ELECTROPHYSIOLOGICAL ASSESSMENT OF NERVE AND MUSCLE HYPEREXCITABILITY

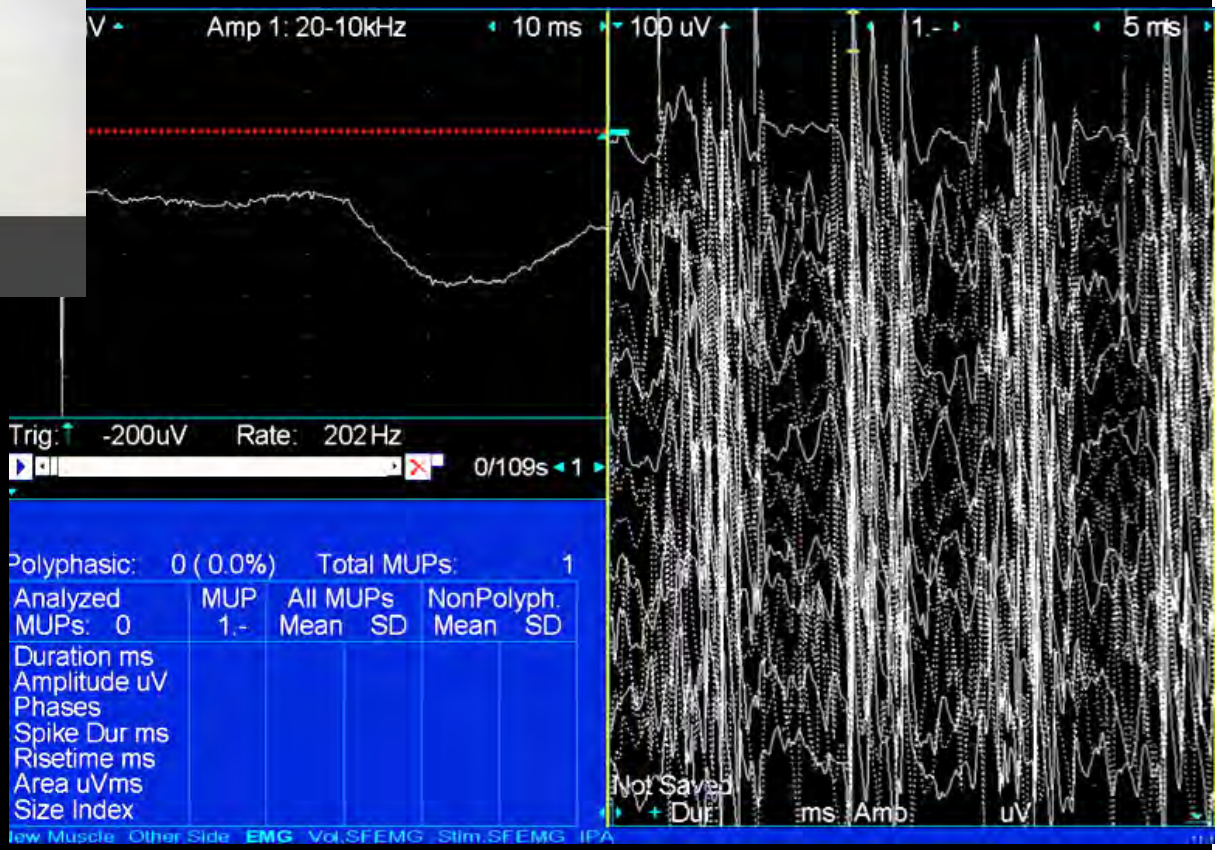
CON YIANNIKAS

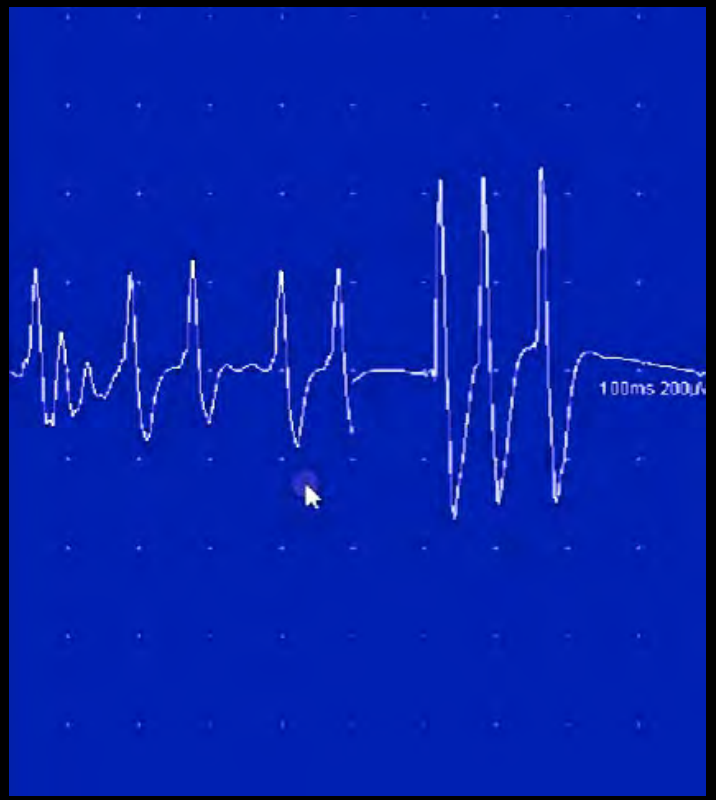
Peripheral Nerve Hyperexcitability

- Spontaneous and continuous muscle fibre activity of peripheral nerve origin.
- Neuromyotonia represents the more severe phenotype of generalized PNH.
- Fasciculation cramp syndrome at the other end.
- Acquired often associated with voltage gated potassium channel antibodies.
- Clinical and/or electrical features may be seen in number of other conditions affecting peripheral nerves

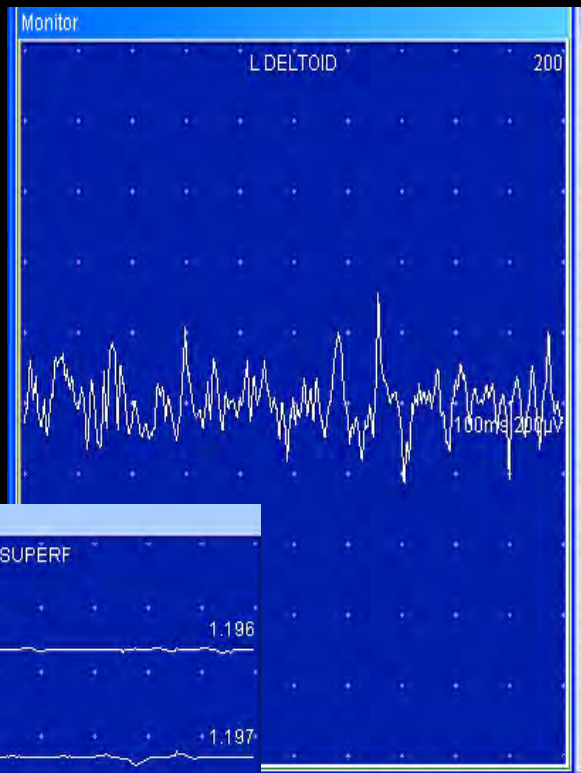
Syndromes of Peripheral Nerve Hyperexcitability		
Autoantibody mediated (Voltage gated potassium Channel Antibodies VGKC)	Non Immune mediated	Fasiculation Cramp Syndrome
Isolated	Genetic Hereditary Neuropathies Schwartz-Jampel syndrome Episodic Ataxia I KCNA1 Gene mutations	With VGKC antibodies Without VGKC antibodies
Paraneoplastic Thymoma(MG/NMG) Small cell Lung Ca Hodgkins Lymphoma Plamacytoma (IgM PP)	Acquired neuropathies Chronic Inflammatory Demyelinating Polyneuropathy Guillaine Barre Syndrome Multifocal motor neuropathy	
Associated with other Autoimmune Disorders MG without thymoma Coeliac Disease Pernicious Amnaemia Hyper thyroidism Hypothyroidism Rheumatoid Disease SLE Systemic Sclerosis Penicillamine induced Diabetes	Drugs Oxaliplatin Gold Toxins Focal Neuropathies/Plexopathies/ Radiculopathies Entrapment Post Irradiation	

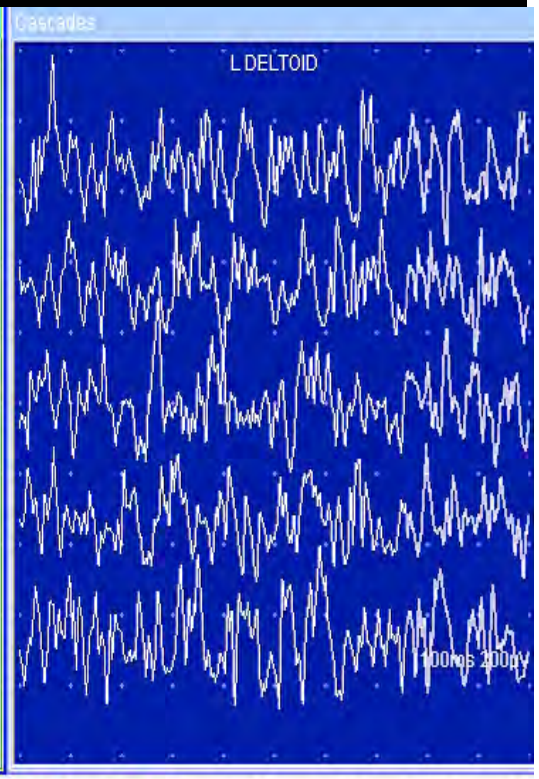

metron

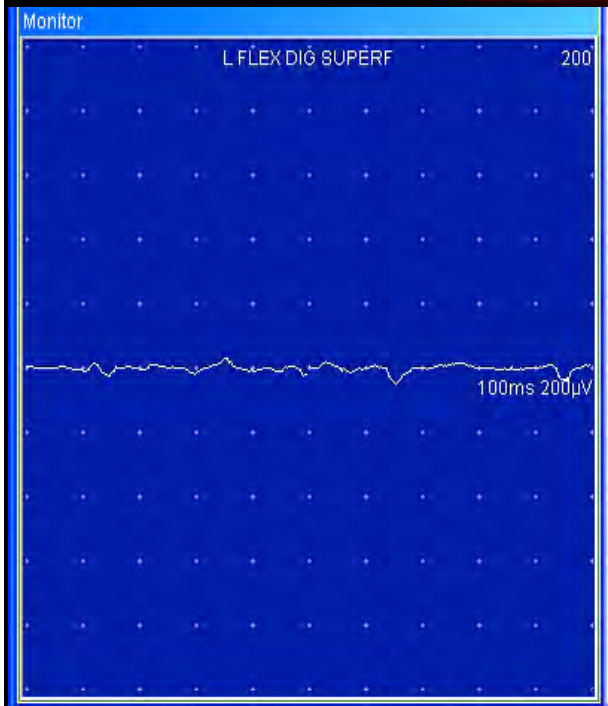

Amp 1: 20-10kHz
10 ms
100 uV
1.-
5 ms
Trig: -200uV
Rate: 202 Hz
0/109s 1
Polyphasic: 0 (0.0%)
Total MUPs: 1
Analyzed MUPs: 0
MUP 1.-
All MUPs Mean SD
NonPolyph. Mean SD
Duration ms
Amplitude uV
Phases
Spike Dur ms
Risetime ms
Area uVms
Size Index
Not Saved
Dur ms Amp uV
Muscle Other Side EMG Vol.SFEMG Stim.SFEMG IPA



MYOKYMIA


Monitor
L DELTOID
200
100ms 200µV


Cascades
L DELTOID
100ms 200µV


Monitor
L FLEX DIG SUPERF
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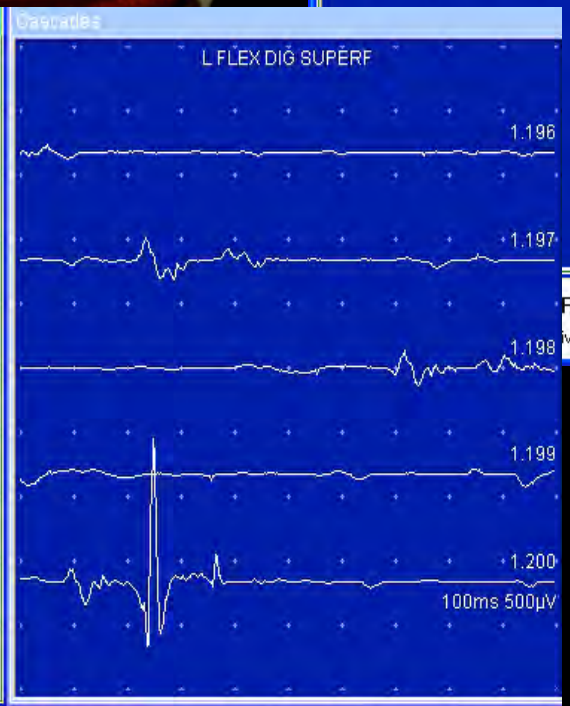
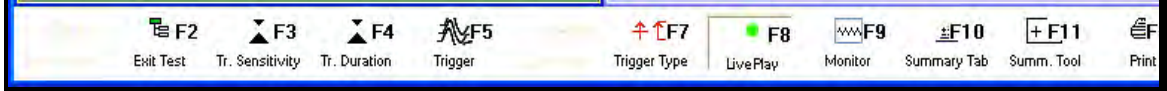
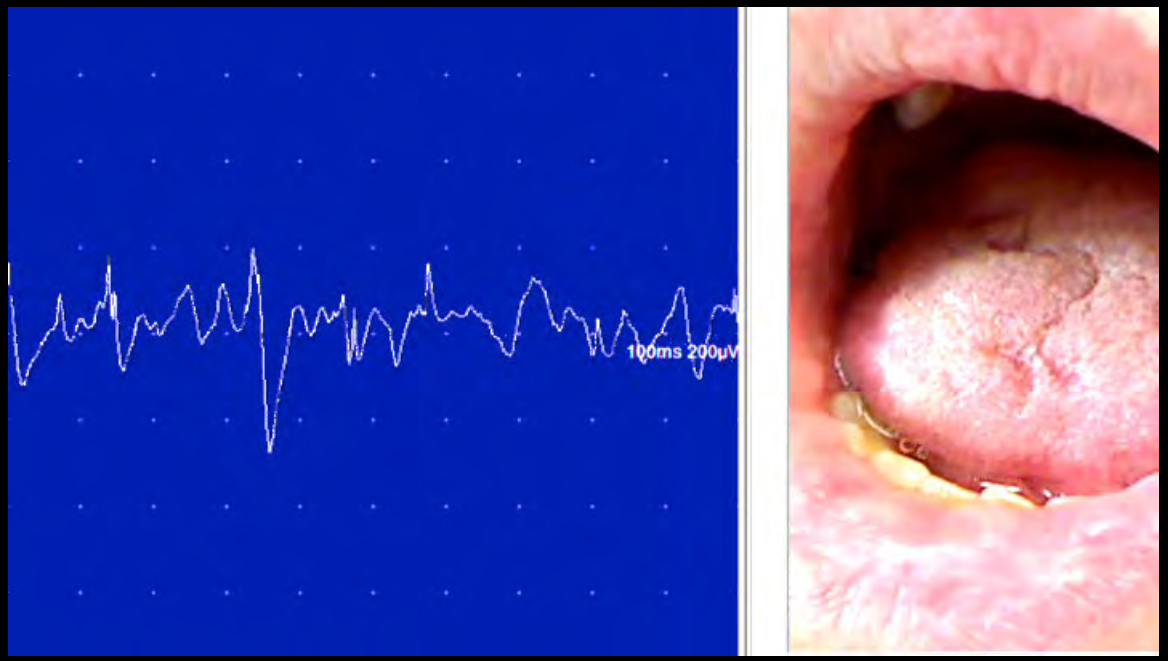
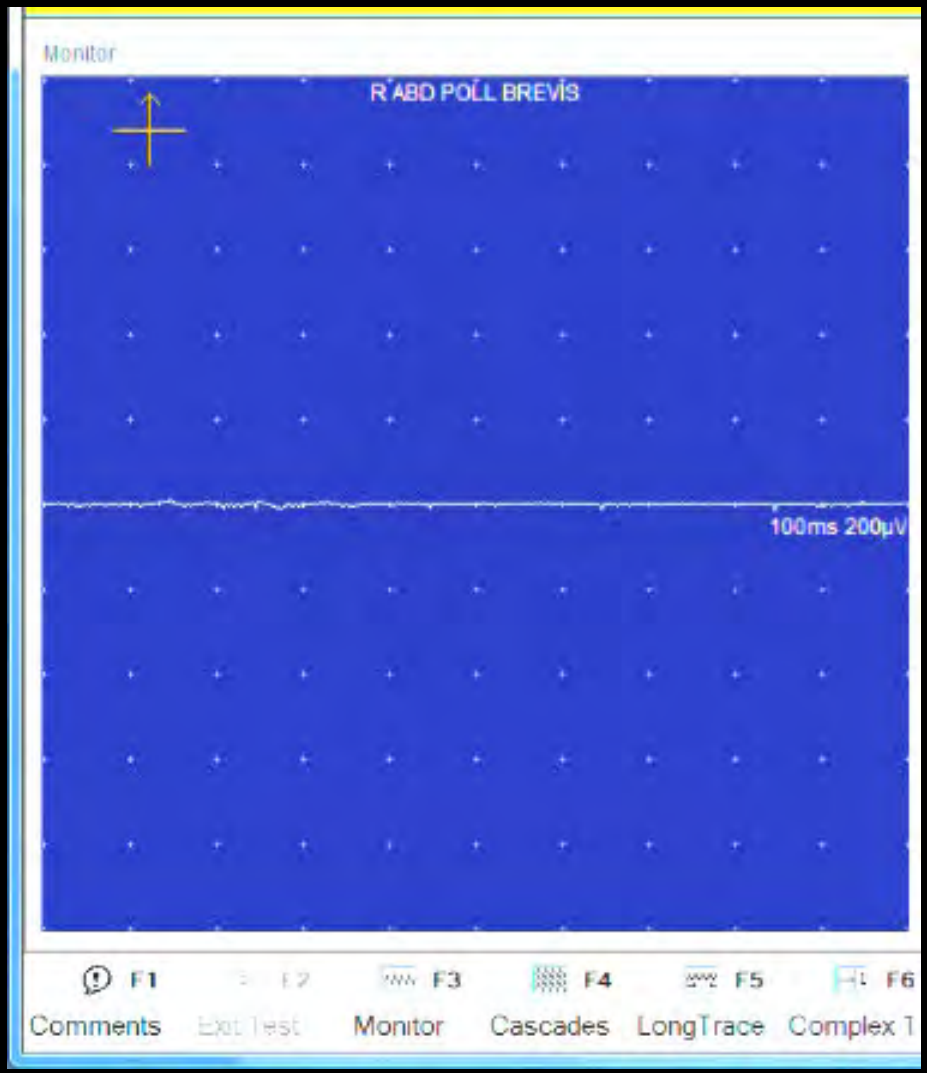
100ms 200µV

