Breathing pattern during and after smoking cigarettes

MARTIN J. TOBIN, ANNE W. SCHNEIDER AND MARVIN A. SACKNER
The Jane & Edward Shapiro Pulmonary Suite, Division of Pulmonary Disease, Department of Medicine, Mount Sinai Medical Center, Miami Beach, Florida, U.S.A.

(Received 6 January 1982; accepted 7 June 1982)

Summary

1. The breathing patterns of ten habitual smokers were monitored in the semi-recumbent position with respiratory inductive plethysmography before and after smoking cigarettes. The subjects smoked a high-tar-content (HTC) and a low-tar-content (LTC) cigarette. The mean (±SD) values and frequency histograms of minute ventilation ($V_{min}$), tidal volume ($V_T$), frequency ($f_R$), inspiratory time ($T_i$), fractional inspiratory time ($T_i/T_{TOT}$) and mean inspiratory flow ($V_T/T_i$) during baseline were compared with the values during and after smoking.

2. On a separate occasion, specific airway conductance (sGaw) and multiple-breath nitrogen washout were measured before and after smoking in six of the subjects.

3. One group of smokers ($n = 4$) had a greatly increased mean (±SD) baseline $V_T/T_i$ (390 ± 39 ml/s) compared with normal non-smokers and another group ($n = 6$) a near normal $V_T/T_i$ (246 ± 36 ml/s). The first group ('deep inhalers') had a significantly higher mean inhalation fraction (volume of inhaled smoke and air/vital capacity; 0.25 ± 0.05). The second group had a lower mean inhalation fraction of 0.14 ± 0.03 ('moderate inhalers').

4. $V_T/T_i$ decreased to 323 ± 33 ml/s in the post-smoking period in the deep inhalers, whereas it increased to 345 ± 65 ml/s in the moderate inhalers during smoking. No systematic difference in $V_T/T_i$ was noted between smoking high- and low-tar cigarettes, although the high-tar brand tended to have a greater effect on $V_T/T_i$. Deep inhalers showed a fall in $V_T$ during and after smoking. Moderate inhalers showed a decrease in $T_i/T_{TOT}$ during and after smoking.

5. sGaw, measured in four moderate inhalers and two deep inhalers, fell in all subjects after smoking HTC (19± 8.7%; $P < 0.01$) and LTC (13.9 ± 10%) cigarettes.

6. ‘Sham’ smoking with an unlit cigarette produced no change in breathing pattern.

7. In moderate inhalers, the increase in respiratory output (as reflected by increased $V_T/T_i$) combined with a reduction in $T_i/T_{TOT}$ appears to reflect the respiratory-centre stimulant effect of nicotine directly or indirectly through bronchoconstriction. This contrasts with the reduced neural drive in deep inhalers, which may relate to some overriding satiating effect of the smoking.

Key words: breathing pattern, respiratory centre, respiratory inductive plethysmography, cigarette smoking.

Introduction

Studies of airway mechanics with spirometry and body plethysmography after acute smoking of cigarettes indicate a broad spectrum of responses ranging from bronchoconstriction through no effect to bronchodilation [1-6]. These inconsistent responses may be partly related to the various protocols of 'smoking challenges' and the variability in the time period after smoking at which the measurements were made, as the maximal effect of cigarette smoke on the airways appears to be brief [4]. Since cigarette smoke is an irritant [7], its inhalation might induce alterations in breathing pattern [8]. By monitoring the breathing pattern with non-invasive means throughout the smoking period, an acute change might be detectable that would have dissipated by the end of the smoking period.
Although changes in lung mechanics after acute smoking have been extensively investigated, we are unaware of any studies on respiratory-centre control despite animal data indicating that nicotine stimulates chemoreceptors and the respiratory centre [9-11]. It is now possible to monitor continuously an index of the components of the breathing pattern, mean inspiratory flow rate \( \left( \frac{V_T}{T_i} \right) \). This variable closely relates to standard indices of respiratory-centre output, such as mouth pressure generated at 0·1 s after the onset of inspiration against an occluded airway \( (P_{0.1}) \) and alteration in minute ventilation \( (V_{min}) \) during \( CO_2 \) stimulation [12, 13].

We examined the effect of smoking on the time and volume components of the breathing pattern using the respiratory inductive plethysmograph, a semi-quantitative non-invasive monitor of ventilation [14, 15]. The purpose of this study was to determine if cigarette smoking produced consistent alterations in the breathing pattern. We assessed the respective effects of high- and low-tar cigarettes and the contribution of intensity of inhalation on breathing pattern and airway mechanics.

