Clinical Neurophysiology Practice 3 (2018) 6–10

Contents lists available at ScienceDirect

Clinical Neurophysiology Practice

journal homepage: www.elsevier.com/locate/cnp

Research paper

Large fasciculation can clinically manifest as spinal myoclonus; electromyographic and dynamic echomyographic studies of four cases with motor neuron disease

Manabu Inoue [a,*], Masayoshi Yamamoto [a], Koji Tsuzaki [a], Toshiaki Hamano [a], Hiroaki Etoh [b], Hiroshi Shibasaki [c]

[a] Department of Neurology, Kansai Electric Power Hospital, Osaka City, Osaka, Japan
[b] Division of Clinical Laboratory, Kansai Electric Power Hospital, Osaka, Japan
[c] Kyoto University Graduate School of Medicine, Kyoto, Japan

ARTICLE INFO

Article history:
Received 21 June 2017
Received in revised form 30 August 2017
Accepted 15 October 2017
Available online 26 November 2017

Keywords:
Large fasciculation
Spinal myoclonus
Motor neuron disease
Dynamic echomyography
Surface electromyography

ABSTRACT

Objective: Patients with motor neuron disease rarely present with fasciculation which is large enough to be clinically recognized as myoclonus. This study is aimed at elucidating the features of large fasciculation manifesting as myoclonus by using surface electromyography (surface EMG) and dynamic echomyography (dynamic Echo).
Methods: Four patients with amyotrophic lateral sclerosis, two of whom clinically presented with both fasciculation and myoclonus, were studied by using the surface EMG and the dynamic Echo.
Results: At rest, all patients had fasciculation in atrophic muscles, and the surface EMG showed occasional discharges of different waveforms corresponding to fasciculation. During voluntary gentle muscle contraction, the surface EMG showed repetitive discharges in the contracting muscle, which were constant in size and waveform within each muscle. The muscle Echo at rest revealed occasional contractions of a small number of muscle fibers corresponding to fasciculation. During voluntary muscle contraction, the number of muscle fibers involved in the involuntary motor phenomena was larger in the patients who clinically presented with myoclonus compared with other patients who clinically presented only with fasciculation. In a patient who presented with myoclonus, there was no contraction in the antagonist muscle.
Conclusions: Fasciculation involving a large number of muscle fibers clinically manifests as spinal myoclonus.
Significance: Fasciculation involving a large number of muscle fibers can be a cause of spinal myoclonus.

1. Introduction

Fasciculation is clinically a random and spontaneous twitch of muscle fibers and is commonly observed in patients with lower motor neuron involvement. Usually fasciculation is visible as a contraction of a part of muscle under the skin or mucous membrane, and is not so large as to be recognized as a joint movement. If it involves small muscles like the hand intrinsic muscles, it may be recognized as a finger movement (Denny-Brown and Pennybacker, 1938; Kimura, 2001).

Myoclonus is defined as shock-like, simple involuntary movements of face and extremities, and anatomically classified into cortical, brainstem and spinal myoclonus according to its estimated sites of origin (Termsarasab and Frucht, 2016; Shibasaki and Hallett, 2016).

Patients with motor neuron disease rarely present with fasciculation which is large enough to be clinically recognized as myoclonus. In the previous case report, we presented a case of bulbospinal muscular atrophy with large fasciculation manifesting as spinal myoclonus (Inoue et al., 2017). The reported case showed brisk, gross contractions of the thigh muscles while the knees were kept in flexion in the supine position, and some movements were large enough to produce joint movements and appeared shock-like. The surface EMG showed occasional discharges corresponding to fasciculation at rest which became larger and more frequent during and

* Corresponding author at: Department of Neurology, Kansai Electric Power Hospital, 2-1-7 Fukushima, Fukushima-ku, Osaka 533-0003, Japan.
E-mail address: ma-inoue@med.osakacity-hp.or.jp (M. Inoue).

https://doi.org/10.1016/j.cnp.2017.10.004
2467-981X/

after voluntary muscle contraction. The duration of the discharges was shorter than 100 ms. The clinical and electrophysiological features of the involuntary movements fulfilled the criteria of myoclonus (Shibasaki, 2000; Shibasaki and Hallett, 2016). Since there was no co-contraction of agonist and antagonist muscles, we interpreted the involuntary movement as the spinal myoclonus caused by large fasciculation.