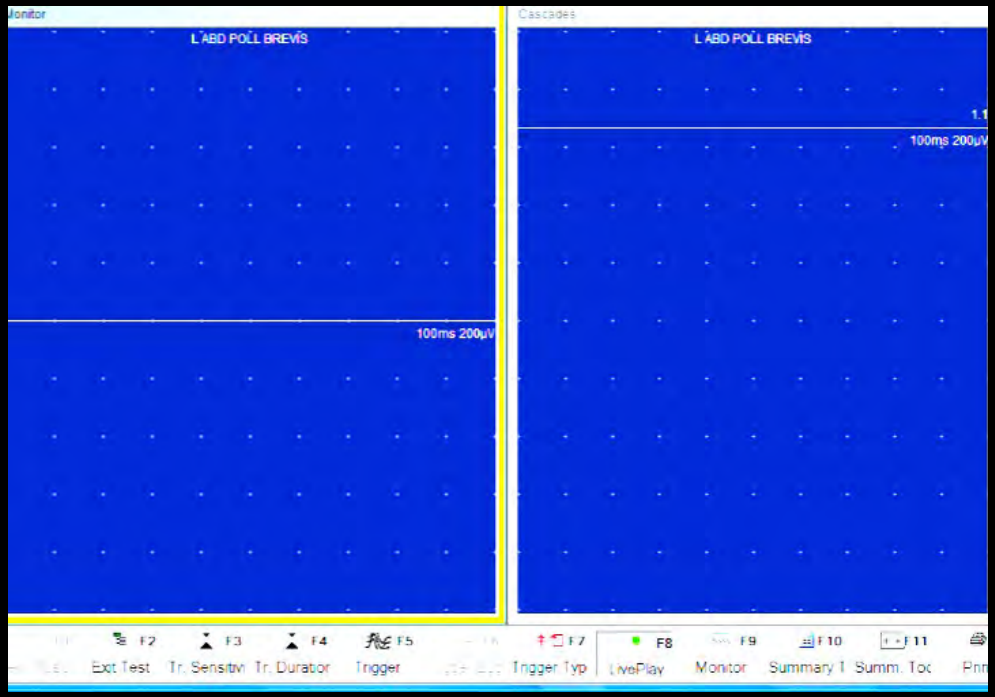

Cascades
L FLEX DIG SUPERF
1.196
1.197
1.198
1.199
1.200
100ms 500µV


F2
Exit Test
F3
Tr. Sensitivity
F4
Tr. Duration
F5
Trigger
F7
Trigger Type
F8
LivePlay
F9
Monitor
F10
Summary Tab
F11
Summ. Tool
Print

Brainstem Irradiation




Monitor
R ABD POLL BREVIS
100ms 200µV
F1
F3
F4
F5
F6
Comments
Monitor
Cascades
LongTrace
Complex T


Monitor
L'ABD POLL BREVIS
100ms 200µV
Cascades
L'ABD POLL BREVIS
100ms 200µV
F2
F3
F4
F5
F7
F8
F9
F10
F11
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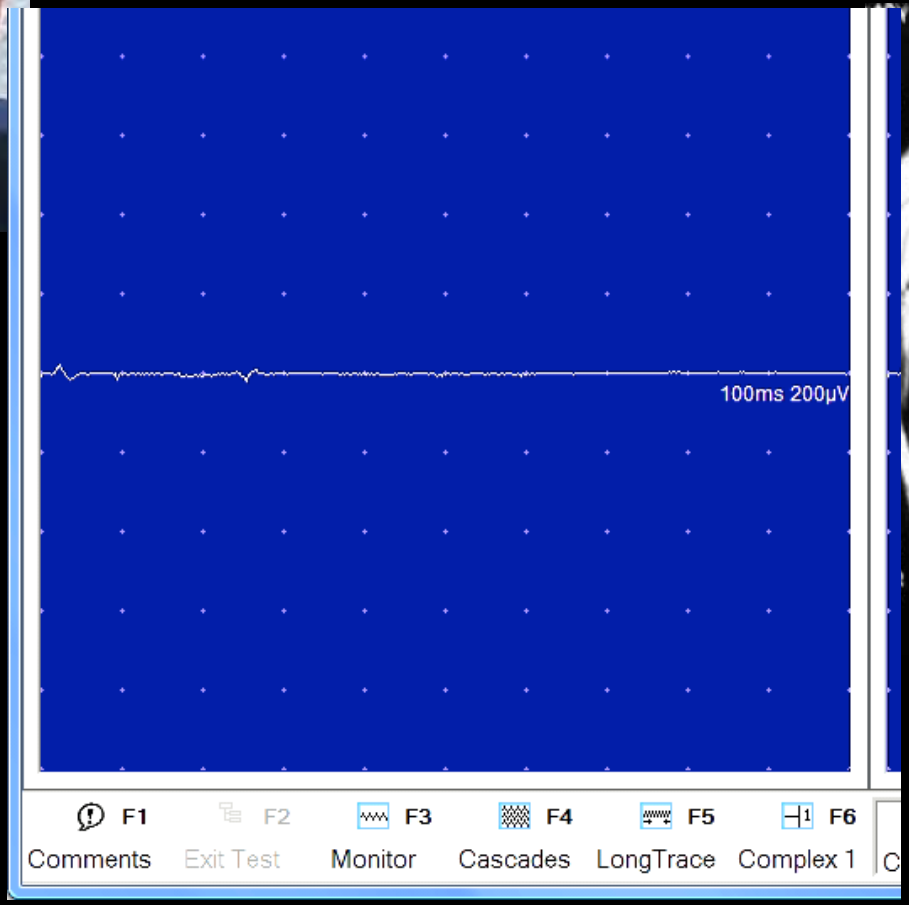
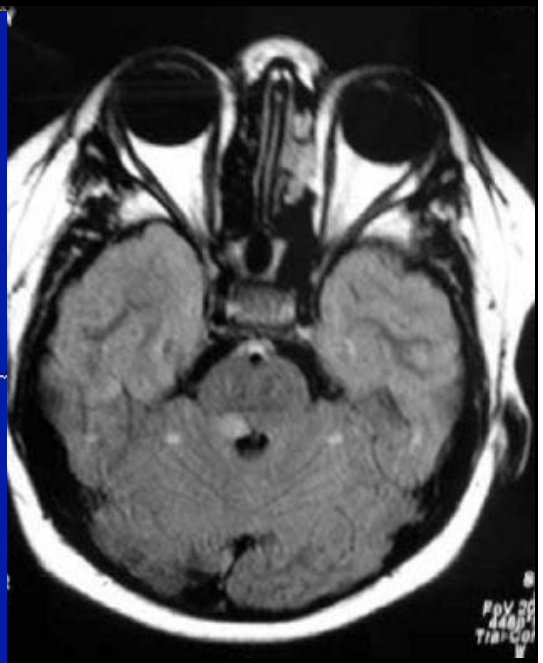
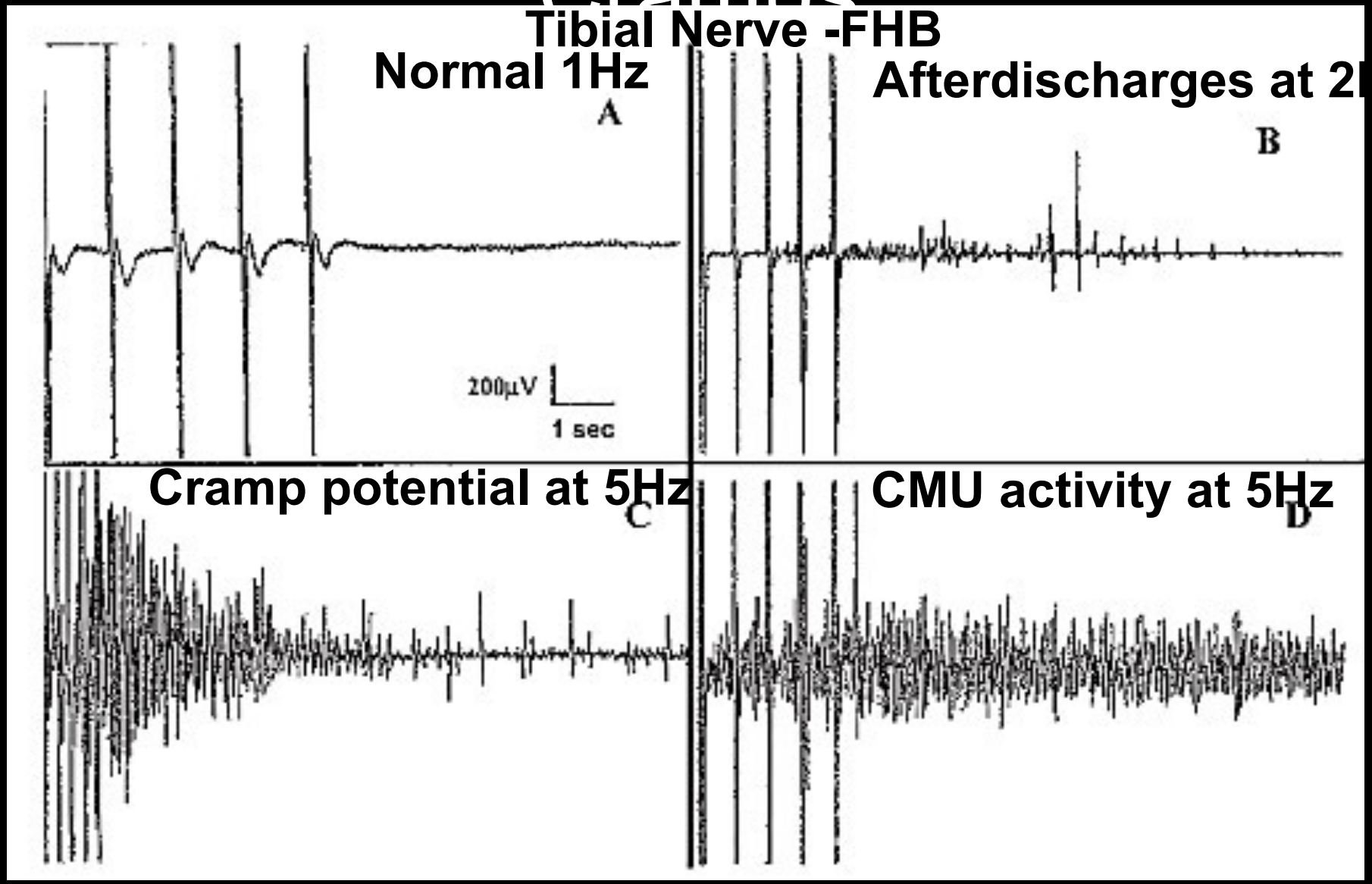
Tr. Sensitivi
Tr. Duration
Trigger
Trigger Typ
LivePlay
Monitor
Summary 1
Summ. Toc

MS Facial Myokymia





RNS- After discharges and Cramps

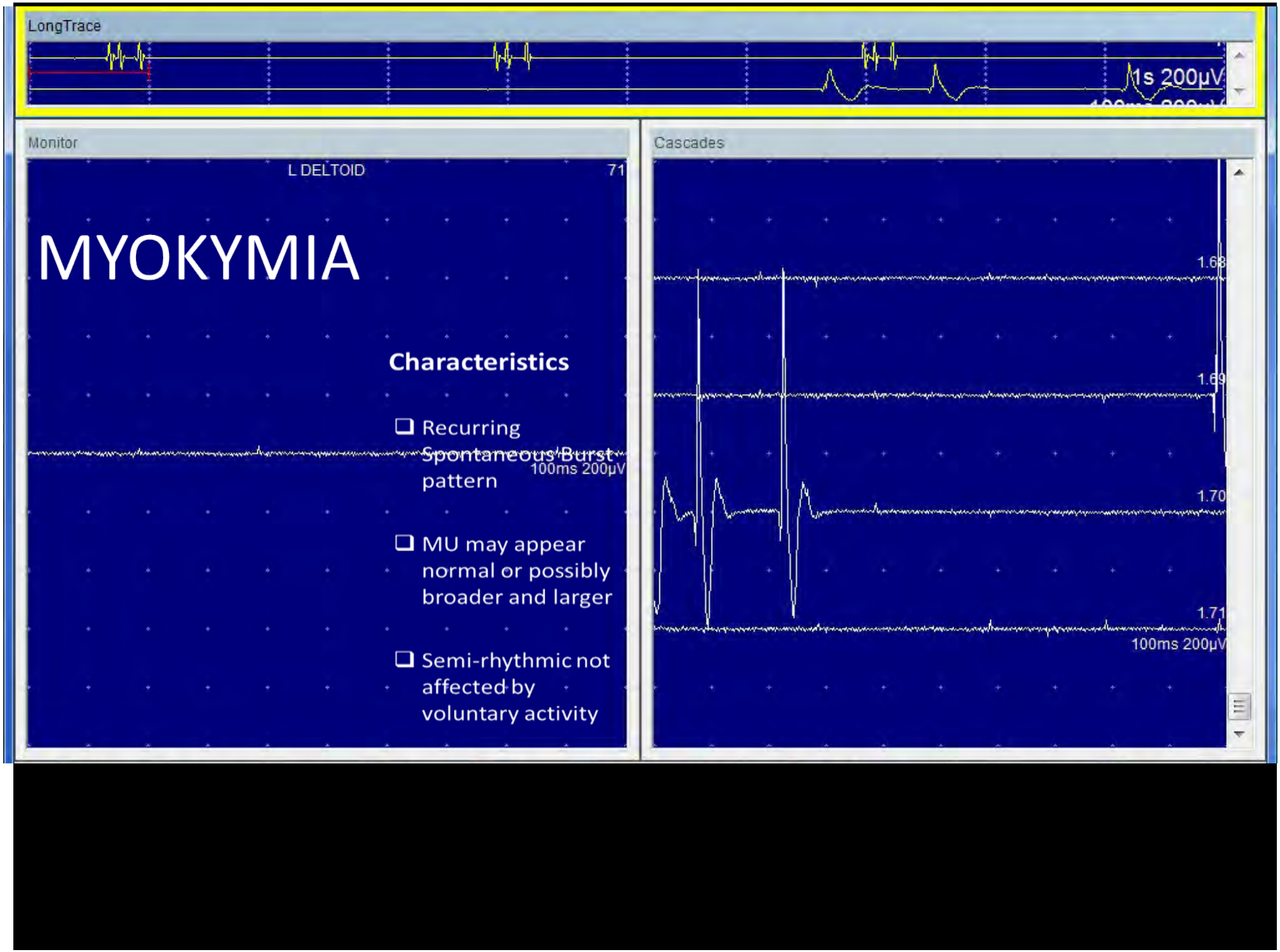


Afterdischarges

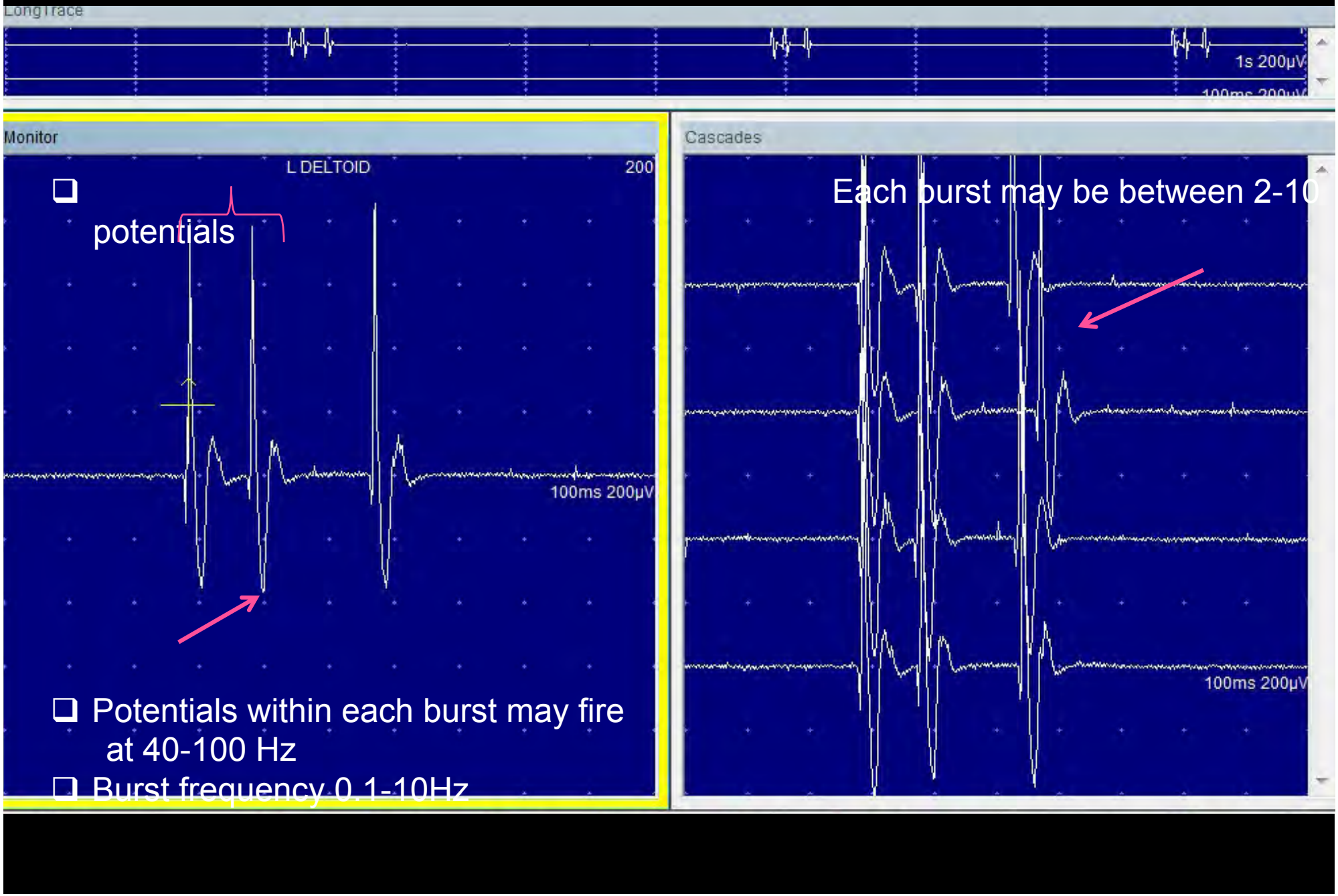
- Frequency dependant
  - 1Hz stimulation greater specifity less sensitive
  - 3-5 Hz Sensitivity above 80% but less specific

Electromyography

- Spontaneous discharges seen
  - Fasciculations
  - Myokymia
  - Neuromyotonia
  - Cramps
  - Continuous motor unit activity.

