TP and 5-HIAA were markedly higher than in age-matched heterozygote mice (dw/+) (TP 6.40 ± 0.33 vs 4.20 ± 0.21 μg/g; 5-HIAA 0.65 ± 0.03 vs 0.33 ± 0.02 μg/g, respectively). Similar to hypox rats, a GH replacement therapy (200 μg i.p. daily for one week) significantly decreased brain TP and 5-HIAA in dwarf mice (TP 6.40 ± 0.3 vs 5.5 ± 0.2 μg/g; 5-HIAA 0.65 ± 0.03 vs 0.57 ± 0.014 μg/g, respectively).

The present findings support the possibility that fluctuations in some essential plasma constituents as a result of hormonal inputs may influence brain TP availability thus altering brain 5-HT metabolism.

Catecholaminergic control of Thyroid Stimulating Hormone (TSH) and Adrenocorticotrophic Hormone (ACTH) secretion

L. ANNUNZIATO, G.F. DI RENZO, G. LOMBARDI, P. PREZIOSI & U. SCAPAGNINI*

Department of Pharmacology, IInd Faculty of Medicine, University of Naples, Naples, Italy

The possibility that central monoaminergic system(s) may take part in controlling secretion of the anterior pituitary hormones has often been suggested (Ganong, 1972). While experimental evidence supports the existence of a central noradrenergic system tonically inhibiting secretion of corticotrophin releasing factor (Scapagnini & Preziosi, 1973), little data is available concerning the role played by central monoamines upon secretion of thyroid releasing hormone (Kotani, Onaya & Yamada, 1973).

In our study, the effect of pretreating rats with α-methyl-*p*-tyrosine (α-MpT), a catecholamine synthesis inhibitor capable of depleting brain catecholamines, was examined with respect to secretion of adrenocorticotrophic hormone (ACTH) and thyroid stimulating hormone (TSH) under basal and cold-stress conditions. Male rats, 200-220 g, were given α-MpT (250 mg/kg, i.p.), 1 h before and in some rats followed by L-Dopa (100 mg/kg i.p.) 45 min before cold stress (exposure to 4°C for 2 h), the latter ostensibly to enhance ACTH and TSH secretion; control rats were given an equivalent volume of saline, i.p. The rats were then decapitated and trunk blood collected for subsequent radioimmunological determination of ACTH (Vague, Oliver, Jaquet & Vague, 1971) and TSH (Jaquet, Franchimont, Rinaldi, Sainty, Codaccioni & Vague, 1971).

Results shown in Table 1 indicate that pretreatment of rats with α-MpT significantly enhanced ACTH secretion both in normal and cold-stressed rats. Concurrent administration of L-Dopa, a catecholamine precursor, reduces this effect in normal rats. TSH secretion was reduced following α-MpT, but only significantly so in the cold-stressed rats.

Our results are compatible with brain catecholamines influencing in an opposite way secretion of ACTH and TSH.

This investigation was supported by a grant from the Italian National Council (CT 73.00732.04).

Table 1

Treatment	*Plasma ACTH*	*Plasma TSH*
Saline	33.6 ± 6.1(10)	4.5 ± 1.3(10)
α-MpT	155.4 ± 16.9(5)*	3.4 ± 0.3(6)
α-MpT + L-Dopa	66.8 ± 9.5(6)*(a)	–
Saline + Cold stress (C.S.) 2 h	89.5 ± 10.9(10)*	18.8 ± 1.8(9)*
α-MpT + C.S.	125.7 ± 11.7(10)**	8.0 ± 1.0(9)***

ACTH and TSH are expressed respectively in pg/ml and uU/ml.
The values shown are means ± s.e. The figures within brackets show the number of rats. Asterisks represent statistical significant differences between mean values of ACTH and TSH for saline treated rats and those given α-MpT, α-MpT + L-Dopa with or without cold-stress (* $P < 0.01$ in comparison to saline treated rats: (a) $P < 0.01$ in comparison to α-MpT treated rats; ** $P < 0.05$ in comparison to cold-stress treated rats; *** $P < 0.01$ in comparison to cold-stress treated rats).

References

GANONG, W.F. (1972). Evidence for a central noradrenergic system that inhibits ACTH secretion. In: *Brain-Endocrine Median Eminence: Structure and Function*, pp. 254-266, Int. Symp. Munich 1971. Basel: Karger.

