Diagnosing ALS: the Gold Coast criteria and the role of EMG

Martin R Turner ©, UK MND Clinical Studies Group

In September 2019, a group of international neurologists gathered in Gold Coast, Australia, to deconstruct the diagnostic process for amyotrophic lateral sclerosis (ALS) and to try to simplify it. A proposal for revised diagnostic criteria emerged1 (box 1) and the initial experience of their application has been positive.2–5 The diagnosis remains fundamentally clinical, and it is timely to reflect on the adjunctive role of electromyography (EMG).

Although motor neurone disease (MND) is undeniably clinically heterogeneous, there is a unifying molecular pathology in 97% of cases, namely cytoplasmic phosphorylated aggregates of the 43 kDa transactive response DNA-binding protein, TDP-43. Since Charcot’s pivotal clinical observations of the simultaneous occurrence of upper motor neurone (UMN) and lower motor neurone (LMN) involvement defining the ‘the most common phenotype of ALS’ a broader spectrum of involvement is now recognised clinically and pathologically.6 At both LMN and UMN clinical extremes, the rate of disease progression is notably slower, but there is no simplistic relationship between the site of onset, the combination of UMN versus LMN signs or rate of disease progression. The historical term progressive muscular atrophy was used to describe the extreme of clinical LMN involvement, but histopathological7 and neuroimaging8 studies have shown that such cases have subclinical corticospinal tract and wider brain involvement, and the modern use of the term ‘LMN-predominant ALS’ reflects this. The other extreme is also a spectrum of ‘UMN-predominant ALS’ in which LMN signs are not clinically obvious until a few years after symptom onset. A minority of these cases, and less than 3% of all MND, can be confidently demarcated as primary lateral sclerosis by virtue of a dramatically slower rate of progression associated with marked spasticity as well as lack of LMN involvement.9 The clinicopathological overlap of ALS with frontotemporal dementia has further extended Charcot’s definition, so that ALS may now be considered a system degeneration variably penetrating the motor cortex and its spinal and cerebral connectome.

The original diagnostic criteria defined at El Escorial, Spain, in 1990 and their subsequent 1998 revision at Airlie House, USA, and in 2006 at Awaji-shima, Japan, employed categories but were created very much with therapeutic trials in mind. Categories were based on the number of body regions (bulbar, cervical, thoracic and lumbosacral) with simultaneous UMN and LMN involvement. The terms used in the various iterations, included some or all of: ‘suspected’, ‘possible’, ‘probable’, ‘probable laboratory-supported’ and ‘definite’ ALS. These categories have been shown to have little independent prognostic value10 and patients with MND deemed to have ‘insufficient’ UMN signs clinically were denied entry to trials, despite similar rates of disability progression as ‘probable’ or ‘definite’ cases. Individuals frequently die from MND never having evolved from their ‘suspected’, ‘possible’ or ‘probable’ categories. It is biologically interesting how little clinical evolution there is between these categories, despite a wide range of disability progression rates common to all of them. Speculatively, the proportions of UMN versus LMN involvement might reflect an individual’s premorbid nervous system architecture to some extent. Most problematic of all, however, was the often psychologically distressing consequences for patients in
The Gold Coast criteria for the diagnosis of amyotrophic lateral sclerosis

1. Progressive motor impairment documented by history or repeated clinical assessment, preceded by normal motor function,

**AND**

2. The presence of upper* and lower† motor neurone dysfunction in at least ONE body region‡, with:
   - upper and lower motor neurone dysfunction noted in the same body region if only one region is involved,
   - or lower motor neurone dysfunction in at least TWO body regions,

**AND**

3. Investigations§ excluding other disease processes.

*Upper motor neurone dysfunction implies at least one of the following:
- Increased deep tendon reflexes, including the presence of a reflex in a clinically weak and wasted muscle, or spread to adjacent muscles.
- Presence of pathological reflexes, including Hoffman sign, Babinski sign, crossed adductor reflex, or snout reflex.
- Increase in velocity-dependent tone (spasticity).
- Slowed, poorly coordinated voluntary movement, not attributable to weakness of lower motor neurone origin or Parkinsonian features.

†Lower motor neurone dysfunction in a given muscle requires either:
- Clinical examination evidence of muscle weakness and muscle wasting, or
- EMG abnormalities that must include both:
  - Evidence of chronic neurogenic change, defined by large motor unit potentials of increased duration and/or increased amplitude (with polyphasia), and motor unit instability regarded as supportive but not obligatory evidence, and
  - Evidence of ongoing denervation, including fibrillation potentials or positive sharp waves, or fasciculation potentials.

‡Body regions are defined as bulbar, cervical, thoracic and lumbosacral. To be classified as an involved region with respect to lower motor neurone involvement, there must be abnormalities in TWO limb muscles innervated by different roots and nerves, or ONE bulbar muscle, or ONE thoracic muscle, either by clinical examination or by electromyography (EMG).

§The appropriate investigations depend on the clinical presentation, and may include nerve conduction studies and needle EMG, MR or other imaging, biofluid studies, or other modalities as clinically indicated.
be conveyed by a clinician with knowledge of that plan.

Further reading


Correction notice  This article has been corrected since it was published Online First. Box 1 has been reordered correctly.

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REFERENCES


