

Brain Water: Regional Changes During the Estrous Cycle in the Rat¹ (35196)

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While evaluating various biochemical parameters which fluctuate in specific areas of the brain during the estrous cycle of the rat (1, 2), it became apparent that the common practice of expressing data in terms of tissue wet weight (3) inherently assumes that the water content of a given area of the brain does not change with the stage of the cycle. In view of the dramatic estrogen dependent changes that occur in the water content of the uterus during the estrous cycle of the rat (4), it seemed worthwhile to determine if discrete areas of the brain are similarly influenced by changing levels of circulating estradiol.

Methods. Six to 10 rats/cycle stage (proestrus, estrus, and diestrus), were selected by vaginal smears from cycling Sprague-Dawley rats (approx 250 g) maintained in 12 hr light and 12 hr dark. After decapitation, the whole brain was rinsed with physiological saline and brain areas (Table I) were rapidly removed and placed in a petri dish on filter paper moistened with saline. Each brain area was placed in a preweighed vial and weighed to the nearest microgram. The tissues were dried in a 60° oven for 7 days at which time constant weight was reached. Prior to weighing, the samples were allowed to cool for 30 min in a desiccator. The percentage of water was calculated for each tissue and signifi-

cance of differences was determined between each stage of the cycle by the Student's *t* test. $p \leq .05$ was considered significant.

Results and Discussion. The data in Table I indicate that of the 7 areas of the brain examined, the water content of the sensory-motor cortex, hypothalamus, and hippocampus is significantly higher during diestrus than at any other stage of the cycle. It is during diestrus that the plasma level of estrogen is significantly lower than that during proestrus or estrus (5).

The inverse relationship between the plasma level of estrogen and the water content of specific areas of the brain was unexpected and may only be indirectly related to decreased estrogen levels. Nevertheless, the three areas of the brain of the female rat which are affected have been shown to contain estrogen sensitive elements (6-8). In contrast, it has been reported that the administration of pharmacologic doses of estradiol to adult male rats does not alter the water content of the cerebral cortex, cerebellum or brain stem (9).

It is apparent that expressing neurochemical data as a function of wet weight may lead to erroneous interpretations concerning changes in specific regions of the brain during the estrous cycle. Even if female rats in the same stage of the cycle are chosen, significant differences in water content *between* brain areas are present; *e.g.*, during proestrus the water content of the hypothalamus is less than that in the sensory-motor cortex ($p < .01$); the hippocampus ($p < .001$); and olfactory bulb ($p < .001$); and greater than that of the corpora quadrigemina ($p < .05$). It may be preferable to express brain data in terms of protein; however, it has not yet

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TABLE 1. Relationship Between the Estrous Cycle and Water Content of Selected Regions of the Rat Brain.

Values shown are the percentage tissue water; mean $\pm$ standard error.

Tissue	Proestrus	Estrus	Diestrus	P vs E	E vs D	P vs D
Cerebellum (left lobe)	78.39 $\pm$ 0.20	78.84 $\pm$ 0.23	78.99 $\pm$ 0.29	NS	NS	NS
Sensory-motor cortex	80.29 $\pm$ 0.12	80.55 $\pm$ 0.33	81.56 $\pm$ 0.42	NS	NS	$p < .02$
Hypothalamus	79.24 $\pm$ 0.24	80.00 $\pm$ 0.34	80.99 $\pm$ 0.15	NS	$p < .05$	$p < .001$
Hippocampus	81.28 $\pm$ 0.32	81.31 $\pm$ 0.32	83.12 $\pm$ 0.16	NS	NS	$p < .001$
Corpora quadrigemina	78.36 $\pm$ 0.26	78.29 $\pm$ 0.28	78.84 $\pm$ 0.30	NS	NS	NS
Head of the caudate nucleus	79.71 $\pm$ 0.19	79.62 $\pm$ 0.35	80.39 $\pm$ 0.33	NS	NS	NS
Olfactory bulb	82.36 $\pm$ 0.38	82.92 $\pm$ 0.35	82.98 $\pm$ 0.20	NS	NS	NS

been shown whether regional concentration of protein or dry weight is equivalent or constant throughout the estrous cycle.

Although highly speculative, it is possible that in the human, the increased incidence of epileptic seizures and other central nervous system symptomology, which occur several days premenstrually, may be related to regional brain changes in water and/or osmotically active molecules (10), subsequent to the withdrawal of estrogen.

Summary. The water content is significantly higher in the hypothalamus, hippocampus, and sensory-motor cortex during the diestrous stage of the estrous cycle than it is during proestrus and estrus.

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