# Single-Fiber Electromyography of the Trapezius in Patients with Myasthenia Gravis

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## ABSTRACT

**Background:** Myasthenia gravis is a chronic autoimmune disease of the neuromuscular junction, clinical and electrophysiological assessment of muscles is necessary for the diagnosis. Repetitive nerve stimulation test is reliable and its sensitivity depends on the distribution and the severity of the affected muscles.

**Objective:** This study aimed to characterize the normal values of jitter for volitional single-fiber electromyography (SFEMG) of the upper trapezius in healthy subjects and patients with generalized myasthenia gravis in Iraq.

**Methods:** Fifty-two patients with myasthenia gravis (mean age, 34.8 years; mean duration of illness, 4.1 years) underwent single-fiber electromyography of the trapezius, frontalis, and extensor digitorum communis (EDC) muscles. In addition, for the control group, 30 healthy subjects (mean age, 32.8 years) were subjected to single-fiber electromyography of the trapezius.

**Results:** The mean jitter of the trapezius in the patient group (67.1 ± 8.7 μs) was significantly higher than that in the control group (18.7 ± 4.1 μs; $p < 0.001$). The normal upper limit of trapezius mean (Mean consecutive differences) MCD of 23 μs /study (mean ± 1 standard deviation) and 26 μs per individual fiber pair, respectively ($95^{th}$ upper percentile, 26.4 μs).

**Conclusion:** These results suggest that volitional SFEMG of the trapezius is a specific investigation for diagnosis of generalized myasthenia gravis even when the examined muscle is not clinically weak. Because of relatively poor patient tolerance and a remote risk of accidental pneumothorax, it is not advisable to examine the upper trapezius.


**Keywords: Single-fiber electromyography, Trapezius, Myasthenia gravis, Repetitive nerve stimulation.**

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Myasthenia gravis, a chronic autoimmune disease of the neuromuscular junction, is characterized by muscle weakness due to destruction of acetylcholine receptors at the neuromuscular junction[1]. The prevalence rate of myasthenia gravis has been reported to be approximately 16 cases per 100,000[2]. Most patients have circulating antibodies to nicotinic receptors ($N_M$) at the neuromuscular junction[3,4]. Consequently, the concentration of acetylcholine available for neurotransmission at the neuromuscular junction is reduced. A common symptom of myasthenia gravis is fluctuating muscle weakness that is relieved by rest[5].

External ocular, bulbar, and proximal limb muscles most commonly exhibit such weakness[6]. The disease typically follows a course of remission and relapse.

Clinical and electrophysiological assessment of muscles is necessary for diagnosis of myasthenia gravis. Clinical diagnosis of myasthenia gravis is achieved by the tensilon test, repetitive nerve stimulation (RNS), SFEMG, and detection of acetylcholine using receptor antibodies and/or muscle-specific tyrosine kinase antibodies[7].

"Repetitive nerve stimulation test is reliable and its sensitivity depends on the distribution and the severity of the affected muscles. The sensitivity of RNS is improved when the proximal rather than distal nerves are stimulated. Facial nerve is the most

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commonly examined cranial nerve, and has a diagnostic yield of 62% in generalized myasthenia gravis"[8]. Limitations of repetitive stimulation of the facial nerve include patient discomfort and necessity for stimulation of the contralateral facial nerve or ipsilateral and contralateral trigeminal nerves.

The trapezius is a proximal muscle, and the sensitivity of the RNS test is high in proximal muscles[2]. Therefore, the rationale of the present study was to induce repetitive supramaximal stimulation of the trapezius. "In addition, supramaximal stimulation of the spinal accessory nerve easily performs and causes less pain (because this nerve is a pure motor nerve). Modification of the maneuver is necessary to counteract the immobilization that faced in practicing the investigation. In brief the subject lay in a supine position, and their shoulder was elevated passively with the hand of the examiner placed on the subject's arm, and thus held upward firmly. The neck of the subject was rotated slightly away from the examined side to secure some space for stimulation"[9].

The present study aimed to identify the cutoff value of jitter for volitional single-fiber electromyography (SFEMG) of the trapezius muscle in healthy Iraqi individuals and to apply the results for evaluation of myasthenia gravis. In addition, the validity of the present results was assessed by comparing the findings of volitional SFEMG (v-SFEMG) and RNS of the same trapezius muscle in patients with generalized myasthenia gravis.

