Effect of Experimental Water Restriction on Brain Water*†

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A decrease in brain volume has obvious advantages in neurological surgery. Hypertonic urea and mannitol have been established as effective agents for cerebral dehydration. Acute changes in tonicity are produced by these hypertonic agents, and the effect on brain water, electrolytes, and osmolality has been well studied.1, 9, 13, 20, 22, 23 In comparison, the results of water restriction have not been as well defined.

The basic precepts for the treatment of dehydration were established during the 1940's when dehydration experiments were carried out in an effort to determine the optimal life-raft ration.5, 8, 13, 24 The difference between a water deprivation dehydration and a salt loss dehydration was clarified.17 Neurological examination remained essentially negative after men were deprived of water for 3 days;13 however, changes in behavior were noted by another group and described as an exaggeration of the individual's temperamental make-up.3 The amount of weight lost was variable.

Water restriction was found to initiate the dehydration reaction17, 19 and to produce a slow change in volume rather than an acute change in tonicity.2 Moore has suggested that this slower form of dehydration is better tolerated by the central nervous system.16 Smith, et al., have shown that a decrease in cerebrospinal fluid production can be effected by dehydration in dogs.21 The possible advantages of fluid restriction have been considered since the classical work of Fay.10 The exact amount of brain water removed during water restriction is not known, and the following study was undertaken primarily to measure this loss.

Variations in the normal brain water values of dogs have been reported with the oven-drying technique. Eichelberger and Richter noted 76.1% with a standard deviation of 0.88%7 while Clasen, et al., found 78.5% with a standard deviation of 1.0%.5 With cats, Bradbury and Coxon were forced to use littermates to achieve a small standard deviation.4 To minimize this variation, a technique that compares direct and indirect measurements of brain water has recently been perfected.15 The standard deviation for the normal brain water values is small enough with this method to allow the measurement of significant changes of water content with dehydration or edema.

Method

Forty-five adult mongrel dogs were used for the purposes of our study. All dogs were environmentally conditioned for at least 5 to 7 days, since unconditioned animals were found to have a much greater variation in brain water values. Animals with evidence of infection or poor water intake were excluded.

The dogs were divided into five groups. Ten conditioned dogs served as controls. For the experimental groups of 10 dogs each, intake was controlled so that each dog received 600 to 800 gm of the food ration and no water for periods of 24, 48, and 72 hours. This was extended to 96 hours with one small group of five dogs. The food ration was Purina Dog Chow, with a water content of less than 12%, protein greater than 24%, fat greater than 8%, and fiber less than 4.5%. Physical discomfort and neurological deficit were not observed during these periods of controlled water intake.

Before and after dehydration, heparinized
blood samples were obtained and the body weight recorded. The dogs were then anesthetized with 30 mg/kg of intravenous pentobarbital. As most pentobarbital solutions contain propylene glycol (a potent freezing-point depressant) as a preservative, care was taken to obtain the blood samples either before giving the pentobarbital or 2 to 3 hours afterwards. Unless these precautions were taken, the plasma osmolality was increased by about 10 mOsm/kg.

All dogs were ventilated on a Harvard respirator, using 20 ml of room air per kg, at a rate of 24 revolutions per minute for 2 hours. This period of relative hyperventilation was standardized for comparison with other experimental preparations. The animals were sacrificed with an intracardiac injection of saturated potassium chloride.

Both cerebral hemispheres were quickly removed with a section of the brain stem at the level of the superior colliculi. The corpus callosum was split longitudinally and the ventricles opened. Excess blood and cerebrospinal fluid were blotted from the ependymal and arachnoid surfaces. The wet weight of each hemisphere was determined under xylene. After homogenization in xylene, the hemispheres were distilled with a large excess of xylene. The amount of water in the distillation receiver was a direct determination of the water in each hemisphere. As a check for experimental error, an indirect water determination was also made from the dry weight of the brain residue, after excess xylene had been removed with flash evaporation. The detailed method is presented elsewhere. At the time of sacrifice, a specimen of temporalis muscle was also obtained for both direct and indirect water determinations.

All blood samples were centrifuged. The plasma was then decanted, covered, and refrigerated at 4°C until used for determinations of osmolality and sodium. Plasma tonicity was measured by freezing point depression with a Fiske osmometer which was calibrated with molal chloride standards. Plasma sodium concentrations were obtained by flame photometry. Each animal served as its own control for changes in plasma sodium and osmolality after dehydration.

Blood water values were estimated with the use of tagged red-blood cells. One hundred µc per kg body weight of radiochromate were used with autogenous cells, which were returned to the circulation at least 20 minutes before sacrifice.

Results

Except in one instance, tissue water determinations were satisfactory in that the direct and indirect water levels matched. A significant decrease in brain and muscle water was seen with all periods of dehydration (Fig. 1). After 1 day of dehydration, there was a decrease in brain water of almost 1% that coincided with a decrease in muscle water of a similar magnitude. Dehydration of 2 and 3 days caused no further decrease in brain water; however, muscle continued to lose water at a rate of about 1% per day. After 4 days of dehydration, the brain water dropped to a level of about 2% less than normal. The muscle water after a similar period was almost 5% below normal. Using Student’s t-test, the difference from the controls for the brain and muscle water determinations was statistically significant at p < 0.05, except the 24-hour muscle water value (Table 1).

A definite parallel exists between the loss of tissue water and dehydration; however,