UK practice for electrodiagnosis of MND
Review of literature and background

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EMG Group

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Purpose of the Audit

- To establish a standard electrodiagnostic approach suitable for the various clinical presentations and the wide symptomatology of MND that would help to avoid misdiagnosis of this condition

- Exclude potentially treatable disorders which mimic MND

- Clarify the role of the neurophysiologist in the diagnosis of pure motor syndromes

Example (1)

- **Reason for referral :**

  No definitive criteria for MND

- **Summary of findings:**

  Only fasciculations found occasionally mainly on bulbar muscles and very rare on both TA.
  Blink reflex normal

- **Conclusion :**

  Not conclusive but possible for MND

Example (2)

- **Reason for referral :** To look for evolution:

- **Summary of findings:**
- Acute and chronic denervation in 2 of 4 regions

- **Conclusion :**
- Partial support for diagnosis of MND

Example (3)

- **Reason for referral**

  No clear cut diagnostic features

  Summary of findings:

  No denervation

- **Conclusion :**

  Most likely PLS variant

DD of primary lateral sclerosis

- Vitamin B-12 Associated Neurological Diseases
- Lyme Disease
- Multiple sclerosis
- Cerebrovascular disease
- Parkinson-plus syndromes
- Multiple system atrophy
- CNS Lymphoma
- Progressive Multifocal Leukoencephalopathy
- Hereditary spastic paraparesis (HSP)
- Spinocerebellar ataxias
- Prion-Related Diseases
- Tropical Myeloneuropathies
- Brain tumours
- Neurolathyrism
- Neurosyphilis
- HIV-Associated Vacuolar Myelopathy

Example (4)

- **Reason for referral:**

  Not mentioned

- **Summary of findings** :
- No neuropathy; no Conduction block; widespread acute denervation, fasciculations and chronic neurogenic changes.
- **Conclusion:**

  Consistent with widespread AHCD

Motor Neuron Diseases

***Amyotrophic lateral sclerosis (ALS)**

Progressive bulbar palsy (PBP)
Primary lateral sclerosis (PLS)
Progressive muscular atrophy (PMA)

***Spinal Muscular Atrophy (SMA)**

Motor Neuron Diseases

***Amyotrophic lateral sclerosis (ALS)**

Progressive bulbar palsy (PBP)
Primary lateral sclerosis (PLS)
Progressive muscular atrophy (PMA)
(Flail arm and Flail Leg)

***Spinal Muscular Atrophy (SMA)**

Amyotrophic Lateral Sclerosis

- The most common form of MNDs (Charcot 1869)
- The cause is unknown although there many theories.
- Sporadic >90% , Familial <10% .
- 75% die within five years from the onset of symptoms
- Prevalence is about 3 per 100,000.
- The incidence is about 1-2 per 100,000.

According to Ammar Al-Chalabi (2006)

- The average GP sees one case per lifetime
- The average neurologist sees one case per month
- The neurophysiologist sees one case per week

ALS: time course

Variable course and severity

First symptom to diagnosis: 2M - >3Yrs

Rapidly progressive
Slowly progressive (25% > 5 yrs)
Arrested "cured"

Amyotrophic Lateral Sclerosis

- Diagnosis: Clinical + EMG + Exclusion
- Typical establishe case: Easy

  UMN and LMN
- Early stage: difficult

  Regionally--Spread

ALS: Early Clinical Features

Limbs (80%)

- Foot drop
- Clumsiness of the hands
- Fasciculations
- Night cramps

Bulbar (20%)

- Dysphagia
- Dysarthria

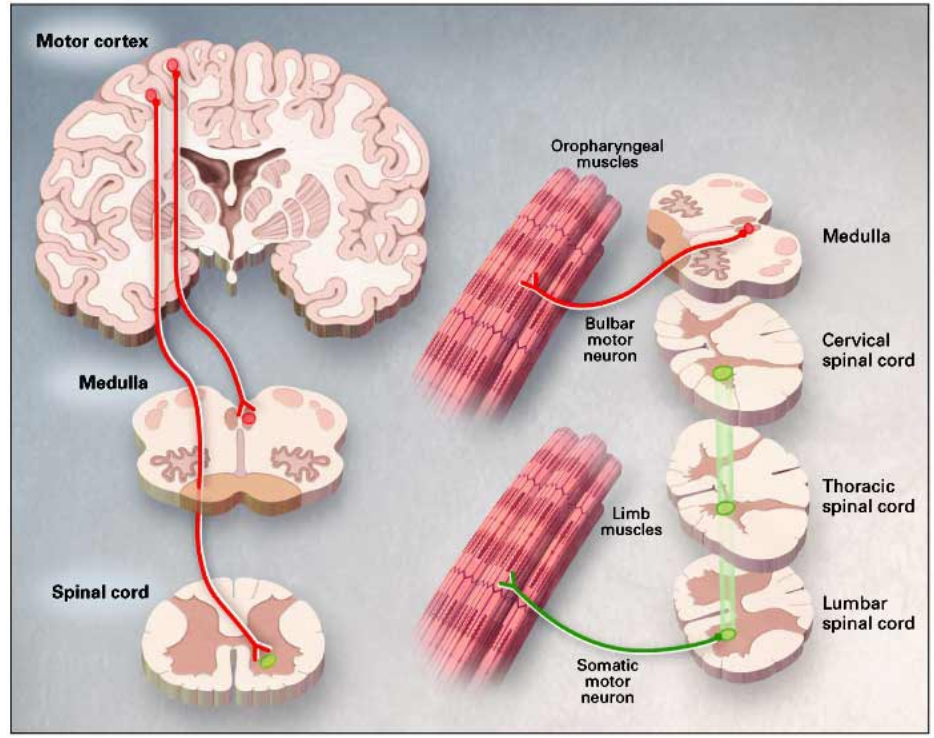
Respiratory (rare)