In this study, we investigated four patients with motor neuron disease by dynamic echomyography (dynamic Echo) and surface electromyography (surface EMG) in order to elucidate the mechanism of large fasciculation manifesting as myoclonus. On interpreting the results, we excluded the ambiguous movements and adopted only fasciculation and myoclonus which fulfilled each criteria unambiguously.

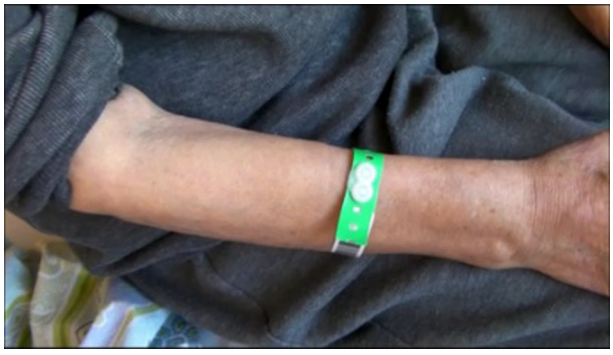
2. Patients

Clinical profiles of four patients are summarized in Table 1. The involuntary motor phenomena of each case and findings of the dynamic Echo are shown on video.

2.1. Case 1

A 76-year-old-woman presented with progressive difficulty in using fingers over a period of five years. On neurological examination, speech was slightly dysarthric. The thenar and dorsal interosseous muscles of the right hand were atrophic. Muscle strength was mildly to moderately weak in the right upper extremity and in the distal part of the right lower extremity. Tendon reflexes were hyperactive in all extremities except for the right upper extremity. The plantar reflexes were flexor bilaterally. About one year later, shock-like involuntary movements appeared in the right upper extremity.

When the patient was asked to move the right elbow or wrist, shock-like involuntary movements appeared in the right upper extremity (see Video 1). Some of the shock-like involuntary movements were large enough to cause flexion of the right elbow. Those movements were not elicited by passive joint movement or by tapping the tendon. In the resting state, there were spontaneous twitches of muscle fibers (fasciculation), but there was no shock-like movement.



Video 1. In cases 1 and 2, some fasciculations of the biceps brachii muscle are large enough to cause shock-like elbor flexion. The dynamic Echo of that muscle shows isolated contractions of a small number of muscle fibers at rest, and frequent contractions of a larger number of muscle fibers during voluntary gentle muscle contraction. In case 1, the dynamic Echo of the antagonist muscle (triceps brachii) during voluntary elbow flexion does not show any contraction. In cases 3 and 4, frequent twitches (fasciculation) are seen in the hand intrinsic muscles. The dynamic Echo of the first dorsal interosseous muscle shows no contraction at rest, and occasional contractions of a small number of muscle fibers during finger extension. In two normal control subjects, the dynamic Echo of the right biceps brachii muscle shows no phasic contractions of muscle fibers even while maintaining the right elbow flexion.

On laboratory data, blood chemistry was normal except for slightly elevated serum creatine kinase. Cervical and lumbar MRI showed atrophy of the paraspinal muscles, but no compression of the spinal cord. Electrophysiologically, motor nerve conduction study showed low amplitude of compound muscle action potentials (CMAP), but normal conduction velocity, in all extremities. Sensory nerve action potentials (SNAP) were normal in waveform and amplitude. Needle EMG suggested the presence of acute and chronic denervation in all extremities and in the paraspinal muscles.

2.2. Case 2

A 65-year-old man noticed of clumsiness of the left hand a year and half prior to the first medical examination. On the initial visit, muscle strength was slightly weak in the left arm. A few fasciculations were seen. Tendon reflexes were hyperactive in all extremities. There was no Babinski sign. Sensory function was normal. Muscle weakness progressed in all extremities, especially on the left over a period of the following four years. There was muscle atrophy of moderate degree with fasciculation in the left shoulder and arm. Then, speech became dysarthric. Muscle tone was spastic in all extremities. The left leg was spastic on walking. Fasciculation has gradually increased in frequency and magnitude. Four years after the first medical examination, shock-like involuntary movements were seen in the left upper extremity while the left elbow was kept in mild flexion (see Video 1). Some of the involuntary movements were large enough to move the left forearm. Those movements were not elicited by passive joint movement or by tapping the tendon.

