Motor Unit Number Estimate and Isometric Hand Grip Strength in Military Veterans with or Without Muscular Complaints: Reference Values for Longitudinal Follow-up

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ABSTRACT Introduction: It remains unclear if Gulf War (GW) veterans have a higher risk of developing motor neuron disorder. We intended to establish baseline neurophysiological values, including thenar motor unit number estimate (MUNE) and isometric hand grip (IHG) strength, to compare future follow-ups of deployed GW veterans with or without muscular complaints. Materials and Methods: We evaluated 19 GW veterans with self-reported weakness, cramps, or excessive muscle fatigue (Ill-19) and compared them with 18 controls without such muscular complaints (C-18). We performed MUNE on hand thenar muscles using adapted multipoint stimulation method for Ill-19 and 15 controls (C-15). We measured IHG strength (maximum force, endurance, and fatigue level) on Ill-19 and C-18 with a hand dynamometer. We performed nerve conduction studies on all study participants to determine which subjects had mild carpal tunnel syndrome (CTS). We compared the MUNE and IHG strength measures between Ill group and controls and between those with CTS and those without CTS. Results: We obtained thenar MUNE of Ill-19 (95% CI of mean: 143–215; mean age: 46 yr) and compared it with that of C-15 (95% CI of mean: 161–230; mean age: 45 yr), and 95% of CI of mean among IHG strength variables (maximum force: 324–381 Newton; endurance: 32–42 s; fatigue level: 24%–33%) compared with C-18 (maximum force: 349–408 Newton; endurance: 35–46 s; fatigue level: 21%–27%). There was no significant difference in either MUNE or IHG strength between Ill-19 group and controls. The MUNE and IHG maximum forces were significantly lower in those with CTS compared with those without CTS. As a surrogate of mild CTS, the median versus ulnar distal sensory latency on nerve conduction study was only weakly associated with MUNE, maximum force, and fatigue level, respectively. Conclusion: To our knowledge, no published study on MUNE reference values of military veteran population has been available. The quantifiable values of both thenar MUNE and IHG strength of military veterans serve as baselines for our longitudinal follow-up of motor neuron function of deployed troops. These reference values are also useful for other laboratories to study veterans' motor system with or without mild CTS.

INTRODUCTION

It is believed that interaction between genetics and environmental factors underlies motor neuron degeneration.[1,2] Despite numerous epidemiological studies suggesting that military veterans have increased susceptibility to amyotrophic lateral sclerosis, few studies have objectively measured baseline motor neuron functions of military veterans with relevant neuromuscular complaints compared with those without.[3–5] Motor unit number estimation (MUNE) is an electromyography method of estimating functional motor units innervating a specific muscle or muscle group and often used in longitudinal follow-up of patients with motor neuron disorder or those with susceptibility to motor neuron disorders. Hand grip strength measurements are used as additional tools of monitoring the disease progression in conjunction of MUNE.[6,7]

To determine if or what impact environmental exposures may have to the motor neuron function of military troops after overseas deployment, we intended to establish baseline MUNE and hand grip strength values in order to longitudinally follow up with these veterans. We selected 19 Gulf War (GW) veterans with self-reported neuromuscular symptoms from a cohort generated from veterans' administration longitudinal epidemiological study entitled "Health of US Veterans of 1991 Gulf War: A Follow-up Survey in 10 Years."[8] Participants from the ill group had at least two of the three self-reported neuromuscular complaints, namely weakness, muscle cramp, or chronic fatigue in that epidemiological survey conducted in 2005, and that many years later at least one of the three muscular complaints remained as a complaint at the time of this study. We selected 18 controls with none of the 3 neuromuscular symptoms. We compared MUNE of hand thenar muscles and isometric hand grip (IHG) strength values between ill group participants and controls. We performed nerve conduction study searching for mild carpal tunnel syndrome (CTS) to determine if those with CTS differed from those without CTS (No-CTS) among outcome measures.