Motor neuron diseases
Clinical Criteria

Purpose: to develop internationally acceptable criteria, that services as algorithm for clinical studies, therapeutic trials and molecular genetic research studies

EL Ecsorial Criteria: WFN 1990, published 1994

MND/Anatomic regions



Rowland & Shneider NEJM 2001, 344: 16688

El Escorial Criteria 1994
Clinical Categories

Definite ALS

UMN and LMN signs in 3 regions

Probable ALS

UMN and LMN signs in 2 regions
UMN sings must be above LMN

Possible ALS

UMN and LMN in only one region
Or UMN alone in two regions

Suspected ALS

LMN signs in 2 or more regions

El Escorial Criteria
EMG signs of definite LMN dysfunction

- SA: Fibrillation potentials
- Large MUP (amplitude, duration)
- Reduced IP with FR > 10Hz

El Escorial Clinical Criteria

Criticisms

Rowland (1998) **J-Neurol-Sci. 160: S6–S24**

Definite ALS

UMN and LMN signs in 3 regions

Probable ALS

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UMN sings must be above LMN

Possible ALS (?)

UMN and LMN in only one region

Or UMN alone in two regions

Suspected ALS (?)

LMN signs in 2 or more regions

El Escorial EMG criteria

Criticisms

Wilbourn 1998: J-Neurol-Sci. 160 : S25–S29

They ignored:

Fasciculations potentials

Staging and severity of the disease

Influence of UMN on firing rate of the motor units

Revised WFN El Escorial Criteria

Airlie House (1998) and Awaji-Shima Criteria (2006)

1. Diagnostic categories: are three: definite, probable and possible

2. Fasciculation potentials (FPs) are equivalent to fibrillations and positive sharp waves in their clinical significance

3. Electrophysiological abnormalities have equal diagnostic significance to clinical findings for the evaluation of LMN dysfunction in a given body region

Revised WFN Criteria

Diagnosis of ALS requires

- Evidence of LMN degeneration by clinical, NP or Npath
- Evidence of UMN degeneration by clinical examination
- Evidence of progression by history or examination
- Absence of NP or Npath evidence of other ds processes
- Absence of neuroimaging evidence that might explain the observed clinical and neurophysiological sings

Revised WFN Criteria

Definite diagnosis of ALS requires:

1. The presence of UMN and LMN signs in multiple regions (bulbar region and at least two of the other spinal regions)

Or

(the presence of UMN and LMN signs in three spinal regions)

and

2. The exclusion of other conditions that explain UMN and LMN signs by neurophysiological, neuroimaging and laboratory examinations

Motor Neuron Diseases

- Amyotrophic lateral sclerosis

  Mimics excluded by neurophysiological, imaging and other lab tests

- MND variants /other forms

  (PMA, Flail arm, Flail leg, early presentation)

  Mimics excluded by neurophysiological, imaging and other lab tests

WFN Criteria

Summary Role of Neurophysiolghist

1. Confirm the presence LMN dysfunction
2. EMG changes in a regional fashion (bulbar, cervical, thoracic and lumbosacral)
   Region: two muscles supplied by two different peripheral nerves and two different nerve roots
3. Detect evidence of LMN in clinically unaffected regions
4. Exclude other problems which may mimic MND

+

Assessment of severity/progression

Neurophysiology

Diagnostic work-up for MND

- **Nerve conduction studies**
- **Needle EMG**
- **Additional tests**
  - **Segmental motor testing**
  - **RST/ SFEMG**
  - **TMS**
  - **MUNE**

