# The Electrophysiology of the Motor Neuron Diseases

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**KEYWORDS**

• Amyotrophic lateral sclerosis • Spinal muscular atrophy
• Primary lateral sclerosis • El Escorial criteria
• Progressive muscular atrophy • Multifocal motor neuropathy

Charcot is credited with the first descriptions of amyotrophic lateral sclerosis (ALS) in the 1860s.[1] He named the disease based on the pathologic features of muscle atrophy (amyotrophy) and sclerosis of the cortical spinal tracts (or lateral columns) in the spinal cord. In the early British literature the disease came to be known as *motor neuron disease*, and since that time the two terms are generally considered synonymous. The illness gained particular notoriety in the United States around 1940 when Lou Gehrig, the famous baseball player for the New York Yankees, was diagnosed with and died of the disease. In the United States, the disease soon became widely known in the lay literature eponymously as Lou Gehrig's disease.

Lou Gehrig offers a unique perspective in ALS that is not possible in most other cases. His baseball statistics offer a nearly daily assessment of his physical abilities. In analyzing these, one can observe when his physical decline began. A review of his batting average indicates that in 1939, his last full year of baseball, a steady and continuous decline occurred in his batting average[2]; this was a full year before the onset of his symptoms in 1940. This fact highlights the difficulty facing experimental treatment trials in ALS; the disease is already well established and advanced before presentation, limiting the potential impact of any disease-modifying therapy.

Also interesting historically was Lou Gehrig's participation in a clinical trial studying the effects of vitamin E in the treatment of ALS. Lou Gehrig was a patient of Dr Wechsler's in New York and appears as index case #4 in Wechsler's publication of this clinical trial.[3] In his case description, Wechsler identifies the classic features of ALS, including the upper motor neuron features of spasticity, slowness of movements, and hyperreflexia, and the lower motor neuron features of atrophy, weakness, and fasciculations. The only missing clinical feature from his description is the asymmetric focal onset that is characteristic of the disease.

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Neurol Clin 30 (2012) 605–620
doi:10.1016/j.ncl.2011.12.006 **neurologic.theclinics.com**
0733-8619/12/$ – see front matter 

Over time, the motor neuron syndromes have been further classified into ALS and other much less common forms, including primary lateral sclerosis (PLS), progressive muscular atrophy (PMA), spinal muscular atrophy (SMA), and X-linked spinobulbar atrophy (SBMA; also known by its eponym, Kennedy disease). The clinical features of each are reviewed in **Table 1**. The clinical syndrome of ALS is characteristic. The role of nerve conduction studies and needle electromyography (collectively referred to as *EMG*) is often straightforward. The objective of EMG is to confirm the clinical suspicion while excluding certain mimic syndromes. As with other ancillary tests, no pathognomonic findings are seen on EMG, but in the proper clinical context it can be diagnostic. Because of its ability to investigate alternative etiologies and provide supportive evidence, EMG is the single most important ancillary testing in evaluating ALS.

## SUMMARY

1. Motor neuron disorders can be separated into ALS, PLS, PMA, SMA, and SBMA. Each has a unique phenotype and prognosis.
2. Motor neuron disease and ALS are considered synonymous terms.

## *ALS*

ALS is the most common of all the motor neuron disorders. Pathologically it can be distinguished by the gliosis and neuronal loss within the motor cortex and the anterior horns of the spinal cord. More recently, pathologic aggregation of the proteins TAR DNA-binding protein 43 (TDP-43) and ubiquilin 2 has been identified in most sporadic cases of ALS.[4,5] This pathology is indistinguishable from that of ubiquitin-positive frontotemporal dementia (u-FTD), raising suspicion that these two disorders may represent separate phenotypes of a common underlying cause.

The incidence of ALS is 1.5 to 2.0 cases per 100,000 population per year.[6] The incidence rate increases with age up to approximately 80 years, followed by a sharp decline in the most senior years. The median survival from diagnosis is approximately 18 months. Age of onset is the most significant prognostic variable.[6] Patients who are younger when diagnosed have a better long-term survival than those who are older. A minority (5%–10%) of cases will live beyond 5 years after diagnosis. The only treatment currently approved by the U.S. Food and Drug Administration (FDA) is riluzole. Two randomized controlled studies showed a dose-dependent mean survival benefit

**Table 1**
**Clinical features of the motor neuron disorders**

| | Onset | Bulbar Involvement | Fasciculations | Lower Motor Neuron Features | Upper Motor Neuron Features |
|---|---|---|---|---|---|
| ALS | Asymmetric and focal | Prominent | Prominent | Prominent | Prominent |
| PMA | Asymmetric and focal | Less prominent | Prominent | Prominent | Absent |
| PLS | Symmetrically usually in lower limbs | Prominent in later stages | None | Absent | Prominent |
| SMA | Symmetrically in proximal limbs | Less prominent | Variable | Prominent | Absent |
| SBMA | Symmetrically in proximal limbs | Prominent | Very prominent | Prominent | Absent |