

SHORT REPORT

Electrophysiological study of diaphragmatic myoclonus

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Abstract

This is the first reported detailed electrophysiological study of diaphragmatic myoclonus. An 86 year old woman had rapid, intermittent epigastric pulsations. Neurological examination and imaging studies of the brain and spinal cord were normal. Needle EMG showed rhythmic contractions of the diaphragm and external intercostal muscles at 4 to 5 Hz. These contractions were often associated with suppression of normal breathing and were capable of maintaining adequate ventilation. Both diaphragms were involved but showed considerable variability in their relative latencies. Automated interference pattern analysis suggested a change in recruitment order, with selective activation of large phrenic motoneurons. The supraspinal mechanisms mediating diaphragmatic myoclonus are different from that of voluntary and involuntary rhythmic breathing, and seem to be unrelated to palatal myoclonus. The generator source is likely related to respiratory centres in the rostral medulla.

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Diaphragmatic myoclonus, also known as diaphragmatic flutter, is a rare disorder associated with repetitive, involuntary contractions of the diaphragm¹ and other inspiratory muscles.² Its pathogenesis is unknown and the pathophysiology has not been studied in detail. We report here the electrophysiological studies of a patient with diaphragmatic myoclonus and discuss its generating mechanisms. Because of the deep location of the diaphragm, surface EMG used in previous reports is imprecise and subject to contamination from chest wall muscles.^{2,3} We used needle EMG of the diaphragm, which allowed unequivocal demonstration of diaphragmatic activity, precise determination of onset latencies and firing patterns, and analysis of the interference pattern.

Methods

Nerve conduction, needle EMG, and median

nerve somatosensory evoked potential studies were performed with standard techniques. The techniques for phrenic nerve conduction studies and needle EMG of the diaphragm have been described.⁴ Monopolar needles were used for needle EMG. Needle EMG of the diaphragm was recorded with a digital audiotape recorder (Sony TCD-D3) for off line automated interference pattern analysis.

AUTOMATED INTERFERENCE PATTERN ANALYSIS

Our methods were modified from those of Nandedkar *et al.*^{5,6} Because the diaphragmatic motor units are generally smaller and more polyphasic than those of limb muscles, the following alterations were made: (1) The amplitude of a turn was reduced from 100 μ V to 50 μ V; (2) the small segment amplitude criteria was decreased to 300 μ V and duration criteria reduced to < 1.5 ms. We have validated these new parameters and obtained normal values with recordings from 25 normal subjects.⁷ Epochs of 500 ms were analysed and results were converted to represent one second. Envelope amplitude, which measures the largest motor unit action potential (MUAP), was defined as the fifth largest peak to peak amplitude in each 500 ms epoch. Activity represents the time within a one second period during which MUAPs were present.⁵ The envelope amplitude and number of small segments per second were plotted against activity for all the epochs analysed.

CASE HISTORY

An 86 year old woman had intermittent, pulsatile abdominal movements for one year. She complained of abdominal discomfort and difficulty falling asleep, but did not have any respiratory symptoms, hiccups or belching. These movements usually persisted for several hours at a time and occurred two to three times per day, but sometimes did not occur for several days. There were no known triggering factors. Observations in hospital confirmed that they did not occur during sleep. Her medical history showed congestive heart failure and complete heart block treated with a permanent pacemaker. She had no history of neurological diseases and she had never taken neuroleptic drugs.

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Examination showed rapid, fluttering epigastric pulsations occurring intermittently. They lasted from 10 seconds to several minutes at a time, stopped, and resumed after a variable period of several seconds to a few minutes. There were no abnormal movements in other parts of the body, including the palate. The remainder of her neurological examination was normal.

A chest radiograph showed mild cardiomegaly. Abdominal ultrasound and CT of the head were normal; CT of the cervical spines showed only minor spondylitic changes with no cord abnormalities. An electroencephalogram showed mildly excessive temporal theta activity but no discharges associated with the epigastric pulsations. Blood gases, including that after 10 minutes of epigastric pulsations, and pulmonary function tests were normal. Temporary stopping of the pacemaker did not alter the abnormal movements.

