

SCIENTIFIC LETTER

Exercise simultaneously increases nasal patency and bronchial obstruction in asthmatic children

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We found that simultaneous post-exercise increase in nasal patency and bronchial obstruction occurs only in children with atopic asthma, but not in sensitized children without asthma. In healthy children, the increase in nasal patency is accompanied by bronchial dilatation.

Key words: asthma, child, exercise, nose, sensitization.

Abbreviations: Δ , post-exercise percentage change; EU, European Union; FEV₁, forced expiratory volume in 1 s; Ig, immunoglobulin; IOS, impulse oscillometry; Rrs5, respiratory resistance at 5 Hz; Rrs51min, Rrs5 at 1 min after exercise; Rrs55min, Rrs5 at 5 min after exercise; Rrs510min, Rrs5 at 10 min after exercise; TMCA, total smallest minimal cross-sectional area (as the sum of both nasal cavities); TVOL, total nasal cavity volume 0–3 cm from the nostril.

In healthy subjects, exercise increases nasal patency by decreasing nasal mucosal congestion, and induces bronchial dilatation through smooth muscle cell relaxation via sympathetic reflexes during¹ and after² exercise. Conversely, exercise induces bronchial obstruction in patients with unstable asthma.³ Still, the post-exercise increase in nasal patency is similar in subjects with rhinitis, asthma or IgE sensitization, and in healthy subjects.^{3–6} Thus, the reactions in nose and distal airways may be different, and the widely proposed suggestion of the united airway disease may not involve these post-exercise reactions. Moreover, simultaneous reactions have not been studied in children. For these reasons, our aim was to study the nasal and bronchial responses after exercise in asthmatic, sensitized and healthy children.

This is a study of a subgroup of children participating in the follow-up studies of Vinku2 ($n = 23$) or the

EU-sponsored multicentre PreDicta ($n = 7$), including consecutive children who successfully underwent acoustic rhinometry.⁶ The study was carried out at the Department of Pediatrics, Turku University Hospital in Turku, Finland. It was approved by the Ethics Committee of the hospital, and commenced after obtaining written informed consent from guardians (Clinical trial registration: NCT00731575 at ClinicalTrials.gov).

Acoustic rhinometry (Acoustic Rhinometer A1, GM Instruments Ltd., Kilwinning, Scotland) assessed nasal acoustic values including total smallest minimal cross-sectional area (TMCA as the sum of both nasal cavities) and the total nasal cavity volume 0–3 cm from the nostril (TVOL)⁷ at baseline and 10 min after exercise testing.⁶ The lung function was assessed by impulse oscillometry (IOS, Jaeger GmbH, Würzburg, Germany) in Vinku2 Study or by spirometry (Medikro Oy, Kuopio, Finland) in PreDicta Study at baseline and 1, 5 and 10 min after exercise testing, which was performed as a free running test designed to measure bronchial hyper-reactivity in children.^{8–10} Air temperature and humidity were measured, and the exercise test was performed outside when air temperature was $\geq 5^{\circ}\text{C}$, otherwise inside. Children had current asthma if they met ≥ 1 of the subsequent criteria during the preceding 12 months: parental/patient chart reports of doctor-diagnosed asthma, and need for daily doctor-prescribed asthma therapy with inhaled corticosteroids, use of oral corticosteroids for asthma exacerbations and/or acute asthma symptoms relieved by repeated use of bronchodilator.⁹ Children had sensitization if they had positivity against any of the tested allergens (food and/or aeroallergens) in skin prick testing (in PreDicta; wheal diameter ≥ 3 mm) or IgE antibodies (in Vinku2; cut-off level ≥ 0.35 kU/L).⁶ Current atopic asthma was asthma with sensitization. Children without asthma and sensitization were considered healthy.