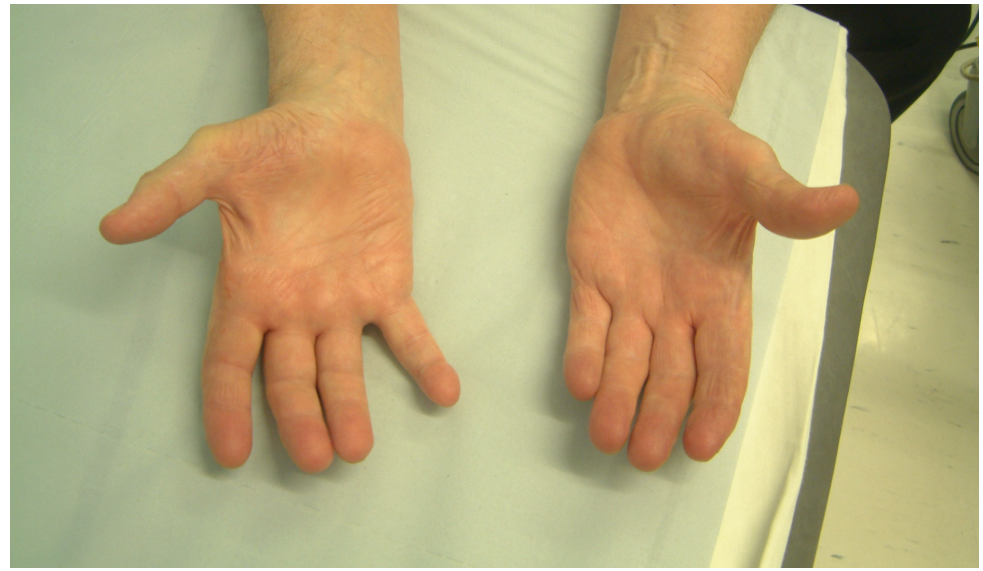
Sensory conduction studies

Typically normal and helps to exclude post-ganglionic pathologies e.g. plexopathy, focal or generalised neuropathies

Motor conduction studies

- Normal: early stages
- Established case :

  Reduced CMAP and CV
- (Split-hand pattern)



No conduction block

F-Waves

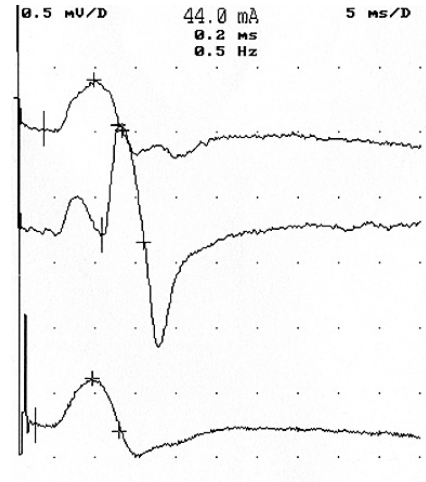
- Slightly prolonged (LMN)
- Increase in amplitude
  - Increase size of the MUP (LMN)
  - Synchronisation of the MUP (UMN)
- Increase persistence (UMN)
- Repeaters (LMN)
- Late late responses (UMN)

+

Proximal conduction block ?

H-reflexes

- Increase amplitude of the soleus H-reflex. H/M ratio > 50%
- Release of H reflexes from other ms.



H-reflex from R Deltoid

EMG procedure

Muscles sampling from 4 regions on one side of the body:

Cervical: FDI , EDC, Biceps, Deltoid

Lumbar: TA, VL, TFL

Thoracic: Mid- thoracic paraspinal, Rectus Abdominis

Bulbar: Genioglossus, OO, Trapezius/SM

Examination of muscles on two sides is optional.

However, it may be useful when patient presents with asymmetrical weakness to detect early neurogenic changes in clinically intact muscles.

Distal> Proximal

Wasted ms.

Muscles with Fasciculations

MND/ EMG findings
Initial stage
well compensated (reinnervation) stage

- **ENEMG:**

  A few fibs, prominent fasc.

  Mild excess of polyphasic stable MUs.
- **SFEMG:**

  FD ++

  Jitter +, No Blocking
- **MacEMG:** Ampl. +

(Rydin, Stalberg, Sanders 1983)

MND/ EMG findings

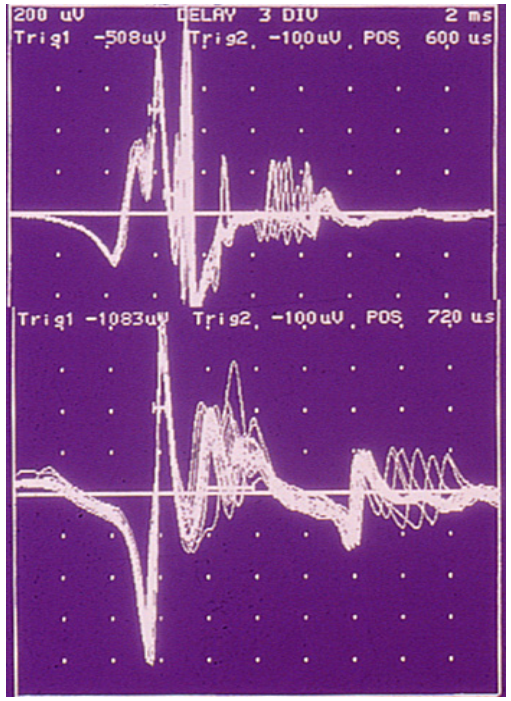
Progressive course (Den>Reinnervation)

Features of instability (Active Neurogenic changes)

