EFFECTS OF ACTIVE AND PASSIVE SIGHS IN NORMOXIA AND HYPEROXIA ON THE BREATHING OF PATIENTS ANAESTHETIZED WITH INFUSIONS OF PROPOFOL

N. W. GOODMAN AND A. C. DOW

SUMMARY
Spontaneous augmented breaths (active sighs) reduced the tidal volume and inspiratory time of succeeding breaths; manual lung inflations (passive sighs) reduced the tidal volume but had little effect on inspiratory time. Sighs in air, whether active or passive, reduced tidal volume more than sighs in hyperoxia (100% oxygen or 33% oxygen in nitrous oxide) after both active and passive sighs (overall difference about 10%); the reduction in inspiratory time after a sigh was less affected by gas mixture. Calculated mean inspiratory flow was reduced after passive sighs, but active sighs were more likely to cause arousal, which complicated the analysis. Tidal volume was reduced after a sigh partly because of reduced peripheral chemoreceptor input, the main effect of which was to reduce inspiratory flow, and partly because inspiratory time was shorter. Although the chemoreceptors may affect inspiratory time after a sigh, the greater effect of active sighs compared with passive sighs makes it likely that the shortening was either part of the neural output that causes spontaneous sighs, or was caused by mechanoreceptor input not mimicked by manual lung inflation. (Br. J. Anaesth. 1993; 70: 536–541)

KEY WORDS

Spontaneous sighs, or augmented breaths [1], transiently change the pattern of breathing. In patients anaesthetized with propofol, the succeeding breaths have shorter inspiratory times and reduced mean inspiratory flows [2], so their tidal volumes are smaller. These changes last about 10 to 20 breaths after the sigh. A sigh causes a transient alteration in the arterial partial pressures of carbon dioxide and oxygen, and these alterations are at least partly the cause of the altered breathing pattern. Khoo and Marmarelis [3] suggested using the response to a sigh to measure the gain of the peripheral chemoreflex. We have investigated the causes of the altered pattern by comparing the effects of spontaneous sighs, which we refer to as "active sighs", with the effects of manual inflations of the lungs, "passive sighs", in patients anaesthetized with propofol and breathing air or hyperoxic mixtures. Our hypothesis was that a sigh in hyperoxia would cause less disturbance than a sigh in air because of reduced peripheral chemoreceptor input; and that from the comparison between active and passive sighs we could show how much of the disturbance was caused by the change in chemical stimulus and how much by other factors.

A preliminary report has been made of this work [4]. Analysis of the effects of hyperoxia on the undisturbed pattern of breathing will be presented separately.

PATIENTS AND METHODS
Patients of slim build and with what we considered easily manageable airways were asked for their consent. We studied 19 patients (16 women), all ASA I, aged 23–52 yr and weighing 49–83 kg. Patients were prescribed a benzodiazepine for premedication if they wished (n = 9).

A venous cannula was placed in the non-dominant arm. A probe for pulse oximetry and a cuff for a non-invasive monitor of arterial pressure were attached. We did not intend to measure arterial pressure unless we were unhappy with the clinical condition of the patient, because of the inevitable disturbance to the breathing caused by arousal when the cuff inflates. Anaesthesia was induced with propofol and a laryngeal mask airway was inserted. Anaesthesia was maintained by a three-step reducing infusion starting at 13 mg kg⁻¹ h⁻¹, stepping after 10-min intervals to 11 mg kg⁻¹ h⁻¹, and then to 9 mg kg⁻¹ h⁻¹. The interval was prolonged if patients were lightly anaesthetized clinically. Patients started by breathing air and were later changed to breathing oxygen, or started by breathing oxygen and later breathed 33% oxygen in nitrous oxide. We used a Mapleson A system with flows of at least 10 litre min⁻¹. We did not change gas mixture or infusion rate within at least 100 breaths (about 5 min) of the other’s being changed, except to add oxygen 1–2 litre min⁻¹ if the saturation was less than 90%. This was necessary for a short time after induction when patients were breathing air, but for only two of these patients later during any study. On more than one occasion, changing from a finger to an ear probe improved the apparent saturation.

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If a patient sighed, we waited 30 breaths and then gave a matching passive sigh by squeezing the reservoir bag, while the patient was breathing in, to augment that breath to about the same tidal volume as the active sigh; otherwise we aimed for a passive sigh about 2.5 times the average tidal volume. In each patient, we aimed for one pair of sighs (one active and one passive) on the first gas mixture, and one pair on the other. If there was time, we changed gas mixtures again.

