

the death your right to say it" – perhaps another expression of Glasnost.

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#### Urinary Tribulin Output in Patients with Panic Attacks

SIR: Tribulin is an endogenous compound present in urine, which has the properties of inhibiting monoamine oxidase (MAO) activity and displacing  $^3\text{H}$ -flunitrazepam binding to brain membrane preparations (Elsworth *et al*, 1986). It has been demonstrated that urinary tribulin output is increased in disorders associated with increased anxiety: alcohol withdrawal (Bhattacharya *et al*, 1982) and benzodiazepine withdrawal (Petursson *et al*, 1982). From these and other studies it was suggested that tribulin may be an endogenous anxiety-promoting agent (Sandler, 1982). If this is the case, then in patients with anxiety disorders, such as panic disorder or agoraphobia with panic attacks, tribulin output would be expected to be elevated compared with normal controls.

We collected 24-hour urine specimens from 23 drug-free normal controls (9 males, 14 females; mean age  $28.5 \pm 7.2$  years) and 22 drug-free patients (7-day washout period) with panic attacks (5 males; 17 females; mean age  $36.0 \pm 10.5$  years). All patients met DSM-III criteria for panic disorder or agoraphobia with panic attacks; controls had no present or past history of psychiatric disorder. Aliquots (50 ml) of the urine were stored frozen at  $-20^\circ\text{C}$  until required. Tribulin was assayed by its ability to inhibit rat liver MAO activity (Glover *et al*, 1980). All urine samples were diluted with water to give a constant creatinine concentration of  $30 \mu\text{g}/100 \mu\text{l}$  acidified to pH1 and extracted into ethylacetate. The organic phase was separated and evaporated to dryness under nitrogen. Samples were reconstituted to half of their original volume in phosphate buffer (100 mM; pH7.4). Aliquots (100  $\mu\text{l}$ ) of the solution were incubated with rat liver homogenate (20  $\mu\text{l}$ ; 2.5% w/v) and  $^{14}\text{C}$ -tyramine (20  $\mu\text{l}$  of 100  $\mu\text{M}$ ; specific activity 56  $\mu\text{Ci}/\mu\text{mol}$ ). Control values were obtained by substituting an equivalent volume of phosphate buffer for the extracted urine specimen. Samples were incubated at  $30^\circ\text{C}$  for 30 min and the incubation terminated by the addition of 100  $\mu\text{l}$  of HCl. The reaction products were extracted into butyl acetate and an aliquot counted. Radioactive substances were obtained from the Radiochemical Centre, Amersham, UK. Assays

were performed in triplicate using analytical reagent grade chemicals from BDH, Sydney, Australia.

Triplicate determinations for individual samples varied by less than 10% of the mean value. In order to assess day-to-day variability we froze aliquots of the same sample and assessed them over 9 days. Mean MAO inhibition was  $42.8 \pm 4.7\%$  of control (CV = 11%;  $n = 19$ ). Mean MAO inhibition for the normal controls was  $35.6 \pm 10.2\%$  (range = 19–49%) and for the patients was  $36.2 \pm 8.2\%$  (range = 21–52%). These values are not significantly different ( $P > 0.1$ ; Mann-Whitney U test).

An increased tribulin output might be predicted in these patients. The failure to find the expected difference suggests that tribulin, postulated to be an endogenous anxiety-provoking agent, is not responsible for producing panic attacks. An alternative explanation might be offered by the nature of the disorder. Panic attacks are episodic, and unless urine samples were collected on the day on which a panic attack had occurred, then an elevation of tribulin output may not be detectable. Although each patient fulfilled DSM-III criteria of at least three panic attacks in the previous three weeks, we did not record if they had panic attacks on the day of urine collection. Nevertheless, panic patients do tend to have high generalised anxiety between attacks and so might be expected to produce more tribulin than controls.

To our knowledge this is the first published report of tribulin output in patients with panic. The absence of a marked difference from controls is difficult to reconcile with the putative anxiety-provoking properties of this substance(s). Studies of tribulin output in lactate-induced panic attacks might prove useful in elucidating the role of tribulin in panic disorders. The identification of the molecule and its metabolites would also clarify its role, if any, in the neurochemical mechanisms involved in anxiety states.

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### HLA-DR2 and Sleep Onset REM Periods in Endogenous Depression

SIR: With rare exceptions (Zietz *et al*, 1986), almost all patients with narcolepsy are HLA-DR2 positive (Billiard & Seignalet, 1985), while the normal population frequency is about 20–35%. To date, this association constitutes the strongest relationship between a given disease and the HLA-system.

Besides clinically relevant symptoms such as cataplexy, excessive daytime somnolence, hypnagogic hallucinations, and sleep paralysis, one main feature of narcolepsy is the occurrence of sleep onset REM periods (SOREMPs) (REM latency  $\leq 25$  min) during daytime and night-time sleep. Recently, a correlation between length of REM latency and possession of HLA-DR2 was reported (Schulz *et al*, 1986). Healthy subjects who were HLA-DR2 positive exhibited significantly shorter REM latencies than those who were not positive. However, this result could not be replicated (Schulz *et al*, 1987).

The fact that narcoleptic patients and patients with endogenous depression share one common feature in their sleep pattern, i.e. the occurrence of sleep onset REM periods, stimulated us to investigate HLA-DR2 in patients with endogenous depression, to clarify if there is a common genetic basis for this deviant sleep pattern.

We have investigated 11 patients with a major depressive disorder of the endogenous subtype according to Research Diagnostic Criteria (Spitzer *et al*, 1977). Seven of them were female, four were male. Mean age ( $\pm$  s.d.) was  $49.6 \pm 8.4$  years. Two of the patients were bipolar II, one patient was bipolar I. Blood samples for HLA-DR2 typing were drawn during a hospital stay and analysed using the micro-lymphocytotoxicity test according to the method of Terasaki.

All of the patients took part in ongoing sleep studies in our sleep laboratory, and had between two and five nights of baseline sleep recordings. The patients were free of any kind of psychoactive medication prior to sleep recording for at least seven days.

Seven of the patients had at least one sleep onset REM period. Four of them were HLA-DR2 positive,

three were negative. Of the four patients showing no sleep onset REM periods, three were HLA-DR2 positive. Calculating a Fisher exact test for the occurrence of SOREMPs (yes/no) and HLA-DR2 positive/negative, a *P* value of 0.42 was attained. This result clearly contradicts the assumption that there is a close relationship between HLA-DR2 positive and sleep onset REM periods in endogenous depression.

Strikingly, however, the HLA-DR2 positive rate of 64% in our sample (7 of 11 patients were positive) of depressed patients by far exceeded the normal population rate of 20–35%. Before definite conclusions can be drawn from this result, larger samples of depressed patients and patients with other psychiatric disorders must be investigated, to clarify whether this result is due to chance or sample selection.

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### Mystical-Ecstatic and Trance States

SIR: Mystical-ecstatic and trance states fall within the general category of depersonalisation symptom and dissociative states. Usually they are pleasant, relaxing, short-lived, and do not have psychopathological consequences (Benson, 1984).

*Case report:* Mr A, a 26-year-old right-handed man, had a life-long interest in mystical and religious philosophy,