How do patients with either asthma or COPD perceive acute bronchodilation?

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ABSTRACT: The purpose of this study was to assess the perception of bronchodilation, as a change in shortness of breath on a bipolar visual analogue scale (VAS), in 16 asthmatics and 20 subjects with COPD.

Bronchodilation was gradually induced by five consecutive terbutaline inhalations (cumulated dose 800 μg). The subjects were categorized into high and low perceivers, on the basis of a cut-off of 25% VAS line length (after the fifth inhalation). The quality of perception was studied on a within-subject basis by linear regression analysis of VAS ratings against changes in lung function, and was characterized in terms of strength of correlation (squared correlation coefficient, r²), slope, and VAS axis intercept.

Fourteen out of 16 asthmatics, and 13 out of 20 COPD subjects, were high perceivers. In the COPD group, the high perceivers had a larger objective response - particularly in inspiratory vital capacity - than the low perceivers. The strongest correlation between subjective and objective response was obtained in asthmatics when the improvement in shortness of breath was evaluated against the decrease in specific inspiratory resistance (median r²=0.831). In COPD low perceivers, subjective and objective response were unrelated, while COPD high perceivers differed from the asthmatics by larger intercepts. The perceptual characteristics were unrelated to the degree of baseline obstruction, whilst a modest relationship (r=-0.51) was found between the increase in forced expiratory volume in one second (FEV₁) and r² of the VAS/FEV₁ analysis.

In conclusion, having characterized the perception of terbutaline-induced bronchodilation, we found that some COPD subjects differed from the asthmatics in that they perceived at a low level, without relationship between VAS ratings and objective response. Other COPD subjects compared well with the asthmatics in terms of strength and slope of the VAS/change in lung function relationship, but differed by a larger intercept, suggesting the presence of a placebo effect.

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In the recent years, there has been a growing interest in the assessment of the perception of airway obstruction by patients with either asthma or chronic obstructive pulmonary disease (COPD). Indeed, respiratory scientists are interested in understanding the physiopathology of respiratory sensations, and there is an increasing awareness that an adequate perception of the severity of airway obstruction is an important key for successful clinical management of these patients. Perception of baseline obstruction and of its spontaneous within-day variability has been reported to be poor in subjects with asthma [1]. Little attention has been given, until now, to the perception of acute changes in airway obstruction measured in the lung function laboratory. Wolkove et al., [2] using a Borg scale, studied the perception of bronchodilation induced by a single salbutamol dose in a large group of COPD subjects, and found no relationship between the subjective responses and the changes in forced expiratory volume in one second (FEV₁). Methodological limitations in the latter study included the use of a Borg scale to assess the perception of bronchodilation in subjects who claimed not to be breathless at all at baseline, and the restriction of lung function analysis to a forced expiratory manoeuvre.

In a previous study [3], in patients with either asthma or COPD, we used a bipolar visual analogue scale (VAS) to assess the subjective perception of an acute inhalation of either saline or terbutaline. This scale allows naive subjects to report either improvement or worsening when moving off from a no change midpoint. This preliminary study suggested that the sensitivity of this scale to bronchodilation is larger in asthmatics than in COPD subjects [3].

The aim of the present study was to further characterize the subjective perception of bronchodilation by these two groups of patients, who inhaled progressively increasing doses of terbutaline. The objective response to terbutaline was monitored by measuring the specific
airway resistance during tidal breathing, as well as the forced inspiratory and expiratory manoeuvres [4]. We studied the relationship between the subjective perception and the changes in lung function indices recorded in the two groups. As there was a suggestion in our previous study that the terbutaline-induced changes in VAS ratings and those in FEV₁ were correlated in subjects with asthma, but not in subjects with COPD, we particularly wished to compare the perceptual aptitude of asthmatics versus COPD subjects.

Patients and methods

Patients

Thirty six out-patients attending the Chest Clinic agreed to participate in a study about respiratory sensations at rest. All had airway obstruction, with a FEV₁ <60% predicted and an FEV₁/inspiratory vital capacity (IVC) ratio <65%. A condition for entry into the study was that lung function testing, including a bronchodilation test with 200 μg salbutamol delivered by a metered dose inhaler, had been previously performed at least three times (with at least one week interval) over a time span of at least 3 months. Subjects were classified as having either asthma or COPD using the criteria that we have described previously [3]. Briefly, the diagnosis of asthma was retained in a lifetime nonsmoker subject with a history of episodic breathlessness and wheeze, provided an increase in FEV₁ exceeding 15% predicted [5, 6] had been obtained at least once following 200 μg salbutamol. The diagnosis of COPD was retained in a smoker or ex-smoker with a history of chronic cough, sputum production and dyspnoea on exertion, provided none of his/her ∆FEV₁ values exceeded 10% predicted.