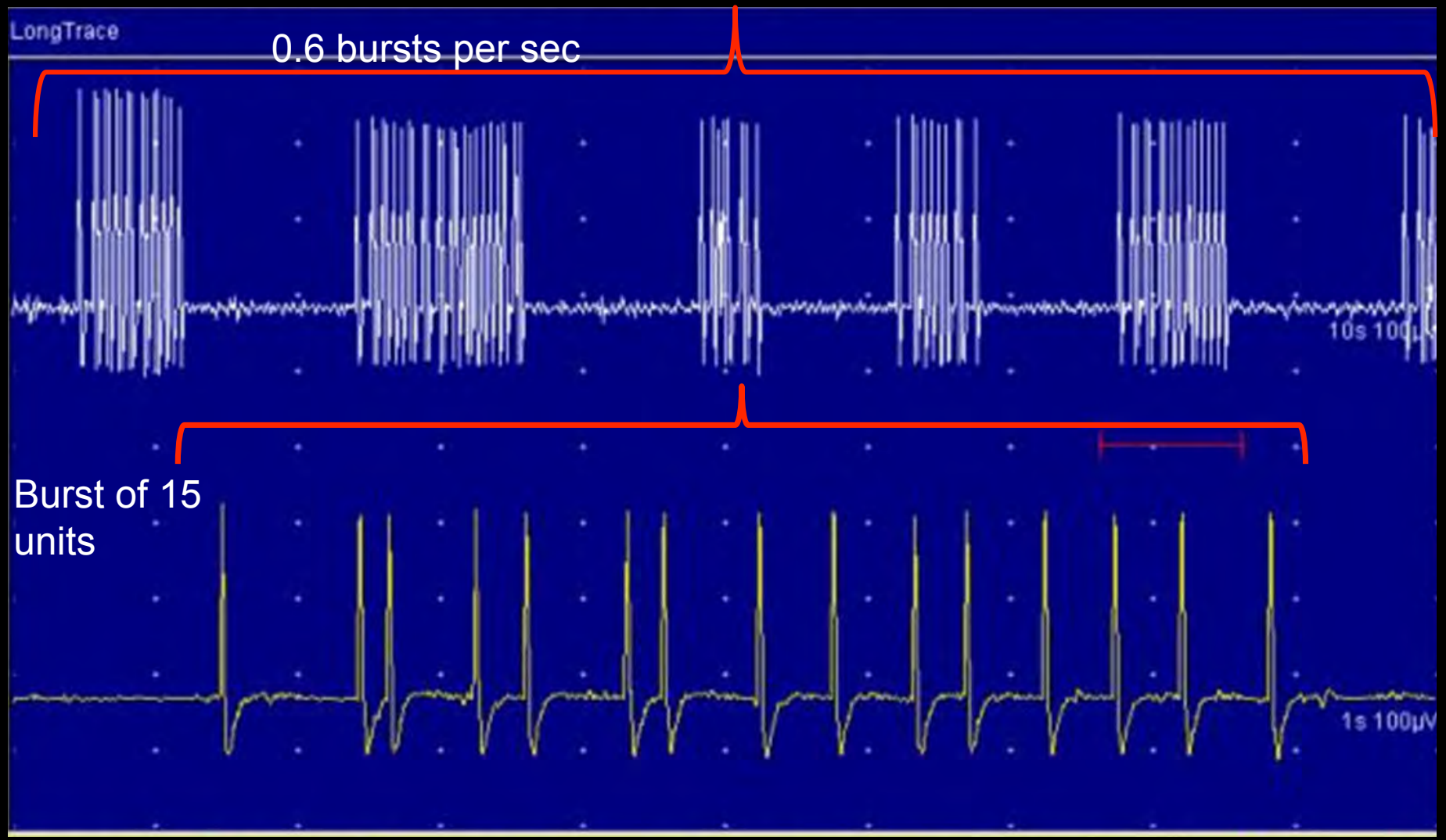

LongTrace
1s 200µV
Monitor
L DELTOID
71
MYOKYMIA
Characteristics
Recurring Spontaneous Burst pattern
100ms 200µV
MU may appear normal or possibly broader and larger
Semi-rhythmic not affected by voluntary activity
Cascades
1.68
1.69
1.70
1.71
100ms 200µV

MYOKYMIA



- ❑ potentials
- ❑ Potentials within each burst may fire at 40-100 Hz
- ❑ Burst frequency 0.1-10Hz

MYOKYMIA

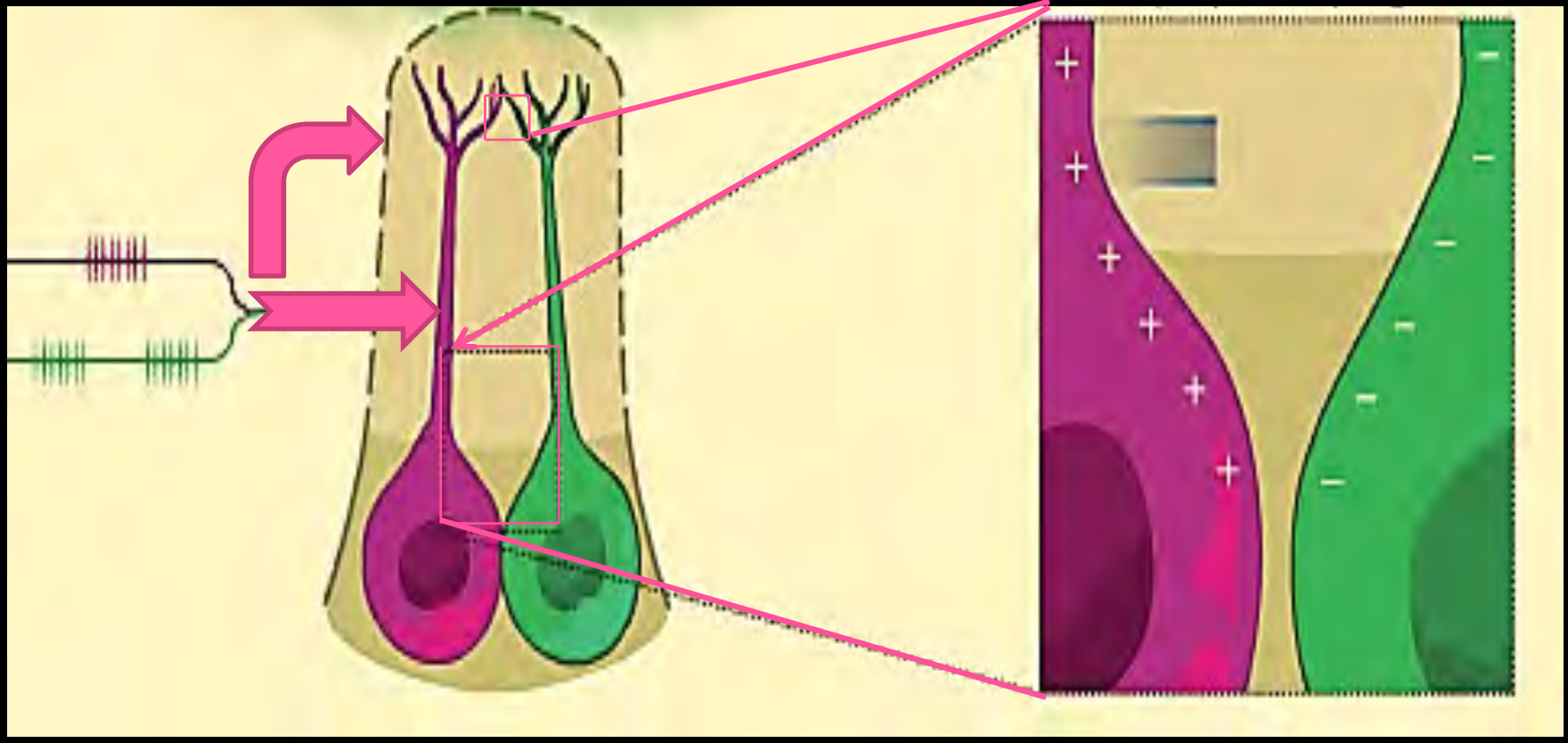

LongTrace
0.6 bursts per sec
Burst of 15 units
10s 100µV
1s 100µV

MYOKYMIA -Mechanism

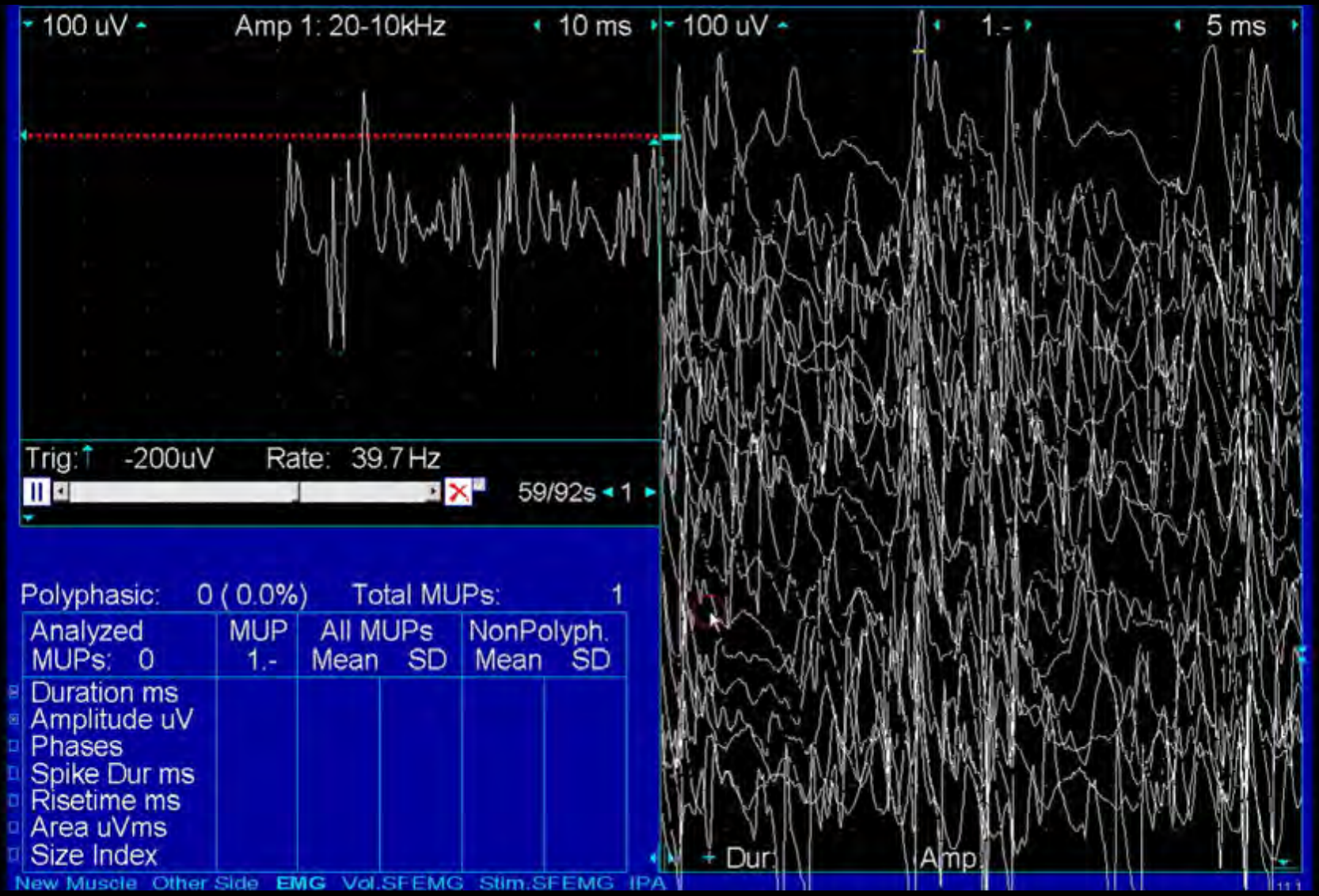
- **Generated by Distal Motor Axons**
  - By a primarily axonal process or by segmental demyelination with secondary axonal dysfunction.
  - spontaneous discharge could initiate volleys of activity or afferent fibers could directly stimulate efferent fibers in the vicinity of the lesion and produce a self-perpetuating reverberating circuit.

- **Transaxonal ephaptic excitation occurs peripherally after focal nerve damage leads to formation of an artificial synapse.**