**Methods**

**Subjects**

Ten smokers participated in this study. The study was approved by the Human Rights Committee of the hospital and informed consent was obtained from all subjects. All received financial remuneration. All completed a respiratory questionnaire, based on that of the British Medical Research Council. Information was obtained on the number of cigarettes smoked each day, age at which smoking was started regularly, whether smoke was inhaled and, if so, whether it was inhaled mildly, moderately or deeply. All had abstained from smoking for at least 3 h before the study.

**Pulmonary-function testing**

All subjects underwent pulmonary-function testing, including measurements of lung volumes by spirometry, functional residual capacity (FRC) and airway resistance (Raw) by body plethysmography, single- and multiple-breath nitrogen washout tests and maximal expiratory flow-volume curves with air and with a helium/oxygen (1:4, v/v) mixture.

**Apparatus**

A detailed description of the d.c.-coupled respiratory inductive plethysmograph (Respirtrace; Non-Invasive Monitoring Systems Inc., Ardsley, NY, U.S.A.) has been published by Sackner et al. [14]. Briefly, it consists of two coils of Teflon-insulated wire sewn into elastic bands encircling the rib cage (RC) and the abdomen (AB), which are connected to an oscillator module. Changes in cross-sectional areas of the RC and AB compartments alter the self inductance of the coils and the frequency of their oscillations, which, after appropriate calibration, reflect tidal volume measured by spirometry. Assuming that the respiratory system moves with two degrees of freedom [16], the device is calibrated using RC, AB and spirometer (SP) volumes and the equation RC/SP + AB/SP = 1 [15]. The subject breathes into a spirometer in two body postures to produce differences in rib-cage and abdominal contributions to tidal volume and the equation is solved graphically. Validation of the calibration of respiratory inductive plethysmography is performed against simultaneous spirometry in the upright and supine positions and the mean percentage error is calculated. In the present study, comparison of tidal volume measured by respiratory inductive plethysmography and spirometry showed a mean \((\pm SD)\) difference of 3·6 + 1·9%.

The signals from the respiratory inductive plethysmograph were recorded on a Grass Polygraph Recorder (Grass Instruments, Quincy, MA, U.S.A.) and a Z-80A-based microprocessor system (Respicomp; Respirtrace Corp., Ardsley, NY, U.S.A.), which sampled the signals at 20 points/s. It continuously calculated respiratory frequency \( (f_R) \), tidal volume \( (V_T) \), minute ventilation \( (V_{min}) \), inspiratory time \( (T_i) \), fractional inspiratory time \( (T_i/T_{TOT}) \) and mean inspiratory flow rate \( (V_T/T_i) \). The microprocessor system plotted the parameters in a variably compressed time scale, calculated the mean and standard deviation and displayed frequency histograms of each parameter.

The onset of puffing was detected by observing the cigarette-end glow and a signal was transmitted to the microprocessor system with an analogue step voltage. The system calculated the subsequent volume of air mixed with smoke inhaled into the lungs and the duration of inhalation with its associated breathhold from the sum signal of the respiratory inductive plethysmograph.

**Procedure**

**Experiment I: breathing pattern before, during and after cigarette smoking.** The subject rested in a semi-recumbent position on a bed for 15 min in
Breathing pattern during and after smoking cigarettes

475

a quiet room while watching television. There-
after, the breathing pattern was continuously
monitored for 15 min before smoking the first
cigarette. Throughout the study period, the
subjects remained in the semi-recumbent position
and were requested to limit body movements to
those involved in the act of smoking. The subjects
smoked two cigarettes with a 15 min interval
between each cigarette and monitoring was
continued for 10 min after the last cigarette. The
cigarettes were commercially available, high-
mg of tar, (4

\[ 1.8 \pm 0.4 \text{ mg of tar} \] (HTC) and low-tar
(4 mg of tar, 0.4 mg of nicotine) (LTC) brands.
The subjects were requested to smoke in their
natural manner.

Upon completion of the study, respiratory
inductive plethysmography was validated against
simultaneous spirometry and the mean (±SD)
percentage difference was 6.9 ± 4.0%.