Sixteen subjects (9 men, 7 women) were considered as having asthma, and 20 (13 men, 7 women) as having COPD. Their anthropometric features were (mean, SEM): age 60 (4) yrs, height 163 (2) cm, weight 65.0 (2.7) kg in the asthma group; and age 62 (3) yrs, height 168 (2) cm, weight 68.9 (3.9) kg in the COPD group. COPD patients were predominantly ex-smokers (17 out of 20). Maintenance drug therapy included (by decreasing frequency) inhaled steroids (n=15), inhaled sympathomimetics (n=14), oral steroids (n=9), oral theophylline (n=7), and inhaled anticholinergics (n=4) in the asthma group, inhaled sympathomimetics (n=14), inhaled steroids (n=13), oral theophylline (n=11), inhaled anticholinergics (n=7), and oral steroids (n=3) in the COPD group. One COPD subject had no regular therapy.

Study design

All of the subjects gave informed consent, and the study protocol was approved by the Ethics Committee of the Hôpital Universitaire Brugmann. The study consisted of consecutive inhalations of terbutaline, with assessment of subjective perception and of lung function, and was single-blind, with the supervisor knowing which agent was inhaled, whilst the subject did not. All of the subjects were naïve to sensory evaluation. All sessions started at 3 pm, and all subjects were asked to abstain from inhaled bronchodilators from 7 am. Oral theophylline preparations were withheld 48 h before testing. Oral and inhaled steroids were not withheld.

After arrival in the lung function laboratory, each subject rested comfortably on a chair for 10 min, and full explanation was given about the method used to evaluate the subjective perception. Baseline lung function was then measured. The patient was then given the first inhalation, and thereafter rested in the sitting position. After a 2 min interval, the subject was invited to rate the change in shortness of breath, and lung function was measured again. Further inhalations were given, and the procedure of subjective response rating and lung function measurement was repeated at each step.

No systematic record of the side-effects from the aerosols was made, but subjects were invited to comment about any possible symptom during the study, as well as about possible difficulties in using the VAS.

Dosage of inhaled agents

A Mefar MB3 dosimeter (Medicali, Brescia, Italy), activated by the subject’s inspiratory manoeuvre, was used [7]. The method of inhalation was the same as that used in our previous study [3]. The solutions used were 1:8 (first two steps), 1:4 (third step), and 1:2 (fourth step) dilutions, followed by the undiluted commercially available 10 mg/ml¹ terbutaline solution (fifth step). The cumulated doses so obtained were 50, 100, 200, 400 and 800 μg terbutaline.

Visual analogue scale

The procedure used to rate the change in shortness of breath using a bipolar VAS [8] was fully described previously [3]. The method used in the present study was the same, with the addition of one minor point: in case of airway obstruction aggravated by the effort of blowing [9], the VAS was shown to the subject immediately after blowing, to obtain an initial measurement before the first inhalation.

Lung function

The methods used for lung function measurements have been fully described previously [3]. Briefly, plethysmography measured the specific inspiratory (sRin), and the specific expiratory resistance (sRex), whilst expiration from total lung capacity of a forced vital capacity (FVCex), followed by inspiration of a forced vital capacity (FVCin), allowed expiratory and inspiratory flow-volume curves to be obtained. Predicted values were those currently used in our department [10].
Statistical analysis

The size of bronchodilation induced by 800 µg terbutaline was reported in terms of median values with 95% confidence intervals calculated using a non-parametric analysis [11]. The Wilcoxon rank sum test was used to compare independent samples (threshold of significance p<0.01). The relationship of the subjective perception assessed with the VAS (reference point: beginning of the session) to the changes in lung function was studied using a linear regression analysis on a within-subject basis, with five points included in each regression. Functional indices studied were sRin, sRex, functional residual capacity (FRC), IVC, FVCex, FEV₁, maximal expiratory flow at 50% FVC (MEF₅₀), FVCin and maximal inspiratory flow at 50% FVC (MIF₅₀). Changes in lung volume were expressed as % predicted, changes in sRin and sRex as cmH₂O·s, and changes in MEF₅₀ and MIF₅₀ as l·s⁻¹.