Ephaptic communication



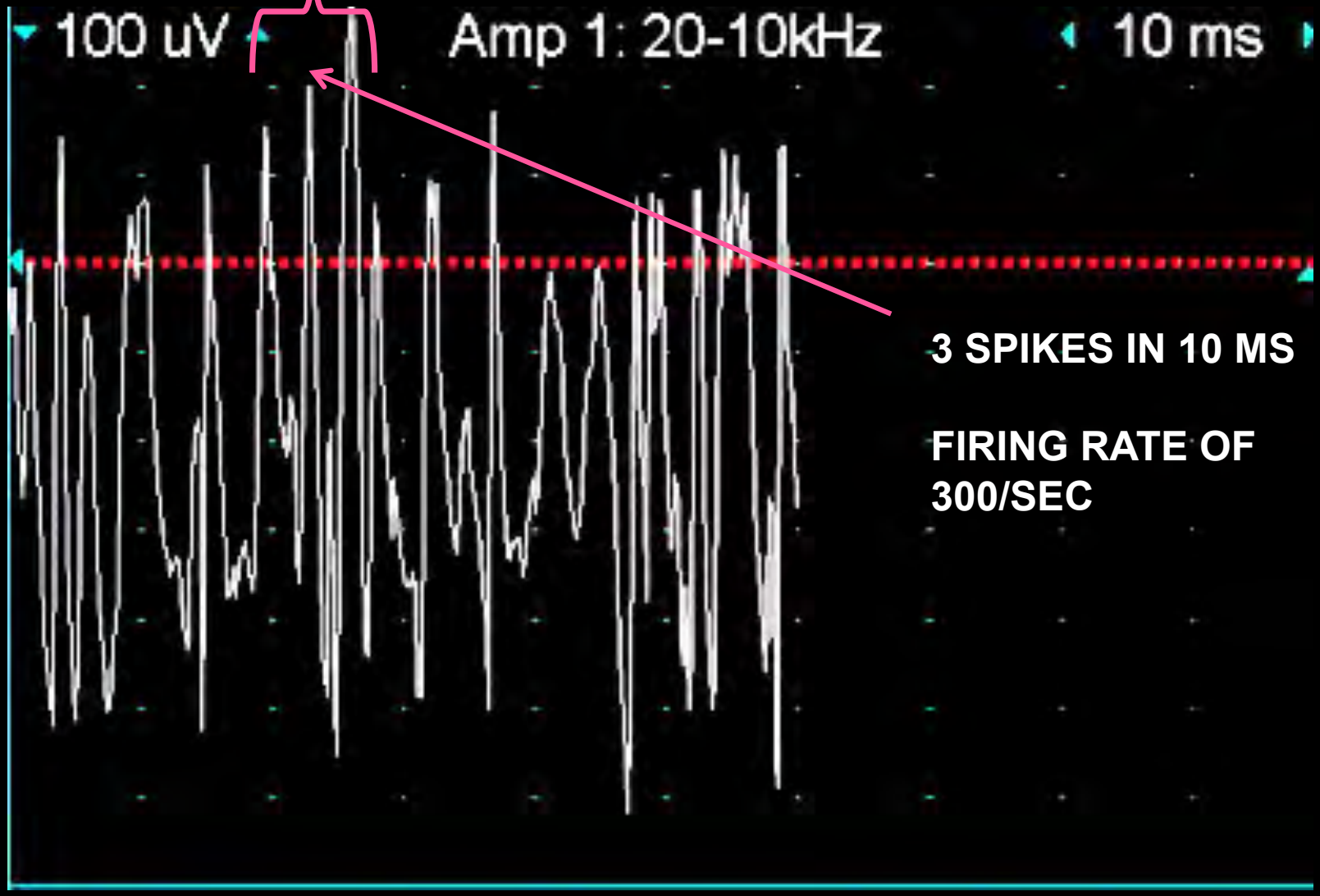
NEUROMYOTONIA



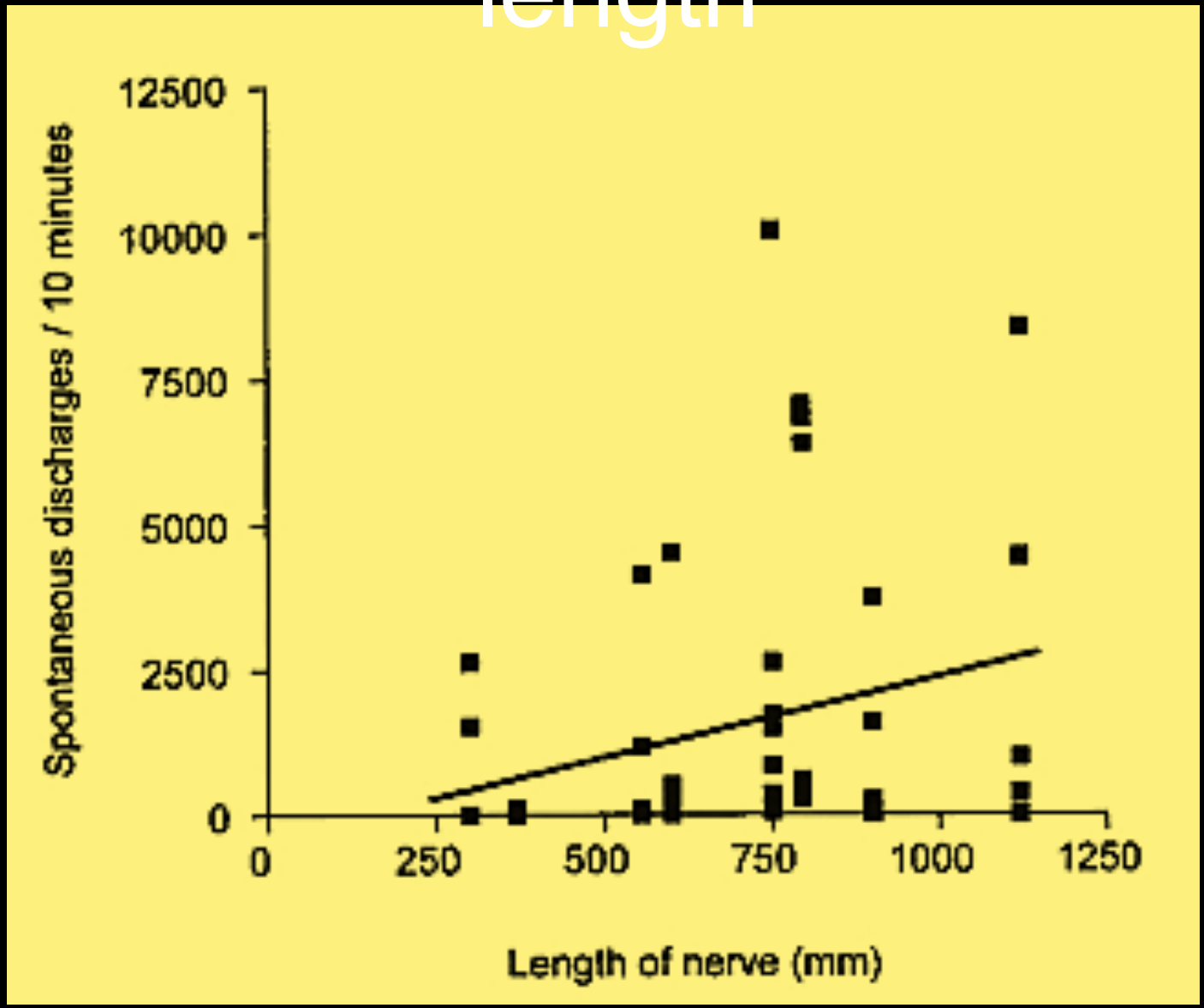
NEUROMYOTONIA

- FEATURES
  - Spontaneous firing of single Motor Unit
  - Firing rate 100-300Hz
  - Long continuous or brief bursts
  - Thought to be distal axon in origin

NEUROMYOTONIA



Frequency related to nerve length



MUSCLE HYPEREXCITABILITY

- Clinical manifestations most commonly seen in muscular dystrophies and non-dystrophic myotonias (channelopathies).

- DM1 and DM2 are inherited muscle disorders

  associated with weakness and other dystrophic features in addition to myotonia

MUSCLE HYPEREXCITABILITY

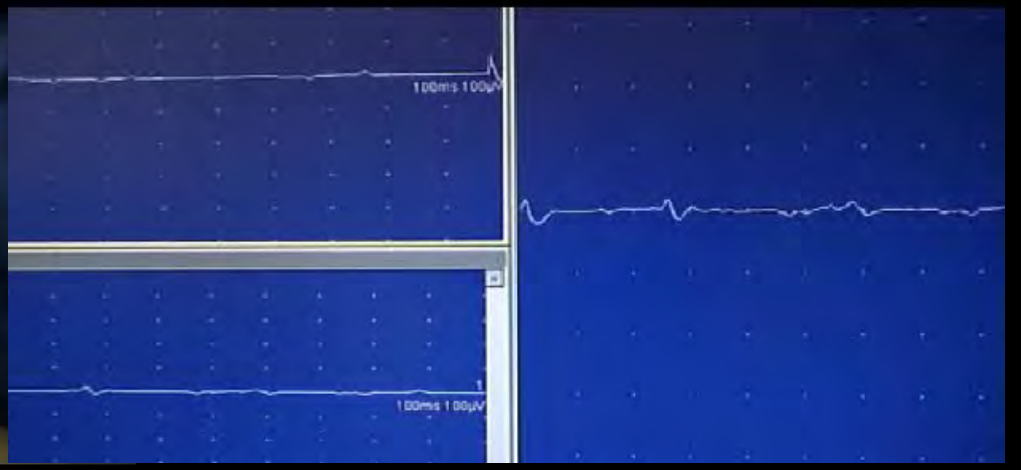
- NDMs, muscle hyperexcitability results in muscle “stiffness” during voluntary movement because of delayed skeletal muscle relaxation caused by repetitive muscle fiber action potentials (myotonia)

- Myotonia may occur electrically without clinical symptoms.

Muscle Hyperexcitability		
Muscle Disorder	**Clinical and Electrical Myotonia**	**Electrical Myotonia**
Muscular Dystrophy		
DM1 and DM2	+	
Myofibrillary myopathies	+	
Muscle Channelopathies	+	
Non Dystrophic myotonia (MC, PMC, PAM)		
Hyperkalemic Periodic Paralysis	+	
Metabolic myopathies		
Acid Maltase deficiency		+
Debrancher deficiency		+
McArdles disease		+

Muscle Hyperexcitability		
Muscle Disorder	**Clinical and Electrical Myotonia**	**Electrical Myotonia**
Toxic Myopathies		
Statin myopathy		+
Colchicine myopathy		+
Endocrine myopathies		
Hypohyroidism		+
Inflammatory myopathies		
Polymyositis		+
Dermatomyositis		+

Percussion Myotonia Thumb



Percussion Myotonia

Eyelid myotonia

Genetics of Myotonia

	Inheritance	Gene	Channel
Dystrophic			
DM1	AD	19q- CGT	Chloride
DM2	AD	3q - CCGT	Chloride
Non-Dystrophic			
dMC (Thomsens)	AD	7q - CLCN-1	Chloride
rMC (Beckers)	AR	7q - CLCN-1	Chloride
PMC	AD	17q - SCN4A	Sodium
PAM	AD	17q- SCN4A	Sodium
HyperPP	AD	17q- SCN4A	Sodium

Clinical Phenotypes

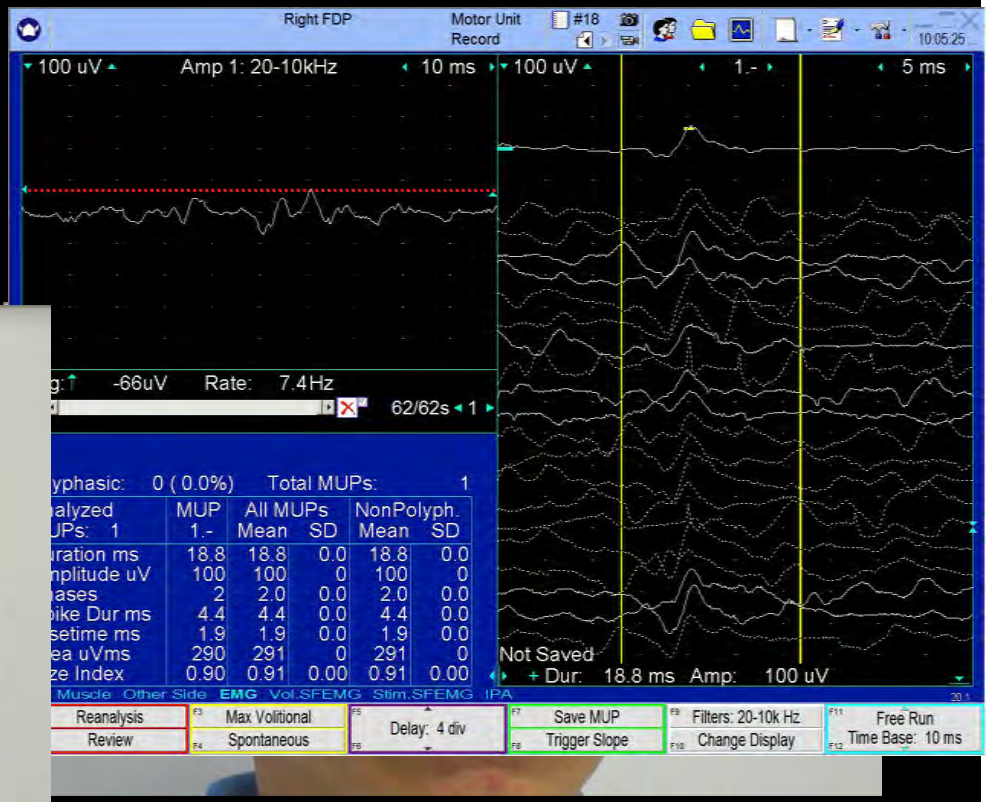
	Myotonia	Exercise	Cold	Weakness	Muscle Hyper	Eyelids	Potassium Sensitive
rMC	Severe	Better	No effect	Transient	Yes	Occ	No
dMC	Mild	Better	No effect	No	Yes	Occ	No
PMC	Severe	Worse	Worse	Transient	Occ	**Yes**	No
PAM	Mild	No Effect	No or delayed effect	No	No	Yes	Yes
HyperPP	Electrical	After exercise	No Effect	Transient	No	No	Elevated levels

Paramyotonia Congenita

Lid Lag sign

Deterioration with cold

Myotonia Congenita

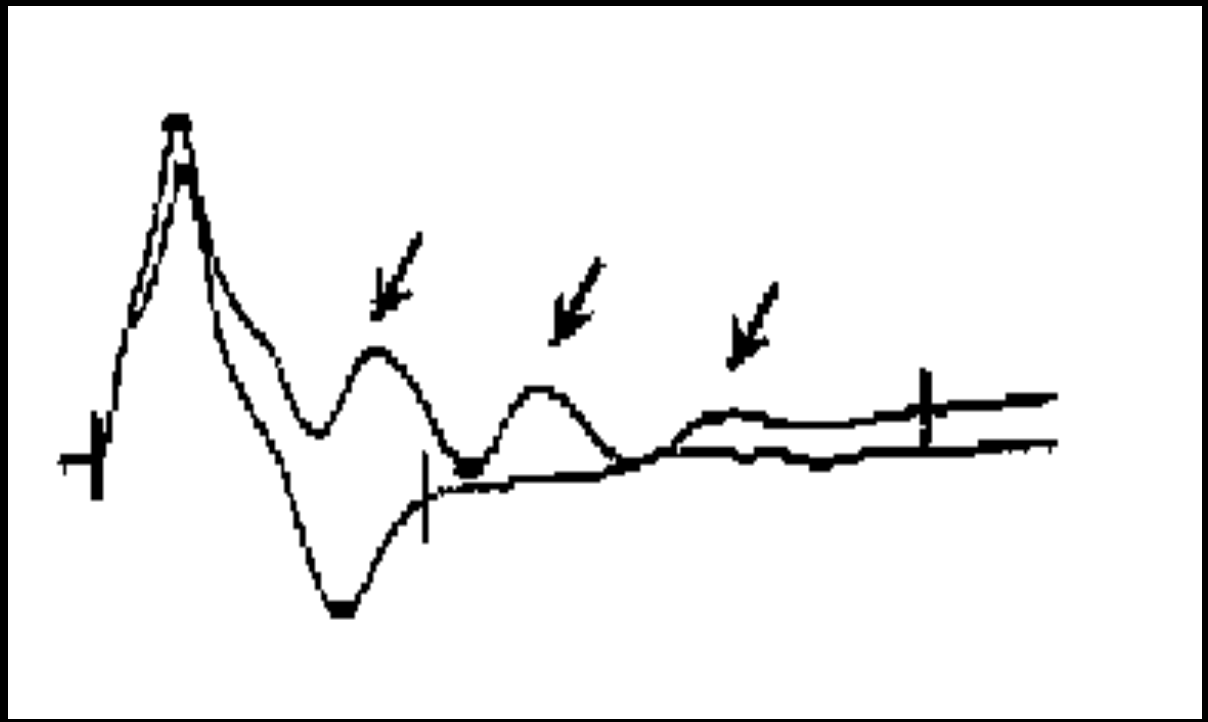


Electrophysiological Features

- Nerve Conduction Studies
  - CMAP amplitude is normal at rest if the temperature is normal.
  - After cooling (23 degrees)
    - Amplitude, duration and area tend to increase in patients with DM1 and MC.
    - Amplitude and area is reduced and duration increased with PC.
  - Small during attack of HyperPP

Nerve Conduction Studies

- Post exercise after potentials (PAP)
  - Following 10 sec of sustained exercise
  - Most PMC
  - Occ MC

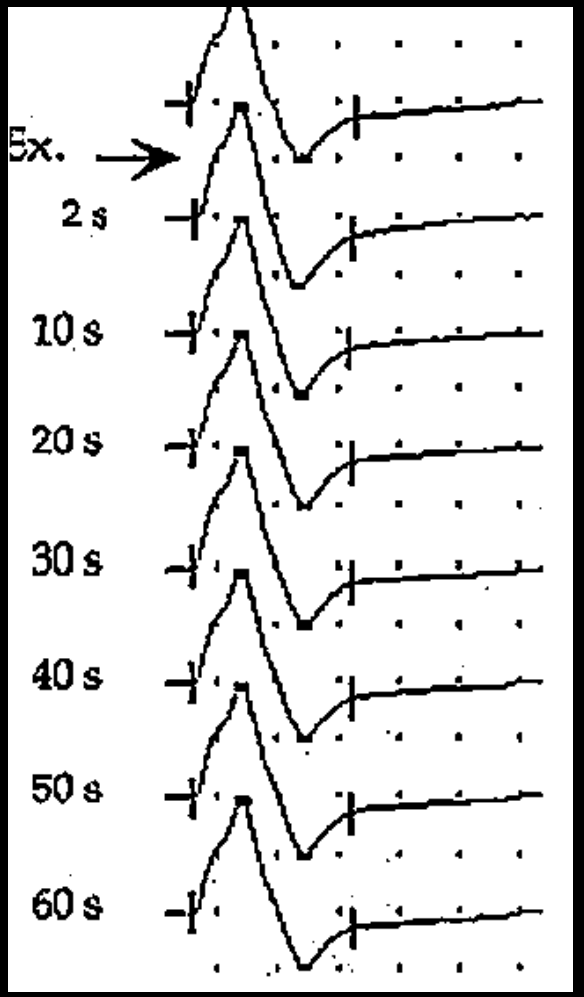


Short Exercise Test

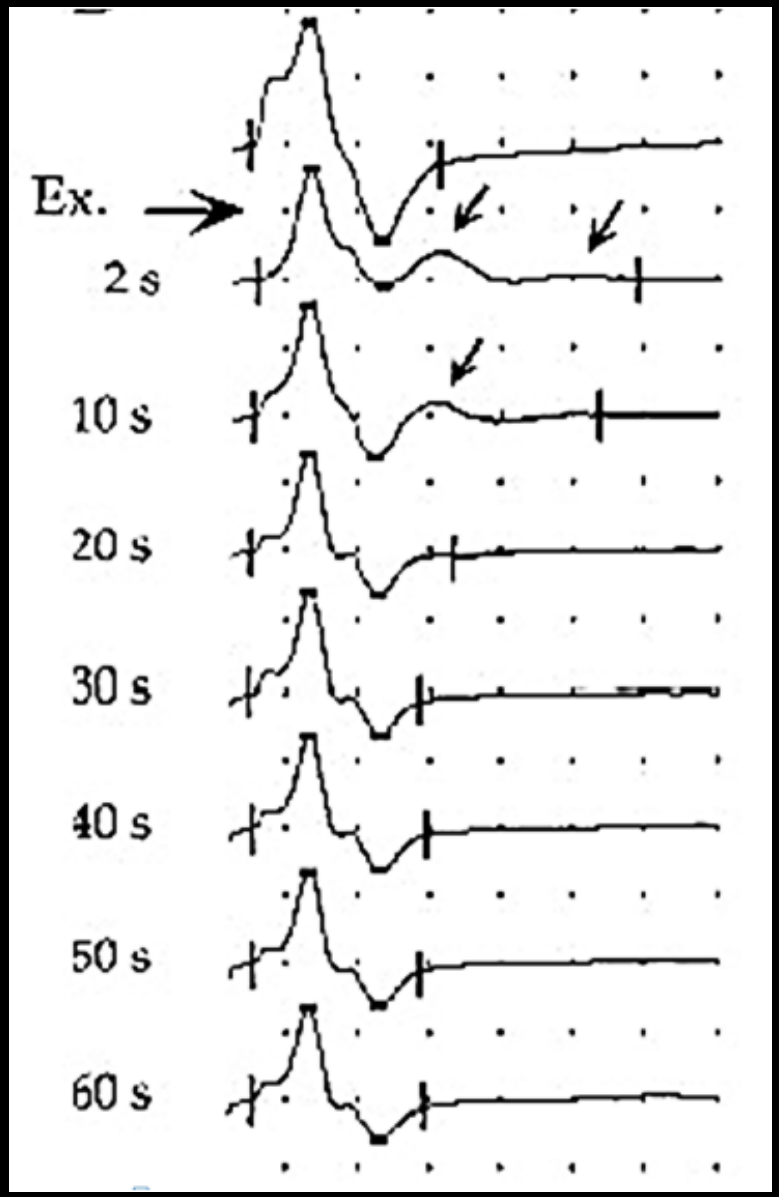
Method

- Supramax CMAPs recorded at baseline
- 10 seconds of sustained contraction of the ADM.
- CMAPs are recorded 2 seconds after exercise and then every 10 seconds for a total of 60 seconds

