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Repetitive ocular vestibular evoked myogenic potentials in myasthenia gravis

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Abstract: **OBJECTIVE** To validate the repetitive ocular vestibular evoked myogenic potentials (RoVEMP) test for diagnostic use in myasthenia gravis (MG) and to investigate its value in diagnostically challenging subgroups. **METHODS** The RoVEMP test was performed in 92 patients with MG, 22 healthy controls, 33 patients with a neuromuscular disease other than MG (neuromuscular controls), 4 patients with Lambert-Eaton myasthenic syndrome, and 2 patients with congenital myasthenic syndrome. **RESULTS** Mean decrement was significantly higher in patients with MG ($28.4\% \pm 32.2$) than in healthy controls ($3.2\% \pm 13.9$; $p < 0.001$) or neuromuscular controls ($3.8\% \pm 26.9$; $p < 0.001$). With neuromuscular controls as reference, a cutoff of 14.3% resulted in a sensitivity of 67% and a specificity of 82%. The sensitivity of the RoVEMP test was 80% in ocular MG and 63% in generalized MG. The RoVEMP test was positive in 6 of 7 patients with seronegative MG (SNMG) with isolated ocular weakness. Of 10 patients with SNMG with negative repetitive nerve stimulation (RNS) results, 73% had an abnormal RoVEMP test. The magnitude of decrement was correlated with the time since the last intake of pyridostigmine ($B = 5.40$; $p = 0.019$). **CONCLUSIONS** The RoVEMP test is a new neurophysiologic test that, in contrast to RNS and single-fiber EMG, is able to measure neuromuscular transmission of extraocular muscles, which are the most affected muscles in MG. Especially in diagnostically challenging patients with negative antibody tests, negative RNS results, and isolated ocular muscle weakness, the RoVEMP test has a clear added value in supporting the diagnosis of MG. **CLASSIFICATION OF EVIDENCE** This study provides Class III evidence that RoVEMP distinguishes MG from other neuromuscular diseases.

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Repetitive ocular vestibular evoked myogenic potentials in myasthenia gravis

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Abstract

Objective

To validate the repetitive ocular vestibular evoked myogenic potentials (RoVEMP) test for diagnostic use in myasthenia gravis (MG) and to investigate its value in diagnostically challenging subgroups.

Methods

The RoVEMP test was performed in 92 MG patients, 22 healthy controls, 33 patients with a neuromuscular disease other than MG (neuromuscular controls), 4 Lambert-Eaton myasthenic syndrome patients and 2 congenital myasthenic syndrome patients.

Results

Mean decrement was significantly higher in MG patients ($28.4\% \pm 32.2$) than in healthy controls ($3.2\% \pm 13.9$; $p < 0.001$) or neuromuscular controls ($3.8\% \pm 26.9$; $p < 0.001$). With neuromuscular controls as reference, a cut-off of $\geq 14.3\%$ resulted in a sensitivity of 67% and a specificity of 82%. The sensitivity of the RoVEMP test was 80% in ocular MG and 63% in generalized MG. The RoVEMP test was positive in 6 out of 7 seronegative MG (SNMG) patients with isolated ocular weakness. Of 10 SNMG patients with negative repetitive nerve stimulation (RNS) results, 73% had an abnormal RoVEMP test. Magnitude of decrement was correlated with the time since the last intake of pyridostigmine ($B = 5.40$, $p = 0.019$).

Conclusions

The RoVEMP test is a new neurophysiological test that, in contrast to RNS and single-fiber EMG, is able to measure neuromuscular transmission of EOMs, which are the most affected

muscles in MG. Especially in diagnostically challenging patients with negative antibody tests, negative RNS results and isolated ocular muscle weakness, the RoVEMP test has a clear added value in supporting the diagnosis of MG.

Classification of Evidence:

This study provides Class III evidence that RoVEMP distinguishes MG from other neuromuscular diseases.

