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ARTICLE

Stimulated jitter with concentric needle in 42 myasthenia gravis patients

Jitter estimulado obtido com agulha concêntrica em 42 pacientes com miastenia *gravis*

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ABSTRACT

Objective: To estimate jitter parameters in myasthenia gravis in stimulated *frontalis* and *extensor digitorum* muscles using the concentric needle electrode. **Methods:** Forty-two confirmed myasthenia gravis patients, being 22 males (aged 45.6±17.2 years-old) were studied. Jitter was expressed as the mean consecutive difference (MCD). **Results:** MCD in *extensor digitorum* was 61.6 µs (abnormal in 85.7%) and in *frontalis* 57.3 µs (abnormal in 88.1%). Outliers represented 90.5% for *extensor digitorum* and 88.1% for *frontalis*. At least one jitter parameter was abnormal in 90.5% of the combined studies. Acetylcholine receptor antibody was abnormal in 85.7% of the cases. **Conclusions:** Stimulated jitter recordings measured from muscles using concentric needle electrode can be used for myasthenia gravis diagnosis with high sensitivity. Extensive normative studies are still lacking and, therefore, borderline findings should be judged with great caution.

Key words: jitter, myasthenia gravis, concentric needle electrode, *Extensor Digitorum, Frontalis*, single-fiber electromyography.

RESUMO

Objetivo: Mensurar os valores do *jitter* em pacientes com miastenia *gravis* nos músculos *frontalis* e *extensor digitorum* pela técnica estimulada, utilizando-se eletrodo de agulha concêntrica. **Métodos:** Foram estudados 42 pacientes, sendo 22 homens (idade 45,6±17,2 anos), com miastenia *gravis* confirmada. O *jitter* foi expresso como a média das diferenças consecutivas (MDC). **Resultados:** A MDC para o *extensor digitorum* foi 61,6 µs (anormal em 85,7%) e para o *frontalis* 57,3 µs (anormal em 88,1%). *Outliers* representaram 90,5% para o *extensor digitorum* e 88,1% para o *frontalis*. Pelo menos um parâmetro do *jitter* foi anormal em 90,5% dos estudos combinados. Anticorpo receptor de acetilcolina estava anormal em 85,7% dos casos. **Conclusões:** *Jitter* estimulado mensurado por meio de eletrodo de agulha concêntrica pode ser utilizado para diagnóstico de miastenia *gravis* com elevada sensibilidade. Estudos normativos mais amplos ainda são necessários e, portanto, valores limítrofes devem ser avaliados com cautela.

Palavras-Chave: *jitter*, miastenia *gravis*, eletrodo de agulha concêntrico, *Extensor Digitorum, Frontalis*, eletromiografia de fibra única.

Neuromuscular junction (NMJ) disorders, such as myasthenia gravis (MG), can be evaluated by single-fiber electromyography (SFEMG), which is a technique developed in the early 1960s by Erik Stålberg and Jan Ekstedt in Sweden[1-3] for measuring neuromuscular jitter parameters. This parameter is the most useful one, together with impulse blocking, for electrodiagnosis of these conditions.

MG is an autoimmune disorder of the NMJ usually associated with antibodies to the postsynaptic acetylcholine receptor (AChR), however it can sometimes be associated with those to muscle-specific tyrosine kinase (MuSK), another protein at the NMJ.

The SFEMG jitter represents the variation in time intervals between pairs of single fiber action potentials (SFAPs) in the voluntarily activated technique or the time measured between stimulation pulse and SFAPs in the stimulated technique. With high jitter values, the neuromuscular transmission is so disturbed that occasional impulse blocking occurs.

The sensitivity of SFEMG has been found to be 88% in ocular MG and 95 to 100% in generalized MG[4]. Similarly, Benatar[5], in a systematic review, confirmed high specificity of SFEMG for the diagnosis of generalized MG. For ocular MG, the sensitivity was ranging from as low as 66% to as high as 98%. Mercelis and Merckaert[6] found a specificity of 97% and

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a sensitivity of 80% for ocular MG in stimulated-SFEMG for *orbicularis oculi* (OOc).

Disposable concentric needle electrodes (CNE) have been tested for measurements of jitter[7,8], due to the increasing concern for the transmission of infections. Some papers have presented normative data and diagnostic value of the test in MG[7-13]. Farrugia et al.[14] found no differences in mean jitter values for *extensor digitorum* (ED) and OOc muscles in 24 MG patients using both SFE and CNE. Papathanasiou and Zamba-Papanicolaou[15] found no significant differences between mean jitter measured by disposable or reusable SFE in 18 MG patients in the OOc muscle stimulation technique.