Breathing was recorded by respiratory inductance plethysmography (Respitrace model 10.9000), calibrated before induction of anaesthesia by double least squares linear regression against a pneumotachograph (Fleisch head: Godart pneumotachograph 7212), itself calibrated against a 1-litre syringe. The calibration and subsequent analysis were by computer program (BBC B+/Macintosh Ilsi running BBC Basic), as reported previously [5].

The change in tidal volume after a sigh is to about 70% of its preceding mean; the SD of tidal volume is about 10% of mean in the anaesthetized patient, but the tidal volumes of the active and passive sighs were normalized to a baseline before comparisons were made. For each sigh, we looked at the tidal volume, inspiratory time and expiratory time of the 10 preceding breaths, the sighs and the 20 succeeding breaths. For the active sighs, we also looked at abdominal contribution. We normalized each sigh to the mean of each variable for the five breaths preceding each sigh. The normalized breaths from all analysed sighs were pooled to give normalized means and 95% confidence limits (t distribution) on those means. For any given pooled breath, therefore, a mean was significantly different from the baseline if its 95% confidence limits did not include unity. Results are given as fractional values—that is, if a variable is given as 0.72, it is 72% of baseline.

Instead of multiple testing breath-by-breath, we used a summary measure of the effect of each sigh by taking a further mean value of the first group of five (normalized) succeeding breaths. Comparisons on pooled data were made by estimating confidence intervals on differences; comparisons on paired data (active sigh on air with passive sigh on air, or active sigh on air with active sigh on oxygen, from the same patient) were by Wilcoxon matched pairs signed rank test.

Correlation of size of sigh with response to the sigh was checked by a scatter plot and tested formally by Spearman Rank correlation.

Results

We recorded 46 active sighs and 44 passive sighs. Thirty-three active sighs and 37 passive sighs were analysable. Because we did not manage strict matched pairs (see Patients and Methods) of analysable sighs in all patients, our main analysis was of unpaired comparisons. Figures 2–4 are the pooled observations breath-by-breath; tables I and II are the summary observations, giving details of the sighs and of the group of five succeeding breaths.

Comparison between active and passive sighs

Overall, active and passive sighs were of similar tidal volumes, but the tidal volumes of the active sighs were largest with patients breathing air and smallest with patients breathing nitrous oxide in
TABLE II. Manual lung inflations (passive sighs) in patients anaesthetized with propofol and breathing different gas mixtures (mean (SD) [range] or mean (95% CL)). Values are normalized to the mean of the five breaths preceding the sigh. VT = tidal volume; TI = inspiratory time; TE = expiratory time; IF = inspiratory flow

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<tr>
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<th>VT of sigh</th>
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<th>VT of next 5 breaths</th>
<th>TI of next 5 breaths</th>
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<th>Mean IF (VT/VT) of next 5 breaths</th>
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<tr>
<td>All (n = 37)</td>
<td>2.42 (0.38) [2.03-3.60]</td>
<td>1.11 (0.23) [0.67-1.76]</td>
<td>1.18 (0.18) [0.85-1.79]</td>
<td>0.92 [0.89-0.95]</td>
<td>0.98 [0.96-0.99]</td>
<td>1.03 [1.00-1.06]</td>
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<td>Air (n = 10)</td>
<td>2.51 (0.49) [2.04-3.36]</td>
<td>— [—]</td>
<td>— [—]</td>
<td>0.84 [0.76-0.93]</td>
<td>0.96 [0.93-0.98]</td>
<td>1.06 [1.01-1.11]</td>
<td>0.88 [0]</td>
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<td>N₂O/O₂ (n = 11)</td>
<td>2.62 (0.29) [2.04-3.00]</td>
<td>— [—]</td>
<td>— [—]</td>
<td>0.96 [0.92-0.99]</td>
<td>1.00 [0.98-1.03]</td>
<td>1.03 [0.96-1.09]</td>
<td>0.95 [0]</td>
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<td>O₂ (n = 16)</td>
<td>2.70 (0.43) [2.03-3.60]</td>
<td>— [—]</td>
<td>— [—]</td>
<td>0.95 [0.91-0.98]</td>
<td>0.97 [0.94-1.00]</td>
<td>1.01 [0.96-1.05]</td>
<td>0.98 [0]</td>
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Active sighs Passive sighs