Introduction

Myasthenia gravis (MG) is an auto-immune disease characterized by fatigable muscle weakness. Ocular muscles are involved at the onset of the disease in approximately 85% of patients, causing diplopia and ptosis.^{1, 2} Early recognition and treatment are of great importance for patients' quality of life.³

Current neurophysiological tests have a major limitation: the most commonly affect muscles, the extra-ocular muscles (EOMs), cannot be measured. Moreover, repetitive nerve stimulation (RNS) has a low sensitivity (0.29) in the patient subgroup in which the diagnosis is most challenging: ocular MG (OMG) patients.⁴ Single-fiber EMG (SFEMG) has a higher sensitivity in OMG (62-97%)⁴, however it requires a skilled neurophysiologist, is time-consuming and operator-dependent.⁵

Measurement of fatigability in the EOMs by using ocular vestibular evoked myogenic potentials (oVEMP) might be a solution to this diagnostic problem (Fig 2).⁶⁻¹⁰ Valko et al. observed a decrement in the n2-p2 amplitude by applying a train of ten repetitive oVEMPs in MG patients, analogous to the decrement observed in RNS.⁶ We will refer to this technique as the Repetitive oVEMP (RoVEMP) test.

We aim to validate and further investigate the diagnostic yield of RoVEMP compared with a control group of patients with a neuromuscular disease other than MG (neuromuscular controls) as well a group of healthy controls. We also analyzed the effect of pyridostigmine use on RoVEMP results. Furthermore, we included a large cohort of MG patients to analyze the sensitivity and specificity of the RoVEMP in diagnostically challenging subgroups (OMG and SNMG patients).

Methods

Primary research question

Does RoVEMP distinguish MG from other neuromuscular diseases in a prospective case control study (Class III evidence)?

Participants

We included a convenience cohort of MG patients who visited the outpatient clinic of Leiden University Medical Center (LUMC) between 2018 and 2019 (fig. 1). The minimum sample sizes for the groups was predetermined based on power calculations with an expected AUC of 0.8. In addition, we included patients with Lambert-Eaton myasthenic syndrome (LEMS) and genetically confirmed congenital myasthenic syndrome (CMS). We also included a group of healthy controls and a group of patients with a neuromuscular disease other than MG (neuromuscular controls). We considered the following diseases: inclusion-body myositis (IBM), facioscapulohumeral muscular dystrophy (FSHD), myotonic dystrophy (DM), myopathy, oculopharyngeal muscular dystrophy (OPMD), chronic inflammatory demyelinating polyneuropathy (CIDP), cranial nerve palsies (III, IV, VI), mechanical diplopia, and Graves' ophthalmopathy (GO). Patients with GO were included from the Ophthalmology Department of the LUMC. GO patients form an important control group as the ocular symptoms in these patients may resemble those of OMG and may cause diagnostic confusion and delay.¹¹⁻¹⁶ MG patients who were being treated with pyridostigmine were not asked to refrain from taking pyridostigmine before the RoVEMP test. All participants were examined for the presence of diplopia prior to RoVEMP testing. We recorded the time between the RoVEMP test and the last intake of pyridostigmine. We retrieved all relevant clinical information or RNS results of MG patients and neuromuscular control patients from their patient records.

The diagnosis of MG was based on a combination of clinically confirmed fluctuating muscle weakness and the presence of serum autoantibodies to the acetylcholine receptor (AChR) or muscle-specific kinase (MuSK). Seronegative myasthenia gravis (SNMG) was defined as fatigable muscle weakness in combination with abnormal decrement (at least 10%) during RNS, increased jitter in SFEMG testing or a positive response to an acetylcholinesterase inhibitor.¹⁷

Standard protocol approvals, registrations, and patient consents

The Medical Ethics Review Committee of the Leiden University Medical Center approved the study and its use of human subjects. All patients provided informed, written consent prior to study participation.

RoVEMP test

In collaboration with the group of Valko et al., we reproduced the measurement setup to perform the RoVEMP test. The oVEMP is a multiphasic wave with the first peak at a latency of 10 milliseconds after stimulation. The placement of the surface electrodes was the same as described in the article of Valko et al., with two surface electrodes directly under each eye to record myogenic activity from the inferior oblique muscles and a ground electrode on the forehead.⁶ We used a stimulation frequency of 20 Hz and applied vibrations in trains of 10 stimuli with a handheld mini-shaker (type 4810, manufacturer: Brüel & Kjær) to the skull. We repeated these trains 40 times to improve the signal-to-noise ratio. The signals were sampled with a rate of 2000 per second and saved using Nim Eclipse software and a Nim Eclipse recording device (Medtronic Xomed, inc). The RoVEMP tests were performed by two physicians (RdM and KK).

