Original Article

Pattern Differences of Small Hand Muscle Atrophy in Amyotrophic Lateral Sclerosis and Mimic Disorders

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Abstract

Background: Amyotrophic lateral sclerosis (ALS) and some mimic disorders, such as distal-type cervical spondylotic amyotrophy (CSA), Hirayama disease (HD), and spinobulbar muscular atrophy (SBMA) may present with intrinsic hand muscle atrophy. This study aimed to investigate different patterns of small hand muscle involvement in ALS and some mimic disorders.

Methods: We compared the abductor digiti minimi/abductor pollicis brevis (ADM/APB) compound muscle action potential (CMAP) ratios between 200 ALS patients, 95 patients with distal-type CSA, 88 HD patients, 43 SBMA patients, and 150 normal controls.

Results: The ADM/APB CMAP amplitude ratio was significantly higher in the ALS patients ($P < 0.001$) than that in the normal controls. The ADM/APB CMAP amplitude ratio was significantly reduced in the patients with distal-type CSA ($P < 0.001$) and the HD patients ($P < 0.001$) compared with that in the normal controls. The patients with distal-type CSA had significantly lower APB CMAP amplitude than the HD patients ($P = 0.004$). The ADM/APB CMAP amplitude ratio was significantly lower in the HD patients ($P < 0.001$) than that in the patients with distal-type CSA. The ADM/APB CMAP amplitude ratio of the SBMA patients was similar to that of the normal controls ($P = 0.862$). An absent APB CMAP and an abnormally high ADM/APB CMAP amplitude ratio (≥4.5) were observed exclusively in the ALS patients.

Conclusions: The different patterns of small hand muscle atrophy between the ALS patients and the patients with mimic disorders presumably reflect distinct pathophysiological mechanisms underlying different disorders, and may aid in distinguishing between ALS and mimic disorders.

Key words: Amyotrophic Lateral Sclerosis; Cervical Spondylotic Amyotrophy; Hirayama Disease; Spinobulbar Muscular Atrophy; Split Hand

Introduction

Amyotrophic lateral sclerosis (ALS) is a relentlessly progressive devastating disorder characterized by degeneration of both upper and lower motor neurons. The median lifespan of ALS patients is 2–4 years from symptom onset.[1] Generally, ALS is observed in middle-aged or older patients, as are cervical spondylosis and spinobulbar muscular atrophy (SBMA). The simultaneous combination of upper motor neuron and lower motor neuron dysfunction in clinical manifestation strongly suggests the clinical diagnosis of ALS.[2] However, early in the course of ALS, the clinical manifestations may be atypical, and muscle weakness and atrophy may be limited to the small hand muscles of ALS patients. Clinically, it is important to distinguish ALS patients from patients with ALS mimic disorders, such as distal-type cervical spondylotic amyotrophy (CSA), Hirayama disease (HD), and SBMA because their prognosis and treatment differ.

CSA is characterized by severe muscle atrophy in the upper extremities with no or insignificant sensory deficits and lower extremity symptoms.[3,4] CSA can be grouped into a proximal type, a distal-type, and a combined type, depending on the most predominantly affected muscle groups.[5] The

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responsible lesion for CSA is in the anterior horn at the C5–C6 cord level for proximal-type CSA, and at the C7–T1 cord level for distal-type CSA.[3] Patients with distal-type CSA, whose muscle atrophy was pronounced in the intrinsic hand muscles, were investigated in the present study. CSA follows a self-limited course, the symptoms of which usually stabilize for years. HD, also known as juvenile muscular atrophy of the distal upper extremity, is characterized by slowly progressive distal amyotrophy of the forearm ulnar muscles.[6] HD mainly affects males early in their lives, and the progression of amyotrophy in HD usually arrests within a few years. Notably, electromyographic studies have revealed diffused subclinical neurogenic changes in some HD patients.[7] SBMA is an X-linked lower motor neuron disease characterized by slowly progressive weakness and atrophy of the bulbar, facial, and limb muscles.[8] Many patients also have symptoms of androgen insufficiency, such as testicular atrophy, gynecomastia, and feminized skin changes.[9] The average life expectancy of patients with SBMA is 15–20 years after symptom onset. It is difficult to discriminate between SBMA and ALS, particularly when patients lack the classic signs for these diseases.[10]

Motoneuron loss can be demonstrated by neurophysiological measures including compound muscle action potential (CMAP) amplitudes, motor unit estimates, and motor unit number indices.[11] What is more, the CMAP amplitude and CMAP amplitude ratio can be obtained via a simple neurophysiological technique that is performed routinely for the diagnosis of ALS. Therefore, in the present study, we evaluated the findings of motor nerve conduction studies of the upper limbs in ALS patients, patients with distal-type CSA, HD patients, and SBMA patients, to investigate the pattern differences of small hand muscle involvement in these similar disorders and find some clues to differentiate between them.

