Regulation of Body Fluid Balance in Spontaneous Dwarf Rats Caused by Isolated Growth Hormone (GH) Deficiency

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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. Several studies have recently shown that GH deficiency (GHD) in man [1, 2] and mice [3] is associated with a reduction in extracellular water (ECW). Depletion of the extracellular fluid volume is a major stimulus which signals changes in the tonicity and volume of total body water, and thereby brings into action the appropriate water and electrolyte regulatory responses [4].

A strain of dwarf rat with autosomal recessive inheritance (gene symbol dr) produces characteristics similar to those of the human disorder, isolated growth hormone deficiency Type I [5]. Although the genetic cause of isolated GH deficiency in the strain of spontaneous dwarf rat was identified [6, 7], little is known about the neural control of body fluid balance in the dwarf rat.

In the present study, to elucidate the neural control of body fluid balance in patients with GHD, we studied water balance in response to drinking behavior in a strain of spontaneous dwarf rats (dr). and is maintained in our laboratory by combinations of crossing hemizygous (dr/+) or homozygous (dr/dr) males with homozygous females (dr/dr). 3–4 month-old homozygous male dwarf rats (dr) of the 36th generation were used. Age matched normal Sprague-Dawley SD male rats (Kiwa Experimental Animal Research Inc., Wakayama, Jpn) were used as normal controls (CNT). All the rats examined were housed in a light- and temperature-controlled room (12 h of light/day; 23–25°C) and allowed access to food and water ad libitum. Daily food and water intake, urine volume, and urinary electrolyte excretion were measured [8]. The rats were then given angiotensin II (A II, 100 μg/kg, s.c.), 40% polyethylene glycol (PEG, 10 mL/kg, s.c.) or 5% NaCl (20 mL/kg, i.p.) for neural stimulation of drinking behavior. Cumulative water intake was measured after the administration of A II, hypertonic saline (for 240 min) or polyethylene glycol (for 360 min). Cumulative urine volume after A II, PEG or NaCl was also measured for 240 min.

The descriptive statistical results are presented as the mean ± SEM. Significance of differences in body weight, daily food intake, water intake and urine volume was calculated by unpaired t test. Group differences in cumulative water intake after administration of A II, hypertonic saline or PEG were each subjected to a two-way repeated-measures of analysis of variance with a computer program StatView 4.0 for Macintosh computer. A P<0.05 was considered significant.

Materials and Methods

A strain of homozygous dr/dr of the 27th generation was gratefully provided by Dr. Okuma,
Results and Discussion

The dr were small (mean ± SEM, BW, n=7: 102.2 ± 2.0 g vs. CNT n=8: 318.6 ± 2.7 g, P<0.01), and showed decreases in daily intake of food (7.1 ± 0.2 g vs. CNT 22.6 ± 0.5 g), water intake (14.9 ± 0.4 g vs. CNT 36.1 ± 0.9 g) and urine volume (7.2 ± 0.4 ml vs. CNT 19.8 ± 0.7 ml) (Table 1).

The rats were injected either with angiotensin II (AII, 100 µg/kg, s.c.), a direct stimulator of the hypothalamic “drinking” center, 40% polyethylene glycol (PEG, 10 ml/kg, s.c.), a indirect stimulator of drinking behavior by reducing circulating blood volume induced by accumulating water in the subcutaneous space, or 5% NaCl (Sal, 20 mL/kg, ip), another stimulator of the “drinking” center by increasing plasma osmotic pressure for the neural stimulation of drinking behavior. Stimulation of drinking behavior by AII (Fig. 1), PEG (Fig. 2) or Sal (Fig. 3) caused significant increases in

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<th>( \text{Table 1. Daily food, water and urine volume in control (SD) and dwarf rats} )</th>
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<tr>
<td>food intake (g)</td>
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<tr>
<td>SD rats (n=8) (BW 318.6 ± 2.70 g)</td>
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<td>Dwarf rats (n=7) (BW 102.24 ± 2.04 g)</td>
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*P<0.05, **P<0.01, ***P<0.001 vs. CNT. The mean ± SD. The numbers in parenthesis indicate values expressed per 100 g BW. npaired t test: *P<0.05, **P<0.01, ***P<0.001.

Fig. 1. Cumulative water intake (ml/100 g BW) induced by administration of angiotensin II (100 µg/kg, s.c.) in SD and dr. The mean ± SD is shown. *P<0.05, **P<0.01, ***P<0.001 vs. CNT.

Fig. 2. Cumulative water intake (ml/100 g BW) induced by administration of 40% polyethylene glycol (10 ml/kg, s.c.) in SD and dr. The mean ± SD is shown. *P<0.05, **P<0.01, ***P<0.001 vs. CNT.

Fig. 3. Cumulative water intake (ml/100 g BW) induced by administration of hypertonic saline (20 ml/kg, i.p.) in SD and dr. The mean ± SD is shown. *P<0.05, **P<0.01, ***P<0.001 vs. CNT.
cumulative water intake in 4 h/100 g BW in dr (P<0.01 vs. CNT).

Since ECW was decreased in dr (Katakami et al., unpublished observation), the present results suggest that neural stimulation of drinking behavior does seem to facilitate water intake in excess to correct dehydration in chronic GH deficiency.

Acknowledgments

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References