![Fig. 1](http://example.com/fig1.png)

![Fig. 2](http://example.com/fig2.png)

**Fig. 1.** A spontaneous augmented breath (active sigh), and a manual inflation (passive sigh) in a patient anaesthetized with propofol and breathing air. Top trace: time (seconds). Middle two: rib cage and abdominal output (uncalibrated, with inspiration upwards) from respiratory inductance plethysmography. Lower: capnogram (minimum is zero %, 1 large square = 1 %). Thirty breaths (about 1.5 min) separated the sighs. The active sigh was 2.95 * baseline; the mean of the five succeeding tidal volumes 0.84. The passive sigh was 2.67 * baseline; the mean of the five succeeding tidal volumes 0.87.

**Fig. 2.** Effect on tidal volume of active and passive sighs under propofol anaesthesia when breathing air and in hyperoxia. Breaths have each been normalized to the mean tidal volume of the preceding five breaths. Each point and error bar are the means and 95% confidence limits on those means calculated from the summed normalized breaths. The actual sighs are omitted.

Oxygen (table I). The tidal volumes of the passive sighs were not different between gas mixtures (table II). We have given only the overall figures for inspiratory and expiratory times of the sighs; both were prolonged more by active than by passive sighs (tables I, II).

Within the limits of measurement, active and passive sighs of similar tidal volume caused similar changes in end-tidal partial pressure of carbon dioxide (fig. 1). The tidal volume of active sighs correlated with the mean tidal volume of the next five breaths (Spearman’s ρ = -0.46; P < 0.01); there was no corresponding correlation for passive sighs (Spearman’s ρ = -0.08; P = 0.6).

The abdominal contribution to the active sighs was 63–127 % of baseline, with a mean of 94 % (95% CL = 89–99 %).

Tidal volume was reduced by about the same amount after active or passive sighs (fig. 2), but inspiratory time was reduced more after an active
than a passive sigh (fig. 3). Expiratory time is more variable and effects were not so easy to distinguish (fig. 4).

**Comparisons between gas mixtures**

Sighs, whether active or passive, had more effect on tidal volume when patients were breathing air than when they were breathing 67% nitrous oxide in oxygen (fig. 2). For active sighs, the difference was 0.17 (95% CL 0.07-0.27; P < 0.001); for passive

| Table III. Paired comparisons of spontaneous augmented breaths (active sighs: AS) and manual lung inflations (passive sighs: PS) in patients anaesthetized with propofol and breathing air or a hyperoxic mixture (ox). Values are normalized to the mean of the five breaths preceding the sigh. The number of comparisons is shown (n), and for each paired comparison: the means, the difference between the means, and the probability by Wilcoxon matched pairs signed rank test. \( V_t \) = tidal volume; \( T_I \) = inspiratory time; \( T_E \) = expiratory time.

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<td>( V_t )</td>
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Sighs with all three gas mixtures affected inspiratory time more if the sigh was active (fig. 3). Only sighs with air prolonged expiratory time, with the same proviso as above concerning variability (fig. 4).
Mean inspiratory flow (calculated as mean tidal volume divided by mean inspiratory time) was reduced after sighs with air but was greater for the five succeeding breaths of an active sigh with a hyperoxic mixture.

**Paired comparisons**

We were able to compare four groups of paired sighs: active sighs on air and passive sighs on air (n = 7, from five patients); active sighs with hyperoxic mixtures and passive sighs with hyperoxic mixtures (n = 17, from 13 patients); active sighs with air and active sighs with hyperoxic mixtures (n = 5, from four patients); and passive sighs with air and passive sighs with hyperoxic mixtures (n = 6, from five patients) (table III). Although small numbers make comparisons imprecise, the trend of the paired comparisons for tidal volume and inspiratory time supports the pooled data, in that tidal volume was affected by gas mixture more than by type of sigh and inspiratory time was affected more by type of sigh than by gas mixture. The change in expiratory time was inconsistent: active sighs with air prolonged expiratory time more than passive sighs with air, and active sighs with oxygen decreased expiratory time.