Treatment with clonazepam (0.5 mg per day) resulted in considerable reduction of the abnormal movements and the patient was no longer symptomatic. Higher doses were not tolerated because of excessive daytime drowsiness.

Results

NEEDLE EMG RECORDINGS

Needle EMG of both diaphragms showed

periods of normal respiration and periods of rhythmic bursts of activity at 4 to 5 Hz (fig 1, A and B), associated with epigastric pulsations. The duration of each burst of activity, timed over 12 bursts, ranged from 88 to 138 (mean 107) ms. The periods of diaphragmatic contractions lasted from a few seconds to 10 minutes. Tapping, auditory startle, or electrical stimulation over the chest, abdomen, face, arm, or leg failed to elicit the diaphragmatic contractions. Sometimes these movements were superimposed on a normal breathing pattern (fig 1A). During most of the recording, however, normal rhythmic breathing was completely suppressed (fig 1B), although the patient could still perform voluntary inspiration or expiration. The abnormal diaphragmatic contractions were capable of maintaining adequate ventilation, as we recorded suppression of normal respiration up to 10 minutes without any respiratory symptom. The contractions could be stopped temporarily by deep inspiration or breath holding, and would resume immediately after these manoeuvres.

The relation between the activity of the two hemidiaphragms was investigated by simultaneous needle EMG recordings. Both diaphragms invariably fired together and seemed to be synchronous at slow sweep speeds, but observations at high sweep speeds showed considerable jitter in their relative latencies. Over 16 bursts measured, the left diaphragm fired first in eight bursts and the right fired first in the other eight bursts. Their relative latencies, with positive values indicating that left preceded right and vice versa, ranged from +30.0 ms to -25.1 ms, with mean (SD) of -0.46 (16.9) ms.

Needle EMG of the external intercostal muscle, in the left seventh intercostal space, showed discharges of 4 to 5 Hz synchronous with epigastric pulsations. Needle EMG of the rectus abdominis, external oblique, levator scapulae, rhomboids, cervical (C3, 4, 5), and thoracic (T2, 7, 10) paraspinal muscles did not show any muscle activity associated with the epigastric pulsations.

AUTOMATED INTERFERENCE PATTERN ANALYSIS

Needle EMG of the left diaphragm was obtained from three different needle positions. Sixty three epochs of normal respiration, which included normal rhythmic breathing and voluntary deep inspiration, and 63 epochs of myoclonic diaphragmatic contractions were analysed. Myoclonic contractions had higher activity than normal respiration but the data points for both myoclonus and normal respiration were within the normal limits in the envelope amplitude-activity plot (fig 2A). Myoclonic contractions had a significantly lower number of small segments compared with normal respiration (fig 2B). There is little overlap between the two groups in the number of small segments-activity plot, with many points representing myoclonic contraction lying outside the normal range.