Methods

Participants

We performed a retrospective chart review of 200 ALS patients, 95 patients with distal-type CSA, 88 HD patients, and 43 SBMA patients, who were diagnosed between 2010 and 2015, to collect demographic, clinical, and electromyographic data. The ALS patients were diagnosed as definite, probable, or probable laboratory-supported ALS according to the revised El Escorial criteria.[12] All the ALS patients were classified into bulbar-, upper limb-, and lower limb-onset ALS according to the site of disease onset. One hundred and fifty healthy volunteers recruited from faculty members served as normal controls. All the patients with ALS, distal-type CSA, HD, or SBMA in this study presented with focal small hand muscle atrophy at the examination.

The diagnostic criteria for distal-type CSA included: (1) the presence of cervical spondylosis; (2) the presence of weakness and atrophy in the intrinsic hand and/or finger extension muscles; (3) absence of gait disturbance; (4) absence of bladder or bowel dysfunction; and (5) the presence of a compressive lesion in the anterior horn of the spinal cord, in the nerve root at the intervertebral foramen, or in both sites as seen on the axial and sagittal images of magnetic resonance imaging or computed tomography myelography.[13] The responsible lesion for distal-type CSA is in the anterior horn at C7–T1.[3]

The diagnostic criteria for HD were as follows: (1) onset before 25 years of age; (2) either unilateral or bilateral muscle weakness and atrophy of the hand and forearm; (3) arrest of the disease course after insidious progression; (4) no involvement of lower extremities; and (5) exclusion of other mimic diseases.[6] Genetic testing was performed in the 43 SBMA patients in the present study, all of whom were found to be positive for the defining triplet repeat (the number of CAGs in the androgen receptor gene more than 40).[14] The disease onset of the SBMA patients was defined as when sensory or motor signs or symptoms began, including progressive muscle weakness and atrophy, significant fasciculation, paresthesia, or dysesthesia. For the patients exhibiting muscle atrophy in both upper limbs, only nerve conduction data from the clinically more affected hand were analyzed in the study. For the normal controls, nerve conduction data from the left upper limb were analyzed. Participants with coincidental carpal tunnel syndrome or cubital tunnel syndrome, diabetes mellitus, alcohol abuse, and other systemic or neurological diseases were excluded from the present study.

Nerve conduction study

Nerve conduction studies were performed by conventional procedures using a Viking IV Electromyography System (Nicolet Biomedical, Madison, WI, USA). The upper limb temperature of the participants under examination was maintained at >32°C. Filters were set between 20 Hz and 10 kHz. For motor nerve conduction study, the median and ulnar nerves were stimulated electrically at the wrist. A surface electrode was positioned over the belly of abductor pollicis brevis (APB) and abductor digiti minimi (ADM), respectively as the recording electrode. The reference electrode was positioned over the first or fifth metacarpophalangeal joint, respectively.

The peak-to-peak CMAP amplitudes, ADM/APB CMAP amplitude ratios, and CMAP amplitude differences of APB–ADM were measured.[15,16] The research protocol was approved by the local research ethics committee and adhered to the principles of *Declaration of Helsinki*, and informed consent was not required as this was a retrospective chart review.

Statistical analysis

The Kolmogorov–Smirnov test was used to assess the normality of data. The Levene test was used to test the homogeneity of variance between different groups. If the data were normally distributed, a univariate analysis of variance (ANOVA) was performed for three-group comparisons with a *post hoc* Newman–Keuls test. If data were not normally

distributed, multiple comparisons between different groups were performed via the Kruskal–Wallis *H* test with a *post hoc* Mann − Whitney *U* test. The significance level was adjusted using Bonferroni adjustment for multiple comparisons. Regression analyses were performed using the Spearman's rank correlation test. A $P < 0.05$ was set as statistically significant. Results are expressed as mean ± standard deviation (SD) for parametric data and median (interquartile range) for nonparametric data. Statistical analyses were performed using SPSS 21.0 (SPSS Inc., Chicago, IL, USA) for Windows.

