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Influence of Repeated Deprivation upon Starvation-Induced Hypovolemia and Plasma Aldosterone Concentration in Rats

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WRIGHT, J. W. AND E. M. SCHULZ. *Influence of repeated deprivation upon starvation-induced hypovolemia and plasma aldosterone concentration in rats.* PHARMAC. BIOCHEM. BEHAV. **16**(5) 697–699, 1982.—Rats exposed to repeated periods of food deprivation during development revealed significant inhibition of starvation-induced hypovolemia as adults. Same age littermates food deprived once as adults indicated severe hypovolemia. Plasma aldosterone (but not angiotensin II) was significantly elevated in the repeatedly fasted group as compared with the control and the singly deprived groups. It is concluded that the repeated application of food deprivation during development results in physiological compensation in the form of increased aldosterone release if starvation is encountered in adulthood. These increments in plasma aldosterone promote greater sodium retention thus lessening the compromising of blood volume necessary to maintain normal plasma osmolality given the lack of dietary sodium.

Food deprivation Hypovolemia Intravascular volume maintenance Angiotensin II Aldosterone Carcass and gut water Rats

A SINGLE food deprivation experience with water available in the adult rat produces a plasma volume deficit of 19% after 2 days and 30–33% after 4 days [9,13] accompanied by carcass water losses of 5 and 10%, respectively, and decreased urinary sodium losses [10]. Similar results have been reported for 4 day food deprived developing rats with plasma volume declines of 39% at 40 days of age, 32% at 60 days and 29% at 100 days [12]. When food deprivation is repeatedly applied throughout development very different results are obtained. Rats deprived of food for 2 days, every 10 days, beginning at 28 days of age and terminating at 100 days (i.e., 8 deprivation experiences), maintained plasma volume equivalent with nondeprived control levels when measured during the last starvation period at 100 days of age, whereas 100 day old animals lost 19% of their plasma volume during one 2 day deprivation period [12]. The repeatedly deprived animals also significantly reduced water consumption during food deprivation as compared with the reductions exhibited by members of the singly deprived group. These observations suggest that a physiological compensation of intravascular fluid volume occurs with repeated exposure to food deprivation during development such that volume is maintained near normal.

The importance of angiotensin II (AII) and aldosterone (ALD) in the maintanence of intravascular volume has been established with the renin-angiotensin-aldosterone system normally activated by stimuli associated with reduced blood pressure, flow or volume, resulting in compensatory increases in each [5]. The present investigation was designed to measure any changes in plasma AII and ALD concentrations that accompany repeated experience with short periods of starvation during development. We hypothesized that elevations in plasma aldosterone would accompany repeated experience with food deprivation thus suggesting a mechanism for sodium retention and maintenance of normal intravascular volume.

METHOD

Animals

The offspring of 12 female Sprague-Dawley rats (Charles River Inc., timed pregnancies) were utilized. Each mother and her litter were maintained under a 12–12 light/dark cycle initiated at 0700 hr at 23–24°C in breeder cages until weaning at 21 days of age.

Procedures

Three male pups were selected at random from each litter and were housed in individual cages (25.4×20.4×17.8 cm) under the previous temperature and light conditions. The thirty-six animals were assigned to 3 independent groups of 12 each, with each litter represented in each group. Water was available throughout the treatment conditions. Subjects in the first group experienced 8 48-hr periods of food deprivation initiated at 10-day intervals beginning at 28 days of age, terminating at 100 days of age with a blood sample. Members of the second group were food deprived once for 48 hr at 98 days of age, terminating with a blood sample at 100 days of age. Each 48-hr deprivation period was initiated at 1100 hr. Members of the third group served as nondeprived controls blood sampled at 100 days of age.

TABLE 1

DEPRIVATION INDUCED CHANGES IN HEMATOCRIT, PLASMA VOLUME, CARCASS AND GUT WATER AND PLASMA ANGIOTENSIN AND ALDOSTERONE IN EACH GROUP

Treatment Group	N	Hematocrit (% RBC)	Plasma Vol* (ml/100 g)	Loss (%)	Carcass water (ml/100 g)	Loss (%)	Gut water (ml/100 g)	Loss (%)	Plasma Concentration AII (pg/ml)	Plasma Concentration ALD (pg/ml)
Group 1										
Repeatedly fd	12	46.2 ± 0.9†	3.19	7.8	54.3 ± 0.5	8.7	3.4 ± 0.1	32.0	86.4 ± 9.4	906.3 ± 137.8
Group 2										
Once fd	12	51.1 ± 0.7	2.48	28.3	54.8 ± 0.4	7.9	2.7 ± 0.1	46.0	88.3 ± 12.3	504.8 ± 59.8
Group 3										
ad lib cont	12	44.4 ± 0.6	3.46	—	59.5 ± 0.6	—	5.0 ± 0.1	—	71.4 ± 14.2	450.9 ± 52.9

*Derived from regression equation, PV=9.94−0.146 (HCT) [13].
†Mean ± standard error of the mean.
Fluid volume losses are presented as percentages of control values.
Abbreviations: fd=food deprived; cont=control.

