Use of flow whole body plethysmography (FWBP) to assess rat strain differential airway responsiveness (AR) and its influence on ozone (O_3) dosimetry.

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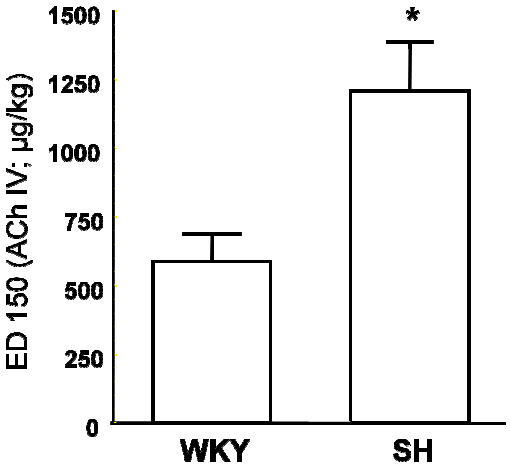
Rationale. Large differences exist in the sensitivity of people to O_3, a principal component of urban smog. Those that are particularly sensitive are known as “responders" because acute exposure induces rapid, shallow breathing and decreased forced expiratory volumes. This restrictive breathing pattern reflects c-fiber-mediated moderate bronchoconstriction which is postulated to allow more even distribution of O_3 within terminal lung regions, thus protecting large conducting airways from its irritant effects. It is not clear whether responders may consequently receive greater overall lung O_3 deposition during chronic exposure. The present study aimed to compare the *effective O_3 dose* of two rat strains with differing degrees of AR, namely the spontaneously hypertensive (SH) rats and their background WKY strain.

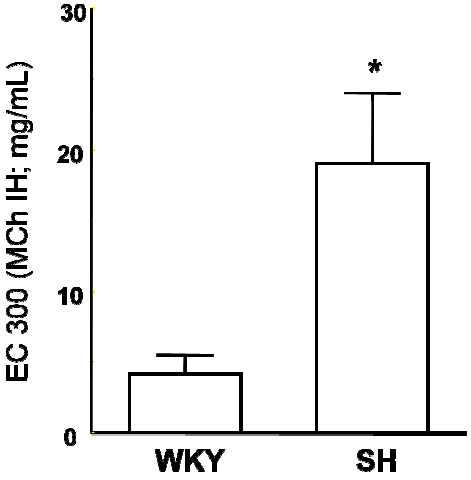
Methods. Having shown that anesthetized WKY rats exhibited increased AR to i.v. acetylcholine based on lung mechanical assessments, we hypothesized that WKY rats would be similarly sensitive to inhaled insults. Herein, awake male 3-mo-old rats inhaled nebulized methacholine (MCh) within FWBP chambers. The concentration required to increase PenH 300% (MCh EC_{300}) was used as an index of non-specific AR. Similarly, FWBP parameters were assessed immediately after nose-only exposure to air or O_3 (at 0.25, 0.5, or 1.0 ppm x 4-h). The *effective O_3 dose* [i.e., product of O_3 concentration (ppm), exposure duration (hr), and minute volume (MV; mL/min/100 g body wt)] was used to assess differential O_3 lung dosimetry.

Results. Based on MCh EC_{300} values, WKY rats again exhibited 3-fold greater AR than SH rats. Immediately after O_3 exposure, both WKY and SH rats had concentration-dependent decreases in MV (20% and 42%, respectively). Compared to SH rats, WKY rats developed significantly greater increases in PenH after 0.5 and 1.0 ppm exposures consistent with moderate bronchoconstriction. At 0.25 ppm, the *effective O_3 dose* in both strains was similar. However, at 0.5 ppm O_3, it was ≈40% reduced in WKY rats; and then rebounded such that at the highest (1.0 ppm) exposure, WKY rats were again equivalent to SH rats.

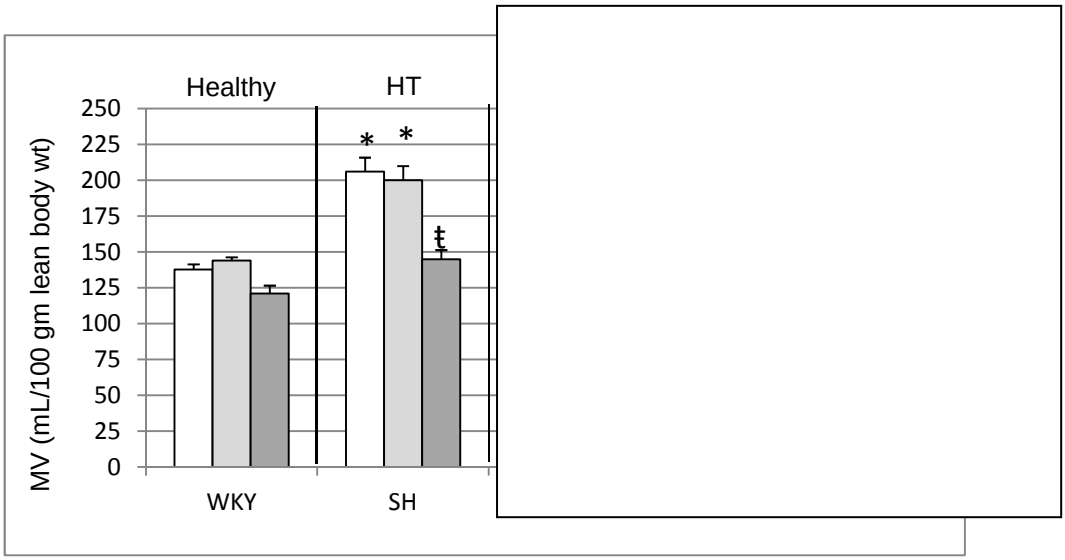
Conclusions. WKY rats consistently exhibited increased AR compared to SH rats. FWBP was capable of discriminating responder and non-responder rat strains. Data further suggest that at moderate pollutant exposures (i.e., 0.5 ppm O_3), bronchoconstriction in responder rats served to reduce overall lung O_3 dosimetry. Conversely, at the highest exposure (i.e., 1.0 ppm), excessive airway narrowing appeared instead to contribute to greater O_3 lung burdens. (This abstract does not reflect USEPA policy).



ED 150 = 50% increase in the baseline airway opening pressure.



EC 300 = 3-fold increase in the post-saline Penh value.



WKY to SH compare: adaptation to WBP

WKY to SH compare MV changes acutely after Air to 1.0 ppm x 4 hr

WKY to SH compare Effective dose vs O3 concentration