In order to relate the inhaled volume of smoke
mixed with air to the subject’s size and body-
build, an inhalation fraction was calculated by
dividing the mean volume of inhalation of smoke
and air by the vital capacity. The mean volume
inhaled from the two cigarettes is reported since
no systematic difference in inhalation volume
between high- and low-tar cigarettes was noted.

Experiment II: pulmonary mechanics before
and after cigarette smoking. Six of the subjects
were available for the second experiment.
Baseline Raw, sGaw and multiple-breath nitro-
gen washout were measured and repeated im-
mediately and again 15 min after smoking a
high-tar-content cigarette. After 1 h, the same
measurements were performed before and after
smoking a low-tar content cigarette.

Experiment III: carboxyhaemoglobin
saturation. Measurements of blood carboxy-
haemoglobin saturation using the technique of
Henderson & Athorp [17] were made in four of
the subjects (one deep and three moderate
inhalers) before and 10 min after smoking an
HTC and an LTC cigarette, with a 15 min
interval between each cigarette.

Mock inhalation. In four subjects (one deep
and three moderate inhalers), the effect of 'sham'
smoking on breathing pattern was studied. The
subjects donned a respiratory inductive plethys-
mograph, which was calibrated and validated
against simultaneous spirometry and the mean
percentage difference was 4.7 ± 1.9%. The
subject rested in the semi-recumbent position for
15 min and thereafter the breathing pattern was
continuously recorded for 15 min. Using an unlit
cigarette, the subjects were requested to take 12
puffs from the cigarette and inhale in a manner
similar to that used during usual smoking. The
breathing pattern was then monitored for a
further 10 min.

Reproducibility of change in breathing pattern
before and after smoking a cigarette. On a
separate occasion, several months after the initial
study, the effect of smoking an HTC cigarette on
breathing pattern was re-studied in two deep and
three moderate inhalers. Validation of the res-
piratory inductive plethysmograph showed a
4.4 ± 2.2% deviation from spirometry. The
experimental protocol was identical with that for
‘mock inhalation’ except that the subjects
smoked an HTC cigarette.

Data and statistical analysis

When analysing the breathing pattern during
smoking, the microprocessor system excluded the
breath accompanying the puff and the preceding
and subsequent breaths as indicated by the
analogue step voltage. Exclusion of these breaths
did not produce a spurious reduction in the
respiratory frequency or minute ventilation
because the respiratory rate was calculated on the
basis of the reciprocal of the duration of each
breath \( (T_{TOT}) \) rather than the number of breaths/
min.

Values were expressed as means \((\bar{x})\) ± SD. Ten
minutes of baseline pre-smoking data were com-
pared with values obtained during smoking and
with values obtained during 10 min immediately
after smoking each cigarette. Differences between
the group mean values were analysed for signifi-
cance by the paired Student’s t-test, and were
considered significant at \( P < 0.05 \). The mean
response in the deep and moderate inhalers was
compared and analysed for significance by the
unpaired Student’s t-test, and was considered
significant at \( P < 0.05 \). To circumvent the
disadvantages of statistical calculations based on
grouped means, the microprocessor compared
the frequency histograms of each breathing
parameter during the pre-smoking, smoking and
post-smoking periods in individual subjects. This
was feasible because of the large number of data
points obtained with continuous monitoring, e.g.
over a 10 min period an average of 20
breaths/min produces 200 data points for each
time and volume component. A significant
monotonic trend in the data of each period was
considered present if the A’ value (a mathemati-
cal term denoting the total number of reverse
arrangements in the data being analysed) was
< 59 or > 130 \((P < 0.025)\) [18]. Differences
between the frequency histograms were analysed
for significance using the Mann–Whitney U Test
of the Medians and the Mann–Whitney U Test of
the Variability and were considered significant at $P < 0.05$. Group changes from baseline in the intra- and post-smoking frequency histograms were analysed by the single-classification chi-square test for independence.

**Results**

**Experiment I**

Respiratory questionnaire and pulmonary-function tests. Selected responses to the respiratory questionnaire are provided in Table 1. Baseline breathing pattern, pulmonary function and inhalation fraction. There was a wide variation in the baseline breathing patterns among the 10 subjects, with $V_T/T_i$ ranging from 201 ml/s to 443 ml/s. It was found that four of the smokers had much greater $V_T/T_i$ values (390 ± 39 ml/s) than normal non-smokers (228 ± 44 ml/s) (M. J. Tobin, T. S. Chadha & M. A. Sackner, unpublished work on 18 normal non-smokers), whereas six had near normal values (246 ± 36 ml/s). This separation was made on a retrospective analysis of the data. Further, the former group had an inhalation fraction of 0.25 ± 0.05 compared with 0.14 ± 0.03 in the latter ($P < 0.02$). We designated the first group 'deep inhalers' and the second 'moderate inhalers'.