For each index, the strength of the correlation was assessed as the squared correlation coefficient (r²). In the VAS/ΔFEV₁ and VAS/ΔsRin analyses, attention was also focused on the slope of the regression, and on the VAS axis intercept, the latter defining the perceived change in shortness of breath when no change had occurred in lung function. The relationship of r², slope, and intercept values with the baseline function and with the amount of induced bronchodilation was subsequently examined by linear regression (threshold of significance: p<0.05). The influence of baseline lung function was also studied using the VAS ratings at FEV₁ levels equal to baseline plus 10% predicted (VASₘₐₓ) calculated by interpolation or extrapolation from the individual regression lines.

Finally, the correlation between the whole set of VAS data, obtained after the five inhalations, and the corresponding data for each lung function index was evaluated using a doubly multivariate repeated measures design (threshold of significance p<0.05). This analysis was made with the SPSS statistical software [12].

Results

Spirometry

The baseline FEV₁ (% predicted) was slightly higher in asthmatics (42.8 (2.8)) than in COPD subjects (37.9 (2.0)), but the difference was not significant. Two subjects with asthma had respiratory manoeuvre-induced bronchoconstriction. All subjects showed at least some degree of improvement in FEV₁ after terbutaline, except for two COPD subjects who remained unresponsive (post-terbutaline, 800 µg, minus baseline FEV₁ = 0). Three out of 16 asthmatics were less responsive to 800 µg terbutaline than to 200 µg salbutamol at the time of the study than to 200 µg salbutamol at the time of inclusion into the study (two with ΔFEV₁ between 10 and 15% predicted, and one with ΔFEV₁ <10% predicted), whilst 9 out of 20 COPD subjects were more responsive (seven with ΔFEV₁ between 10 and 15% predicted, and two with ΔFEV₁ >15% predicted).

Pattern and level of perception

Individual VAS ratings are shown in figure 1. Four patterns of subjective response were identified. Four
COPD subjects rated nearly no change (VAS ≤5%) throughout the protocol. In eight subjects, perceived improvement did not start until either the second (two asthmatics), the third (one COPD subject), or the fourth inhalation (one asthmatic), or the final inhalation (one asthmatic and three COPD subjects). Two subjects from the COPD group perceived an improvement from the first (or the first two) inhalation(s), but did not perceive additional improvement. Finally, 22 subjects (12 asthmatics and 10 COPD subjects) perceived a gradual improvement.

In an attempt to analyse the level of perception, we categorized the subjects into low and high perceivers. The cut-off, chosen on the basis of the results of our first study [3], was VAS=25% after a cumulated dose of 800 μg terbutaline. Thus, 14 out of 16 asthmatics, and 13 out of 20 COPD subjects, were high perceivers (fig. 1). In the COPD group, a subgroup analysis was performed, whilst in the asthma group the very small number of low perceivers precluded such an analysis. The median VAS ratings (95% confidence interval) obtained after 800 μg terbutaline were, respectively, +60% (+45 to +78%) in the asthmatics, +50% (+45 to +65%) in the COPD high perceivers, and +5% (0 to +18%) in the COPD low perceivers.

Subjects' comments

Three asthmatics reported palpitations, and two throat irritation, following terbutaline. Three COPD subjects reported terbutaline-induced tremor, and one nervousness. Three other COPD subjects reported a bad taste after the fifth terbutaline inhalation.

Table 1. – Size of terbutaline-induced (800 μg) bronchodilation in 36 subjects with airway obstruction

