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Tribulin output in neurological disorders

The high incidence of psychiatric morbidity in neurological patients has previously been highlighted (Bridges & Goldberg, 1984). We describe here a biochemical observation that may relate to it.

We have examined the urinary output of tribulin in epileptic and other neurological patients, as well as in controls. Tribulin is the name we have given (Sandler, 1982) to an endogenous monoamine oxidase inhibitor (MAO I) which also appears to inhibit benzodiazepine binding to its receptor (BZ I). Although its structure is not yet known, it has now been very highly purified and its presence cannot be accounted for by any known monoamine or major monoamine metabolite (Glover *et al.*, 1980). Both activities BZ I and MAO I are distributed in parallel in rat tissues (Armando *et al.*, 1986). They are particularly high in sympathetic ganglia but absent from the adrenal gland. The urinary output of tribulin is raised in a variety of conditions connected with stress, anxiety or agitation (Glover *et al.*, 1981; Petursson *et al.*, 1981; Bhattacharya *et al.*, 1982).

Twenty-four hour urine samples were collected from a group of epileptic inpatients, from other inpatients with a range of neurological disorders, and from a group of laboratory personnel, to serve as normal controls. All were free from benzodiazepines and some from all drugs. The urine samples were diluted to constant creatinine concentration and analysed for MAO I and BZ I by incorporating extracts into standard assays (Clow *et al.*, 1983). The results are shown in Table 1.

Table 1 Inhibition of monoamine oxidase (MAO I) and benzodiazepine receptor binding (BZ I) in the urine of control subjects, epileptic inpatients and other neurological inpatients. The results are expressed as a percentage of control values $\pm$ s.e. mean

	n	MAO I	BZ I
a. Normal controls	10	100 $\pm$ 13	100 $\pm$ 12
b. Epileptic inpatients	21	141 $\pm$ 11*	156 $\pm$ 13**
c. Other neurological inpatients	12	155 $\pm$ 16*	151 $\pm$ 19*
d. Drug-free patients from groups b and c	14	154 $\pm$ 14*	160 $\pm$ 18*

** $P < 0.01$ compared with normal controls.

* $P < 0.05$

There was a highly significant correlation between output of BZ I and MAO I in all urine samples studied ($n = 43$, $r = 0.48$, $P < 0.001$). Each patient group had significantly higher urinary tribulin output values compared with normal controls, with epileptic patients being similar to other neurological patients. Drug treatment had no significant effect on output.

Epileptic patients not uncommonly show high levels of anxiety and depression (Brown *et al.*, 1985). Our findings suggest that raised tribulin output may be common to neurological patients as a whole. As it possibly may be an index of stress or anxiety, we are now trying to determine whether tribulin output is correlated with any specific psychiatric dimension in this particular clinical group.

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The Royal College of Physicians of London reports

In the editorial of March 1987 on the relationship between physicians and the pharmaceutical industry, Professor Laurence states that the Association of the British Pharmaceutical Industry (ABPI) and the British Medical Association have objected publically to declaration of investigators financial interests to Ethics Committee. This attribution probably comes from a letter in 1983 jointly from Dr Eric Snell when Medical Director of the ABPI and Dr John Ball, when Chairman of the General Medical Services Committee; this did express the opinion as quoted above on the basis of the views then held by many physicians and company medical directors.

Since then the ABPI has debated the subject more widely and has had the benefit of the 1984 RCP Report on Ethics Committees. The ABPI view now is that appropriate disclosure of payment to investigators to Ethics Committees is a

reasonable measure in the interests of research standards. This is expressed in the recently published 'Report on Clinical Trials (Medico-Pharmaceutical Forum 1987) in the following terms (para 16 [a]): 'It is ethically acceptable for a clinician to be paid for clinical trial work provided his employing authority permits this. The level of payment is relevant and should realistically relate to the work done, the time spent and the skill involved. The clinician should declare his financial interest and the ethics committee should note this . . .'

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