

showed an abnormal ratio after oral testing and 29.3% (s.d. = 17.7%) in those with a normal ratio, over a five-hour period, concluding that there was no significant difference between these two groups of patients in the metabolism or excretion of this probe molecule after absorption. These recovery rates after intravenous injection are extremely low; indeed, in their previous work (Cobden *et al.*, 1985) a mean cellobiose recovery rate of 52.0% (s.d. = 14.3%) was reported, and Menzies (unpublished) obtained an 83.4% recovery rate in normal subjects over the same time period. Irrespective of whether the patients had a normal or abnormal cellobiose/mannitol recovery ratio, due to the low cellobiose recovery intravenously in both populations one might conclude that considerable systemic metabolism of this probe marker had occurred. However, cellobiose, in common with most other disaccharides, is not known to be significantly metabolised within the body (Menzies, 1974). As intravenous cellobiose was not administered to a population free of psychiatric illness, these results would equally well support the hypothesis that patients with chronic psychiatric illness demonstrate abnormal systemic metabolism of cellobiose.

The authors acknowledged the low recovery rates of both probe molecules, postulating that this may have been due to inaccurately timed urine collections, leading to a similar reduction in recovery of both molecules, leaving the cellobiose/mannitol ratio unaffected. However, the mean mannitol recovery rate of 49.45% (mean, abnormal/normal patients) is almost identical to the 49.9% recovery in normal controls (Cobden *et al.*, 1985), but the cellobiose recovery ratio is some 23.35% lower (52.0%, compared with 28.65%). This disproportionate lowering of the cellobiose recovery rate is not compatible with error introduced by inaccurately timed urine collections.

Furthermore, it is unclear whether the test solution administered was hyperosmolar. If it was, it is important that subjects refrain from drinking water for at least two and a half hours before and after the commencement of the study, as water would act to dilute the hyperosmolar stress, leading to difficulties in interpreting the results. As the authors have alluded to difficulties in obtaining complete timed urine collections in this group of patients, it would be reassuring to know that 'fasting' included preventing the subjects swallowing water throughout this period, a somewhat natural reaction after ingesting an extremely sweet sugary drink.

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References

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SIR: We are grateful to McGauley for drawing attention to the low five-hour recovery of cellobiose after i.v. injection in patients with chronic psychiatric disorder. As stated, the recovery is some 23% lower than in the previous study in fit, co-operative volunteers. In theory this could be due to altered metabolism, but may reflect difficulty ensuring complete bladder emptying before starting and at completion of the test in the patients we studied. It is incorrect to presume that the abnormality demonstrated in the oral test could have been due to metabolic differences, as this would have given rise to an apparent reduction in permeability to cellobiose, whereas in fact we have demonstrated the opposite.

The purpose of the i.v. test was to compare the group of psychiatric patients with abnormal oral tests with those who had a normal oral sugar test. The i.v. injection was given before the patient was allowed away from his bed and after a urine specimen was collected. The patients did not have access to food or water during the five-hour period when all urine passed was collected. Endoscopy was performed at the end of the i.v. test and no excessive gastric contents were noted. The i.v. test therefore confirmed no significant difference in metabolism or excretion in the two groups studied.

The composition of the oral test solution is clearly stated in the method section. Patients were asked not to drink, but in order to retain co-operation some freedom was allowed and it is possible that some may have drunk water during the study. However, this would tend to reduce permeability to cellobiose, whereas in fact the study demonstrated an increased permeability to cellobiose in the abnormal group.

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Mental handicap and double-blind trial design

SIR: The title "Lithium in the treatment of aggression in mentally handicapped patients: a double-blind trial" (*Journal*, May 1987, **150**, 685–689) raises an interesting question about how the limited conceptual ability implicit in mental handicap might interact with the conceptual sophistication necessary to understand a double-blind design. That the