Acoustic myography as a diagnostic test for myasthenia gravis

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Background

Myasthenia Gravis (MG) is an autoimmune disorder in which animals produce antibodies against acetylcholine receptors at the neuromuscular junction. The disease manifests as exercise intolerance and aspiration pneumonia resulting from megaesophagus. The latter condition is responsible for a roughly 50% mortality rate within 6 months.

Current diagnostic tests have limitations:

- **Clinical signs**: Lacks specificity and sensitivity.
- **AchR Ab titer**: Gold standard but requires 5-7 days for processing.
- **Edrophonium:** (Tensilon) challenge: Lacks sensitivity and specificity, (unavailable)
- **Electrophysiology**: Fatigue of compound muscle action potential requires general anesthesia (needle electrodes) and is high risk for patients.

Acoustic myography (AMG) may provide comparable results to standard needle electrophysiology without anesthesia. By using a piezoelectric receptor to measure the sound of muscle contraction (rather than the electrical potential), and a surface field generator to stimulate muscle contraction, AMG may provide a novel MG diagnostic modality.
The aim of this experiment is to establish normal healthy dog reference interval values for percent decrement in AMG readings during electrical stimulation of the cranial tibial muscle.

Hypothesis

Repetitive skin surface nerve stimulation and AMG recording of muscle contractions will be feasible and provide consistent responses in normal dogs.

Specific Aim

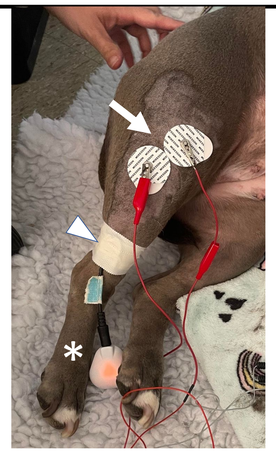
- Define reference values for variability in AMG response to surface field stimulation in normal dogs.

Methods

12 normal dogs, L+R pelvic limbs (24 assessments)
Surface stimulation superficial peroneal nerve

- Repetitive stimulation (X10) at 1, 3, 5, 7, 15, 20 Hz
- AMG recording- Cranial tibial muscle (CURO MkII)
- Recording repeated 3 times (Intra-procedure variability)
- Recordings repeated 2nd day (Inter-procedure variability)
- Peak and total area of AMG calculated using R pipeline

Fig 1. Piezoelectric AMG sensor



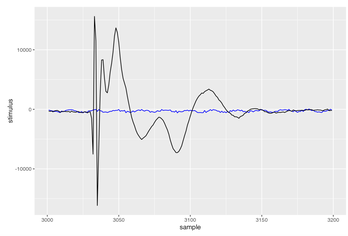


Fig 2. AMG procedure with surface electrodes (arrow), sensor (arrow head) and CURO MkII blue tooth unit (asterix) A typical single AMG tracing resulting from myofiber contractions is shown.

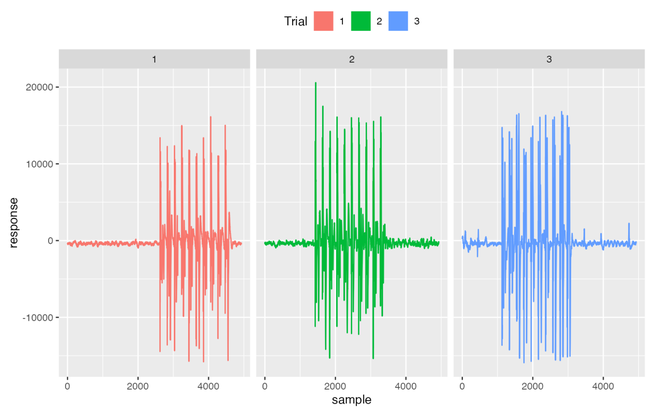


Fig 3. **Dog 2**: 5 hz stimulation Leg 1

Visualization of 3 separate sets of 10 stimuli at 5 Hz
AMG recordings are present at all stimulations and are similar in amplitude and areas in all recordings

Results

- Recordings from 3/12 dogs were acquired and data collected.
- Analysis pipeline using R was established to allow data visualization
- AMG areas were successfully measured using WavePad and ImageJ.
- Hardware and software issues precluded collection of additional data

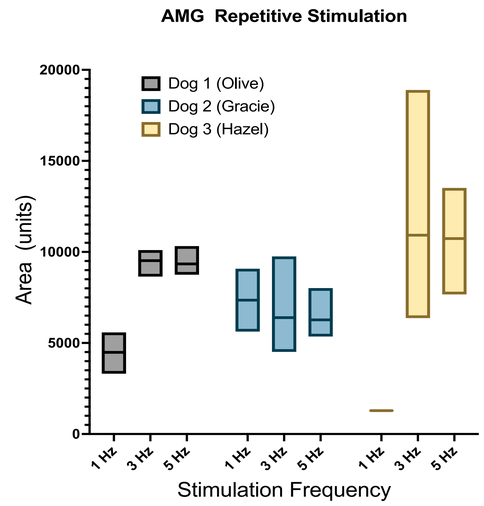
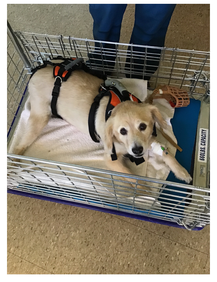
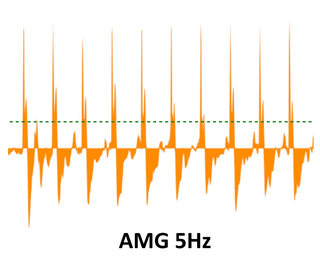


Fig 4. Visualization of variability in repeated stimulations at 1, 3, and 5Hz. Area value represents total area of waves 2+3+4 at one stimulation time. Boxes represent the variability over the 3 repeats. Variability is low for Dogs 1 and 2. Dog 3 was agitated and the high variability likely represents voluntary muscle contractions superimposed on stimulated contractions.

This is less likely to be an issue in clinically weak animals.

Sedation may be beneficial





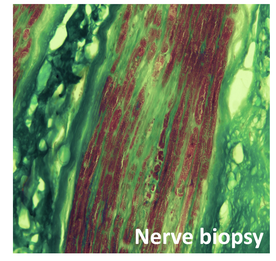


Fig 5. Clinical patient with weakness and suspected myasthenia gravis. Similar to study control dogs, the AMG showed no decrement, which would be expected in MG due to neuromuscular junction fatigue. A final diagnosis of polyneuropathy was consistent with the AMG findings.

Conclusions and Future Directions

- Surface stimulated repetitive AMG is feasible in conscious dogs
- AMG recordings have limited variability in compliant animals.
- Collection of additional data and definition of analysis parameters with minimum variability will define reference values against which MG patients can be compared.

Acknowledgements

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