Title: CHANGES IN RESPIRATION AFTER THYROIDECTOMY AND PARATHYROIDECTOMY

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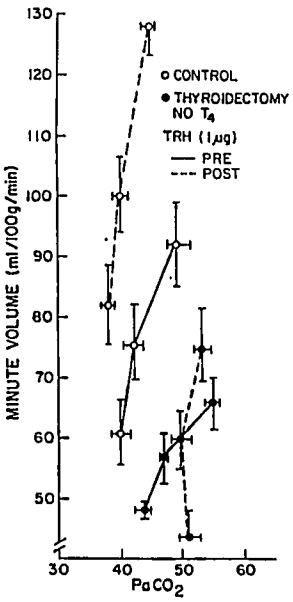
Introduction. It is well recognized that inadvertent damage to the parathyroid glands may occur in the course of thyroidectomy. Although usually respiratory distress after this operation is on an obstructive basis, no systematic investigation has been made of the importance of hypocalcemia or hypothyroidism in respiratory control. The present investigation sought to establish how thyroid/parathyroidectomy alters respiratory control in halothane anesthetized rats. In addition, the respiratory and cardiovascular responses to thyrotropin releasing hormone, an important determinant in shock states, were examined in these animals.

Methods. Measurement of Respiration. Sprague-Dawley rats of either sex, weighing 200-300g were lightly anesthetized with ether to permit placement of cannulae in the tail or femoral artery, the trachea and the lateral cerebral ventricle. Following the surgical procedures, the animal was given 0.7% halothane in oxygen to breathe and placed in a closed body plethysmograph to permit recording of respiratory tidal volume, frequency and inspiratory time (T_I).[1,2] Body temperature was monitored and maintained constant. After a stabilization period of 20 minutes, mechanical responsiveness to CO_2 was tested using mixtures of 2.5 and 5% CO_2 in O_2 and halothane. Arterial blood (0.2ml) was removed immediately after each measurement of mechanical response for measurement of $PaCO_2$. When the respiratory parameters had returned to near pre-CO_2-exposure values, TRH or saline was given via the i.c.v. cannula. At 5-minute intervals, measurements of blood pressure, heart rate, respiratory rate, tidal volume and T_I were made. After the 15-minute values were recorded, the two above sequential CO_2 exposures were repeated. The plethysmograph was calibrated at the end of the experiment with each rat. Statistical analysis employed two tailed t tests and/or analysis of variance using Tukey's procedure to assess significance of differences.

Results. Rats thyroidectomized and parathyroidectomized 2 weeks before respiratory studies had a minute volume-$PaCO_2$ response curve which was shifted to the right (see Fig.). T_I and T_I/T totals were not altered. Although supplementation with 25µg/kg/day thyroxine during the two-week period tended to keep the curve in the normal position, the curve remained displaced to the right. Administration of a submaximal respiratory stimulating dose of TRH (1µg i.c.v.) shifted the $PaCO_2$-minute volume curve to the left in control rats and T_4 supplemented rats, but did not shift the curve of thyroidectomized rats (see Fig.). The minute volume response to TRH was significantly less ($P<.05$) and delayed in thyroidectomized rats relative to control rats, and this was antagonized by T_4 maintenance. Since serum calcium values (control=9.9mg%) were reduced in the thyroidectomized/parathyroidectomized rats (7.2mg%) TRH was given to rats parathyroidectomized 2-3 weeks previously. The minute volume-$PaCO_2$ curve was not significantly altered in these hypocalcemic rats with normal T_4 levels, and the respiratory stimulant effect of TRH was unaltered. Administration of propylthiouracil, sufficient to reduce plasma T_4 values to the range seen in thyroidectomized rats, also shifted the $PaCO_2$-minute volume curve to the right, though this change was less marked than after thyroidectomy/parathyroidectomy. Though heart rate was significantly lower in the thyroidectomy/parathyroidectomy and PTU-treated rats, blood pressure was not altered. The slight (20-22%, $P<.05$) bradycardia observed after TRH in control rats was not seen in animals with deficient thyroid function.

Discussion. The decrease in basal CO_2 responsiveness which develops after thyroidectomy/parathyroidectomy is a result of altered thyroid function, not changes in plasma calcium availability. The central respiratory stimulant effect of TRH is also a function of thyroid state, though it is probably not secondary to the acute release of thyroid hormone. The minor effects of TRH on the cardiovascular system are not apparent in hypothyroid rats.



References.
1. Mueller RA, Lundberg DB, Breese GR: Alteration of aminophylline-induced respiratory stimulation by perturbation of biogenic amine systems. J Pharmacol Exp Ther 218:593-599, 1981
2. Lundberg DB, Breese GR, Mueller RA: Aminophylline may stimulate respiration in rats by activation of dopaminergic receptors. J Pharmacol Exp Ther 217: 215-221, 1981