Control



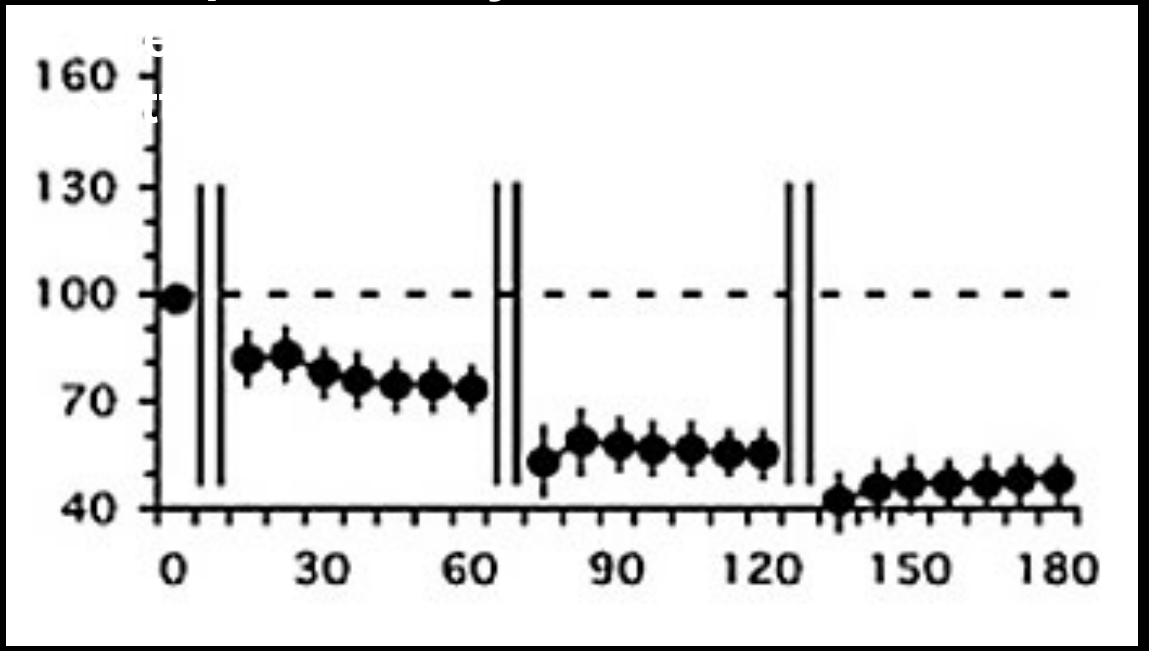
PMC



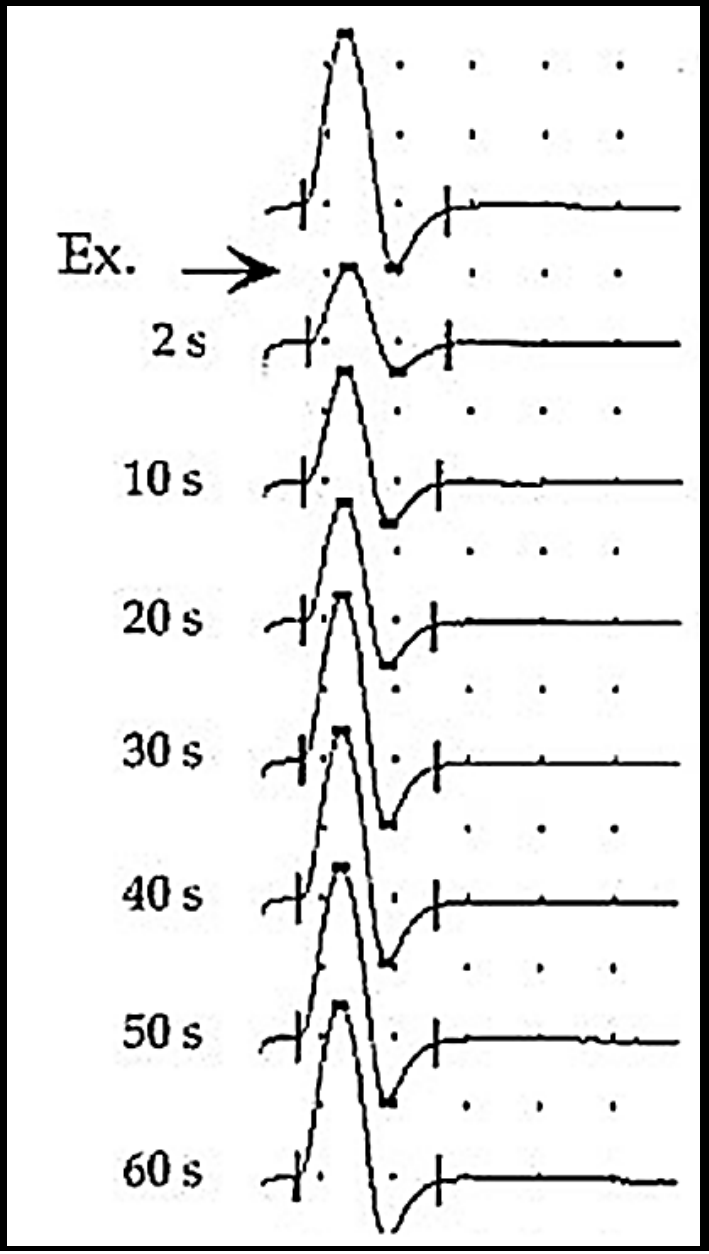
Sustained reduction in CMAP amplitude

This pattern becomes worse with repetition and cooling.

This pattern may be seen with PAM



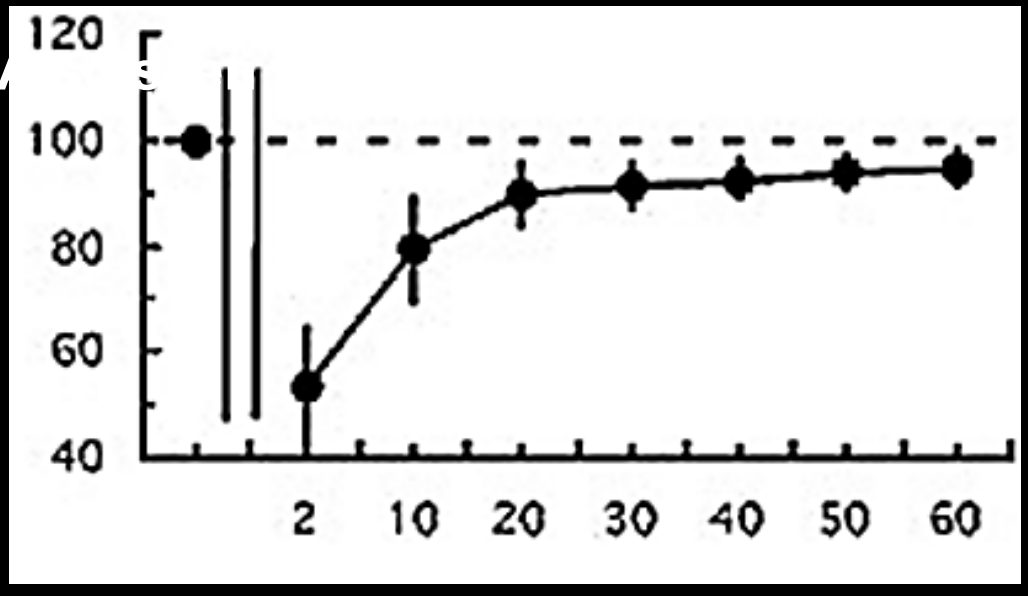
MC (warming up)



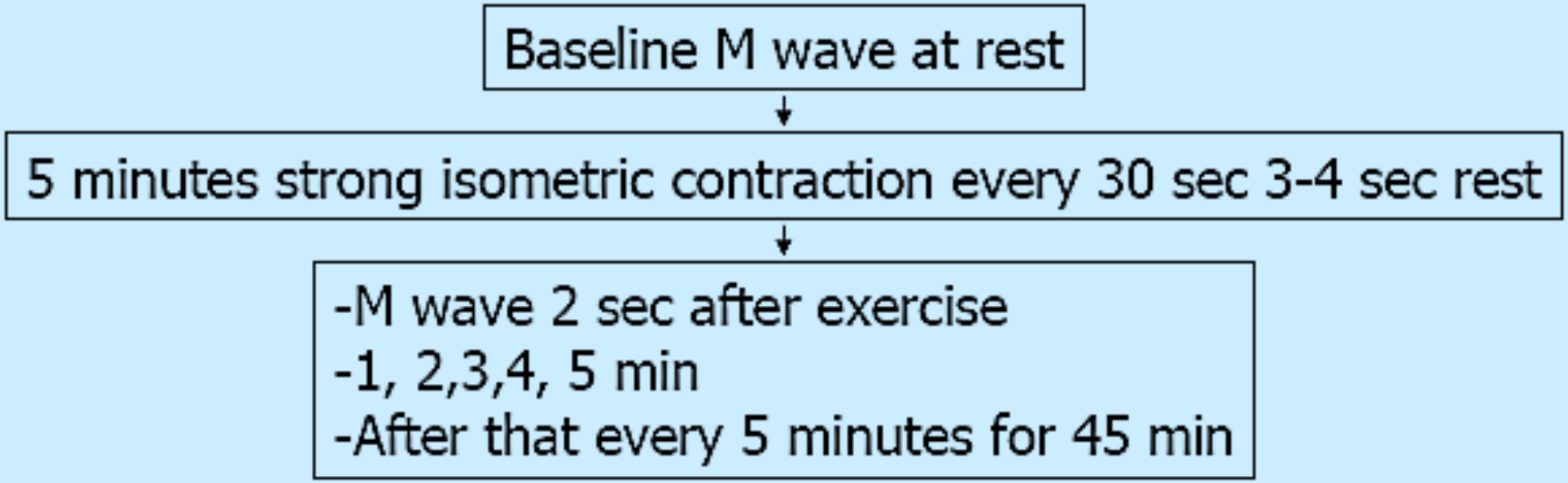
Initial postexercise CMAP decrement, which repairs by 60 seconds

Less pronounced on subsequent trials.

This amplified by cooling



Long Exercise Test



Of no further use in NDM –useful to differentiate from PP.

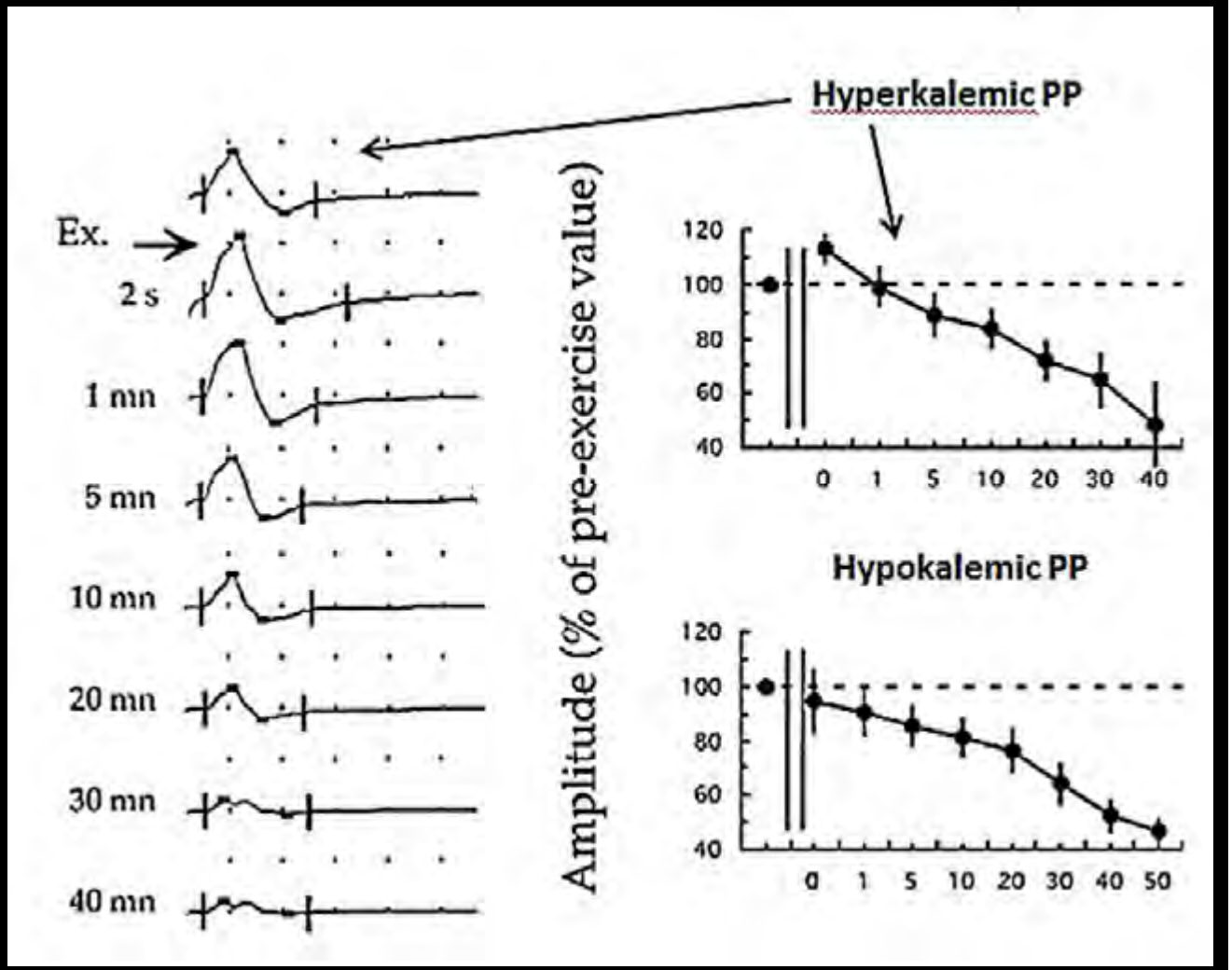
LET

HyperPP

Initial increase in the CMAP followed by a significant decrement with time (greater than 30%)

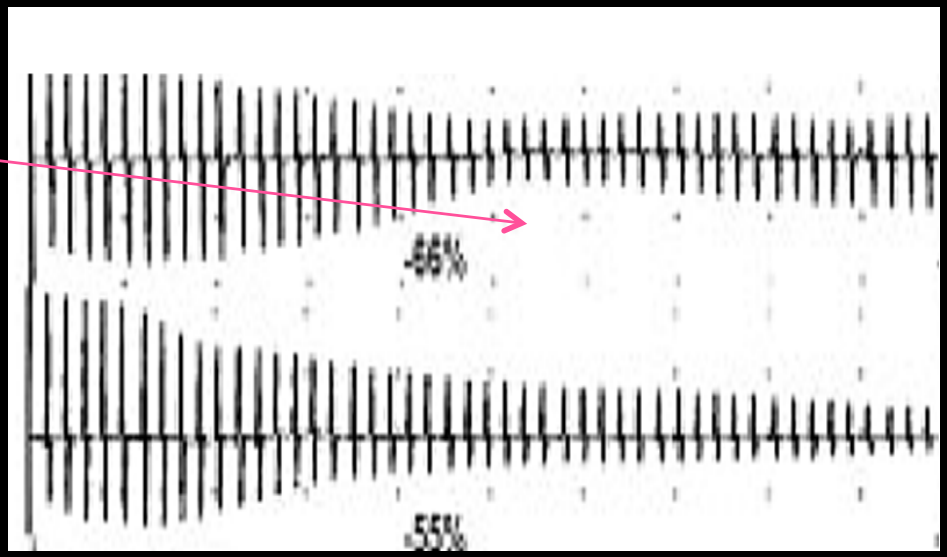
HypoPP (a calcium channel disorder)

Decrement without an initial increment.

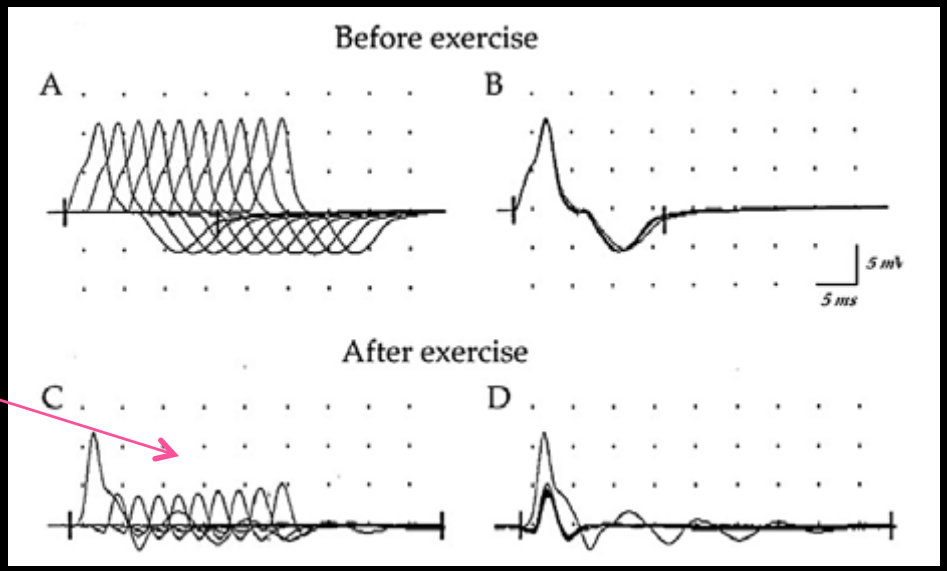


Repetitive Stimulation

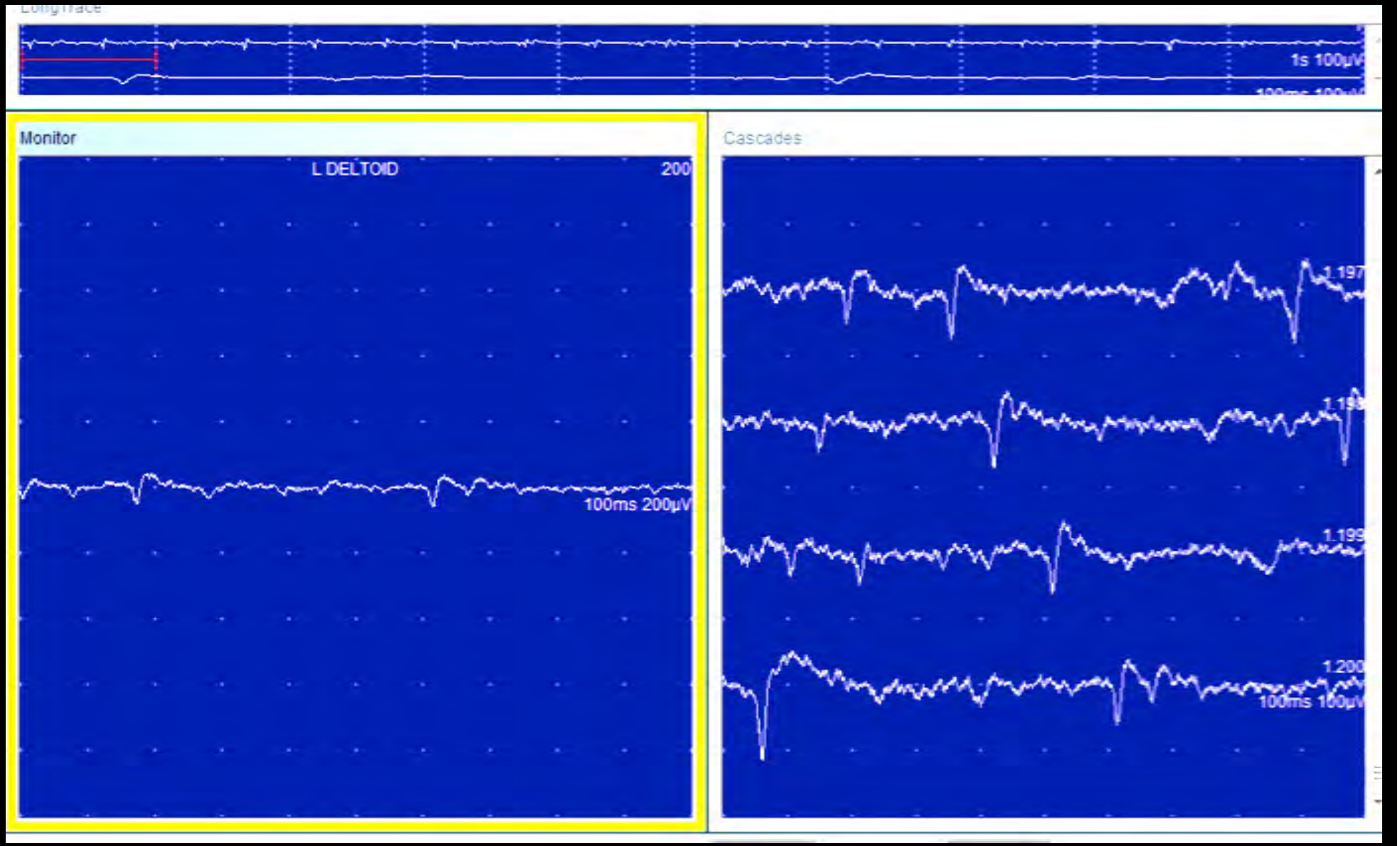
- **10Hz RS**
  - At room T°, patients with AR MC and DM exhibit a decrement in CMAPamp that is more pronounced with cooling
  - PC exhibited a decrement only with cooling.