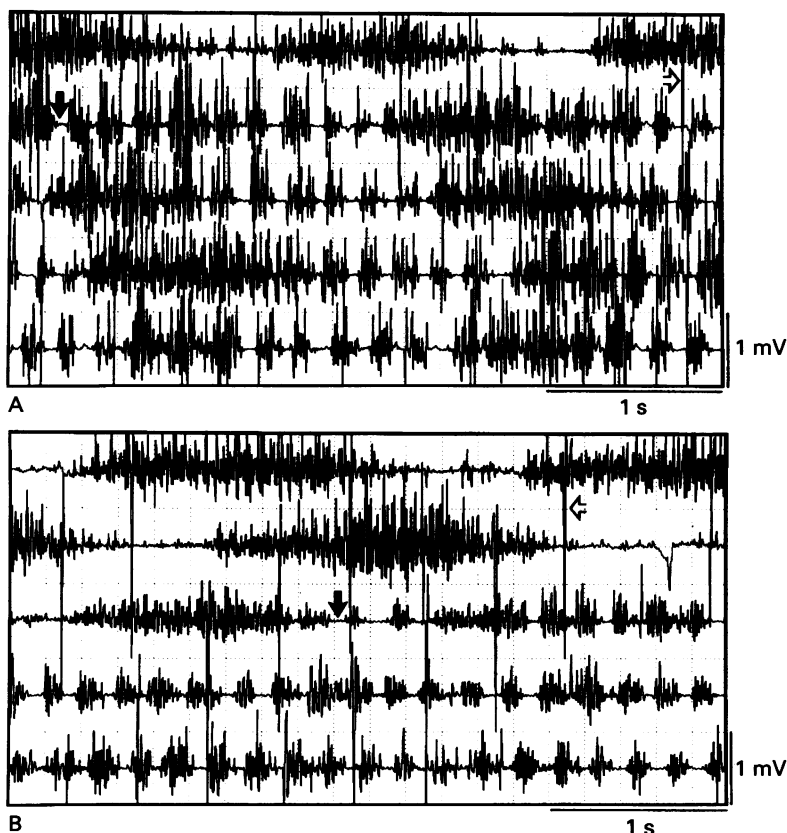
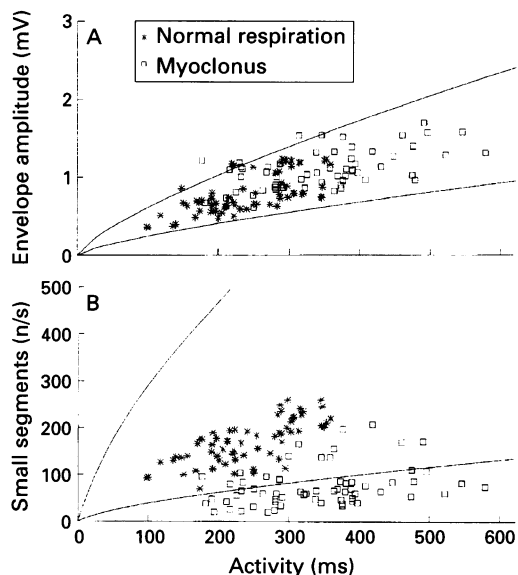


Figure 1 Needle EMG of the right diaphragm. (A) The first four seconds shows normal respiration with diaphragmatic activity associated with inspiration. The onset of myoclonic diaphragmatic activity of 4-5 Hz, superimposed on normal rhythmic breathing, is marked by the black arrow in the second line. (B) Rhythmic breathing occurs in the first 10 seconds and the onset of diaphragmatic myoclonus, with suppression of normal respiration, is marked by the black arrow. The open arrows point to pacemaker artifacts.

Figure 2 Automated interference pattern ("cloud") analysis of diaphragmatic EMG. The lines in each graph delineate the area that contains 90% of the epochs recorded from 25 normal subjects. (A) Plot of envelope amplitude against activity per second. The data points for normal respiration and myoclonus are both within normal limits. (B) Plot of number of small segments against activity. The data points for myoclonus have lower numbers of small segments and many points outside the normal limits.



The right median nerve somatosensory evoked potentials and nerve conduction studies, including phrenic nerves, were normal.

Discussion

Our patient had myoclonus strictly limited to inspiratory muscles, similar to some reported cases of diaphragmatic myoclonus.^{2,3} This condition is more commonly known as diaphragmatic flutter and was first described by Antony van Leeuwenhoek, "father of the microscope", who himself was afflicted with the disorder.² Diaphragmatic flutter is not a distinct disease entity, and can be caused by peripheral or central lesions. Cases associated with peripheral phrenic nerve irritation are usually unilateral.¹ Epigastric pulsation is the commonest manifestation,¹ but patients can also present with dyspnoea, respiratory distress,¹ hyperventilation,⁸ hiccups or belching,³ and difficulty weaning from the ventilator.⁹ In most cases the diaphragmatic contractions are intermittent¹ and may disappear during sleep,^{8,10} as found in our patient. The frequency of contractions ranged from 0.5 to 15 Hz,^{1,3} with most cases around 2.5 Hz.¹ These contractions are usually superimposed on a normal breathing pattern.^{1,3,8} Our patient is unusual in that normal breathing was often suppressed and yet the high frequency diaphragmatic contractions were adequate for ventilatory functions. This phenomenon has previously been reported in only one patient, after intravenous pethidine.⁸

