

Letter to the Editor

Inspiration through the nose increases the bronchoprotective effect of lung inflation

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The nose plays an important role in the function of the respiratory system.¹ For example, nasal breathing can protect the airways of asthmatic subjects from exercise-induced bronchospasm.² Inversely, inflammatory events in the nasal mucosa can be accompanied by functional and tissue changes in the lower airways, effects that have been described as the “vertical relationship” between rhinitis and asthma.³ There are probably several mechanisms through which the nose could influence the lower airways (air conditioning, nasobronchial reflexes, and systemic inflammatory responses). We herein report that in healthy nonasthmatic individuals deep inspirations through the nose, as opposed to the mouth, provide greater bronchoprotection from a bronchospastic stimulus. Deep inspiration-induced bronchoprotection is a phenomenon that plays a significant physiologic role in lower airway patency, and its loss is strongly associated with airways hyperresponsiveness and asthma.^{4,5}

We tested 20 subjects who had no history of asthma or any chronic upper or lower respiratory tract disease with normal baseline spirometry, no evidence of airways hyperresponsiveness on routine methacholine inhalation challenge, and negative epicutaneous skin test results to common aeroallergens. To measure bronchoprotection by deep inspiration, we used single-dose methacholine challenges, as previously described. The characteristic of these challenges is that after baseline spirometry, subjects abstain from taking deep inspirations for 20 minutes before inhaling a single dose of methacholine with 5 tidal breaths. Three minutes after the challenge, single spirometry is performed. The single-dose challenge needs to be repeated with increasing doses on different days to determine the dose that causes a 20% or greater reduction

in FEV₁. Once this dose was identified, our subjects returned for an additional 2 single-dose challenges using the determined threshold dose of methacholine: on each occasion, immediately before the methacholine challenge, subjects were asked to take 5 consecutive, slow deep inspirations through their nose (mouth closed) or through their mouth (nose-clip in place) in randomized sequence. The choice of 5 deep inspirations is based on previous work.⁶ Bronchoprotection by deep inspiration was determined by comparing the reduction in FEV₁ or forced vital capacity (FVC) from baseline in the challenges in which deep inspirations were taken before methacholine to the no-deep-inspiration challenge. The study was approved by the Johns Hopkins Bayview Medical Center Institutional Review Board, and all subjects provided written informed consent.

The median concentration of methacholine required to achieve the targeted reduction in FEV₁ in the absence of deep inspiration was 75 mg/mL. The actual reduction in FEV₁ and FVC by that dose was $38\% \pm 3.5\%$ and $24\% \pm 1.7\%$, respectively (mean $\pm$ SEM). Deep inspirations conferred protection against methacholine (Fig 1), with the percentage of bronchoprotection based on FEV₁ being $57\% \pm 4.1\%$ with nasal and $41\% \pm 7.2\%$ with oral deep inspirations ($P = .04$). Bronchoprotection based on FVC yielded similar results ($P = .04$). To rule out the possibility that differences in the velocity of the inspiratory maneuver affected the outcome of the study, we asked 5 different healthy nonasthmatic subjects to perform slow deep inspiratory maneuvers through the nose and through the mouth and measured inspiratory vital capacity, peak inspiratory flow, and midinspiratory flow at 50% of vital capacity. The time of the inspiratory maneuvers was kept between 3 and 5 seconds. In no parameter did we detect significant differences between nasal and oral maneuvers (nose vs mouth: inspiratory vital capacity, 3.99 ± 0.44 vs 4.15 ± 0.39 L, $P = .12$; peak inspiratory flow, 1.80 ± 0.33 vs

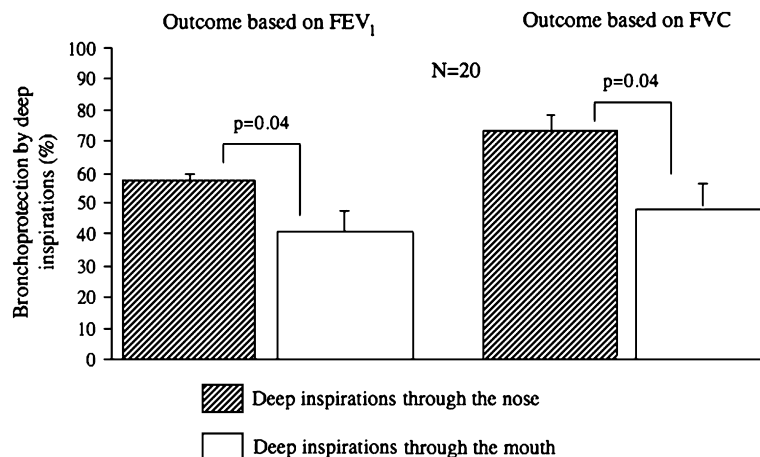


FIG 1. Bronchoprotection by 5 deep inspirations based on FEV₁ or FVC with the deep inspirations taken through the nose versus the mouth. Bars represent means $\pm$ SEM.

2.12 ± 0.33 L/s, $P = .36$; midinspiratory flow at 50% of vital capacity: 1.45 ± 0.31 vs 1.46 ± 0.28 L/s, $P = .96$).

This study demonstrates that the bronchoprotective effect of deep inspiration in healthy, nonasthmatic human subjects is approximately 40% stronger when air is inhaled through the nose compared with through the mouth, with this difference not being accounted for by differences in inspiratory airflow. The mechanism through which nasal inspiration confers this effect is unknown, but 2 hypotheses can be raised: (1) nasal breathing enriches inhaled air with a natural product that increases bronchoprotection, and (2) deep inspiration through the nose initiates a central reflex that potentiates the bronchoprotective effect of deep inspiration. This hypothesis can be tested by anesthetizing the nose, but we have not done this at this time. In the context of the first hypothesis, the primary candidate to play a bronchoprotective role is nitric oxide, which is produced in large amounts by the sinus and nasal mucosa,⁷ has substantial bronchodilatory activity,⁸ and has been shown to play a role in airways hyperresponsiveness.⁹ However, the role of nitric oxide in deep inspiration-induced bronchoprotection has yet to be examined.

In conclusion, by determining that the bronchoprotective effect of deep inspiration is stronger when air is inhaled through the nose, we have identified another possible mechanism through which the upper airways can benefit the lower airways. This observation adds to our knowledge of the mechanisms of nose-lung interaction.

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