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Focal nerve enlargement is not the cause for increased distal motor latency in ALS: Sonographic evaluation

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HIGHLIGHTS

- Focal conduction slowing at the median nerve at the wrist in ALS has been frequently reported, but its etiology has been elusive.
- Sonography of the median nerve showed lack of swelling of the median nerve at the wrist in ALS despite of focal conduction slowing.
- The mechanism of selective focal conduction dysfunction in ALS is unlikely to be compressive or demyelinative, rather might be related to preferential involvement of the distal portion of the median nerve.

ABSTRACT

Objective: To elucidate the mechanism of focal conduction slowing in the median nerve in ALS.
Methods: The patients with ALS and CTS and normal control subjects were tested with sonography of the median and ulnar nerves. The cross-sectional areas (CSAs) and the wrist–forearm CSA ratios were compared with the parameters of nerve conduction study.
Results: The median motor distal latency was frequently prolonged in ALS and CTS. CSA and the wrist–forearm ratio of the median nerve were smaller in ALS than in CTS. The ulnar nerve sonography was similar in all the groups.
Conclusions: Selective conduction slowing of the median nerve at the wrist in ALS is unlikely due to secondary compressive neuropathy, as seen in carpal tunnel syndrome.
Significance: Unique vulnerability of the median nerve in ALS may explain the selective conduction slowing.

1. Introduction

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease. Although the primary pathogenesis of ALS is motor neuron death and axonal degeneration, previous neurophysiological studies have indicated complex phenomenon suggesting superimposed "demyelinating features" such as a prolonged distal latency by motor conduction study. Previous studies have suggested that the median nerve at the wrist is prone to focal neuro-conductive dysfunction, as evidenced by prolonged distal latency by nerve conduction study (Kollewe et al., 2011; Kothari et al., 1996; Mohammadi et al., 2007). The etiology for selective prolongation has been elusive. Regardless of the presumptive etiology, because the distal motor latency tends to increase proportionally to axon loss and muscle wasting, the distal latency has been incorporated in a neurophysiological index to measure disease

Abbreviations: ADM, abductor digiti minimi; ALS, amyotrophic lateral sclerosis; APB, abductor pollicis brevis; BMI, body mass index; CMAP, compound muscle action potential; CSA, cross-sectional area; DL, distal latency; FDI, first dorsal interosseous; WF ratio, wrist–forearm ratio.

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progression in ALS (de Carvalho and Swash, 2000; Swash and de Carvalho, 2004).

The recent advent of sonography of a peripheral nerve has shed light on the pathophysiology of peripheral nerve diseases and ALS (Cartwright and Walker, 2013; Cartwright et al., 2011; Nodera et al., 2014). Furthermore, compressive neuropathy such as CTS is sensitively diagnosed by sonography (Cartwright and Walker, 2013; Tai et al., 2012). Thus, our aim was to depict the electrophysiologic and sonographic characteristics of the median nerve at the wrist that could elucidate the pathophysiology of ALS.

2. Methods

2.1. Inclusion criteria of the subjects

The following three groups were recruited and prospectively assessed: (1) ALS: the patients who fulfilled the criteria for definite or probable ALS according to the revised El Escorial ALS criteria (Brooks et al., 2000) combined with the Awaji electrodiagnostic criteria (de Carvalho et al., 2008). (2) CTS: patients who were otherwise healthy but had typical sensory symptoms (a combination of at least two of the following: nocturnal or work-related paresthesias in the median distribution, positive Tinel sign, positive Phalen sign) and met the diagnostic criteria (Keith et al., 2009). (3) Controls: asymptomatic persons who had no neurological symptom or sign. Specifically, an individual who reported symptoms suggesting cervical radiculopathy (e.g., neck pain, radicular pain, a history of whiplash injury), carpal tunnel syndrome (e.g., hand pain/paresthesia, nocturnal exacerbation, use-related exacerbation) and ulnar neuropathy (e.g., hand pain/paresthesia, elbow injury, elbow pain) were excluded. The study was approved by the Institutional Review Board of Vihara Hananosato Hospital and Tokushima University. The subjects gave written informed consent at the time of the testing.

