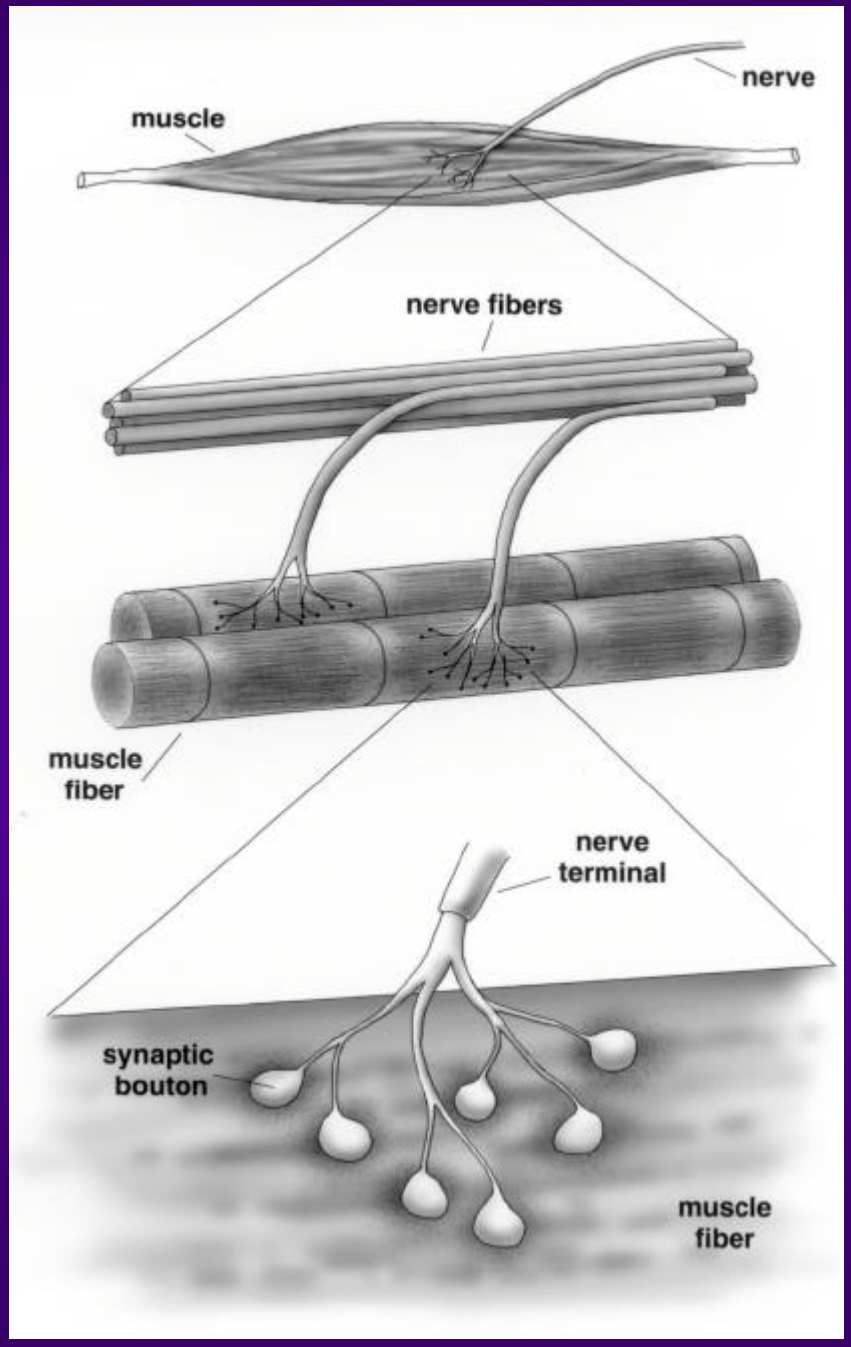
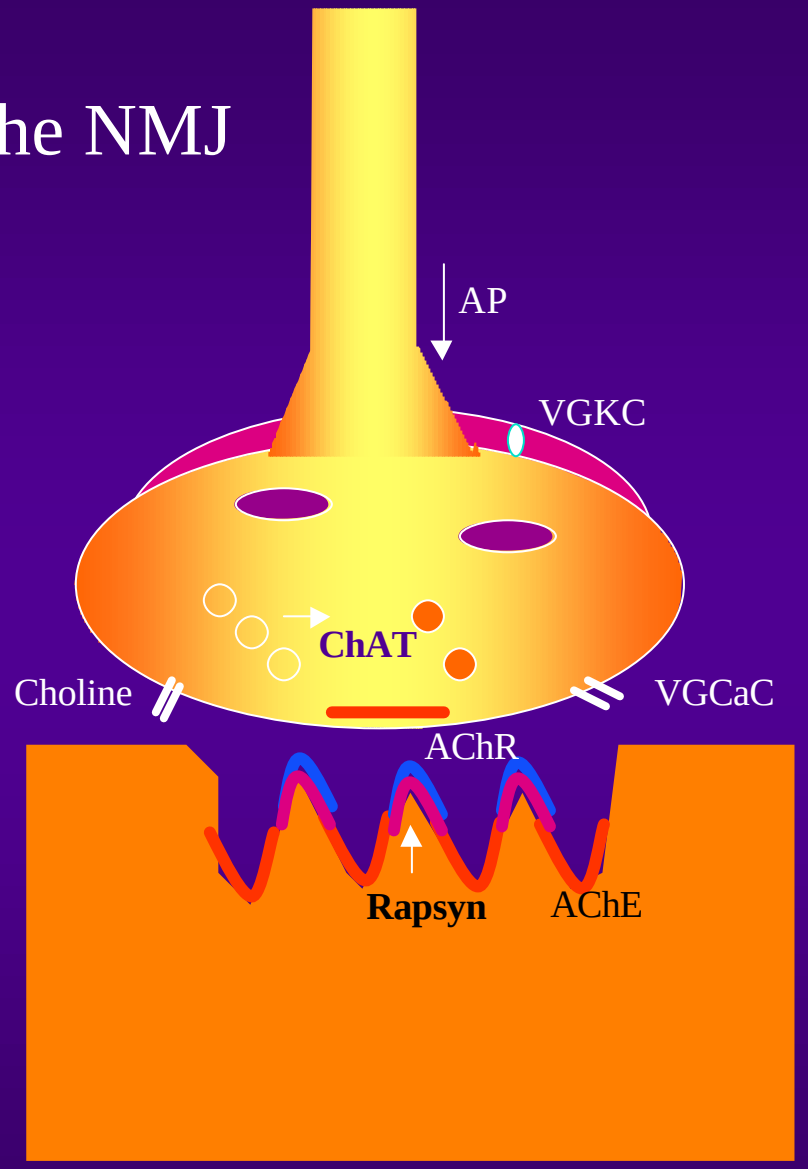
# Neuromuscular disorders

Stålberg

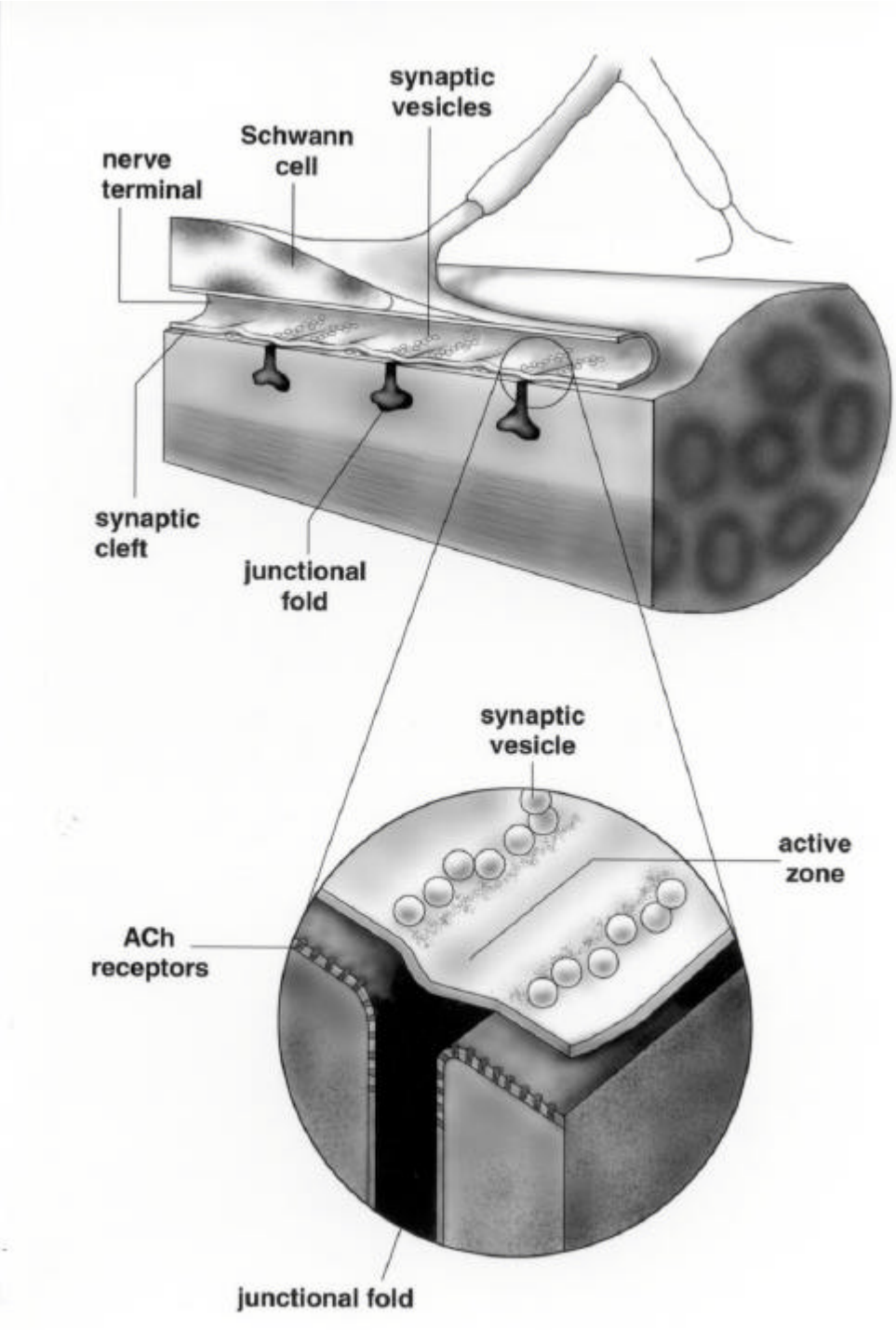



Howard in
Stålberg, 2003

# Multiple targets at the NMJ



# *The neuromuscular junction*




Howard in Stålberg 2003

# *Myasthenic disorders*

- **Non-familial**
  - **Autoimmun MG**
  - **LEMS**
  - **Toxins, drugs**
- **Congenital syndromes**
  - **presynaptic, synaptic, postsynaptic**