<table>
<thead>
<tr>
<th></th>
<th>Asthma n=16</th>
<th>p(1)</th>
<th>COPD high perceivers n=13</th>
<th>p(2)</th>
<th>COPD low perceivers n=7</th>
<th>p(3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ΔRin cmH₂O·s⁻¹</td>
<td>-19.8 (-4.6 to -27.5)</td>
<td>&gt;0.10</td>
<td>-9.7 (-3.6 to -23.0)</td>
<td>&lt;0.02*</td>
<td>-6.0 (-4.0 to -6.8)</td>
<td>&lt;0.05*</td>
</tr>
<tr>
<td>ΔRex cmH₂O·s⁻¹</td>
<td>-23.3 (-4.6 to -44.7)</td>
<td>&gt;0.10</td>
<td>-16.6 (-4.8 to -36.2)</td>
<td>&lt;0.02*</td>
<td>-7.6 (-4.8 to -8.6)</td>
<td>&lt;0.02*</td>
</tr>
<tr>
<td>ΔFRC % pred</td>
<td>-30.2 (-10.4 to -58.1)</td>
<td>&gt;0.10</td>
<td>-28.5 (+9.8 to -39.7)</td>
<td>&gt;0.10</td>
<td>-15.4 (-2.9 to -26.3)</td>
<td>&lt;0.10*</td>
</tr>
<tr>
<td>ΔVFC % pred</td>
<td>+20.0 (+6.1 to +33.8)</td>
<td>&gt;0.10</td>
<td>+11.2 (+9.0 to +24.2)</td>
<td>&lt;0.01*</td>
<td>+5.0 (0 to +8.3)</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>ΔFVCex % pred</td>
<td>+20.9 (+10.4 to +35.3)</td>
<td>&gt;0.10</td>
<td>+12.5 (+9.9 to +26.9)</td>
<td>&lt;0.10*</td>
<td>+9.5 (+8.0 to +13.6)</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>ΔFEV₁ % pred</td>
<td>+20.9 (+12.7 to +33.2)</td>
<td>&gt;0.10</td>
<td>+9.5 (+0.4 to +17.5)</td>
<td>&gt;0.10</td>
<td>+9.5 (+2.0 to +14.0)</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>ΔMEF₂⁰ l·s⁻¹</td>
<td>+0.55 (+0.25 to +0.80)</td>
<td>&gt;0.05*</td>
<td>+0.20 (+0.05 to +0.80)</td>
<td>&gt;0.10</td>
<td>+0.10 (0 to +0.60)</td>
<td>&lt;0.02*</td>
</tr>
<tr>
<td>ΔFVCin % pred</td>
<td>+15.8 (+7.6 to +31.1)</td>
<td>&gt;0.10</td>
<td>+13.2 (+8.0 to +26.9)</td>
<td>&lt;0.02*</td>
<td>+7.8 (+6.4 to +11.7)</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>ΔMIF₂⁰ l·s⁻¹</td>
<td>+0.45 (+0.10 to +1.00)</td>
<td>&gt;0.10</td>
<td>+0.50 (+0.05 to +1.05)</td>
<td>&lt;0.02*</td>
<td>+0.15 (+0.10 to +0.35)</td>
<td>&lt;0.05*</td>
</tr>
</tbody>
</table>

Median value with 95% confidence interval (non-parametric analysis) in parenthesis. p(1) p(2) p(3): significance level for the comparison asthma versus COPD high perceivers (1), COPD high perceivers versus COPD low perceivers (2), and COPD low perceivers versus asthma (3). Asterisks indicate p values <0.10. COPD: chronic obstructive pulmonary disease; sRin: specific inspiratory resistance; sRex: specific expiratory resistance; FRC: functional residual capacity; IVC: inspiratory vital capacity; FVCex: expiration of a forced vital capacity; FEV₁: forced expiratory volume in one second; MIF₂⁰ maximal expiratory flow at 50% FVC; FVCin: inspiration of a FVC; MIF₂⁰: maximal inspiratory flow at 50% FVC.

Size of bronchodilation

As shown in table 1, all of the indices studied improved significantly more in the asthmatics than in the COPD low perceivers. When the comparison involved the asthmatics and the COPD high perceivers, only the indices derived from the forced expiratory manoeuvre (FEV₁, MIF₂⁰ and, to a lesser extent, FVCex) showed a larger response in the asthmatics. Finally, within the COPD group, the high perceivers showed a larger improvement than the low perceivers in most indices (except for FEV₁, MIF₂⁰ and PRC), the best discriminator being IVC.

