The Hering-Breuer reflex in anesthetized infants: end-inspiratory vs. end-expiratory occlusion technique

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1Department of Anaesthesia, Montreal Children's Hospital, Montreal, Quebec, Canada H3H 1P3; 2Portex Anaesthesia, and Intensive Therapy and Respiratory Medicine Unit, Institute of Child Health, London, WC1N 1EH, United Kingdom; and 3Department of Anaesthesia and Intensive Care, The Chinese University of Hong Kong, Hong Kong, People's Republic of China

Brown, K., J. Stocks, C. Aun, and P. S. Rabbette. The Hering-Breuer reflex in anesthetized infants: end-inspiratory vs. end-expiratory occlusion technique. J. Appl. Physiol. 84(4): 1437–1446, 1998.—Both end-inspiratory (EIO) and end-expiratory (EEO) occlusions have been used to measure the strength of the Hering-Breuer inflation reflex (HBIR) in infants. The purpose of this study was to compare both techniques in anesthetized infants. In each infant, HBIR activity was calculated as the relative prolongation of expiratory time during EIO and EEO, respectively. Respiratory drive was assessed from the change in airway pressure during inspiratory effort against the occlusion, both at a fixed time interval of 100 ms (P0.1) and a fixed proportion (10%) of the occluded inspiratory time (P10%). Twenty-two infants [age 14.3 ± 6.4 (SD) mo] were studied. No HBIR activity was present during EIO [−11.8 ± 15.9 (SD) %]. By contrast, there was significant, albeit weak, reflex activity during EEO [HBIR: 27.2 ± 17.4%]. A strong HBIR (up to 310%) was elicited in six of seven infants in whom EIO was repeated after lung inflation. P0.1 was similar during both types of occlusions, whereas mean ± SD P10% was lower during EEO than during EIO: 0.198 ± 0.09 vs. 0.367 ± 0.15 kPa, respectively (P < 0.01). These data suggest a difference in the central integration of stretch receptor activity in infants during anesthesia compared with during sleep.

healthy infants; halothane; sevoflurane; anesthesia; respiratory drive; control of breathing; Hering-Breuer inflation reflex
METHODS

Study Population

All infants were participating in a randomized controlled trial of the ventilatory effects of sevoflurane vs. halothane, the results of which are described elsewhere (2). The study population comprised infants aged 6–24 mo who were healthy, had fasted, had no history of cardiovascular disease or chest wall deformity, and were undergoing elective peripheral limb surgery or hypospadias repair. The study received institutional ethics committee approval and written informed parental consent.

Anesthetic Management

Patients were premedicated orally with atropine (20 µg/kg) and randomized to receive either halothane or sevoflurane in 33% oxygen in nitrous oxide (6 l/min) for induction and maintenance of anesthesia. All infants were monitored with pulse oximetry, which was maintained above 95% saturation. After induction of anesthesia, an appropriately sized laryngeal mask was inserted and the anesthetic vapor concentration was adjusted to 1 MAC (where 1 MAC, a measure of anesthetic depth, is the minimum alveolar concentration (MAC) of anesthetic required to prevent movement in 50% of the population). The age-adjusted MAC of halothane and sevoflurane were assumed to be 0.9 (14) and 2.5% (26), respectively. After induction of anesthesia, a regional block was performed with bupivacaine (0.25%). Infants received either a caudal block (0.75 ml/kg) for hypospadias and lower limb surgery or a brachial plexus block (0.5 ml/kg) for upper limb surgery. The patients were then placed in the supine position, and data recording commenced.

Recording Equipment

Airflow was measured with a heated Hans Rudolph pneumotachograph (no. 3500, linear range 0–35 l/min, Kansas City, KS) attached to a piezoresistive pressure transducer (±0.2 kPa, 431 SCXL0040N, Sensym, Milpitas, CA). Volume (V) was integrated digitally from the flow signal. The pressure at the airway opening (Pao) was measured with another pressure transducer (±5.0 kPa, 511 SCX010N, Sensym) via a side port attached to the laryngeal mask. A pneumatically activated, hand-operated balloon-type shutter (series 9300, Hans Rudolph) was used to produce EIO. To perform EEO, it was necessary to interpose an appropriately sized, nonrebreathing valve (Hans Rudolph 2200) between the pneumotachograph and the shutter to separate the inspiratory and expiratory airflow. Airway occlusions were timed from the real-time display of flow.