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# *Myasthenia Gravis*

- Autoimmun disorder
- Other autoimmune disorders in MG
- Incidence 1 / 100.000 per year
- Female : male  3 : 2

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# *Myasthenic disorders*

- Myasthenia gravis
  - **reduced AChR**
  - **antibodies to AChR**
- LEMS
  - **reduced release of Ach**
  - **antibodies to presynaptic Ca-channels**
  - **autonomic symptoms**
  - **malignancy in 65%**

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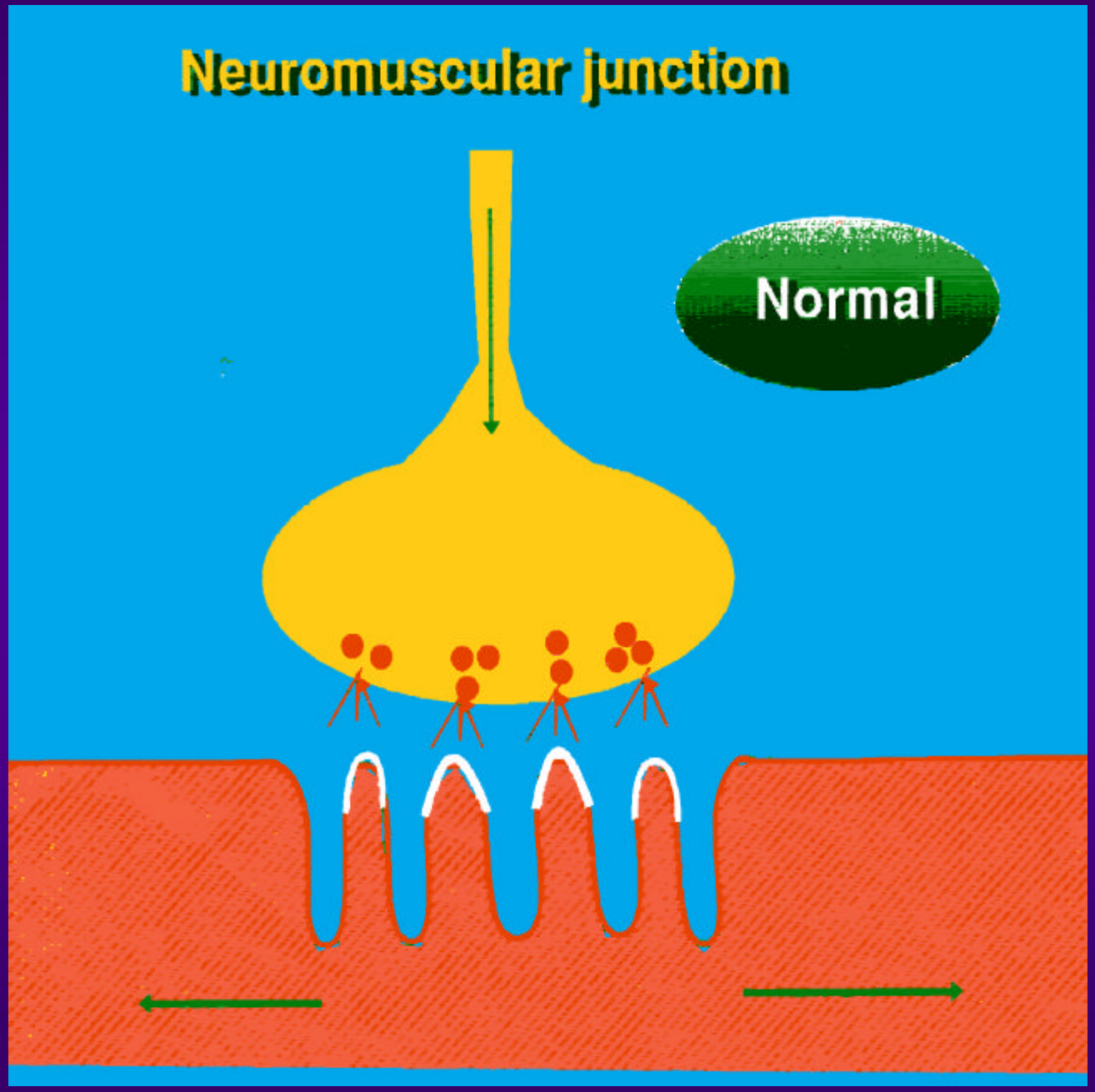


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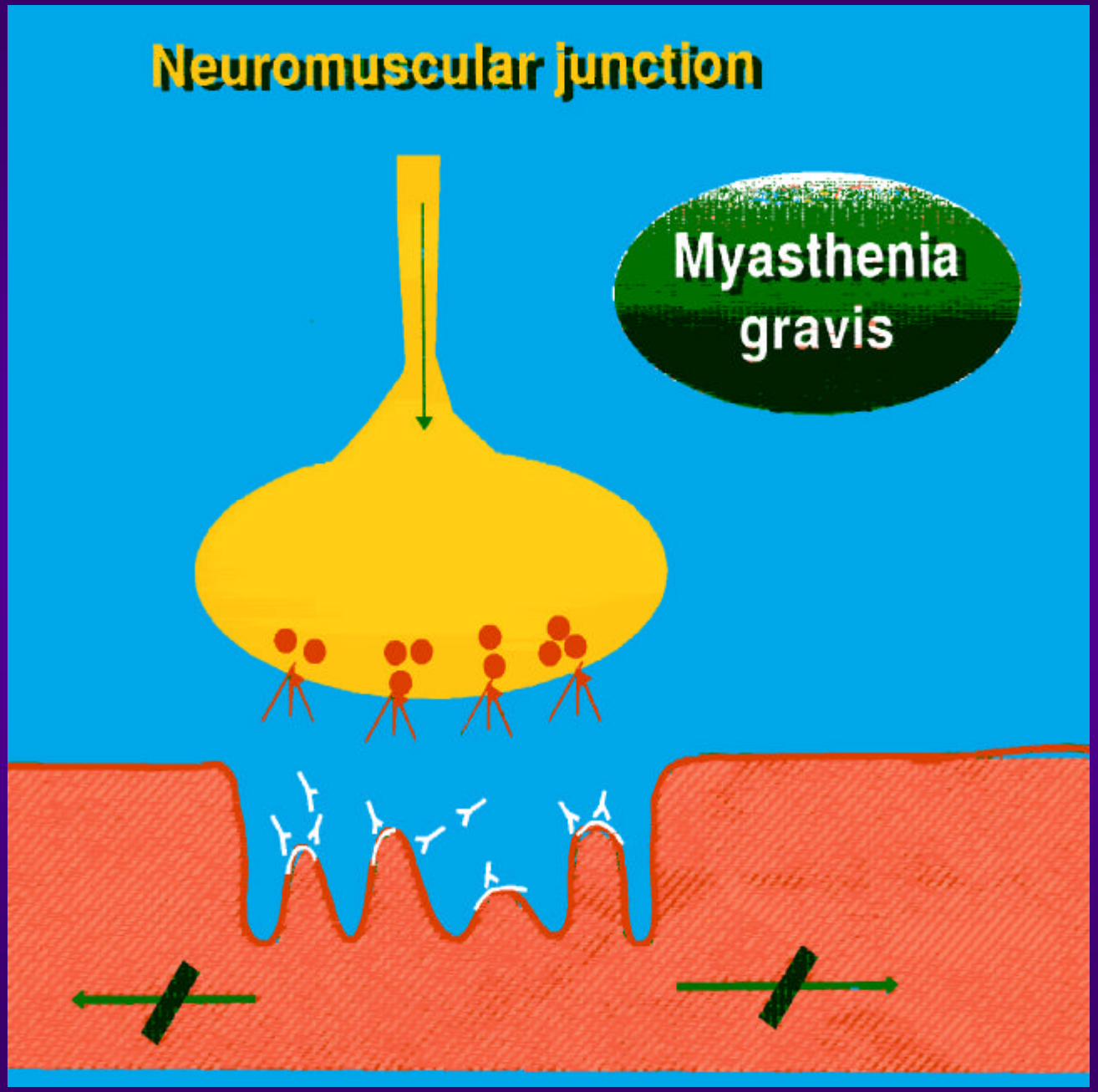