To maximize the number of study children, we included children from both the studies with different lung function methods. This was enabled by linearly re-scaling the forced expiratory volume in 1 s (FEV₁) values of spirometry to the counterpart respiratory resistance at 5 Hz (Rrs5) values of IOS at analogous moments. The correlation coefficient of 2.3 was used in

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this re-scaling as the correlation of Rrs5 and FEV1 has been demonstrated with challenge testing in asthmatic children.^{10–13} With bronchial obstruction, the respiratory resistance increases and therefore the values of Rrs5 in IOS increase versus FEV1 by spirometry which decreases.^{8,10,11} The nasal and bronchial responses after exercise were determined as percentage changes (Δ) between baseline and post-exercise in nasal acoustic (Δ TMCA and Δ TVOL at 10 min) and IOS (Δ Rrs5 at 1 min (Δ Rrs51min), 5 min (Δ Rrs55min) and 10 min (Δ Rrs510min) after exercise) values. Then, the associations between nasal and bronchial responses after exercise were assessed with bivariate Pearson correlations based on the normality of the data. A two-sided *P*-value of 0.05 was considered statistically significant. Analyses were made using IBM SPSS 21.0 software (SPSS Inc, Chicago, IL, USA).

This study included 30 children (mean age: 5.1 years; range: 4.1–6.4 years; SD: 0.1 years, 20 males). Current

asthma was diagnosed in 12 children, of whom 11 had atopic asthma, but only one child had non-atopic asthma and therefore was not included in analyses. Daily asthma controller therapy was used by 10 of 12 asthmatic children. Sensitization occurred altogether in 18 children, of whom 7 had no asthma, but 11 were the above-mentioned atopic asthmatic children. Eleven children were considered healthy without asthma or sensitization. No significant differences were found in the pooled estimates of nasal or bronchial responses after exercise in asthmatic versus non-asthmatic, sensitized versus non-sensitized or healthy versus sensitized and/or asthmatic children.

Overall, no correlations were found between nasal and bronchial responses after exercise ($P > 0.14$) (Fig. 1A). Interestingly, a significant correlation between simultaneous post-exercise increase in nasal patency (Δ TMCA) and bronchial obstruction (Δ Rrs51min and Δ Rrs55min) was demonstrated in children with current