Cervical MRI did not show any abnormality. Electrophysiologically, motor nerve conduction study showed prolongation of distal latency in the bilateral median nerves. Needle EMG suggested active and chronic denervation in the muscles of all extremities and the paraspinal muscles.

2.3. Case 3

A 74-year-old woman noticed of twitches in the fingers of both hands four years prior to the first examination. Subsequently muscle weakness appeared and progressed in all extremities. Neurologically, the thenar and dorsal interosseous muscles of both hands were atrophic and moderately weak. Fasciculation was seen in both hands, especially when the fingers were kept extended (see Video 1). Tendon reflexes were hyperactive in the lower extremities more on the left. The plantar reflexes were extensor on the right and flexor on the left. Tactile and vibration senses were mildly decreased in both feet with paresthesia.

Serum antiganglioside antibodies were negative. Electrophysiologically, motor nerve conduction study showed low amplitude of CMAP in all extremities, and mildly decreased conduction velocity in the lower extremities. SNAPs were mildly decreased in amplitude in the lower extremities. Needle EMG revealed the presence of chronic denervation in the abductor digiti minimi muscles.

One year later, she developed difficulty in walking.

2.4. Case 4

An 84-year-old man has had twitches in both hands, predominantly in the left hand, and gait disturbance over a period of one year. Subsequently he also noticed of speech difficulty. Neurologically, speech was slightly dysarthric. Tongue was not atrophic. The thenar muscles and dorsal interosseous muscles of both hands were atrophic. Muscle strength was moderately weak in the neck and fingers bilaterally. Fasciculation was seen in both hands, especially when fingers were extended (see Video 1). Tendon reflexes

Table 1
Clinical profile of the four patients studied.

	Case 1	Case 2	Case 3	Case 4
Age	76	65	74	84
Sex	Female	Male	Female	Male
Diagnosis	Probable ALS	Probable ALS	Possible ALS	Probable ALS
Involuntary motor phenomena	Myoclonus	Myoclonus	Fasciculation	Fasciculation
Distribution of involuntary motor phenomena	Right upper extremity	Left upper extremity	Fingers	Fingers
Appearance of involuntary motor phenomena	6 years after the clinical onset	5.5 years after the clinical onset	At the clinical onset	At the clinical onset

ALS: amyotrophic lateral sclerosis.

were hyperactive in the lower extremities. The plantar reflexes were flexor. Vibration sense was mildly decreased in the feet.

The blood chemistry was within normal limits. Electrophysiologically, motor nerve conduction study showed low amplitude of CMAP and normal conduction velocity in all extremities. SNAPs were normal. Needle EMG revealed the presence of active and chronic denervation in the muscles of all extremities and the paraspinal muscles.

Two years later, he developed difficulty in walking.

3. Methods

Surface EMG was recorded with Neurofax PlexScan L367 (Nihon Kohden Co., Ltd, Tokyo, Japan) in cases 1, 2 and 3. A pair of silver-coated electrodes was placed on the skin over the belly of the corresponding muscle with the inter-electrode distance of 3 cm. Muscle activities were recorded at rest and during gentle muscle contraction.

Dynamic Echo was performed in all cases with the Aplio™ 500 ultrasound machine (Toshiba Medical Systems Co., Ltd, Otawara, Japan) with linear 4.8–11.0 MHz transducers and elastography software. The probe (PLT-704SBT) was positioned on the skin over the corresponding muscle. The involuntary contractions of muscle fibers were recorded at rest and during gentle muscle contraction. In order to obtain control data, dynamic Echo was recorded in two healthy subjects from the right biceps brachii muscle during continuous right elbow flexion.

On interpreting the results, we excluded the ambiguous movements and adopted only fasciculation and myoclonus which fulfilled each criteria unambiguously.

4. Results

4.1. Surface EMG

In the three cases in whom surface EMG was studied (cases 1, 2 and 3), occasional discharges of different waveforms corresponding to fasciculation were observed in the resting condition (Fig. 1). During continuous gentle muscle contraction, irregular discharges corresponding to fasciculation were superimposed on the discharges related to voluntary muscle contraction in the contracting muscle. In other muscles of the same extremity, repetitive discharges corresponding to fasciculation and/or myoclonus appeared and remained for a few seconds after the voluntary contraction was stopped (Fig. 2).