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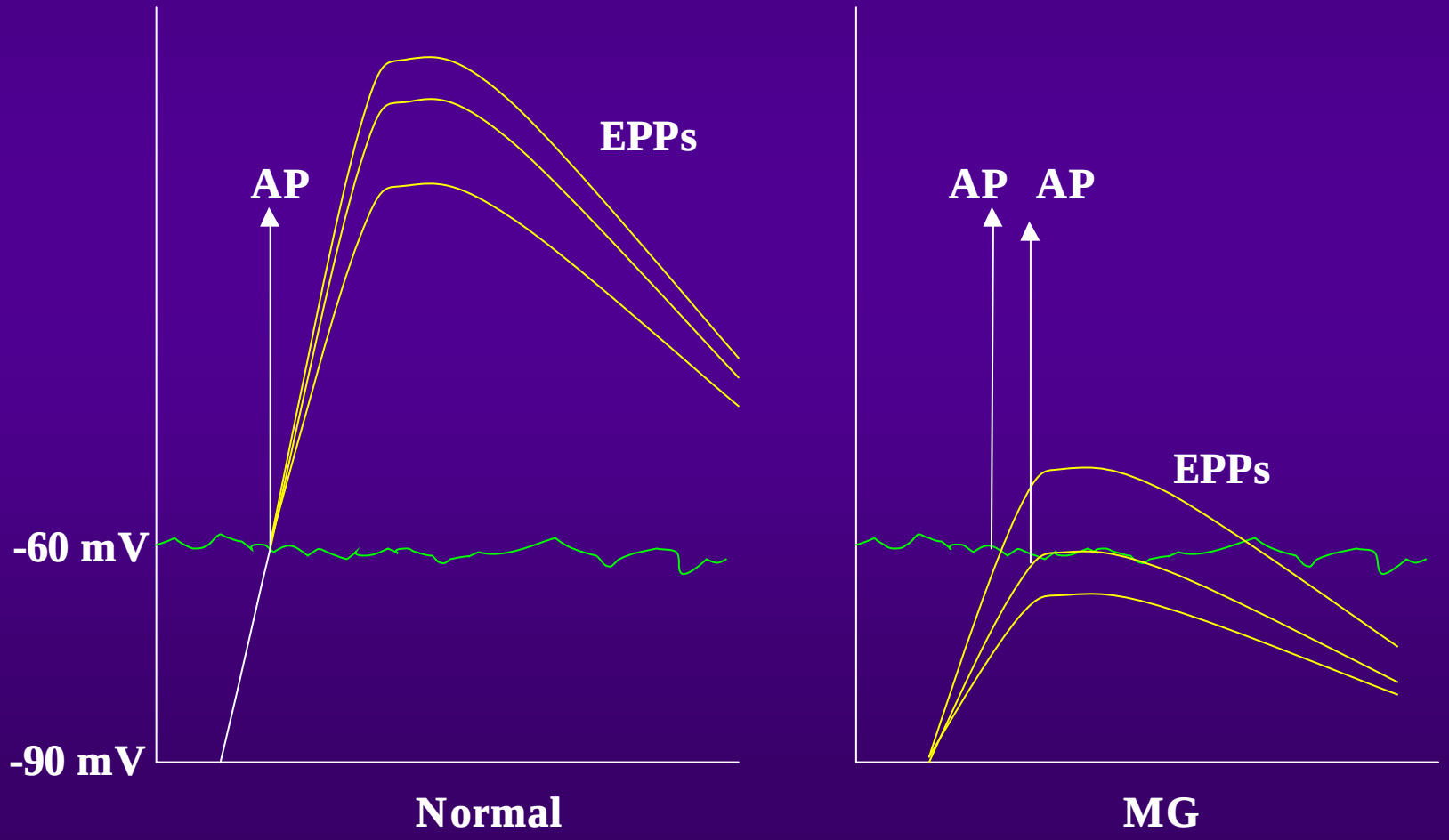
# *Intracellular recordings, - action potentials not shown*

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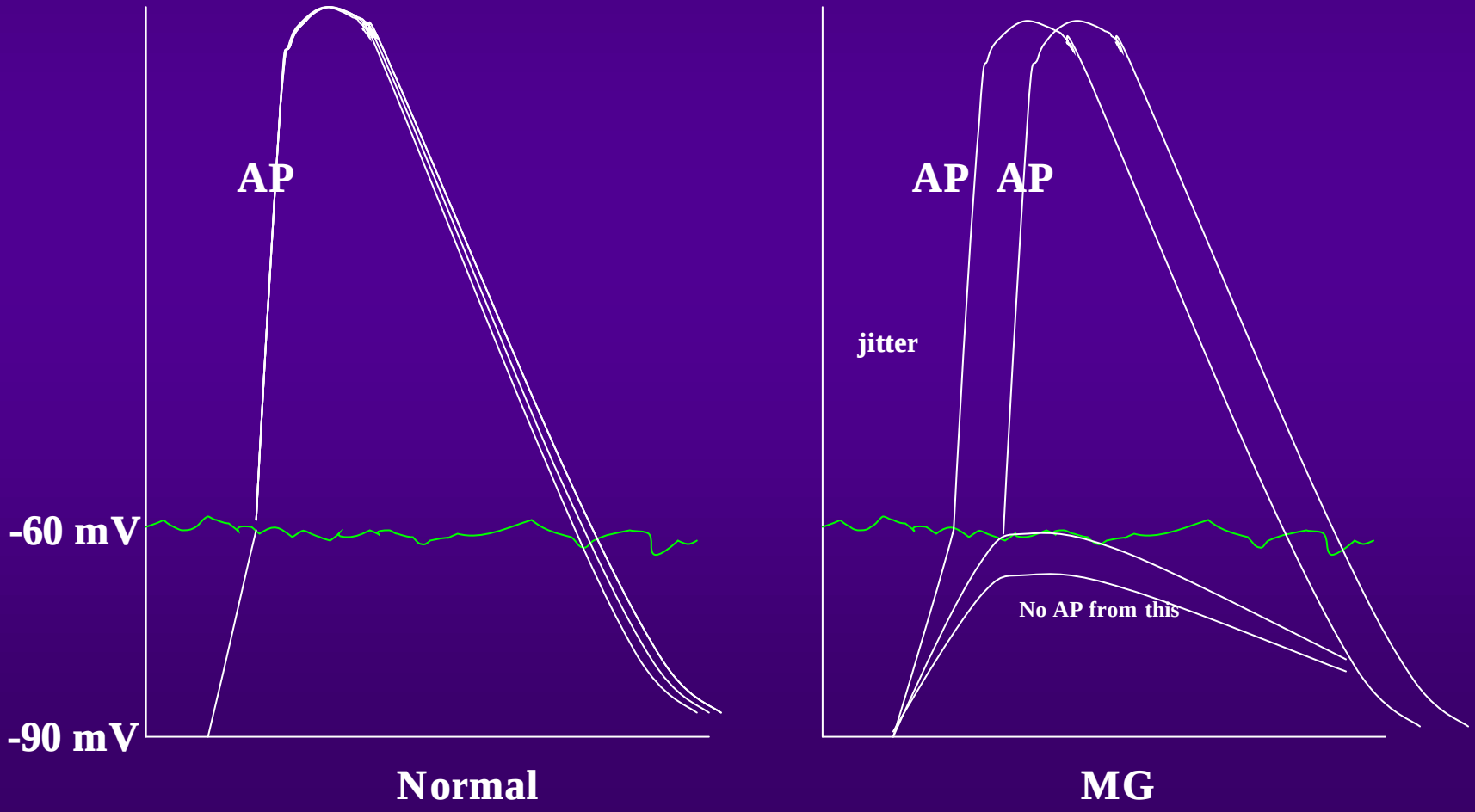
# *Intracellular recordings, schematic with APs*

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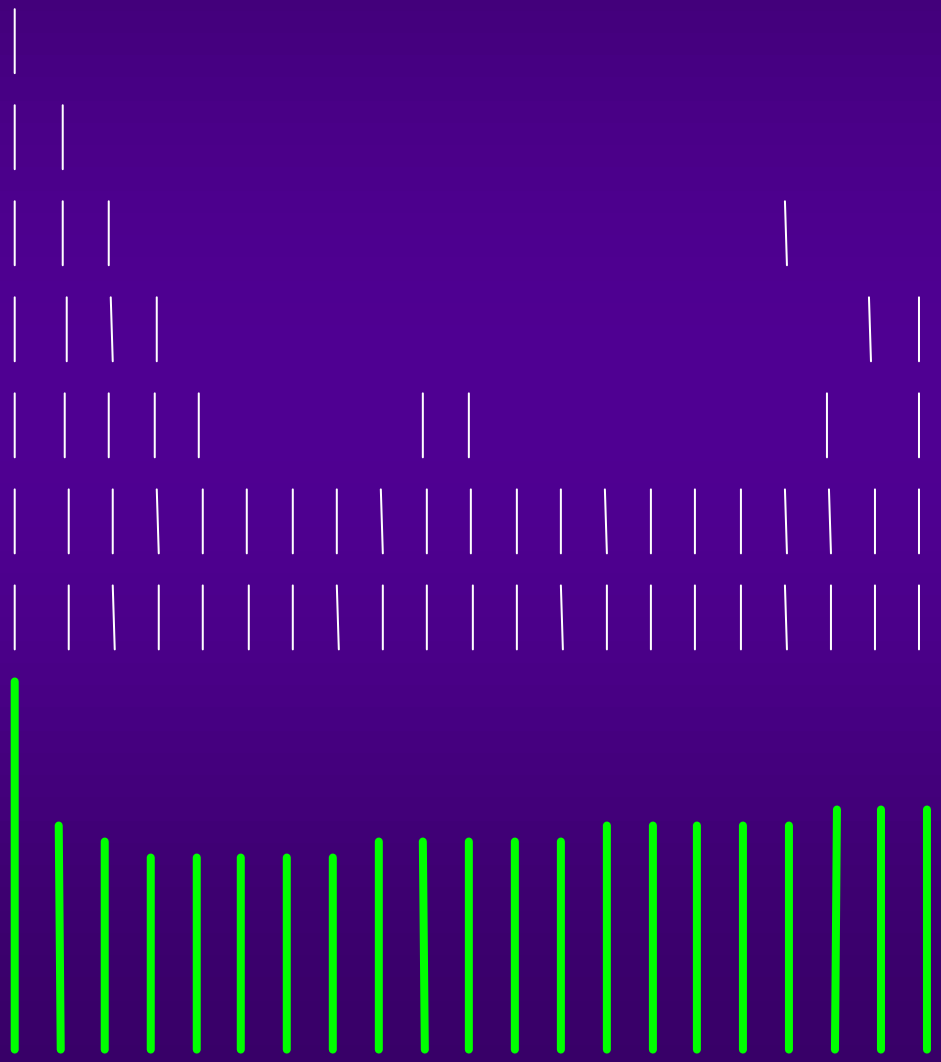
# *Schematic explanation to the myasthenic decrement*



**All or none reponse of individual motor end-plates**

**CMAP representing the sum of above**

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# *Tests for MG*

- **CLINICAL**
  - **History**
  - **Tests** → **fatigue, Tensilon, curare**
- **EMG**
  - **Rep nerve stimulation** → **slow-fast, postactivation, ischemia, curare, stair-case, paired stimuli**
  - **Needle-EMG** → **shape variability**
  - **SFEMG** → **jitter**
- **INTRACELL REC**
- **STAPEDIUS REFLEX**
- **OCULOGRAPHY**
- **TONOMETRY**
- **ACHR ANTIBODIES**