Flow was calibrated with rotameters, and the volume was validated with a volumetric 100-ml syringe (Hans Rudolph) containing the 66% nitrous oxide-in-oxygen mixture used for anesthetics. Pressure was calibrated against a water manometer. Pressure transducers were checked at the start and end of each study. At a flow of 100 ml/s, the resistance of the apparatus was 0.31 kPa·l⁻¹·s during EIO and 0.88 kPa·l⁻¹·s during EEO. The dead space of the measuring apparatus, estimated by water displacement, was ~9 ml. The analog outputs of flow and Pao were sampled at 100 Hz, digitized (Data Translation DT2801, Mississauga, Canada), interpolated, and recorded on a personal computer (ANADAT RHT InfoDat, Montreal, Quebec).

Protocol

After steady-state equilibration of the inspired anesthetic, a time period between 15 and 20 min, measurements of flow and Pao were recorded during spontaneous ventilation.

Data were collected during 1) baseline spontaneous ventilation, 2) respiratory efforts against an occluded airway after EIO, 3) respiratory efforts against an occluded airway after EEO, and 4) respiratory efforts against an occluded airway after a passive lung inflation. The EIO was performed at an occluded volume (Vocc) within 15% of end-tidal inspiration and held for the duration of a complete respiratory effort (Fig. 1A). The EEO was achieved by inflating the balloon shutter during expiration such that the subsequent inspiratory effort was occluded, thereby ensuring occlusion exactly at end expiration. The EEO was held for the duration of two consecutive respiratory efforts (Fig. 1B). A minimum of eight breaths was allowed between consecutive EIO and EEO. In addition, a single, passive lung inflation, coordinated with the onset of a spontaneous inspiratory effort, was performed whenever possible. The airway was occluded at a Vocc two to three times that of the spontaneous tidal volume (VT) (Fig. 1C).

Data Analysis

Acceptance criteria for the occlusion data were a stable end-expiratory level, no evidence of a volume leak (11), and a Vocc of zero during EEO and of at least 85% of the VT during EIO. Data within five breaths of a spontaneous sigh were excluded. An additional acceptance criterion during the inflation technique was evidence of a passive lung inflation coordinated with the spontaneous inspiratory effort.

Analysis of flow and volume VT and various parameters of ventilatory timing [the total cycle time (TT), inspiratory time (TI), TE and the inspiratory duty cycle (TI/TT)] were calculated. Reported values for the baseline spontaneous ventilation data were the mean of eight consecutive breaths. The Vocc was measured as the volume excursion between the prior end-expiratory level and the volume plateau during airway occlusion (Fig. 1, A and C).

Analysis of airway pressure. During the EIO, TEocc was measured from the expiratory zero flow crossing and rise in Pao to the onset of negative deflection on the Pao trace (Fig. 1A). TIocc was measured from the initial negative deflection to the upswing of the Pao trace. The effect of EIO on the duration of expiration (HBIRel) was assessed by the prolongation of Teocc relative to Te such that

\[
\text{HBIRel} [%] = \left( \frac{\text{Teocc} - \text{Te}}{\text{Te}} \right) \times 100
\]

During the EEO, both occluded inspiratory efforts obtained during EEO were analyzed. During airway occlusion, Tiocc was measured from the initial negative deflection to the upswing of the Pao trace (Fig. 1B). The effect of EEO on the duration of inspiration (HBIRint) was assessed from the prolongation of Tiocc relative to Ti during EEO such that

\[
\text{HBIRint} [%] = \left( \frac{\text{Tiocc} - \text{Ti}}{\text{Ti}} \right) \times 100
\]

A physiologically significant reflex was defined as an HBIR exceeding 25%, that is, when Te or Ti increased by at least 25% relative to baseline values during EIO and EEO, respectively. This value was chosen to represent the upper 95% confidence limits for within-subject variability of Ti or Te in infants (i.e., mean plus 2 SD) (35, 36).

