Regulation of Body Fluid Balance in Human GH-Releasing Hormone (hGHRH)-Transgenic Rats

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GH stimulates longitudinal bone growth and also exerts a wide variety of other biological actions, such as a water-retaining effect. Chronic excess of GH causes various degrees of edema due to increased extracellular water through an antinatriuretic action in the kidneys as seen in patients with acromegaly [1-3]. Recently mechanisms underlying the neural control of body fluid balance have been elucidated [4], but little is known about the neural control of body fluid balance in patients with acromegaly. We have established a strain of human GH-releasing hormone (GHRH)-transgenic rats [5] as an animal model for human giantism and acromegaly. In the present study, we studied water balance and urinary sodium excretion in response to changes in drinking in hGHRH-transgenic conscious rats (Tg).

Materials and Methods

Male Tg (n=8) and their control Sprague-Dawley rats (CNT, n=8) of three-month-old were housed individually in metabolic cages under constant light and dark cycles (lights on: 0600–1800 h). All the Tg showed integration of hGHRH gene and high plasma hGHRH concentrations (over 5,000 pg/ml, vs. CNT: below the least detectable levels 0.2 pg/ml). Daily food and water intake, urine volume, and urinary electrolytes excretion were measured. The rats were then given angiotensin II (A II, 100 ug/kg, s.c.), 40% polyethylene glycol (PEG, 10 mL/kg, s.c.) or 5% NaCl (20 mL/kg, i.p.) for the neural stimulation of drinking behavior. Cumulative water intake was measured after administration of A II, hypertonic saline (for 240 min) and polyethylene glycol (for 360 min). Cumulative urine volume after A II, PEG or NaCl was also measured for 240 min.

Results and Discussion

The Tg were large in size (mean ± SEM, BW n=8: 598.7 ± 19.6 g vs. CNT n=8: 493.4 ± 15.3 g, P<0.01), and showed increases in daily intake of food and excretion of sodium (2.09 ± 0.05 mEq/day, vs. CNT 1.71 ± 0.06 mEq/day, P<0.01) and potassium (4.25 ± 0.12 mEq/day, vs. CNT 3.32 ± 0.1 mEq/day, P<0.01) without significant changes in daily intake of water or urine volume (Table 1).

We then applied to the rats three different stimuli to induce drinking behavior [5]. Neither A II, a direct stimulator of the hypothalamic “drinking” center, nor PEG, a indirect stimulator of drinking behavior by reducing circulating blood volume induced by accumulating water into the subcutaneous space, caused significant differences in daily intake of water or urine volume (Table 1).

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When Tg (n=7) were given with 5% NaCl, another stimulator of the “drinking” center by increasing plasma osmotic pressure, they showed increases in both urine volume (3.2 ± 0.1
ml vs. CNT 2.4 ± 0.2 mL, P<0.025) and sodium excretion (0.83 ± 0.02 mEq, vs. CNT n=8, 0.63 ± 0.05 mEq, P<0.025) without any significant change in cumulative water intake (Fig. 3).

These results suggest that chronic GH excess does not seem to alter the neural control of drinking behavior as assessed by individual animals, but does increase sodium and potassium turnover as is observed in patients with acromegaly. The hGHRH-transgenic rat provides a useful animal model for the study of body fluid balance in acromegaly.

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References