Signal analysis

The recorded signals were analyzed for outliers using a median absolute deviation algorithm. The median absolute deviation of the signal between the stimulus artifacts is a measure for baseline fluctuations and other high voltage artifacts, which are most commonly caused by eye-blinking during the measurement. Measurements with a median absolute deviation higher or lower than two standard deviations from the mean were considered outliers and were excluded. The remaining recorded signals were averaged. The average was high-pass filtered at 20Hz with a butterworth filter to correct for additional baseline fluctuations.

Decrement calculation

After averaging all measurements, the peaks and troughs of the oVEMP signal were analyzed and the amplitude of the oVEMP response was calculated using an in-house developed Matlab script (MATLAB 2016a, The Mathworks of Natick, Massachusetts, USA). Per measurement all peaks and troughs were automatically analyzed (thresholding using a minimal peak prominence of 0.8μV) and the correct peaks and troughs were automatically selected, using subject-specific latency values based on visual inspection of the averaged signals. The amplitudes from all second negative peaks (n2) to the second positive peaks (p2) were calculated. The N2P2 amplitude was used to calculate decrement as this ‘reference’ (instead of N1P1 for example) was shown to result in the highest diagnostic yield. As a measure of neuromuscular transmission, the RoVEMP decrement was calculated for each eye as described previously by Valko et al. using the following formula:

$$\text{Decrement} = 100\% - \frac{\text{Average of } n2p2\text{Amplitude}_{5th-9th}}{n2p2\text{Amplitude}_{2nd}} * 100\%$$

Of the two decrements found in the two eyes of the subject, the highest was considered as the RoVEMP decrement in that subject. An additional analysis was performed using the lowest decrement for each subject.

Statistical Analysis

For comparison of decrement and other numerical variables between groups, we used an unpaired t-test. To compare categorical variables between groups we used a chi-square test. To determine optimal oVEMP cut-off values, we created receiver operating characteristics (ROC) curves. Data are presented as number of patients (%) for categorical variables and as mean $\pm$ SD for continuous variables. P-values < 0.05 were considered significant. Statistical analyses were performed using SPSS version 23 (IBM Corp., Armonk, NY).

Data availability

Anonymized data and the study protocol presented in this article will be made available at the request of a qualified investigator. Requests should be made to dr. Tannemaat (m.r.tannemaat@lumc.nl).

Results

Participant characteristics

We included 92 MG patients, 22 healthy controls, 33 neuromuscular controls, 4 LEMS patients and 2 CMS patients. Two MG patients had a follow-up visit at which the RoVEMP test was performed for a second time. The mean age and percentage of males was comparable between MG patients (57 years $\pm$ 18; 48%), healthy controls (51 years $\pm$ 14; 46%) and neuromuscular controls (58 years $\pm$ 12; 46%). Diplopia upon examination prior to RoVEMP

testing was found in 58% of MG patients and 67% of neuromuscular controls. Thirty-five MG patients had used pyridostigmine $\leq 4,5$ hours before the RoVEMP test. The RoVEMP results of one MG patient, 2 healthy controls and 2 neuromuscular controls were not analyzable due to excessive blink artifacts and were excluded. In one neuromuscular control (DM), increment was truncated at 100%. None of the participants reported major discomfort due to the RoVEMP test and all patients that had experienced RNS or SFEMG before, reported that the RoVEMP test was less unpleasant. Demographic and clinical baseline characteristics of all MG patients subdivided by antibody status are shown in table 1.

