

causally related, but they do have in common a disturbance of hypothalamic dopamine function and at least one reported patient with NMS (Wedzicha & Hoffbrand, 1984) has been observed to drink excessively and to develop hyponatraemia. Given the difficulties in recognising compulsive drinking before serious consequences occur, in awareness of the possibility is essential.

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Switch Mechanism in Affective Illness and Oral S-Adenosylmethionine (SAM)

SIR: A mechanism for switching manic-depressives out of depression has been postulated (Bunney *et al*, 1970). The spontaneous switch rate from depression to hypomania or mania in untreated unipolar and bipolar depressives was reported to be 10–14% over a six-month period (Bunney, 1978; Lewis & Winokur, 1982). Drugs acting on brain biogenic-amines, like tricyclic anti-depressants, are known to give rapid switches of mood from depression to mania; increases in these amines are thought to underlie these changes. The possibility of switching retarded, potentially suicidal depressives into a less hazardous euphoric state has long excited speculation (Bunney, 1978; Lewis & Winokur, 1982). There would be advantages if this could be effected by means of a naturally occurring physiological brain metabolite given by a non-intimidating procedure rather than by the use of drugs or ECT.

We have recently reported (Carney *et al*, 1983) switching in three of 12 depressives receiving i.v. SAM. We calculated that the probability of such an event occurring by chance within six days of starting SAM was remote ($P < 0.001$) and it was probably associated with SAM. However, there was no certainty that oral SAM, unavailable during the previous study, would have the same effect as i.v. SAM.

At Northwick Park Hospital we gave SAM in daily doses of 500–1600 mg orally for 14–42 days in an open study to six endogenous depressive in-patients (Newcastle score 6 or more (Carney *et al*, 1965)).

Three became hypomanic during the trial. Thus, a 26-year-old female teacher whose brother had developed mania after receiving i.v. SAM in the previous study became hypomanic. A 50-year-old female clerk who had become hypomanic when given i.v. SAM in the former study showed a similar reaction. A 70-year-old man with no previous or family history of affective illness, unresponsive to other anti-depressant treatments, including ECT (the other two patients were considered for ECT), developed hypomania. All had been retarded, non-verbal, seclusive, and exhibited nihilistic or intrapunitive delusions. Each went through a brief euthymic period of 1–3 days before suddenly becoming elated, with marked increases in the production of speech and activity, and all developed grandiose ideas. One had heightened libido. Over the trial period the mean plasma SAM level in four of these patients increased from 30.5 to 144.0 ng/ml, i.e. from 2 to 10 times the basal mean value.

We have already demonstrated that SAM can cross the blood-brain barrier and influence monoamine metabolism (Bottiglieri *et al*, 1984). These results with oral SAM support the earlier report of switching (Carney *et al*, 1983) associated with the use of i.v. SAM and again suggest that some apparently endogenous depression is SAM-responsive (Reynolds *et al*, 1984). SAM is the major source of methyl groups in the brain, and intimately connected with brain and amine metabolism and membrane and neuro-transmitter function. Further studies of oral SAM in endogenous depression would be worthwhile. We are currently undertaking double-blind placebo-controlled trials of i.v. and oral SAM in patients with endogenous depression.

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A HUNDRED YEARS AGO

Causes of Idiocy

Although Dr Down's patients came from every variety of social rank, he could not draw any safe deductions as to the influence of various occupations of the parents on the causation of idiocy. He had collected 400 cases with fair social antecedents, and had found that 75 per cent were the children of merchants, country gentlemen, officers in the army and navy, gentlemen of independent means and liberal education, and members of the titled aristocracy. No less a proportion than 25 per cent were the children of members of one or other of the three *learned professions*. Of these, 18 per cent were children of members of the clerical profession. Mr Galton finds that the legal profession (which procreates fewest

idiots) gives birth to 11 per cent of the foremost men of eminence; that the medical profession (which procreates 1 per cent more of idiots than the legal) gives origin to 9 per cent of scientific men; while the clerical profession, which procreates the maximum amount of idiocy, gives birth to only 6 per cent of men of science. These statistics illustrated the process of natural selection.

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