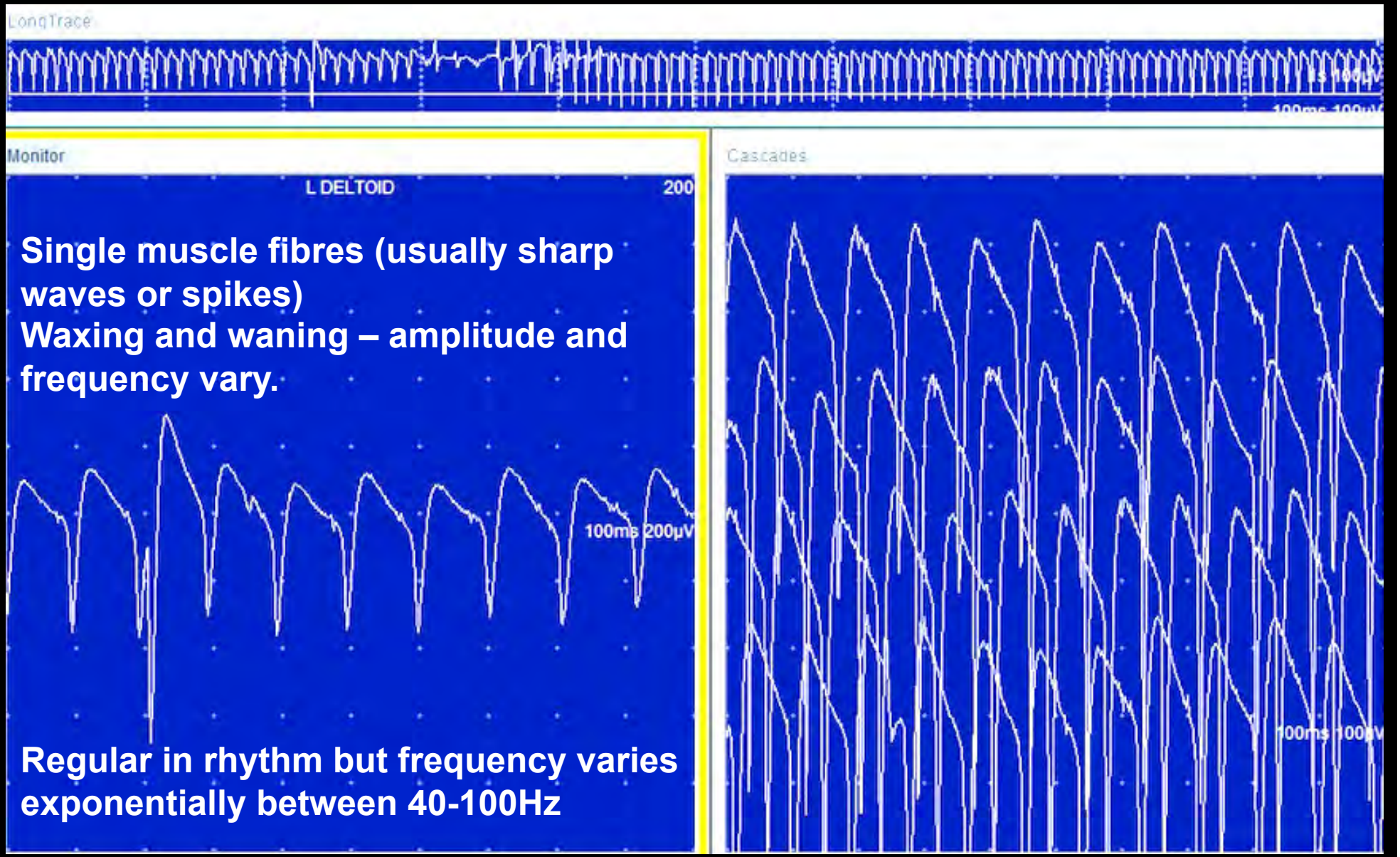
- **3 Hz RS**
  - **PC after exercise** a decrease of CMAPamp with persistence of PAPs



Electromyography- Myotonia



Myotonia


LongTrace
Monitor
L DELTOID
200
Single muscle fibres (usually sharp waves or spikes)
Waxing and waning – amplitude and frequency vary.
100ms 200µV
Regular in rhythm but frequency varies exponentially between 40-100Hz
Cascades

Myotonia Patterns

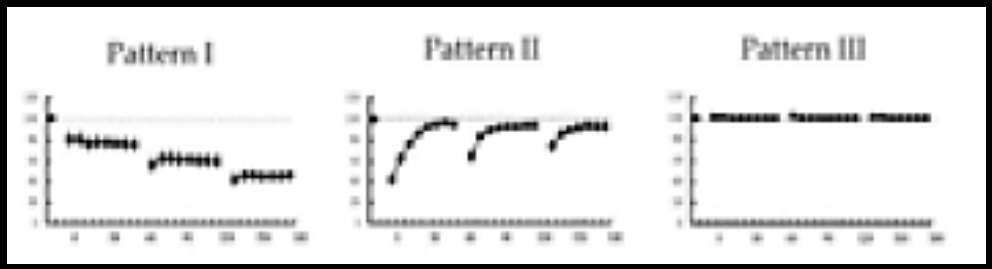
- DM1
  - More distal than proximal
  - Waxing and waning
  - Easily elicitable
- DM2
  - Proximal and distal
  - Waning pattern
  - Less easily elicitable
- NDM
  - Proximal and distal
  - Profuse and easily elicitable

Electromyography of muscle channelopathies		
Disease	EMG	
	Spont	Vol
Dystrophic		
DM1	Myotonia-Waxing/ Waning Distal	Myopathic
DM2	Myotonia -Waning Proximal	Mild Myopathic
Non Dystrophic		
MC CICN1)	Myotonia Better with exercise	Normal- occasional Myopathic in rMC
PC (SCN4)	Myotonia Worse with exercise	Normal
PAM(SCN4)	Myotonia	Normal
Periodic Paralysis		
HyperKPP	Myotonia	Inc Inser Fib/Sharp waves Polyphasic units
HypoKPP	Nil	Normal or Myopathic

Protocol for evaluation of myotonia

Clinical Exam and EMG → Myotonia - No myopathy → myopathy → DM1, DM2

SET on hand and cold SET contralateral hand



SCN4A (MC genes) CLCN1 SCN4A (PAM genes)

Syndromes of electromyographic silence as a manifestation of clinical hyperexcitability.

- **Rippling muscle disease**

- Mutations in the CAV3 gene although antibody mediated cases have been described.
- Stretching the muscle causes visible ripples to spread across the muscle, lasting 5 to 20 seconds.
- They may experience fatigue, cramps, or muscle stiffness, especially after exercise or in cold temperatures.
- EMG may show myopathic changes but electrical activity at the time of the ripple is silent and is most likely mechanical in origin

Electrical Silence

- **Myoedema**
  - Classical sign of hypothyroid myopathy
  - Mounding of muscle tissue occurring after a light pressure stimuli.
  - It is due to prolonged muscle contraction caused by delayed calcium reuptake by sarcoplasmic reticulum, following local calcium ion release brought out by percussion or pressure

Electrical Silence

- **Mcardles Disease**

  - Affects the contractile mechanism because of lack of phosphorylase which is involved in the breakdown of muscle glycogen to glucose-6-phosphate.

  - The most prominent symptom is painful exertional cramp.

  - The EMG during a cramp following exercise is silent and is a contracture due to shortage of ATP during exercise.

Conclusion

- “We are still confused,
- But on a much higher level “
- Winston Churchill

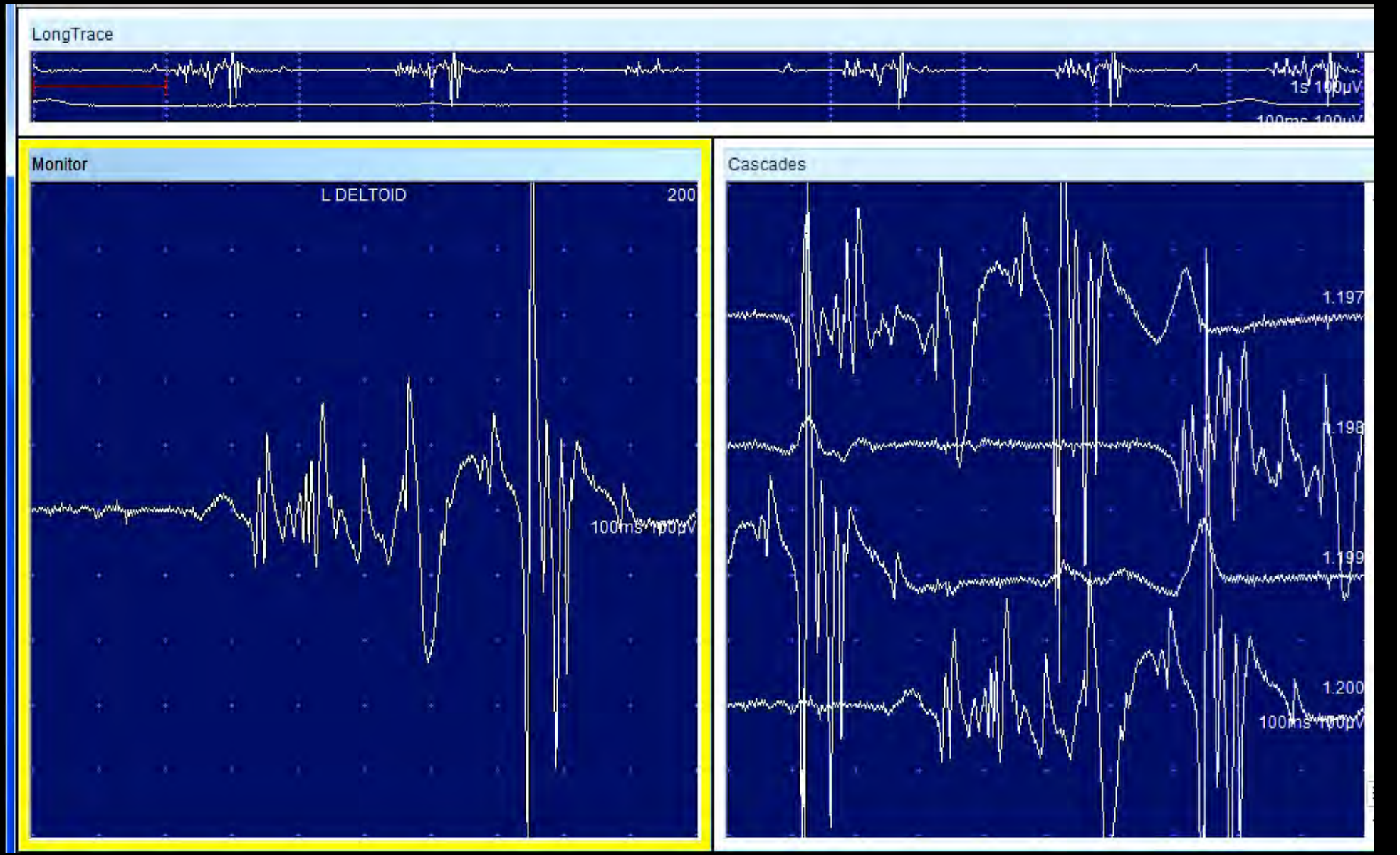
Recessive Myotonia Congenita

Transient weakness

Episodes of collapse with sudden movements

Severe myotonia

Complex Repetitive Discharges



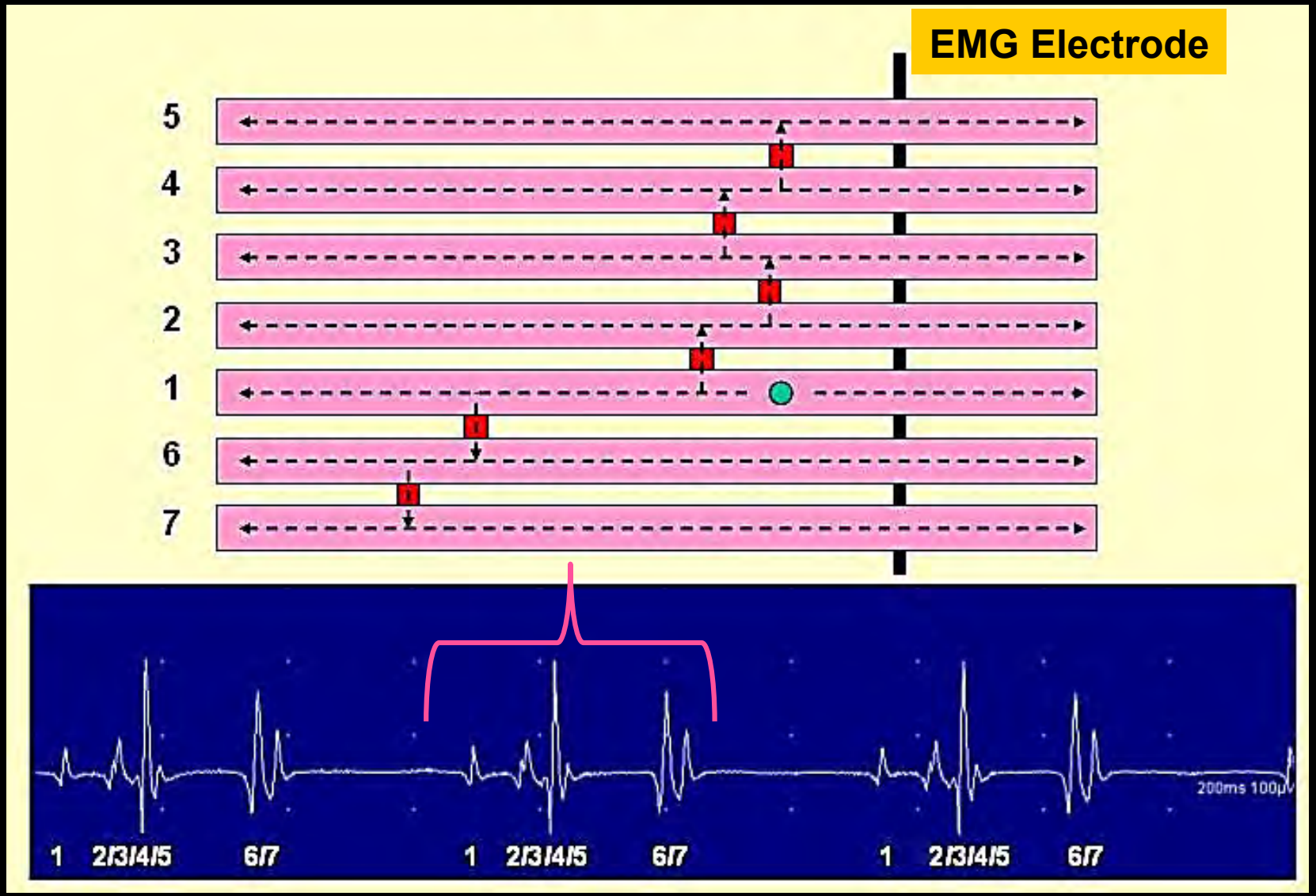
COMPLEX REPETITIVE DISCHARGES

- Spontaneous potentials from groups of muscles fibres
- Repetitive regular and almost synchronous
- Not from the same motor unit
- Ephaptic activation of groups of adjacent fibres
- Number of fibres activated may vary and continue until circuit complete and repeats itself.