## Methods

The study was conducted at the Department of the Neurophysiology, Al-Yarmouk Teaching Hospital, between June 2015 and June 2017. Informed consent was obtained from all patients and healthy subjects, and the ethics committee of the hospital approved the study. The control group included 30 healthy volunteers (male, 12; female, 18) recruited from among the staff of Al-Yarmouk Teaching hospital. The control subjects were all apparently healthy and symptom-free, with no history or clinical evidence of neurological deficit. The patient group included 52 patients (male, 24; female, 28) who were referred to the hospital by consultant neurologists for confirmation of clinical diagnosis of myasthenia gravis.

The patients were forbidden medication with acetylcholinesterase enzyme inhibitors for 12 hours prior to the electrophysiological study. The SFEMG and RNS tests were performed using the Nihon Kohden MEB-9400 EMG system.

Motor and sensory nerve conduction studies of upper- (right median and ulnar) and lower- (right and left fibular and left sural) limb nerves were performed to rule out neuropathic processes and to confirm that the nerves that were to be assessed by RNS were normal. Moreover, to rule out primary muscle diseases, the EMG study was performed using a concentric needle.

Repetitive nerve stimulation of facial (orbicularis oculi muscle), spinal accessory (upper trapezius), and ulnar (abductor digiti minimi) nerves was administered at a low frequency of 3 Hz for a train of 10 responses. Maximal stimulation was usually administered using a current of 10–15 mA. The intensity of the stimulus was adjusted to correspond to two times the maximum stimulus (i.e., < 30 mA).

Since the spinal accessory nerve descends along the posterior border of the sternocleidomastoid muscle, it was stimulated using a surface-stimulating electrode. The active electrode was placed over the upper trapezius at the angle of the neck and shoulder. The stimulating electrodes were manually secured when a stimulation point with the lowest threshold was detected. The recording electrode was placed over the upper border of the trapezius, midway between the spinous process of the seventh cervical vertebra and the acromion, with the reference electrode being placed over the acromion.

The result of the RNS test was considered positive when the amplitude decreased between the first and fourth

responses by 20% or more for the facial nerve and by 10% or more for the spinal accessory and ulnar nerves. A positive result observed at rest necessitated 10 s of voluntary muscle exercise in order to obviate the decrement (post-exercise facilitation), while a negative result at rest necessitated 1 min of voluntary muscle exercise.

Continuous stimulation was repeated every minute for 4 min after the running exercise. Once decrement was recorded, patients were requested to perform the most strenuous exercise for 10 s or more. This exercise involved shrugging shoulders against resistance; the surface skin temperature was maintained at 32℃ to avoid false-negative results.

Volitional single-fiber electromyography (v-SFEMG): The upper trapezius, frontalis, and extensor digitorum communis muscles were evaluated by v-SFEMG using the following parameters: gain, 0.05 mV/division; sweep time, 1 msec /division; and band pass, 10–500 Hz.

"The patient was instructed to activate the upper trapezius muscle, and to sustain that contraction. Five to six insertions were done to report 10 to 20 pairs of single muscle fiber action potentials. The needle was reallocated as far as a single muscle fiber potential was optimally placed, then a search for a second action potential that was time locked to the first action potential, imply that it was from the equivalent motor unit. Numerus, successive firing of the muscle fiber action potential pairs were ultimately registered" [10].

The criteria for acceptable potential pairs were [11] "an amplitude of more than 200 μV, and a rise time of less than 300 μs". "At least 20 pairs were requested from control subjects. Jitter was considered abnormal if 2 out of 20 pairs exceeded the normal value for that muscle or if mean consecutive difference (MCD) of jitter exceeded the 95 percentile value" [12].

The criteria for abnormal SFEMG were as follows: mean jitter > 50 μs and/or > 10% of pairs exhibiting jitter > 55 μs with or without blocking. Blocking was defined as discharges dropped during consecutive discharging at MCD ≥ 80 μs. Reference values for SFEMG of healthy EDC and frontalis muscles were derived from previous studies[13,14].

Qualitative and quantitative analysis of variables was performed using the Statistical Package for Social Sciences (SPSS) version 16.1. Intergroup differences in quantitative variables were evaluated by the unpaired two-tailed Student's t-test. A p value of 0.05 was considered as the highest limit of significance.