oVEMP decrement in MG and other groups

Mean decrement was significantly higher in MG patients ($28.4\% \pm 32.2$) than in healthy controls ($3.2\% \pm 13.9$; $p < 0.001$) and neuromuscular controls ($3.8\% \pm 26.9$; $p < 0.001$) (fig 3A). Mean decrement in LEMS patients ($41.8\% \pm 40.4$) and CMS patients ($29.1\% \pm 16.2$) was elevated, but due to the low numbers in these groups, statistical comparisons were not feasible. The results in neuromuscular controls shown for each disease separately are shown in figure 6. Using ROC analysis we identified optimal decrement cut-offs for distinguishing between MG patients and healthy controls ($\geq 11.3\%$; sensitivity 71% [95% CI: 61-79], specificity 86% [95% CI: 67-95]; area under the curve (AUC) 0.78 [95% CI: 0.69-0.86]), and between MG patients and neuromuscular controls ($\geq 14.3\%$; sensitivity 67% [95% CI: 57-76], specificity 82% [95% CI: 66-91]; AUC 0.74 [95% CI: 0.65-0.83]) (fig 4A&B). The positive and negative predictive values are 96% (95% confidence interval (CI) = 88 – 98) in the former ROC analysis and 41% (95% CI = 33 – 50) in the latter. The positive and negative predictive values in the latter ROC analysis are 91% (95% CI = 83 – 96) and 47% (95% CI = 39 – 56), respectively. When a cut-off value of 11.3% is applied to the measurement with the

lowest decrement in each subject, specificity increases to 91%, but sensitivity is reduced to 54% comparing healthy controls to MG patients, as described previously⁶.

RoVEMP decrement in MG subgroups

Mean decrement was comparable in AChR ($27.5\% \pm 33.0$), MuSK ($29.7\% \pm 42.2$) and SNMG patients ($32.6\% \pm 23.2$). The mean decrement in OMG ($32.1\% \pm 23.7$) and GMG patients ($27.1\% \pm 34.9$) was also comparable (fig 3B). With a cut-off of $\geq 11.3\%$, a non-significant trend towards a higher occurrence of an abnormal RoVEMP test was found in OMG (84%) compared to GMG patients (66%, $p = 0.086$). With a cut-off of $\geq 14.3\%$, a similar difference was found (80% vs. 63%, $p = 0.115$). The RoVEMP was abnormal in similar frequencies in AChR, MuSK or SNMG patients (table 1). In 6 out of 7 SNMG patients with isolated ocular weakness the RoVEMP test was clearly abnormal with decrements above 22%.

Comparison RoVEMP and RNS

Abnormal RNS findings (decrement $\geq 10\%$) occurred significantly more often in seropositive MG patients (47%) than in SNMG (9%; $p = 0.019$) patients and more often in GMG (51%) than in OMG patients (16%; $p = 0.008$). The percentage of patients with an abnormal RoVEMP test and a negative RNS was significantly higher in SNMG patients (73%) compared to seropositive (AChR or MuSK) MG patients (40%; $p = 0.047$). These results were identical with cut-off values $\geq 11.3\%$ and $\geq 14.3\%$.

Pyridostigmine effect on RoVEMP decrement

Mean decrement was significantly higher in MG patients who did not use pyridostigmine before the RoVEMP test ($33.2\% \pm 35.4$), compared to MG patients who did use pyridostigmine $\leq 4,5$ hours before the RoVEMP test ($19.8\% \pm 23.7$; $p = 0.033$) (fig 5A). However, the percentage of patients with a RoVEMP decrement $\geq 11.3\%$ was similar in both groups (73% and 67%, respectively; $p = 0.530$). With a cut-off value of $\geq 14.3\%$, a non-significant trend towards a higher occurrence of an abnormal RoVEMP test was found in the former (73%) compared to the latter group (58%, $p = 0.133$). Magnitude of decrement was correlated with the time since the last intake of pyridostigmine ($B = 5.40$, $p = 0.019$) (fig 5B). In the two patients with a follow-up visit, RoVEMP decrements were lower on the day in which pyridostigmine was taken an hour before the test (29% and 24%) than on the day in which the patients did not take pyridostigmine prior to the test (66% and 45%).

Discussion

In this study, we showed that the RoVEMP test accurately differentiates between MG and patients with other neuromuscular diseases as well as healthy controls. Interestingly, the RoVEMP test had a high sensitivity in the diagnostically most challenging myasthenia subgroup: ocular SNMG patients. Six out of 7 of these patients had a positive RoVEMP test.