In order to improve recording selectivity and successfully use a CNE for jitter measurement, the low-frequency filter should typically be raised from 500 Hz to 1 or 2 kHz to suppress the activity from distant muscle fibers[7,8]. A filter setting with a 1 kHz high-pass filter, rather than higher, has been suggested for optimal quality[16]. This setting seems to provide good balance between the desired effect of low frequency suppression with a reasonably preserved original signal shape and an acceptable signal-to-noise ratio.

As the signals obtained with CNE recording do not always represent a single-fiber action potential, but rather a summation of many, the term jitter recording with CNE from apparent single fiber action potential (ASFAPs) is preferable, rather than SFEMG with CNE.

Jitter studies for MG electrodiagnosis using CNE are still incipient and relatively few of them have been done. In our previous report[17], we have used electrical stimulation for jitter measurements in 20 MG patients. The aim of this study was to evaluate in a larger cohort whether stimulated CNE in the ED and *frontalis* (FR) muscles in MG patients could give similar results as described with the SFE.

MATERIAL AND METHODS

Patients

Forty-two MG patients were studied between August 2009 and December 2011 for jitter measurement using CNE. All of them had confirmed MG based on the clinical picture (fluctuating weakness), unequivocal clinical response to edrophonium and/or pyridostigmine, positive acetylcholine receptor antibody (AChRAb) titer, and/or decrement of at least 10% on slow (from 2 to 3 Hz) repetitive nerve stimulation studies (RNS) from the first to fourth responses. None of them had previous jitter measurements. All patients stopped pyridostigmine at least 24 hours before testing. Cholinesterase inhibitors may mask abnormal jitter when the abnormality of neuromuscular transmission is mild[18].

The MG Group consisted of 22 men and 20 women with a mean age of 45.6±17.2 years-old (range, from 21 to 82). The mean time of MG symptoms was 75.6±72.6 months (range, from 2 to 288). The mean time since diagnosis was 55.5±61.7 months (range, from 1 to 246). The mean age of debut was 39.3 years-old (13 to 80).

Disease severity was determined at each clinic visit according to the MG Foundation of America (MGFA) clinical classification from I, ocular weakness, to II-V, generalized weakness[19]. In the worst period, it comprised: I (6 patients), IIb (5), IIIa (5), IIIb (4), IVa (11), IVb (2), and V (9). The classification profile at the time of CNE jitter measurement was I (8 patients), IIa (8), IIb (1), IIIa (10), IIIb (3), and IVa (3); nine patients were asymptomatic but eight of those were still taking pyridostigmine. Worst MGFA was considered for ocular (6 cases, 14.3%) and generalized (36 cases, 85.7%) distinctions; in all but one ocular case the time of symptoms was more than 24 months.

CNE jitter recordings and antibody measurements, either to AChRAb or MuSK, were studied at the same day. The most pronounced RNS decrements were taken from the files at any time from the MG diagnosis and included several nerve — muscle settings either distal, proximal, or facial.

Reference jitter parameters for CNE in the stimulated ED muscle were taken from our previously published data[20]: upper limit of normal (ULN), 97.5% (non-Gaussian), for mean consecutive difference (MCD)=22.6 μs and for outliers=30 μs. The results for the stimulated FR muscle were also taken from our previously published data[21] as follows: ULN, mean +2 SD (Gaussian), for MCD=21.5 μs and 97.5% (non-Gaussian) for outliers=30 μs.

Jitter recording

A KeypointNet electromyograph (Medtronic Skovlunde, Denmark) with built-in jitter software was used for recording and analyzing all patients, using a peak detection algorithm for time measurements. The recordings were performed using a CNE with a diameter of 0.30 mm and a recording area of 0.019 mm^2 (this CNE is the smallest "facial needle" from Medtronic/Alpine bioMed, Denmark).

