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Comparative diagnostic yield of median and ulnar nerve repetitive nerve stimulation in generalized myasthenia gravis

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Abstract

Background & Objective: Ulnar nerve repetitive nerve stimulation (RNS) is widely used in the electrophysiological evaluation of myasthenia gravis (MG), but its limited diagnostic sensitivity remains a challenge. This study aimed to directly compare the diagnostic sensitivity of low-frequency (3 Hz) median and ulnar nerve RNS in generalized MG patients positive for acetylcholine receptor (AChR) or muscle-specific kinase (MuSK) antibodies. *Methods:* In this retrospective single-center study, 35 patients diagnosed with generalized MG and seropositive for AChR or MuSK antibodies were evaluated. All underwent both median and ulnar nerve RNS testing. Electrophysiological recordings were obtained from the abductor pollicis brevis (APB) muscle for the median nerve and the abductor digiti minimi (ADM) muscle for the ulnar nerve. *Results:* Abnormal decremental responses were more frequent in median nerve RNS than in ulnar nerve RNS, especially among newly diagnosed patients and those with higher AChR antibody levels, although this difference was not statistically significant. Importantly, the mean decrement magnitude was significantly greater in the median nerve compared to the ulnar nerve (17.1% vs. 9.4%; $p = 0.018$). This difference was particularly notable in patients with mild MG symptoms (MGFA class II and III).
Conclusion: Median nerve RNS showed higher sensitivity and greater decrement magnitude than ulnar nerve RNS, particularly in mild generalized MG cases. These findings suggest that median nerve RNS is a valuable complementary diagnostic tool in MG, especially during early disease stages.

Keywords: Myasthenia gravis, repetitive nerve stimulation, ulnar nerve, median nerve, low-frequency stimulation, decrement

INTRODUCTION

Myasthenia gravis (MG) is an autoimmune disorder targeting the neuromuscular junction, characterized by fluctuating skeletal muscle weakness.[1] The autoimmune process is mediated by autoantibodies, most commonly directed against acetylcholine receptors (AChR) at the postsynaptic membrane of the neuromuscular junction.[2] The clinical spectrum ranges from mild ocular involvement to severe generalized weakness affecting limb, bulbar, and respiratory muscles. Although MG is a treatable condition, delayed diagnosis may result in significant morbidity and mortality.

The diagnosis of MG typically requires a multifaceted approach that incorporates clinical assessment, serological testing, and electrophysiological studies.[3] Repetitive nerve stimulation (RNS) is a widely used and reliable electrodiagnostic technique to assess neuromuscular transmission. However, its diagnostic sensitivity varies depending on the muscle groups examined and disease severity. In clinical practice, the ulnar and facial nerves are most commonly selected for RNS testing. Nevertheless, recent studies suggest that median nerve RNS may provide higher diagnostic yield, particularly in generalized MG.[4] To date, however, no study has directly compared the diagnostic performance of median and ulnar nerve RNS in the same cohort of seropositive (AChR- or MuSK-positive) generalized MG patients.

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This study aimed to evaluate and compare the diagnostic sensitivity and decrement percentage of low-frequency (3 Hz) median and ulnar nerve RNS in seropositive generalized MG patients.

METHODS

This study included patients diagnosed with generalized myasthenia gravis (MG) who underwent electrophysiological evaluation for diagnostic purposes in the neurophysiology laboratory between December 1, 2023, and January 1, 2025. Inclusion criteria required seropositivity for acetylcholine receptor (AChR) or muscle-specific kinase (MuSK) antibodies and mild-to-moderate clinical symptoms, corresponding to Myasthenia Gravis Foundation of America (MGFA) class II–III. Exclusion criteria were age under 18 or over 75 years, ocular MG, seronegative status, and MGFA class I or IV.

The study protocol was approved by the local ethics committee (Protocol No: 227/2025) and conducted in accordance with the principles of the Declaration of Helsinki.

Data analysis was performed using IBM SPSS Statistics version 23. The Shapiro–Wilk test was applied to assess normality of distribution. Concordance between abnormal responses in 3 Hz median and ulnar RNS was evaluated using the McNemar test. Since the data were not normally distributed, the Wilcoxon signed-rank test was employed to compare median and ulnar RNS decrement values. The independent samples t-test was used to compare normally distributed variables between two groups, while the Mann–Whitney U test was applied for non-normally distributed data. Pearson's correlation coefficient was used for normally distributed quantitative variables, while Spearman's rho was applied for non-normally distributed variables. Associations between categorical variables were examined using the Yates correction and Monte Carlo-adjusted Fisher's exact test. For comparisons across three or more groups, one-way ANOVA was applied for normally distributed variables (with Bonferroni correction for multiple comparisons), and the Kruskal–Wallis test for non-normally distributed variables.