JAQUET, PH., FRANCHIMONT, P., RINALDI, J.P., SAINTY, J.M., CODACCIONI, J.L. & VAGUE, J. (1971). Le dosage radioimmunologique de TSH plasmatique. *Annales d'endocrinologie*, **32**, 495-507.

KOTANI, M., ONAYA, T. & YAMADA, T. (1973). Acute increase of thyroid hormone secretion in response to cold and its inhibition by drugs which act on autonomic or central nervous system. *Endocrinology*, **92**, 288-294.

SCAPAGNINI, U. & PREZIOSI, P. (1973). Role of brain noradrenaline in the tonic regulation of hypothalamic hypophyseal adrenal axis. In: *Progress in Brain Research*, ed. Zimmermann, E., Gispen, W.H., Marks, B.H. & De Wied, D., pp. 171-184. Amsterdam–London–New York: Elsevier Scientific Publishing Company.

VAGUE, PH., OLIVER, C.H., JAQUET, PH. & VAGUE, J. (1971). Le dosage radioimmunologique de l'ACTH plasmatique. *Revue Europeenne d'études clinique et biologiques*, **16**, 485-493.

A metabolic profile of patients receiving prophylactic lithium therapy

N.J. BIRCH*, A.A. GREENFIELD & R.P. HULLIN

Department of Biochemistry, University of Leeds and The Computing and Statistics Section, B.I.S.R.A., Sheffield

Previous findings have indicated that lithium might affect bone metabolism due to its similarity to calcium and magnesium (Birch & Jenner, 1973; Birch, 1974). Since this is a potential long-term side effect it was thought essential to screen a large number of patients for any resultant metabolic abnormalities and to use the opportunity to determine other interrelationships.

Ninety patients receiving lithium therapy for recurrent affective disorder were investigated during one of their regular visits to the out-patient clinic during which a sample is routinely taken for lithium estimation. The patient series is essentially that described by Hullin, McDonald & Allsopp (1972). A 'spot' urine sample was taken in addition to a 25 ml blood sample. The patient was interviewed and body weight and height were determined. Lithium, sodium, potassium, magnesium, calcium, phosphate, chloride, urea and creatinine were determined in both serum and urine. Serum alkaline phosphatase was also estimated.

In order to obtain values for the excretion rates and clearance of the estimated parameters, algebraic transformations were carried out on the data and a total of ninety variables was subjected to correlation analysis. Preliminary conclusions may be drawn from the results of the correlation analysis though it is expected that further findings will emerge following more detailed statistical analysis.

There is no evidence of gross abnormality in alkaline earth metal excretion. However, osteoporosis may not be readily detectable by normal clinical chemical techniques (Gallagher, Young & Nordin, 1972). Urine lithium/creatinine ratio is correlated with urine magnesium/creatinine ratio ($P < 0.01$).

Males appear to excrete lithium at a lower rate with respect to creatinine than females though this may be related to lean body mass. Premenopausal females receive a higher dose/body weight than both males and post-menopausal females ($P < 0.05$) and yet maintain a lower serum lithium. Clearance of lithium is negatively correlated with age ($P < 0.05$) in agreement with Schou (1968) though this conflicts with Fyrö, Petterson & Sedvall (1973). There is no correlation between urine lithium/creatinine ratio and urine volume/creatinine ratio indicating that lithium excretion is not apparently controlled by urine excretion rate. The lithium : creatinine clearance ratio in all groups was about 0.17, somewhat lower than that found by Geisler, Schou & Thomsen (1971).

We gratefully acknowledge the assistance of nursing and technical staff of High Royds Hospital, Ilkley, and The Medical Research Council for financial support.

References

BIRCH, N.J. (1974). Lithium accumulation in bone following oral administration in rat and in man. *Clin. Sci. & Mol. Med.*, **46**, 409-413.

BIRCH, N.J. & JENNER, F.A. (1973). The distribution of lithium and its effects on the distribution and excretion of other ions in the rat. *Br. J. Pharmac.*, **47**, 586-594.

FYRÖ, B., PETTERSON, U. & SEDVALL, G. (1973). Pharmacokinetics of lithium in manic-depressive patients. *Acta psychiat. scand.*, **49**, 237-247.

GALLAGHER, J.C., YOUNG, M.M. & NORDIN, B.E.C.