Lung inflation. Inflation was analyzed in a similar fashion to that for EIO data (Fig. 1C). The effect of inflation on the duration of expiration (HBIRinf) was assessed by the prolonga-
Fig. 1. End-inspiratory occlusion (EIO; A), end-expiratory occlusion (EEO; B), and inflation technique (C) in an anesthetized infant. $T_{Eocc}$, occluded expiration; $V_{occ}$, occluded volume; $P_{max}$, maximal excursion of airway opening pressure ($P_{ao}$) during occluded inspiratory effort; $T_{E}$, unoccluded expiratory time; $T_{Iocc}$, occluded inspiration; $T_{I}$, unoccluded inspiratory time. Derivation of various indexes of respiratory timing and drive are also indicated. Note change in scale to accommodate larger lung inflation (C).
of spontaneous breathing, causing an increase in VT administered.

 Scatterplots indicate the type of anesthetic agent admin-
istered.

(i.e., techniques equivalent to 1 SD of the main outcome variables
such that measured mean HBIR EI was
shorter than TE in the majority of infants (Fig. 3A),
such that measured mean HBIR EI was −12% (Fig. 4, Table 1). Four of the five infants with values of HBIR EI below −25% were <12 mo old, and all but one had been anesthetized with halothane (Fig. 5). Many of the Pao waveforms showed an upward convexity during the brief TEocc, suggestive of some expiratory muscle activity.

EEO. Tiocc was significantly longer than the baseline
Ti in the majority of infants (Fig. 3B) such that the
mean HBIREE for the pooled data was 27.2 ± 17.4%
(Fig. 4, Table 2). No relationship between age and
HBIREE was seen (Fig. 5). The Tiocc, and hence HBIREE,
for the second EEO were similar to values for the first
occluded effort (Table 1). The mean (95% CI) difference in
HBIR (EIO – EEO) was −39% (−50, −29%, P < 0.01).

Respiratory Drive

Although the second inspiratory effort during EEO
was recorded in all 22 infants, data from one infant had
to be excluded because of an r² < 0.97 (see METHODS).
Values of P0.1, P10%, and Pmax for the second EEO were similar to those derived from the first EEO (Table 1).
Similar values for P0.1 were also obtained during EIO and
EEO. However, the mean Tiocc (0.4 s) during the
EIO was lower than that during EEO (0.7 s, P < 0.01).
When corrected for this shorter Tiocc, the respiratory
drive index, P10%, was lower during the EIO [mean (95%
During inflation, Vocc ranged from 10 to 23 ml/kg. To our knowledge, this is the first published comparison of paired measurements of the EIO and EEO technique in infants. These findings suggest an important influence of the technique on results in anesthetized infants, with respect to both the respiratory timing and drive components of the HBIR. Results obtained from the EEO technique indicated the presence of an active, albeit weak, HBIR in the majority of anesthetized infants, whereas results obtained from the EIO technique suggested that there was no physically significant HBIR over the tidal range. Furthermore, there were marked differences in respiratory drive according to the technique used. These results are in marked contrast to those reported in sleeping infants of similar age and suggest differences in the central integration of stretch receptor activity during anesthesia compared with sleep.

Unpublished data (35) of paired EIO and EEO measurements from naturally sleeping newborns showed a mean prolongation in TEocc and TIocc of 98 and 99%, respectively, suggesting that the two techniques give similar results when the strength of the HBIR is being assessed. More recently, these findings have been confirmed in 15 older infants (mean age 12 mo), in whom the strength of the HBIR was 48 and 44% during EIO and EEO, respectively (95% CI of difference: −14 and 22%; P. S. Rabbette, personal communication). The

Table 1. Comparison of ventilatory parameters before and during end-inspiratory and end-expiratory occlusions