Deep inhalers breathed with a greater $V_T/T_i$ than moderate inhalers ($P < 0.001$) and also had a greater $V_1$ ($P < 0.01$) and $V_{mln}$ ($P < 0.02$). Selected pulmonary-function indices (forced expiratory volume in 1 s, vital capacity, total lung capacity, functional residual capacity, airways resistance, maximal mid-expiratory flow rate and alveolar uniformity) showed no consistent difference in pulmonary function between the two groups except for volume of isoflow ($V_{iso}$; percentage of vital capacity) [19], which was significantly higher in deep inhalers (21.8 ± 1.7%) than in moderate inhalers (12.8 ± 9.0%) ($P < 0.05$). On regression analysis of inhalation fraction and baseline $V_T/T_i$, the correlation coefficient was +0.833 ($P < 0.005$) (Fig. 1).

![FIG. 1. Regression analysis of inhalation fraction and baseline mean inspiratory flow rate.](image)

### Table 1. Characteristics and smoking habits of subjects

<table>
<thead>
<tr>
<th></th>
<th>Deep inhalers</th>
<th>Moderate inhalers</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 2 3 4</td>
<td>5 6 7 8 9 10</td>
</tr>
<tr>
<td>Age (years)</td>
<td>31 37 38 39</td>
<td>23 39 23 31 20 32</td>
</tr>
<tr>
<td>Sex</td>
<td>F M M M</td>
<td>F M M F F M</td>
</tr>
<tr>
<td>Number of cigarettes per day</td>
<td>20–25 40 20–30 30–40</td>
<td>30 30 20–30 30 20 20</td>
</tr>
<tr>
<td>Age started smoking regularly (years)</td>
<td>17 16 14 15</td>
<td>16 16 16 18 17 12</td>
</tr>
<tr>
<td>Mean baseline tidal volume (ml) ± SD</td>
<td>527 ± 104 472 ± 166 700 ± 100 485 ± 101</td>
<td>401 ± 270 365 ± 80 328 ± 168 420 ± 215 298 ± 210 436 ± 250</td>
</tr>
<tr>
<td>Mean volume of inhalation (ml determined by respiratory inductive plethysmography)</td>
<td>694 1286 1104 1570</td>
<td>717 963 362 645 329 596</td>
</tr>
<tr>
<td>Inhalation index [volume inhaled/vital capacity (ml) × 100]</td>
<td>21.0 23.9 22.6 32.4</td>
<td>17.4 13.5 9.2 17.2 11.8 14.9</td>
</tr>
<tr>
<td>Mean duration of inhalation and breath-hold (s)</td>
<td>6.9 8.9 7.4 6.92</td>
<td>4.1 9.6 3.0 3.1 3.23 7.0</td>
</tr>
<tr>
<td>$V_{iso}$ (% vital capacity)</td>
<td>24 20 21 22</td>
<td>5 5 7 25 12 23</td>
</tr>
</tbody>
</table>
**Breathing pattern during smoking (Tables 2 and 4).** A monotonic trend was present in 13% of the data, including baseline, during-smoking and post-smoking periods. These trends were small, occurred in a random manner and were disregarded, since they did not affect overall comparisons made from the frequency histograms.

$V_T$ was significantly reduced by smoking in deep inhalers with both HTC and LTC ($P < 0.05$ and $P < 0.01$ respectively) cigarettes. Analysis of frequency histograms indicated that all four deep inhalers had a significant reduction in $V_T$ and variability of its measurement during smoking. Three of the six moderate inhalers showed an increase in $V_T$ while smoking, with no significant change for the group. No consistent changes in respiratory frequency were noted. There was a significant reduction in $V_{min}$ in deep inhalers while smoking LTC cigarettes ($P < 0.05$) and an increase in $V_{min}$ while smoking HTC cigarettes in the moderate inhalers ($P < 0.05$). Three of the four deep inhalers individually showed significant reductions of $T_j/T_{TOT}$ during smoking but the group means did not differ from baseline; a significant reduction in $T_j/T_{TOT}$ was observed while smoking both HTC and LTC cigarettes in the moderate inhalers ($P < 0.02$ and $P < 0.01$ respectively).

