Brain and Serum Glutamine in Nephrectomized, Uremic Rats[1] (37416)

ABRAHAM G. WHITE[2]

Department of Medicine, Mount Sinai School of Medicine, City University of New York, and the Bernstein Institute Medical Service, Department of Medicine, Beth Israel Medical Center, New York, New York 10003

The biochemical disturbances underlying uremic cerebral dysfunction are not fully known (1). Because glutamine plays a special role in cerebral metabolism (2), it seemed of interest to study the effect of uremia on the concentration of brain glutamine. Serum glutamine concentrations also were measured in some uremic and control animals.

Materials and Methods. Bilateral nephrectomy was performed under ether anesthesia on male Wistar white rats weighing 400 to 550 g. These rats, as well as simultaneous control, sham-operated animals, were allowed water *ad libitum,* but no food, during the next 24 hr. At 24 hr postoperatively, the rats were sacrificed by exsanguination under brief ether anesthesia, and the brains were removed. Some experiments were performed in which both water and food were withheld during the 24 hr postnephrectomy period.

Glutamine concentrations were measured by a modification of the method of Ramadan and Greenberg (3). *E. coli* glutaminase (Worthington) was used, with its optimal pH of 4.9 provided by acetate buffer. The Seligson method (4) was used to measure the ammonia released by the glutaminase. In all determinations of brain and serum glutamine, the ammonia released in the absence of the glutaminase was subtracted from the ammonia released in the presence of glutaminase, thus giving a specific measure of the amide nitrogen converted to ammonia by the enzyme.

Glutamine determinations on standard solutions, performed in all experiments, yielded approximately 98 to 102% recovery of calculated amide nitrogen.

Results. Table I indicates the concentrations of glutamine (mg/100 g tissue wet wt) of normal and uremic rat brains. The uremic brains showed significantly lower concentrations of glutamine.

Table II demonstrates that the concentrations of serum glutamine (mg/100 ml) are significantly lower in uremic animals than in normal controls.

Discussion. The glutamine content of normal rat brain, 64.4 ± 2.8 mg/100 g, in the present study falls within the range of previously reported values, 48 to 70 mg/100 g (2). Dawson (5) reported values ranging from 61 to 84 mg/100 g in the brains of normal, fed rats.

Williams *et al.* (6) did not report any significant effects of brief, light ether anesthesia on either brain glutamate or glutamine.

Shear (7) found, as we did, a lowering of blood plasma glutamine in bilaterally nephrectomized rats. Thus, in Shear's report, blood plasma glutamine averaged 7.01 mg/100 ml in normal rats and 6.82 mg/100 ml in uremic rats; however, this difference was not statistically significant in his series. One difference between the two investigations is that Shear used a Beckman automated amino

TABLE I. Glutamine Content of Brain Tissue from Normal and Uremic Rats.

Group	No. expt	Glutamine[a] (mg/100 g tissue wet wt)
Normal	23	64.4 ± 2.8
Uremic	16	50.4 ± 1.4[b]

[a] Glutamine concentration of brain tissue; mean value ± SEM.

[b] Significantly different from normal $p < 0.001$.

[1] Abstr. in Proc. Annu. Meet. Amer. Soc. Nephrol., 5th, p. 90, 1971.

[2] Reprint requests to Bernstein Institute, 307 Second Ave., New York, N. Y. 10003.

TABLE II. Glutamine Content of Serum from Normal and Uremic Rats.

Group	No. expt	Glutamine[a] (mg/100 ml)
Normal	7	7.94 ± 0.27
Uremic	7	6.08 ± 0.22[b]

[a] Glutamine concentration of serum; mean value ± SEM.

[b] Significantly different from normal $p < 0.001$.

acid analyzer for the glutamine determination while the values in this report were obtained with a specific, sensitive enzymatic method. Another point of difference is that the animals in the present experiments weighed 400 to 550 g while the rats in Shear's series weighed about 220 g.

The mechanisms underlying the presently observed lowering of brain and serum glutamine in uremic rats remain to be elucidated.

Summary. The concentrations of brain and serum glutamine were found to be significantly lower than normal in bilaterally nephrectomized, uremic rats.

The technical assistance of Mr. Barry Sonkin is gratefully acknowledged.

1. Teschan, P. E., Amer. J. Med. **48**, 671 (1970).

2. Waelsch, H., *in* "Advances in Protein Chemistry" (M. L. Anson, K. Bailey and J. T. Edsall, eds.), Vol. 6, p. 299. Academic Press, New York (1951).

3. Ramadan, M. E. A., and Greenberg, D. M., Anal. Biochem. **6**, 144 (1963).

4. Seligson, D., and Seligson, H., J. Lab. Clin. Med. **38**, 324 (1950).

5. Dawson, R. M. C., Biochem. J. **47**, 386 (1950).

6. Williams, A. H., Kyu, M. H., Fenton, J. C. B., and Cavanagh, J. B., J. Neurochem. **19**, 1073 (1972).

7. Shear, L., J. Clin. Invest. **48**, 1252 (1969).

Received Mar. 21, 1973. P.S.E.B.M., 1973. Vol. 143.