Determinants of diaphragm motion in unilateral diaphragmatic paralysis

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Scillia, Pierre, Matteo Cappello, and André De Troyer. Determinants of diaphragm motion in unilateral diaphragmatic paralysis. J Appl Physiol 96: 96–100, 2004. First published August 29, 2003; 10.1152/japplphysiol.00761.2003.—Cranial displacement of a hemidiaphragm during sniff is a cardinal sign of unilateral diaphragmatic paralysis in clinical practice. However, we have recently observed that isolated stimulation of one phrenic nerve in dogs causes the contralateral (inactive) hemidiaphragm to move caudally. In the present study, therefore, we tested the idea that, in unilateral diaphragmatic paralysis, the pattern of inspiratory muscle contraction plays a major role in determining the motion of the inactive hemidiaphragm. We induced a diaphragmatic paralysis in six anesthetized dogs and assessed the contour of the diaphragm during isolated unilateral phrenic nerve stimulation and during spontaneous inspiratory efforts. Whereas the inactive hemidiaphragm moved caudally in the first instance, it moved cranially in the second. The parasternal intercostal muscles were then severed to reduce the contribution of the rib cage muscles to inspiratory efforts and to enhance the force generated by the intact hemidiaphragm. Although the change in pleural pressure (ΔPpl) was unaltered, the cranial displacement of the paralyzed hemidiaphragm was consistently reduced. A pneumothorax was finally induced to eliminate ΔPpl during unilateral phrenic nerve stimulation, and this enhanced the caudal displacement of the inactive hemidiaphragm. These observations indicate that, in unilateral diaphragmatic paralysis, the motion of the inactive hemidiaphragm is largely determined by the balance between the force related to ΔPpl and the force generated by the intact hemidiaphragm.

METHODS

The experiments were carried out on six adult mongrel dogs (body weight 15–25 kg) anesthetized with pentobarbital sodium (initial dose 30 mg/kg iv), as approved by the Animal Ethics and Welfare Committee of the Brussels School of Medicine. The animals were placed in the supine posture and intubated with auffed endotracheal tube, and a venous catheter was inserted in the forelimb to give maintenance doses of anesthetic. The abdomen was then opened by a midline incision, and rows of five lead spheres (diameter of 4–5 mm) were stitched to the peritoneal surface and superficial muscle fibers of the left and right hemidiaphragms in the coronal midplane, as described in our laboratory’s previous communication (3). After the abdomen was sutured, the C3 and C6 phrenic nerve roots were isolated bilaterally through a midline incision of the neck, and the animal was placed supine in a radiolucent fabric sling. The C3 and C6 left and right phrenic nerve roots were then laid over two pairs of insulated stainless steel stimulating electrodes, and a differential pressure transducer (Validyne, Northridge, CA) was connected to a side port of the endotracheal tube to measure airway opening pressure (Pao).

The animal was connected to a mechanical ventilator (Harvard pump, Chicago, IL) and made apneic by hyperventilation, and anteroposterior radiographs of the lower rib cage and upper abdomen were taken first during relaxation at functional residual capacity, then during separate, supramaximal stimulation of the right and left phrenic respiratory muscles; mechanics of breathing

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nerve roots with the endotracheal tube occluded. Each nerve was stimulated successively at 15, 20–25, and 35–40 impulses/s. After completion of these measurements, the C5, C6, and C7 phrenic nerve roots were sectioned on the right side of the neck in three animals and on the left side in the other three, and spontaneous breathing was allowed to resume. When the breathing pattern was stabilized, the endotracheal tube was occluded at end expiration for a single breath, and a radiograph was taken at peak inspiration. Two occluded breaths were recorded in each animal.

In four animals, the rib cage was subsequently exposed on both sides of the chest from the first through the eighth rib, and the parasternal intercostal muscles in interspaces 1–7 were severed. Two occluded breaths were also recorded in this condition. These animals were finally reconnected to the ventilator, a pneumothorax was induced by sectioning the intercostal muscles laterally in the second left and right interspace, and the C5-C6 phrenic nerve roots on the active side were stimulated again at a frequency of 15 impulses/s.

Data analysis. In each animal, in each condition, we measured the change in Pao (ΔPao), the axial (cranio-caudal) displacement of the inactive hemidiaphragm, and the change in length of the active hemidiaphragm. The procedures used to make these measurements have been previously described in detail (3); by convention, a negative axial displacement indicates a displacement in the caudal direction, and a negative length change indicates a muscle shortening below its relaxation length (Lr). Stimulating the right or the left phrenic nerve at a given frequency produced similar changes in diaphragm configuration and length and induced similar ΔPao; these changes, therefore, were averaged for each individual animal. The changes observed in the two occluded breaths recorded before and after section of the parasternal intercostals were also averaged for each animal, and they were then averaged across the animal group. Statistical assessment of the effects of parasternal section on the changes during occluded breaths and of the effects of pneumothorax on the changes during phrenic nerve stimulation was made by using paired t-tests. The criterion for statistical significance was taken as P < 0.05.

