

# How Can We Assess the Perception of Induced Dyspnea in Chronic Obstructive Pulmonary Disease?

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**OBJECTIVE:** To evaluate various methods for studying the perception of dyspnea in chronic obstructive pulmonary disease (COPD) using a new parameter, the change in Borg scale rating, and others already in use: the linear regression slope and the application of Stevens' law to the response-perception curve—ie change in forced expiratory volume in 1 second ( $\Delta FEV_1$ )—change in dyspnea ( $\Delta$ dyspnea).

**PATIENTS AND METHODS:** A bronchial challenge test was performed on 70 patients with stable COPD and no contraindications for performing the test (European Respiratory Society criteria), during which dyspnea was measured (Borg scale) after each nebulization. Perception was analyzed using: *a*) the linear regression slope of  $\Delta FEV_1$  plotted against ( $\Delta$ dyspnea); *b*) the exponent *n* of Stevens' law ( $\psi = k\phi^n$ , in which  $\psi$  is  $\Delta$ dyspnea and  $\phi$  is  $\Delta FEV_1$ , with perception being poor when  $n < 1$  and good when  $n > 1$ ), and *c*) change in Borg: difference between dyspnea when  $FEV_1$  has fallen 20% and dyspnea after saline inhalation. Subjects were classified according to the slope and change in Borg as hypoperceivers, normal perceivers, or hyperperceivers. These 2 methods of classification were compared using the  $\kappa$  statistic.

**RESULTS:** According to the exponent *n*, all patients were hypoperceivers ( $n < 1$ ). According to the slope, there were 33 hypoperceivers, 28 normal perceivers, and 9 hyperperceivers. The change in Borg classified 37 subjects as hypoperceivers, 23 as normal perceivers, and 10 as hyperperceivers. All except 5 subjects were classified in the same way by the slope and the change in Borg ( $\kappa = 0.88$ ). In most of the 5 cases of discrepancy, the slope classified subjects as better perceivers.

**CONCLUSIONS:** The *n* exponent is not valid for evaluating the perception of dyspnea induced by a bronchial challenge test in COPD. Change in Borg is at least as useful as the slope for evaluating perception of dyspnea. The percentage of patients with this disease who are hyperperceivers is high.

**Key words:** Perception. Dyspnea. Chronic obstructive pulmonary

disease. Bronchial challenge test.

¿Cómo valorar la percepción de la disnea inducida en la EPOC?

**OBJETIVO:** Valorar varios métodos para el estudio de la percepción de la disnea en la enfermedad pulmonar obstructiva crónica (EPOC) usando un nuevo parámetro, el cambio en Borg (CB), y otros ya utilizados: la pendiente de la regresión lineal y la aplicación de la ley de Stevens a la curva respuesta-percepción—cambios en el volumen espiratorio forzado en el primer segundo ( $\Delta FEV_1$ )—cambio en la disnea ( $\Delta$ disnea).

**PACIENTES Y MÉTODOS:** Se realizó un test de broncoprovocación a 70 pacientes con EPOC estable, sin contraindicaciones para dicha prueba (criterios de la European Respiratory Society), durante el que se midió la disnea (escala de Borg) después de cada nebulización. La percepción se analizó mediante: *a*) la pendiente de la regresión lineal entre  $\Delta FEV_1$  y  $\Delta$ disnea; *b*) el exponente *n* de la ley de Stevens ( $\psi = k\phi^n$ , donde  $\psi$  es  $\Delta$ disnea y  $\phi$  es  $\Delta FEV_1$ ; cuando  $n < 1$ , la percepción es mala, y cuando  $n > 1$ , buena), y *c*) el CB: diferencia entre la disnea cuando el  $FEV_1$  ha caído un 20% y la disnea tras inhalación de salino. Se clasificó a los sujetos según la pendiente y el CB en hipoperceptores (HPO), normoperceptores (NP) e hiperperceptores (HPR). Se compararon ambas clasificaciones mediante el estadístico kappa.