Results

The demographics of the participants are summarized in Table 1. The age at disease onset was the lowest in the HD patients. The disease duration before electromyographic examination was the shortest in the ALS patients compared with those in the other disease groups.

Table 2 shows the results of motor nerve conduction studies. Figure 1 shows the distribution of absolute CMAP amplitudes of the APB and the ADM as well as the ADM/APB CMAP amplitude ratios of the ALS patients, the HD patients, the SBMA patients, the patients with distal-type CSA, and the normal controls. Figure 2 shows the typical examples of CMAP responses recorded from the APB and ADM of an ALS patient (a), a patient with distal-type CSA (b), a patient with HD (c), a patient with SBMA (d), and a normal participant (e). In the normal participants, the APB and the ADM CMAP amplitudes were similar; hence, the mean ADM/APB CMAP amplitude ratio was nearly 1 and the mean APB–ADM CMAP amplitude difference was nearly zero. When these data were plotted against the participants' ages, absolute CMAP amplitudes declined with age; there were weak inverse relationships between age and absolute CMAP amplitude of the APB ($r = -0.256$, $P = 0.002$) and the ADM ($r = -0.165$, $P = 0.044$). However, there was no significant correlation between age and the ADM/APB CMAP amplitude ratio ($r = 0.090$, $P = 0.276$). No significant correlation was detected between age and the APB–ADM CMAP amplitude differences as well ($r = -0.114$, $P = 0.164$).

For the ALS patients, an abnormally low APB CMAP amplitude (<6.0 mV) was found in 167 (83.50%) patients, and an abnormally low ADM CMAP amplitude (<5.5 mV) was identified in 100 (50.00%) patients. Three ALS patients with absent APB CMAP were excluded from the CMAP amplitude and CMAP amplitude ratio analyses. In the ALS patients, there was no significant relationship between disease duration and the ADM/APB CMAP amplitude ratios ($r = 0.123$, $P = 0.086$) or the APB–ADM CMAP amplitude differences ($r = -0.031$, $P = 0.667$), which indicated that dissociated small hand muscle involvement may occur at an early stage of ALS. The CMAP amplitude of the APB in the patients with distal-type CSA was significantly lower than that of the HD patients ($t = 0.792$, $P = 0.004$), while the ADM in the patients with distal-type CSA and the HD patients were affected similarly ($t = -1.019$, $P = 0.379$). The mean ADM/APB CMAP amplitude ratio in the HD patients ($z = 3.511$, $P < 0.001$) was significantly reduced, and the mean APB–ADM CMAP amplitude difference in the HD

Table 1: Demographics of participants in this study

Characteristics	ALS	CSA	HD	SBMA	NC
Number of subjects	200	95	88	43	150
Gender (male:female), *n*	133:67	64:31	86:2*,‡	43:0*,‡	98:52
Age at examination (years), mean ± SD (range)	52.8 ± 11.4 (22−77)	54.9 ± 9.7 (267−797)†	21.0 ± 5.0 (13−49)*,‡	48.0 ± 18.0 (35−69)	50.9 ± 12.8 (20−83)
Disease duration (years), mean ± SD (range)	1.0 ± 0.8 (0.2−5.0)	1.0 ± 3.3 (0.1−11.0)§	3.0 ± 4.0 (0.3−30.0)‡	7.0 ± 5.0 (0.5−20.0)‡	NA

*P<0.001, †P<0.010 compared with the normal controls; ‡P<0.001, §P<0.050 compared with the ALS patients. ALS: Amyotrophic lateral sclerosis; CSA: Cervical spondylotic amyotrophy; HD: Hirayama disease; NA: Not applicable; NC: Normal controls; SBMA: Spinobulbar muscular atrophy; SD: Standard deviation.

