대한임상신경생리학회지 6(2):85~91, 2004 ISSN 1229-6414

근위축성 측상경화증 환자에서 등세모근의 신경생리학적 검사

서울대학교 의과대학 신경과학교실

조중양 · 전종은 · 이광우

The Electrophysiological Studies of the Trapezius Muscle in Patients with Amyotrophic Lateral Sclerosis

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Background: Needle electromyography (EMG) and motor evoked potential (MEP) of the genioglossus (tongue) are difficult to perform in evaluations of the craniobulbar region in amyotrophic lateral sclerosis (ALS). Therefore, we investigated the yields of needle EMG and MEP recorded from the upper trapezius, since it receives innervation from the lower medulla and upper cervical cord.

Methods: Needle EMG and MEP of the upper trapezius were obtained in 17 consecutive ALS patients. The needle EMG parameters recorded included abnormal spontaneous activity and motor unit action potential (MUAP) morphology. An upper motor neuron (UMN) lesion was presumed when either response to cortical stimulation was absent, or the central conduction time was delayed (>mean+2SD).

Results: Of the five patients with bulbar-onset ALS, four had abnormalities in the upper trapezius and four in the tongue by needle EMG. In contrast, of the 12 patients with limb-onset ALS, 11 had abnormalities in the upper trapezius, and only five in the tongue. When MEP was performed, it was found that three of the five patients with bulbar symptoms and three of the six patients with isolated limb involvement had abnormal MEP findings.

Conclusions: Electrophysiological studies of the upper trapezius are more sensitive those of the tongue in patients without bulbar symptoms. Thus, needle EMG and MEP of the upper trapezius are alternative tools for assessing bulbar and rostral neuraxial involvement in the diagnosis of ALS.

Key Words: Amyotrophic lateral sclerosis, Needle EMG, MEP, Upper trapezius

Introduction

Amyotrophic lateral sclerosis (ALS) is a clinically well-defined disorder of the pyramidal and spinal motor neurons.[1] Muscle weakness develops with the progressive loss of both upper motor neurons (UMN) and lower motor neurons (LMN). Due to the progressive and fatal course of ALS, diagnostic testing must be as certain as possible and false positives minimized. The electrophysiological diagnostic criteria of ALS require abnormalities in at least three of four areas of the neuraxis (craniobulbar, cervical, thoracic, or lumbosacral) and in at least one area beyond the cervical and lumbosacral segments to assure widespread motor neuron involvement. It is well known that electromyographic (EMG) findings and motor evoked potentials (MEP) of the lower cranial nerve innervated muscles, such as, of the genioglossus (tongue) and masseter, have been detected in cases of craniobulbar dysfunction. However, these methods have some limitations, as they are difficult to perform and uncomfortable to patients.[2-5] The objectives of this study

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were to compare the relative utilities of EMG of the tongue, SCM, and upper trapezius muscles in the evaluation of LMN dysfunction, and to investigate MEP by transcranial magnetic stimulation (TMS) in the upper trapezius muscles of ALS patients, finally we examined the value of electrophysiological studies of the upper trapezius muscle as alternative tools for assessing craniobulbar involvement in the diagnosis of ALS.

Material & methods

1. Patients and normal subjects

The study was performed in 17 ALS patients (12 males and 5 females; aged 35~72 years, mean±SD=54.7±11.0). Their mean duration of illness was 20.9±11.8 months at the time of this investigation. A diagnosis of ALS was made based on clinical and electrophysiological examinations based according to El Escorial criteria.[1] To determine the normal parameters of MEP, 21 healthy subjects (7 males and 14 female; aged 30~71 years, mean±SD=52.9±12.7) were included. These controls had no neurological abnormalities, and had electrophysiological study results within normal limits. All subjects provided informed consent, and the study was approved by our institutional ethics committee.

2. Procedures

1) Needle EMG of the upper trapezius

Needle EMG was performed as previously described.[5,6] Though the number of muscles studied per patients varied, needle EMG was performed in bulbar, limbs, and paraspinal muscles. In particular, attention was focused on the tongue, SCM, and upper trapezius muscles. EMG abnormalities in muscles were assessed by following a standard protocol.[7,8] We first looked for abnormal spontaneous activity in the form of positive sharp waves and fibrillation potentials with muscles at rest. Abnormal spontaneous activity was defined as abnormal activity in two separate sites within a muscle. Motor unit action potential (MUAP) configuration was assessed during a minimal muscle contraction, and was considered complex when polyphasic (greater than four action potentials crossing the baseline) or polyturn (greater than five turns without crossing the baseline).[7] The pattern of MUAP recruitment was excluded due to faster firing rates of the bulbar muscles.[6]

2) MEP of the upper trapezius

Corticobulbar projections were investigated by TMS, and evoked potentials were recorded via surface electrodes placed on the upper trapezius muscle, as previously described.[9] In brief, the active electrode was taped 1~2 cm below the upper margin of the muscle, approximately midway between the acromion and the C7 spinous process. The reference electrode was placed over the acromion. For TMS, a standard circular coil (diameter 90 mm, Cadwell MES-100) with a peak magnetic field of 2.0 tesla was used and potentials were registered using a conventional unit (Cardwell Excel EMG instrument). The coil was applied tangentially to the skull with its center placed over the vertex or slightly laterally toward the stimulated hemisphere. In order to evoke muscle responses with shortest latencies and largest amplitudes, the subjects were asked to contract the target muscle by lifting the shoulder of interest against resistance applied by an examiner to the wrist.