**RESULTADOS:** Según el exponente *n* todos los pacientes fueron HPO ( $n < 1$ ). Según la pendiente hubo 33 HPO, 28 NP y 9 HPR. El CB clasificó como HPO a 37 sujetos, como NP a 23 y como HPR a 10. La pendiente y el CB clasificaron igual a todos, excepto a 5 sujetos ( $\kappa = 0,88$ ). En la mayoría de casos discordantes, la pendiente clasificó a los sujetos como mejor perceptores.

**CONCLUSIONES:** El coeficiente *n* no es válido para estudiar la percepción de la disnea inducida mediante test de broncoprovocación en la EPOC. El CB es, al menos, tan útil como la pendiente para estos estudios. La proporción de HPO entre los pacientes con dicha enfermedad es elevada.

**Palabras clave:** Percepción. Disnea. Enfermedad pulmonar obstructiva crónica. Prueba de provocación bronquial.

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## Introduction

The pathogenesis of dyspnea in chronic obstructive pulmonary disease (COPD) is complex<sup>1</sup> and involves factors of a psychosocial nature.<sup>2</sup> Individuals with similar degrees of bronchial obstruction may therefore perceive symptoms differently. The fundamental question is how a subjective sensation like dyspnea can be measured objectively. For a long time studies of respiratory sensations in COPD have been few and have most often been approached from the standpoint of psychophysics, using external resistive loading.<sup>3</sup> In other diseases, however, (such as asthma) the perception of dyspnea is usually measured by inducing acute bronchoconstriction.<sup>4</sup> Three methods for evaluating whether subjects are good or poor perceivers of dyspnea have been described: *a*) perception score of breathlessness when the subject presents a 20% decrease in forced expiratory volume in 1 second (FEV<sub>1</sub>) (PS<sub>20</sub>),<sup>5</sup> which considers only a single point on the response-perception curve and does not evaluate change; *b*) the slope of the regression line between the stimulus (degree of obstruction) and the sensation (dyspnea rating)<sup>6</sup>; and *c*) the application of Stevens' law,<sup>7</sup> according to which the magnitude of the sensation (breathlessness) depends exponentially on the stimulus applied.

In this study we sought to improve our understanding of respiratory sensations in COPD and facilitate the assessment of perception of dyspnea by inducing it through stimuli similar to those that provoke breathlessness spontaneously. For this purpose we studied a new parameter for distinguishing between good and poor perceivers of dyspnea—the change in Borg (CB) scale rating—and compared it with the slope of the regression line and the application of Stevens' law. CB is easy to calculate in clinical practice, is mathematically simple, and assesses changes in perception in a way that is related to changes in bronchial obstruction.

## Patients and Methods

### Patient Selection

The study was carried out in 101 consecutive subjects (age range, 41-81 years) with COPD (according to American Thoracic Society<sup>8</sup> criteria) in outpatient pneumology departments. The patients were clinically stable (no respiratory infections or changes in usual treatment in the previous 6 weeks). None of the subjects suffered from diseases that could cause airflow obstruction or serious comorbidity. Patients who had asthma, chronic respiratory insufficiency, other diseases that cause dyspnea, psychiatric disorders, or who had applied for disability were excluded. All patients consented to participate in the study once they had been informed of its objectives and the protocol had been duly explained.

### Histamine Challenge Test

As patients with absolute contraindications for this test (according to the European Respiratory Society [ERS]<sup>9</sup>) were

excluded, the test was performed on 70 of the 101 initial patients. Bronchodilators were withheld during the 12 hours preceding the test. Histamine phosphate was prepared in sterile vials by the pharmacy department and was administered according to ERS<sup>9</sup> procedures by continuous flow and consecutive inhalation.<sup>10</sup> Before the test, basal spirometric values were obtained as well as values after saline inhalation. The latter were used to calculate change in FEV<sub>1</sub> ( $\Delta$ FEV<sub>1</sub>). The test was discontinued when FEV<sub>1</sub> had decreased by at least 20%, at which point 600  $\mu$ g of salbutamol was administered through a pressurized inhaler and a spacer. After 20 minutes another spirometry test was performed to ascertain whether bronchoconstriction had resolved.