Mean $V_T/T_j$ (Fig. 2) did not change in deep inhalers but in the six moderate inhalers it significantly increased while smoking HTC cigarettes ($P < 0.02$) but not LTC cigarettes. The comparison of mean changes in $V_T/T_j$ between the two groups revealed significant differences during smoking, with deep inhalers showing a decrease and moderate smokers an increase in $V_T/T_j$ ($P < 0.01$).
Within groups, change from baseline to intra-smoking value was analysed by paired Student’s t-test. Comparison of change from baseline to intra-smoking values between deep and moderate inhalers was analysed by unpaired Student’s t-test. Results are means ± SD. Significant changes with groups are indicated by: * P < 0.05; ** P < 0.01. Significant changes between groups are indicated by: † P < 0.05; ‡ P < 0.01.

**Table 3. Comparison of change in breathing pattern between deep and moderate inhalers after smoking**

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>HTC cigarettes</th>
<th>LTC cigarettes</th>
</tr>
</thead>
<tbody>
<tr>
<td>$V_{\text{min}}$ (l/min)</td>
<td>Deep</td>
<td>9.17 ± 1.99</td>
<td>7.75 ± 1.28</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>6.00 ± 1.33†</td>
<td>6.29 ± 1.43†</td>
</tr>
<tr>
<td>$V_T$ (ml)</td>
<td>Deep</td>
<td>535 ± 86</td>
<td>430 ± 74**</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>376 ± 53††</td>
<td>379 ± 62††</td>
</tr>
<tr>
<td>$f_b$ (breaths/min)</td>
<td>Deep</td>
<td>17.7 ± 4.1</td>
<td>19.1 ± 5.4</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>16.8 ± 1.4</td>
<td>17.7 ± 1.8</td>
</tr>
<tr>
<td>$T_I$ (s)</td>
<td>Deep</td>
<td>1.38 ± 0.16</td>
<td>1.35 ± 0.26</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>1.58 ± 0.14†</td>
<td>1.39 ± 0.13**†</td>
</tr>
<tr>
<td>$T/T_{\text{tot}}$</td>
<td>Deep</td>
<td>0.40 ± 0.06</td>
<td>0.40 ± 0.04*</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>0.42 ± 0.03</td>
<td>0.38 ± 0.04*</td>
</tr>
<tr>
<td>$V_T/T_I$ (ml/s)</td>
<td>Deep</td>
<td>390 ± 39</td>
<td>323 ± 33**</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>246 ± 36††</td>
<td>282 ± 39††</td>
</tr>
</tbody>
</table>

**Table 4. Significant changes in the medians and variability of frequency histograms of breathing pattern during and after smoking in deep and moderate inhalers**

MW-M = Mann-Whitney U Test for the Medians; MW-V = Mann-Whitney U Test for Variability.

**Experiment II**

**Pulmonary functions** (Table 5). Lung mechanics were measured in four of the moderate inhalers and two of the deep inhalers. Immediately after smoking HTC cigarettes, all subjects showed a decrease in sGaw ranging from 6 to 26%, with a mean fall of 19 ± 8.7% (P < 0.01). This reduction was not related to the inhalation fraction of each subject and the decreases in the two deep inhalers were 26% and 22% and in the moderate inhalers they were 26%, 24%, 10% and 4%. At 15 min after smoking, mean sGaw for all six subjects was still 10% below the baseline value (P < 0.05).
Breathing pattern during and after smoking cigarettes

A less marked fall in sGaw was observed immediately after smoking LTC cigarettes with a mean decrease of $14 \pm 10\%$. In contrast with HTC cigarettes, the deep inhalers showed less decrease in sGaw compared with the moderate inhalers. Specific conductance (sGaw) at 15 min after smoking was comparable with the baseline value.

There were minimal changes in FRC with either cigarette. The multiple-breath nitrogen washout test showed two compartments in four subjects and a single compartment in two subjects (one a deep inhaler, the other a moderate inhaler). This distribution was not changed by cigarette smoking.