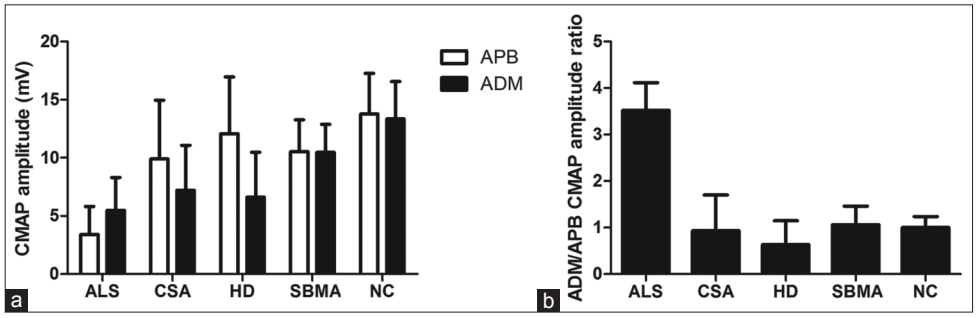

Figure 1: Absolute compound muscle action potential amplitudes of the abductor pollicis brevis and the abductor digiti minimi (a), as well as the abductor digiti minimi/abductor pollicis brevis compound muscle action potential amplitude ratios (b) in the patients with amyotrophic lateral sclerosis, the patients with distal-type cervical spondylotic amyotrophy, the patients with Hirayama disease , the patients with spinobulbar muscular atrophy, and the normal controls. Error bars indicate standard deviation.

patients ($t = -3.798$, $P < 0.001$) was significantly increased, compared with those in the patients with distal-type CSA. For the SBMA patients, an abnormally low APB CMAP amplitude was identified in 2 (4.65%) patients, and no patients presented with an abnormally low ADM CMAP amplitude.

Table 3 shows the results of ADM/APB CMAP amplitude ratios in the ALS patients, the patients with distal-type-CSA, the HD patients, the SBMA patients, and the normal controls. An ADM/APB CMAP amplitude ratio that was <0.6 or >1.7 was considered as abnormal.[15,17] A value of ADM/APB CMAP amplitude ratio >1.7 was considered to be evidence of the split hand sign.[15] The split hand sign was observed in 53.78% of the ALS patients (including the patients with absent APB CMAP). An abnormally low ADM/APB CMAP amplitude ratio (<0.6) was observed predominantly in the HD patients and the patients with distal-type CSA. The ADM/APB CMAP amplitude ratio was in the normal range in 93.02% of the SBMA patients. An extremely high ADM/APB CMAP amplitude ratio (≥4.5) and an absent APB CMAP were observed exclusively in the ALS patients. Using a cut-off value of ADM/APB CMAP amplitude ratio >1.7 or an absent APB CMAP for diagnosing ALS yielded 51% sensitivity and 99% specificity versus the normal controls [Figure 3a], and 91% specificity versus the patients with ALS mimic disorders [Figure 3b]. Notably, an extremely high ADM/APB CMAP amplitude ratio (≥4.5) or an absent APB CMAP was observed exclusively in the ALS patients.

Table 2: CMAP amplitudes of APB and ADM, ADM/APB CMAP amplitude ratios, and APB–ADM CMAP amplitude differences

Groups	APB (mV)	ADM (mV)	ADM/APB ratios	APB–ADM (mV)
ALS	3.20 (3.96)*	5.40 (4.08)*	1.75 (2.24)*	–2.10 (3.70)*
CSA	10.20 (6.50)*†	7.50 (5.80)*†	0.77 (0.49)*†	1.80 (5.90)*†
HD	12.30 (6.50)†	6.80 (6.40)*	0.56 (0.43)*†	5.15 (6.03)*†
SBMA	10.30 (3.20)*†	10.50 (3.10)*†	0.98 (0.39)†	0.20 (4.10)†
NC	13.68 (5.25)†	12.90 (4.63)†	0.98 (0.30)†	0.40 (4.05)†

*P<0.001, compared with the normal controls; †P<0.001, compared with the ALS patients. The data are expressed as mean ± SD, or median (interquartile range). ADM: Abductor digiti minimi; APB: Abductor pollicis brevis; ALS: Amyotrophic lateral sclerosis; CMAP: Compound muscle action potential; CSA: Cervical spondylotic amyotrophy; HD: Hirayama disease; NC: Normal controls; SBMA: Spinobulbar muscular atrophy; SD: Standard deviation.

The distributions of the ADM/APB CMAP amplitude ratios in the patients with upper limb-, lower limb-, and bulbar-onset ALS, and the normal controls are shown in Figure 4. In our study, the disease was of bulbar-onset in 58 (29.00%) ALS patients, upper limb-onset in 130 (65.00%) ALS patients, and lower limb-onset in 32 (16.00%) ALS patients. The significantly increased ADM/APB CMAP amplitude ratio was a uniform finding across the ALS patients, with different regions of disease onset compared with that in the normal controls. Subgroup analysis disclosed that the ADM/APB CMAP amplitude ratios were comparable between the ALS patients with different sites of disease onset.