### Evaluation of Dyspnea

Thirty seconds after the administration of saline aerosol and each dose of histamine, patients were questioned about their perception of dyspnea at that moment and asked to rate it on the modified Borg scale.<sup>11</sup> After recording the dyspnea ratings, flow-volume curves were obtained. For the rating of dyspnea, subjects were instructed to ignore such sensations as nasal or pharyngeal irritation, unpleasant taste, or cough; they were unaware of what substance they had been given and what effects it might have on breathing. With the results of dyspnea ratings and FEV<sub>1</sub> values a curve was plotted for each patient, with  $\Delta$ FEV<sub>1</sub> on the x-axis and dyspnea rating on the y-axis.

### Parameters for Assessing Perception of Dyspnea

We used 3 parameters to assess perception of dyspnea:

1. The exponent *n* of Stevens' law<sup>7</sup>:  $\psi = k\phi^n$ , where  $\psi$  represents change in dyspnea ( $\Delta$ dyspnea),  $\phi$  change in FEV<sub>1</sub> ( $\Delta$ FEV<sub>1</sub>) and *k* is a constant. In order to determine the value of the exponent *n*, the logarithm of  $\psi$  is plotted against the logarithm of  $\phi$  to transform the response-perception curve into a straight line, the slope of which is *n*:  $\log_{\psi} = \log_k + (n \times \log_{\phi})$ .

However, the Borg scale includes the value 0, which cannot be transformed logarithmically. In order for Stevens' law to hold, the original relationships between points on the scale must be maintained. For this reason, a simple sum of a constant to avoid the value 0 is not possible.<sup>12</sup> The Borg scale is categorical and its original values can only be transformed by multiplying a constant, such that the problem of the value 0 remains unsolved. However, Stevens' law does contemplate transformations, including summation, to bring the curve as close as possible into a straight line.<sup>13</sup> A way to achieve a logarithmic transformation of the original 0 values and still maintain relationships as similar as possible to those on the original scale is to multiply the scores by the highest possible constant (for practical purposes, by 10), first adding a small decimal amount (in our case, 0.1) to the score. As changes in FEV<sub>1</sub> are expressed on an ordinal scale, they can be subjected to any kind of transformation that does not alter the order, and we therefore subjected them to the same transformation as the Borg scale.

2. The slope of the regression line between  $\Delta$ FEV<sub>1</sub> (percentage of basal value) and  $\Delta$ dyspnea.<sup>6</sup> We also calculated the coefficient of determination (*r*<sup>2</sup>).

3. CB, which is the mathematical difference between PS<sub>20</sub><sup>5</sup> and dyspnea after histamine inhalation:

CB = PS<sub>20</sub> — Borg score after saline inhalation

PS<sub>20</sub> was obtained by linear interpolation between the dyspnea scores just before and after the 20% decrease in FEV<sub>1</sub>

### Classification of Perception of Dyspnea

According to Stevens' law,<sup>14</sup> subjects in whom the exponent  $n$  is less than 1 would be considered "poor perceivers" and those in whom  $n$  is greater than 1, "good perceivers." Subjects were classified by CB and the slope as follows: those with a score less than 0 were considered hypoperceivers. For the rest of the subjects who perceived some change in dyspnea we obtained 25th and 75th percentiles for both parameters. Those who scored below the 25th percentile were added to the group of hypoperceivers, those who scored between the 25th and the 75th percentile were considered normal perceivers, and those who scored above the 75th percentile were classified as hyperperceivers. The classifications obtained by the slope and by CB were compared using the  $\kappa$  statistic.

