UK practice for electrodiagnosis of MND
Review of literature and background
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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
• **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 are 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 establishes 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 serves as algorithm for clinical studies, therapeutic trials and molecular genetic research studies

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


**Definite ALS**
- UMN and LMN signs in 3 regions

**Probable ALS**
- UMN and LMN signs in 2 regions
- UMN signs 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


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
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

2. 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 Neurophysiologist

1. Confirm the presence of 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

**CNEMG**
- Fibs +++
- Small, unstable MUs ++

**SFEMG:**
- FD 0
- Jitter and Blocking ++

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

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

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.