Results were reported as mean (standard deviation) or median (minimum–maximum) for quantitative variables, and as frequency (percentage) for categorical variables. A p-value < 0.05 was considered statistically significant.

RESULTS

Patient population

As part of the same study session, RNS was performed on the median and ulnar nerves in a total of 35 patients. The baseline characteristics are presented in Table 1. MG was newly diagnosed in 11 patients during RNS assessment, whereas 24 patients had a previously established diagnosis. In these patients, RNS was conducted either to confirm the diagnosis or to evaluate functional status. All patients included in the study were seropositive for AChR or MuSK antibodies.

MGFA classification

The severity of MG was defined during RNS evaluation according to the MGFA classification.[5] Only patients classified as MGFA class II–III were included. No statistically significant differences were observed in 3 Hz ulnar, 3 Hz median, or overall decrement values between MGFA class II and III subgroups (Table 2).

Electrodiagnostic tests

Cholinesterase inhibitors were discontinued 12 hours before testing.[6] RNS and nerve conduction studies (NCS) were performed using a Natus EMG device by a single neurophysiologist. The protocol included: unilateral sensory and motor NCS of the median nerve (to exclude carpal tunnel syndrome); 3 Hz RNS of the APB muscle via the median nerve; and 3 Hz RNS of the ADM muscle via the ulnar nerve. Ten stimuli were delivered, and abnormal decrement was defined as a >10% reduction in CMAP amplitude between the first and fourth responses.[7] If a positive decrement occurred, RNS was repeated after a 10-second maximal isometric contraction. Limb temperature was maintained at ≥32°C. Across subgroups, median and ulnar decrement percentages and the proportions of significant decrement responses (≥10%) are reported. The Wilcoxon test compared continuous variables, and the McNemar test compared proportions. (Table 3)

Abnormalities in either median, ulnar, or both nerves were detected in 23 patients (64.3%). The proportion of abnormal responses was slightly higher in the median nerve compared with the ulnar nerve (51.4% vs. 45.7%; $p = 0.046$). The mean decrement percentage was significantly greater in the median nerve than in the ulnar nerve

Table 1: Patients' characteristics (N= 35)

Features	
Age, in years, median (range)	50.0 (19-75)
Females (%)	22 (62.9%)
Median duration of symptoms before RNS testing (range, in months)	33.3 (1-240)
Treatment before RNS testing	
New diagnosis	11
Immunotherapy	13
Pyridostigmine only	11
Antibody result	
Number of AChR-Ab+ /	28
Number of MuSK-Ab+ /	7
MGFA classification	
Class II	22
Class III	13
Thymectomy	
Yes	5
None	30

(17.1% vs. 9.4%; p = 0.018) (Figures 1- Median and ulnar nerve RNS decrement percentages in two sample patients). These findings were consistent across MGFA class II–III.

No significant difference was observed between patients with and without thymectomy. All patients underwent sensory and motor NCS of the median nerve on the side ipsilateral to RNS. An EDX diagnosis of median neuropathy at the wrist was established in 16 patients. Among them, 7 showed abnormal decrement in median nerve RNS (2 severe, 5 mild–moderate). In 9 patients with median neuropathy, no decrement was observed. There was no significant

Table 2: Comparison of 3 Hz ulnar, 3 Hz median, and overall decrement values according to MGFA classification groups

	MGFA			
	Score 2	**Score 3**	**Test statistics**	**P**
3 Hz-Ulnar RNS				
non-significant	8 (36.4)	8 (61.5)	1.96	0.274
Significant	14 (63.6)	5 (38.5)		
3 Hz-Median RNS				
non-significant	10 (45.5)	8 (61.5)	0.325	0.569
Significant	12 (54.5)	5 (38.5)		
Overall decrement				
Ulnar nerve	4 (28.6)	1 (11.1)	4.894	0.097
Median nerve	5(42.9)	1 (11.1)		
Both ulnar and median nerves	4 (28.6)	7 (77.8)		

Table 3: Results of repetitive nerve stimulation (RNS) of the median and ulnar nerves in subgroup analyses

Group	Subgroup	N	Median% (mean)	Ulnar% (mean)	Median significant (%)	Ulnar significant (%)	Wilcoxon p	McNemar p
New diagnosis	Yes	11	17.9	14.2	63.6	54.5	0.273	1.000
	No	24	13.2	12.5	45.8	41.7	0.889	1.000
Thymectomy	Yes	5	12.5	11.2	60.0	60.0	0.180	0.617
	No	30	15.6	13.6	50.0	43.3	0.721	0.724
AchR level	Low (<median)	22	14.8	12.4	36.4	36.4	0.600	0.683
	High (≥median)	13	15.3	13.9	76.9	61.5	0.753	0.683

Median and ulnar nerve decrement percentages and rates of significant decrement (≥10%) in each subgroup, based on 3 Hz repetitive nerve stimulation (RNS) testing. Continuous variables were compared using the Wilcoxon test, and proportions of significant decrement were analyzed with the McNemar test

association between median neuropathy and abnormal median RNS (p = 0.801) (Table 4).