## Results

### Patients

Of the 70 subjects studied, COPD was mild in 22 cases, moderate in 44, and severe in 4 (according to ERS criteria<sup>15</sup>). All but 2 patients showed bronchial hyperreactivity, with provocation concentration of histamine causing a 20% decrease in  $FEV_1$  ( $PC_{20}$ ) of <8 mg/mL). In the 2 patients who were not hyperreactive,  $PC_{20}$  was 12.8 mg/mL and 9.81 mg/mL respectively. In 6 patients the histamine challenge test used only 2 doubling doses of histamine. In no cases were there complications related to the test and none of the patients showed significant bronchoconstriction after saline inhalation. Patient characteristics are shown in Table 1.

### Perception of Respiratory Sensation

In absolute values, perception of dyspnea before the histamine challenge dyspnea and  $PS_{20}$  varied widely among subjects (Figure 1). The median dyspnea score was 0.5 after saline provocation (25th-75th percentile, 0-2.5). Median CB was 0.58 (25th-75th percentile, 0-2.06). The median decrease in  $FEV_1$  was 296 mL at the moment when a 20% decrease had been induced (25th-75th percentile, 258-368). The median  $PS_{20}$  was 2 (25th-75th percentile, 0.5-4).

### Comparison of the 3 Parameters for Perception of Dyspnea

The median value of  $n$  was 0.28 (25th-75th percentile, 0-0.58; range, 0-0.84) (Figure 2). In all patients, therefore,  $n$  was less than 1.

The median slope was 0.035 (range, -0.9-0.24). The median value of  $r^2$  was 0.91 (range, -0.93-1) Patients with a slope of less than 0.03 were classified as hypoperceivers; those with a slope between 0.03 and 0.14, as normal perceivers; and those with a slope of more than 0.14, as hyperperceivers. Thus, based on slope, 33 patients (9 of whom had negative slopes and

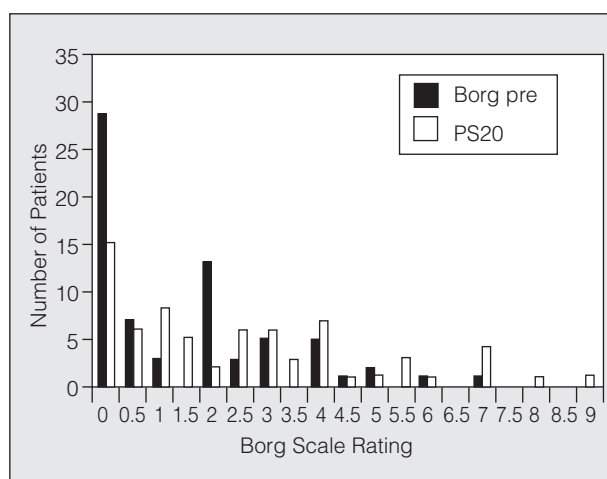


Figure 1. Frequency scatterplot of dyspnea after aerosol saline inhalation and  $PS_{20}$ . Borg pre indicates perceived dyspnea after saline inhalation;  $PS_{20}$ , perceived dyspnea when a 20% decrease in forced expiratory volume in 1 second had been induced.

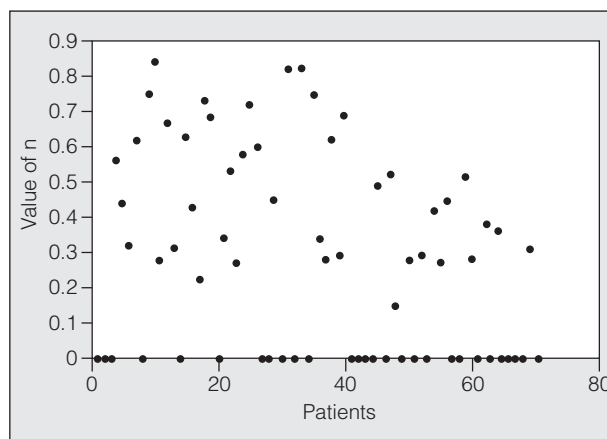


Figure 2. Values of exponent  $n$ .