## Results

Table 1 shows the characteristics of the patients included in this study. The patient group (mean age, 32.8 years; age range, 23–63 years) included 24 men (46.1%; mean age, 42.3 years) and 28 women (53.8%; mean age, 34.2 years). The mean and median disease durations in the patients group were 4.1 ± 5.4 years (range, 2 months to 21 years) and 1.3 years, respectively, (Table 1). The control group (mean age, 32.8 ± 13.5 years; age range, 20–58 years) included 12 men (40%) and 18 women (60%).

The results of the RNS test were negative in all control subjects. In the patient group, the results of the RNS test were negative in 18 patients and positive for one, two, and three nerves in 5, 20, and 9 patients, respectively, (Table 1).

The results of SFEMG are presented in Table 2. In the control group, SFEMG findings of the trapezius revealed minimum and maximum MCD values of 13.2 and 27.9 μs, respectively, with mean ± standard deviation values of 20.6 ± 4.2 and 20.4 μs, respectively. The 95$^{th}$ percentile for a single-fiber pair was 26.7 μs. The proportion of abnormal pairs was 2.72 and no instances of blocking were observed, (Table 2, Figure 2).

In the patient group, SFEMG results of the trapezius muscle revealed abnormal MCD values for all subjects (100%); 48

(92.3%) patients exhibited significant percentages of abnormal pairs, and 19 (38.4%) exhibited blocking, (Table 2, Figure 2). The SFEMG results of the frontalis muscle also revealed abnormal mean MCD values; 48 (92.3%) patients exhibited significant percentages of abnormal pairs, and 16 (30.7%) exhibited blocking, (Table 2). In case of the EDC, 47 (90.3%) patients exhibited abnormal MCD values and significant percentages of abnormal pairs, and 14 (26.9%) patients exhibited blocking, (Table 2).

There were significant differences between the control and patient groups in terms of mean MCD ($p < 0.001$), percentage of abnormal pairs ($p < 0.001$), and percentage of blocking ($p = 0.02$) of the trapezius muscle. In the patient group, there was no statistically significant difference in percentage of abnormal pairs ($p = 0.175$) among the EDC (59.2%), frontalis (70.1%), and trapezius (70.3 %) muscles. However, significant differences in percentage of blocking were observed among the three groups (EDC, 26.9%; trapezius, 38.4%; frontalis muscle, 40.3%; $p = 0.001$). The sensitivity of mean MCD of the trapezius, frontalis, and EDC muscles were 100%, 100%, and 90%, whereas the sensitivity of the RNS test was approximately 63%.

**Table 1: Patient characteristics.**

| Variable | Results No. (%) |
|---|---|
| Age, years | 32.8 ± 10.8 |
| Sex | |
| Male | 24 (46.1) |
| Female | 28 (53.8) |
| Duration of illness, years | 4.1 ± 5.5 |
| Repetitive nerve stimulation findings | |
| Negative | 18 (34.6) |
| Positive — one nerve | 5 (9.6) |
| Positive — two nerves | 20 (38.4) |
| Positive — three nerves | 9 (17.3) |

Values are expressed as mean ± standard deviation or number (percentage).

**Table 2: SFEMG data of the trapezius, frontalis, and EDC muscles.**

| SFEMG parameters | Control group Trapezius | Patient group Trapezius | Patient group Frontalis | Patient group EDC |
|---|---|---|---|---|
| Median MCD, µs | 21.3 | 67.8 | 68.9 | 73.5 |
| Mean MCD, µs | 21.9 ± 4.2 | 64.2 | 65.1 | 71.2 ± 11.3 |
| Abnormal pair, % | 3.2 ± 3.4 | 70.3 ± 29.2 | 70.1 ± 27.3 | 59.2 ± 22.3 |
| Blocking, % | 0 | 38.4 | 40.3 | 26.9 |

Values are expressed as number (percentage) or mean ± standard deviation.
SFEMG, single fiber-electromyogram; EDC, extensor digitorum communis; MCD, mean consecutive difference.

