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Motor neuron diseases

Amyotrophic lateral sclerosis or not: Keys for the diagnosis

T. Lenglet [a,b], J.-P. Camdessanché [c,d,*]

[a] Département de neurophysiologie clinique, Hôpital de la Salpêtrière, Assistance Publique-Hôpitaux de Paris, France
[b] Centre Référent Maladies du Motoneurone et SLA, Hôpital de la Salpêtrière, Assistance Publique-Hôpitaux de Paris, France
[c] Service de Neurologie, Hôpital Nord, CHU de Saint-Etienne, France
[d] Centre Référent Maladies du Motoneurone et SLA, CHU de Saint-Etienne, France

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ABSTRACT

Amyotrophic lateral sclerosis (ALS) is a degenerative motor neuron disease (MND) which prognosis is poor. Early diagnosis permit to set up immediately adapted treatment and cares. Available diagnostic criteria are based on the detection of both central and peripheral motor neuron injury in bulbar, cervical, thoracic and lumbar regions. Electrodiagnostic (EDX) tests are the key tools to identify peripheral motor neuron involvement. Needle examination records abnormal activities at rest, and looks for neurogenic pattern during muscle contraction. Motor unit potentials morphology is modified primary to recruitment. Motor evoked potentials remain the test of choice to identify impairment of central motor neurons. In the absence of diagnostic biomarker of ALS and among essential investigations of suspected MND, a careful clinical and neurophysiological work-up is essential to rule out the differential diagnosis.

1. Introduction

Amyotrophic lateral sclerosis (ALS) which prognosis is poor, is a degenerative disease of both central and peripheral motor neurons leading to gradual installation of motor deficits that may affect limbs, respiratory muscles, phonation and deglutition [1]. Its pathophysiology remains unclear and to date, riluzole is the only one drug that may influence survival in ALS patients [2]. Nevertheless, other types of care, respiratory management or nutrition for example, isolated or part of a multidisciplinary care, may impact survival or quality of life in ALS [1]. Thus, reaching the diagnosis of ALS as early as possible remains a challenge for the neurologist.

Discovery of clinical, biological, genetic, radiological and neurophysiological biomarkers of ALS is one of the biggest challenges of our scientific community [3–5]. At the moment, clinics and electrodiagnostic (EDX) tests remain the arms of

* *Corresponding author at*: Service de Neurologie, Hôpital Nord, CHU de Saint-Etienne, 42055 Saint-Etienne cedex 02, France.
E-mail address: j.philippe.camdessanche@chu-st-etienne.fr (J.-P. Camdessanché).
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ALS diagnosis based on El Escorial diagnostic criteria successively updated in Airlie House and Awaji-shima criteria [6–8].

Diagnosis of ALS is horrific for the patient and the clinician who will announce it. This is why diagnosis needs to be as sure as possible. The main objective of this article is to highlight the central role of electrophysiological investigations in the diagnosis of ALS in an evocative context and to provide to the clinicians and the neurophysiologists tools necessary for diagnosis and differential diagnosis.

2. Diagnostic criteria

ALS is the most frequent form of motor neuron disease (MND), a common adult-onset neurodegenerative disorder, also comprising progressive muscle atrophy (PMA) and primary lateral sclerosis (PLS) in which motor neurons loss is restricted to lower motor neuron (LMN) and upper motor neuron (UMN) respectively. ALS is characterized by the typical association of UMN and LMN loss, producing a characteristic mixed picture. In the absence of definitive diagnostic test, diagnosis of ALS is made clinically with support of the electroneuromyography while all other investigations are tailored to exclude ALS mimics. Formal diagnostic criteria, known as El Escorial criteria were first agreed in 1994 to standardize patients enrolment in clinical trials [6]. Overall, they defined four levels of diagnosis certainty, namely definite, probable, possible or suspected, depending on the dissemination of both central and peripheral motor neuron damage in four defined anatomical regions: bulbar, cervical, thoracic and lumbar area. Considered as too stringent they were revised in 2000 to improve diagnostic sensitivity. The revised criteria introduced the contribution of electrophysiological investigations to the diagnosis of ALS by adding a ''laboratory-supported probable ALS'' category [9]. Although the resulting Airlie House criteria reached good specificity, their sensitivity remained disputable, especially in the early stages of the diseases, resulting in detrimental diagnostic delay and limitations in the recruitment of ALS patients in clinical trials [10]. In 2008, a committee of experts in neurophysiology published new diagnostic criteria – Awaji-shima criteria – including recommendations to use electrophysiological data in the diagnosis of ALS [8]. First these new criteria gave to EDX tests the same weight as clinical abnormalities for the diagnosis of LMN damage and so the category ''laboratory-supported probable ALS'' disappeared. These criteria also raised the diagnostic value of fasciculation potentials (FPs), considered as equivalent to fibrillation potentials or positive sharp waves to illustrate acute denervation, what is essential in terms of clinical practice as FPs often occur earlier [11]. Many studies have illustrated the best sensitivity of Awaji-shima criteria for the diagnosis of ALS in comparison to the revised El Escorial criteria [12–14], especially in cases of bulbar onset ALS [15–17]. Airlie House criteria updated regarding Awaji-shima criteria are available in Table 1.

3. Clinical findings

The time that elapses between the appearance of the first symptoms and diagnosis of ALS may be incredibly long [18]. However, acknowledge of classical clinical ALS presentation should allow to shorten this delay i.e. a – painless weakness in one limb then spreads typically to the contralateral one; b – speech or swallowing problems followed by motor involvement in the limbs; c – progressive muscle stiffness and spasticity with muscle cramps and fasciculations; d – unexplained restrictive respiratory disease with a pattern suggestive of diaphragmatic weakness; e – head drop with upper motor neuron signs [19]. Concerning upper limb motor involvement, split hand syndrome is common corresponding to selective hand intrinsic muscles atrophy in C8-T1 myotomes can be confirmed with a more pronounced reduction of CMAP in *abductor pollicis brevis* and first *interosseous dorsalis* muscles with relative sparing of *adductor digiti minimi* [20]. The split hand syndrome constitutes an early clinical and neurophysiological feature of ALS that can facilitate the diagnosis of ALS but also helps to discriminate it from other

Table 1 – Amyotrophic lateral sclerosis (ALS) criteria according to Airlie House criteria (El Escorial revised criteria) in light of Awaji-shima consensus recommendations [8]. ALS: amyotrophic lateral sclerosis. LMN: lower motor neuron. UMN: upper motor neuron.

ALS diagnosis requires
1 – Presence of evidence of LMN degeneration by clinical, electrophysiological or neuropathological examination
2 – Presence of evidence of UMN degeneration by clinical examination
3 – Presence of progressive spread of symptoms or signs within a region or to other regions, as determined by history, physical examination, or electrophysiological tests
4 – Absence of electrophysiological or pathological evidence of other disease processes that might explain the signs of LMN and/or UMN degeneration
5 – Absence of neuroimaging evidence of other disease processes that might explain the observed clinical and electrophysiological signs
Diagnostic categories
Definite ALS: clinical or electrophysiological evidence by the presence of LMN as well as UMN signs in the bulbar region and at least two spinal regions or the presence of LMN and UMN signs in three spinal regions
Probable ALS: clinical or electrophysiological evidence by LMN and UMN signs in at least two regions with some UMN signs necessarily rostral to (above) the LMN signs
Possible ALS: clinical or electrophysiological signs of UMN and LMN dysfunction in only one region or UMN signs alone in two or more regions or LMN rostral to UMN signs
Neuroimaging and clinical laboratory studies will have been performed and other diagnoses must have been excluded