19 a slope of 0) were classified as hypoperceivers, 28 were classified as normal perceivers, and 9 as hyperperceivers. In our study there were 12 cases with  $r^2 < 0.71$ , 9 of whom were classified (according to both the slope and CB) as hypoperceivers and 2 as normal perceivers. One case was discordant.

CB classified subjects with a score below 0.75 as hypoperceivers, those with a score between 0.75 and

TABLE 1  
Patient Characteristics\*

	Mean (SD)	Range
Age, years	62.33 (7.74)	41-81
$FEV_1$ , mL	1716 (419)	1240-3320
$FEV_1$ , % expected	65.53 (12.42)	38-93
$PC_{20}$ , mg/mL	0.895 (2.2)	0.035-12.8
Smoking, S/ex	18/52	
Sex, M/W	68/2	

\* $FEV_1$  indicates forced expiratory volume in 1 second;  $PC_{20}$ , provocation concentration of histamine causing a 20% decrease in  $FEV_1$ ; S, smoker; ex, ex-smoker; M, man; W, woman.

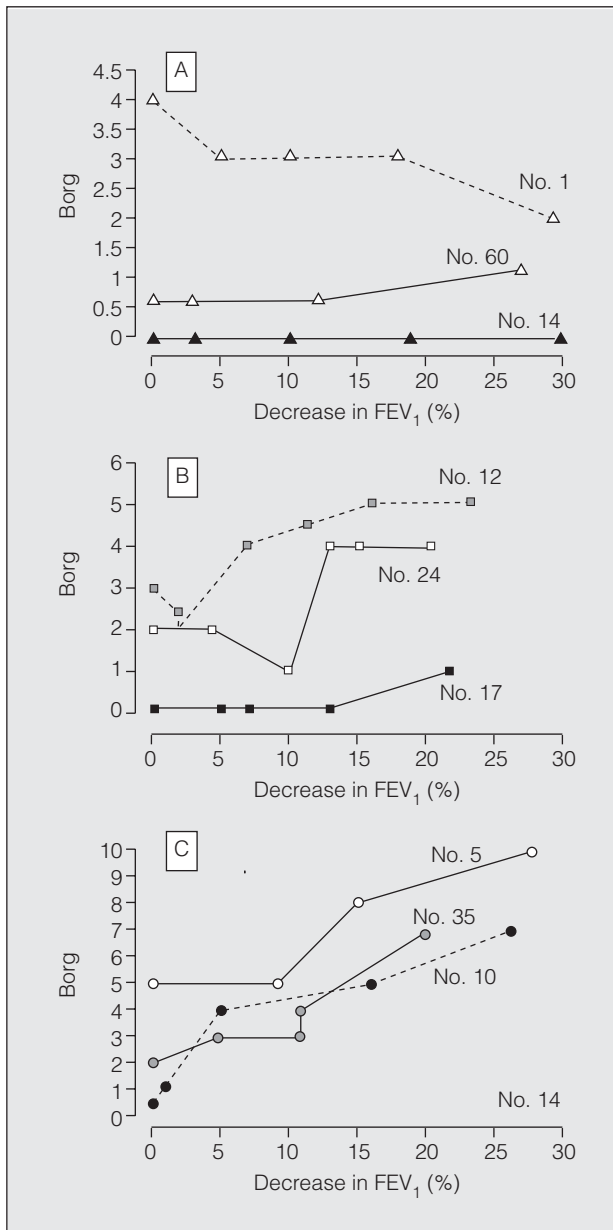


Figure 3. Relationship between dyspnea and changes in forced expiratory volume in 1 second (FEV<sub>1</sub>) in the various types of perceivers. We present the “decrease in FEV<sub>1</sub>-perception” curves for 3 subjects chosen at random within each group of perceivers. A: hypoperceivers; B: normal perceivers; C: hyperperceivers.