MATERIALS AND METHODS

Study Participants

The survey entitled "Health of US Veterans of 1991 Gulf War: A Follow-up Survey in 10 Years" conducted in 2005 found

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that many 1991 GW veterans who were previously deployed reported weakness, muscle cramp, or chronic fatigue.[8] Based on this survey, we generated a pool of potential study participants with self-reported complaints determined by their response to the specific survey questions that inquired whether they experienced (i) weakness, (ii) muscle cramp, or (iii) chronic fatigue since deployment to the Gulf Theater. Veterans in the initial ill group ($n = 540$) had at least two of the three above self-reported neuromuscular complaints. We administered telephone interviews with potential study participants from the initial pools to determine their eligibility for the on-site clinical study if any one of the the previously reported muscle weakness, cramp, or excessive fatigue remained as a complaint at the time of this study. The method of recruiting study participants was described in detail in our published report.[9] Exclusion criteria of the study included veterans with (i) conditions interfering with independent travel for the on-site study, (ii) prior known diagnosis of mononeuropathies or polyneuropathy involving hand such as CTS or a history of brain/spine/nerve invasive procedures, and (iii) active medical conditions that explain the muscle weakness, cramp, or excessive fatigue.[10] A total of 19 GW veterans constituted the final Ill-19 group (Ill-19). Those in the control group of 18 GW veterans (C-18) were without any 1 of the 3 above self-reported neuromuscular complaints at the time of this study. All 37 study participants were deployed to Gulf Theater at some time between 1990 and 2002. The study was approved by the Research & Development Committee/Institutional Review Board of VA hospital in Washington D.C.

Measures and Procedures

We performed the nerve conduction study (NCS; Cadwell, Kennewick, WA, USA) on all 37 study participants using the standard transcarpal method to search for median neuropathy at wrist (CTS). CTS was diagnosed if (i) median distal sensory latency across the wrist was equal to or exceeding 2.3 ms or (ii) median–ulnar distal sensory latency across wrist differed by more than 0.3 ms. Compound muscle action potential (CMAP) was recorded at abductor pollicis brevis by stimulating distal median nerve above the wrist, which was 7 cm from the CMAP recording point. We performed MUNE using adapted multipoint stimulation method as described.[11] Briefly, a surface G1 recording electrode of 2 × 2 cm was placed on the abductor pollicis brevis of the thenar eminence in each hand and G2 over the abductor pollicis brevis tendon near the bony prominence. The average size of at least 10 single-motor units obtained through stimulation at median nerve from wrist to elbow was calculated, and then compound muscle action potential area was divided by that value to derive motor unit number estimates. Three study participants of the C-18 group could not complete the MUNE procedure, but none of the three had CTS by NCS.

We performed IHG strength testing on both hands of each of the 37 participants on at least two separate days after sufficient times of training before the formal testing. We used a commercially available digital hand dynamometer connected to a computer where the data were analyzed by a software program (MIE Myometer; MIE Medical Research Ltd., England).[12] The best performance of at least three independent tests was used for the purpose of this study. Three IHG strength outcome measures, maximum force (Newton), endurance (s), and fatigue level (%), were obtained as described.[13–15] To the original testing, we added the following modifications. The endurance test participants were instructed to maintain the grip on the dynamometer for as long as possible in the range from 70% to 90% of the maximum force and duration maintained within this range was recorded as endurance. For fatigue-level measurements, participants were instructed to grip as hard as possible for 10 s, rather than 5 s, before release of the grip. The fatigue level was calculated by percentage loss of grip from the peak force (PF) to the end force (EF) at the point of grip release ([PF − EF] x 100/PF) as described.[13,16] The correlation coefficiency (r) between best IHG strength performance of day 1 and that of day 2 is 0.94 for maximum force, 0.91 for endurance, and 0.87 for fatigue level.

Data Analysis

If the distribution of a variable was approximately normal by the Shapiro–Wilk normality test, the null hypothesis was examined with the two-tailed Student's t-test. If the distribution failed the normality test, we used the nonparametric Mann–Whitney U test. The Pearson correlation coefficient (r) was obtained with the SigmaPlot 11.2 software package (San Jose, CA, USA).

RESULTS

Participant Characteristics

Table I showed participant demographics and basic characteristics relevant to the comparison of MUNE and IHG strength between Ill-19 group and controls. At the time of this study, the age, BMI, forearm circumference, blood CK level, and post-deployment years were comparably similar between III-19 group participants and 18 controls. Normal reference values of blood CK (U/L) in our hospital ranged between 20 and 300. There was slightly more CTS among Ill-19 ($n = 12$) compared with C-18 ($n = 8$), but no statistical significance ($p > 0.05$). A total of 20 hands were diagnosed with CTS out of a total of 72 hands of all participants by NCS. Among these 20 CTS hands, 2 in Ill-19 and 1 in C-18 had distal median motor latency equal to or exceeding 4.5 ms, which were considered more than mild severity of CTS.