<table>
<thead>
<tr>
<th>Parameter</th>
<th>EIO</th>
<th>EEO</th>
<th>2nd EEO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vt, ml/kg</td>
<td>6.2 ± 0.8</td>
<td>6.2 ± 0.9</td>
<td>As for EEO</td>
</tr>
<tr>
<td>Vocc, ml/kg</td>
<td>5.8 ± 0.8</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Tr, s</td>
<td>1.50 ± 0.3</td>
<td>1.53 ± 0.4</td>
<td></td>
</tr>
<tr>
<td>Ti, s</td>
<td>0.52 ± 0.1</td>
<td>0.54 ± 0.1</td>
<td></td>
</tr>
<tr>
<td>Te, s</td>
<td>0.98 ± 0.3</td>
<td>0.99 ± 0.3</td>
<td></td>
</tr>
<tr>
<td>Ti/Tt</td>
<td>0.35 ± 0.04</td>
<td>0.35 ± 0.04</td>
<td></td>
</tr>
<tr>
<td>HBIR, %</td>
<td>−11.8 ± 16.9*</td>
<td>27.2 ± 17.4</td>
<td>24.5 ± 13.7</td>
</tr>
<tr>
<td>P0.1, kPa</td>
<td>0.54 ± 0.37</td>
<td>0.58 ± 0.33</td>
<td>0.57 ± 0.27†</td>
</tr>
<tr>
<td>P10%, kPa</td>
<td>0.20 ± 0.09*</td>
<td>0.37 ± 0.15</td>
<td>0.37 ± 0.15†</td>
</tr>
<tr>
<td>Pmax, kPa</td>
<td>1.34 ± 0.50*</td>
<td>1.94 ± 0.81</td>
<td>2.12 ± 0.78*</td>
</tr>
<tr>
<td>Fgocc, s</td>
<td>0.87 ± 0.3</td>
<td>0.69 ± 0.2</td>
<td>0.67 ± 0.13</td>
</tr>
<tr>
<td>TIocc, s</td>
<td>0.42 ± 0.1†</td>
<td>0.79 ± 0.74</td>
<td>0.67 ± 0.13</td>
</tr>
<tr>
<td>HBIR inf, %</td>
<td>14 ± 3.15</td>
<td>25 ± 4.5</td>
<td>20 ± 5.0</td>
</tr>
</tbody>
</table>
| P10% (EIO − EEO)   | −0.17 kPa (−0.25, −0.09 kPa, P < 0.01) | (Fig. 6) | Pmax was also smaller (P < 0.01) during the EIO than during the EEO (Table 1).
reasons for these discrepancies are probably related to both specific effects of anesthetic agents on the control of breathing and to the reduction in both lung volume (9) and VT (4, 12) induced by inhalation of volatile anesthetics such as halothane (13). They might also reflect some interdependence between chemo- and mechanoreflexes because any degree of hypoventilation, such as commonly occurs in anesthetized subjects during spontaneous breathing (2), would be expected to inhibit HBIR activity (19, 20, 28). However, before the results can be interpreted more fully, it is necessary to consider factors that could have potentially influenced them.

Potentially Confounding Factors

Several aspects of the study design could have potentially influenced our findings. ANOVA suggested an effect of an anesthetic agent on the activity of the HBIREI, such that HBIREI was lower, and the relative increase in HBIR between the EIO and EEO techniques was greater, in those infants who received halothane. Rather than analyzing the two groups separately, which would have reduced the power of study, we have indicated which agent was used in all illustrations. Of importance, halothane affected the magnitude but not direction of the response (Figs. 3–5). No difference in HBIREI activity was observed between halothane and sevoflurane, which agrees with findings in adults (21).

Although infants were premedicated with atropine, an agent known to decrease vagal activity, the oral dose of 20 µg/kg is minimal compared with the

**Table 2. Results of inflation technique, arranged in ascending order of TEocc during the inflation, and corresponding EIO data**