RESULTS

The changes in diaphragmatic silhouette observed in a representative animal during isolated stimulation of the left C5-C6 phrenic nerve roots and during an occluded breath after section of the right phrenic nerve are reproduced in Fig. 1. As anticipated (3), stimulating the right or the left phrenic nerve (Fig. 1A) induced a fall in Pao and elicited a large shortening and caudal displacement of the ipsilateral hemidiaphragm, as well as a marked shift and tilt of the central tendon toward the stimulated side. The contralateral (inactive) hemidiaphragm also moved invariably in the caudal direction, and all of these changes increased progressively in magnitude as the frequency of stimulation was increased from 15 to 35–40 Hz. Consequently, both the fall in Pao and the caudal displacement of the inactive hemidiaphragm were closely related to the amount of shortening of the stimulated muscle fibers, as shown in Fig. 2.

The ΔPao obtained during occluded breaths in the six animals averaged (mean ± SE) −11.3 ± 1.2 cmH2O, which was similar to that measured during phrenic nerve stimulation at 15 Hz (−11.8 ± 1.3 cmH2O). However, whereas the amount of shortening of the active hemidiaphragm during 15-Hz stimulation of the phrenic nerve was −31.2 ± 0.8% Lr, during occluded breaths it was only −5.6 ± 0.7% Lr. Also, whereas the inactive hemidiaphragm moved in the caudal direction during phrenic nerve stimulation, during occluded breaths it moved in the cranial direction in every animal (Fig. 1B); for the six animals, this cranial displacement averaged 5.2 ± 0.7 mm. As a result, the data points obtained during occluded breaths lay well above the relationships obtained for phrenic nerve stimulation (Fig. 2).

The effects of sectioning the parasternal intercostal muscles on the changes occurring during occluded breaths in the individual animals studied are summarized in Fig. 3. Sectioning the muscles had no consistent effect on the peak ΔPao (before, −10.6 ± 1.8 cmH2O; after, −10.9 ± 1.1 cmH2O; P = not significant). However, the amount of shortening of the active hemidiaphragm increased substantially from −5.4 ± 1.0 to −10.2 ± 1.0% Lr (P < 0.02), and the cranial displacement of the inactive hemidiaphragm decreased from 4.5 ± 0.9 to 2.4 ± 1.1 mm (P < 0.02). In one animal (animal 4), this cranial displacement was even abolished.

The amount of diaphragm shortening observed during 15-Hz stimulation of the ipsilateral phrenic nerve remained unchanged in the presence of pneumothorax (before, −31.8 ± 1.2% Lr; after −32.7 ± 1.7% Lr; P = not significant). As shown in Fig. 4, however, the caudal displacement of the inactive hemidiaphragm was consistently greater than before.

![Fig. 1. Contours of the diaphragm seen on anteroposterior radiographs in a representative animal during relaxation (solid line), during isolated tetanic (25 Hz) stimulation of the left C5-C6 phrenic nerve roots (dashed line in A), and at the peak of an occluded breath after section of the right phrenic nerve (dashed line in B). The two short bars on each contour correspond to the junctions of the muscle fibers with the central tendon. The change in airway opening pressure was −14.5 and −13.0 cmH2O in A and B, respectively.](jap.org)
pneumothorax. For the four animals, this displacement thus increased from $7.2 \pm 2.3$ to $12.9 \pm 2.2$ mm ($P < 0.05$).

**DISCUSSION**

The present findings have confirmed our recent observation (3) that, in the dog, isolated stimulation of one phrenic nerve causes the contralateral hemidiaphragm to move caudally. In every animal, this caudal displacement increased gradually in magnitude as tension in the stimulated muscle fibers was increased (Fig. 2B). However, when the animals performed spontaneous inspiratory efforts after section of one phrenic nerve, the inactive hemidiaphragm moved cranially, and this difference is fully consistent with the idea that the pattern of inspiratory muscle contraction plays a major role in determining the direction of displacement of the paralyzed hemidiaphragm in unilateral diaphragmatic paralysis. Specifically, whereas selective stimulation of one phrenic nerve causes isolated contraction of the ipsilateral hemidiaphragm, occluded breaths involve coordinated contraction of one hemidiaphragm and the rib cage inspiratory muscles. The $\Delta P_{\text{pl}}$ during such breaths is therefore greater than anticipated on the basis of the hemidiaphragmatic contraction alone.