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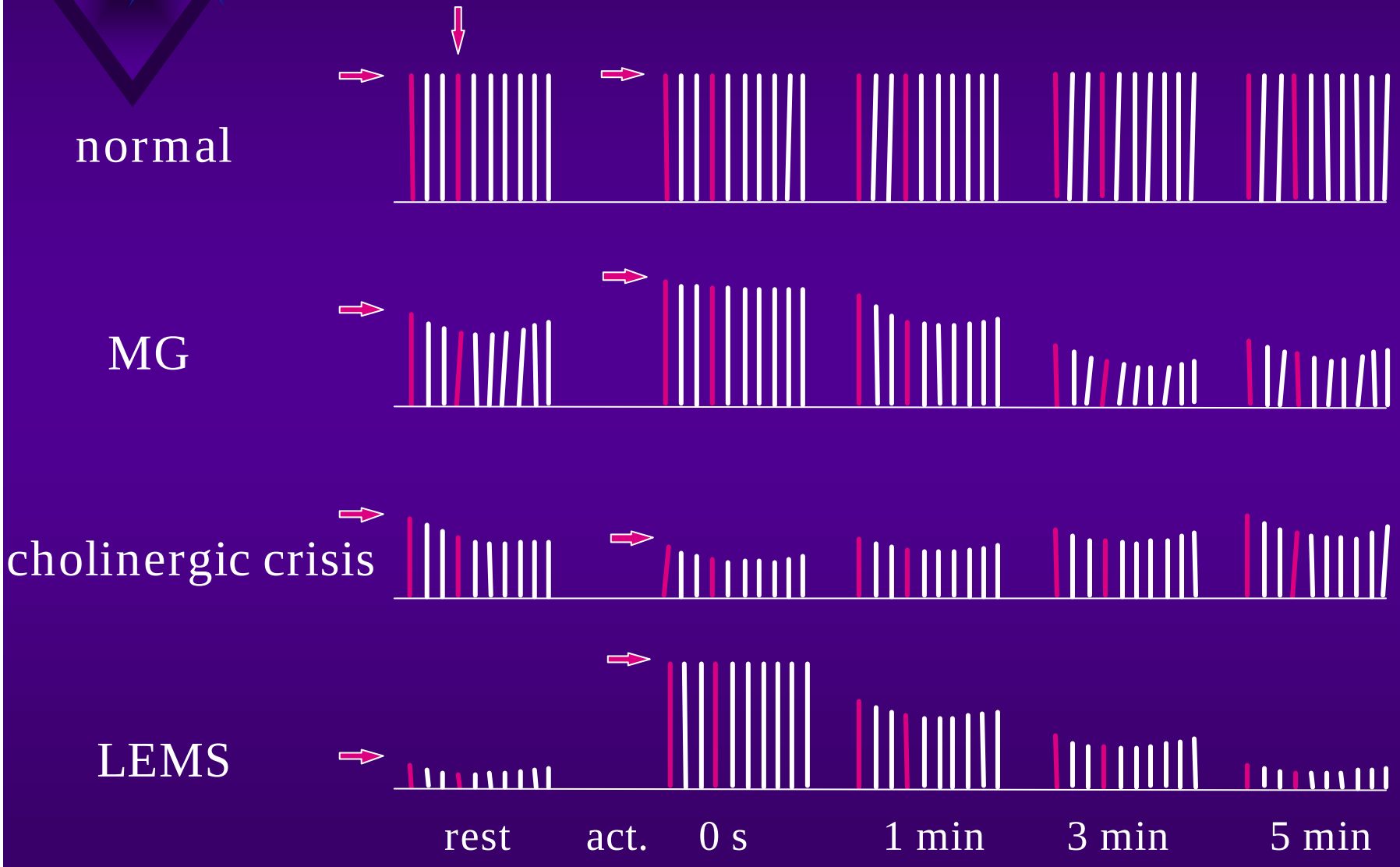
# Decrement protocol

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# *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

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# *Parameters to analyse*

- initial amplitude
- decrement
- amplitude after activity (postactivation facilitation)
- decrement after activity
- ampl and decrement after 1, 3 and 5 min (postactivation exhaustion)

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# *Rep.nerve stimulation: considerations*

- distal / proximal muscle
- rest / fatigue
- on / off treatment
- cold / warm
- stim. frequency
- muscle fixation

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# *Muscles to test*

- Deltoideus
- Trapezius
- Anconeus
- Nasalis
- Orbicularis oculi
- EDB
- Rectus femoris

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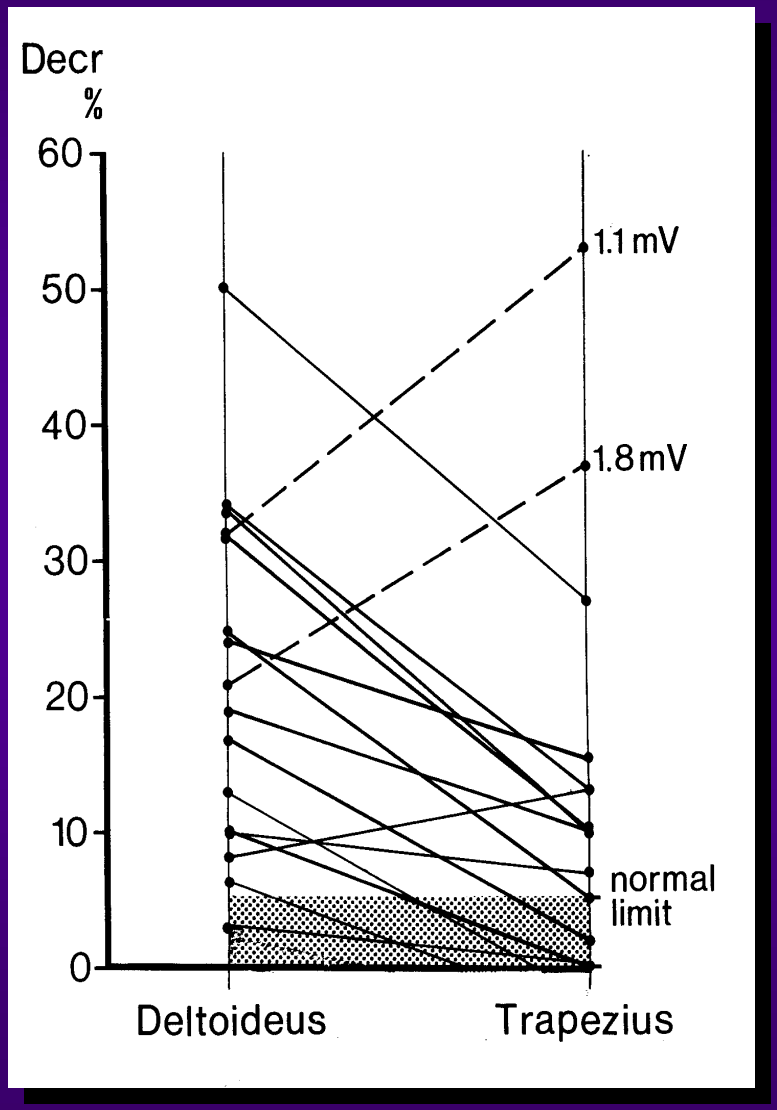
# Decrement in 2 proximal muscles




| | | |
|---|---|---|
| **Mean decrement** | **24.8** | **15.8** |
| **Mean amplitude** | **8.0** | **6.4** |

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# *Decrement at rest*


**M. abd dig min** **M. deltoideus** **M. anconeus**

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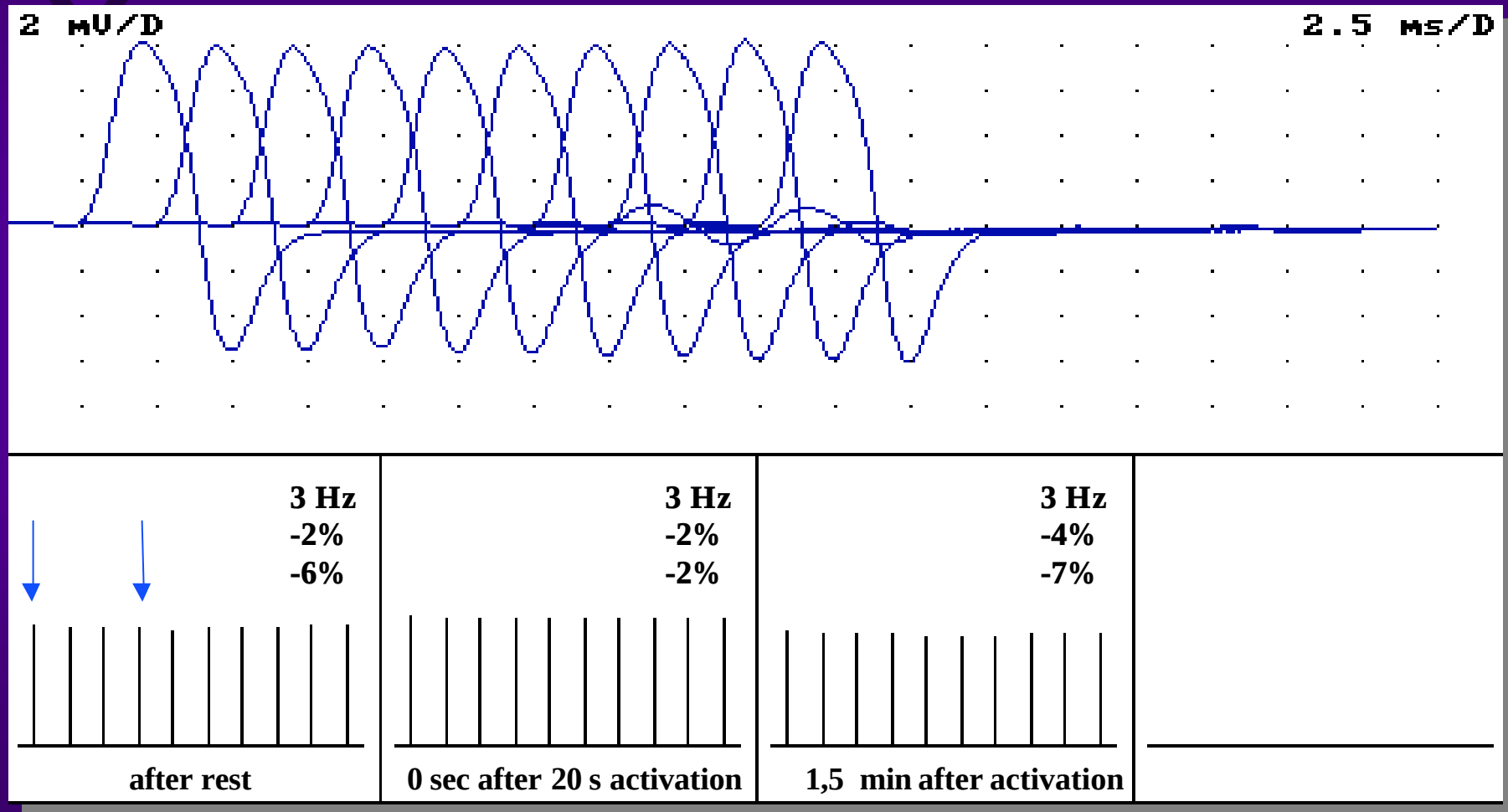
# *Is there?*