The parameter analyzed was the central motor conduction time (CMCT). CMCT was defined as the difference between the shortest onset latency of the MEP and the latency of the compound muscle action potentials (CMAP). Peripheral CMAP was obtained by the spinal accessory nerve (SAN), which was electrically stimulated with surface electrodes slightly above the midpoint between the clavicle and mastoid process along the posterior border of the SCM.[10] Strictly speaking, this parameter was not a true central conduction time, since it included the proximal segment of the accessory nerve. An UMN-lesion was assumed when either the cortically evoked response was absent or the CMCT was delayed (> mean+2SD) with the normal nerve conduction study of spinal accessory nerve. The stimulation intensity was increased to 100% of the maximal output of the stimulator before a response was regarded absent. Absence of potential was defined as no reproducible response in four consecutive trials.[11,12]

3) Statistical analysis

Correlations between bulbar dysfunction and

MEP findings were analyzed using Fisher's test and Sperman's correlation coefficients. The clinical severity of bulbar dysfunction was evaluated by using Appel ALS rating scale (AALSRS).[13] To compare MEP findings and AALSRS score, we divided the patients into two groups according to MEP abnormalities. The difference of bulbar AALSRS score between two groups were statistically investigated using the Mann-Whitney U test, and the level of statistical significance was set at $P<0.05$. Statistical analyses were performed using the SPSS statistical software package.

Results

1. Normal subjects

The mean CMAP amplitude of the upper trapezius in normal subjects was 13.2±4.6 mV (range: 4.8~25.5 mV), and its mean latency was 2.1±0.3 ms (range: 1.4~3.0 ms). MEP was easily elicited from the upper trapezius muscle in all subjects although maximal MEP amplitudes often required a higher level of voluntary contraction, and a higher magnetic stimulation strength. The mean MEP latency was 8.7±0.85 ms (range: 7.0~10.8 ms), and the mean CMCT was 6.42±1.25 ms (range: 1.8~85 ms) and normal limiting values were defined as the mean value + 2SD (≤8.92 ms).

2. Patients

1) Needle EMG of the upper trapezius

EMG abnormalities in limb-onset ALS were more frequent in the upper trapezius (11/12) than in the SCM (8/11) or in the tongue (5/12). Patients with limb-onset ALS were further divided into those who had no bulbar symptoms (n=6) and those who had bulbar symptoms (n=6). In patients with no bulbar symptoms, EMG abnormalities of the upper trapezius and SCM were detected in five and three ALS patients, respectively, but EMG tongue abnormalities were found in only one patient. In patients with bulbar symptoms, EMG abnormalities were found in the upper trapezius (n=6) and tongue (n=4). We also analyzed our data in an alternative way by dividing the 17 patients into those with no bulbar symptoms (n=6) and those with bulbar symptoms (n=11), regardless of the location of symptom-onset (Table 1, Table 2).

2) Upper trapezius MEP

The upper trapezius MEP was abnormal in 12 of 17 patients. Four patients had a prolonged CMCT with a normal CMAP latency value. MEP included no potential or only poor potential in eight patients. A clinical examination performed at the time of trapezius MEP revealed that six patients had the symptoms and signs of UMN involvement, such as, hyperactive jaw reflexes or reduced tongue motility with spastic dysarthria and dysphagia. Three of the five patients with bulbar symptoms such as tongue atrophy and fasciculation showed evidence of additional subclinical coricobulbar tract involvement. In three of six patients with isolated limb involvement,

Table 1. EMG abnormalities* in 17 ALS patients

	tongue	SCM†	upper trapezius
bulbar onset (n=5)	4	3	4
limb onset (n=12)			
with bulbar symptoms and signs (n=6)	4	5	6
without bulbar symptoms and signs (n=6)	1	3	5

* EMG abnormalities mean denervation potentials and/or giant motor unit action potentials
† sternocleidomastoid muscle

Table 2. Electrophysiological findings of 17 ALS patients

	EMG abnormalities*			upper trapezius MEP	
	tongue	SCM†	upper trapezius	abnormal	normal
with bulbar symptoms and signs (n=11)	8	5	10	9	2
without bulbar symptoms and signs (n=6)	1	3	5	3	3

* EMG abnormalities mean denervation potentials and/or giant motor unit action potentials
† sternocleidomastoid muscle

subclinical corticobulbar tract dysfunction was demonstrated (Table 2).