2.76 as normal perceivers, and those with a score above 2.76 as hyperperceivers. Thus, we found 37 hypoperceivers, 23 normal perceivers, and 20 hyperperceivers. As with the slope, there were 9 hypoperceivers in whom dyspnea decreased with respect to baseline after a 20% decrease in FEV<sub>1</sub> had been induced and 19 who experienced no change in dyspnea (CB=0) (Figure 3A).

Only 5 subjects were classified differently by slope and by CB (Table 2). There was, therefore, high agreement between the 2 methods ( $\kappa=0.88$ ). In the

TABLE 2  
Agreement Between Classification of Perception According to the Change in Borg Scale Rating and According to the Slope of the Regression Line\*

	HPO	NP	HPR
Slope			
HPO	33		
NP	4	23	1
HPR			9

\* $\kappa=0.88$ .  
HPO indicates hypoperceivers; NP, normal perceivers; HPR, hyperperceivers.

TABLE 3  
Values for the Slope of the Regression Line and Change in Borg Scale Ratings in Patients Classified Differently by the 2 Parameters\*

Patient	Slope	Change in Borg
21	0.03 (NP)	0.5 (HPO)
22	0.13 (NP)	3 (HPR)
37	0.03 (NP)	0.67 (HPO)
52	0.03 (NP)	0.71 (HPO)
61	0.06 (NP)	0 (HPO)

\*HPO indicates hypoperceiver; NP, normal perceiver; HPR, hyperperceiver.

discordant cases, the slope was near the reference limits established between groups of perceivers in all but 1 case (patient 61) (Table 3). This patient’s response was anomalous in that there was a paradoxical bronchodilator response to the first doses of histamine and improvement in dyspnea, which did not worsen with respect to baseline after bronchoconstriction was induced. In the discordant cases, the slope usually classified subjects as better perceivers than did CB.

## Discussion

The study of respiratory sensations has aroused considerable interest recently. As with pain, it is the individual experiencing breathlessness who can provide the best description of it.<sup>16</sup> Studies carried out on the “language of breathlessness” have shown that dyspnea is qualitatively different in different diseases,<sup>17,18</sup> but it has also often been shown to be quantitatively different in individuals with the same disease and degree of severity. Disturbances in respiratory perception can have clinical implications, as in the case of patients with asthma who are poor perceivers of dyspnea, and whose prognosis is poorer than that of good perceivers.<sup>19,20</sup> There is also the added problem that we have no reliable method to distinguish between good and poor perceivers. For this reason, the present study was designed to investigate the validity in COPD of methods already described for assessing the perception of dyspnea and to compare them with a new parameter, CB. In selecting indicators of perception we rejected PS<sub>20</sub>, as it is a measure that reflects only a single point on the response-perception curve. Also, since it is

dependent on baseline values, it is difficult to establish comparisons among individuals. This does not mean, however, that it is not a useful indicator for the study of dyspnea, as it provides us with the absolute magnitude of dyspnea during an episode of bronchoconstriction.

Determining the exponent  $n$  of Stevens' law is an attempt to provide a psychophysical estimation of the perception of breathlessness. Stevens' law, however, has several drawbacks. For one, we can only study a portion of the response-perception curve, as the induced decrease in  $FEV_1$  is rarely more than 20%, while Stevens' law was intended to apply to a wider range of stimuli and responses. Moreover, the value of the exponent  $n$  varies according to the stimulus studied, and we do not know what its value for bronchoconstriction is. It also became evident after the publication of Stevens' law that the value of  $n$  was dependent on the context of investigation: stimulus level and duration as well as sensory adaptation caused changes in perceived response. The aim of the present study was not to determine the value of  $n$  for bronchoconstriction, and we therefore assumed a general value of 1 to differentiate between good and poor perceivers. But this implies that only in cases where the value of  $n$  is 1 would the changes in dyspnea be linear with respect to physiological changes, while it is most probable that values near 1 are reflections of "normal" perception, and those further above or below 1 are an expression of "good" or "poor" perception, respectively. With the data obtained, we could not even make an approximation of this kind, as all subjects showed values of  $n$  less than 1. Finally, Stevens' law has the added disadvantage of being complicated to calculate, making it difficult to apply in daily clinical practice.