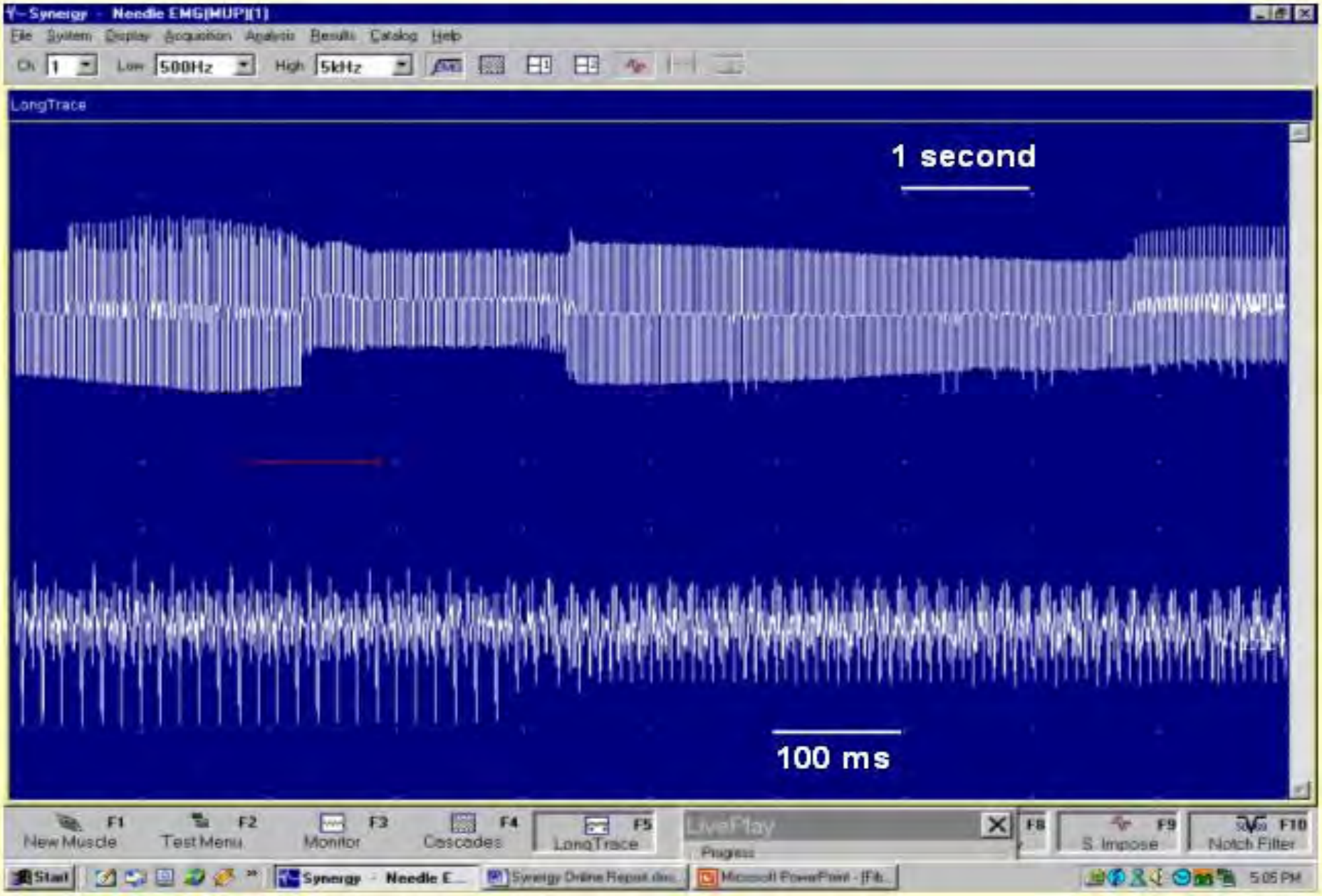
CRD

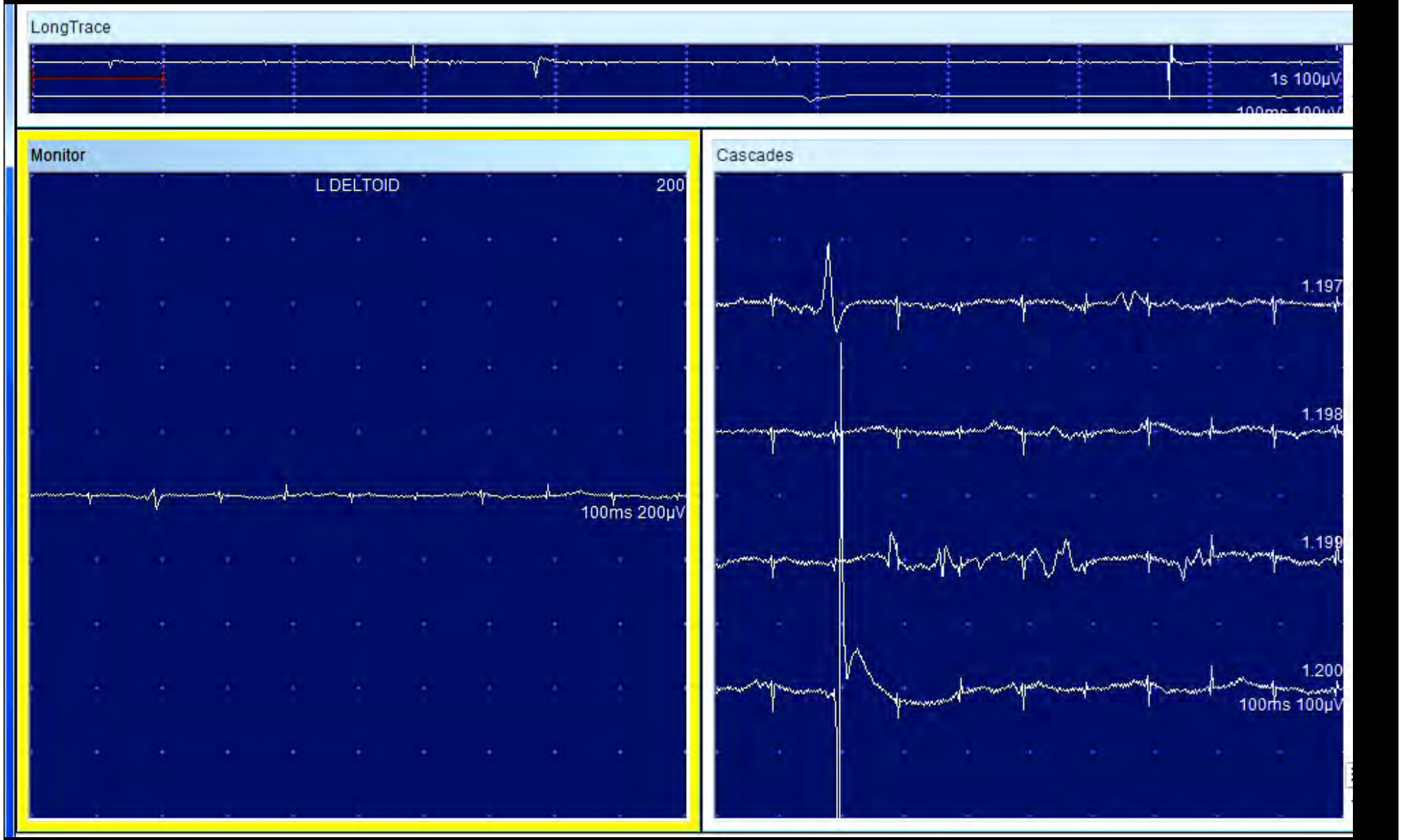
- Each spike is a single muscle fibre
- Regular
- Abrupt onset and cessation
- Configuration may change during it.
- Firing rate 3-40Hz
- Shape variable 3-10 spikes
- Duration brief up to 50ms amplitude 500uV

CRD Generation

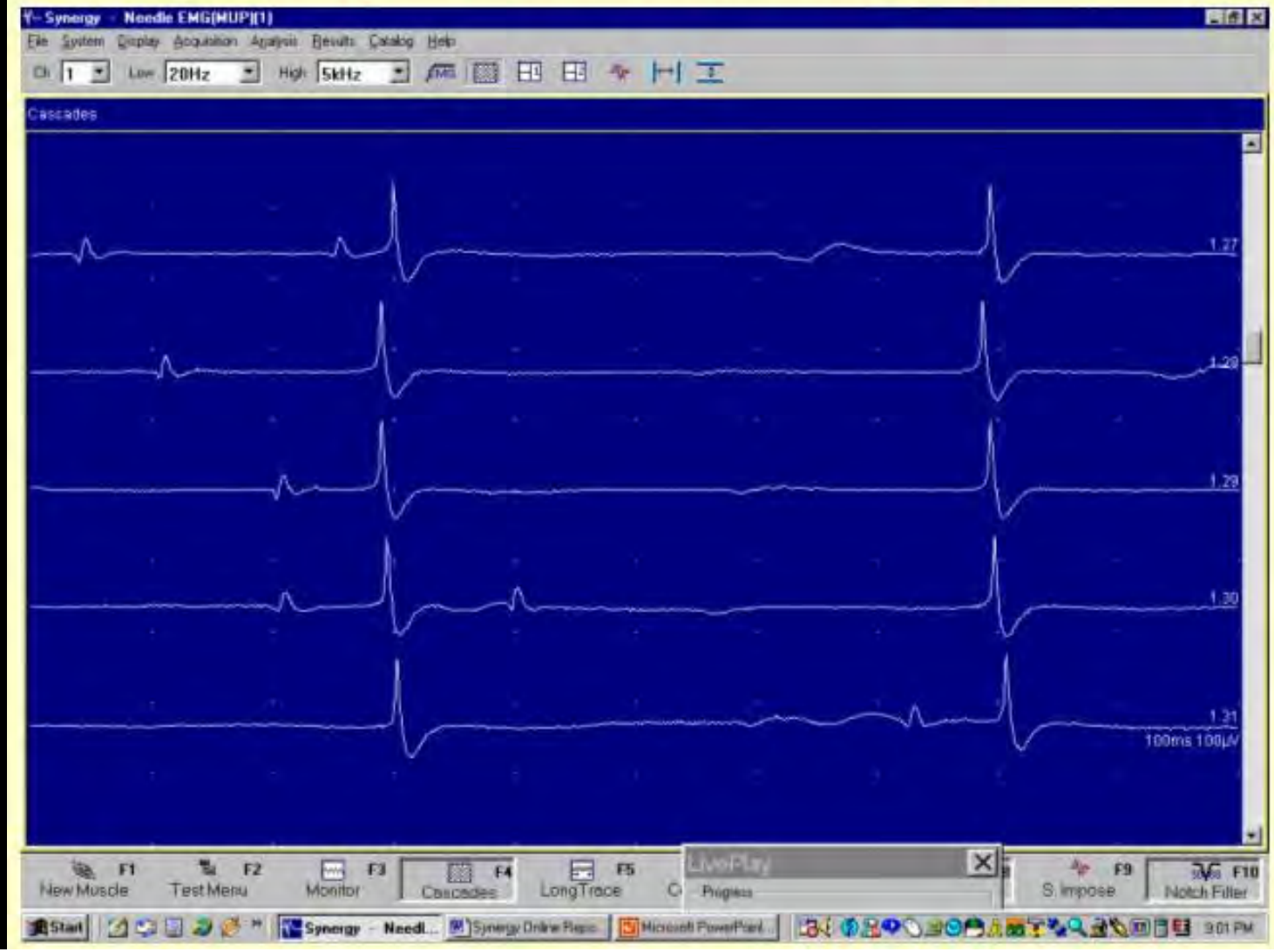


CRD : Change in Configuration




LongTrace
1s 100µV
Monitor
L DELTOID
200
100ms 200µV
Cascades
1.197
1.198
1.199
1.200
100ms 100µV

Simple Iterative Discharge (SID)



Neuromuscular disorders with myotonia

Muscular dystrophies:

- Myotonic dystrophy type 1 and 2
- Myofibrillar myopathies[1]

Muscle channelopathies:

- Nondystrophic myotonia (myotonia congenita, paramyotonia congenita, sodium channel myotonia)
- Hyperkalemic periodic paralysis

Metabolic myopathy:

- Acid maltase deficiency[a,2,3]
- Debrancher deficiency[a,4]
- McArdle disease (myophosphorylase deficiency)[a,4]

Toxic myopathies[a]:

- Chloroquine/hydroxychloroquine myopathy[5,6]
- Statin myopathy[7]
- Colchicine myopathy[8]

Endocrine myopathies[a]:

- Hypothyroidism[4]

Inflammatory myopathies[a,4]

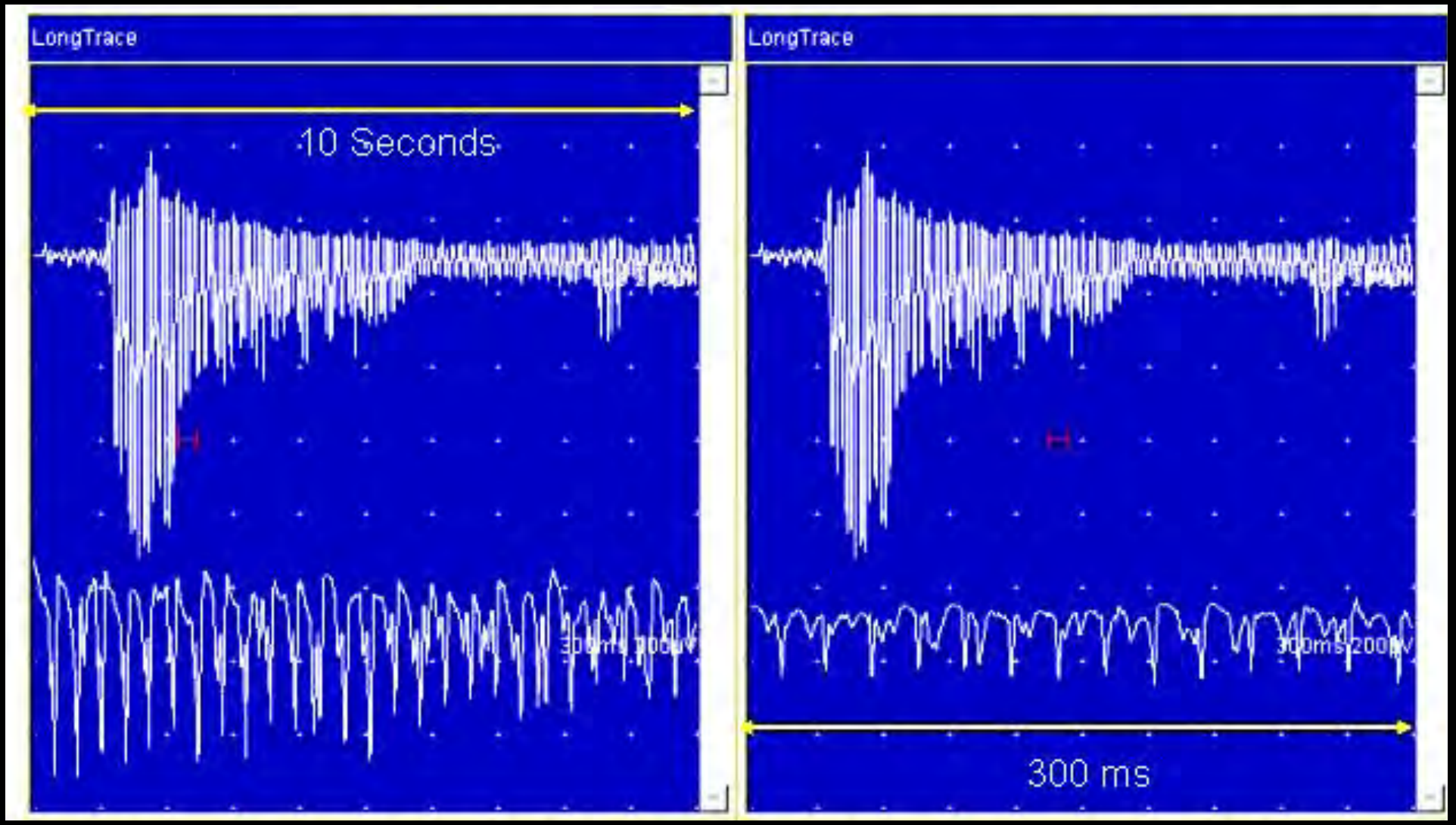
- Polymyositis
- Dermatomyositis

[a] Electrical myotonia without clinical myotonia.