2.2. Nerve conduction study

Compound motor action potential (CMAP) was recorded at the median and ulnar nerve using conventional techniques using Viking Quest (Natus, San Carlos, CA) (Kimura, 2013). Specifically, the wrist stimulation was performed at 2 cm proximal to the wrist crease for the median and ulnar nerves, therefore the distances between the stimulating and recording electrodes were not uniform because of variable body size. Terminal latency index for the median motor study was calculated as distal conduction distance (mm)/(conduction velocity [m/s] × distal motor latency [ms] (Cocito et al., 2001; Simovic and Weinberg, 1997).

2.3. Sonography

The sonographic examinations were performed using LOGIQ7 (GE) with an 11-MHz linear-array transducer. A single technician (N.T.) who was blinded to the diagnosis performed the sonography. The participants were tested in the supine position with the arm supinated and abducted at body level. The cross-sectional area (CSA) were measured by tracing the nerve just inside the hyperechoic rim, corresponding to the epineurium (Sugimoto et al., 2013b).

The right median and ulnar nerves were imaged at the wrist, 2 cm proximal to the wrist crease and in the mid–forearm. The room temperature was maintained at 23–25 degrees Centigrade. The skin temperature at the forearm and the hand was measured and maintained >32 degrees Centigrade by covering a blanket. The wrist–forearm ratio (WF ratio) in each nerve was determined by dividing the CSA at the wrist by the CSA at the forearm.

2.4. Data analysis

SPSS version 20.0J (Tokyo, Japan) was used for statistical analysis, using Welch's test, One-way ANOVA with Games–Howell post hoc test, Fisher's exact test, Chi-square test, and Spearman's correlation coefficient where applicable. A statistically significant P value was set at 0.05.

3. Results

The characteristics of the subjects are summarized in Table 1, showing no significant difference of the gender, age, height, weight, and body mass index among the three groups. The distances between the cathode and the recording electrode were similar between the ALS and CTS patients in the median and ulnar nerve, respectively (median nerve: 7.3 ± 0.3 (ALS), 7.2 ± 0.3 (CTS); $P = 0.3$/ulnar nerve: 6.8 ± 0.2 (ALS), 6.9 ± 0.3 (CTS); $P = 0.3$). Nerve conduction study in the ALS and CTS patients showed reduced median CMAP amplitudes and prolonged median DL. Of note, the median DL was frequently prolonged in both groups (62% in ALS and 100% in CTS), while the conduction velocity of the median nerve in the forearm segment was normal in the majority of the

Table 1
Characteristics of the subjects and the nerve conduction study.

	ALS	CTS	Control	P values
Number (man: woman)	21 (17:4)	14 (8:6)	30 (20:10)	0.2 (Chi square)
Age (years)	68.3 ± 9.1	63.9 ± 16.8	61.8 ± 18.1	0.4 (ANOVA)
Height (cm)	159.9 ± 9.9	158.5 ± 6.2	161.9 ± 9.7	0.6 (ANOVA)
Weight (kg)	53.4 ± 11.2	60.3 ± 10.1	59.7 ± 11.2	0.1 (ANOVA)
Body mass index (BMI)	20.9 ± 4.2	24.0 ± 4.2	22.6 ± 3.0	0.07 (ANOVA)
Median CMAP amplitude (mV)	2.8 ± 4.0	2.7 ± 2.9	N/A	0.6
(% abnormal)	81%	73%		0.9
Median distal latency (ms)	4.7 ± 1.1	7.0 ± 2.9	N/A	0.02
(% abnormal)	62%	100%		0.01
Median forearm CV (m/s)	53.9 ± 6.9	47.2 ± 7.0	N/A	<0.01
(% abnormal)	23%	50%		0.15
Terminal latency index (normal: 0.39–0.41)*	0.29 ± 0.06	0.23 ± 0.06	N/A	0.02
Ulnar CMAP amplitude (mV)	4.7 ± 2.2	7.0 ± 1.1	N/A	<0.01
(% abnormal)	70%	14%		<0.01
Ulnar distal latency (ms)	3.1 ± 0.6	3.2 ± 0.6	N/A	0.9
(% abnormal)	15%	28%		0.4
Ulnar forearm CV (m/s)	56.6 ± 4.7	54.5 ± 5.0	N/A	0.2
(% abnormal)	5%	14%		0.6

* The reference range of the terminal latency index was obtained from 76 healthy control subjects (Cocito et al., 2001).