Abnormal decrement was observed exclusively in the median nerve in 7 patients and exclusively in the ulnar nerve in 5 patients. In patients with newly diagnosed MG and those with high AChR antibody levels, decrement was more pronounced in the median nerve. In all 11 patients with abnormal responses in both nerves, the median nerve decrement was greater than the ulnar.

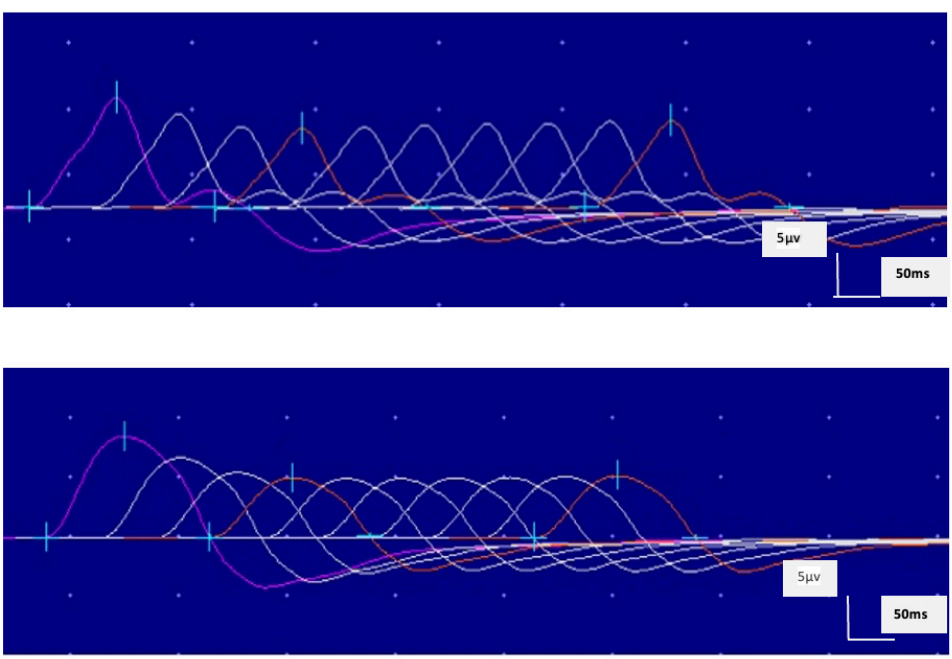

Figure 1. Decrement percentages observed during repetitive nerve stimulation (RNS) of the median and ulnar nerves in two representative patients.

The ulnar nerve demonstrated a 20.8 % decrement in compound muscle action potential amplitude when recorded from the ADM muscle.

The median nerve demonstrated a 40.5% decrement in compound muscle action potential amplitude when recorded from the APB muscle

Tablo 4: Assessment of 3 Hz repetitive nerve stimulation parameters of the median nerve across carpal tunnel syndrome severity groups

	Median neuropathy				P
	None	Mild	Moderate	Heavy	
3 Hz-Median RNS					
non-significant	9 (47.4)	6 (66.7)	3 (60)	0 (0)	0.463
Significant	10(52.6)	3 (33.3)	2 (40)	2 (100)	
	12.5 (10-27.8)	14.9 (10.3-19.8)	15.4 (10.5-24.6)	-	0.801

DISCUSSION

In this study, we compared the diagnostic yield of low-frequency (3 Hz) RNS of the median and ulnar nerves in seropositive generalized MG patients. Abnormal responses were observed in nearly two-thirds of the cohort, a figure comparable to previously reported positivity rates of 54–83% when multiple nerves are examined.[8] This confirms that RNS remains a valuable tool in the electrodiagnostic evaluation of MG, particularly when more than one nerve is tested.

Our results showed that the mean decrement percentage was significantly greater in the median nerve compared with the ulnar nerve (17.1% vs. 9.4%), and the frequency of abnormal responses was also slightly higher in the median nerve (51.4% vs. 45.7%). This is in line with reports suggesting that the choice of nerve and muscle substantially influences diagnostic sensitivity.[6] Studies evaluating distal hand muscles such as the APB have demonstrated higher decrements compared with the ADM, supporting our finding that median nerve RNS may have superior sensitivity.[4]

The superiority of median nerve RNS was particularly evident in newly diagnosed patients and those with higher AChR antibody titers. This observation is consistent with earlier studies showing that RNS abnormalities are more frequent in early disease and correlate with antibody burden.[9,10] Detecting such abnormalities at the time of diagnosis is clinically important, as delayed recognition of neuromuscular transmission failure is associated with worse outcomes.[11]