<table>
<thead>
<tr>
<th>Infant</th>
<th>Inflation</th>
<th>Vocc, ml/kg</th>
<th>TEocc, s</th>
<th>HBIREI, %</th>
<th>T1occ, s</th>
<th>P10%, kPa</th>
<th>P10%, kPa</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10</td>
<td>0.89</td>
<td>-3</td>
<td>0.42</td>
<td>0.15</td>
<td>0.06</td>
<td>0.15</td>
</tr>
<tr>
<td>2</td>
<td>6</td>
<td>1.21</td>
<td>54</td>
<td>0.40</td>
<td>0.45</td>
<td>0.18</td>
<td>0.26</td>
</tr>
<tr>
<td>3</td>
<td>6</td>
<td>0.69</td>
<td>-12</td>
<td>0.36</td>
<td>0.73</td>
<td>0.26</td>
<td>0.42</td>
</tr>
<tr>
<td>4</td>
<td>15</td>
<td>1.61</td>
<td>82</td>
<td>0.25</td>
<td>0.74</td>
<td>0.19</td>
<td>0.19</td>
</tr>
<tr>
<td>5</td>
<td>6</td>
<td>0.90</td>
<td>-3</td>
<td>0.36</td>
<td>1.18</td>
<td>0.42</td>
<td>0.42</td>
</tr>
<tr>
<td>6</td>
<td>16</td>
<td>1.85</td>
<td>171</td>
<td>0.29</td>
<td>0.19</td>
<td>0.05</td>
<td>0.11</td>
</tr>
<tr>
<td>7</td>
<td>5</td>
<td>0.59</td>
<td>-16</td>
<td>0.31</td>
<td>0.35</td>
<td>0.11</td>
<td>0.11</td>
</tr>
<tr>
<td>8</td>
<td>23</td>
<td>2.66</td>
<td>44</td>
<td>0.59</td>
<td>0.26</td>
<td>0.15</td>
<td>0.15</td>
</tr>
<tr>
<td>9</td>
<td>5</td>
<td>1.91</td>
<td>-4</td>
<td>0.66</td>
<td>0.28</td>
<td>0.19</td>
<td>0.19</td>
</tr>
<tr>
<td>10</td>
<td>13</td>
<td>3.16</td>
<td>290</td>
<td>0.21</td>
<td>0.13</td>
<td>0.03</td>
<td>0.12</td>
</tr>
<tr>
<td>11</td>
<td>5</td>
<td>0.79</td>
<td>-4</td>
<td>0.34</td>
<td>0.34</td>
<td>0.12</td>
<td>0.12</td>
</tr>
<tr>
<td>12</td>
<td>11</td>
<td>3.71</td>
<td>310</td>
<td>0.33</td>
<td>0.08</td>
<td>0.03</td>
<td>0.03</td>
</tr>
<tr>
<td>13</td>
<td>5</td>
<td>0.95</td>
<td>3</td>
<td>0.39</td>
<td>0.41</td>
<td>0.16</td>
<td>0.16</td>
</tr>
</tbody>
</table>

HBIREI, relative prolongation of expiration during an EIO.
The intravenous dose required for ablation of a vagal response in dogs (1.5 mg/kg) (34).

The use of a laryngeal mask, positioned above the larynx, may have allowed vagally mediated volume-dependent modulation from the upper airway to influence the duration of inspiration (48). Weight-corrected VT was higher in this study than is usually reported during anesthesia (38), which probably reflects the lower resistive load imposed by a laryngeal mask compared with that by an endotracheal tube (39). As expected (30), the resistance of the occlusion devices changed the pattern of breathing compared with the unloaded pattern, resulting in an increase in VT and a slowing of respiration (Fig. 3). Nevertheless, VT remained lower than in nonanesthetized infants (37), which could have contributed to the diminished HBIR, as discussed below. Importantly, the need to use different devices for the EEO and EIO did not result in any detectable differences in the baseline ventilation between the two techniques (Table 1).

It has been suggested that, because stretch receptor activity is obviously dependent on volume changes, the magnitude of VT should be taken into account when the strength of the HBIR is being calculated (5, 15, 42). However, the model proposed by Grunstein et al. (15), which was developed from work in anesthetized cats, is not directly applicable to human infants, particularly when the relative strength of the HBIR at the extremes of VT is being investigated. While marked increases in VT do occur during early life, reflecting the rapid growth over this period, they are accompanied by parallel increases in respiratory compliance (37, 44). Consequently, elastic recoil of the respiratory system at end inspiration remains at ~1 kPa throughout the first year of life. This means that, under any given measurement conditions, a remarkably constant volume (and pressure) stimulus is presented to infants by occluding the airway at end inspiration, as indicated in this study by the consistency of the weight-corrected VT (Table 1).

