Clinical neurophysiology in the diagnosis of amyotrophic lateral sclerosis: The Lambert and the El Escorial criteria

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Abstract

For many years, the only published criteria for the electrodiagnostic (EDX) recognition of amyotrophic lateral sclerosis (ALS) were those formulated by Lambert (1957; 1969). In 1990, different EDX guidelines were incorporated in the all-inclusive diagnostic criteria formulated by a subcommittee on ALS of the World Federation of Neurology, which met in El Escorial, Spain. Unfortunately, particularly in regard to the EDX requirements, the ‘El Escorial criteria’ have several flaws which compromise their usefulness. These include: (1) they ignore the fact that whenever upper and lower motor neuron disorders co-exist, as they characteristically do with ALS, the motor unit potential firing pattern is controlled by the upper motor neuron lesion; (2) they markedly devalue the usefulness of detecting fasciculations and, through presumably typographical error, state that the ‘absence’ rather than the ‘presence’ of fasciculations supports the diagnosis of ALS; this view is in direct conflict with the opinions expressed by most electromyographers; (3) they contain a statement regarding how the diagnosis of ALS is confirmed by the EDX studies which is confusing and, for two of the body regions (bulbar; thoracic), unrealistic; (4) finally, many of the EDX features they listed supporting the recognition of possible LMN degeneration appear to be mislabeled, while a few features in the EDX criteria are incorrect. © 1998 Elsevier Science B.V. All rights reserved.

Keywords: Amyotrophic lateral sclerosis; ALS; Motor neuron disease; MND; El Escorial criteria; Lambert criteria; EMG; Electrodiagnosis

The electrodiagnostic (EDX) examination is the premier laboratory procedure for assessing the peripheral neuromuscular system. Serving in this role, it has been used in the evaluation of patients with clinically suspected amyotrophic lateral sclerosis (ALS) for nearly 50 years. During the 1950’s, several publications-including the first book on Electromyography, authored by Marinacci-reported that the EDX examination was a valuable ancillary procedure in the diagnosis of ALS; most of these focused on the fact that fasciculation potentials, and particularly fibrillation potentials, often were widespread with this disorder, frequently being detected in clinically normal limbs [4,18,24,28]. Nonetheless, it was the two publications by Lambert [21,22] that firmly established the utility of the EDX examination in the assessment of patients with ALS, not only to assist in the diagnosis of that disease, but also to exclude other disorders, principally of the peripheral neuromuscular system, that could be confused with it.

In his later publication on the topic, Lambert [20] listed a combination of four EDX findings that he considered highly supportive of the clinical diagnosis of ALS; two of these concerned the nerve conduction studies (NCS), and two the needle electrode examination (NEE) (Table 1). These changes have since been referred to as the ‘Lambert criteria’ for the EDX confirmation of ALS. It is pertinent to note, however, that in both of his publications Lambert [20,21] himself was careful to emphasize the limitations of the EDX examination in this regard. He stressed that the mixture of EDX abnormalities seen with ALS ‘is not

Table 1

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<th>The Lambert criteria for the electrophysiological confirmation of amyotrophic lateral sclerosis*</th>
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<td>1. Normal sensory NCS</td>
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<td>2. Motor NCS CVs that are normal when recording from relatively unaffected muscles and are not less than 70% of the age-based average normal value when recording from severely affected muscles.</td>
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<td>3. Fibrillation and fasciculation potentials in muscles of the upper and lower extremities or in the muscles of the extremities and the head.</td>
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<td>4. MUPs which are reduced in number and increased in duration and amplitude.</td>
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* (MUPs, motor unit potentials; NCS, nerve conduction studies).
pathognomonic’ for it, but may occur with other chronic, diffuse intraspinal canal disorders, as well as with certain chronic polyneuropathies [21].

In 1990, a three-day workshop on the ‘Clinical Limits of ALS’ was held in El Escorial, Spain, by the World Federation of Neurology Subcommittee on Motor Neuron Disease (Amyotrophic Lateral Sclerosis). Its purpose “was to develop diagnostic criteria for ALS which are workable, internationally acceptable, and provide an algorithm which will enhance clinical studies, therapeutic trials, and molecular genetic research studies.” Over the next several months, these were reviewed, amended, and accepted by the participants, as well as by many other individuals and members of organizations concerned with ALS. The ultimate result was an eight-page document describing features considered ‘definite’, ‘probable’, ‘possible’, and ‘inconsistent’ for and with ALS, in regard to the clinical examination, EDX examination, neuroimaging studies, clinical laboratory studies, and neuropathological findings. These criteria were published in 1994 [12].