A potential limitation of using the median nerve is the coexistence of carpal tunnel syndrome, which is relatively common in the general population. However, in our study, abnormal decrement responses were not significantly more frequent in patients with electrodiagnostically confirmed median neuropathy, suggesting that mild-to-moderate entrapment neuropathy does not confound RNS interpretation. This finding is reassuring and is supported by reports noting that a decrement in MG reflects neuromuscular junction dysfunction rather than axonal or demyelinating changes.[12]

We also observed that abnormal decrement occurred exclusively in the median nerve in seven patients and exclusively in the ulnar nerve in five patients. This underlines the importance of testing multiple nerves, as previously emphasized by AAEM guidelines, which recommend examining at least two clinically relevant muscles to maximize sensitivity.[6] Our results echo earlier findings that abnormalities may be site-specific and testing only one nerve risks missing the diagnosis.

It is well established that MG leads to weakness predominantly in proximal and facial muscles, and clinical assessments tend to focus on the strength and electrophysiological features of these muscle groups. In contrast, the evaluation of distal extremity muscle strength—particularly that of muscles such as the APB is not routinely documented in MG patients and is often excluded from many MG outcome measures. However, evidence suggests that distal upper extremity weakness is not uncommon in MG and may, in some cases, be more prominent than proximal muscle weakness.[13] In a study involving 70 seropositive MG patients, distal upper extremity weakness was found to exceed proximal weakness in 37% of cases.[14] These findings are consistent with our clinical observations that weakness of the APB and finger extensor muscles is common among patients with generalized MG. Our study demonstrated that neuromuscular transmission abnormalities

are more pronounced in distal muscles in patients with MGFA score 2. This observation suggests that synaptic dysfunction may initially manifest in distal muscles before proximal muscles are affected, highlighting a potential early site of disease activity. In particular, the APB muscle, innervated by the median nerve, consists of small motor units with high activation frequency, making it especially susceptible to early postsynaptic receptor dysfunction. Similar findings have been reported in previous electrophysiological studies, which emphasize the vulnerability of distal muscles in early-stage MG. Conversely, in patients with MGFA score 3, despite more pronounced clinical weakness and broader muscle involvement, distal RNS responses appeared less sensitive. This reduced sensitivity may be explained by compensatory remodeling, a ceiling effect in decremental amplitudes, or secondary neuropathic changes associated with longer disease duration and prior treatment exposure. These findings suggest that electrophysiological detection of neuromuscular transmission failure in advanced MG may be influenced by adaptive mechanisms, potentially masking early distal involvement.

Overall, our results indicated that distal muscle involvement was more prominent in the MGFA score 2 group, which corresponds with the higher rate of positive RNS responses observed in Table 2. These data support the concept that neuromuscular transmission failure in distal muscles may occur early in the disease course, preceding the onset of generalized clinical weakness. Clinically, this highlights the importance of targeted electrophysiological assessment of distal muscles, particularly the APB, in the early detection and management of MG, and aligns with emerging evidence emphasizing site-specific vulnerability in neuromuscular disorders. From a practical perspective, median nerve RNS offers advantages over proximal or facial nerve testing, including technical ease, reduced movement artifacts, and improved patient comfort. The frequent daily use of the APB may render it more susceptible to fatigue and neuromuscular junction dysfunction, potentially explaining the higher magnitude of decrement observed in our cohort.[15]

Previous studies have reported variable sensitivities for different nerve–muscle combinations, ranging between 30% and 70% in generalized MG. Ulnar RNS is widely used but has been shown to have limited sensitivity in mild or early disease. Alternative muscles, including the trapezius and deltoid, have been explored with varying success. [10] Our study extends this evidence by providing a direct within-patient comparison of median and ulnar nerves, thereby minimizing inter-patient variability and strengthening the argument for routine inclusion of median nerve RNS in diagnostic protocols.

The strengths of this study include the within-patient design, which reduces confounding, and the restriction to seropositive generalized MG, which ensures diagnostic homogeneity. Limitations include the modest sample size and the single-center, retrospective design. Despite these limitations, our results provide novel evidence that median nerve RNS can improve diagnostic sensitivity in MG. Future multicenter, prospective studies with larger patient populations are warranted to validate these findings and to explore the role of additional nerve–muscle pairs.

In conclusion, taken together, our results indicate that median nerve RNS is a valuable complementary tool in the electrodiagnostic evaluation of MG, particularly in early-stage or antibody-high patients. Its inclusion in standard protocols may enhance sensitivity and support earlier diagnosis and treatment.

DISCLOSURE

Data availability: The datasets generated and/or analyzed during the current study can be available from the corresponding author on reasonable request.

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