- **CNEMG:**

  Fibs ++,

  Polyphasic, LD and unstable ++, SP



- **SFEMG:**

  Increase fibre density

  Very abnormal jitter and marked blocking

- **MacEMG:** Normal or moderate increase

MND/ EMG findings

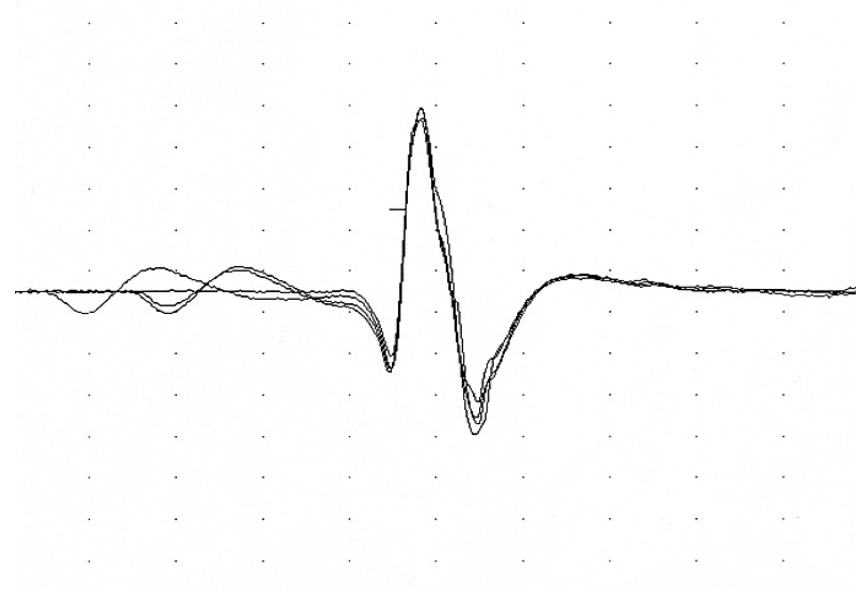
Progressive course (End stage denervation)

Features of failed reinnervation

<u>CNEMG</u>

Fibs +++

Small, unstable MUs ++



<u>SFEMG</u>:

FD 0

Jitter and Blocking ++

<u>MacEMG</u>: small

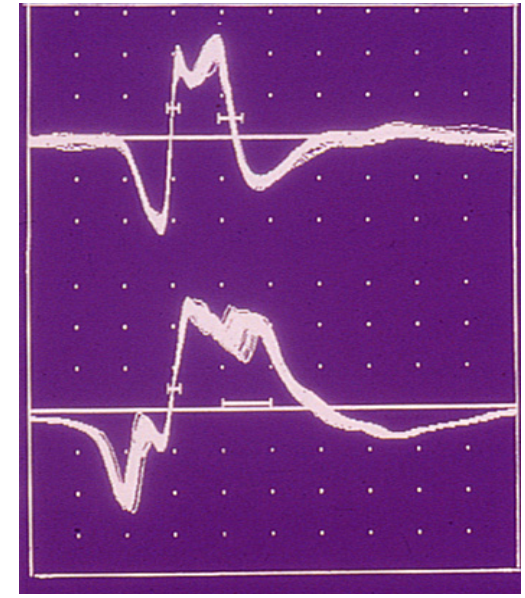
MND/ EMG findings

slow course (Chronic neurogenic changes)

CNEMG

Fibs 0

Large stable MUs +++



SFEMG:

FD +++

Jitter + , Blocking 0

MacEMG: ampl +++

Bad prognostic features

- Profuse fibrillations
- Unstable motor units
- RNS: Decrement of responses
- SFEMG: Increased Jitter and blocking

Other Neurophysiological tests (Form A)

- Segmental motor studies
- RNS and SFEMG
- Transcranial Magnetic Stimulation
- Motor unit number estimation (MUNE)

Segmental motor testing

Young patient

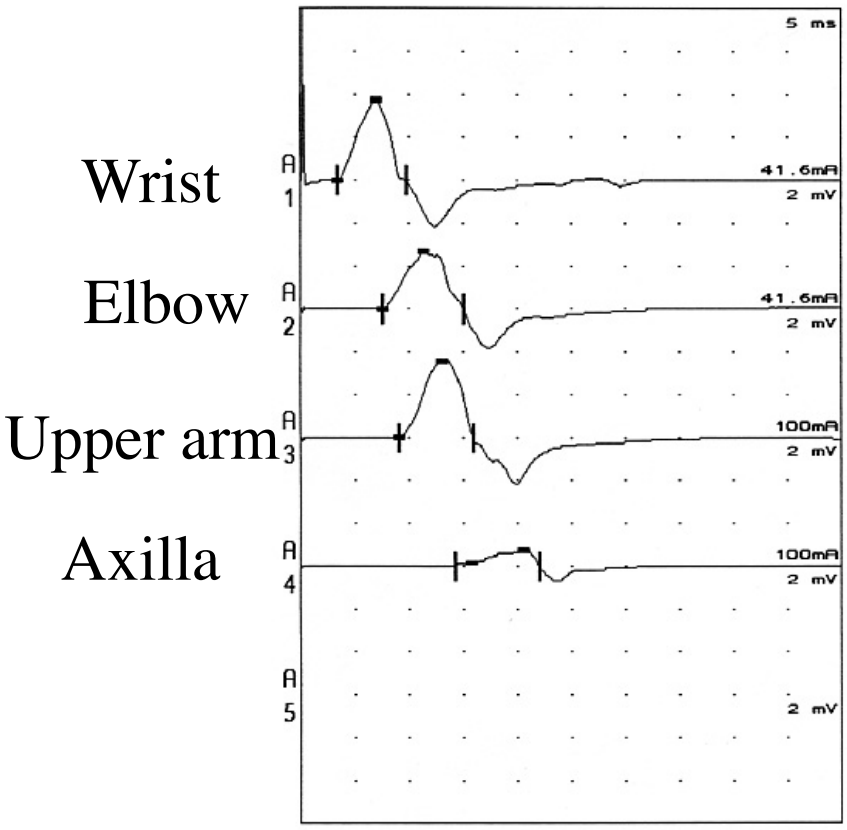
Asymmetrical lower motor neuron weakness