Nerve Conduction Variables

There was no significant group differences between Ill-19 and controls among selected nerve conduction variables (Table II). Calculated from all hands diagnosed with CTS (Table II; $N = 20$), the group average value 4.2 ms of the median motor distal

latency was within the limit of the normal upper cutoff 4.5 ms for diagnosing CTS with motor fiber involvement; however, this median motor distal latency 4.2 ms of CTS group was significantly prolonged compared with that of all hands without CTS (Table II; $N = 54$; 3.7 ms). The average median distal sensory latency across the wrist of CTS group obtained by the standard transcarpal method was 2.3 ms, which was just at the borderline prolongation for diagnosing sensory CTS (Table II), and the average difference of median–ulnar distal sensory latency across the wrist of CTS group was slightly more than the normal upper cutoff 0.3 ms (Table II; 0.5 ms).

Baseline MUNE

There was no significant difference of MUNE between Ill-19 and controls (Table III; $p = 0.317$). Three controls in the C-18 could not complete the MUNE procedures; however, none of the three had CTS on either left or right hand. The average MUNE (137) of all hands diagnosed with CTS ($N = 20$ [12 in Ill-19 plus 8 in C-15]) was significantly lower than that (207) of No-CTS (Table III; $N = 48$ [26 in Ill-19 plus 22 in C-15]; $p = 0.003$). The 95% CI of mean of MUNE from hands without CTS in Ill-19 (150–241; $N = 26$) was not significantly different from that of hands without CTS in C-15 (177–261; $N = 22$; $p = 0.222$).

TABLE I. Demographics and Characteristics of Participants

Group	Ill-19	C −18
Age (mean ± SD)	46.6 ± 6.2	45.3 ± 3.1
Sex (m/f)	14/5	14/4
Post-deployment (yr)	21.6 ± 3.4	21.8 ± 2.6
BMI (mean ± SD)	29.7 ± 4.3	29.5 ± 7.2
Forearm circumference (cm)		
Right (mean ± SD)	28.8 ± 2.8	28.2 ± 2.5
Left (mean ± SD)	28.5 ± 2.6	27.9 ± 2.6
Blood CK (mean ± SD)	210 ± 97	228 ± 101
Dominant hand		
Right/left	13/6	15/3
No. of hands evaluated by NCS	38	36
No. of hands with CTS		
Right	5	4
Left	7	4

Ill-19 denotes a group of 19 participants with muscular complains; C-18, a group of 18 participants without muscular complaints; CK, muscle enzyme expressed in U/L; No., numerical numbers.

Baseline IHG Strength

IHG strength and endurance test results of one healthy volunteer without CTS was illustrated in Figure 1A and B, respectively. None of the three IHG strength variables (maximum force, endurance, and fatigue level) showed significant difference between Ill-19 and controls (Table III). The maximum force of all hands diagnosed with CTS ($n = 20$) was significantly lower than that of No-CTS (Table III; $N = 54$; $p = 0.001$), whereas the two other IHG outcome measures of CTS group, endurance and fatigue level, were not significantly different from that of No-CTS.

Correlations Between MUNE and Variables of Interest

There was no strong correlation between thenar MUNE and variables of either IHG strength or NCS. MUNE was weakly correlated with endurance ($r = 0.300$), CMAP amplitude ($r = 0.368$), and the difference of median–ulnar distal sensory latency across the wrist ($r = -0.252$), respectively (Table IV; $p < 0.05$). There were no significant correlations between MUNE and (a) maximum force, (b) fatigue level, or (c) CMAP distal latency, respectively (Table IV; $p > 0.05$). Among three IHG strength variables, both maximum force ($r = -0.326$) and fatigue level ($r = 0.309$) were weakly associated with the difference of median–ulnar distal sensory latency, a NCS surrogate of mild CTS, whereas endurance was not associated with the difference of median–ulnar distal sensory latency (Table IV; $p = 0.468$).

TABLE II. Nerve Conduction Variables (Mean ± SD)

No. of Hands	Ill-19 38	C-18 36	*p*-Value Ill-19 vs. C-18	CTS 20	No-CTS 54	*p*-Value CTS vs. No-CTS
Median CMAP						
Amplitude (mV)	7.8 ± 2.9	9.0 ± 2.5		7.7 ± 3.1	8.6 ± 2.6	
95% CI	6.8–8.7	8.1–9.9	0.061	6.2–9.1	7.9–9.4	0.186
Latency (ms)	3.8 ± 0.4	3.8 ± 0.3		4.2 ± 0.5	3.7 ± 0.2	
95% CI	3.7–4.0	3.7–3.9	0.970	3.9–4.4	3.6–3.7	<0.001*
Median SNAP						
Amplitude (μV)	50.0 ± 10.2	47.0 ± 13.7		38.7 ± 11.2	52.2 ± 10.3	
95% CI	46.6–53.4	42.3–51.7	0.577	33.4–43.9	49.4–55.0	<0.001*
Latency (ms)	2.1 ± 0.2	2.0 ± 0.2		2.3 ± 0.1	1.9 ± 0.1	
95% CI	2.0–2.2	1.9–2.1	0.333	2.2–2.4	1.9–2.0	<0.001*
M-U diff (ms)	0.15 ± 0.23	0.12 ± 0.32		0.50 ± 0.19	0.01 ± 0.16	
95% CI	0.07–0.23	0.01–0.23	0.442	0.40–0.59	−0.02–0.06	<0.001*

