefficients
Grip force	0.96
Pinch force	0.93
FDI_CMAP	0.62
FDI_MUNIX	0.67
Thenar_CMAP	0.64
Thenar_MUNIX	0.72

p<0.001