**Experiment III**

*Carboxyhaemoglobin levels.* There was wide variation in carboxyhaemoglobin levels in the four subjects before smoking (Table 6). Similarly, repeat measurements 10 min after smoking showed a variable increase in the subjects, which bore little relationship to the subjects' inhalation fraction.
Mock inhalation

The group mean volume inhaled during mock inhalation was 0.92 ± 0.33 litre compared with 0.59 ± 0.20 litre during subsequent smoking ($P = $ not significant). However, the duration of inhalation was longer during mock inhalation (7.7 ± 2.4 s compared with 4.2 ± 0.77 s during smoking) ($P < 0.05$). No significant changes took place in the breathing pattern (Table 7).

Reproducibility of change in breathing pattern after smoking an HTC cigarette

Repeat measurements of baseline breathing pattern and alteration after smoking an HTC cigarette in two deep and three moderate inhalers are listed in Table 8. The difference between baseline breathing pattern in the two groups is comparable with that observed in Experiment I. Similarly, the directional changes in breathing parameters after smoking an HTC cigarette follow the pattern observed in the first experiment, although the changes do not reach statistical significance because of the smaller number of subjects involved.

Discussion

Lung mechanics

All six subjects showed a significant reduction in specific airway conductance after smoking HTC cigarettes and an insignificant fall after LTC cigarettes. This is consistent with previous studies [1, 2] where airway narrowing was consistently observed after smoking but is in conflict with some recent reports showing a variable airway response after smoking [5, 6]. We found a greater airway response after smoking HTC than after LTC cigarettes, and this change was more prominent in the deep inhalers. By using non-commercial cigarettes of similar tar but varying nicotine content, Da Silva & Hamosh [4] noted that airway narrowing was less marked with low nicotine cigarettes. The absence of change in the multiple-breath nitrogen washout test is in agreement with a similar finding by Angelo et al. [3] and suggests that the acute airway response to cigarette smoking is probably localized in the larger airways.

Mean inspiratory flow

The response of the respiratory control centre to chemical or physical stimuli has been generally expressed in terms of minute ventilation ($V_{\text{min}}$). However, 50 years ago, Barcroft & Margaria [20] recognized that in elucidating the mechanisms regulating respiration, $V_{\text{min}}$ should be further analysed in terms of the duration of the phases of the respiratory cycle ($T_i$, $T_e$ and $T_{TOP}$) and the rates of air flow during inspiration and expiration. For the next 40 years, this analytical approach aroused little interest until the publication of Clark & von Euler’s work [21]. They

### Table 7. Effect of mock inhalation on breathing pattern in four subjects

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>After mock inhalation</th>
</tr>
</thead>
<tbody>
<tr>
<td>$V_{\text{min}}$ (l/min)</td>
<td>7.23 ± 1.17</td>
<td>7.14 ± 1.45</td>
</tr>
<tr>
<td>$V_r$ (ml)</td>
<td>386 ± 54</td>
<td>371 ± 53</td>
</tr>
<tr>
<td>$f_a$ (breaths/min)</td>
<td>18.9 ± 1.6</td>
<td>19.6 ± 0.95</td>
</tr>
<tr>
<td>$T_i$ (s)</td>
<td>1.38 ± 0.13</td>
<td>1.36 ± 0.17</td>
</tr>
<tr>
<td>$T_{TOP}$</td>
<td>0.43 ± 0.02</td>
<td>0.43 ± 0.01</td>
</tr>
<tr>
<td>$V_r/T_i$ (ml/s)</td>
<td>281 ± 39</td>
<td>281 ± 59</td>
</tr>
</tbody>
</table>

### Table 8. Reproducibility of effect of smoking HTC cigarettes on breathing pattern in two deep inhalers and three moderate inhalers