PN distribution

Median and/or ulnar F- responses: absent

MMNCB

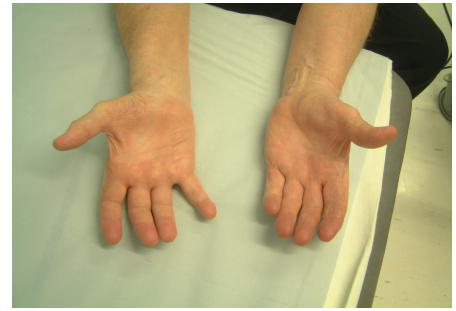
Median nerve CB



Rt. Median N.

Young
Asymmetrical weakness: No wasting,
ULs> LLs, PN distribution
Distal > Proximal
Fasciculations
Reflexes: normal or brisk
Sensation: normal
Elevated Anti-GM1 Abs (60%)

MMN



MND

RNS and Single fibre EMG

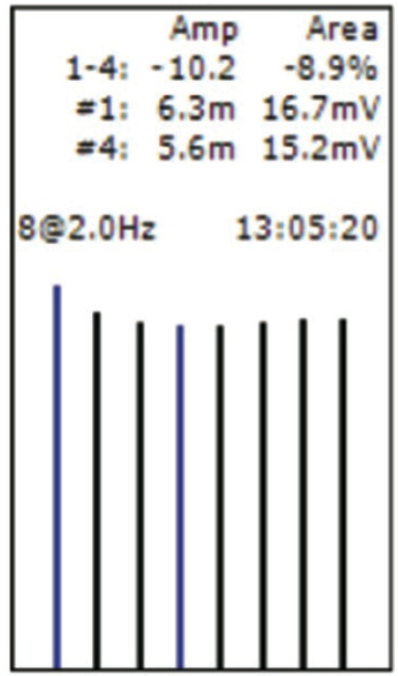
Repetitive nerve stimulation and SFEM are performed in patients with bulbar symptoms when routine EMG does not show denervation to support MND

RNS in MND

- 1. Decrement : Distal > Proximal muscles
- 2. Decrement but not decrement-increment pattern

Typical Myasthenia Gravis Pattern

A



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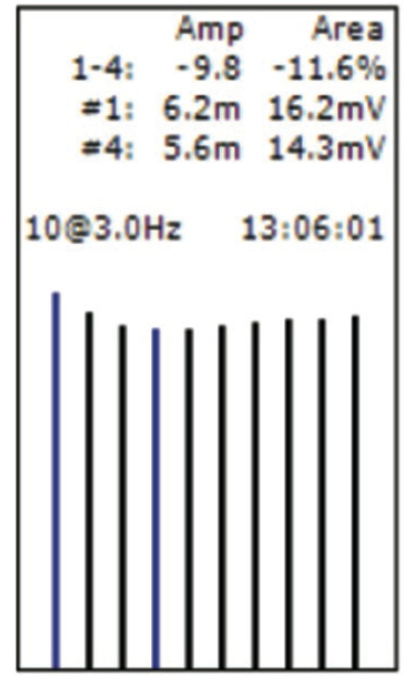