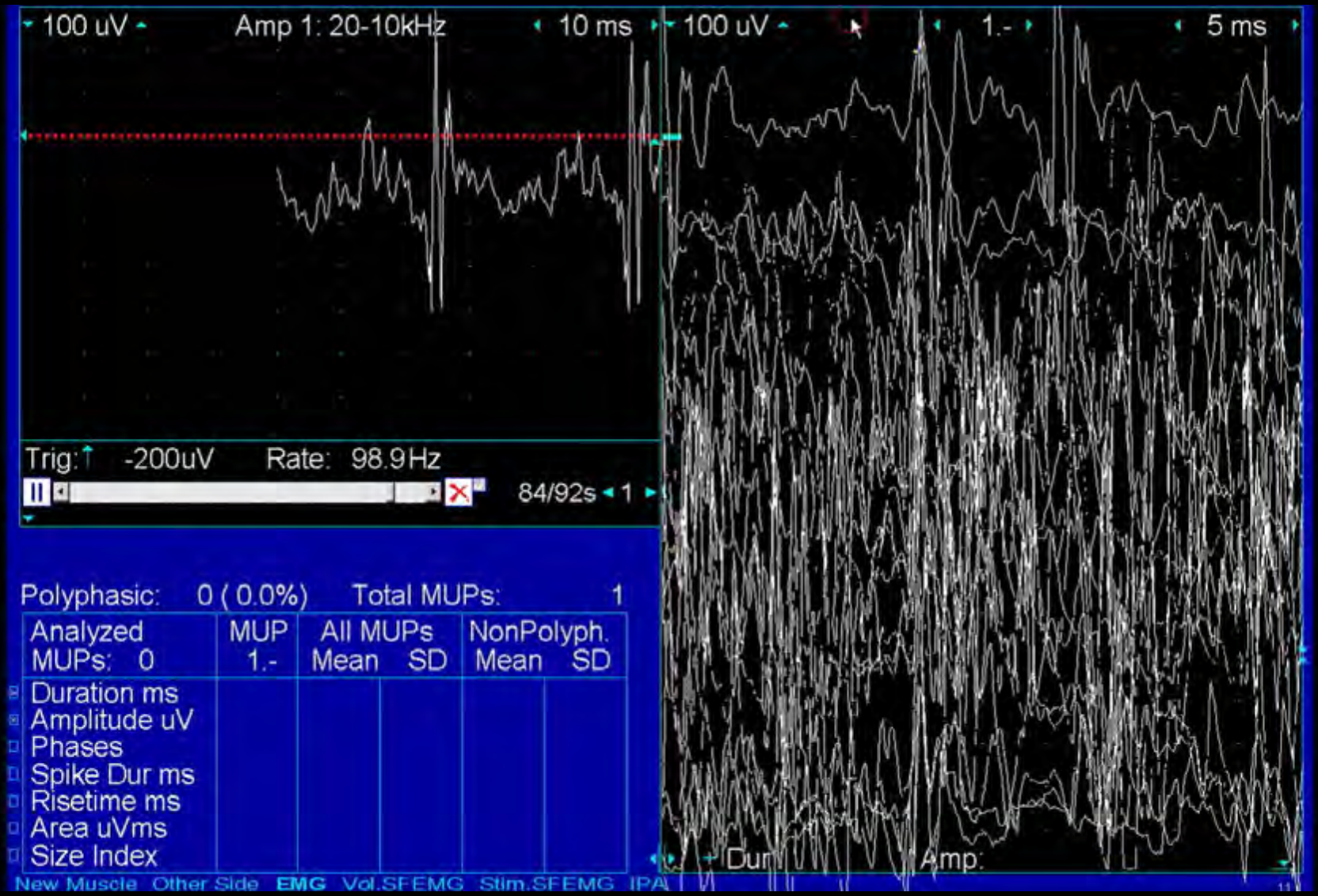
Classification of ion channels

Channel	Muscle	Gene
Sodium channel	Hypokalemic periodic paralysis	SCN4A
	Hyperkalemic periodic paralysis	SCN4A
	Paramyotonia congenita	SCN4A
	Potassium-aggravated myotonia	SCN4A
Chloride channel	Myotonia congenita:	CLCN1
	Thomsen's (AD) and Becker's (AR)	
Calcium channel	Hypokalemic periodic paralysis	CACNA1S
Potassium channel	Andersen's syndrome	KCNJ2
	Hypokalemic periodic paralysis	KCNE3
	Hyperkalemic periodic paralysis	KCNE3

Amplitude and Frequency variation

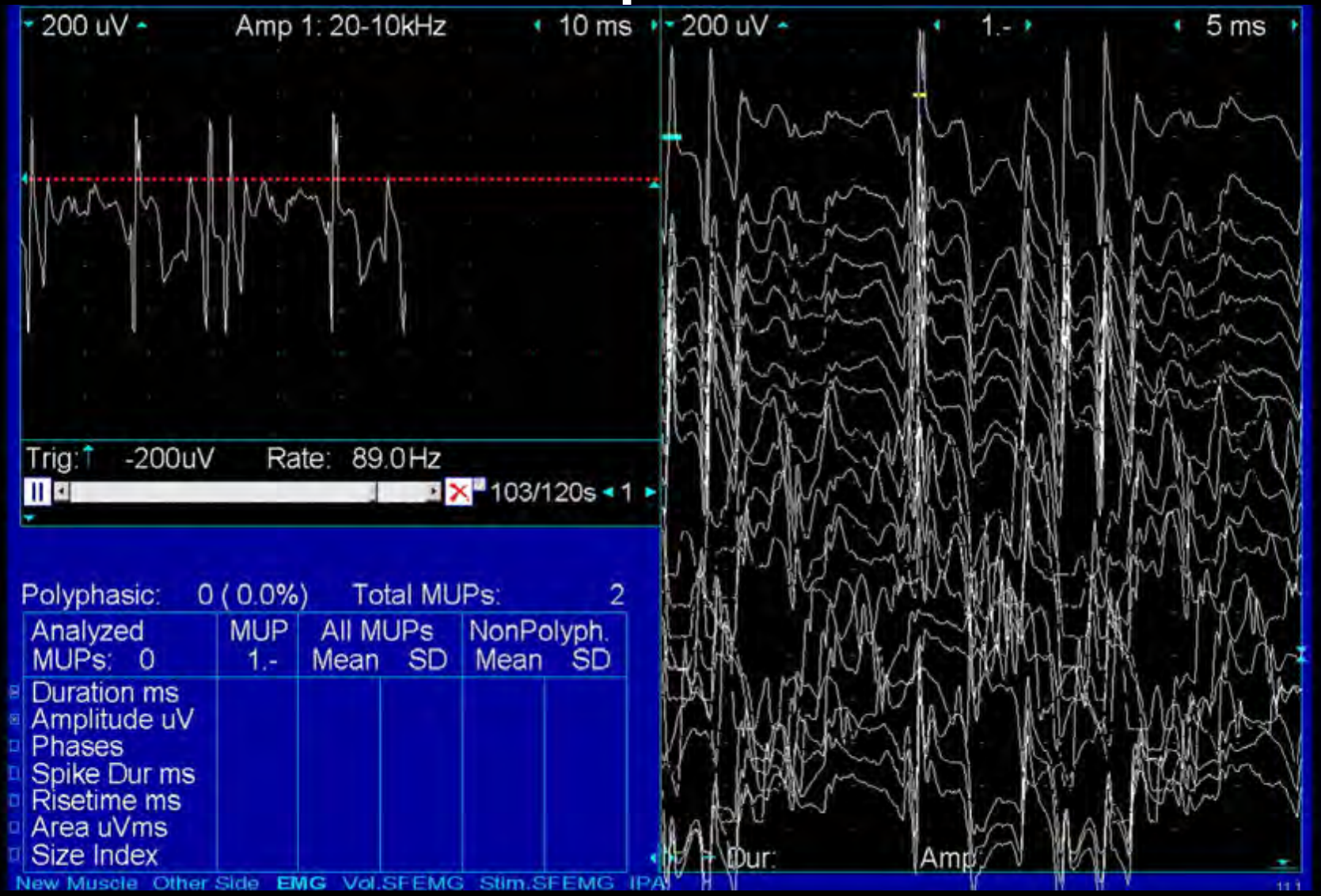


Doublets

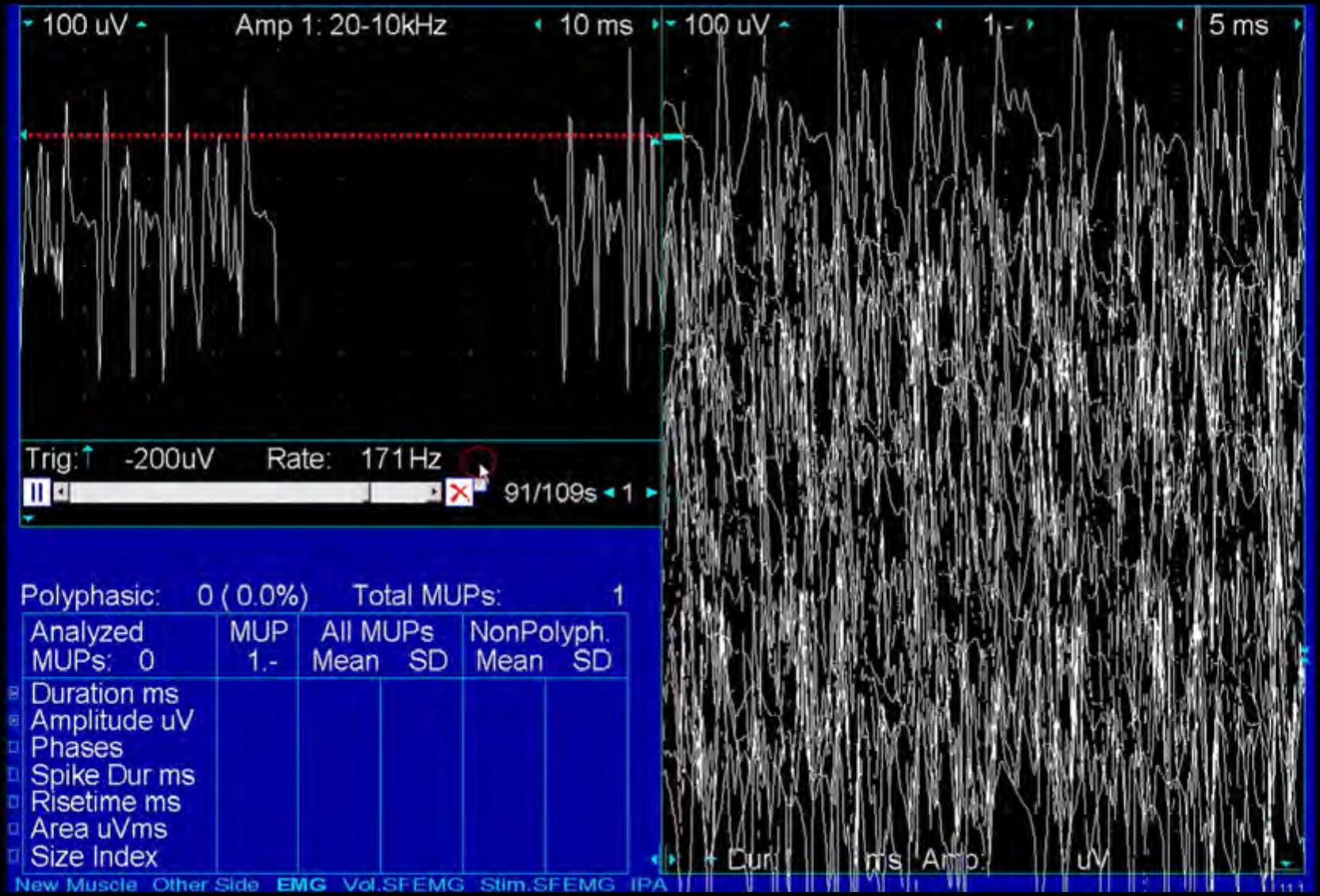

100 uV
Amp 1: 20-10kHz
10 ms
100 uV
1.-
5 ms
Trig: -200uV
Rate: 98.9Hz
84/92s 1
Polyphasic: 0 (0.0%)
Total MUPs: 1
Analyzed MUPs: 0
MUP 1.-
All MUPs Mean SD
NonPolyph. Mean SD
Duration ms
Amplitude uV
Phases
Spike Dur ms
Risetime ms
Area uVms
Size Index
Dur
Amp:
New Muscle
Other Side
EMG
Vol.SFEMG
Stim.SFEMG
IPA

Doublets

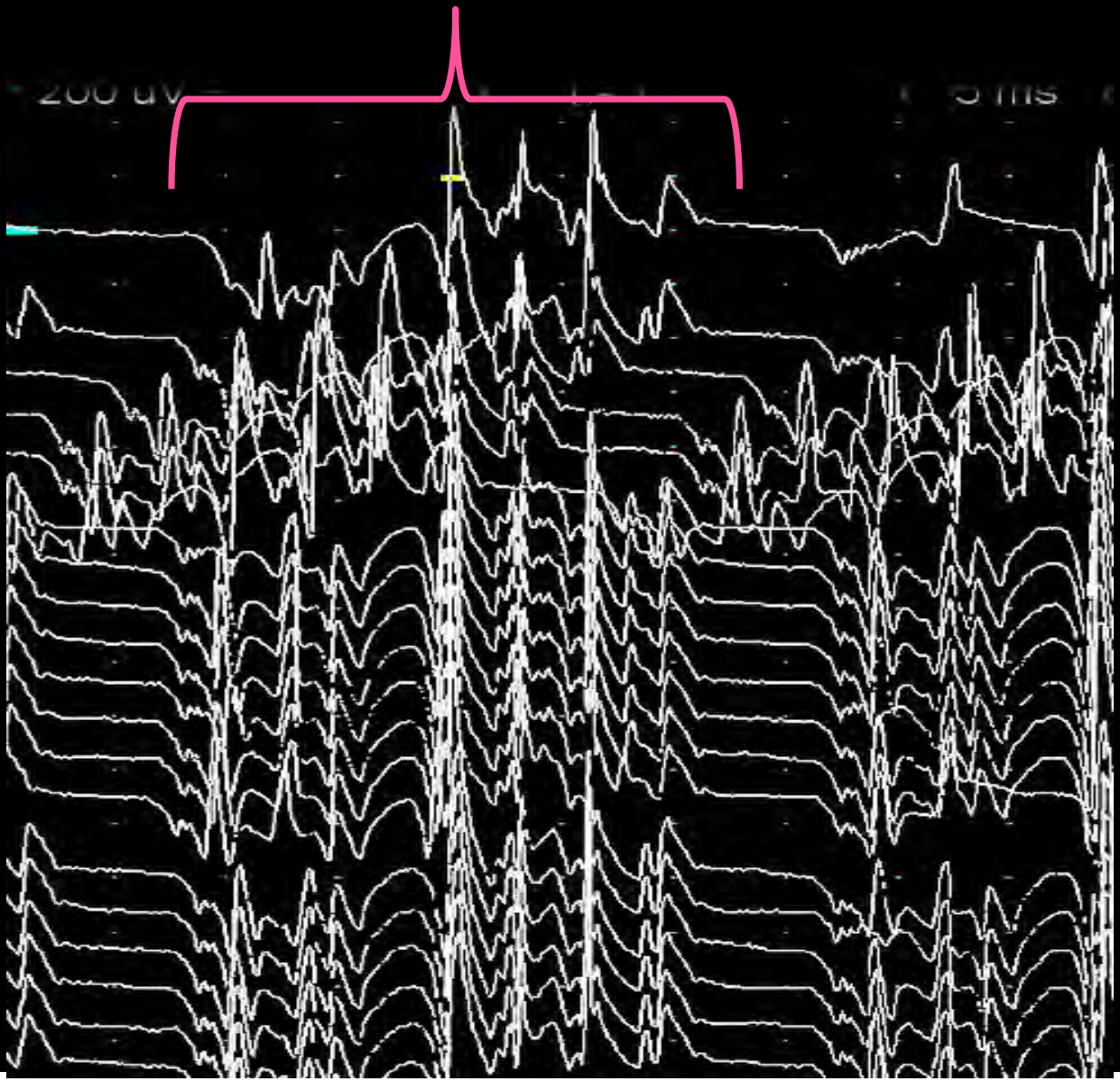
Triplets


200 uV
Amp 1: 20-10kHz
10 ms
Trig: -200uV
Rate: 89.0 Hz
103/120s 1
Polyphasic: 0 (0.0%)
Total MUPs: 2
Analyzed MUPs: 0
MUP 1.-
All MUPs Mean SD
NonPolyph. Mean SD
Duration ms
Amplitude uV
Phases
Spike Dur ms
Risetime ms
Area uVms
Size Index
New Muscle
Other Side
EMG
Vol.SFEMG
Stim.SFEMG
IPA
200 uV
1.-
5 ms
Dur:
Amp:

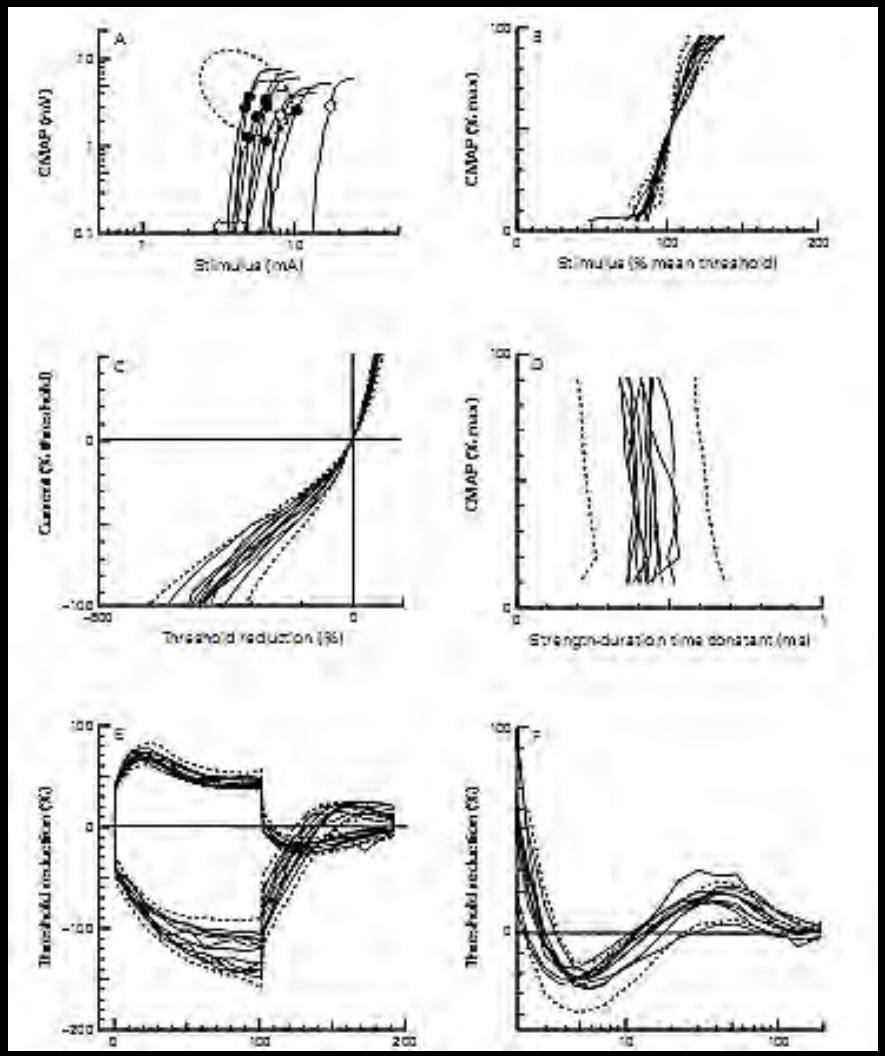
Bursts


100 uV
Amp 1: 20-10kHz
10 ms
100 uV
1.-
5 ms
Trig:
-200uV
Rate:
171 Hz
91/109s
1
Polyphasic: 0 (0.0%)
Total MUPs: 1
Analyzed MUPs: 0
MUP 1.-
All MUPs Mean SD
NonPolyph. Mean SD
Duration ms
Amplitude uV
Phases
Spike Dur ms
Risetime ms
Area uVms
Size Index
Dur
ms
Amp
uV
New Muscle
Other Side
EMG
Vol.SFEMG
Stim.SFEMG
IPA

Neuromyotonia burst pattern



Axonal excitability studies



Kiernan and Bostock 2001

- Excitability normal
- Fast Potassium channels not nodal and antibodies have no effect.
- Site of ectopic generator probably at motor terminals or adjacent nodes where K channel blockade leads to superexcitability.