ALS: Making the Diagnosis

Jennifer M. Martinez-Thompson, MD
October 18, 2019
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• No conflicts of interest
• No discussion of off-label or investigational drug use
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Goals

By the end of this talk, you should be able to:

- Describe the approach to diagnosing ALS using existing clinical criteria
- Identify common electrodiagnostic (EDX) findings in ALS
- Recognize EDX findings that may prompt evaluation for mimickers
Diagnosing ALS

• Can be challenging
  o Clinical diagnosis
  o Phenotypic heterogeneity
  o Early in disease course

• Most do not meet criteria for a definite diagnosis early on
  o Limitations to existing criteria
History of ALS Diagnostic Criteria

1957: Lambert criteria published
1991: El Escorial criteria
1997: Airlie House guidelines
2000: Revised El Escorial/Airlie House criteria
2006: Awaji-Shima criteria
2010s: Continued guideline revisions (clinical trials)
Regions/segments

• **UMN signs**
  - Weakness without atrophy
  - Hyperreflexia (preserved reflexes in atrophic muscles)
  - Primitive reflexes (Babinski sign)
  - Spasticity

• **LMN signs**
  - Weakness with atrophy
  - Low or normal tone
  - Reflex loss
  - Fasciculations

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## Revised El Escorial Criteria

<table>
<thead>
<tr>
<th>Degree of diagnostic certainty</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Definite ALS</strong></td>
<td>UMN + LMN signs in 3 regions</td>
</tr>
<tr>
<td><strong>Probable ALS</strong></td>
<td>UMN + LMN signs in 2 regions (some UMN signs rostral to LMN)</td>
</tr>
<tr>
<td><strong>Laboratory-supported probable ALS</strong></td>
<td>UMN+ LMN signs in 1 region OR UMN in ≥ 1 region(s) + EMG evidence of active denervation in ≥ 2 segments (≥ 2 muscles of different root and nerve origin)</td>
</tr>
<tr>
<td><strong>Possible ALS</strong></td>
<td>UMN + LMN signs in 1 region, UMN signs only ≥ 2 regions, LMN signs rostral to UMN signs</td>
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</tbody>
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Fibrillations or positive sharp waves
Awaji Criteria

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- Includes both clinical and EMG findings
- Active denervation
  - Fibrillations or positive sharp waves
  - Fasciculations with chronic neurogenic changes
- Literature suggests helpful in bulbar-onset ALS for earlier diagnosis
Why perform EMG/NCS?

• Confirm extent of lower motor neuron involvement

• Exclude ALS mimickers
  o Motor-predominant neuropathies (CIDP, MMN)
  o Inclusion body myositis
  o BFS or CFS
  o Other motor neuron diseases (need clinical context)
    • SMA, SBMA, PLS, PBP
Common EMG/NCS Changes
Fibrillations
Positive sharp waves
Fasciculations
Reinnervation
MUP instability
MUP complexity
Long, tall MUPs
Satellite potentials
Reduced recruitment
NCS in ALS

• **Sensory NCS** usually normal

• **Motor NCS** normal early on
  - Slow, progressive motor axon loss + compensatory reinnervation
  - CMAP amplitude drops once # of functioning motor units are ~50% normal *(later finding)*
  - Distal latencies and conduction velocities normal until amplitudes are very low
Motor NCS in ALS (con’t)

• **F-waves** usually **normal**
  - May be absent if CMAP amplitude very low
  - F-wave persistence or decreased variability
  - F-wave latency should not be prolonged relative to F-estimate (think of proximal slowing)

• May need to exclude proximal conduction block
  - Beware of pseudo-conduction block
R**eptitive stimulation (NCS)**

- Decrement has been reported in up to 50% of patients with ALS

- Typically $< 10\%$ with baseline 2-Hz repetitive stimulation

- Can partially repair with brief exercise and worsen several minutes after exercise
Sounds of EMG in ALS
Spontaneous activity
Voluntary activation
Temporal EMG/NCS Changes

Within single muscle:

**Early**
- Reduced recruitment
- MUP instability
- Fibrillations

**Late**
- Low CMAP amplitude
- F-wave persistence or loss

MUP complexity
- Large MUPs

Fibrillations
Approach to EMG/NCS
NCS

**If weakness isolated to lower limb:**
- Peroneal (EDB) + F-wave
- Tibial (AH) + F-wave
- Sural sensory

**If weakness isolated to upper limb:**
- Ulnar (ADM) + F-wave
  - Consider 4-point or proximal stimulation if LMN findings only on exam
- Median (APB) + F-wave
- Ulnar and median antidromic sensory

**If weakness generalized:**
- Peroneal (EDB) + F-wave
- Sural sensory
- Ulnar (ADM) + F-wave
- Median antidromic sensory
Needle EMG

- In obvious cases, may only need to do enough to show the process is diffuse

- Sample several muscles in each segment
  - Different root and nerve contribution
  - Relaxed muscle to assess for fasciculations
  - Distal/weak muscles higher yield

- If bulbar-onset may need to do cranial nerve-innervated muscles
  - Masseter, genioglossus, orbicularis oris

- Bulbar (if needed)
- Cervical (3 muscles) FDI, Biceps, Triceps
- Thoracic paraspinals (2 levels) Lumbosacral (3 muscles) TA, MG, VM
When to think about mimickers...

**NCS**
- True proximal conduction block on motor NCS
- Absent or prolonged F-waves with near normal motor amplitudes
- Prominent distal latency and conduction velocity abnormalities on motor NCS
- Sensory NCS abnormalities without pre-existing *peripheral neuropathy* or mononeuropathies

**Needle EMG**
- Absence of fasciculation potentials
- Large MUP of simple morphology
- Normal MUP (*UMN syndrome, BFS/CFS*)

Motor-predominant/demyelinating neuropathies

MMN (conduction block)

Kennedy's disease (SBMA)
Take-home points

- Making the diagnosis of ALS can be challenging
  - Requires combination of clinical and EDX findings
  - Revised El Escorial criteria used clinically
- EMG/NCS can:
  - Confirm extent of lower motor neuron involvement
  - Exclude ALS mimickers
- Standard NCS are typically normal with low CMAP amplitudes later in the disease
- Needle EMG shows
  - Fasciculations, fibrillations
  - Long duration, high amplitude, unstable, complex MUP with reduced recruitment

EMG/NCS can:
- Confirm extent of lower motor neuron involvement
- Exclude ALS mimickers
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