Electrodiagnostic Testing for the Diagnosis and Management of Amyotrophic Lateral Sclerosis

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KEYWORDS

• Amyotrophic lateral sclerosis • Electrodiagnosis • Motor neuron disease
• Biomarkers • X-linked bulbospinal atrophy

KEY POINTS

- Careful history and physical examinations should guide a thorough diagnostic evaluation, with laboratory and electrodiagnostic studies to exclude the possibility of treatable mimic diseases.
- The Awaji modifications to the El Escorial diagnostic criteria have increased the sensitivity for diagnosis of amyotrophic lateral sclerosis by making electromyography findings of equal importance to clinical examination findings.
- Evidence of subclinical disease by electromyography in clinically normal muscles can foreshadow progression of weakness and relate to poorer prognosis.
- Diaphragmatic denervation on needle electromyography may suggest impaired neuromuscular respiratory function and should trigger evaluation to maximize respiratory management.
- Several electrodiagnostic measures have been proposed as biomarkers to monitor progression and may be useful measures for research or clinical use to assess response to disease-modifying medications.

INTRODUCTION

Amyotrophic lateral sclerosis (ALS) is the most common adult-onset motor neuron disease with an estimated prevalence of approximately 3.9 per 100,000 persons in the United States.[1] Despite the classic presentation of mixed upper and lower motor neuron signs and symptoms, a great deal of phenotypic heterogeneity exists in ALS, which adds to the challenge in establishing a diagnosis.[2–6] Electrodiagnostic testing provides key insight into subclinical aspects of disease in ALS. For this reason,

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it serves an important role in establishing the diagnosis and excluding other competing diagnoses. Although some investigators may limit consideration of electrodiagnostic testing in ALS only to the role of confirming a clinical diagnosis, to stop there may prematurely constrain the full usefulness of this tool. Electrodiagnostic testing may provide useful information to guide management or track disease progression. Mapping the extent of subclinical disease may help to guide the clinician to appropriate supportive interventions. Finally, there is considerable interest in establishing biomarkers to monitor progression of disease over time. Electrodiagnostic biomarkers have the benefit of being more sensitive to change than traditionally used outcome measures and do not require specialized equipment.

This article details the usefulness of electrodiagnostic testing across the disease spectrum in ALS, including to establish a diagnosis, identify common ALS mimic disorders, monitor progression for ongoing management, and predict prognosis. Before delving into specific electrodiagnostic studies for motor neuron disease, a brief review of clinical presentations and differential diagnoses is presented. Emerging applications of electrodiagnostic studies to guide management and assess response to treatment interventions are then presented. We conclude with considerations for clinical practice.

CLINICAL PRESENTATION OF AMYOTROPHIC LATERAL SCLEROSIS

The heterogeneity of clinical presentation in ALS often leads to long delays between the onset of symptoms and a diagnosis, which in turn limits access to disease-modifying medications and investigational therapeutics, as well as supportive interventions that may prolong life expectancy, improve quality of life, or maintain function. Major advances in disease awareness have done little to decrease the diagnostic lag time. A delay of 1 year between symptom onset and diagnosis is still common; 1 study found no evidence of improvement in this metric in Great Britain over a 20-year period despite efforts to fast track evaluations for suspected motor neuron disease.[7]

Initial symptoms of weakness may present in the limbs (~60%), bulbar muscles (~30%), or, more rarely, in the respiratory muscles (~3%). Weakness is generally asymmetric and progresses regionally to adjacent myotomes and body regions; however, some variants of ALS demonstrate prolonged periods of disease isolated to a single body region, for example, in brachial amyotrophy (Hiramaya disease). Bulbar weakness may present as dysphagia or dysarthria. Respiratory weakness is common as the disease progresses; initial symptoms may be subtle and involve orthopnea or sleep-disordered breathing. Although cognition and behavior was once thought to be spared from the disease process in ALS, frontotemporal dementia is now recognized as part of the disease spectrum[8]; symptoms may either precede muscle weakness or manifest with disease progression. Other signs and symptoms frequently associated with ALS are weight loss, fatigue, and musculoskeletal complaints. Although not thought to be a common presenting feature of ALS, pain is reported in about one-half of all patients as a consequence of muscle imbalance and progressive loss of muscle mass and mobility.[9] Common pain complaints include shoulder pain, back and neck pain, and pain related to medical procedures (gastrostomy, tracheostomy tube placement). Neuropathic pain, however, is an uncommonly reported symptom in persons with ALS.

The evaluation of a patient suspected of having ALS begins with a detailed history and physical examination. Cranial nerve function, sensory examination, and cerebellar examinations should be normal. Bladder and bowel function are generally intact. Weakness, atrophy, hypotonia, hyporeflexia, and fasciculations are signs of lower motor neuron pathology. Neck extensor weakness is a manifestation of muscle weakness