Presumably, one of the reasons that new EDX criteria were formulated by the El Escorial group was because the Lambert criteria were considered too stringent; as a result, only patients with rather advanced disease were likely to satisfy them. Behnia and Kelly [3], for example, reported that, of 133 patients with clinical ALS they assessed, 50 (38%) did not meet the Lambert criteria, principally because their EDX changes were not sufficiently widespread.

Unfortunately, the EDX portion of the El Escorial criteria contain several flaws, which limit their use by electrodiagnostic physicians. These will be discussed as separate four topics.

1. Of the three electrophysiologic features required to identify ‘definite’ primary lower motor neuron (LMN) degeneration, one is unrealistic and often cannot be met. The features required for the indisputable recognition of denervation in a muscle include not only fibrillation potentials and suggestive chronic motor unit potential (MUP) changes, but also that the MUP firing pattern be indicative of a LMN lesion, i.e. MUPs must be present in reduced numbers “... with firing rates over 10 Hz” [12]. Stipulating that the MUPs fire at faster than their basal firing rate (5–10 Hz) would be reasonable if only a LMN disorder were present. However, ALS, by definition, has an upper motor neuron (UMN), as well as a LMN, component, and UMN pathology manifests as an impairment of motor control. With such “central paresis,” there is not only a reduction in the number of MUPs, because fewer motor units can be recruited, but also a reduction in the firing frequency of those MUPs that can be activated. As a result, with UMN lesions the MUPs fire in reduced numbers, at a slow rate. As Hallett [16] noted two decades ago, the fact that “the maximal firing frequency of motor units is limited (with UMN disease) is not well-documented in the literature, although most electromyographers recognize its validity.” Moreover, when an UMN and a LMN lesion coexist, and both influence the activation of a given muscle, the UMN component dictates the MUP firing pattern. Consequently, in the presence of widespread spasticity, the provision that MUPs fire at ‘rates over 10 Hz’ may not be met during the NEE assessment, even though fibrillation potentials and chronic neurogenic MUP changes are prominent [1,2,6,8,20,25,30,35].

If the MUPs in the muscles assessed in a particular limb cannot fire at greater than their basal firing rate because of superimposed UMN influence, then the El Escorial criteria [12] require that the EDX findings in that limb be classified as ‘probable,’ rather than ‘definite’ evidence of LMN involvement. This downgrading can affect how the entire EDX examination is classified, since definite evidence of LMN involvement is required in at least two of the four body regions (bulbar, cervical, thoracic, and lumbosacral). ‘Probable’ evidence is not conclusive, although two ‘probable’ regions can equal one ‘definite.’ As a result, if fibrillation potentials and chronic neurogenic MUP changes are present diffusely in muscles of all four limbs, but because of marked spasticity the MUPs fire at slow rates throughout, the end result will be only one ‘definite’ body region. Thus, the firing rate requirement for the ‘definite’ category appears quite unrealistic. Ironically, by the Lambert criteria (which presumably were replaced because they were considered too demanding) these findings would, very reasonably, be considered evidence of a widespread LMN disorder, consistent with ALS.

2. Fasciculation potentials are defined incorrectly in the Clinical section, unjustifiably minimized in the EDX section, and the opinions expressed about them in the two sections are inconsistent with one another. Fasciculations clinically are random, spontaneous twitchings of groups of muscle fibers, which may be visible through the intact skin. Fasciculation potentials seen on NEE are the electrical initiators of fasciculations; they have the dimensions of a MUP, occurring spontaneously and usually sporadically [9]. The site of origin of fasciculation potentials has been debated for decades and still remains unclear. Probably most originate along the more distal portion of the motor axon, although some may arise proximally, and the level of origin may change during the course of the disease [10,15,17,27,34].

Fasciculations have been considered a prominent feature of ALS since the latter was first established as a distinct condition by Charcot in 1874 [14,25]. They are mentioned in virtually every clinical publication dealing with ALS. Their clinical significance typically is reported to be as described by Mitsumoto and co-workers [25] in a recently published textbook: “Fasciculations are found in nearly all ALS patients . . . (if they) are not found in a patient who is suspected to have ALS, one must be cautious in the diagnostic process.”

In the Clinical section of the El Escorial criteria [12], fasciculations are listed as one of the features, along with
weakness and wasting, ‘required for the diagnosis of ALS.’ However, they are misidentified as a sign of LMN degeneration. In fact, fasciculations are being generated by intact motor units which may or may not be under voluntary control; consequently they cannot be due to denervation. Rather, they are evidence of motor unit irritation, probably resulting from marked fluctuations in the excitability of the motor neuron soma or its axon [34].