Relationship of subjective perception to changes in lung function

The results of linear regression analysis on a within-subject basis are shown in table 2. Median r² values reflecting the strength of the correlation for the whole group were the highest in the asthma group, the best linear relationship being observed in asthmatics with ΔsRin (median r=0.831). As shown in table 2, the relationship of VAS ratings to the changes in lung function was significantly stronger in both asthmatics and COPD high perceivers than in COPD low perceivers for all the indices being evaluated. Individual regressions of VAS ratings against the changes in IVC are illustrated in figure 2. It is clear from this figure that the relatively high r² values obtained in the COPD low perceivers were mainly a result of hazard, as based on points grouped very close to zero for both ΔVFC and VAS variables.
Table 2. Linear regression analysis of the perception of acute bronchodilation assessed on a within-subject basis

<table>
<thead>
<tr>
<th></th>
<th>Asthma n=16</th>
<th>COPD high perceivers n=13</th>
<th>COPD low perceivers n=7</th>
</tr>
</thead>
<tbody>
<tr>
<td>sRin</td>
<td>0.831 (0.099-0.978)</td>
<td>0.760 (0.000-0.960)</td>
<td>0.279 (0.000-0.716)</td>
</tr>
<tr>
<td>FEV&lt;sub&gt;1&lt;/sub&gt;</td>
<td>0.810 (0.085-0.981)</td>
<td>0.740 (0.033-0.958)</td>
<td>0.133 (0.006-0.624)</td>
</tr>
<tr>
<td>sRex</td>
<td>0.780 (0.097-0.977)</td>
<td>0.712 (0.008-0.950)</td>
<td>0.271 (0.013-0.670)</td>
</tr>
<tr>
<td>IVC</td>
<td>0.776 (0.092-0.979)</td>
<td>0.647 (0.010-0.944)</td>
<td>0.200 (0.157-0.830)</td>
</tr>
<tr>
<td>FVC inclination</td>
<td>0.769 (0.086-0.970)</td>
<td>0.650 (0.005-0.920)</td>
<td>0.198 (0.000-0.666)</td>
</tr>
<tr>
<td>FVCex</td>
<td>0.766 (0.085-0.972)</td>
<td>0.625 (0.005-0.949)</td>
<td>0.190 (0.000-0.302)</td>
</tr>
<tr>
<td>FRC</td>
<td>0.727 (0.089-0.942)</td>
<td>0.574 (0.000-0.910)</td>
<td>0.048 (0.000-0.329)</td>
</tr>
<tr>
<td>MEF&lt;sub&gt;50&lt;/sub&gt;</td>
<td>0.643 (0.048-0.930)</td>
<td>0.636 (0.000-0.946)</td>
<td>0.169 (0.006-0.608)</td>
</tr>
<tr>
<td>MEF&lt;sub&gt;25&lt;/sub&gt;</td>
<td>0.561 (0.016-0.929)</td>
<td>0.608 (0.043-0.918)</td>
<td>0.041 (0.000-0.540)</td>
</tr>
</tbody>
</table>

Data in the table are median and range (in parenthesis) for squared correlation coefficient (r<sup>2</sup>) in linear regression of VAS against change in lung function. Indices are ranked by decreasing median r value in the asthma group. For explanation of p(1) p(2) p(3) see legend to table 1. VAS: visual analogue scale. For further abbreviations see legend to table 1.

![Graph showing VAS ratings against change in IVC](image)

Fig. 2. Within-subject regression analysis of VAS ratings against the change in IVC: individual examples with 5 points corresponding to the 5 terbutaline inhalations. In each of the three groups, patients showing the best (upper figure) and the worst (lower figure) r<sup>2</sup> value have been chosen. IVC: inspiratory vital capacity. For further abbreviations see legend to figure 1.

Table 3. Perception of acute bronchodilation (within-subject analysis): slope and intercept

<table>
<thead>
<tr>
<th></th>
<th>Asthma n=16</th>
<th>COPD high perceivers n=13</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV&lt;sub&gt;1&lt;/sub&gt;</td>
<td>+2.7 (+0.3 to +4.7)</td>
<td>+2.1 (-1.9 to +20.7)</td>
</tr>
<tr>
<td>Slope</td>
<td>+5 (-44 to +28)</td>
<td>+36 (-5 to +69)</td>
</tr>
<tr>
<td>Intercept</td>
<td>0 (-34 to +26)</td>
<td>+25 (-64 to +57)</td>
</tr>
</tbody>
</table>