4.2. Dynamic Echo (see Video 1)

In the two cases who clinically manifested only fasciculation (cases 3 and 4), the muscle Echo at rest revealed rare contractions of muscle fibers, and the dynamic Echo during continuous gentle muscle contraction revealed small and repetitive contractions of a small number of muscle fibers. In cases 1 and 2 who clinically manifested both fasciculation and myoclonus, the muscle Echo at rest showed isolated contractions of a small number of muscle fibers, and the dynamic Echo during continuous gentle muscle contraction revealed frequent and repetitive contractions of a large number of muscle fibers. The frequent and repetitive contractions were seen independently in different parts of a muscle. There was no contraction in the antagonist muscle (the right triceps brachii of Case 1). In two healthy control subjects, dynamic Echo during continuous gentle muscle contraction revealed no phasic contraction of muscle fibers (see the last two cases of Video 1).

5. Discussion

In all four cases presented here, the neurologic signs suggested involvement of the upper and lower motor neurons, and the needle EMG revealed an evidence of acute and chronic denervation. According to the EI Escorial criteria for amyotrophic lateral sclerosis (ALS), the three cases (1, 2 and 4) were diagnosed as clinically probable-laboratory-supported ALS (Brooks et al., 2000; Geevasinga et al., 2016). The neurologic signs of case 3 suggested involvement of the upper and lower motor neurons, and the needle

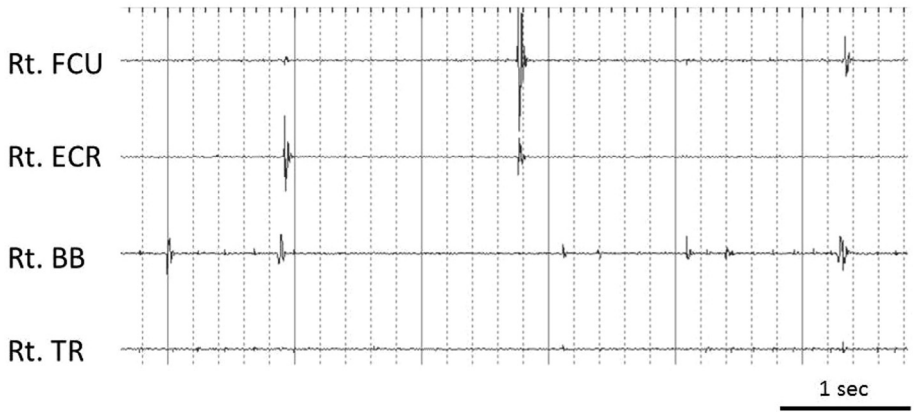


Fig. 1. Surface EMG recorded at rest in case 1. Note occasional EMG discharges of short duration and various magnitude corresponding to fasciculations. FCU: flexor carpi ulnaris, ECR: extensor carpi radialis, BB: biceps brachii, TR: triceps brachii, Rt: right.