Although the possible contribution of these methodological factors can be acknowledged, their potential influence seems too small to account for the magnitude of the difference in HBIR activity between EIO and EEO in anesthetized infants, with respect to both respiratory timing and drive components. Hence, other explanations need to be considered.

Respiratory Timing

Although stretch receptor activity is important in determining responses to both EEO and EIO, the actions at the level of central respiratory control differ. The lengthening of Ti during an EEO is believed to be due to an inhibition of inspiratory neurons, whereas the lengthening of Ti during an EEO is due to a lack of inhibition of inspiratory neurons during mid- to late inspiration. The pulmonary stretch receptors responsible for mediating the HBIR (10) are frequently separated into phasic and tonic components. The prolongation of Ti during EEO may reflect tonic changes induced by excitation of rapidly adapting irritant receptors, as well as the functional blockade of the slowly adapting receptors. By contrast, during EIO, the phasic activity of slowly adapting receptors causes progressive increases in Ti and hence inhibition of inspiration with progressive stretch receptor activity (20).

Experimental evidence suggests that lung volume is an important modulator of expiratory duration (45). In a canine model, a decrease in tonic lung volumes decreased expiratory duration (1). Alterations in end-expiratory lung volume also have a marked effect on expiratory duration in newborn infants (27), analogous to the vagally mediated control of Ti with changes in FRC reported in anesthetized animals (1). Indeed, the shortening of Ti and rise in respiratory rate associated with a reduction in end-expiratory lung volume has
been identified as an important mechanism to defend lung volume (22).

In this study, we found that although prolongation of 

TI did occur during EEO, as previously demonstrated in 

nonanesthetized infants (37), occlusion at end-tidal 

inspiration did not result in any inhibition of the 

inspiratory neurons and was frequently associated 

with a decrease in the duration of TEocc relative to TE 

(Fig. 4), resulting in a negative mean value of HBIREI of 

−12% (range −53 to 1%).

Potential Influence of Volume

Our results suggest that, during tidal breathing in 

anesthetized infants, a critical volume threshold suffi-

cient to elicit the HBIR during EIO had not been 

attained. An HBIREI of ~50% (range 26–125%) has 

been reported in 1-yr-old sleeping infants (37), in whom 

the volume stimulus of ~10 ml/kg was considerably 

greater than that observed in this study (~6 ml/kg). In 

addition, inhalational anesthesia is accompanied by a 

reduction in lung volume (9, 17). The volume stimulus 

at EIO was therefore undoubtedly lower in our study 

than that presented by using the same technique in 

healthy, sleeping infants (37). Indeed, the absolute lung 

volume of an anesthetized infant during EIO (i.e., the 

sum of FRC and VT) could well be lower than that at 

EEO in a nonanesthetized infant. It is of interest to 

note that, whereas in healthy infants the strength of 

the HBIR declines with increasing age (37, 44), in the 

present study the lowest levels of HBIREI activity were 

observed in the youngest infants (Fig. 5). This may 

reflect the fact that the reduction in lung volume 

associated with anesthesia is inversely proportional 

to age (9). The prolongation of TEocc relative to TE in all 

the infants in whom the airway could be occluded at 

volumes >10 ml/kg above FRC is consistent with the 

notion of a critical volume threshold to elicit the 

expiratory pause associated with the HBIR in infants.

Although the notion of a volume dependence for 

inspiratory-inhibitory activity in infants is consistent 

with present concepts of ventilatory control (37, 44, 47), 

additional mechanisms may have contributed to the 

shortening of TEocc during EIO, such as activation of 

expiratory muscles during halothane anesthesia (41). 

During this study, we noticed that Pao waveforms often 

showed an upward convexity during airway occlusions, 

consistent with active expiratory efforts. Anesthesia is 

known to be associated with a blunting of HBIR activity 

when measured by EEO (3, 21). The response of other 

pulmonary reflexes has also been shown to depend on 

the depth of anesthesia. The cough reflex, excited by 

tactile irritation of the larynx and trachea, is easily depressed, whereas the 

cough reflex to an identical stimulus is not (31). 