Previous studies have established that, in anesthetized dogs, the contribution of the parasternal intercostals to inspiration is much greater than that of the external intercostals (1, 4). Also, such animals do not contract the scalenes or the sternomastoids during breathing, including during breathing against elevated inspiratory airflow resistance (2). By severing the parasternal intercostals in all interspaces, it was therefore expected that the pressure contributed by the rib cage inspiratory muscles during occluded breaths would be markedly reduced and that the shortening of the intact hemidiaphragm would be enhanced. Indeed, after the parasternal intercostal muscles were sectioned, every animal showed a marked increase in the amount of shortening of the intact hemidiaphragm. Every animal showed a smaller cranial displacement of the paralyzed hemidiaphragm as well (Fig. 3). However, sectioning the parasternal intercostals did not cause any loss in $P_{\text{ao}}$ (pleural) during occluded breaths, which might have contributed to the observed decrease in cranial displacement. On the other hand, when a
pneumothorax was performed to eliminate ΔPpl during isolated unilateral phrenic nerve stimulation, the causal displacement of the contralateral hemidiaphragm was enhanced, even though the amount of shortening of the stimulated muscle fibers was unaltered (Fig. 4). These observations altogether thus lead to the conclusion that, in unilateral diaphragmatic paralysis, the direction of motion of the paralyzed hemidiaphragm is largely determined by the balance between ΔPpl and the degree of shortening of the contralateral hemidiaphragm. The present data, in fact, allow this balance to be analyzed in a more quantitative manner, as shown in Fig. 5. In this figure, the values (means ± SE) of axial motion of the inactive hemidiaphragm per unit length change of the contralateral (active) hemidiaphragm measured during isolated stimulation of one phrenic nerve with the chest intact, during occluded breaths before and after section of the parasternal intercostals, and during stimulation of one phrenic nerve after pneumothorax, are plotted on the y-axis, and the corresponding values of ΔPao per unit length change of the active hemidiaphragm are plotted on the x-axis. There was a close linear relationship (r = 0.998) between all of the data, such that, for a given shortening of the active hemidiaphragm, a larger ΔPao yielded a larger cranial displacement of the inactive hemidiaphragm. If the axial displacement of this hemidiaphragm is denoted A_in and the length change of the active hemidiaphragm is denoted ΔL_da, one can therefore write the following equation

\[ A_{in} / \Delta L_{da} = a + b(\Delta Pao/\Delta L_{da}) \] (1)

Rearranging this equation yields

\[ A_{in} = a \Delta L_{da} + b \Delta Pao \] (2)

The coefficients a and b thus describe the relative effects of the length change of the active hemidiaphragm and Pao (pleural) on the axial displacement of the inactive hemidiaphragm. Because the linear relationship yields a = 0.46 mm/% Lr and b = −0.70 mm/cmH2O, it may, therefore, be concluded that, in these animals, the caudal displacement of the inactive hemidiaphragm produced by a 3% shortening of the active hemidiaphragm counterbalances the cranial displacement produced by a ΔPpl of 1 cmH2O. In other words, the inactive hemidiaphragm would remain stationary during an inspiratory maneuver in which ΔPpl per unit shortening of the active hemidiaphragm is 0.65 cmH2O/% Lr; it would move cranially during inspiratory efforts, such as occluded breaths, with a ΔPpl-to-ΔL_da ratio of >0.65, whereas it would move caudally during efforts with a ΔPpl-to-ΔL_da ratio of <0.65, such as during isolated contraction of the contralateral hemidiaphragm (Fig. 2A).

The present demonstration that, in the dog, the displacement of a paralyzed hemidiaphragm is largely determined by the balance between ΔPpl and the amount of shortening of the intact hemidiaphragm should be applicable to humans as well. However, the central tendon in humans is more tightly attached to the mediastinal structures, in particular the pericardium, than in the dog. Therefore, it would be expected that contraction of one hemidiaphragm in humans would induce a smaller shift of the central tendon and a smaller lengthening of the contralateral, inactive muscle fibers. As a result, these fibers should develop smaller passive tension. Furthermore, the present studies and our laboratory’s previous observations (3) were made with the animals in the supine posture. In contrast, fluoroscopic examination of diaphragmatic displacement in clinical practice is generally performed with the subject standing, and a change from the supine to the standing posture is well known to elicit, through the action of gravity on the abdominal visceral mass, a substantial shortening of the diaphragm at end expiration. The standing posture, therefore, should enhance the reduction in passive tension in the diaphragmatic muscle fibers, and hence one would predict that, for a given ΔPpl-to-ΔL_da ratio, the displacement of the inactive hemidiaphragm in humans would be less caudal or more cranial than in the dog. In other words, the relationship shown in Fig. 5 would be displaced to the left, and the “stationary value” would be lower than that obtained in our animals (i.e., 0.65). And indeed, Sarnoff et al.
(7) have reported that isolated stimulation of one phrenic nerve in several subjects with pulmonary tuberculosis and one healthy individual causes only a moderate shift of the mediastinum and a slight cranial, rather than caudal displacement of the contralateral hemidiaphragm. Cranial displacement could be more prominent in patients with long-standing hemidiaphragmatic paralysis, in whom the paralyzed hemidiaphragm is atrophied (8) and may develop even less passive tension.

GRANTS
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REFERENCES