Diaphragmatic myoclonus had been successfully treated with phenytoin,² carbamazepine,³ and haloperidol.⁸ Temporary effects were noted with benzhexol.¹⁰ In many cases phrenic nerve block or transection was used.¹ We chose clonazepam because of its efficacy in other cases of segmental myoclonus.¹¹ It was highly effective in our patient.

In automated interference pattern analysis, the number of small segments reflects the number of small amplitude MUAPs.^{5,12} The

decreased number of small segments in myoclonus is likely due to activation of only large amplitude motor units whereas normal respiration contains both large and small amplitude motor units. This cannot be accounted for by the motor units activated in myoclonus being closer to the recording needle by chance alone, as we recorded many motor units from three different needle positions and obtained similar results. Summation of different MUAPs firing simultaneously in myoclonus is also unlikely because the effect of motor unit summation on the mean amplitude of the interference pattern is minor compared with the amplitude of individual motor units and did not feature significantly in the calculation of the number of small segments.¹² The predominance of large amplitude MUAPs in myoclonus, therefore, is most likely due to a change in the recruitment order, with selective activation of large motoneurons. In normal muscle activity, large motoneurons are activated only after smaller motoneurons are recruited, in accordance with the size principle.¹³ This change in recruitment order is not simply secondary to the rapid onset of contraction as recruitment order is preserved in ballistic movements.¹⁴

The activation of different phrenic motoneuron pools in diaphragmatic myoclonus, compared with both quiet rhythmic breathing and voluntary deep inspiration, suggests that they are mediated by different supraspinal mechanisms. The dissociation between normal breathing and diaphragmatic myoclonus in our patient also suggests different generators for these rhythms. Other involuntary, non-rhythmic respiratory reflexes such as cough¹⁵ and hiccups¹⁶ are also believed to have central mechanisms independent of rhythmic respiration.

The cause of diaphragmatic myoclonus in our patient is unknown. In view of her age, the lack of progression of her symptoms and the normal imaging studies, a small vascular lesion seems to be the most likely cause. The origin of diaphragmatic myoclonus in our case and other cases with bilateral involvement^{1,2,8,10} is clearly central. A spinal cord generator source is unlikely in our case as both diaphragms, but no other C3 to C5 innervated muscles, were involved and there was no evidence of myelopathy. A cortical generator source is also unlikely because it cannot explain the isolated, bilateral inspiratory muscle involvement and voluntary breathing was not affected.

It has been suggested that diaphragmatic myoclonus is related to palatal monoclonus (tremor).² Symptomatic palatal myoclonus, however, is steady in intensity and not appreciably affected by sleep,¹⁷ and these are not features of diaphragmatic myoclonus. Isolated involvement of the palate and diaphragm, without involvement of the face, eyes, or arms, has not been reported. Moreover, the pathological features of symptomatic palatal tremor with hypertrophy of the inferior olive and lesions in the

dentato-olivary pathway has not been shown in diaphragmatic myoclonus. Therefore, palatal tremor and diaphragmatic myoclonus seem to be different conditions.

It seems likely that the generator source for diaphragmatic myoclonus is associated with the medullary respiratory centres, which can explain isolated, bilateral activation of inspiratory muscles. Experimental cold block in the rostral medulla causes a bilateral symmetric increase in respiratory rate.¹⁸ The jitter and bilateral involvement are similar to reticular reflex myoclonus, which likely originates in the rostral medulla.¹⁹ The considerable jitter in the relative latency of the two diaphragms suggests variable spread in a complex, polysynaptic pathway.

In conclusion, diaphragmatic myoclonus is associated with a change in recruitment order, with selective activation of large phrenic motoneurons. Its generator source is likely closely associated with medullary respiratory centres.

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