Karunaratne K, Taube D, Khalil N, et al. Pract Neurol 2018;18:115–125

Neurophysiological tests
Upper Motor Neuron

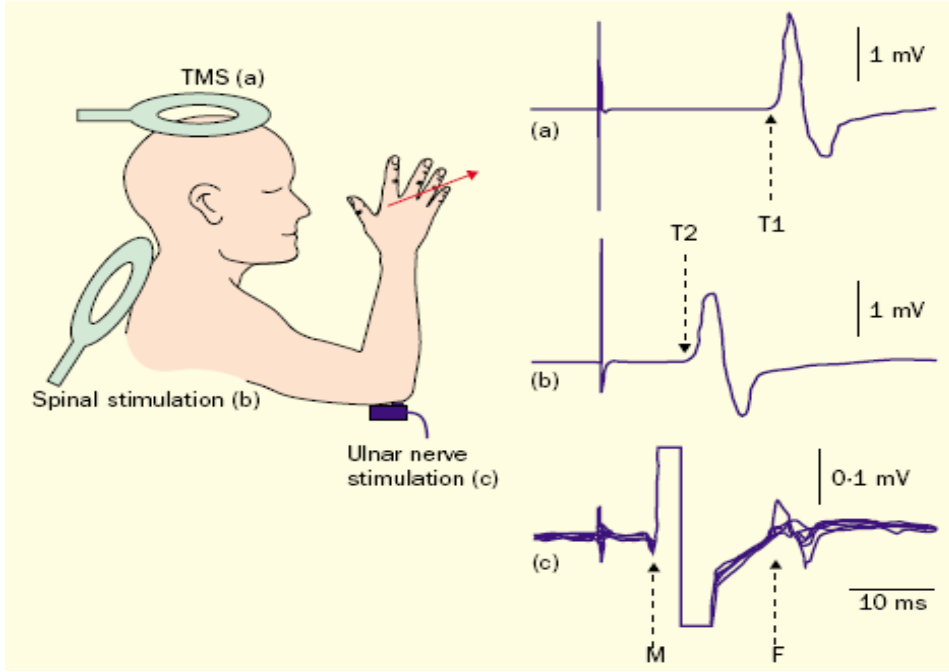
- This is not a requirement EMG test by WFN Criteria
- Upper motor neuron signs on routine NCS/EMG
- Transcranial Magnetic Stimulation (TMS)

NCS/ EMG

Upper motor neuron signs

- Increased amp. & persist. of F waves
- Increased amp. of the H-reflexes
- Release of H reflexes from the small ms of the hand
- Enhanced H-reflex recovery curve
- Increased amplitude of the Blink reflex
- Enhanced Blink reflex recovery curve
- Reduced silent period
- Abnormal firing pattern of the MU (JIH)
- Reduced RP at a low firing rate
- Enhanced Fasciculations

Transcranial Magnetic Stimulation (TMS)



CMCT= Scalp Latency – Spinal latency

CMCT= Scalp latency - Peripheral conduction

(M+F-1)/2

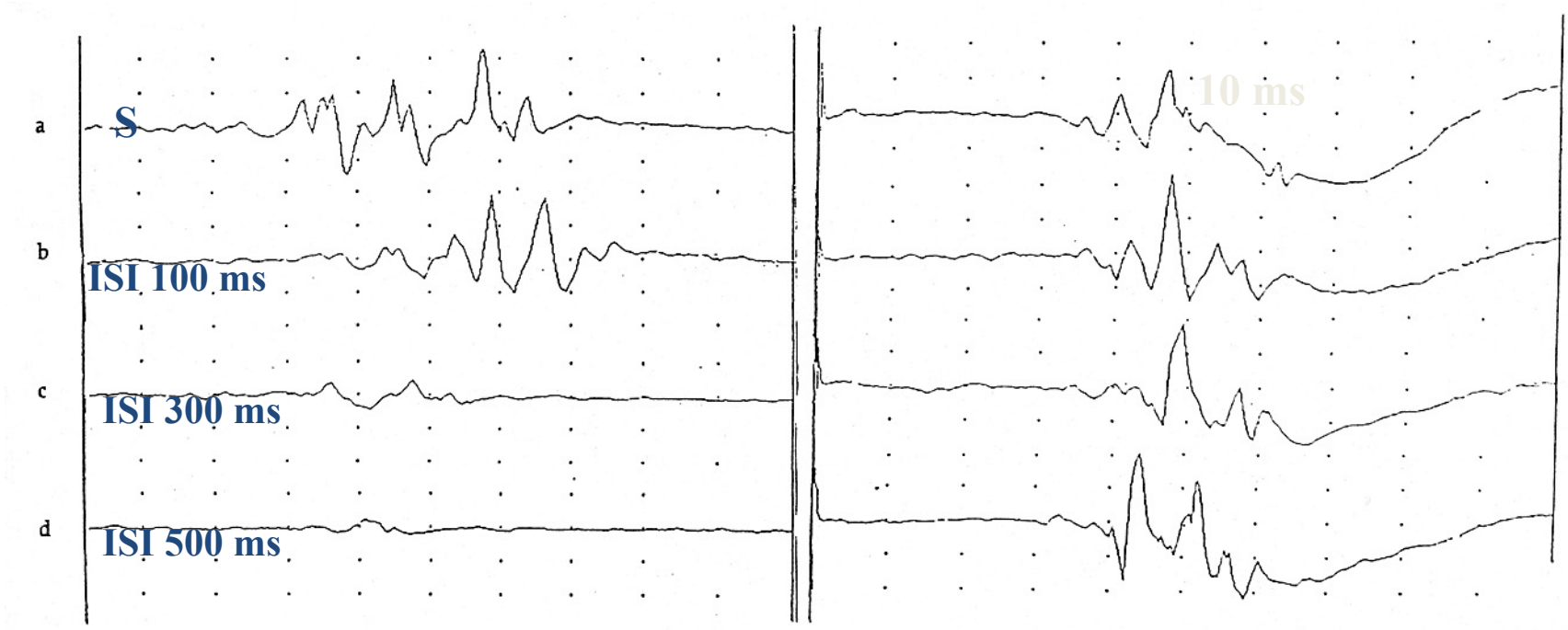
Transcranial Magnetic Stimulation (TMS)