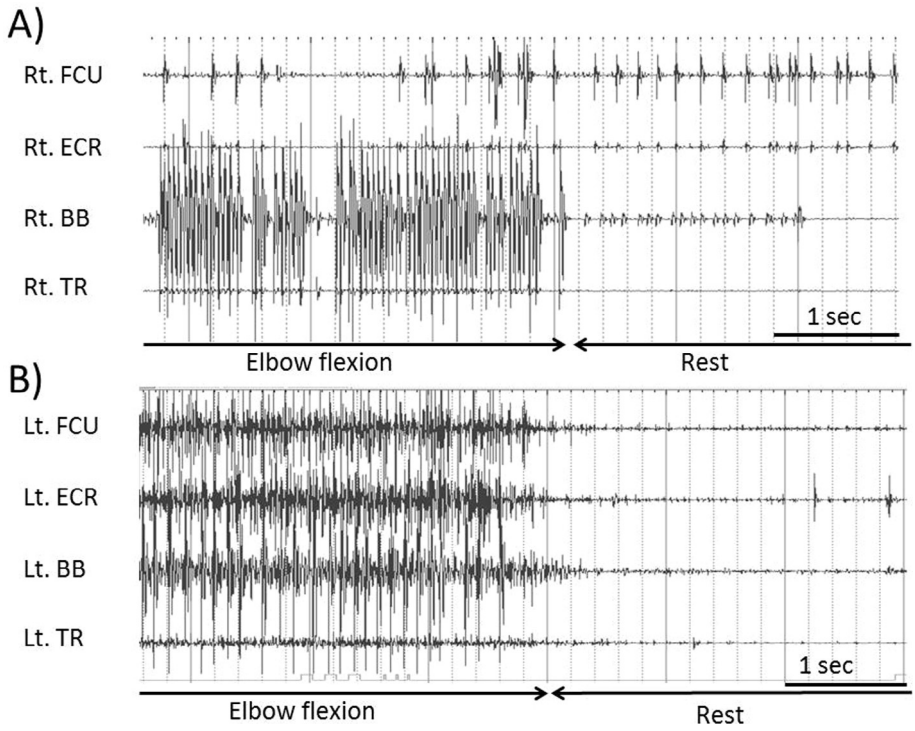


Fig. 2. Surface EMG during voluntary gentle muscle contraction in case 1 (A) and case 2 (B). (A) Note repetitive EMG discharges in the FCU during and after flexion of the right elbow. (B) Note frequent high amplitude discharges in all muscles during flexion of the left elbow. In the FCU, ECR and BB, those discharges are superimposed on the continuous discharges associated with voluntary muscle contraction. Abbreviations are the same as for Fig. 1. Lt: left.

EMG revealed an evidence of chronic denervation. According to the EI Escorial criteria for ALS, case 3 was diagnosed as clinically possible-laboratory-supported ALS.

Clinically, cases 1 and 2 showed frequent shock-like movements in the upper extremity. Those movements were occasionally seen in the resting condition, and they were enhanced especially during voluntary gentle contraction of the corresponding muscles. Some of the shock-like movements were large enough to produce joint movements, manifesting as myoclonus. Cases 3 and 4 showed frequent and fine movements in the contracting hand intrinsic muscles, but those movements were not large enough to cause shock-like joint movement. Cases 1 and 2 could elevate the upper extremities and walk independently more than five years after the clinical onset. Myoclonus in these two cases appeared about six and five years, respectively, after the clinical onset. Since life span of cases with ALS is about three years, both cases had slower progression (Logroscino et al., 2008). The previously reported case with BSMA also showed long clinical course (Inoue et al., 2017). Although the number of cases is limited in this study, the above finding might suggest that MND cases of long duration tend to show large fasciculation manifesting as myoclonus.

In three cases in whom the surface EMG was recorded (case 1, 2 and 3), it showed occasional discharges corresponding to fasciculation at rest which became much more frequent during voluntary muscle contraction.

In the two cases who clinically manifested only fasciculation (cases 3 and 4), the muscle Echo at rest revealed rare contraction of muscle fibers, and the dynamic Echo during continuous gentle muscle contraction revealed frequent contractions of a small number of muscle fibers corresponding to repetitive fasciculation. In cases 1 and 2 who clinically manifested myoclonus caused by large fasciculation in addition to small muscle contraction, the muscle Echo at rest showed isolated contractions of a small number of muscle fibers corresponding to fasciculation, and the dynamic Echo during continuous muscle contraction revealed frequent and repetitive contractions of a larger number of muscle fibers. Thus, the number of muscle fibers involved in myoclonus was larger than that in fasciculation. To the authors' knowledge, the findings of the dynamic Echo of large fasciculation which clinically manifested as myoclonus have not been reported.

Misawa et al. (2010) reported that dynamic Echo of spinal segmental myoclonus showed passive and repetitive contraction of the whole muscle. Osaki et al. (2015) reported that dynamic Echo of myokymia showed repetitive, brief but sustained, tractive movements of the surface of the muscle. Features of large fasciculation observed in the present dynamic Echo were different from those in the reported cases of spinal myoclonus which showed repetitive contractions of a whole muscle or myokymia which showed repetitive contractions of a bundle of muscle fibers with lower frequency.

Although the surface EMG and the dynamic Echo were not recorded simultaneously in the present study, the clinical observation combined with these two data suggests that large fasciculation involving a large number of muscle fibers clinically manifests as myoclonus whereas small fasciculation restricted to a small motor unit territory manifests as fine muscle twitch.