<table>
<thead>
<tr>
<th></th>
<th>First study</th>
<th>Second study</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>After HTC cigarettes</td>
</tr>
<tr>
<td>$V_{\text{min}}$ (l/min)</td>
<td>Deep</td>
<td>8.63 ± 1.46</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>6.82 ± 1.01</td>
</tr>
<tr>
<td>$V_r$ (ml)</td>
<td>Deep</td>
<td>501 ± 102</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>367 ± 47</td>
</tr>
<tr>
<td>$f_a$ (breaths/min)</td>
<td>Deep</td>
<td>18.4 ± 0.1</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>18.8 ± 2.0</td>
</tr>
<tr>
<td>$T_i$ (s)</td>
<td>Deep</td>
<td>1.40 ± 0.07</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>1.39 ± 0.15</td>
</tr>
<tr>
<td>$T_{TOP}$</td>
<td>Deep</td>
<td>0.41 ± 0.64</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>0.43 ± 0.03</td>
</tr>
<tr>
<td>$V_r/T_i$ (ml/s)</td>
<td>Deep</td>
<td>369 ± 63</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>264 ± 26</td>
</tr>
</tbody>
</table>
showed that the control of the breathing cycle consists of two mechanisms, a central inspiratory drive and a respiratory timing element that determines the duration of inspiration and expiration. Since the neural impulses controlling inspiratory drive are independent of reflex activity once inspiration has been initiated, the rate of inspiratory flow ($V_{TOT}/T_I$) reflects central inspiratory drive, as it is the mechanical transformation of this neural activity. A disadvantage of this index is that its final expression may be modified by the mechanical properties of the respiratory system, but, in the presence of normal to near normal mechanics, it correlates well with the standard indices of respiratory-centre output, $P_{0.1}$ and $V_{min}$ during CO₂ stimulation [12, 13, 20], despite variable changes in $V_T$ and $f_R$. All of our subjects had normal baseline $sgaw$. Furthermore, work in our laboratory has shown that methacholine-induced decreases in $sgaw$ of 25%, 35% and 55% produced parallel increases in $V_{TOT}/T_I$ [22]. This suggests that the changes in $V_{TOT}/T_I$ could be interpreted as an expression of respiratory-centre drive.

When our smokers were divided into two groups on the basis of baseline mean $V_{TOT}/T_I$, those smokers with greatly elevated values ($390 \pm 39$ ml/s) compared with normal non-smokers had higher inhalation fractions than the six with normal $V_{TOT}/T_I$ values ($246 \pm 36$ ml/s). In 18 normal non-smokers, the baseline semi-recumbent $V_{TOT}/T_I$ value was 228 ± 43 ml/s (M. J. Tobin, T. S. Chadha & M. A. Sackner, unpublished work). All subjects in this study had abstained from smoking for at least 3 h before the study, which might have been more stressful for the deep inhalers, as their daily consumption of cigarettes was also greater than the moderate inhalers. The resulting anxiety may have been reflected by the increased respiratory-centre output. Also, a higher level of circulating nicotine may have persisted in the deep inhalers than in the moderate inhalers, and so may have been responsible for the increased inspiratory drive [9–11], although serum nicotine levels were not measured. Another possibility is that since signs of small airway obstruction were greater in deep inhalers as reflected by a significantly higher $V_{iso\Phi}$, this may have stimulated stretch receptors within the airways resulting in a reflexly increased respiratory drive [22]. However, two of the moderate inhalers had an increased $V_{iso\Phi}$ without an increase in $V_{TOT}/T_I$.

During and after smoking, the pattern of change in $V_{TOT}/T_I$ markedly differed between the two groups. Since nicotine stimulates the respiratory centre either directly or through the chemoreceptors or both [9–11], a rise in $V_{TOT}/T_I$ would have been predicted during the smoking period. The airway narrowing consequent to smoking would have been expected to produce a further increase in respiratory-centre output, since development of minimal bronchoconstriction, i.e. a fall in $sgaw$ of 35%, causes an increase in $V_{TOT}/T_I$ [23]. The reduction in $V_{TOT}/T_I$ observed in the deep inhalers, which was more marked in the post-smoking period, was unexpected and might have been due to a reduction in neural drive related to a satiating effect of smoking that overcame the nicotine effect. One of the constituents in cigarette smoke might have acted directly or indirectly, through the release of endogenous substances, on the respiratory centre to diminish inspiratory drive. This central depressant effect might be related to reduced stress so often claimed by smokers [24].

Moderate inhalers showed an increase in $V_{TOT}/T_I$ during smoking, which persisted, albeit less markedly, into the post-smoking period. In previous animal studies of abnormal breathing patterns after inhalation of irritants, changes in $V_{TOT}/T_I$ have not been observed [25]. This increase in inspiratory drive is similar to that found after provocation of bronchoconstriction in normal and asthmatic subjects [23]. Cigarette smoke is known to produce bronchospasm and this may have been the mechanism for the increased inspiratory drive observed in the moderate inhalers. The rise in $V_{TOT}/T_I$ could have been further potentiated by nicotine stimulation of the respiratory centre [9–11].

That the changes observed in breathing pattern after smoking are related to some constituent in cigarettes (rather than simply a result of the respiratory manoeuvres involved in the act of smoking) is suggested by the absence of effect of ‘sham’ smoking on the breathing pattern.