Discussion

The preferential wasting of the thenar complex, including the APB and the first dorsal interosseous (FDI), along with the relative preservation of the ADM, appears to be specific to ALS. This pattern of dissociated atrophy of intrinsic hand

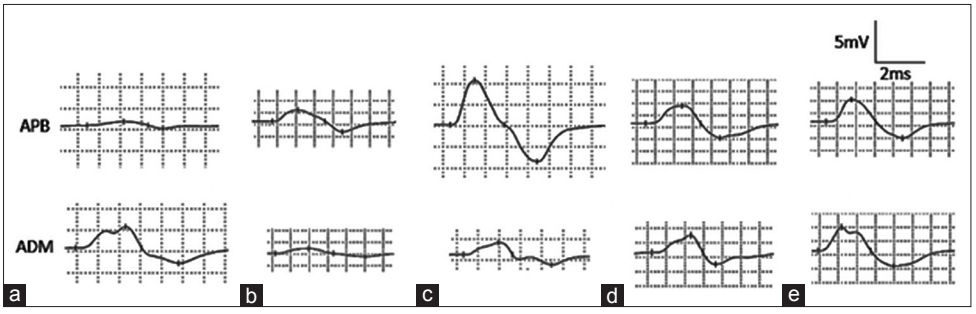

Figure 2: The compound muscle action potential responses recorded from the abductor pollicis brevis and the abductor digiti minimi of an amyotrophic lateral sclerosis patient (a), a patient with distal-type cervical spondylotic amyotrophy (b), a patient with Hirayama disease (c), a patient with spinobulbar muscular atrophy (d), and a normal participant (e). For the amyotrophic lateral sclerosis patient, the amplitude of abductor pollicis brevis compound muscle action potential was 1.63 mV, the amplitude of abductor digiti minimi compound muscle action potential was 8.5 mV, and the abductor digiti minimi/abductor pollicis brevis compound muscle action potential amplitude ratio was 5.21; for the patient with distal-type cervical spondylotic amyotrophy, the amplitude of abductor pollicis brevis compound muscle action potential was 9.2 mV, the amplitude of abductor digiti minimi compound muscle action potential was 3.5 mV, and the abductor digiti minimi/abductor pollicis brevis compound muscle action potential amplitude ratio was 0.37; for the patient with Hirayama disease, the amplitude of abductor pollicis brevis compound muscle action potential was 19.2 mV, the amplitude of abductor digiti minimi compound muscle action potential was 5.3 mV, and the abductor digiti minimi/abductor pollicis brevis compound muscle action potential amplitude ratio was 0.28; for the patient with spinobulbar muscular atrophy, the amplitude of abductor pollicis brevis compound muscle action potential was 13.5 mV, the amplitude of abductor digiti minimi compound muscle action potential was 9.9 mV, and the abductor digiti minimi/abductor pollicis brevis compound muscle action potential amplitude ratio was 0.73; for the normal participant, the amplitude of abductor pollicis brevis compound muscle action potential was 15.4 mV, the amplitude of abductor digiti minimi compound muscle action potential was 14.0 mV, and the abductor digiti minimi/abductor pollicis brevis compound muscle action potential amplitude ratio was 0.91.

Table 3: Results of ADM/APB CMAP amplitude ratios in study subjects

Groups	*n*	ADM/APB CMAP amplitude ratio, *n* (%)			Absent APB response, *n* (%)	Absent ADM response, *n* (%)
		<0.6	0.6–1.7	>1.7		
ALS	200	9 (4.57)	85 (43.15)	103 (52.28)	3 (1.50)	0
CSA	95	35 (36.84)	49 (51.58)	11 (11.58)	0	0
HD	88	47 (53.41)	36 (40.91)	5 (5.68)	0	0
SBMA	43	1 (2.33)	40 (93.02)	2 (4.65)	0	0
NC	150	3 (2.00)	146 (97.33)	1 (0.67)	0	0

Numbers within parentheses indicate percentages of patients in each disease category. APB: Abductor pollicis brevis; ADM: Abductor digiti minimi; ALS: Amyotrophic lateral sclerosis; CMAP: Compound muscle action potential; CSA: Cervical spondylotic amyotrophy; HD: Hirayama disease; NC: Normal controls; SBMA: Spinobulbar muscular atrophy.