Stimulation technique for Frontalis muscle

Stimulation was performed with a bar electrode of the facial nerve temporal branch. Its parameters were 10 Hz frequency using rectangular pulses of 0.10 ms duration. The intensity was adjusted to produce a slight visible twitch of the FR muscle. In general, this could be achieved at about 5 to 7 mA. The recording position and stimulus intensity were adjusted to provide a minimum number of spikes in the response. An extremely important part of this method is to assure that each spike accepted for analysis has supramaximal stimulation. If a spike showed increased jitter, the intensity was

raised, ever so little. In case of submaximal stimulation, the jitter decreased, otherwise it was unchanged. To be accepted for measurements, the ASFAPs should have a fast rising phase without notches or shoulders, be constant at consecutive discharges, i.e., have parallel rising phases seen on superimpositions of the signals separated by more than 150 µs, and have a well-defined peak.

Jitter was expressed as the mean of MCD values. On average, 31.6 potentials were analyzed per patient. For each jitter analysis, a minimum of 50, and ideally 100, consecutive traces was recorded. The filter settings were from 1 to 10 kHz. The Keypoint software also calculated the mean peak latency.

Stimulation technique for *extensor digitorum* muscle

In this muscle, small nerve branches cannot be reached outside it, therefore intramuscular axonal stimulation must be used. Stimulation was made with a disposable monopolar needle electrode, 15x0.35 mm, 28 G (Medtronic, Denmark) inserted near the motor end-plate zone, between the proximal and middle thirds of ED. A disposable scalp needle electrode, 10x0.30 mm, 30 G (Medtronic, Denmark), was used as the anode and was inserted subcutaneously about 2 cm away from the cathode. Stimulation parameters were 10 Hz using rectangular pulses of 0.04 ms duration. In general, this could be achieved at about 2 to 6 mA. As described, special and time-consuming adjustments must be done to assure that the spike under study be supramaximally stimulated. Jitter was expressed as the mean of MCD. On average, 28.8 potentials were analyzed per patient. Other parameters were similar to the FR muscle stimulation.

Abnormal jitter parameters

Stimulation jitter was considered abnormal, after technical one due to submaximal stimulation was excluded, if: the mean MCD was above the ULN; and equal or more than 10% of individual jitter values for the ASFAPs for each study were above the ULN for outliers.

Ethics

The study was approved by the Ethics Committee, and informed consent was obtained from each subject.

RESULTS

Patients

The AChRAb was positive in 36 cases (85.7%). The worst MGFA classification in the six negative cases was: I (two), IIb (one), IIIa (two), and IVa (one). The mean abnormal AChRAb value was 11.62±8.14 nmol/L (range from 0.18 to 31.3). Antibodies to MuSK were negative in all 6 AChRAb negative MG patients. Antibodies to striated muscle tissue were found in 3 out of 41 MG patients (7.3%); in one of them, a thymoma was found. In the retrospective analysis, the following number of RNS studies were: ulnar-*Abductor Digiti Minimi* in 37/42, median-*Abductor Pollicis Brevis* in 24/42, accessory-*Trapezius* in 10/42, facial-OOc in 7/42, facial-*Nasalis* in 7/42, facial-*Orbicularis Oris* in 4/42, radial-*Anconeus* in 3/20, and fibular-*Extensor Digitorum Brevis* in 2/42 patients. Abnormal decrement was found in 37 from 42 patients (88.1%) in any time of the disease. Nine patients were asymptomatic at the time of jitter and antibody studies, however only one was completely drug free (remission). Thymectomy was performed in 16 from 42 patients (38.1%), and thymoma was found in five of them. Thirty-eight patients (90.5%) were on pyridostigmine from 60 to 420 mg a day. Twenty patients (47.6%) were using prednisone; 12 from 5 to 40 mg every other day, and 8 from 2.5 to 60 mg every day. Five participants (11.9%) were taking azathioprine from 100 to 150 mg every day.

Jitter parameters in *extensor digitorum*

The total number of ASFAPs analyzed was 1,209, varying from 13 to 35 for each patient except in one case in whom only five ASFAPs with very high jitter were obtained. The mean MCD was 61.6±43.0 µs (from 12.4 to 221). Abnormality was found in 85.7%, and 36 from 42 patients had a MCD greater than 22.6 µs.

Using the criterion for outliers, abnormality was found in 90.5% of the patients, meaning that 38 from 42 patients had at least 10% of ASFAPs with a MCD greater than 30 µs. In 4 of 42 patients, both MCD and outliers still remained normal, therefore the abnormality in any was 90.5%. The mean latency between stimulus and each spike was 6.9±3.0 ms (1.34 to 19.5).

There were no hematomas in the patients studied; the test duration was about 40 to 60 minutes, and it was reported to be more painful than in FR, since more needle insertions and position corrections (stimulation and recording) were necessary.