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

# Repetitive nerve stimulation
# Anconeus muscle

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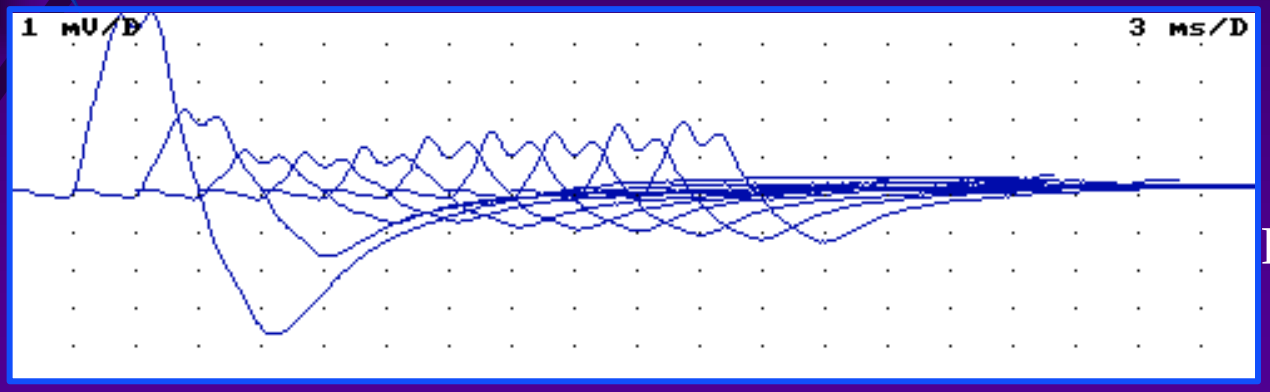
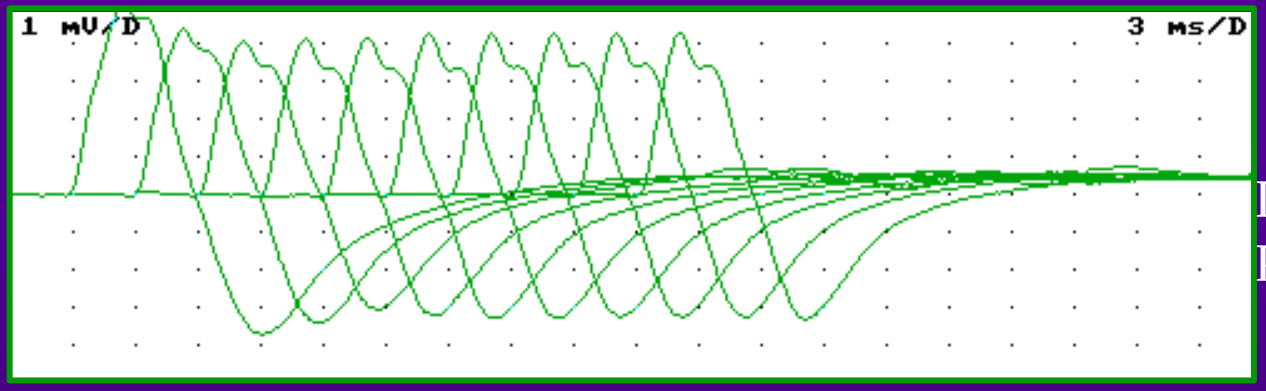
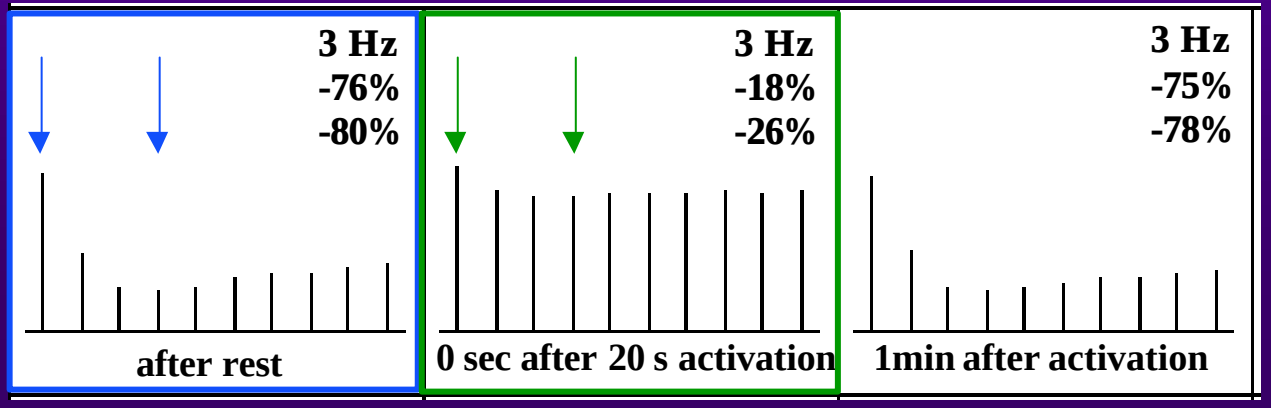
# *Repetitive nerve stimulation in a patient with severe MG*




Rest, 3 Hz 10 stim




Directly after 20 s act.
Post-act facilitation




Left ADM

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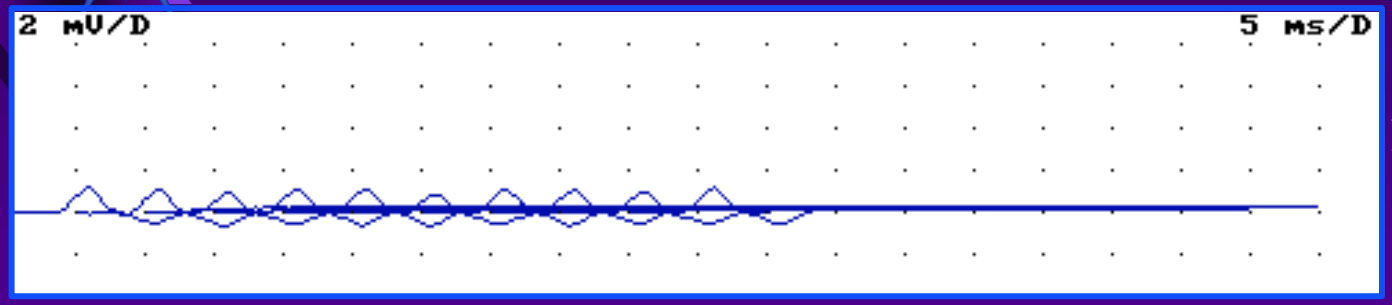
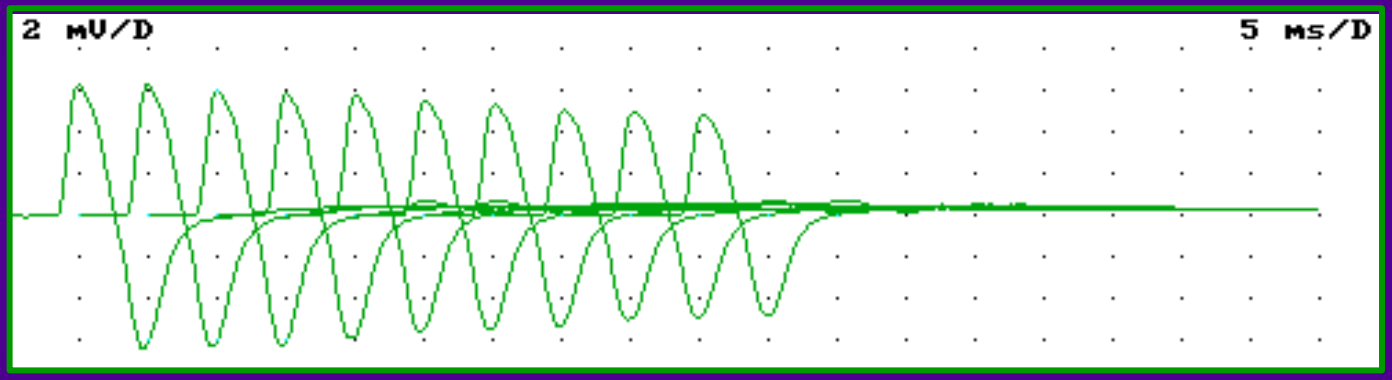
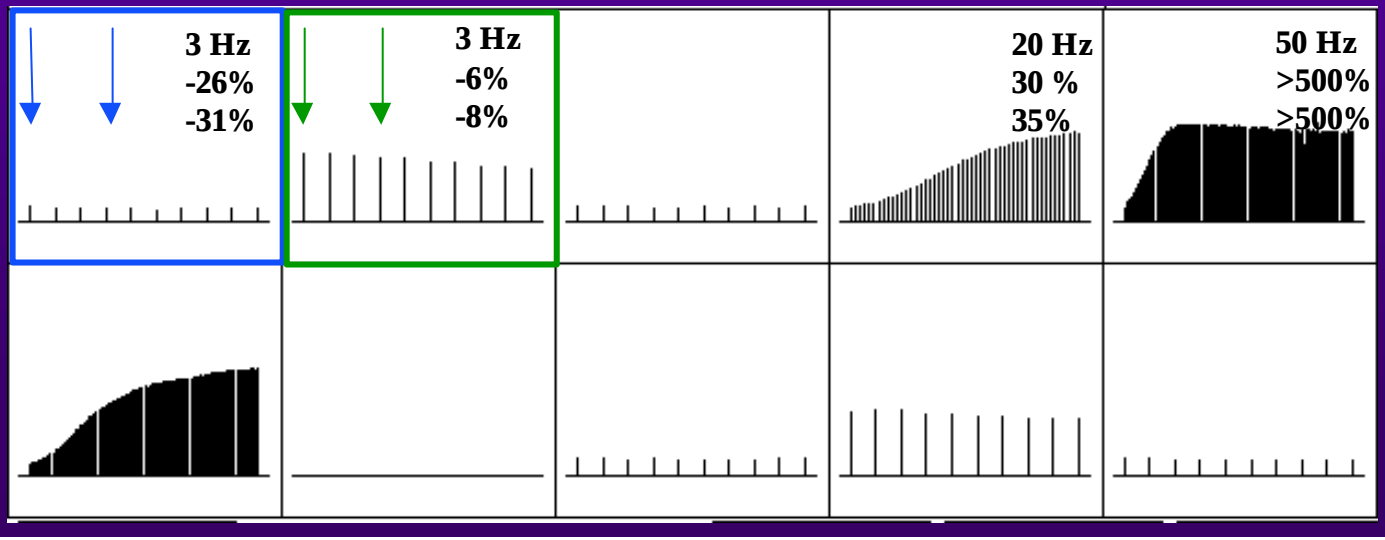
# LEMS, *Repetitive nerve stimulation at rest*