Median CMAP, distal median motor nerve evoked compound muscle action potential recorded at abductor pollicis brevis; median SNAP, median nerve evoked sensory nerve action potential across the wrist; M-U diff, the difference between median and ulnar distal sensory latency by standard transcarpal method.
*Values significant.

TABLE III. Reference Values of Thenar MUNE and Hand Grip Strength

	Ill-19	C-18	*p*-Value Ill-19 vs. C-18	CTS	No-CTS	*p*-Value CTS vs. No-CTS
MUNE						
Mean ± SD	179 ± 110	195 ± 92		137 ± 80	207 ± 104	
95% CI	143–215	161–230	0.317	99–174	176–237	0.003*
No. of hands	38	30		20	48	
Max-Force (*N*)						
Mean ± SD	352 ± 86	379 ± 86		312 ± 83	384 ± 81	
95% CI	324–381	349–408	0.195	273–351	362–406	0.001*
No. of hands	38	36		20	54	
Endurance (S)						
Mean ± SD	37.2 ± 14.9	40.9 ± 14.8		35.0 ± 15.2	40.1 ± 14.7	
95% CI	32.3–42.1	35.9–46.0	0.285	27.9–42.1	36.1–44.1	0.196
No. of hands	38	36		20	54	
Fatigue level (%)						
Mean ± SD	29.0 ± 12.6	24.6 ± 8.9	0.251	31.3 ± 14.0	25.2 ± 9.4	
95% CI	24.8–33.1	21.6–27.6		24.7–37.9	22.6–27.8	0.092
No. of hands	38	36		20	54	

MUNE, motor unit number estimate; 95% CI, 95% confidence interval; N, Newton; S, seconds.
*Values significant.

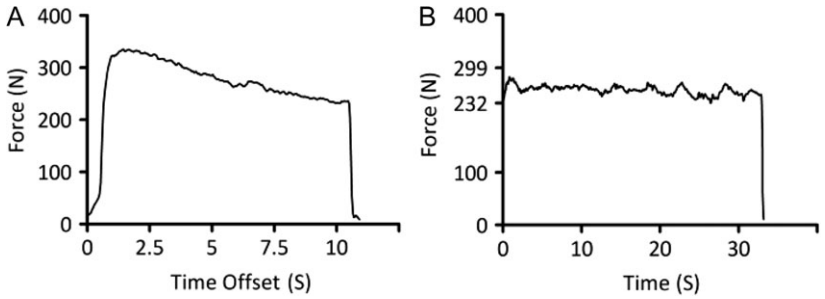

FIGURE 1. Grip strength test (A). Maximum force: 332 (N); end force: 232 (N); fatigue level: 30%. Endurance test (B). Endurance: 32 s.

DISCUSSION

Over years, many studies have been conducted with a focus on objectively examining GW veterans with post-deployment neuromuscular complaints.[9,17–19] The neurological symptoms of some of these veterans have resolved over time or remained as manifestations of metabolic or immune disturbances due to subclinical diseases such as prediabetes, and among others.[9] It remains unclear, however, if some patients with persisting complaints may develop expedited aging, or even evolve into a notable neuromuscular degenerative disorder. To our knowledge, no published study on MUNE reference values of military veteran population has been available. As an off-shoot clinical study of the large-scale longitudinal epidemiological study "Health of US Veterans of 1991 Gulf War: A Follow-up Survey in 10 Years" conducted by the Department of Veterans' Administration, we quantitatively assessed the number of functioning motor units present in a hand muscle among some deployed GW veterans.[8] We have established a baseline thenar MUNE and IHG strength values for our longitudinal follow-up of deployed GW veterans.

