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F wave study in amyotrophic lateral sclerosis: Assessment of balance between upper and lower motor neuron involvement

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Abstract

Objective: We sought to record significant F wave variable changes in ALS patients having no advanced disease. Furthermore, an interpretation of these F wave abnormalities in the context of upper (UMN) and lower motor neuron (LMN) dysfunction was attempted.

Methods: Standard motor and sensory conduction study was performed to the ulnar nerves of 23 patients with ALS (13 males and 10 females with mean age 67.2 ± 5.3 years), having a clinically predominant LMN syndrome. A series of 40 electrical stimuli were also delivered to both their ulnar nerves in order to obtain F waves. The following F wave variables were estimated: F persistence, F wave latency, amplitude, duration and F chronodispersion. Twenty-three, age-and gender-matched healthy volunteers served as controls.

Results: Both the distal and proximal ulnar a-CMAPs ($P = 0.001$) and the MCV ($P = 0.014$) values were significantly decreased in patients, than the controls. The sensory conduction study was normal. The ulnar F wave persistence in the ALS patients was significantly lower than that of the controls ($P = 0.0007$). The mean ($P = 0.0001$), minimal ($P = 0.0001$) and maximal ($P = 0.0001$) F wave latencies were significantly prolonged, the F wave amplitudes ($P = 0.0001$) were significantly higher and the F wave chronodispersion ($P = 0.014$) was significantly increased in the patients than the controls.

Conclusions: Significant F wave abnormalities occur in patients with ALS, even those patients having no advanced disease. Increased F wave amplitudes combined with low persistence is a pattern consistent with ALS.

Significance: Our results show that patients with ALS having predominantly LMN involvement also have electrophysiological UMN dysfunction.

Keywords: ALS; Upper motor neuron; Lower motor neuron; Nerve conduction; F waves

1. Introduction

Amyotrophic lateral sclerosis (ALS) is a progressive degenerative disorder of the motor system that affects both upper motor neurons (UMN) and lower motor neurons (LMN) in various combinations (Rowland, 1991). The reportedly annual incidence rates of the disease vary from 0.5 to 2.6 per 100,000 population (Argyriou et al., 2005; Bracco et al., 1979; Koerner, 1952).

Muscle weakness and wasting are the two main clinical characteristics of ALS, and these are generally considered to be apparent as a result of LMN loss (Kelly et al., 1990). Signs and symptoms of LMN damage can be relatively easy disclosed by clinical examination, whereas electrodiagnostic studies, including sensory and motor nerve conduction studies, repetitive motor nerve stimulation and needle electromyography (EMG), are expected to confirm the diagnosis.

Although sensory action potentials abnormalities have been previously reported (Shefner et al., 1992), it is widely accepted that sensory conduction parameters are within normal limits in ALS, even in proximal segments (Ertekin, 1967). As concerning the motor conduction studies, several abnormalities have been recognized in ALS patients. The amplitude and area of compound muscle action potentials may be decreased (de Carvalho and Swash, 2000), whereas increased distal motor latencies have been commonly

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reported (Mills and Nithi, 1998). Motor conduction velocity is usually normal in ALS (Cornblath et al., 1992), with the exception of advanced disease, where mild to moderate slowing of velocities may occur (Iijima et al., 1991).

Among other tests that have been used for the assessment of the motor neuron pool integrity, F waves have been also proposed as indicators of UMN dysfunction (Lin and Floeter, 2004). There are several inconsistent reports of F wave abnormalities in ALS patients, including increased F wave latencies and amplitudes with normal F wave frequencies (Fisher, 1992; Milanov, 1992) and slowing of F wave velocities with decreased F wave frequency (Chroni et al., 1996).

The current study aimed to record significant F wave variable changes in ALS patients having no advanced disease. Furthermore, an interpretation of these F wave abnormalities in the context of upper and lower motor neurons dysfunction was attempted.