The 1.5–2.0 ml blood samples were taken by heart puncture under light Metafane anesthesia (Methoxyflurane, Pitman-Moore, Inc., Washington Crossing, NJ). Sampling was completed within 2 min of removal from the home cage, in an adjacent room. A portion of the whole blood was used to prepare microhematocrit capillary tubes in duplicate and the remainder was transferred to culture tubes (12×75 mm) containing 20 units of sodium heparin. These tubes were then centrifuged to obtain the plasma fraction and two 100 μl aliquots of plasma were immediately frozen at −20°C for the later determination of AII concentration. The remaining plasma was pipetted into a third tube and also frozen for later determination of ALD concentration. Plasma AII and ALD levels were measured in duplicate by radioimmunoassay according to previously described procedures [2, 11, 14]. Both assays had sensitivities to 5 pg/100 μl.

At the conclusion of blood sampling each animal was killed by cervical dislocation. A midventral incision was made to expose the gastrointestinal tract which was clamped at the entrance to the stomach and at the distal end of the large intestine, removed and weighed. The carcass was also weighed and both were dried to constant weight at 85°C. The differences between wet and dry weights were then calculated on the basis of predeprivation bodyweight.

RESULTS AND DISCUSSION

Hemotocrit, estimated plasma volume, carcass, and gut water measures for each group are summarized in Table 1. Each data set was submitted to a one-way analysis of variance with posttest comparisons accomplished with Tukey's procedure [3]. As predicted from earlier investigations there were differences among the groups with respect to estimated plasma volume with the once food deprived group indicating the greatest volume loss while the repeatedly food deprived and control groups did not differ, $F(2,33)=18.64$; posttests $p<0.01$ and $p>0.05$, respectively. There were group differences in levels of carcass water with each treatment group revealing significant losses compared with the control group, $F(2,33)=33.74$; posttests $p<0.01$. There were also differences in gut water among the groups. The treatment groups revealed losses as compared with the control group, and the singly deprived group showed the greatest loss, $F(2,33)=97.78$; posttests $p<0.01$.

These results suggest significant plasma volume savings in those animals repeatedly food deprived but not in animals deprived once as adults. The total carcass water losses were not different for the treatment groups, however, the once deprived animals lost more gut water than members of the repeatedly deprived group.

There were anticipated differences in the final day predeprivation (98 days of age) body weights among the groups, $F(2,33)=10.18$, with the repeatedly food deprived group revealing a 14.7% lower weight than the control group and 9.7% less than the group to be deprived for the first time. However, the two treatment groups did not differ with respect to body weight loss at the completion of 48 hours of deprivation. The repeatedly food deprived group showed a 10.4% loss while the once deprived group an 11.4% loss.

Plasma AII and ALD concentrations are also presented in Table 1. There were no differences in circulating levels of AII among the groups, $F(2,33)=0.61$; however, there were differences in ALD concentrations with the repeatedly food deprived group revealing a doubling over that measured in the control group and a 67% elevation over that of the once deprived group, $F(2,33)=6.90$) posttest $p<0.01$.

These results indicate that experience with two day periods of food deprivation, repeatedly applied during development, promotes significant inhibition of starvation-induced hypovolemia in adulthood. This acquired ability to maintain near normal intravascular volume appears to be, in part, dependent upon an elevation in circulating aldosterone levels. Such elevations were not measured in animals deprived of food for two days as adults. We were somewhat surprised to note that plasma angiotensin II concentrations in the repeatedly food deprived animals were not different from the singly food deprived group, or from nondeprived controls. However, the half-life of aldosterone in circulation is much longer than that of angiotensin [4,6]. The function of increased aldosterone secretion in repeatedly food deprived animals likely derives from its ability to increase sodium retention and potassium excretion in renal tubules [8]. Greater sodium retention by food deprived animals lessens the compromising of blood volume necessary to maintain

normal plasma osmolality given the lack of dietary electrolytes. Angiotensin receptor density in adrenal glomerulosa tissue, and aldosterone secretion in response to angiotensin, are increased by sodium restriction [1] and by chronic angiotensin infusions in rats [7]. Given that repeated food deprivation encourages sodium retention we would predict increased numbers of angiotensin receptors in the adrenal glomerulosa tissues of these animals and such an analysis should be included in further investigations of this phenomenon.

In summary, the present results support the view that repeated food deprivation experiences during development result in physiological compensation if deprivation is encountered in adulthood, specifically in the form of increased plasma aldosterone. With respect to inhibition of starvation induced hypovolemia, these elevations in aldosterone appear to aid in the maintenance of normal intravascular volume.

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