Valko et al. reported an optimal decrement cut-off of $\geq 15.2\%$ in a cohort of 13 ocular and 14 generalized MG patients compared to a healthy control group ($n = 28$) and found a sensitivity of 89% and a specificity of 64%. The overall sensitivity of the RoVEMP test compared to healthy controls found in our study was somewhat lower (71%). This is probably due to the fact that our cohort contained a lower percentage of ocular MG patients (27% (25/92)) than

the cohort of Valko et al. (48% (13/27)). This is supported by the higher sensitivity found in ocular MG patients of our cohort (84%).

As previously described, RNS is often negative in SNMG or OMG patients.⁴ In our study, RNS was abnormal in only 9% of SNMG patients and in 16% of OMG patients. Compared to previous studies, the sensitivity of the RNS was lower in our cohort (both in OMG and GMG). We hypothesize that this may have been caused by the fact that our patients were not newly diagnosed, and treatment for a longer period of time may have lowered the sensitivity of RNS. This hypothesis also entails the possibility that the RoVEMP test may have a higher sensitivity in a cohort of treatment-naïve patients.

In SNMG, the RoVEMP test was abnormal in 73% of patients that had a normal RNS. In seropositive MG patients, the RoVEMP test also appeared to be more sensitive than RNS (40% of patients with a negative RNS had an abnormal RoVEMP), however this additional diagnostic value was significantly lower than in SNMG. This difference is probably due to the higher number of ocular MG patients in the SNMG group. This study shows that the RoVEMP test is the only diagnostic test for MG that does not have a lower sensitivity in SNMG or OMG. To the contrary, sensitivity of the RoVEMP test in ocular SNMG patients, usually the most difficult subgroup to diagnose, was relatively high.

In this study, we included a low number of MuSK MG patients (N = 7) that had a similar percentage of positive RoVEMP tests (71%) compared to AChR MG patients. RNS has been reported to be less sensitive in MuSK MG.⁵ Although the numbers are too low draw

conclusions, we suspect that the relatively high sensitivity of the RoVEMP test in MuSK MG may be due to the frequent presence of some degree of ocular weakness in this subgroup, whereas limb weakness is often absent. In fact, all of our 7 MuSK MG had diplopia at the time of RoVEMP testing. As RNS is also used in LEMS and CMS patients, we included a small number of these patients to explore the potential value of the RoVEMP test in LEMS and CMS. 3 of 4 LEMS patients and 2 of 2 CMS patients had an abnormal RoVEMP test in our study. Although promising, these results should be confirmed in larger cohorts.

We used an ROC analysis to identify optimal cut-off values to distinguish between MG patients and healthy controls, and between MG patients and neuromuscular controls. Sensitivity, specificity and area under the curve were similar in the two ROC analyses. The optimal cut-off values were also similar. As neuromuscular controls form a better reference than healthy controls, we propose to use the more conservative cut-off value found in the ROC analysis with neuromuscular controls ($\geq 14.3\%$), with an overall sensitivity of 67% and a specificity 82%. The calculated positive predictive value of 91% and negative predictive value of 41% show that the RoVEMP is more valuable for ruling in MG patients than in ruling them out. Although this cut-off value lies 3.0% above that of the ROC analysis with healthy controls, sensitivity in SNMG or OMG patients is not affected. This cut-off value also lies closer to that proposed by Valko et al. ($\geq 15.2\%$).

Pyridostigmine use $\leq 4,5$ hours before the RoVEMP test was associated with a lower magnitude of RoVEMP decrement. However, the sensitivity was not significantly different between patients that did or did not use pyridostigmine before the test. Still, we would recommend asking patients not to use pyridostigmine $\leq 4,5$ hours before the RoVEMP test.

We also found a significant correlation between the magnitude of decrement and the time since the last intake of pyridostigmine and observed considerably lesser decrements in two patients when taking pyridostigmine compared to not taking pyridostigmine. These findings support that RoVEMP decrement reflects reversible neuromuscular transmission failure, probably analogous to RNS decrement. In addition, we showed that RoVEMP decrement is not a measure for diplopia in general, as the prevalence of diplopia was similar in our MG patients and neuromuscular controls.