The links between ALS, fasciculation potentials, and the EDX examination extend to a time long before the EDX examination became a recognized diagnostic procedure. Sixty years ago, in a landmark article, Denny-Brown and Pennybacker [7] coined the term “fasciculations” and distinguished them from fibrillation potentials. Many of the electrical potentials they analyzed in their paper were recorded from patients with ALS. This was six years before the publication of the article by Weddell et al. [33], which generally is considered to have introduced NEE into clinical use, and it was 18 years prior to the publications by Lambert [22] and by Simpson [29], which independently initiated sustained interest in the clinical application of NCS.

The fact that fasciculation potentials are regularly seen with ALS was stressed by the early electromyographers [4,18,24,28]. In his later publication, Lambert [20] stated that “The EMG discloses fasciculation so regularly in ALS as to make the diagnosis unless it is demonstrated.”

Despite the views expressed above, and even though fasciculations are easier to detect on NEE than on clinical examination [9,31], in the EDX Section of the El Escorial criteria fasciculation potentials are markedly devalued. They are not included among the ‘required for diagnosis,’ or even the ‘supports probable diagnosis’ categories. Instead, they are relegated to the ‘supports possible diagnosis’ category, and even among this large group they are denigrated, appearing eleventh, and last, on the list. Moreover, due to what one hopes is a typographical error, the phrase reads, ‘11. absence of fasciculations,’ rather than ‘11. presence of fasciculation potentials,’ as it should [12].

Why fasciculation potentials are trivialized in this manner is unclear. Certainly, their being assigned such a minor role among the EDX changes suggestive of ALS receives very little support in the more recent or current literature. With rare exceptions [1,3], every EDX publication on the topic over the past two decades, of which I am aware, has emphasized the value of fasciculation potentials [5,9,11,14,19,23,25,26,30–32,35]. In most of these publications, opinions are expressed similar to those stated by Daube [6] in a review article on the EDX examination with ALS: “Fasciculation potentials are particularly prominent in most patients with ALS and can be an important clue that a patient may have the disease”.

One possible explanation for fasciculation potentials being considered so insignificant in the El Escorial criteria is that they are a non-specific finding, a fact emphasized in most EMG publications. However, fasciculation potentials are not unique in this regard, since virtually all of the EDX findings with ALS are non-specific. In fact, fibrillation potentials, the other type of spontaneous activity crucial for diagnosis, are far more non-specific, being found with disorders of the anterior horn cell, motor axon, neuromuscular junction, muscle fiber, and, according to some reports, the UMN [9]. In contrast, if the ‘myogenic fasciculations’ described by Stalberg and Sanders [31] are excluded, fasciculation potentials actually are rather specific, in that they are at least neurogenic in origin.

When the opinions regarding the value of fasciculation potentials in the diagnosis of ALS that appear in the Clinical section and the EDX section of the El Escorial criteria [12] are compared, it is apparent that the two views are incompatible. The Clinical section declares the presence of fasciculations essentially mandatory for diagnosis, whereas the EDX Section states that their absence supports the diagnosis. Fasciculations obviously have no satisfactory niche in the rigid framework used to formulate the El Escorial criteria. They are neither a sign of an UMN disorder, nor of LMN degeneration; unfortunately, the El Escorial criteria mandate that every abnormality must result from one or the other of these two pathological processes. Nonetheless, fasciculation potentials are seen in nearly all patients with ALS, and their presence narrows the diagnostic possibilities. If these facts are ignored when diagnostic criteria are formulated, the risk of misdiagnosis is increased [35].