3) Comparison between upper trapezius MEP and the AALS rating scale

AALS ratings were performed on all ALS patients. Upper trapezius MEP abnormalities were not found to be correlated with the severity of bulbar dysfunction. However, bulbar AALSRS scores were higher in patients with an abnormal MEP (13.7±6.5, 6-24) than in patients with a normal MEP (7.2±1.6, 6-9), (p=0.034), (Fig. 1).

Discussion

In ALS, a loss of UMN affects central motor drive, which leads to contraction speed and repetitive movement retardation, weakness, reduced muscle activation, hyperreflexia, and spasticity.[14,15] A loss of LMN results in muscle atrophy, fasciculations, hyporeflexia, and a comparable loss in both voluntary and electrically stimulated muscle force.[16] Thus, needle EMG and MEP of the craniobulbar muscles have become standard methods of assessing the functional integrity of the corticobulbar system. However, recordings from craniobulbar muscles such as of the tongue, present practical and interpretative difficulties.[8] As a means of investigating electrophysiologically the craniobulbar region in ALS, we selected the upper trapezius muscle as an alternative to the lower cranial nerve innervated muscles, because this muscle, together with the SCM, is innervated by the SAN, and because such investigations are easier in this muscle or cause less patients discomfort.

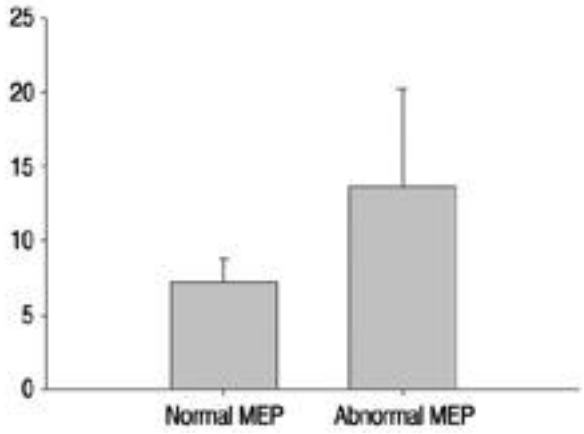

Figure 1. The difference of bulbar Appel ALS rating scale score between two groups. Bulbar AALSRS scores were higher in patients with an abnormal MEP than in patients with a normal MEP using the Mann-Whitney U test (p=0.034). The normal MEP group was defined to have a CMCT of ≤8.92 msec.

In a previous study, the tongue and buccinator muscles were used for investigating UMN dysfunction in the craniobulbar region.[4] In this study, of 30 ALS patients , only 6% showed clinical evidence of UMN involvement, whereas the MEP of orofacial and tongue muscles were impaired in 57% and 50%, respectively. However, interpretations of tongue MEP are limited owing to some peculiarities of peripheral hypoglossal nerve conduction and excitability.[17,18] Abnormalitie of masseter MEP were previously compared for ALS patients and cervical spondylotic myelopathy patients.[19] In 30 patients with ALS, 63.3% (regardless of the presence or absence of bulbar signs) showed masseter MEP abnormalities, but all CSM patients were normal in this respect. Recently, MEP of the upper trapezius was performed to evaluate the usefulness of MEP as a diagnostic aid for the differentiation of ALS and CSM.[9] Upper trapezius MEP abnormalities were detected in all ALS patients, but only one of nine CSM patients. This suggests that MEP of the upper trapezius might be useful in the differential diagnosis of spinal cord compression disorders mimicking ALS due to the combination of UMN and LMN signs.

The EMG of facial, glossal, and masticatory muscles in ALS patients were also compared the relative value between them.[5] The tongue (50%) most commonly showed abnormal findings in bulbar-onset patients, but in limb-onset patients, abnormal findings were similar for these techniques (2/13 tongue, 3/13 masseter, 2/12 frontalis). However, this method has many limitations;[2,3] which include; (1) needle EMG of the craniobulbar muscles causes discomfort to the patient and to the electromyographer, (2) some of the craniobulbar muscles are difficult to investigate because of inadequate relaxation and inadequate voluntary contraction, and (3) the assessment of spontaneous craniobulbar muscle activity is difficult, because the MUAP is small and may resemble fibrillation potentials, and because craniobulbar muscles are more difficult than the relaxation of larger muscles. Thus, in the recent study, SCM was used as alternative lower cranial nerve

innervated muscle for EMG in ALS.[6] Of 21 ALS patients, six showed bulbar-onset ALS, and of these six three had abnormalities in the SCM and three had abnormalities in the tongue. In contrast, for the 15 patients with limb-onset ALS, nine had abnormalities in the SCM, and only three had abnormalities in the tongue. These results indicated that needle EMG of the SCM is useful for evaluating the craniobulbar region in ALS patients. Though EMG of the SCM was less difficult than that of the tongue and masseter, some limitations remain.