Jitter parameters in *frontalis*

The total number of ASFAPs analyzed was 1,327, varying from 25 to 46 for each patient. The mean MCD was 57.3±27.3 µs (from 12.3 to 124). Abnormality was found in 88.1% of the patients, meaning that 37 from 42 patients reached a MCD greater than 21.5 µs.

Abnormality based on outliers was found in 88.1% of the patients, meaning that 37 from 42 patients had at least 10% of ASFAPs with a MCD greater than 30 µs. In 5 of the 42 (same patients), both MCD and outliers were normal, so the abnormality in any remained 88.1%. The mean latency between stimulus and each spike was 9.1±3.5 ms (2.3 to 19.3).

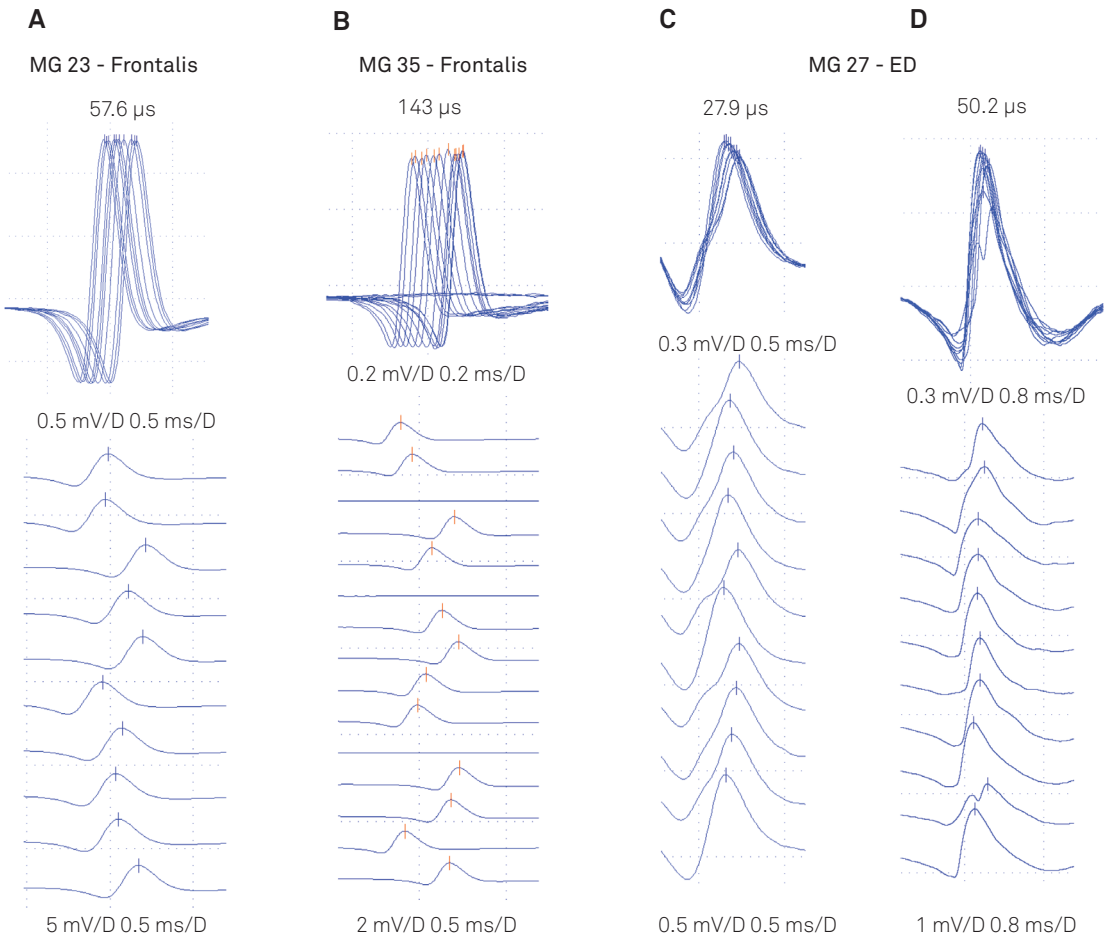

Figure. Stimulation concentric needle jitter in myasthenia gravis cases. (A and B): highly abnormal jitter (57.6 and 143 µs) with impulse blocking on B. Notice fast rising phase spikes without notches or shoulders and well-defined peak without shape changes at consecutive discharges. (C and D): false jitter (27.9 and 50.2 µs). Note summation with notches, shoulders, and nonparallel rising phases, not suitable for analysis. For all spikes shown in the figure, the stimulation strength was checked to be supramaximal.