We found an abnormal RoVEMP test in 2 healthy controls and 6 neuromuscular controls. Some of these controls showed a relatively high variation in the latency of the detected peaks and a low signal to noise ratio. In this study, we decided to exclude RoVEMP results only when there were evident blink artifacts that disrupted the RoVEMP signal (overall exclusion rate 3%). In further research, we will focus on quantifying the signal to noise ratio and establishing a method to objectively determine the confidence bounds of a single RoVEMP measurement to increase the diagnostic yield.

Limitations of this study include the single center of inclusion and our study population within a tertiary referral center that may not fully reflect the total MG population due to a referral bias. Our control group of neuromuscular patients did not reflect the whole range of patients with diplopia due to a neuromuscular disease other than MG. However, we included control patients with disorders that were previously reported to cause diagnostic confusion and delay due to similarities in presenting symptoms compared to OMG.¹⁸ Methodological limitations of our study are the fact that inter-rater reliability was not formally assessed and the fact that investigators were not blinded to clinical status. These methodological limitations

are likely to have a minimal impact as the role of the investigator is limited to placing electrodes, encouraging the patient to relax and placement of the mini-shaker, but further studies on reliability will still be needed to prove this. All post-processing and decrement calculation was fully automated by a matlab script. Another limitation is the (current) impossibility of including patients with excessive blinking in response to the vibrations. In this study, we have excluded 3% of the participants due to this problem. By further optimizing stimulus parameters, altering the procedure of testing in patients with excessive blinking (e.g. lowering the stimulus intensity) as well as optimizing post-processing, diagnostic yield could be increased in future studies¹⁹.

The RoVEMP results of one MG patient, 2 healthy controls and 2 neuromuscular controls were not analyzable due to excessive blink artifacts and were excluded.

The RoVEMP test is a new neurophysiological test that, in contrast to RNS and single-fiber EMG, is able to measure neuromuscular transmission of EOMs, which are the most affected muscles in MG. As the test is quick (10-15 minutes), less invasive than RNS and single-fiber EMG and easy to perform, we recommend including the RoVEMP test in the routine diagnostic evaluation of patients with suspected MG. Especially in diagnostically challenging patients with negative antibody tests, negative RNS results and isolated ocular muscle weakness, the RoVEMP test has a clear added value in supporting the diagnosis of MG.

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Author contributions

RH, KR, MA, KP, JJ and MR have contributed to conception and design of the study. RH, KR, UA and MR have contributed to the acquisition and analysis of data. RH, KR, JJ and MR have contributed by drafting a significant portion of the manuscript or figures.

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Figure Legends

Figure 1. STARD flow diagram: Included participants with RoVEMP results and diagnosis

Figure in image file

STARD flow diagram showing the included participants and the results for the RoVEMP test at the lowest determined cut-off point. The corresponding study group is included in the bottom for myasthenia gravis (MG), neuromuscular disease control (NMC) and healthy controls (HC).

Figure 2. Ocular vestibular evoked myogenic potentials (oVEMP) recordings

Figure in image file

RoVEMP test results of a neuromuscular control (Graves' opthalmopathy) (A) and an MG patient (B) are shown. The oVEMP response is a multiphasic wave. For the RoVEMP test, the amplitude between the second peak (n2) and the second trough (p2) of the oVEMP response is used (n2 and p2 are indicated by colored asterixis). Decrement is calculated by comparing the n2-p2 amplitude after the second stimulation with the mean of the fifth to ninth amplitudes.

Figure 3. Individual and mean RoVEMP decrements in MG patients, healthy controls and neuromuscular disease controls

Figure in image file

A. Scatter dot plots showing RoVEMP decrements in the five groups that participated in this study. Mean and 95% CI are shown by lines and error bars.

Abbreviations: HC = healthy control, NMD = neuromuscular disease control

Figure in image file

B. Scatter dot plots showing RoVEMP decrements in AChR, MuSK and SNMG patients, subdivided by ocular and generalized phenotype. Mean and 95% CI are shown by lines and error bars.

Figure 4. Receiver operating characteristic curve (ROC) analyses to determine optimal cut-off values

Figure in image file

A. ROC analysis with healthy controls as reference. Optimal cut-off value: >11.3%, sensitivity: 71%, specificity: 86% and area under the curve (AUC): 0.78.

