Testing Neuromuscular transmission

Erik Stålberg

The neuromuscular junction

Multiple targets at the NMJ

Tests for MG

- CLINICAL
  - History
  - Tests
- EMG
  - Rep nerve stimulation
  - Needle-EMG
- INTRACELL REC
- STAPEDUS REFLEX
- OCULOGRAPHY
- TONOMETRY
- ACHR ANTIBODIES

fatigue, Tensilon, curare
slow-fast, postactivation, ischemia, curare, staircase, paired stimuli
shape variability jitter

Howard in Stålberg, 2003
Intracellular recordings,
- action potentials not shown

Schematic explanation to the myasthenic decrement

Myasthenic disorders
- Non-familial
  - Autoimmun MG (post)
  - LEMS (pre)
  - Toxins, drugs (pre or post)
- 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%
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 analyze

- 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

Generalized MG
- Deltoidus
- Trapezius
- Anconeus
- Nasalis

Bulbar MG
- Nasalis
- Anconeus
- Trapezius

Ocular MG
- RNS is quite insensitive
- Nasalis
- Start with SFEMG jitter
Decrement in 2 proximal muscles

<table>
<thead>
<tr>
<th>Decr %</th>
<th>Muscles</th>
<th>Mean decrement</th>
<th>Mean amplitude</th>
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<tbody>
<tr>
<td></td>
<td>Distal</td>
<td>24.8</td>
<td>8.0</td>
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<tr>
<td></td>
<td>Proximal</td>
<td>15.8</td>
<td>6.4</td>
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Is there?

- myasthenia
- good/ bad effect of AchE inhibs
- cholinergic overdose
- LEMS
- McArdle, myotonia

Repetitive nerve stimulation

Anconeus muscle

3 Hz -4% 3 Hz -2% 3 Hz -2%

Rest, 3 Hz 10 stim

Facilitation after exercise in LEMS

Controls

LEMS

MG

Left ADM

Rest, 3 Hz 10 stim

Facilitation after 20 s activation

Tim and Sanders, M&N, 1994
Facilitiation with 20 Hz stimulation in LEMS

Time and Sanders, M&N, 1994

Single fiber action potentials

Intramuscular stimulation and SFEMG recording

Measuring jitter with Concentric Needle electrodes

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Uppsala, Sweden
Four types of EMG electrodes

Recording surface: width (µm), length (µm), area (mm²)

- Monopolar: 680, 0.240
- Concentric: 150, 580, 0.070
- Concentric, facial: 80, 300, 0.019
- SFEMG: 25, 25, 0.0005

Three types of EMG electrodes

- CN, 0.070 mm²
- SFEMG, 0.0005 mm²
- CN, 0.019 mm²

Three types of EMG electrodes

SFEMG

Jitter with cone needle electrode
Jitter SF vs Conc, mixed diagn

#>10 values, total mtrf; n=92

MUSCLE: edc

CNE in EDC, vol: mean MCD in 1340 individual pairs (67 subjects)

EDC: Extensor Digitorum Communis; MCD: mean consecutive difference; ULN: upper limit of normality

Mean 23.50
SD 7.328
N1 3 4 0

95% 99%

Kouyoumdjian, Stålberg 2006
Muscle | MCD mean | 95% SFEMG # | Pool mean | 95% SFEMG # | 99% SFEMG # |
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<td>Voluntary Activation</td>
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<tr>
<td>EDC</td>
<td>67</td>
<td>23.6</td>
<td>29.7</td>
<td>32.8 (35.4)</td>
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<tr>
<td>OQ</td>
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<td>24.7</td>
<td>31.0</td>
<td>34.1 (40.4)</td>
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<tr>
<td>PR</td>
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<td>19.8</td>
<td>23.6</td>
<td>26.4 (31.5)</td>
<td>19.9</td>
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<td>Electrical Stimulation (* intramuscular microaxonal ** bar electrode)</td>
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<tr>
<td>EDC *</td>
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<td>18.2</td>
<td>22.6</td>
<td>24.8 (25.0)</td>
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<td>OQ **</td>
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<tr>
<td>Frontalis **</td>
<td>20</td>
<td>16.0</td>
<td>21.5</td>
<td>24.2 (23.0)</td>
<td>16.0</td>
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Reference data
Kouyoumdjian & Stålberg (2007 - 2012)

Diagnostic tests for MG
% positive results from a total of 291 patients

<table>
<thead>
<tr>
<th>Group</th>
<th>SFEMG</th>
<th>Decrement ADM</th>
<th>Delt</th>
<th>Stapedius reflex</th>
<th>Anti-AChr</th>
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<tr>
<td>Ocular</td>
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<tr>
<td>EDC + Frontalis</td>
<td>Ocular</td>
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<td>Mild generalized</td>
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<td>Mod-severe generalized</td>
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<td>Remission</td>
<td>Ocular</td>
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Sensitivity of Diagnostic Tests in MG

- 550 patients with acquired MG
- All tests performed before immunotherapy or thymectomy
- Ocular myasthenia (OMG)
  - weakness only in ocular muscles
- Generalized MG (GMG)
  - weak in any non-ocular muscle

Sensitivity of initial tests
550 untreated MG patients

Some links
Sfemg.info (SFEMG meetings videos)
Keypointclub.com (simulators)