Data are presented as median and range in parenthesis. Slopes are expressed in % of VAS line length divided by change in FEV<sub>1</sub> expressed as % predicted (or by change in sRin, expressed as cmH<sub>2</sub>O·s), intercepts in % of VAS line length p: significance level for the comparison asthma versus COPD high perceivers. For abbreviations see legend to tables 1 and 2.
Slopes and intercepts obtained in asthmatics and COPD high perceivers are given in table 3. The intercept was significantly larger in COPD high perceivers in the analysis against ΔFEV₁ and, to a lesser extent, in that against ΔRin. On the other hand, there was little difference in median slopes, with, however, a much larger between-subject range in COPD high perceivers. The characteristics of perception were unrelated to either baseline lung function or to the size of bronchodilation, except for a modest correlation between r² and the size of bronchodilation, in the VAS/ΔFEV₁, (r=0.513, p<0.01) as well as in the VAS/ΔRin analysis (r=0.353, p<0.05). The former regression (r² of the VAS/ΔFEV₁ relationship against ΔFEV₁) is illustrated in figure 3. No significant relationship was found between the calculated VAS₄₀ ratings and the baseline FEV₁, (r=0.22).

Correlation coefficient values obtained from the multivariate analysis of the whole set of data are shown in table 4. The analysis was made separately in the three groups. In the asthma group, the correlation reached significance with ΔIVC and ΔFEV₁ (and drew near significance with ΔRex and ΔRin); in COPD high perceivers, significance was achieved with ΔRin, ΔFCVcin and ΔRin (and nearly achieved with ΔIVC). No significant correlation was found in COPD low perceivers, except for a paradoxical negative VAS/ΔMEF₅₀ relationship, which we considered as fortuitous. The scatter of VAS ratings, plotted either against ΔFEV₁ data, or against ΔIVC data, is shown in figures 4 and 5. It is clear from these figures that no correlation could be expected in COPD low perceivers, as most VAS ratings were close to zero.

**Discussion**

In a previous study we showed that a bipolar VAS is convenient for assessing the subjective perception of the airway response to an inhaled agent in patients with...
asthma or COPD. The level of perception recorded as a line length on the scale was found to be high in some of the COPD subjects ("high perceivers") for both saline and terbutaline, whilst it was low in other COPD subjects ("low perceivers"). A sensitivity analysis showed that the asthmatics had the highest post-terbutaline improvement in shortness of breath, after normalization for the post-saline variability [3].

In the present study, we have induced acute bronchodilation in 16 asthmatics, and in 20 COPD subjects, with different degrees in baseline airway obstruction. The doses of terbutaline were low in the initial steps, so that bronchodilation occurred very gradually. As in our previous study, considerable effort was made to keep the subject unaware of the nature of the aerosols. We again found that the COPD subjects could be categorized into:

![Scattergrams](image)

Fig. 4. – Scattergrams to illustrate the relationship of the perceptual response to the change in FEV₁ (point of reference: baseline status), for asthmatics (n=82) (left); COPD high perceivers (n=65), (middle); and COPD low perceivers (n=35) (right). Significance of the relationship can be found in table 4. For abbreviations see legend to figures 1 and 3.

![Scattergrams](image)

Fig. 5. – Scattergrams to illustrate the relationship of the perceptual response to the change in IVC (point of reference: baseline status), for asthmatics (n=82) (left); COPD high perceivers (n=65) (middle); and COPD low perceivers (n=35) (right). Significance of the relationship can be found in table 4. For abbreviations see legend to figures 1 and 2.
high and low perceivers. The high perceivers had a larger terbutaline-induced increase in IVC, but not in FEV₁, a finding in agreement with our previous results [3], and with the claim by Bellamy and Hutchison [13] that only those COPD subjects who improve in IVC are able to perceive bronchodilation.

The relationship between the VAS ratings and the parallel changes in lung function was studied primarily on a within-subject basis, as recommended by Stark [14]. We characterized individual perception in terms of strength of correlation with parallel change in lung function, slope, and VAS axis intercept. We found that both asthmatics and COPD high perceivers showed some degree of relationship between VAS ratings and changes in lung function, COPD high perceivers differing from the asthmatics by a larger VAS axis intercept, while subjective and objective response were unrelated in COPD low perceivers.

The size of the improvement in FEV₁ was significantly larger in the asthmatics than in the COPD subjects, and this was expected as it simply reflected the selection criteria. However, three asthmatics had a ΔFEV₁ <15% predicted, indicating a decreased responsiveness at the time of the study [15]. Conversely, nine COPD subjects showed a ΔFEV₁ >10% predicted. Long-term, time-related changes in bronchodilator responsiveness are known to occur in COPD subjects also [16]. However, a more attractive explanation is that terbutaline at a 800 μg dose was more potent than 200 μg salbutamol [17], especially as the use of a dosimeter method is expected to enhance lung deposition [18].