Rest, 3 Hz 10 stim




Directly after 20 s activation = facilitation




Right ADM

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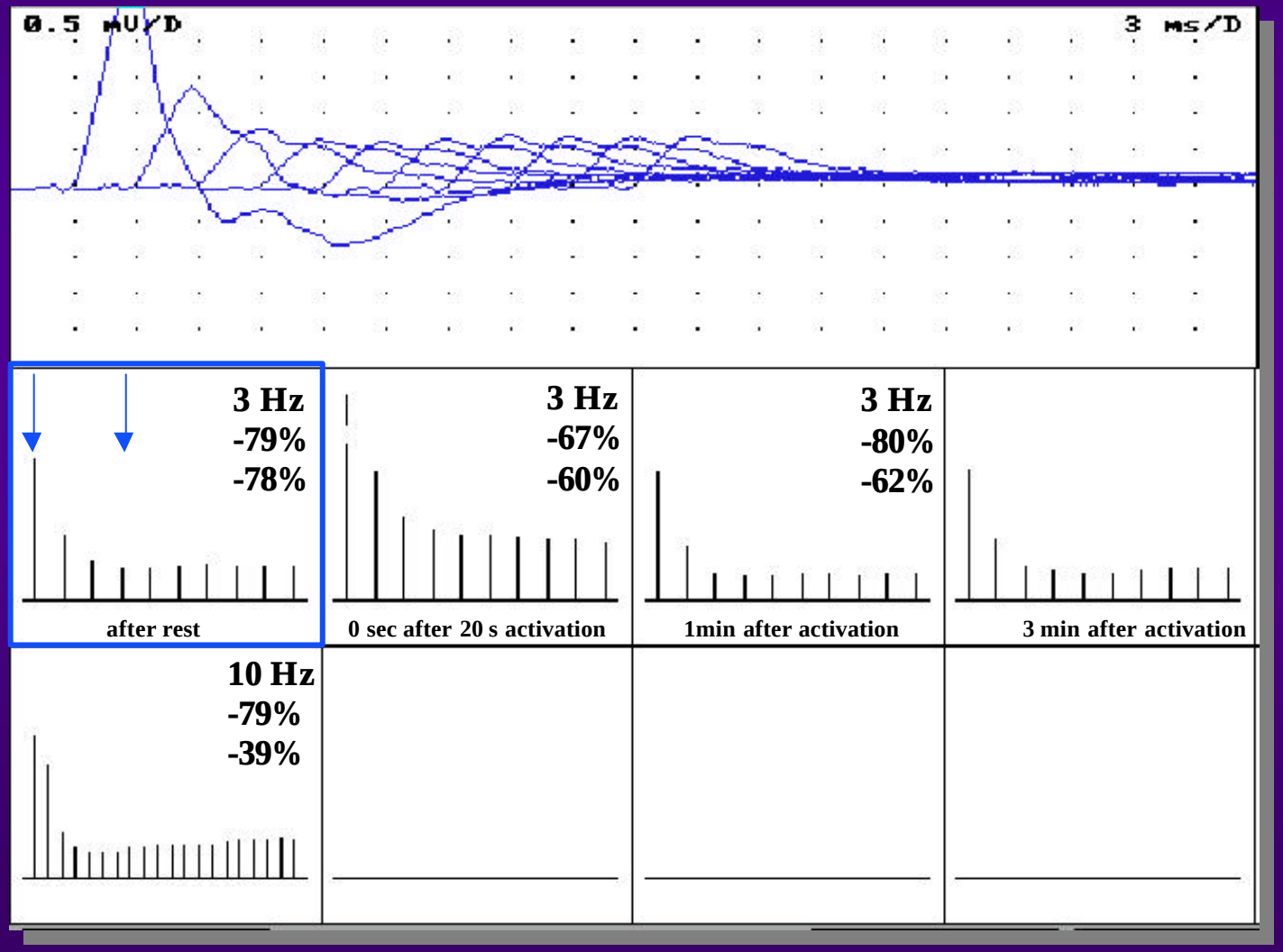
# *Congenital myasthenia* *(slow channel)*

## Repetitive nerve stimulation

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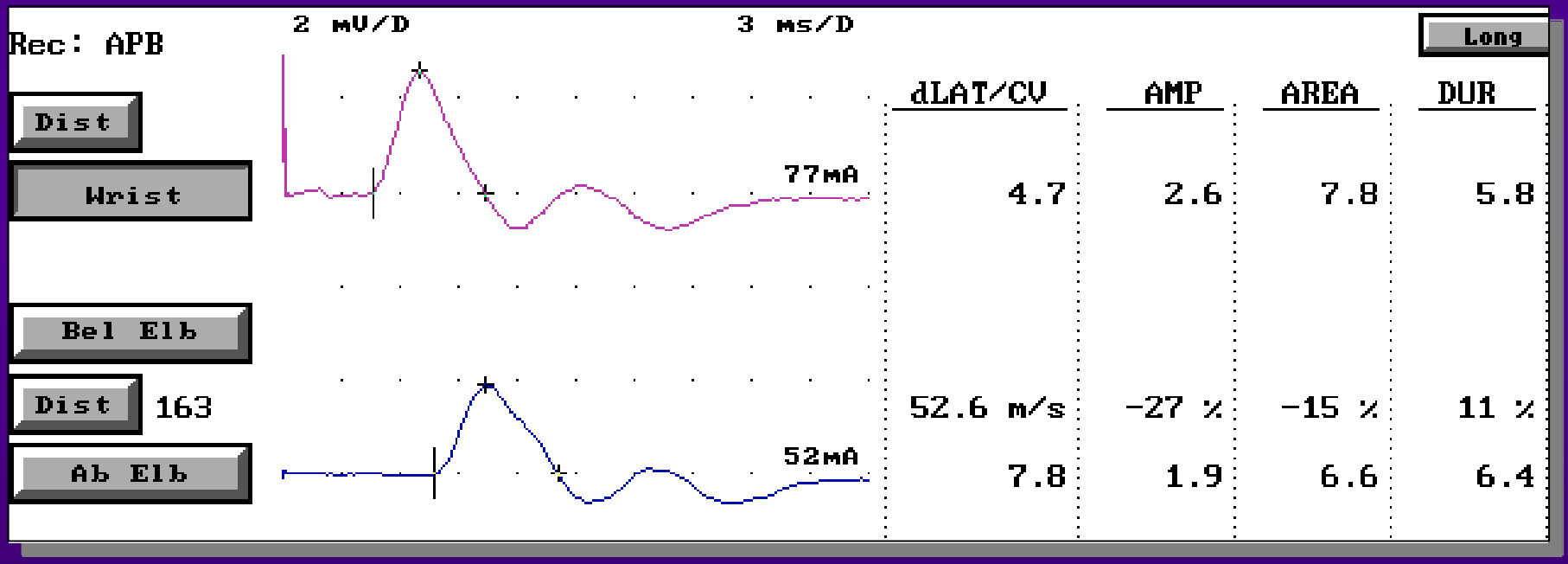
# *Congenital myasthenia* *(slow channel)*

## Abnormal CMAP

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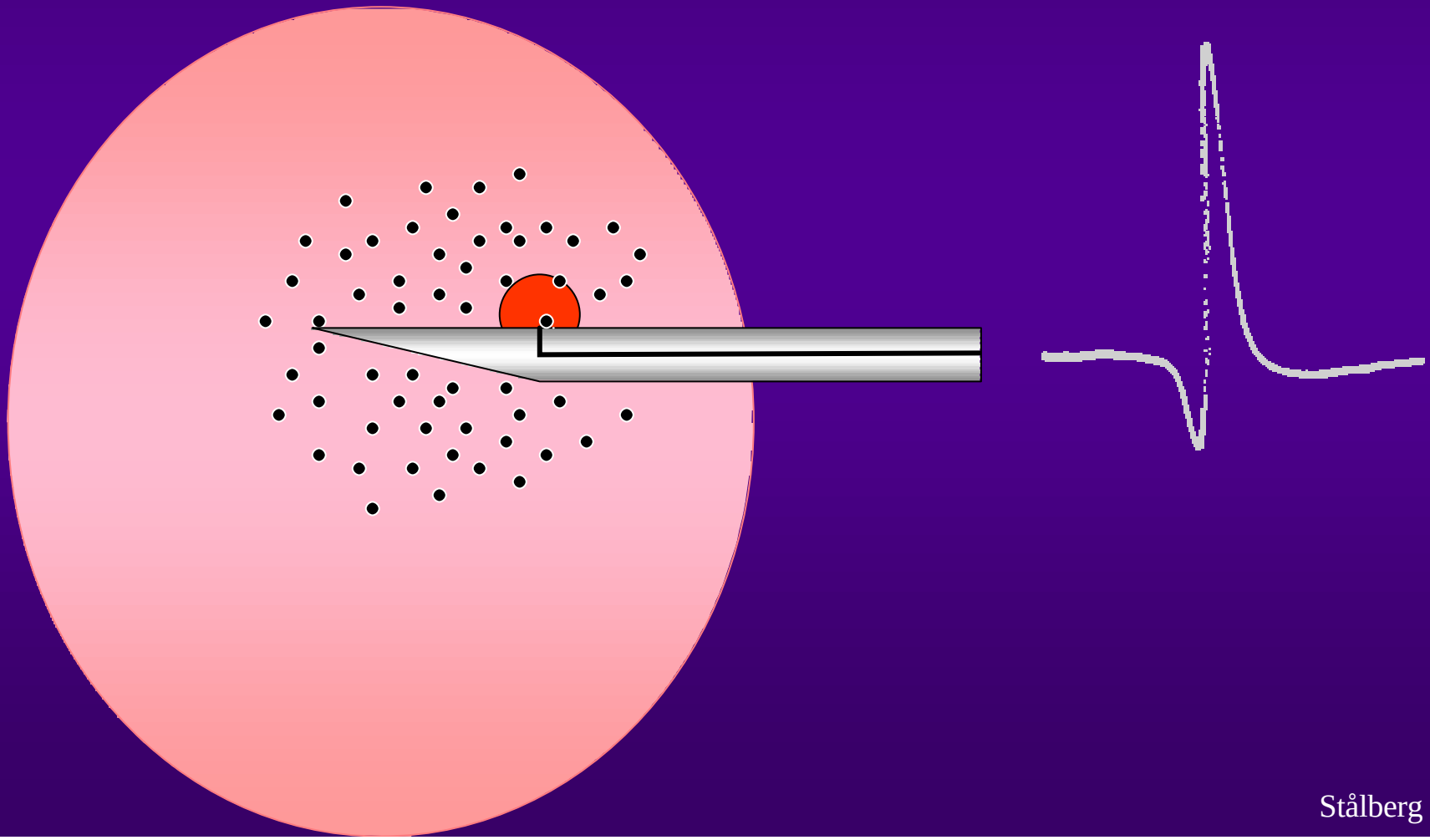
# SFEMG (Single Fibre EMG) signal from 1 muscle fibre



