Muscle Velocity Recovery Cycles to Examine Muscle Membrane Properties in Patients with Myasthenia Gravis

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Introduction

Although myasthenia gravis (MG) is caused by antibodies against the acetylcholine receptors (AChR) in the neuromuscular junction (NMJ), there is also evidence of postsynaptic membrane destruction leading to voltage gated sodium channel (VGSC) loss, which may decrease muscle excitability.

Muscle velocity recovery cycles (MVRC) is a method to evaluate the muscle membrane potential in vivo, with which the muscle cell excitability of MG patients can be studied independent of the neuromuscular transmission.

Aim

To investigate whether changes in muscle membrane potential can be detected in myasthenia gravis.

Methods

- 10 MG patients vs. 12 healthy volunteers (HV)
- MVRCs were performed in the morning at baseline, 3.5 hours later, and 5 hours later (only in HV).
- Main inclusion criteria MG patients:
  - Diagnosis of AChR+ MG
  - MGFA-classification II-IV
  - If applicable, pyridostigmine was stopped in the morning until after the last MVRC
- Stimulation was guided by QTRACS
- A repeated measures mixed model ANOVA was performed for statistical analysis

Results

- Increased interstimulus interval corresponding to early supernormality (ESN@) and residual supernormality (RSN) in MG vs. HV; 1.38ms (95%CI: 0.08, 2.69; p=0.0395) and 0.183% (95%CI: 0.008, 0.357; p=0.0407) respectively
- RNS was very variable with CV's >400% in HV, possibly type I error

Conclusions

- Findings suggest MG patients have a normal resting membrane potential with a slower "post-spike recovery"
- Possibly due to an elevated firing threshold caused by VGSC loss in the motor endplate, decreasing muscle excitability
- MVRC can be used to differentiate between MG and HV and evaluation of its sensitivity to detect pharmacological effects could prove its usefulness as a biomarker for drugs targeting abnormal muscle excitability in MG patients

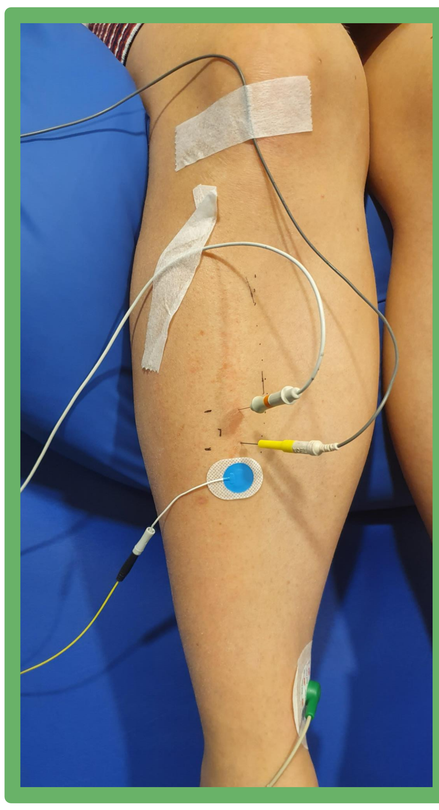

Figure 1: MVRC set-up

Demographics	MG N=10	HV N=12
Gender (Male)	10%	100%
Age (years) Range	43 (±19) 21-74	24 (±5) 19-41
Weight (kg)	70 (±9)	74 (±12)
BMI (kg/m^2)	24 (±3)	23 (±2)
MGFA- classification: II III IV	 7 3 0	 NA NA NA

Table 1: Demographics

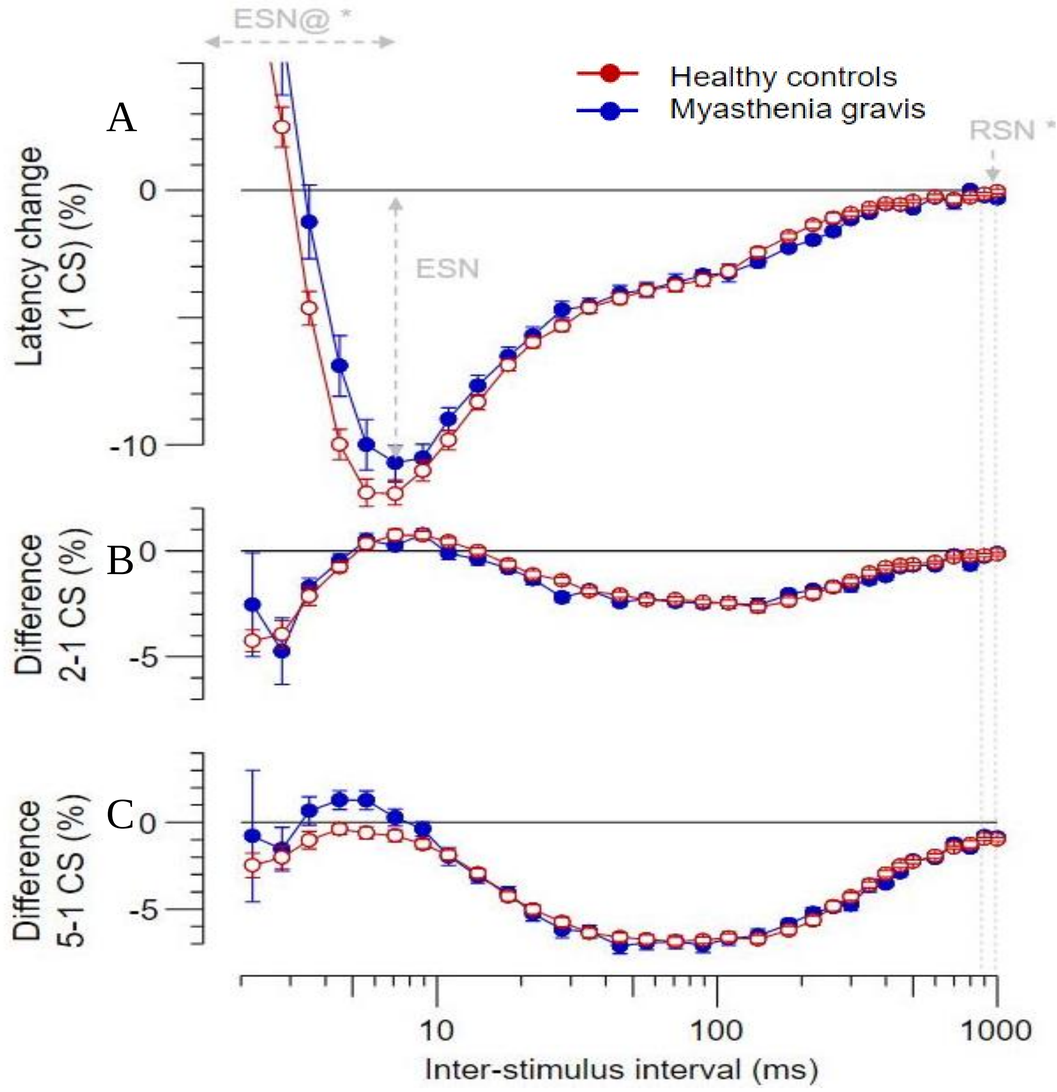

Figure 2: Mean MVRC recordings of 10 MG and 12 HV
A: Mean latency of muscle action potential after single conditioning stimulus at different interstimulus intervals
B: Difference in latency after 2 - 1 conditioning stimuli
C: Difference in latency after 5 – 1 conditioning stimuli

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