The pathophysiology of myoclonus during voluntary muscle contraction has not been precisely clarified. Myoclonus observed in the present cases can be explained as extremely large fasciculation of anterior horn cell origin, because it was enhanced by voluntary muscle contraction. Moreover, lack of co-contraction of agonist and antagonist muscles suggests myoclonus of spinal cord origin rather than of cortical origin (Shibasaki, 2000). Spinal myoclonus is divided into spinal segmental myoclonus and propriospinal myoclonus. Spinal segmental myoclonus is usually symptomatic of a localized lesion of the spinal cord. Propriospinal myoclonus involves propriospinal pathways, in which myoclonic jerk starts from a certain thoracic segment and spreads rostrally

as well as caudally with relatively slow conduction velocity (Brown et al., 1991, 1994). However, the distribution of myoclonus in the present cases was not compatible with either isolated spinal segmental or propriospinal myoclonus (Brown et al., 1994; Hopkins and Michael, 1974; Jankovic and Pardo, 1986). In the present cases, therefore, it is reasonable to consider myoclonus as spinal myoclonus originating from multiple segments.

Conflict of interest

The authors declare that they have no conflicts of interest and nothing to disclose.

Acknowledgments

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

Brooks, B.R., Miller, R.G., Swash, M., Munsat, T.L., World Federation of Neurology Research Group on Motor Neuron Diseases, 2000. El Escorial revisited: revised criteria for the diagnosis of amyotrophic lateral sclerosis. Amyotroph Lateral Scler Other Motor Neuron Disord 1, 293–299.

Brown, P., Thompson, P.D., Rothwell, J.C., Day, B.L., Marsden, C.D., 1991. Axial myoclonus of propriospinal origin. Brain 114, 197–214.

Brown, P., Rothwell, J.C., Thompson, P.D., Marsden, C.D., 1994. Propriospinal myoclonus: evidence for spinal "pattern" generators in humans. Mov. Disord. 5, 571–576.

Denny-Brown, D., Pennybacker, J.B., 1938. Fibrillation and fasciculation in voluntary muscle. Brain 61, 88–96.

Geevasinga, N., Menon, P., Scherman, D.B., Simon, N., Yiannikas, C., Henderson, R.D., et al., 2016. Diagnostic criteria in amyotrophic lateral sclerosis: a multicenter prospective study. Neurology 87, 684–690.

Hopkins, A.P., Michael, W.F., 1974. Spinal myoclonus. J. Neurol. Neurosurg. Psychiatry 37, 1112–1115.

Inoue, M., Kojima, Y., Kanda, M., Tsuzaki, K., Shibata, Y., Hamano, T., et al., 2017. A case of bulbospinal muscular atrophy with large fasciculation manifesting as spinal myoclonus. Clin. Neurophysiol. Pract. 2, 62–64.

Jankovic, J., Pardo, R., 1986. Segmental myoclonus clinical and pharmacologic study. Arch. Neurol. 43, 1025–1031.

Kimura, J., 2001. Electrodiagnosis in Diseases of Nerve and Muscle: Principles and Practice. Oxford University Press, New York, p. 905.

Logroscino, G., Traynor, B.J., Hardiman, O., Chio', A., Couratier, P., Mitchell, J.D., et al., 2008. Descriptive epidemiology of amyotrophic lateral sclerosis: new evidence and unsolved issues. J. Neurol. Neurosurg. Psychiatry 79, 6–11.

Misawa, S., Hayakawa, S., Himuro, K., Sawai, S., Akaogi, Y., Ito, S., et al., 2010. Spinal myoclonus in the periscapular muscles after mastectomy assessed by FDG-PET. Clin. Neurol. Neurosurg. 112, 527–529.

Osaki, Y., Takamatsu, N., Shimatani, Y., Mori, A., Maruyama, K., Miyazaki, Y., et al., 2015. Ultrasonographic evaluation of myokymic discharges. Clin. Neurophysiol. 126, 1638–1639.

Shibasaki, H., 2000. Electrophysiological studies of myoclonus. Muscle Nerve 23, 321–335.

Shibasaki, H., Hallett, M., 2016. The Neurologic Examination: Scientific Basis for Clinical Diagnosis. Oxford University Press, New York, p. 172.

Termsarasab, P., Frucht, S.J., 2016. Myoclonus. In: Louis, E.D. (Ed.), Merritt's Neurology. 13th ed. Lippincott Williams & Wilkins, Philadelphia, pp. 660–665.