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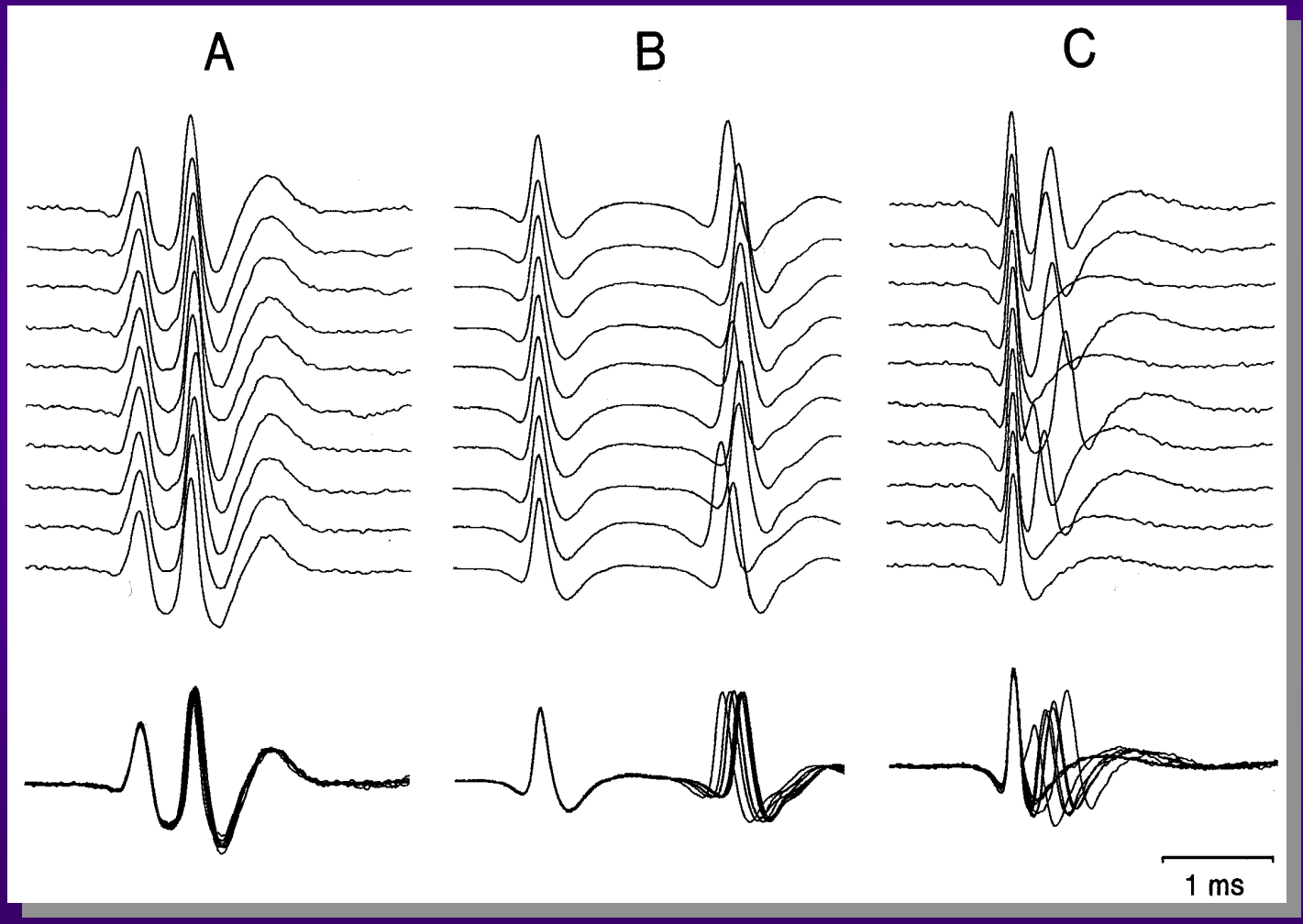
# *Single fiber action potentials*

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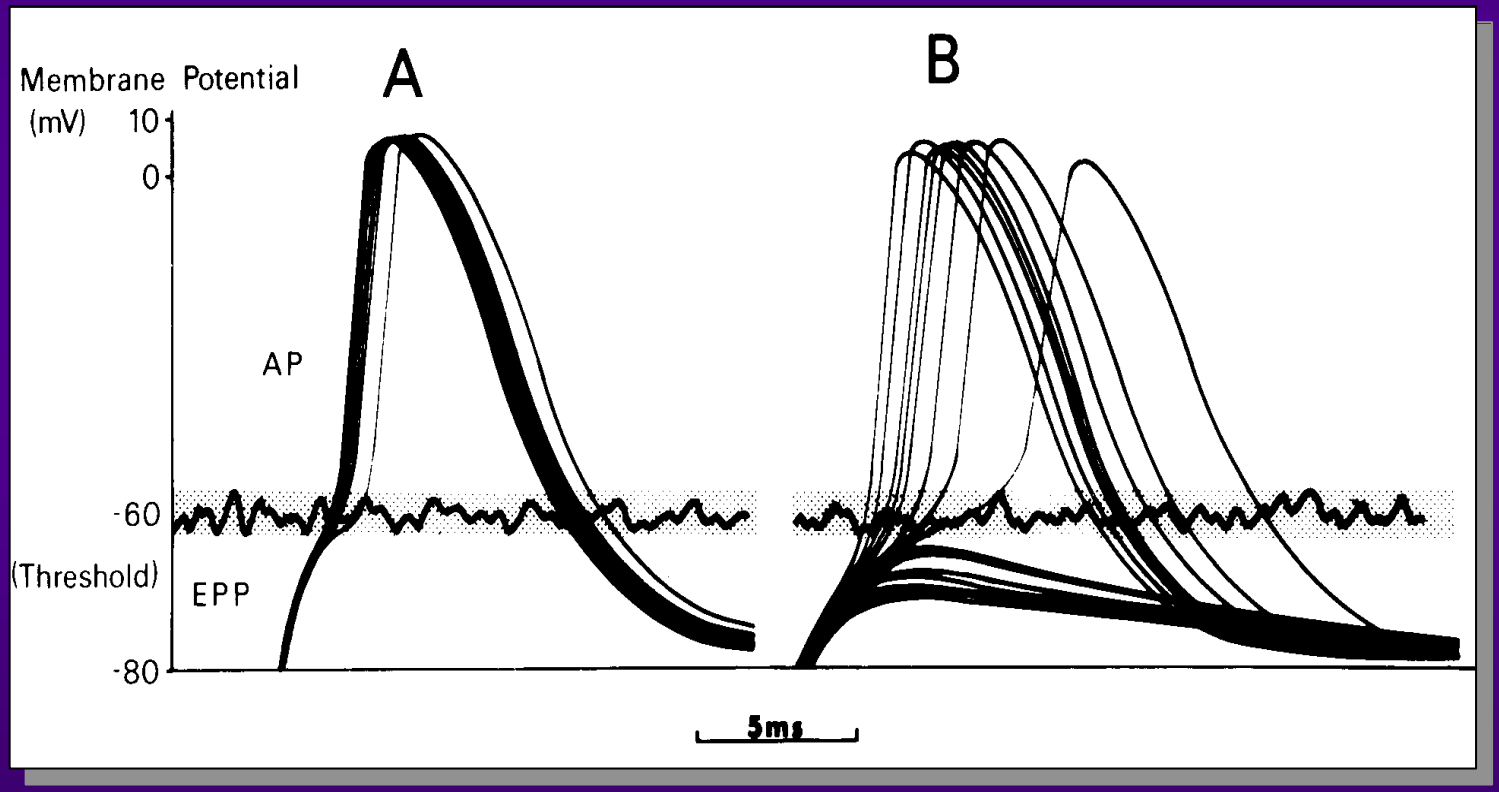
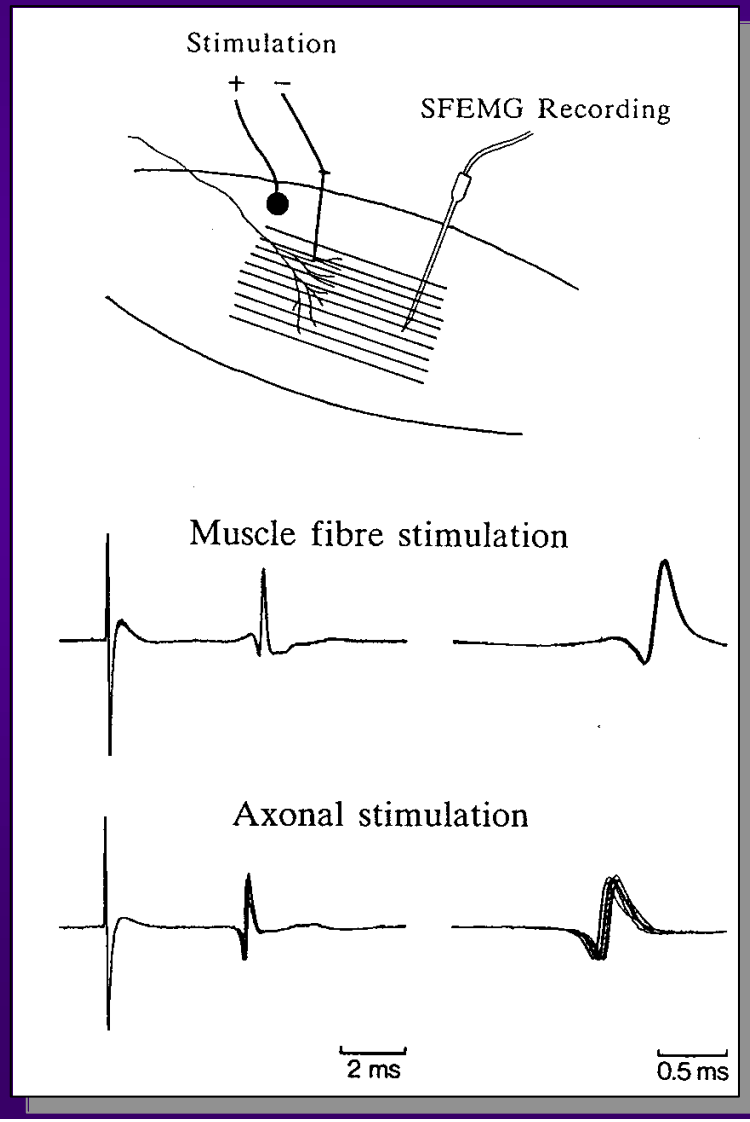
# EPP, AP