- Central motor conduction time: slightly prolonged
- Cortical threshold: reduced early stages but it becomes higher later on.
- Motor evoked potential (MEP) amplitude:

  Increase in early stages, becomes smaller later on
- Cortical Silent period: shorter than normal (reduced cortical inhibitory interneurons)

- Paired-stimulus technique: (reduced cortical inhibitory mechanisms)
- Triple stimulation technique: (early detection of corticomotor dysfunction)

Blink reflex paired stimuli



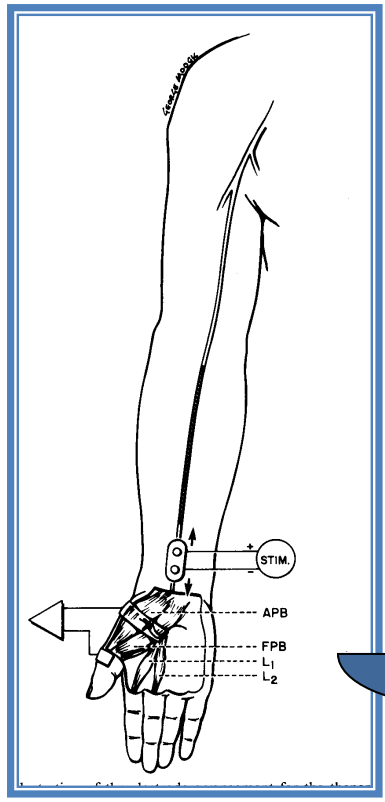
Normal **Patient**

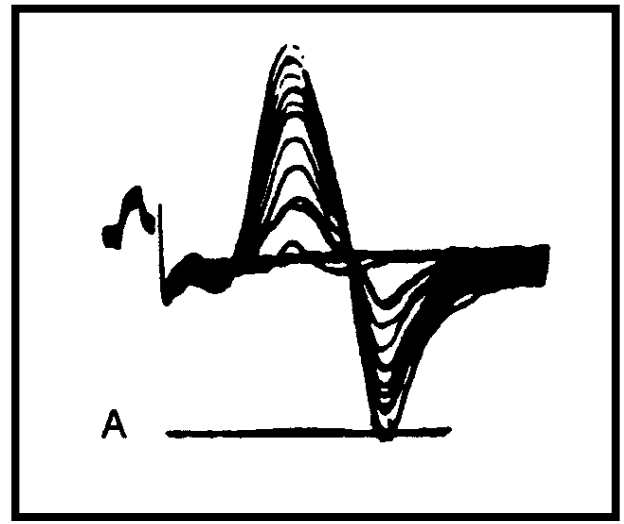
Blunt, Khalil, Perkin (1997)

Motor Unit Number Estimation (MUNE)

- Is not part of the routine NCS/EMG tests
- It may be useful to document motor neuron loss in any progressive motor syndrome
- It is an established biomarker of MU loss in research and in clinical trials of MND

Motor Unit Number Estimation





Size of M-potential

Mean S-MUP Size

= MUNE

McComas et al. 1971

Motor unit index (MUNIX)
Motor unit size index (MUSIX)

- A new technique was developed by Sanjeev Nandekar (2004) for assessment of number (MUNIX) and size (MUSIX) of the motor units.
- Using the compound muscle action potential (CMAP) and surface interference pattern (SIP) at different force levels.
- MUNIX is calculated from the area and power of CMAP and SIP.
- MUSIX is derived by CMAP / MUNIX.

Muscle Ultrasound

Muscle ultrasound can be used as an additional tool to needle EMG to increase detection of generalized lower motor neuron disease.

(Misawa et al., 2011)

Exclusion of MND Mimics

1. Regional – one body region
2. Spinal- PMA type
3. Spinal and Bulbar –ALS type
4. Bulbar alone

MND mimics

Clinical presentation involving one body region

Focal peripheral nerve lesion

Radiculopathies : L5 , S1

Diabetic amyotrophy

Neuralgic amyotrophy

Monomelic amyotrophy

MND Mimics

Clinical presentation involving two body regions

(PMA-type picture)

- Neuropathies: Inflammatory and paraproteinemic
- Lymphoma-related motor Neuropathy/Neuronopathy
- Multifocal motor neuropathy with or without CB
- Radiation-related motor neuropathy
- Myopathies: IBM and Ca-P Homeostasis
- Cervical spondylotic myelopathy
- Adult-onset SMA
- Post-polio syndrome
- Neuromuscular hyperexcitability syndromes
- LEMS

MND Mimics

Clinical presentation involving Spinal and Bulbar regions (AlS-Type)

- Kennedy disease (X-linked bulbospinal MA)
- Oculopharyngeal muscular dystrophy (OPMD)
- Lithium myopathy

MND Mimics

Clinical presentation involving bulbar region

- Myasthenia
- Thymoma-related motor neuropathy
- Post-radiation bulbar neuropathy

Neuromuscular hyperexcitability syndromes

- Neuromyotonia
- Cramp-fasciculation syndrome
- Rippling muscle disease
- Focal neuromuscular hyperexcitability
- Marvan’s syndrome

Definite electrodiagnosis of MND

- A definite electrodiagnosis of MND requires demonstration of denervation in four body regions (or three body regions including bulbar, cervical and lumbosacral) with lack of conduction block and normal sensory potentials.