In our study, to solve the electrophysiological study problems associated with recording from the lower cranial nerve innervated muscles such as tongue and masseter, the upper trapezius were examined as alternatives. MEP of the upper trapezius in ALS patients revealed abnormalities in 12 of 17 patients. In patients with bulbar symptoms, three of the five patients showed evidence of additional subclinical corticobulbar tract involvement, and this finding was also demonstrated by three of the six patients with isolated limb involvement. Therefore, MEP of the upper trapezius was found useful for evaluating UMN dysfunction of the corticobulbar tract in ALS patients, especially in those without bulbar symptoms.

When we performed EMG of the upper trapezius to investigate LMN dysfunction, abnormalities were found in 15 of 17 patients. EMG of the upper trapezius was found to be as similar sensitive as that of the tongue in ALS patients with bulbar symptoms. Moreover, in patients without bulbar symptoms, EMG of the upper trapezius was found to be more sensitive than that of the tongue. Similar findings were obtained in patients with limb-onset ALS. The findings of a previous study, which compared EMG sensitivities of the SCM and the tongue, concur with our findings.[6]

We easily obtained MEP of the upper trapezius, as has been reported by others.[20,21] The latencies of responses in our control subjects were similar to those found by these authors. However, MEP amplitude may not be a reliable parameter, because of a marked variability that led to a broad range of normal values.[22] Sometimes, the MEP amplitude was larger than the CMAP stimulated by SAN. This may has been due to the recording of volume-conducted activity from muscles other than the upper trapezius, such as the levator scapulae or supraspinatus, which can be co-activated by TMS.[9]

Since the amplitudes of cortically evoked responses showed considerable inter-individual variation,[26,27] the parameter analyzed was the central motor conduction time (CMCT), where CMCT abnormalities were defined as absent or delayed (> mean+2SD) responses. In previous study, the MEP/CMAP amplitude ratio was used as an additional parameter to assess corticobulbar and corticospinal tract dysfunction.[9,22] However, because the CMAP amplitude might not reflect the number of intact lower motoneurons during the early stage of the disease,[28] and because MEP amplitude was found to have a broad range of normal values,[22] we have excluded the MEP/CMAP amplitude ratio from our considerations.

The trapezius arises from the external occipital protuberance and the medial third of the superior nuchal line of the occipital bone, from the ligamentum nuchae, the spinous process of the seventh cervical, the spinous processes of all thoracic vertebrae, and from the corresponding portion of the supraspinal ligament. From this origin, the upper fibers proceed downward and laterally (descending part), the lower fibers upward and laterally (ascending part), and the middle fibers horizontally (transverse part). It receives innervation from the SAN with occasional contribution from the cervical roots at C3 and C4.[23] However, recent studies have demonstrated that the upper trapezius gains its motor innervation from a small branch of the SAN, and that the upper trapezius branches of the cervical plexus do not contribute significantly to the muscle's motor innervation.[24,25] On the basis of cadaver study, the SAN and the trapezius branches of the cervical plexus merge and pass together to the transverse and ascending parts of the trapezius, but the descending part of the muscle is innervated solely by a single fine branch of the SAN.[25] Though the upper trapezius is mainly innervated by the SAN, which originates from the accessory nucleus, controversies remain. This nucleus extends from the lower medulla to upper cervical cord. A unresolved issue is whether the upper trapezius also receives innervation from anterior horn cells in the cervical cord. It is reasonable to presume that the upper trapezius receives innervation both the

lower medulla and upper cervical cord, since the accessory nucleus lies in both segments.[6]

MEP abnormalities were not found to be correlated with bulbar dysfunction severity, which is consistent with previous studies.[19,29] This lack of correlation may be related to the fact that MEP was absent in about a half of the patients (8/17).[19] However, the difference of the score of bulbar AALSRS between two groups proved significant. This suggests that bulbar dysfunction is more severe in patients with an abnormal MEP. The possible explanations are that an increasing cortical threshold or a reduced cortical excitability leads to a degeneration of corticobulbar fibers and bulbar symptoms in ALS patients.[30] However, the upper trapezius is not pure a bulbar muscle and only a small number of patients were included, further studies are needed to resolve this relation.

In conclusion, although the upper trapezius is not a "pure" bulbar muscle, needle EMG of the upper trapezius was found to be has more sensitive than of the tongue in patients without bulbar symptoms, and MEP was found to detect early and subclinical corticobulbar tract involvement in the pathway to the upper trapezius. Thus, electrophysiological studies of the upper trapezius could prove diagnostically useful for the evaluation of the craniobulbar region in ALS.

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