Stimulated Single-Fiber EMG In The Ocular Myasthenia Gravis And In Some Ocular Myopathies

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Citation

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Abstract

The aim of this study was to evaluate the role of stimulated single fiber electromyography (ST□SFEMG) in differentiating ocular myasthenia gravis (OMG) from some myopathies with ocular involvement. We performed ST□SFEMG in the orbicularis oculi muscle in 65 patients diagnosed with OMG, in 11 chronic progressive external ophthalmoplegia and 3 oculopharyngeal muscular dystrophy. 97% of OMG and 21.4% of myopathic patients had 10% o more motor potentials (MP) exceeding 35 µs. 95% of OMG and 14.3% of myopathic patients had 15% o more MP exceeding 35 µs. 89% of OMG and 7.1% of myopathic patients had 20% o more MP exceeding 35 µs. 72% of OMG and 0% of myopathic patients had 25% o more MP exceeding 35 µs. It is possible to discern between OMG and ocular myopathy by ST□SFEMG and that the cutoff criteria is 25% MP with jitter over 35□s in orbicularis oculi muscle.

INTRODUCTION

Myasthenia gravis (MG) is an autoimmune disorder caused by antibodies against acetylcholine receptors (AChR) or muscle-specific tyrosine kinase (MuSK) at the neuromuscular junction and affects approximately 3 out of 10,000 people. The development of an assay of serum for AChR antibodies was a major advance in the diagnosis of MG, although circulating ACh receptor antibodies are not detectable in all patients with MG. Electrodiagnostic studies, in particular single fiber electromyography (SFEMG), remain the most sensitive test for the diagnosis of ocular mysthenia gravis (OMG), although it may be abnormal in conditions that mimic OMG, such as chronic progressive external ophthalmoplegia (CPEO) and oculopharyngeal muscular dystrophy (OMD) [1,2] .

The aim of this study was to evaluate the role of stimulated single fiber electromyography (ST SFEMG) in differentiating OMG from some myopathies with ocular involvement, such as CPEO and OMD, because ocular involvement is the most common presenting form of MG.

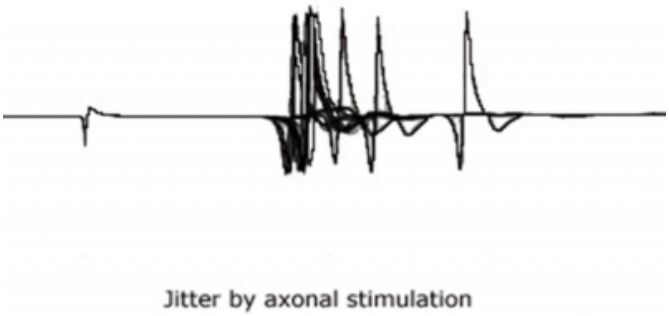
MATERIALS AND METHODS

Patients. Sixty-five patients with a definite diagnosis of MG, 38 men and 27 women, whose age ranged from 17 to 92 years (mean age, 62.6 ± 14.43) were studied. The diagnosis of MG was based on the history of illness, clinical findings, electrophysiological examination, response to anticholinesterase drugs, and abnormal acetylcholine receptor antibody titer. None of the patients showed symptoms or signs suggestive of other muscle involvement. In all cases, cranial magnetic resonance imaging was normal and systemic diseases such as hyperthyroidism were excluded. The results were compared with those of 14 patients with a definite diagnosis of myopathy with ocular involvement, 11 CPEO and 3 OMD cases with ages ranging between 54 and 71 years (63.2 ±5.2), 6 men and 8 women.

All subjects provided their informed consent to participate, and the protocol was approved by our institutional review board.

Methods. ST SFEMG was performed using technical recommendations and criteria defining normal results (published previously [3,4,5,6]) in 65 orbicularis oculi muscle.

Figure 1



Jitter by axonal stimulation

Special care was taken with some aspects of the ST SFEMG recordings. Spikes with MCD values lower than 5□s were not taken into account. Great care was taken with stimulation; one potential per recording (Figure); if there was more than one potential, they were done separately and supramaximal stimulation for the axons was maintained throughout the jitter measurements.