Some recordings from ED and FR, with abnormal jitter and impulse blocking, are shown on Figure. Detailed results from jitter parameters, AChRAb, RNS, and MGFA-w class are provided in Table 1.

Comparisons of jitter abnormalities between ED and FR are shown in Table 2. When ED or FR were together considered, abnormality was found in 90.5% either as MCD or outliers.

Jitter parameters in ocular *versus* generalized cases

In spite of the small cohort, comparison between ocular (worst MGFA class I, 6 patients) and generalized MG (worst MGFA class II to V, 36 patients) was made for the same parameters (Table 3). Follow-up for ocular form (2–93 months) revealed that three patients (50%) considered themselves asymptomatic (all taking pyridostigmine), and the remaining three (50%) were unchanged. Follow-up for generalized forms (from 2 to 288 months) revealed that 6 patients (16.6%) considered themselves asymptomatic (all but one taking pyridostigmine), 4 (11.1%) were unchanged, 1 (2.8%) was worsened, and the remaining 25 (69.4%) were improved.

DISCUSSION

We studied a small and heterogeneous MG cohort regarding age, MGFA class, time of disease, thymus pathology, use of acetylcholinesterase inhibitors, and ongoing immunosuppressive treatment. Patients selected for jitter analysis and AChRAb titer determination only included confirmed MG cases under treatment for months or years from diagnosis. Nine patients were asymptomatic but only one was completely free from medication. This study was designed to study the general feasibility of stimulation CNE jitter analysis in MG, and the results do not represent sensitivity and specificity of the technique.

Jitter was found abnormal in 90.5% of the subjects in either or both ED and FR in all patients regardless ocular or generalized, similar to the 90% in our previous article[17],

and also close to results described by others[18] that found abnormality with voluntary SFEMG in either or both ED or FR in 92%.

The analysis of the four patients with normal jitter parameters showed one case with both RNS and AChRAb normal, one with AChRAb abnormal and RNS normal, one with both RNS and AChRAb abnormal, and one with RNS abnormal and AChRAb normal.

The AChRAb titer was abnormal in 66.7% for the ocular MG (mean value of 3.49 nmol/L) and in 88.8% for the generalized MG (mean value of 12.63 nmol/L). In a previous similar study with 20 MG patients[17], the present authors found 75.0 and 87.5%, respectively. In larger published reports, the AChR antibody titer was increased in 55% of those with ocular MG and in 80% of those with generalized MG[18].

RNS was abnormal in 66.7% for ocular MG and in 94.4% for generalized MG cases. An abnormal decrement was found in muscles described in 75% of patients with generalized MG, and in 50% of those with ocular MG[18]. The higher percentage of RNS abnormality in this and previously study[17] compared to others[18] gives an impression of the general severity of our patients; also, it should be emphasized that RNS was collected from the files and sometimes were done more than three times over the disease duration (months or years).

Patients with ocular MG had abnormal mean MCD in 66.7% for ED and 83.3% for FR. Outliers were 83.3% in both ED and FR. In our previous study[17] with 20 MG cases, we found 75% for both parameters and muscles. Sanders and Howard[4] found MCD abnormality in 63% ED and in 88% if any of ED and facial (FR, OOc or *orbicularis oris*) muscles were tested close to our present results.

Patients with generalized MG had abnormal mean MCD in 88.9%, both ED or FR. Outliers were 91.7% for ED and 88.9% for FR. In our previous study[17] with 20 MG cases, we found 93.7% when both ED and FR were considered. Others have found abnormality ranging from 81.4 to 95% in ED[18]. Again, the results found here are quite similar to other previously described studies.

Impulse blocking was found in 25.8% of ED and 25.3% of FR in generalized MG and in 16% for ED and in 27.1% for FR in ocular MG. Overall, impulse blocking was found in 24.3% for ED and 25.6% for FR.

Impulse blocking in MG cases after therapy (similar to this study) was found in 5.2% (ED) and 20.6% (FR) for ocular and in 9.9 to 38.3% (ED) and 20.6 to 47.6% (FR) for generalized forms[18]. In our previous study[17] with 20 MG cases, it was found 21.6% (ED) and 23.3% (FR) for ocular form, and 31% (ED) and 38.3% (FR) for generalized ones. We found much more impulse blocking in ED for ocular form both in this and in the previous paper. This could indicate that patients may have had unsuspected generalized symptoms during the disease evolution (months or years).

