Neuromuscular disorders

Erik Stålberg

The neuromuscular junction
Multiple targets at the NMJ

AGRIN / MUSK SIGNALERING

ACh synthesis and storage
Miniature end-plate potentials

End-plate activity - monophasic

Intracellular recordings, - action potentials not shown
**Intracellular recordings, schematic with APs**

![Intracellular recordings, schematic with APs](image)

**Schematic explanation to the myasthenic decrement**

![Schematic explanation to the myasthenic decrement](image)

**Myasthenic disorders**

- Non-familial
  - Autoimmune MG
  - LEMS
  - Toxins, drugs
- Congenital syndromes
  - Presynaptic, synaptic, postsynaptic
Myasthenic disorders

- Myasthenia gravis
  - reduced AChR
  - antibodies to AChR (85%)
- Seroneg MG
  - normal ACHR density
  - anti-MUSK antibodies in 2/3
- LEMS
  - reduced release of Ach
  - antibodies to presynaptic Ca-channels
  - autonomic symptoms
  - malignancy in 65%
Decrement protocol

- normal
- MG
- cholinergic crisis
- LEMS

Tests for MG

- History
  - Tests
    - fatigue, Tensilon, curare
- EMG
  - Rep nerve stimulation
    - slow-fast, postactivation, ischemia, curare, stair-case, paired stimuli
  - Needle-EMG
    - shape variability
  - SFEMG
    - jitter

Protocol

- 3 Hz, 10 stimuli
- immobilize the muscle
- max stim strength, 125%
- test at: rest after 20 sec of act, after 1,3,5,10 minutes
**Parameters to analyse**
- initial amplitude
- decrement
- amplitude after activity (postactivation facilitation)
- decrement after activity
- amplitude and decrement after 1, 3 and 5 min (postactivation exhaustion)

**Rep.nerve stimulation: considerations**
- distal/proximal muscle
- rest/fatigue
- on/off treatment
- cold/warm
- stim. frequency
- muscle fixation

**Muscles to test**
- Deltoideus
- Trapezius
- Anconeus
- Nasalis
- Orbicularis oculi
- EDB
- Rectus femoris
Decrement in 2 proximal muscles

<table>
<thead>
<tr>
<th></th>
<th>Outliers</th>
<th>Trajectory</th>
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<tbody>
<tr>
<td>Decr 1</td>
<td></td>
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<tr>
<td>Decr 2</td>
<td></td>
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<tr>
<td>Mean Decr</td>
<td>24.8</td>
<td>15.8</td>
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<tr>
<td>Mean Amplitude</td>
<td>8.0</td>
<td>6.4</td>
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Is there?

- myasthenia
- good/ bad prognosis
- cholinergic overdose
- LEMS
- McArdle, myotonia

Repetitive nerve stimulation
Anconeus muscle

<table>
<thead>
<tr>
<th></th>
<th>3 Hz</th>
<th>3 Hz</th>
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<tbody>
<tr>
<td>after rest</td>
<td>-2%</td>
<td>-2%</td>
<td>-4%</td>
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<tr>
<td>1 min after 20 s activation</td>
<td>-7%</td>
<td>-9%</td>
<td>-10%</td>
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Repetitive nerve stimulation in a patient with severe MG

Rest, 3 Hz 10 stim
Directly after 20 s act.
Post-act facilitation

Rest, 3 Hz 10 stim
Directly after 20 s activation = facilitation

Facilitation after exercise in LEMS
Facilitation with 20 Hz stimulation in LEMS

Tim and Sanders, M&N, 1994

Congenital myasthenia (slow channel)

Abnormal CMAP

5-year old girl with rapsyn deficiency
Thenar muscles 15 Hz stim for 5 minutes

RNS with 3 Hz stim following prolonged activation 15 Hz 5 min