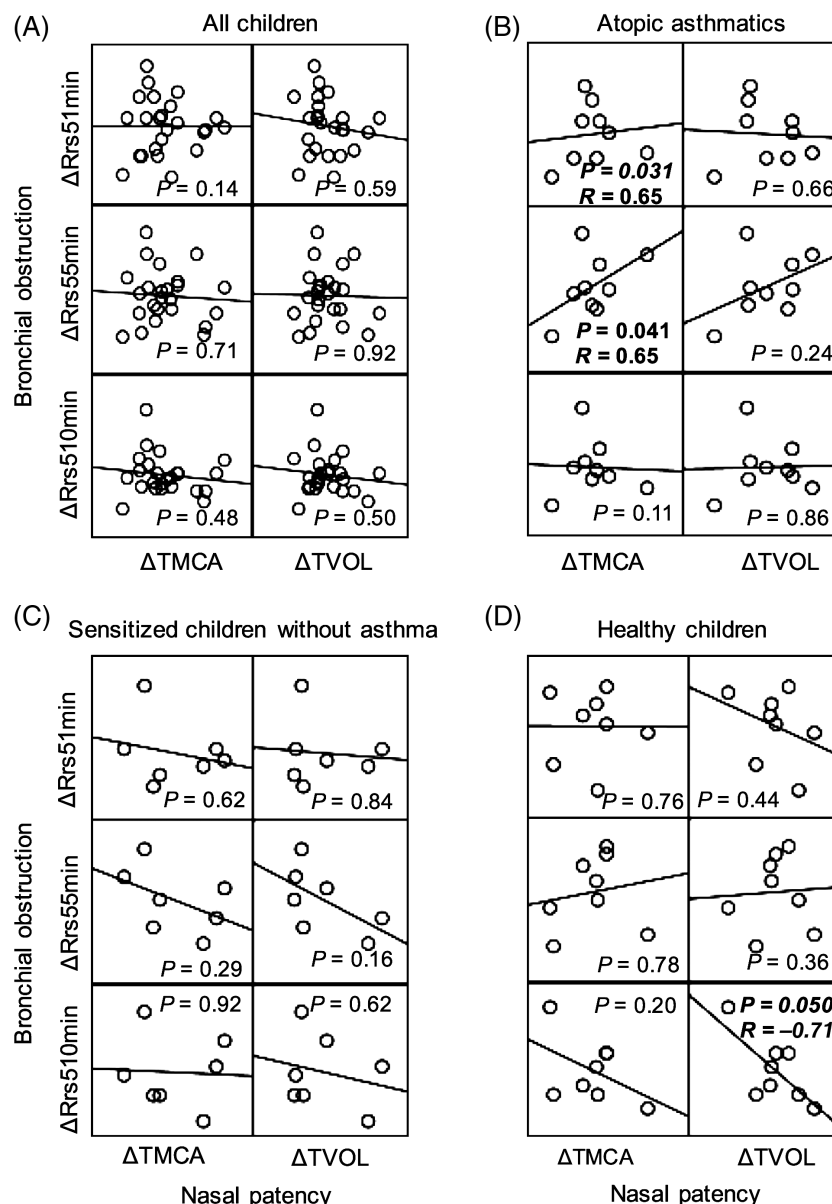


Figure 1 Pearson correlations (*R*) and statistical significances (*P*) between simultaneous reactions (A) in all children ($n = 30$), and in children with (B) current atopic asthma ($n = 11$), (C) sensitization without asthma ($n = 7$) and (D) in healthy children with no asthma and sensitization ($n = 11$). Δ , post-exercise percentage change; Rrs5, respiratory resistance at 5 Hz; Rrs51min, Rrs5 at 1 min after exercise; Rrs55min, Rrs5 at 5 min after exercise; Rrs510min: Rrs5 at 10 min after exercise; TMCA, total smallest minimal cross-sectional area (as the sum of both nasal cavities); TVOL, total nasal cavity volume 0–3 cm from the nostril.

atopic asthma ($P = 0.041$) (Fig. 1B), but not in sensitized children without asthma ($P > 0.16$) (Fig. 1C). An increase in nasal patency (Δ TVOL) and bronchial dilatation (Δ Rrs510min) was seen in healthy children ($P = 0.050$) (Fig. 1D). The results were consistent when analysed separately for IOS and spirometry.

Physical exercise increases nasal patency independently from sensitization or asthma status.^{3–6} We found that this post-exercise increase in nasal patency is accompanied by simultaneous bronchial obstruction in children with atopic asthma, but not in sensitized children without asthma. Bronchial dilatation occurs in healthy children.¹⁴ The mechanism mediating these exercise-induced reflexes may be different for upper and lower airways, and thus the dogma 'one airway—one disease' in light of physiological stimuli may be questioned.^{3,5} However, baseline nasal acoustic values are lower in asthmatic children⁶ and adults¹⁵ compared with controls independent of sensitization status. This may provide evidence of persistent changes to whole airway system due to asthma inflammation, and conversely, support the one-airway paradigm. Although the majority of physiological phenomena are similar in children and adults, this is the first study demonstrating these simultaneous physiological reactions in children.

The post-exercise increase in nasal patency suggests natural response to stress via sympathetic reflexes.^{2–6} In healthy subjects, the bronchial dilatation during exercise may occur through smooth muscle cell relaxation via activated bronchial β -adrenergic receptors and decreased vagal tone.¹ Children with mild/moderate asthma, as observed in this study, often have normal lung function at baseline. Still, in asthmatic children, the responses after exercise appear to be different in upper and lower airways as exercise induces bronchial hyper-reactivity in the form of obstruction. This would be caused by loss of water from airways, and thereby changes in respiratory mucosa causing release of inflammatory mediators, smooth muscle cell contraction and ultimately bronchial obstruction.^{5,10} This cascade is the target for daily asthma controller therapy.⁹ Thus, the post-exercise obstruction could not be demonstrated in asthmatic children due to daily asthma controller therapy in most asthmatic children. However, despite the fact that post-exercise obstruction per se did not reach significance, our finding of positive correlation between increase in nasal patency and bronchial obstruction only in asthmatic children raises a theory that the therapy targets of nasal patency and post-exercise bronchial obstruction might be different.

In conclusion, we found that exercise causes simultaneous increase in nasal patency and bronchial obstruction in asthmatic, but not in healthy, children. The sensitization status did not affect this reaction.

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