Table 1. Summary of concentric needle jitter parameters from 42 myasthenia gravis cases in stimulation *extensor digitorum* (ED) and *frontalis* (FR) techniques. Muscle specific tyrosine kinase antibody (MuSK) was negative in all AChRAb negative cases.

Case	MCD		Outliers		AChRAb	RNS-w	MGFA-w
	ED	FR	ED*	FR*	nmol/L	ab ≥10%	Class
1	24.4	23.6	16.7	23.3	<0.10	n	I
2	30.7	112	50	96.7	16.5	ab	IIb
3	29.2	50.1	36.7	96.7	15.5	ab	V
4	21.5	85.6	10	93.3	7.35	ab	IVb
5	48.8	38.5	64.3	60.7	6.32	ab	I
6	104	124	72.2	100	15.7	ab	IIIa
7	29.6	114	40	100	11.61	ab	IIb
8	23.6	14.4	10	0	<0.10	ab	IIIa
9	78.9	75.1	90.6	90.6	6.48	ab	IVa
10	35.6	62.7	55.2	94.1	3.82	ab	IIIb
11	90.2	65.2	96	97.1	4.98	ab	IIIb
12	64.9	80.6	76.7	85.3	3.44	ab	I
13	17.6	16.7	8.8	9.1	1.53	n	I
14	79.2	68.6	89.7	87.5	18.5	ab	IIb
15	12.4	12.3	0	0	<0.10	n	IIb
16	79.8	74.2	96.8	88.2	15.8	ab	V
17	221	54.6	100	83.9	16.6	ab	IVa
18	39	57.7	66.7	81.8	15.4	n	IIIb
19	55.2	58.3	78.6	79.4	3.1	ab	IIIa
20	144	77.6	84.6	93.9	22.3	ab	IVa
21	79.3	91.2	91.2	97.8	2.22	ab	V
22	157	88	100	96.9	10.8	ab	V
23	121	57.9	93.7	83.3	0.18	ab	V
24	34.4	23.3	48.6	18.2	1.47	ab	IVa
25	45	54.6	63.6	67.5	2.7	ab	I
26	22	15.5	3.3	3.3	12.5	ab	IVa
27	40.6	45.5	67.6	87.1	6.8	ab	V
28	40.7	64.3	63.6	83.3	26.0	ab	IIIa
29	95.2	46.5	100	63.3	28.0	ab	IVa
30	75.4	50.1	96.7	63.3	31.3	ab	IVb
31	31.6	38.8	45.5	63.3	16	ab	IIb
32	57.9	33.2	60	46.7	<0.10	ab	IIIa
33	28.1	29.8	26.7	26.7	19.5	ab	V
34	17	15.7	0	3	<0.10	ab	IVa
35	22.3	77.9	23.3	77.8	<0.10	ab	I
36	74.6	54	81.2	78.8	12.7	ab	IVa
37	70.2	70.8	90	90.9	17.9	n	V
38	60.4	74.8	70	85.2	2.91	ab	IVa
39	43.7	43.7	65.6	59.4	20.6	ab	IIIb
40	116	59.9	100	90	8.54	ab	IVa
41	56.4	55.3	75	76	6.56	ab	V
42	67.6	45.1	86.7	66.7	6.59	ab	IVa
Limit	22.6 µs	21.5 µs	30 µs	30 µs			
Ab	85.7%	88.1%	90.5%	88.1%	85.7%	88.0%	

MCD: mean consecutive difference (microseconds); AChRAb: acetylcholine receptor antibody; RNS-w: worst repetitive nerve stimulation since diagnosis; MGFA-w: Myasthenia Gravis Foundation Association classification, worst; ab: abnormal; n: normal; *percentage above limit (abnormal ≥10%).

Table 2. Comparison of concentric needle electrodes jitter parameters in stimulated *extensor digitorum* (ED) and *frontalis* (FR) in 42 myasthenia gravis patients.