# *Intramuscular stimulation and SFEMG recording*

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# *STIM SFEMG can be used to study*

- muscle membrane parameters
- n-m transmission
- axonal conduction
- spinal reflexes
- central pathways

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# *SFEMG INDICATIONS*

- *Neuromuscular transmission in diseases*
- *Experimental studies of n-m transmission*
- *Spatial organisation of MUs in diseases*
- *Firing pattern*
- *Spike triggering*
- *Propagation velocity*

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# Diagnostic tests for MG

% positive results from a total of 291 patients

| Group | SFEMG | Decrement ADM | Decrement Delt | Stapedius reflex | Anti-AChr |
|---|---|---|---|---|---|
| **Ocular** | | | | | |
| EDC + Frontalis | 85 | 4 | 19 | 90 | 76 |
| **EDC** | 59 | | | | |
| **Mild generalized** | 96 | 31 | 68 | 91 | 76 |
| **Mod-severe generalized** | 100 | 68 | 89 | 63 | 88 |
| **Remission** | 62 | 0 | 0 | 83 | |

Stålberg Sanders 1981

# MG

## Protocol

**Repetitive nerve stim** — **normal** — **abnormal** → STOP

**SFEMG** — **normal** — **abnormal** → STOP

**EMG ( 2 dist, 1prox)** — **normal** — **abnormal**

↓

**Neurography, MCS, SCS** — **normal** — **abnormal** → STOP

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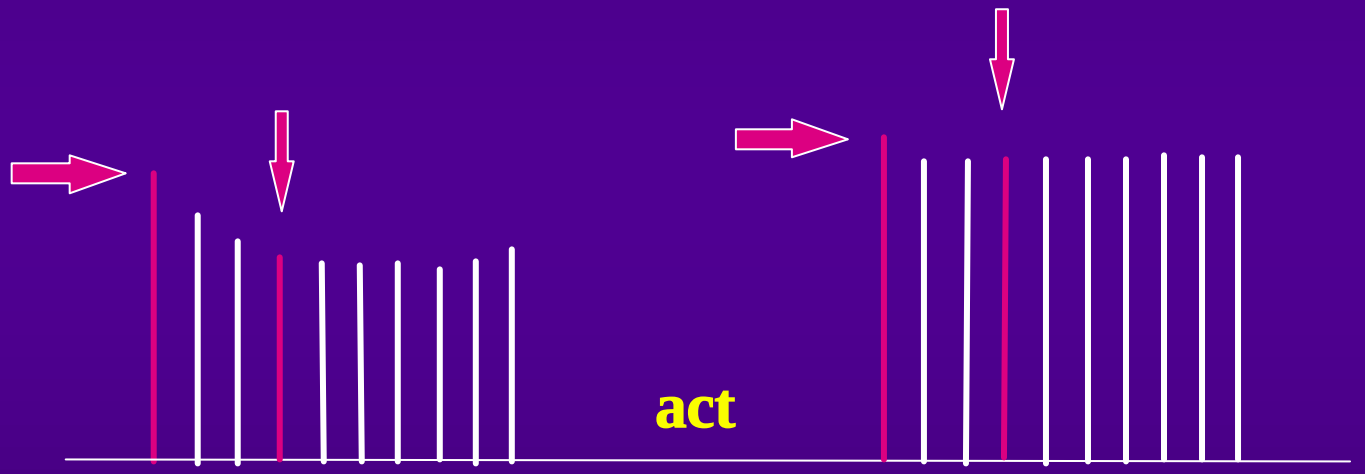
# *Comparison of diagnostic tests in 550 untreated Myastenia Gravis patients*

| | SFEMG any muscle | SFEMG EDC | RNS | AchR-Ab |
|---|---|---|---|---|
| Ocular | 97 | 60 | 48 | 55 |
| Generalized | 99 | 89 | 76 | 80 |

RNS= Repetitive nerve stimulation; ADM= abductor dig min; AchR-Ab= acetylcholine receptor antibodies

Sanders, Massey and Howard.
Unpublished, with permission.

# *Decrement protocol*

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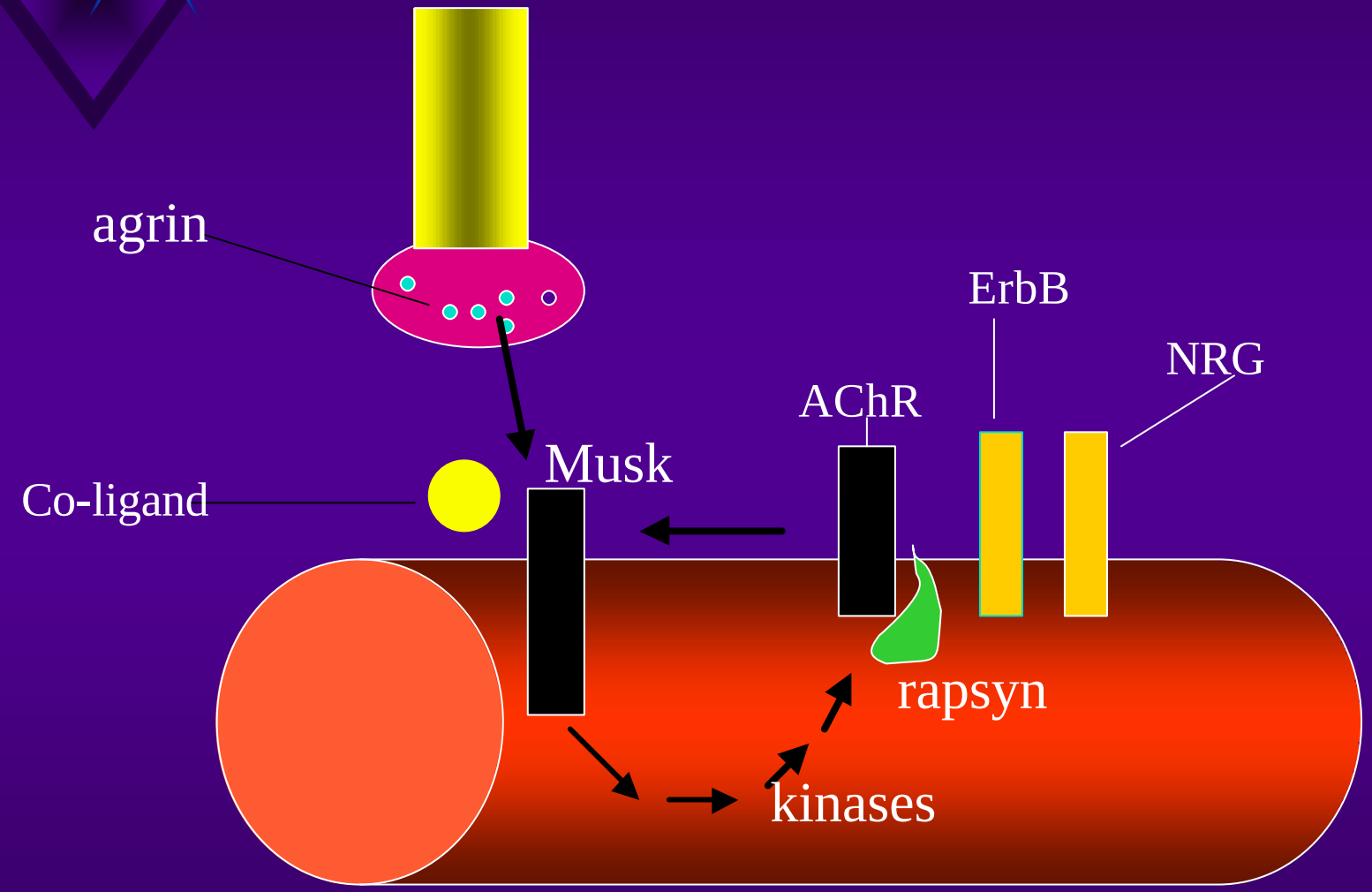
## Seroneg MG= no AChR antibody titer (15%)

10% of these have antibodies to Muscle Specific tyrosine kinase, MuSK

# AGRIN / MUSK SIGNALLING



# *Motor end-plate in AChR ab+ and MuSK ab+ muscles*

**AChR ab+:**

Significant reduction of postsynaptic area
Reduced membrane density

Deposition of complement C3

**MuSK ab+:**

Preserved AChR
Slight reduction of postsynaptic area
Preseved membrane density
Complement C3