Why only a proportion of patients with chronic airflow limitation develop CO₂ retention remains an enigma. It is not due to differences in respiratory mechanics, as pulmonary function is similar in patient cohorts with and without CO₂ retention. A reduction in inspiratory muscle activity in hypercapnic patients has been demonstrated in studies utilizing mouth occlusion pressures and diaphragmatic electromyogram [26, 27]. Studies of the pathogenesis of lung destruction in this disorder have been directed toward understanding the role of cigarette smoking as the most important risk factor but no attention has been paid to this factor to explain the development of CO₂ retention. Since smokers show marked variability in respiratory-centre output and some develop a significant reduction
in drive after smoking a cigarette, perhaps some constituent of cigarette smoke, directly or indirectly, may contribute to the development of hypercapnia in those smokers who subsequently develop chronic airflow limitation.

**Pattern of breathing**

In this study, we show that changes in the breathing pattern during and after smoking correlated with the baseline respiratory drive and the depth of smoke inhalation. The deep inhalers developed a fall in tidal volume during smoking and a decrease in mean inspiratory flow in the immediate post-smoking period. The moderate inhalers showed a pattern of increased mean inspiratory flow during smoking. The difference in the change in \( V_{T}/T_{i} \) during smoking in the two groups was considerable, with a maximal reduction of 18% in the deep inhalers and a maximal increase of 17% in the moderate inhalers. Both groups showed a decrease in \( T_{i} \) and \( T_{i}/T_{TOT} \), which was greater in the moderate inhalers. The decrease in \( T_{i} \) may be due to a central effect of cigarette smoke on the rhythmicity of the respiratory centre or local activation of pulmonary reflexes by stimulating irritant, stretch or J-type receptors [28]. Although both \( T_{i} \) and \( T_{E} \) were reduced with smoking the decrease in \( T_{i}/T_{TOT} \), particularly in the moderate inhalers, indicates a relative shortening of \( T_{i}/T_{TOT} \). This may be related to the development of airflow limitation during expiration, with relative prolongation of \( T_{E} \) [29]. This is consistent with the increased \( V_{T}/T_{TOT} \) seen in this group, which has been observed to occur with minimal and graded increase of bronchoconstriction [22, 23].

In contrast with the change in breathing pattern observed in our study, Rees & Clark reported the breathing pattern during 3 min of smoking and noted a consistent increase in \( V_{T} \) with a marginal increase in \( T_{E} \) [30]. Using only a single pair of magnetometer coils, these authors did not account for the fact that the respiratory system moves with two degrees of freedom [16]. It is not clear if the breaths taken during actual inhalation of the smoke, with its associated breath-hold, were included or excluded from the data analysis. Changes in breathing parameters other than \( V_{T} \), \( T_{i} \) and \( T_{E} \) were not reported, nor did they relate changes in breathing pattern to depth of smoke inhalation. They stated that the volume of inhalation was approximately twice the tidal volume, but provide no information on the degree of variation in depth of inhalation. In our subjects, the volume of inhalation varied from 1.1 to 3.2 times the tidal volume. A significant decrease in \( V_{T} \) was observed in our deep inhalers with no significant change in moderate inhalers and unlike the bradypnoea observed by Rees & Clark [30], our subjects showed a reduction in \( T_{i} \) and \( T_{i}/T_{TOT} \).

Animal studies [7, 8, 25, 31] have shown that mechanical or chemical stimulation of irritant receptors produce an abnormal breathing pattern characterized by rapid shallow breathing. However, as pointed out by Guz [32] none of the wide variety of stimuli used in these experiments are specific to these receptors. Also, unlike animals, humans can report if they feel that their airways are being irritated. In our study, deep inhalers had reduced tidal volume with no significant increase in \( f_{R} \) and moderate inhalers an increase in \( V_{T} \) with smoking. Overall, the magnitude of change was much less than that observed in animal studies and despite smoking two cigarettes in less than 20 min our smokers did not complain of an irritant effect.

**Acknowledgments**

We are grateful to Mr Donald G. Ford for performing the pulmonary-function testing and Mr Gilbert Jenouri for performing the measurements of blood carboxyhaemoglobin saturation. This work was supported in part by the National Heart, Lung and Blood Institute (Grant no. HL 10622).

**References**

Breathing pattern during and after smoking cigarettes


