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Airway Sensory Nerve Hyperinnervation in Obese Mice with Airway Hyperreactivity

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Keywords

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Abstract

Background

Obese asthmatic patients often have severe symptoms and poor responses to treatment. The molecular mechanisms of obesity-related asthma and associated airway hyperreactivity remain unclear, limiting our ability to develop new therapeutic strategies. In humans, increased airway innervation contributes to the pathogenesis of airway hyperreactivity. Here we tested if diet-induced obese mice have nerve-mediated airway hyperreactivity and increased airway sensory nerve innervation.

Methods

Wild type (C57BL/6J) mice were fed a normal or high fat diet for 19 weeks. Mice were fasted, anesthetized, ventilated, and paralyzed for airway measurement experiments. Airway response to increasing doses of inhaled serotonin was measured before and after vagotomy to test airway nerve-mediated reflex bronchoconstriction. Airway epithelial nerves were immunostained for substance P in optically cleared whole-mount tracheas and density was quantified using confocal microscopy and three-dimensional nerve modeling. Food intake, body weight, body fat, fasting glucose, and fasting insulin were measured.

Results

Body weight was increased in high fat chow fed mice. Reflex mediated bronchoconstriction in response to inhaled serotonin was increased in these obese mice, and there was increased length and branching of airway epithelial sensory nerves. Body fat, fasting glucose, and fasting insulin were significantly higher in the mice fed a high fat diet.

Conclusion

Diet-induced obese mice have nerve-mediated reflex airway hyperreactivity and airway sensory nerve hyperinnervation suggesting a mechanism for obesity-related airway hyperreactivity.