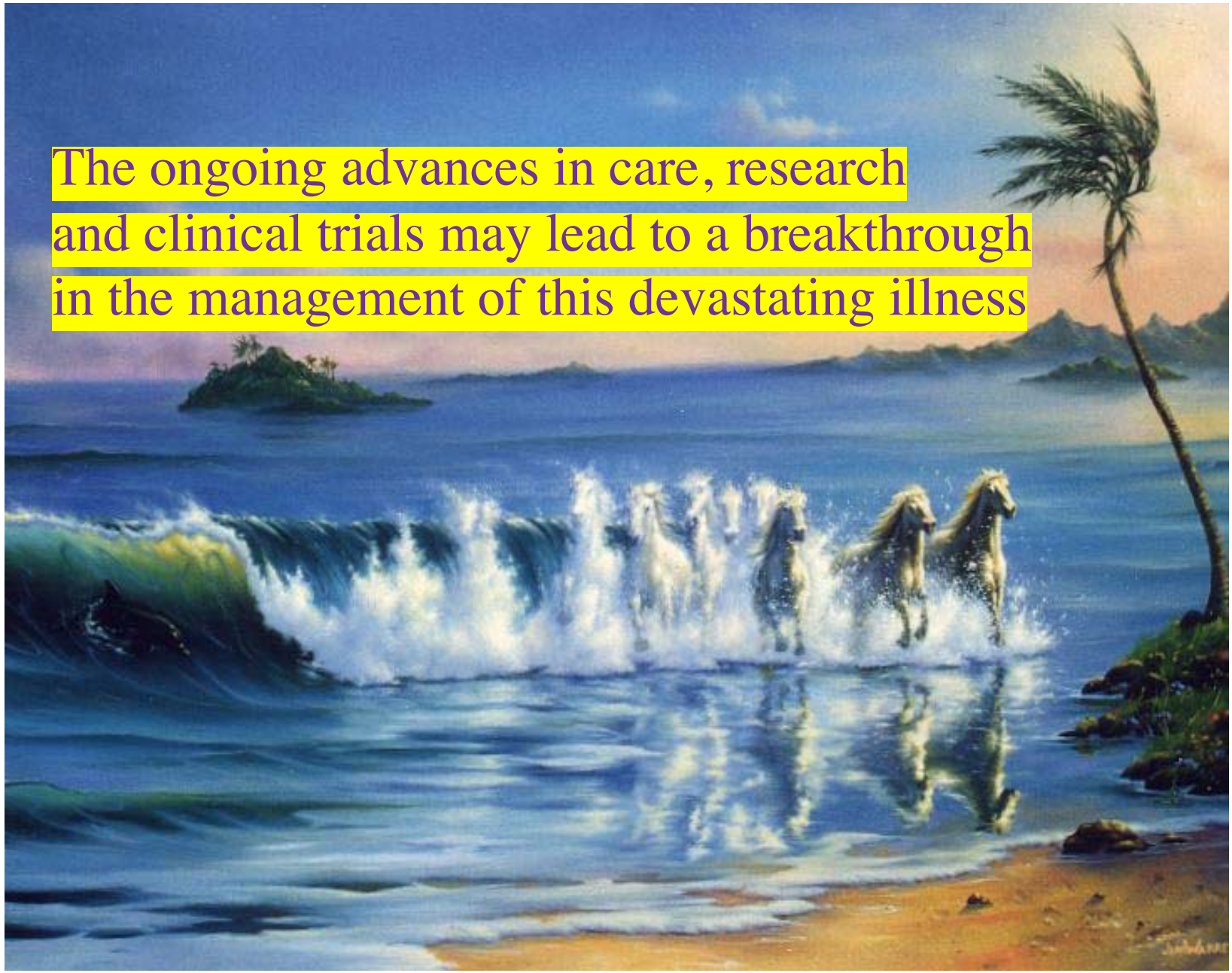
- Avoid using suspected, possible or probable MND in the conclusion as these are clinical terms originally used in the El Escorial Criteria and their use is later discouraged.

- If denervation is not found in four body regions (particularly the bulbar muscles) the differential diagnosis should be wide open to include acquired or hereditary pathology of the motor neurons and/or their motor axons innervating the affected muscles/body region (s).

- A follow-up study in a few months is recommended to check on progression.

- Findings suggest pathology of the motor neurons and/or their axons innervating muscles in (….body regions) with normal sensory potentials and lack of conduction block.

- This will ensure the DD will include any motor unit pathology from the anterior horn cells to the muscle fibres.


The ongoing advances in care, research
and clinical trials may lead to a breakthrough
in the management of this devastating illness