Figure in image file

B. ROC analysis with neuromuscular controls as reference. Optimal cut-off value: >14.3%, sensitivity: 67%, specificity: 82% and area under the curve (AUC): 0.74.

Figure 5. Correlation between decrement and pyridostigmine intake

Figure in image file

A. Scatter dot plots showing RoVEMP decrements in MG patients that did not use pyridostigmine (pyridostigmine -) and MG patients that did use pyridostigmine ≤ 4.5 hours before the RoVEMP test (pyridostigmine +). Mean and 95% CI are shown by lines and error bars.

Figure in image file

B. Analysis of the relation between decrement and time since last pyridostigmine intake in 39 MG patients. The correlation between these two variables is shown by the linear regression line (red).

Figure 6. Individual and mean RoVEMP decrements in neuromuscular disease controls subdivided by neuromuscular disease

Figure in image file

Scatter dot plots showing RoVEMP decrements in all the disease groups that together constituted the neuromuscular control group. Mean and 95% CI are shown by lines and error bars.

Tables

Table 1. Comparison of demographic, clinical and diagnostic characteristics between AChR MG, MuSK MG and SNMG patients

	AChR MG N=71	MuSK MG N=7	SNMG N=14	p Value
Age, y	57.1 ± 18.3	54.0 ± 20.3	57.1 ± 14.4	0.908
Age at onset, y	46.3 ± 18.7	46.4 ± 17.6	46.0 ± 15.1	0.998
Gender				
Male	36 (51)	4 (57)	4 (29)	0.278
Female	35 (49)	3 (43)	10 (71)	
Phenotype				
Ocular	18 (25)	0 (0)	7 (50)	0.040
Generalized	53 (75)	7 (100)	7 (50)	
Thymectomy				
Yes, with thymoma	7 (10)	0 (0)	0 (0)	0.138
Yes, without thymoma	21 (30)	1 (14)	1 (7)	
No	43 (60)	6 (86)	13 (93)	
Medication use				
Pyridostigmine	49 (69)	1 (14)	10 (71)	0.013
Prednisone	38 (54)	5 (71)	7 (50)	0.622
Other immunosuppressants	33 (47)	4 (57)	5 (36)	0.622
Repetitive nerve stimulation				
Abnormal decrement	24/49 (49)	2/6 (33)	1/11 (9)	0.048
RoVEMP				
Decrement	27.5 ± 33.0	29.7 ± 42.2	32.6 ± 23.2	0.861
Decrement ≥ 11.3%	50 (70)	5 (71)	10 (71)	0.996
Decrement ≥ 14.3%	47 (66)	5 (71)	10 (71)	0.904

Baseline characteristics of 92 patients with MG included in this study. Data are presented as number of patients (%) for categorical variables and as mean ± SD for continuous variables.

Appendix Author Contributions

Name	Location	Role	Contribution
Robert de Meel, MD	Leiden University Medical Center, Leiden	Author	Design and conceptualized study; analyzed the data; major role in the acquisition of data; drafted the manuscript for intellectual content
Kevin Keene, MD	Leiden University Medical Center, Leiden	Author	Design and conceptualized study; analyzed the data; major role in the acquisition of data; drafted the manuscript for intellectual content
Magdalena Wirth, MD	University Hospital Zurich, University of Zurich, Switzerland	Author	Design and conceptualized study; Interpreted the data; revised the manuscript for intellectual content
Konrad Weber, MD	University Hospital Zurich, University of Zurich, Switzerland	Author	Design and conceptualized study; Interpreted the data; revised the manuscript for intellectual content
Umesh Badrising, MD PhD	Leiden University Medical Center, Leiden	Author	Major role in the acquisition of data; Interpreted the data; revised the manuscript for intellectual content
Jan Verschuuren, MD PhD	Leiden University Medical Center, Leiden	Author	Design and conceptualized study; drafted the manuscript for intellectual content
Martijn Tannemaat, MD PhD	Leiden University Medical Center, Leiden	Author	Design and conceptualized study; analyzed the data; major role in the acquisition of data; drafted the manuscript for intellectual content

A. Neuromuscular control

B. MG patient