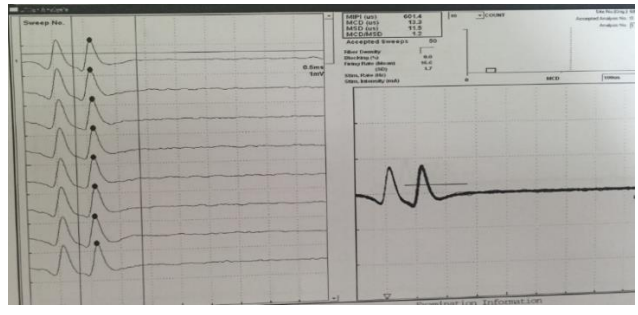

**Figure 1: Normal single-fiber EMG of the upper trapezius.**

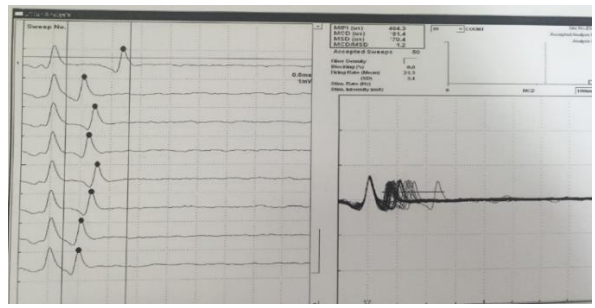

**Figure 2: Abnormal single-fiber EMG of the upper trapezius.**

## Discussion

Repetitive nerve stimulation is a valid technique for assessment of generalized myasthenia gravis[15]. "However, the sensitivity of RNS, is variable and it depends on the severity of disease, distribution of the involved muscles, use of acetylcholinesterase inhibitor drugs, and the examined nerves. The sensitivity of conventional RNS is low in mild myasthenia gravis, therefore single fiber EMG could serve as a confirmative diagnostic test"[16].

In the present study, the proportion of women was slightly higher than that of men, who presented with myasthenia gravis at a younger age than did women[17]. Single-fiber EMG is the most valuable clinical test for diagnosis of myasthenia gravis; serial measurements of jitter can be useful for disease follow-up and assessment of treatment effects. This test should be administered when RNS test findings are negative or equivocal[15]. "When abnormal NMT has been demonstrated by RNS, the finding of abnormal jitter does not add to the diagnosis, although it may be useful in providing baseline values for comparison with the results of subsequent studies"[5].

Several studies have reported normal MCD values of the frontalis (42.6 ± 6.8 µs) and EDC (42.68 ± 6.1 µs) muscles like Balci et al[18] and Farqad et al[19].

Kokubun et al[20] reported an MCD value of 56.8 µs for v-SFEMG of the frontalis muscle. These differences in MCD values among various studies might be attributable to differences in technique, muscle type, and subject age.

In the present study, the sensitivity of SFEMG of the EDC among patients with myasthenia gravis was 90%; previous studies involving patients with generalized myasthenia gravis have reported sensitivity values of 96.4%[16], 99%[20], and 74%[12]. A possible explanation for these differences in sensitivity among various studies is the difference in proportion of patients who did not experience muscle weakness at the time of examination. Two of the present subjects exhibited normal SFEMG results for the EDC and did not experience muscle weakness. In the present study, SFEMG of the trapezius and frontalis muscles exhibited 100% sensitivity, which corresponds with the results reported by Kokubun et al[20] in patients with generalized myasthenia gravis. In addition, 42 patients in the present study exhibited normal findings upon SFEMG of the trapezius, while the remaining 10 patients exhibited minimal to moderate weakness of the upper trapezius.

These findings support the assumption that SFEMG of the trapezius is an extremely hypersensitive diagnostic method for myasthenia gravis, even in the absence of clinical muscle deficit. The high sensitivity of SFEMG of the trapezius in myasthenia gravis corresponds with SFEMG findings in other faciocranial muscles, such as the frontalis and sternocleidomastoid muscles (volitional mode of measurement)[9] and the orbicularis oculi[10]. The trapezius and frontalis muscles exhibited a significantly

higher percentage of blocking than did the EDC, because of its little safety element. In this study, SFEMG of the trapezius exhibited 100% sensitivity, which is in agreement with the findings of Stalberg et al[8], who reported a sensitivity of approximately 90% for the combined results of ocular and generalized myasthenia gravis.

In conclusion; The present study determined the normal limits of MCD values of the trapezius. Volitional SFEMG of the trapezius is an extremely sensitive tool for diagnosis of generalized myasthenia gravis, and its sensitivity is related not to muscle weakness but to disease severity. Upper trapezius SFEMG analysis is not recommended because patients have better tolerance to sampling of the frontalis muscle than to sampling of the upper trapezius. Moreover, upper trapezius SFEMG carries a relatively high risk of pneumothorax.

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