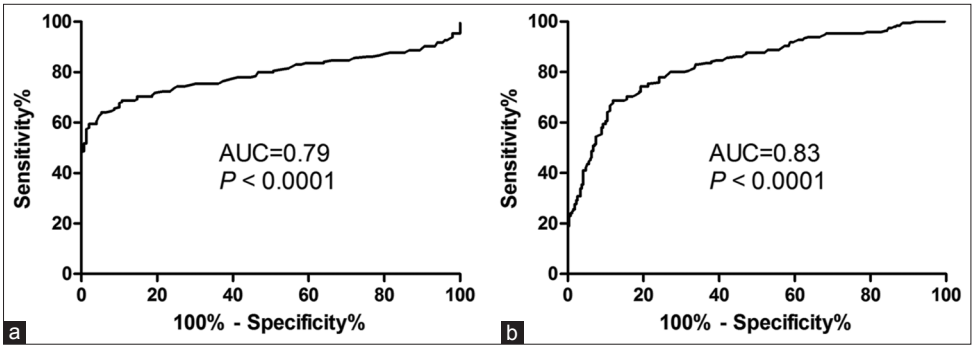

Figure 3: (a) Receiver operating characteristics curve analysis revealed that the abductor digiti minimi/abductor pollicis brevis compound muscle action potential amplitude ratio reliably differentiated amyotrophic lateral sclerosis from the normal controls, with an area under the curve of 0.79 ($P < 0.0001$). (b) Receiver operating characteristics curve analysis revealed that the abductor digiti minimi/abductor pollicis brevis compound muscle action potential amplitude ratio reliably differentiated amyotrophic lateral sclerosis from amyotrophic lateral sclerosis mimic disorders, with an area under the curve of 0.83 ($P < 0.0001$).

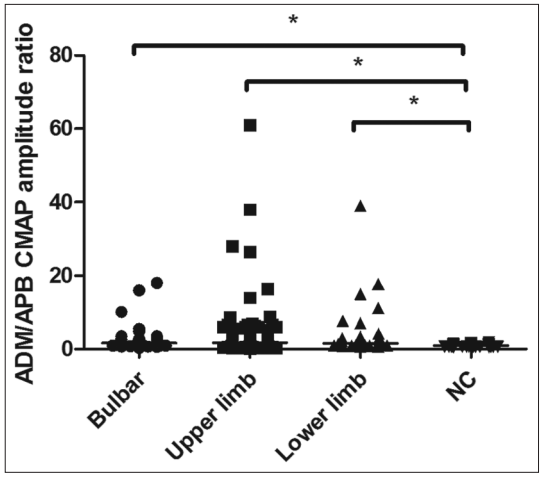

Figure 4: Distribution of the abductor digiti minimi/abductor pollicis brevis compound muscle action potential amplitude ratios in the patients with bulbar-, upper limb-, and lower limb-onset amyotrophic lateral sclerosis, and the normal controls (*$P < 0.001$).

muscles has been termed the split hand.[18] In the present study, the APB was more severely affected than the ADM in the ALS patients. The split hand sign was predominantly observed in the ALS patient group. Our findings did not provide evidence of dissociated small hand muscle atrophy in aging.[16] In the present study, the absolute CMAP amplitudes of APB and ADM declined with aging, but the extent of the decrease did not significantly differ between the APB and the ADM. The split hand phenomenon was not limited to the ALS patients. A reverse split hand sign, which indicates that the ADM is more severely affected, was noted in 9 (4.57%) ALS patients in the present study. Nevertheless, preferential involvement of APB has a high degree of specificity to ALS patients.[15,17] The ADM/APB CMAP amplitude ratios were comparable between the patients with bulbar-, upper limb-, and lower limb-onset ALS. This suggested that neurophysiological evidence of the split hand sign was evident in the ALS patients, independent of the clinical regions of onset.[19] A noteworthy observation was that the APB and the ADM appeared to be more or less equally affected in several ALS patients, especially in the advanced stage of the disease.[18] An ADM/APB CMAP amplitude ratio that was ≥4.5 was detected only in the ALS patients and not in the patients with ALS mimic disorders. The increase in ADM/APB CMAP amplitude ratio may be an early feature of patients with ALS.