**Sighs not included for analysis**

Twenty sighs were not analysed (13 of them active sighs). Eight were part of—or triggered—an obvious arousal reaction (fig. 5, left), in which there was limb movement or transient tachycardia. Two sighs caused a short apnoea (fig. 5, middle). One passive sigh triggered an active sigh (fig. 5, right), and was excluded. Two active sighs occurred too soon after a change of gas mixture. Two could not be analysed because of sudden shifts in the Respitrace signal shortly after the sighs. The other five excluded sighs occurred when breathing was unstable or irregular, and the sigh was imposed on a pattern of changing tidal volume.

**DISCUSSION**

The alteration in breathing pattern caused by sighs was, in general, much as described previously [2]. The similarity of reduction in tidal volume after active and passive sighs, and the way this reduction was less in hyperoxia, supports the hypothesis that the reduction is mediated by the chemoreceptors.

As in the previous study [2], most (16 of 19) of our patients were women. We did not record stage of menstrual cycle, or if they were receiving oral contraceptives, so can make no comment on whether differences between patients were influenced in any way by progestagens.

Active sighs shortened inspiratory time more than passive sighs did, and gas mixture had less effect on inspiratory time than on tidal volume. We cannot say that the change in chemoreceptor input had no effect on inspiratory time (there may be some difference between the effect of passive sighs in air and in hyperoxia), but we suggest that much of the effect on inspiratory time is either an in-built response of the respiratory centre when the sigh is generated, or caused by a mechanoreceptor afferent response not mimicked by a passive sigh.

We could not distinguish an effect of nitrous oxide on the pattern after the sigh. Active sighs with nitrous oxide had smaller tidal volumes than sighs with either air or oxygen. We cannot say if this was because of the nitrous oxide. Overall, hyperoxic active sighs had smaller tidal volumes than active sighs with air, which could have affected the tidal volume response to the sigh. As tidal volume was also affected more after a passive sigh with air, when the tidal volumes of the actual sighs were not affected by gas mixture, we believe that hyperoxia does modify the tidal volume response.

What is clear from this study, and which we did not notice during the previous work, is that a sigh can cause, or is part of, arousal. One difference from
SIGHS UNDER PROPOFOL ANAESTHESIA

the previous study [2] was the use of the laryngeal mask airway. Afferents from the larynx form part of many reflexes in the control of breathing. It is unlikely that the laryngeal mask alters the general pattern of the response to sighs—our observations of the effect of active sighs was much the same in this study as in the previous one—but perhaps a sigh is more likely to cause arousal if there is a laryngeal mask in place. Arousal, easy to identify when accompanied by an increase in heart rate occurring with the sigh and continuing for a few beats, complicates analysis of the effects of sighs. The chemical change reduces the tidal volume, but arousal increases it, and there is no easy way of distinguishing between these opposing effects. If there was obvious arousal, we did not include that sigh in the analysis. Arousal was more common with active sighs than with passive sighs. When the arousal had subsided, breaths then followed the usual post-sigh pattern, but the smallest tidal volume after a sigh was the third or fourth breath or later.

We suggest that the increase in mean inspiratory flow after hyperoxic active sighs was caused by this arousal, and that the decrease in flow after hyperoxic passive sighs is a truer reflection of the effect of the change in chemical stimulus: less than occurs with air. In work on cats [6], the rate of increase in phrenic activity after spontaneous and provoked sighs was usually greater and the inspiratory time shorter after the sigh; this study did not include the effect of simple passive inflations.

There was correlation between the tidal volume of active sighs, but not of passive sighs, with the subsequent effect on tidal volume, which we suggest is because of the wider range of tidal volumes of active sighs. There are many sources of variability between tidal volume of sigh and effect: the calibration of inductance plethysmography varies with tidal volume; the end-tidal measurement of carbon dioxide is not the arterial partial pressure; and chemoreceptor reflex sensitivity varies between individuals.

As previously [2], the effect of sighs on expiratory time was unclear, partly because of its greater variability. The only unreported observation on expiratory time in anaesthetized patients about which we are certain is that the expiratory time of a passive sigh—of the breath on which it is imposed—is usually prolonged: the next breath is delayed. Bowes, Andrey and Kozar [7] reported in dogs that this prolongation did not occur if the carotid bodies were denervated. We saw no differences in the expiratory times of passive sighs between gas mixtures.

That a sigh can cause arousal, which then affects the ventilatory drive of a breath or two after the sigh, is another reason why the suggestion of Khoo and Marmarelis [3], of using the effect of a sigh to estimate the gain of the peripheral chemoreflex, might not be easy to apply to anaesthetized man.

REFERENCES