3. The statement in the EDX section regarding the findings necessary for the ‘confirmation of the diagnosis of ALS’ is both confusing and, at least for two of the body regions, unrealistic. According to the El Escorial criteria [12], confirming the clinical diagnosis of ALS with the EDX examination “depends on finding electrophysiologic evidence of LMN degeneration in at least two muscles of different root or spinal nerve and different cranial or peripheral nerve innervation in two or more of the four (bulbar, cervical, thoracic, lumbar) regions.” Some components of this sentence are redundant while others are illogical. Thus, ‘root’ and ‘spinal nerve’, as far as the NEE is concerned, have essentially the same meaning, and neither of them is applicable to ‘cranial nerve . . . innervation.’ The sentence, moreover, is extremely complex and, therefore, open to more than one interpretation. However, if it is assumed that the localization approach stated here is similar to that used to diagnose radiculopathies, i.e. abnormalities must be found in two or more muscles innervated by the same root via different peripheral nerves [36] then the ease with which these criteria can be met varies significantly among the four body regions. Most of the cervical and lumbar spinals segments innervate multiple limb muscles, so these requirements pose no difficulty for those two regions. However, a much different situation is encountered for the bulbar and thoracic regions.
Regarding the bulbar region, the tongue technically can be a very trying muscle to examine. Detecting fibrillation potentials in it is often problematic, because relaxation frequently is impossible to achieve, and the MUPs in the normal tongue are very similar, in both their size and configuration, to fibrillation potentials [13,35]. Chronic neurogenic MUP changes (MUPs of increased duration and amplitude) are readily recognized in the tongue, if sufficient relaxation can be obtained to permit assessment of individual MUPs, which is often a most difficult task. Finsterer et al. [13] recently reported demonstrating such MUP configurational changes, as well as MUP firing pattern alterations, in the tongue in a high proportion of ALS patients, especially those with the bulbar form. However their results must be duplicated by others, and the specialized techniques they used currently are not widely employed. Another difficulty concerning this region is that it can be quite difficult to find NEE changes in muscles innervated by more than one cranial nerve, even though the El Escorial criteria require that abnormalities be found in “at least two muscles of... different cranial... nerve innervation”.

Regarding the thoracic region, there also are several problems. For practical purposes, only the thoracic paraspinal and the upper abdominal muscles can be evaluated. The latter are rarely sampled during ALS assessment. The thoracic paraspinal muscles can be technically difficult to examine, since sufficient muscle relaxation often cannot be achieved, and some small MUPs, similar in configuration to fibrillation potentials, may be present and cause confusion. Moreover, because of the cascade innervation present throughout the paraspinal muscles, an abnormality of a single spinal cord segment or root can produce fibrillation potentials throughout a rather extensive longitudinal paraspinal area [36]. Consequently, to find changes “in at least two muscles of... different root... innervation, as the El Escorial criteria [12] mandates, can be problematic. For practical purposes, to meet this requirement fibrillation potentials must be found in two regions of the ipsilateral thoracic paraspinal muscles, separated by a region in which no fibrillation potentials are present. Because of the technical difficulties encountered when assessing the thoracic paraspinal muscles, attempting to accomplish this can be a time consuming, and often frustrating, task.

4. Many of the EDX features listed in the category of “support the identification of possible primary LMN degeneration” appear to be mislabeled. In fact, the majority of items in this category of the El Escorial criteria [12] are more appropriately described as “being not inconsistent with”, rather than “being supportive of”, possible LMN degeneration. The distinction is an important one. Thus, no experienced electrodiagnostic physician would consider polyphasic MUPs, low amplitude MUPs, or low amplitude compound muscle action potentials (CMAPs) alone to be supportive of the diagnosis of ALS; each of these findings would require some definite qualification. Low amplitude CMAPs, for example, would only be accepted if NEE of the recorded muscle demonstrated severe denervation. Certainly, if the NEE showed no abnormalities, or changes more suggestive of a myopathy than a chronic denervating process, a low amplitude CMAP alone would not support the diagnosis of primary LMN degeneration. Thus, without accompanying explanations, most of the listings in this category are best characterized as being not inconsistent with ALS.

5. Finally, a few features contained in the EDX section simply are incorrect. One example of an error in the El Escorial criteria [12] has already been cited: considering fasciculations as being indicative of denervation, as occurs in the Clinical section. Another instance can be found in the EDX section. Under the features listed as being inconsistent with the diagnosis of ALS are motor conduction velocities (CVs) (and) ... H-wave amplitudes which are more than 30% above established normal values [12]. While these EDX changes are inconsistent with the diagnosis of ALS, to my knowledge they are equally inconsistent with the diagnosis of any other type of peripheral neuromuscular disorder. The usual causes for such findings, in fact, are technical error in the performance of the procedure, and the failure to recognize a nerve anomaly, e.g. a spuriously fast median motor forearm CV due to a Martin-Gruber Anastomosis coexisting with a carpal tunnel syndrome [9].

In conclusion, the El Escorial criteria have several flaws which should be rectified. The criteria need to be revised within a less rigid framework, so that fasciculations can be given the emphasis they merit. Moreover, during the revision, each section needs to be carefully scrutinized, with particular attention directed towards clarifying certain confusing statements, and correcting some obvious inaccuracies. [8,11]

References