results of the chemical estimation also showed an increased concentration of 5-HT after treatment of the animals with the amine.

The localization of the uptake of 5-HT in the cellular population was investigated by Nissl staining after fluorescence microscopy. Glial cells identified on the basis of Nissl staining exhibited a green fluorescence after the injection of 5-HT. The results of model (droplet) experiments indicate that the colour of the formaldehyde induced fluorescence of 5-HT in a certain range of concentration is green, instead of yellow, as is usually reported. It is thus suggested that glial cells in the area postrema are capable of taking up 5-HT.

REFERENCES

ECCLESTON, D., ASHCROFT, G. W., CRAWFORD, T. B. B. & LOOSE, R. (1966). Some observations on the estimation of tryptamine in tissues. *J. Neurochem.*, **13**, 93–101.

FALCK B. & OWMAN, C. (1965). A detailed methodological description of the fluorescence method for the cellular demonstration of biogenic monoamines. *Acta Univ. lun d. Sect.* II. No. 7., 1–23.

LASZLO, I. (1972). Investigation on the histochemical demonstration of noradrenaline and 5-hydroxytryptamine in the area postrema of the rabbit by fluorescence microscopy. (Demonstration at this meeting.)

MOIR, A. T. B. & DOW, R. C. (1970). A simple method allowing perfusion of cerebral ventricles of the conscious rabbit. *J. appl. Physiol.*, **28**, 528–529.

Effect of cortisol on a central response to 5-hydroxytryptophan

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It has been suggested that steroid-induced depression could be attributed to underactivity of central 5-hydroxytryptamine (5-HT) neurones, consequent on reduced 5-HT synthesis (Lapin & Oxenkrug, 1969). Cortisol activates liver tryptophan oxygenase (Thomson & Mitkuta, 1954) and hence could reduce the availability of tryptophan and/or pyridoxal phosphate (co-decarboxylase) to the brain.

Although a fall in brain 5-HT has been shown to follow a single large (5 mg/kg) dose of cortisol (Curzon & Green, 1968) no direct evidence for alteration in central tryptaminergic responsiveness has previously been obtained.

In the present experiments the 5-hydroxytryptophan (5-HTP)-head twitch response in mice (Corne, Pickering & Warner, 1963) has been used as a test of central tryptaminergic function, since the incidence of head twitches has been shown to be proportional to the amount of free 5-HT in the brain (ibid). Groups of 4 male albino mice were housed in quiet surroundings for 7 days, during which time they received the appropriate number of daily subcutaneous injections of either arachis oil (vehicle) or cortisol 75 μg/kg in arachis oil. Mice were injected with 5-HTP (180 mg/kg i.p.) 24 h after the last injection, and the number of twitches occurring in each group determined over alternate 2 min periods for up to 1 h. At least five replicates were performed for each pretreatment schedule.

The effect of cortisol depended upon the duration of pretreatment. A single dose caused a significant increase in the 5-HTP response; two daily injections had no significant effect, while 3–5 daily injections caused a progressive decline in responsiveness to 5-HTP. After five daily cortisol injections the peak 5-HTP response was only 53% of that of vehicle pretreated animals ($P<0.05$).

To test for altered receptor sensitivity to 5-HT, 5-HT (20 μg) was injected intraventricularly (Brittain & Handley, 1967) in pretreated mice. Four daily cortisol injections had no significant effect on the twitch-response. However, preliminary results suggest that a single injection of cortisol 24 h previously could cause a marked elevation in the peak response to 5-HT.

Thus changes in receptor sensitivity could possibly account for the early potentiation of 5-HTP but not the fall in responsiveness following continued pretreatment.

Unlike the effect of cortisol on 5-HT levels in the rat, which had returned to normal following 5 days pretreatment (Curzon & Green, 1968) the reduced responsiveness to 5-HTP described here became more intense with continued pretreatment. A possible mechanism for this effect is the development of a functional lack of pyridoxal phosphate (co-decarboxylase). Preliminary experiments suggest that pyridoxal phosphate (1·0 mg/kg s.c.), 30 min before 5-HTP, is capable of restoring the response to normal in 3-day pretreated animals.

REFERENCES

BRITTAIN, R. T. & HANDLEY, S. L. (1967). Temperature changes produced by the injection of catecholamines and 5-hydroxytryptamine into the cerebral ventricles of the conscious mouse. *J. Physiol., Lond.*, **192**, 805–813.

CORNE, S. J., PICKERING, R. W. & WARNER, B. T. (1963). A method for assessing the effects of drugs on the central actions of 5-hydroxytryptamine. *Br. J. Pharmac.* **20**, 106–120.

CURZON, G. & GREEN, A. R. (1968). Effect of hydrocortisone on rat brain 5-hydroxytryptamine. *Life Sci.*, **7**, 657–663.

LAPIN, I. P. & OXENKRUG, G. F. (1969). Investigation of the central serotoninergic processes as a possible determinant of the thymoleptic effect. *Lancet*, **i**, 132–136.

THOMSON, J. F. & MIKUTA, E. T. (1954). The effect of cortisone and hydrocortisone on the tryptophan peroxidase-oxidase activity of rat liver. *Endocrinology*, **55**, 232–233.