Between 20 and 40 different muscle potentials (MP) were sampled in each of the patients.

The equipment used was a Medelec – Oxford Synergy EMG machine (Oxford Instruments Medical, Surrey, UK).

RESULTS

MP in excess of 35□s (mean MCD of individual MP in normal subjects plus 3 SD in orbicularis oculi muscles) [6] ranged from 0 to 100% in OMG patients . The mean value was 41.2% (SD 24.2%). The mean MCD was 50.9□s (SD 25.9) and ranged from 11 to 119. Sixty-three (97%) of the 65 patients with OMG had 10% or more MP exceeding 35 µs, the mean MCD was increased above 23□s in 58 patients (89%).

MP in excess of 35□s in myopathic patients ranged from 0 to 23%. The mean value was 6.5% (SD 6.75%). The mean MCD was 21.36□s (SD 4.89) and ranged from 15 to 31. Three patients (21.4%) of the 14 myopathic had 10% or more MP exceeding 35 µs. The mean MCD was increased above 23□s in 5 of them (35.7%). Two (18.2%) of the 11 CPEO had 10% or more MP exceeding 35 □s, and the mean MCD was increased above 23□s in 4 CPEO (36.7%). One (33.3%) of the 3 OMD had 10% or more MP exceeding 35□s, and the mean MCD was increased above 23□s in one of the OMD (33.3%).

Figure 2

Table 1: Sensitivity/specificity at different cutoffs in OMG. Cutoff I: 10% individual MP >35?s. Cutoff II: 15% individual MP >35?s. Cutoff III: 20% individual MP >35?s. Cutoff IV: 25% individual MP >35?s. Cutoff I: mean MCD >23?s. Cutoff II: mean MCD >26?s. Cutoff III: mean MCD >29?s. Cutoff IV: mean MCD >32?s.

	Individual MP			Mean MCD	
	Sensitivity	**Specificity**		**Sensitivity**	**Specificity**
cutoff I	0.97	0.79		0.89	0.64
Cutoff II	0.95	0.86		0.83	0.79
cutoff III	0.89	0.93		0.74	0.93
cutoff IV	0.72	1		0.71	1

Using cutoff criteria I for abnormal ST SFEMG (table 1), the sensitivity in OMG was 0.97 (63/65), and the specificity was 0.79 (1-(3/14)) for individual MP, and for the mean MCD, the sensitivity was 0.89 (58/65) and the specificity was 0.64 (1-(5/14)) (Table 2a,b).

Figure 3

Table 2a: Percentage of muscle potentials (MP) >35□s at different cutoffs in ocular myasthenia (OMG) and myopathies (CPEO+OMD)

	10% MP>35µs	**15% MP>35µs**	**20% MP>35µs**	**25% MP>35µs**
	OMG	**OMG**	**OMG**	**OMG**
Exp	65	65	65	65
Ab	63	62	58	47
%	96,9	95,4	89,2	72,3
	CPEO+OMD	**CPEO+OMD**	**CPEO+OMD**	**CPEO+OMD**
Exp	14	14	14	14
Ab	3	2	1	0
%	21,4	14.3	7.1	0

Figure 4

Table 2b: Different mean MCD (MMCD) in OMG and myopathies

	MMCD>23 µs	**MMCD>26 µs**	**MMCD>29 µs**	**MMCD>32 µs**
	OMG	**OMG**	**OMG**	**OMG**
Exp	65	65	65	65
Ab	58	54	48	46
%	89,2	83	73,8	70,8
	CPEO+OMD	**CPEO+OMD**	**CPEO+OMD**	**CPEO+OMD**
Exp	14	14	14	14
Ab	5	3	1	0
%	35.7	21.4	7.1	0

Considering as abnormal 15% MP in excess of 35□s, sixty-two (95%) OMG had 15% or more MP exceeding 35 µs, and a mean MCD exceeding 26□s in 54 patients (83%).

Two myopathic patients (14.3%) had 15% or more MP exceeding 35 µs, and a mean MCD exceeding 26□s in three (21.4%).