The slope of the regression line of the response-perception curve has proven to be a good index of perception of bronchoconstriction in patients with asthma.<sup>7</sup> In the study by Bijl-Hofland et al<sup>7</sup> the authors pointed out that if the value of  $r^2$  of the linear regression is less than 0.71, the calculation of the slope may be less exact. Such cases might correspond to hypoperceivers, although the authors obtained similar results regardless of whether such patients were included or not. However,  $r^2$  in isolation is not valid for the study of perception. We have an example in those subjects who experienced no change in breathlessness despite a 20% decrease in  $FEV_1$ ; in these patients, the slope was 0 and while  $r^2$  was 1—the maximum—they must nevertheless be considered hypoperceivers. Subjects for whom  $r^2$  was low might simply be patients for whom breathlessness does not correspond clearly to  $FEV_1$  rather than hypoperceivers per se. Given that agreement between the slope and CB was still good even with low  $r^2$  values, we do not think that such cases should be excluded from the analysis.

The agreement between the classification of perception by slope and by CB is worthy of note. The  $\kappa$  statistic was 0.88 and only in 5 cases were subjects classified differently by the 2 methods. In these cases the slope usually fell near the reference limits and

worsening of dyspnea occurred only after the last doubling dose of histamine. Dyspnea in such cases was mild in absolute terms, probably explaining the low CB values and the fact that the slope stayed within reference limits. In addition to good agreement with slope, the principal advantage of CB lies in its simplicity: it is extremely easy to calculate and the value does give us some information (albeit intuitive) about how a subject perceives bronchoconstriction.

The present study has certain limitations. For one, we cannot establish with certainty the reference limits that differentiate between good and poor perceivers of dyspnea induced by bronchoconstriction. Those established in our study may not be the only acceptable ones and we believe that the only affirmation we can make with confidence is that subjects who perceive breathlessness to be the same or less once  $FEV_1$  has decreased by 20% are hypoperceivers. The difficulty in establishing reference limits is due, in part, to the fact that the distributions obtained for the values of the slope,  $PS_{20}$ , and CB were not normal because of the high percentage of patients who perceived no change in dyspnea despite bronchoconstriction. These results differed from those of patients with asthma, in whom the percentage of hypoperceivers was lower<sup>5</sup>; the results, however, are not completely comparable, as the method used was different. We could not establish a control group either, as results would not be comparable with subjects in different clinical stages of COPD. Another limitation is that in COPD dyspnea during bronchoconstriction is not due to a decrease in bronchial caliber alone. The resulting muscular tensions and air trapping also play an important role, although all the parameters used to assess dyspnea have been related to changes in  $FEV_1$ . However, the high percentage of subjects who experienced no worsening of breathlessness during bronchoconstriction would indicate that they perceived not only changes in airway caliber poorly, but also that they were poor perceivers of any air trapping that might have occurred. Given the design of our study, however, we cannot know "how much" of the dyspnea was due to air trapping or "how much" to decrease in bronchial caliber.

We believe that we can conclude that CB is at least as useful a parameter as slope to study perception of dyspnea in subjects with COPD. It presents the added advantage that only 2 points on the response-perception curve (initial dyspnea and  $PS_{20}$ ) are needed to calculate it, whereas calculation of the slope requires linear regression. In our study we noted a high percentage of patients with COPD who were unable to perceive acute bronchoconstriction properly. The clinical relevance of this observation is in need of further study.

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