2. Patients and methods

2.1. Patients selection

Twenty-three patients, 13 males and 10 females with mean age 67.2 ± 5.3 years (range 58–75) and mean height 168.4 ± 4.8 cm, diagnosed as having definite or probable ALS, were studied. Recruitment of patients and overall electrophysiological tests were made at their first admission to our Department for establishment of a diagnosis. The diagnosis of ALS was based on the El Escorial criteria (1994), requiring clinical findings of a progressive pure motor disorder with muscle weakness, atrophy, fasciculation and pyramidal signs in the absence of sensory defects and sphincter disturbances.

At the time of investigation, the disease duration from first symptom ranged between 3 and 32 months (mean 14.1 ± 9.2 months). Clinical examination revealed muscle weakness, which was restricted on one side in 8 patients, whilst in the remaining 15 patients included all limbs. UMN involvement in the upper limbs was suggested by the presence of clonus, increased tone, increased tendon reflexes and positive Hoffman signs. The strength of the examined muscles was estimated by manual muscle testing, using the MRC scale.

Other conditions with analogous manifestations, i.e. cervical myelopathy, pseudobulbar palsy of vascular origin, etc. were excluded by means of appropriate laboratory and neuroimaging investigations. Patients with diabetes mellitus, alcohol abuse and other systemic or neurological diseases were excluded from the study. Patients with severely atrophied muscles, resulting in unobtainable M or F responses, were also excluded. At the time of investigation, none of the patients were taking riluzole or antispasticity drugs.

2.2. Nerve conduction studies

Routine nerve conduction study including motor conduction of the median, ulnar and peroneal nerves and sensory conduction study of the ulnar and sural nerves were performed to support the diagnosis of ALS. Particular emphasis was paid to exclude the possibility of conduction block by applying proximal stimulation of the median and ulnar nerves in the axilla and Erbs' point and by comparing the amplitude of the CMAP response between different stimulus sites. Concentric needle EMG studies were also performed in at least 4 muscles in order to evaluate spontaneous activity and motor unit recruitment.

For the purposes of the study, the investigation was focused around ulnar nerve function. The ulnar nerve was preferred over the median, because carpal tunnel syndrome, which is a common condition, would confuse the results. A Keypoint, Medtronic-Dantec (Medtronic-Dantec Electronics, Skovlunde, Denmark) electromyographic unit performed the electrophysiological studies. All subjects were examined reclining on a couch with the arm in a supine position. Complete relaxation of the examined limb was ensured by audio feed-back and the skin temperature of the examined limb has been maintained between 32 and 34 °C. Both ulnar nerves were studied in each patient ($n = 23$, nerves = 46), employing standard methods and the widely accepted criteria for comparison of parameters were used (Kimura, 2001). Ulnar nerves were stimulated at the wrist and the elicited compound muscle action potential (CMAP) was recorded with surface electrodes over abductor digiti minimi (ADM) muscles. A belly-tendon, silver electrode, surface montage was used to record ADM responses. The ulnar nerve was stimulated at the wrist, 6–7 cm from the proximal active recording electrode (G1) on the ADM, using supramaximal surface stimulation. The same distance between stimulator and G1 was kept in all recordings. Ulnar motor conduction parameters included measurements of peak to baseline amplitude of compound muscle action potential (a-CMAP), distal motor latency (DML) and motor conduction velocity (MCV).

Sensory conduction of ulnar (orthodromic technique) nerves with measurements of peak-to-peak amplitude of sensory action potentials (a-SAP) and sensory conduction velocities (SCV), were also recorded. Concentric needle EMG studies were additionally performed in ADM muscles.

2.3. F wave studies

Forty consecutive supramaximal stimuli were delivered to both ulnar nerves of patients with a frequency of 1 Hz and the obtained F waves were stored for subsequent analysis. Acquisition conditions included a filter setting of 2 Hz to 10 kHz, a sweep speed of 10 ms per division and an amplifier gain of 0.1–0.5 mV per division for the F waves, and 0.5–5 mV for the CMAP.