The distinction between HD, CSA, and ALS may be difficult, given the potential overlapping clinical manifestations. From a clinical point of view, it is important to distinguish HD and CSA from ALS. For example, early diagnosis of CSA and timely treatment may contribute to significant improvement of clinical manifestations in patients with CSA.[20] In the patients with distal-type CSA and the HD patients, the ADM appeared to be more severely involved than the APB, which was in contrast with the pattern in the

ALS patients.[17] HD and CSA share similar pathogenesis and clinical features, apart from distinct ages of symptom onset. There has been little discussion about the differences in the clinical and neurophysiological manifestations between HD patients and patients with distal-type CSA to date. Compared with the patients with distal-type CSA, the APB in the HD patients was relatively spared. Presumably, the APB is innervated primarily from the T1 root, and the ADM seems to be innervated predominantly from both the C8 and T1 roots.[21] In the HD patients, pathological findings revealed anteroposterior flattening of the cord, predominantly at the C7 and C8 cord level; additionally, the number of anterior horn cells was decreased most severely at the C7 and C8 cord level,[22-24] while the patients with distal-type CSA had responsible lesion in the C7–T1 cord level.[4] One pathophysiological mechanism of HD is the anterior shift of the cervical dural sac induced by neck flexion with subsequent ventral spinal cord compression and local circulatory insufficiency resulting in anterior horn cell dysfunction.[6] Two different pathophysiological mechanisms have been proposed in the development of CSA. One is selective ventral motor root lesions[25], and the other is vascular insufficiency of the corresponding anterior horn cells, as a result of the compression of posteriorly herniated cervical disks.[26]

In our study, 95.35% of the SBMA patients demonstrated symmetrical disease onset. Consistent with previous studies,[27] the CMAP amplitude abnormalities of the SBMA patients were less frequent and less pronounced, compared with those of the ALS patients. The CMAP amplitude abnormalities were only found in 2 of 43 SBMA patients (4.65%), in agreement with a very chronic and slowly progressive denervation process, in which reinnervation via collateral sprouting can keep pace with anterior horn cell loss.[28] In addition, prior studies have reported that the proximal limb muscles were usually more severely affected than the distal limb muscles in SBMA patients.[29,30] The thenar and hypothenar muscles were affected to a similar extent in the SBMA patients. Diffuse testosterone-dependent nuclear accumulation of the mutant androgen receptor in the lower motor neurons is a cardinal pathogenesis process underlying the neurological manifestations in SBMA.[31] Based on our results, it can be reasonably speculated that lower motor neurons are affected diffusely and nonselectively in patients with SBMA.

Motor unit number estimation has demonstrated a greater and faster loss of motor units in the APB compared with that in the ADM in ALS patients.[32] However, the precise mechanism underlying the preferential involvement of the APB compared with the ADM in ALS patients remains unknown. Both cortical and peripheral mechanisms have been proposed in the development of the split hand sign in ALS patients.[33,34] Previous studies have demonstrated the existence of stronger corticomotoneuronal input to the thenar complex than to the hypothenar complex in healthy subjects.[34] This might cause the thenar complex to preferentially degenerate in ALS patients through glutamate-induced excitotoxicity.[35] The corticomotoneuronal input to the thenar complex is preferentially affected in ALS patients, which indicates that corticomotoneuronal dysfunction may be the prime contributor to the split hand sign in ALS patients.[34] Peripheral axonal excitability studies have suggested that the APB motor axons have increased persistent sodium currents and reduced potassium currents compared with the ADM axons in ALS patients, which results in higher excitability and thereby more ready degeneration of the APB motor axons.[36,37]

The limitations of our study must be acknowledged. Because this is a retrospective study, we could not evaluate data from the FDI muscles though it has been suggested that the APB/ADM CMAP amplitude ratio appears to be more sensitive and specific than the FDI/ADM CMAP amplitude ratio.[15] In addition, the retrospective approach made the data problematic to record with accuracy.

In conclusion, the patterns of small hand muscle atrophy differentiated between the ALS patients and the patients with mimic disorders as a result of distinct pathophysiological mechanisms underlying different disorders. The ADM/APB CMAP amplitude ratio cannot absolutely distinguish ALS patients from patients with mimic disorders. However, an increased ADM/APB CMAP amplitude ratio in patients with suspected ALS carries a high positive predictive value. The findings of the nerve conduction study, especially the ADM/APB CMAP amplitude ratio, may play a potential role in not only facilitating the clinical diagnosis of ALS but also providing information on a different and potentially treatable diagnosis.

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Conflicts of interest

There are no conflicts of interest.

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