Therefore, the reflex arcs that mediate the inspiratory-

inhibitory activity of the HBIR measured by EIO or 

EEO may also exhibit a differential sensitivity to the 

anesthesia. During EEO, the intercostal-phrenic inhibi-

tory reflex (16) may have decreased the relative prolonga-

tion of TIocc resulting in a diminished HBIREE. 

Although this reflex has usually been observed only in 

preterm infants, the loss of intercostal tone and rise in 

chest wall compliance associated with inhalational 

anaesthesia could potentially have activated this reflex 
in at least some of the infants.

Respiratory Drive

Respiratory drive was lower when measured with the 

EIO technique than with the EEO technique. Contro-

versy has arisen regarding the validity of the occluded 

airway pressure waveform in infants because they are predis-

posed to chest wall retraction during an inspiratory 

effort, so that the contraction against the occluded 

airway may not be truly isometric (5). Analysis of the 
Pao, a mechanical transform of neural output, is there-

fore an imperfect method of assessing respiratory drive 
in infants.

The use of P0.1, i.e., Pao at the fixed interval of 100 

ms, has been used to minimize the behavioral and 

reflex modulation of the occlusion pressure (49). How-

ever, for any given respiratory drive, if the duration of 

inspiration were to shorten, the rate of change in pressure, and hence P0.1, would have to increase (5). 

Because the mean duration of TIocc was 0.7 s for the 

EEO compared with 0.4 s for the EIO, the potential 

influence of inspiratory duration on P0.1 must be consid-

ered. Furthermore, whereas a fixed interval of 100 ms 

represents <10% of TI in an adult breathing at 12 

breaths/min, it will be >30% of TI in an infant breathing 

at 30 breaths/min. Therefore, the use of a fixed 

propportion might better reflect breath drive in situa-

tions 

where TIocc is variable and deviates appreciably 

from 1 s.

In this study, P10% was higher during EEO than EIO 

(Fig. 7, Table 2). Although the duration of occlusion 

preceding the EIO inspiratory effort was longer than 

that of the EEO, it is improbable that chemoreceptive 

modulation of respiratory drive was an important 

influence because P10% and indeed all other indexes of 

respiratory drive and timing were remarkably similar 

during the first and second respiratory efforts.

Potential influence of lung volume on respiratory 

drive. Lung volume may influence P10% in two ways. 

First, it may alter the conformation of the diaphragm 

and thereby its resting length. However, studies in 

adult men are have shown either no (25) or minimal 

(29) effect of P0.1 with relatively large changes in lung 

volume. Furthermore, although configurational change 

in the curvature of the diaphragm may have occurred 

at the higher volumes achieved during inflations, this 

is less likely to have occurred with the relatively small 

Vocc of ~6 ml/kg during the EIO. This suggests that, 

unlike in the adult, the resting length of the infant's 

diaphragm may be affected by even small changes in 

lung volume, or that other mechanisms are involved.

Lung volume may also affect the performance of the 
diaphragm through vagal and nonvagal pulmonary 

reflex arcs (1, 18, 34, 40). Reflex-enhanced contractility 

of the diaphragm at the low lung volume associated 

with EEO in an anesthetized infant is equally plau-

sible.
Conclusions

During this comparison of HBIR activity by using the EIO and EEO techniques in 22 anesthetized infants, we found that both the drive and timing components of the HBIR depended on which technique was used. The EIO method suggested an inactive HBIR and lower respiratory drive compared with the EEO method. The suggestion of a different volume threshold for excitation in low-lung-volume states, which could also be relevant in nonanesthetized infants.

The finding of a higher respiratory drive, evidenced by a higher P10%, during EEO suggests a phasic volume stimulus affecting the measurement of respiratory drive and challenges the validity of a single value for respiratory drive in infants. Although the results apply primarily to anesthetized infants, a volume-sensitive, reflex increase in the contractility of the diaphragm, coupled with evidence of expiratory-inhibitory activity, may represent a protective reflex to defend alveolar ventilation in low-lung-volume states, which could also be relevant in nonanesthetized infants.

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