Muscle	MCD				ASFAP			
	n	Mean (µs)	Range	ab* (%)	n	Mean (µs)	Range	ab** (%)
ED	42	61.6	12.4–221 µs	85.7	1,209	55.5	6.3–299 µs	90.5
FR	42	57.3	12.3–124 µs	88.1	1,327	48.4	6.6–268 µs	88.1
ED or FR				90.5				90.5

MCD: mean consecutive difference; ASFAP: apparent single fiber action potentials; n: number; ab: abnormal; *>22.6 µs (ED) and 21.5 µs (FR); **outliers, at least 10% >30 µs (ED and FR).

Table 3. Some parameters comparing generalized to ocular myasthenia gravis.

Parameters	Generalized	Abnormal (%)	Ocular	Abnormal (%)
n	36		6	–
Age at debut	43.8 (21–82)		56.7 (27–78)	–
Symptoms duration	82.4 months (2–288)		34.3 months (2–93)	–
Mean MCD ED*	65.6 µs (12.4–221)	88.9	37.2 µs (17.6–64.9)	66.7
Mean MCD FR*	58.7 µs (12.3–124)	88.9	48.7 µs (16.7–80.6)	83.3
Outliers ED*		91.7	–	83.3
Outliers FR		88.9	–	83.3
Some blocking ED*		25.8	–	16.0
Some blocking FR*		25.3	–	27.1
AChRAb nmol/L*	12.63 (0.18–31.3)	88.8	3.49 (1.53–6.32)	66.7
RNS (1-4)**	–	94.4	–	66.7
Thymectomy**	16/36 (44.4%)		0/36 (0%)	–

MCD: mean consecutive difference; ED: *extensor digitorum*; FR: *frontalis*; AChRAb: acetylcholine receptor antibody; RNS: repetitive nerve conduction studies; *present; **any time.

In voluntary jitter, the percentage of recordings with blocking may be higher compared to stimulation jitter since the fact that the block in one of two fibers may be counted as a blocking pair.

In the present study, abnormal percentage of outliers was greater (ED) or equal (FR) than abnormal mean MCD, similar to our previous study[17]. The MCD value is usually a more sensitive index of abnormality than the number of outliers for voluntary SFEMG[18]. This disparity may be because the jitter in voluntary recording is obtained with two motor end plates. If one has low normal jitter, and the other barely above normal values for individual neuromuscular junctions, the combined jitter of the two would be normal.

Measuring jitter and impulse blocking is technically easier in FR than in ED, and this is due to small motor units in FR. Spikes are more separated and easier to record without riding, notches, and shoulders in FR.

Stimulation technique is quite dependent on the physician's ability to avoid insufficient stimulation that will give a false large jitter. Therefore, in order to be accepted for analysis, the spike under study must fulfill the ASFAP criteria and be checked for supramaximal stimulation.

Individual spikes obtained with CNE are not always obtained from single-muscle fibers[16,22], but represent summation of more than one SFAP. For the stimulation technique, the risk of summation is even worse, since many axons are often stimulated.

One must be careful to obtain spikes with a fast rising phase without notches or shoulders, parallel rising phases on consecutive discharges with spikes separated by more than 150 µs. The peak should be well-defined without shape changes on consecutive discharges. The recordings should show clear spikes for reliable increased jitter and impulse blocking analysis.

In CNE jitter studies, we can get SFAPs and ASFAPs (summated), and therefore separate normative data should be collected for this kind of needle. We have done it in some previous reports for ED and OOc muscles, both for voluntary and stimulated techniques and FR stimulated[10,20-24]. A few studies that have compared jitter values from SFEMG and from CNE in healthy controls and patients with MG reported a good correlation between results[6-8].

After some previous reports on stimulation jitter analysis with CNE in healthy subjects[20,21,24] and patients with MG[17], we have noticed that in FR the individual single fiber signals may be shorter and definitely more separated in time from each other compared to ED. This technique can be applied in pediatric patients[25] after collection of reference values for younger groups. Large limb muscles like ED are less recommended for stimulation studies.

The present study confirms that CNE can be used for jitter analysis and impulse blocking in definite MG patients. However, larger studies should be done for

sensitivity and specificity in suspected cases. We found a very high rate of abnormality for MCD (85.7% for ED and 88.1% for FR), outliers (90.5% for ED and 88.1% for FR), and blocking (24.3% for ED and 25.6% for FR) in this small cohort of 42 proven MG cases. This is similar to what has been reported in larger series with SFEMG. In spite of encouraging results for abnormal jitter detection, some caution must be maintained before a study using CNE is declared abnormal or normal in situations of borderline jitter values. Technically, jitter measurement was more easily obtained, less painful, and less time-consuming for FR than ED.

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