Using cutoff criteria II for abnormal ST SFEMG (Table 1), the sensitivity was 0.95 (62/65) in OMG and the specificity was 0.86 (1-(2/14)) for individual MP, and for the mean MCD the sensitivity was 0.83 (54/65) and the specificity was 0.79 (1-(3/14)).

Considering as abnormal 20% MP in excess of 35□s, fifty-eight (89%) OMG had 20% or more MP exceeding 35 µs,

and a mean MCD exceeding 29μs in 48 patients (74%) (Table 2a,b).

One myopathic patient (7.1%) had 20% or more MP exceeding 35 μs, and a mean MCD exceeding 29μs in one (7.1%).

Using cutoff criteria III for abnormal ST SFEMG (Table 1), the sensitivity was 0.89 (58/65) in OMG and the specificity was 0.93 (1-(1/14)) for individual MP, and for the mean MCD 0.74 the sensitivity was (48/65) and the specificity was 0.93 (1-(1/14)).

Considering as abnormal 25% MP in excess of 35μs (Table 2a,b), forty-seven (72%) OMG had 25% or more MP exceeding 35 μs, and a mean MCD exceeding 32μs in 46 patients (71%).

No myopathic patients (0%) had 25% or more MP exceeding 35 μs, and a mean MCD exceeding 32μs in none of them (0%).

Using cutoff criteria IV for abnormal ST SFEMG (Table 1), the sensitivity was 0.72 (47/65) in OMG and the specificity was 1 (1-(0/14)) for individual MP, and for the mean MCD the sensitivity was 0.71 (46/65) and the specificity was 1 (1-(0/14)).

DISCUSSION

Several authors (Stalberg [7] , Sanders [8] , Cruz-Martinez [9] , Nogues [10]) have demonstrated the high degree of sensitivity of SFEMG for diagnosing MG, but they have also found alterations of jitter in different conditions such as myopathies and neuropathies, [1,2,10] although they all agree that these changes appear to be relatively minor. Discerning between MG and myopathies is not difficult. The jitter is often significantly high in MG and low in myopathies (<25% MP), as we observed in our study. Jitter can be increased in neuropathies if limb muscles are examined, but it is not usually increased in the OO, except for Guillain-Barré's syndrome and Bell's palsy.

Rouseev et al studied 41 patients with isolated weakness of the eyelids or extraocular muscles through voluntary single fiber electromayography [11] and concluded that the criteria of abnormality was >8/20 pairs (40%) with jitter >45μs, or a mean jitter of 20 pairs >50μs for a definite diagnosis of MG. In our study the criteria of abnormality was significantly lower, 25% MP with MCD >35μs or a mean MCD of >32μs, probably because of the technique used (ST SFEMG).

As to the diagnosis of OMG, we think it is more reliable to take into account the percentage of altered MP than the mean MCD, because the latter is less sensitive in the diagnosis of OMG and is altered slightly more in myopathies, especially in lower cutoff (I and II) criteria (Table 2b). We must also take into account that the average age of ocular myopathies, especially of the CEPO, is high (mean 63 years in our series) and that in normal elderly patients the mean MCD is higher than in young patients. [12]

We think it is better to diagnose myasthenia on the basis of the percentage of abnormal MP. According to this study, the diagnosis of possible myasthenia could be with 15% MP exceeding 35 μs, probable myasthenia with 20% MP exceeding 35 μs, and definite myasthenia with 25% or more of MP exceeding 35 μs.

In conclusion it is possible to distinguish between ocular myasthenia and myopathy by ST SFEMG. The cutoff criteria is at 25% MP with jitter exceeding 35μs. The case in not so clear when the jitter is less than 25% MP exceeding 35μs. If there is a significant clinical effect (ophthalmoparesis) and low jitter (<25% MP), myopathy is very likely. If there is little clinical involvement and 10% MP with jitter exceeding 35μs, the likelihood of myasthenia is 79%. If there is little clinical involvement and 15% MP with jitter exceeding 35μs, the likelihood of myasthenia is 86%. If there is little clinical involvement and 20% MP with jitter exceeding 35μs, the likelihood of myasthenia is 93%.

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