A major objective of the present study was to evaluate the relationship between the subjective response recorded on the VAS and the change in lung function. Using a within-subject linear regression analysis, we found that some correlation between VAS ratings and changes in lung function was present in asthmatics and COPD subjects with a high level of perception, but not in those COPD subjects with low perception. Data available in the literature about the perception of acute bronchodilation by patients with airway obstruction are scarce. In qualitative studies, non-perceivers have been described among asthmatics and COPD high perceivers [19, 13, 20]. Using a Borg scale to quantitate the perception of a single dose salbutamol, Wolkove et al. [2] found no relationship between the subjective response and the change in FEV₁, in a group of 65 COPD subjects. The analysis made in the present study included a wide variety of lung function indices. The reasons for choosing any particular index have been discussed elsewhere [3]. In the three groups analysed, the subjective response showed the highest correlation with the change in sRin. Two factors may account for this finding. Firstly, the decrease in specific resistance is a better reflection of acute bronchodilation than the increase in forced expiratory volumes or flows, as it is free from any bronchodilator induced increase in large airways collapsibility [21], or decrease in lung elastic recoil [22]. Secondly, shortness of breath was taken as a marker of the perception of airway obstruction, and dyspnoea is known to be a predominantly inspiratory sensation [23].

The ability to discriminate a change in airway obstruction, assessed as the slope of VAS ratings against changes in FEV₁ or sRin, was not significantly different between asthmatics and COPD high perceivers. On the other hand, the median VAS rating recorded when no change had occurred in FEV₁ was found to be markedly higher in COPD high perceivers (+36%) than in asthmatics (+5%) and COPD low perceivers (+2%). These figures compare well with the perceived effect on shortness of breath of isotonic saline, as assessed in similar populations in our previous study [3]: +43% in COPD high perceivers, +9% in asthmatics, and +5% in COPD low perceivers (median values). These results suggest that the high level of perception of terbutaline obtained in some of the COPD subjects is predominantly a placebo effect.

In a study focused on the perception of acute bronchoconstriction, Burdon et al. [24] found larger perceptual responses in asthmatics with normal baseline function than in asthmatics with baseline obstruction, and hypothesised that temporal adaptation following repeated bronchoconstriction might be responsible for decreased perception. We examined the influence of baseline obstruction on the characteristics of perception, and were unable to find any significant correlation. The possible influence of baseline FEV₁ was also studied by looking at the VAS ratings obtained at a given level of FEV₁, a method previously used by several groups [24, 25], and we again found no relationship. Finally, as stronger correlations are expected when data are widely distributed than when they are closely grouped, we evaluated the influence of the size of bronchodilation on perception. The fact that our COPD high perceivers - defined on the basis of the size of the VAS ratings - were found to have a larger response in some indices to terbutaline, and also a stronger relationship between subjective and objective response, made this evaluation even more necessary. Here, we found a significant relationship between r² values characterizing the perception and the amount of bronchodilation. However, the correlation was weak, variations in ΔFEV₁ accounting for only 25% of variations in r² of the VAS/ΔFEV₁ analysis.

As a final step, the evaluation of the relationship between the improvement in shortness of breath and that in lung function included an analysis of the whole set of data. In this multivariate analysis, the between-subject variability was factored out before assessing the effect of the successive inhalations of terbutaline. The results suggest that some indices influenced the perceived improvement in shortness of breath, either in asthmatics but not in COPD high perceivers (e.g. FEV₁), or in COPD high perceivers but not in asthmatics (e.g. FRC), whilst IVC and sRin seemed to play a role in both groups.

A few previous studies have given some support to the hypothesis that the perception of airway obstruction is less accurate in subjects with COPD than in asthmatics, e.g. a study with magnitude estimation of added resistive loads [26], and an evaluation of the relationship between the baseline dyspnoea index [27] and the FEV₁, in the present study, we measured in the lung function laboratory the terbutaline-induced perceived improvement in shortness of breath, and we analysed the level of
perception in relation to the objective change in lung function. We found that some, but not all, COPD subjects had perception of low level and unrelated to the change in lung function.

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**References**