Motor unit loss over healthy aging is about 1% per year after 20 yr of age and about 50% of the motor neuron loss occurs at 70 yr of age.[20,21] The motor unit loss plays a significant role in the age-related reduction in maximal isometric muscle contraction.[22] The similar demographics of our study participants in Ill-19 group compared with controls ensured the success of future investigating chronic degenerative disorders versus normal aging. Our investigative scopes were comprehensive by studying the thenar MUNE together with IHG strength, considering that MUNE or IHG strength testing alone may not be feasible in the distant future if severe co-morbidities occur in ill veterans. Our results were consistent with previous similar studies on civilian population in that the presence of even very mild CTS would severely affect the MUNE.[23–25] Exceeding 17% maximal voluntary hand contraction force was associated with the development of CTS in civilian workers with occupations involving heavy object maneuvering.[12] In this study on military veterans, there were 20 hands diagnosed with CTS out of a total of 74 hands of the 37 study participants and that both MUNE and IHG maximum force were significantly reduced because of the presence of mild CTS, emphasizing the need for screening CTS before MUNE testing or IHG measuring among military veterans with or without neuromuscular complaints, who were all at high risk for having subclinical CTS revealed in this study.

TABLE IV. Correlations Among Variables of Interest

	MUNE		Fatigue (%)		Max-Force (N)		Endurance (S)	
	p-Value	*r*	*p*-Value	*r*	*p*-Value	*r*	*p*-Value	*r*
Fatigue (%)	0.343	−0.117						
Max-Force	0.776	0.035	0.127	−0.179				
Endurance	0.013	0.300*	0.077	−0.207	0.011	0.293*		
CMAP amplitude	0.002	0.368*	0.132	−0.177	0.072	0.210	0.303	0.121
CMAP latency	0.130	−0.186	0.022	0.266*	0.489	−0.081	0.794	0.030
M-U Diff	0.037	−0.252*	0.007	0.309*	0.004	−0.326*	0.468	−0.085

MUNE, motor unit number estimate; N, Newton; S, seconds; *r*, Pearson correlation coefficient. CMAP, compound muscle action potential recorded at thenar muscle by stimulation of distal median nerve; M–U Diff, the difference between median and ulnar distal sensory latency by standard transcarpal method. *Significant at *p*-value less than 0.05.

The absolute MUNE values we obtained among GW veterans were within normal historical values obtained by others from civilian population of the same age group.[21] The MUNE obtained in veterans without CTS (mean = 207, SD = 104; age: 37–55 yr) appeared to be slightly lower in average numbers and wider in standard deviation than that of the historical value (mean = 258, SD = 64; age: 41–58 yr) by the same adapted multipoint stimulation method.[11] The differences were probably due to (a) the recording G1 electrode we used was smaller and (b) the No-CTS group in our study comprised both ill veterans with neuromuscular complaints and controls who might not simply be healthy volunteers because our recruitment criteria did not exclude many non-muscular diseases. There was no strong correlation between thenar MUNE and any one of the three IHG strength measures, consistent with historically published results, due to either small numbers of our study participants or measuring median nerve innervated thenar MUNE without measuring ulnar innervated hand muscle.[6] The weak correlation between MUNE and the difference of median–ulnar distal sensory latency across the wrist on nerve conduction study, but not the median motor distal latency across the wrist, was due to the better sensitivity of sensory nerve conduction study for detecting CTS than motor study and that the current study had no sufficient power to show the expected correlation between MUNE and motor distal latency across the wrist. It was known that the endurance measured by the hand dynamometer, rather than the maximum force, was more preserved in later life than earlier life during normal aging.[26,27] Given our finding that among three IHG strength measures endurance was the least affected by CTS, we speculate that endurance testing described in this study might be an important addition to MUNE for the longitudinal follow-up of motor neuron function among veterans with CTS.

This study has limitations. Because the study design was observational and that the numbers of total study participants ($N = 37$) including both Ill-19 and controls were small, our results may not be representative of most of the previously deployed veterans. Some participants in our control group were not healthy volunteers compared with participants of historical studies on civilian population. Hidden brain and spinal cord disorders, for example, asymptomatic C8-T1 radiculopathies, might potentially cause underestimation of MUNE and IHG strengths. It was also desirable to obtain MUNE of an ulnar nerve innervated hand muscle in addition to median nerve innervated thenar MUNE, which would make the correlation between MUNE and IHG strength measures more meaningful because hand muscle strength is mainly determined by both median and ulnar innervated C8-T1 muscles.

CONCLUSION

There was no group difference of both MUNE and IHG strength measures between deployed GW veterans with self-reported neuromuscular complaints and controls. To the best of our knowledge, we are the first to provide quantifiable values of thenar MUNE among deployed military veterans. The thenar MUNE and IHG strength values we have established here serve as (a) baselines for our longitudinal follow-up of motor neuron function among previously deployed troop and (b) references for other laboratories to study veterans' motor system with or without mild CTS.

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