studies. In addition to our reports[1,2], Nies *et al.*[4] observed significantly reduced MAO activity in schizophrenics, as did Meltzer and Stahl[5], who also noted differences in substrate specificity differentiating chronic from acute patients. Our recent study of acute schizophrenics revealed normal MAO activity[6], while a replication study of chronic schizophrenics again documented reduced MAO activity unexplained by differences in thyroid or sex steroid hormones, iron metabolism or drug treatment (in preparation). This distinction between chronic and acute schizophrenics is interesting in view of studies of adopted-away children of schizophrenics indicating that chronic and acute schizophrenia may be genetically distinct disorders[7].

While the non-overlapping low-high distribution of MAO activities observed by Shaskan and Becker in 24 schizophrenics might represent a split between chronic and acute patients, the bimodal distribution in eight alcoholic and seven staff controls suggests the possibility of sampling inequities or technical differences in this very small sample. A typical unimodal distribution pattern for platelet MAO was observed in 167 normals[8]. Whether alcoholics should be included as 'controls' is problematic, as alcoholism has been linked to affective disorders, and patients with bipolar affective disorder have reduced MAO activity[9].

We have also found platelet MAO activity to be a generally stable characteristic of individuals. We continue to view MAO differences as possibly related to vulnerability issues (which might, for example, result in chronicity) rather than to overt psychiatric disorders themselves[2,8]. Shaskan and Becker's observation that low MAO patients may be relatively treatment-resistant is congruent with this concept. In studying non-hospitalised, drug-responsive patients, however, Shaskan and Becker have not replicated the conditions of our first study of chronic schizophrenics, but instead may have accomplished a combination study of schizophrenic subgroups. We look forward to further examination by them and others of the relationships between MAO activity, behaviour and behavioural disorders.

National Institute of Mental Health
Bethesda

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Chloride ions cancel out inhibition of β-galactosidase activity by acid mucopolysaccharides

A SERIES of short reports on the effect of glycosaminoglycans on β galactosidase have been published[1-3]. Kint[3] has shown that cetylpyridinium chloride or albumin can partially overcome the inhibition of β galactosidase by the glycosaminoglycans accumulated in autopsy liver homogenates from mucopolysaccharidoses patients. We report that this inhibition is completely cancelled out by a pure physiological agent, that is, chloride ions, required for enzyme activity[4-6].

The effect of various glycosaminoglycans and synthetic sulphated polymers on acid β-galactosidase activity is summarised in Table 1, which shows that hyaluronic acid was not inhibitory whereas all the sulphated polymers were inhibitory to varying extents. Chondroitin sulphate A and keratan sulphate were only mildly inhibitory but the synthetic sulphates were very strongly so. Chloride ions cancelled out all inhibition completely. The lowest concentration of chloride ions which prevented inhibition resulting from 83 μg ml^{-1} heparitin sulphate was about 1.6 meq.

Other salient observations were as follows. (1) Chloride ions prevented inhibition if added simultaneously with inhibitor in the incubation mixture. Preincubation of enzyme with inhibitor at 37° C led to irreversible inactivation after 5–10 min and subsequent addition of chloride ions did not restore enzyme activity. (2) Inactivation of enzyme by glycosaminoglycans required heat and acidic *p*H (below 4.5). A mixture of enzyme and inhibitor maintained at 0° C did not result in inactivation or complex formation. The same mixture

Table 1 Effect of glycosaminoglycans on acid β galactosidase activity in the presence or absence of chloride ions

Addition	Enzyme activity (%) −Chloride	+Chloride
None	100	138
Hyaluronic acid	116	139
Chondroitin sulphate A	73	135
Keratan sulphate	73	134
Dermatan sulphate	51	126
Heparitin sulphate	20	133
Dextran sulphate	7	88
Polyvinyl sulphate	5	80

A 15% homogenate of liver in distilled water was diluted 1:20 with water or 0.2 M NaCl and assayed for β galactosidase activity using 4-methylumbelliferyl-β-galactoside as substrate[6]. Incubations were carried out for 15 min at 37° C. The final concentration of chloride ions in the assay mixture was 33.3 meq., that of glycosaminoglycans/sulphated polymers 83 μg ml^{-1}.

Table 2 Effect of chloride ions on β-galactosidase activity in mucopolysaccharidoses patients and in controls

Liver homogenates	Enzyme activity Chloride	− Chloride
Control (1)	160	180
Control (2)	264	309
Hurler (MP-I)	7	22
Hunter (MP-II)	5	30
Sanfilippo (MP-III)	15	58

Conditions are as in Table 1. Enzyme activity is expressed as nmol substrate hydrolysed per h per mg protein.

on starch gel electrophoresis at 4° C (ref. 6) gave an isoenzyme pattern indistinguishable from controls.

The effect of chloride ions on β-galactosidase activity in liver homogenates from mucopolysaccharidoses patients and from controls is shown in Table 2. The results indicate that the apparent restoration in enzyme activity in the mucopolysaccharidoses patients was incomplete, suggesting that irreversible enzyme inactivation had occurred. Further inactivation of enzyme was prevented, however, by the presence of chloride during incubation, as evidenced by the three to fourfold increase in activity in all patients when chloride was included in the assay mixture.

It is now clearly established that the β-galactosidase abnormality in the mucopolysaccharidoses patients[7] is not the primary genetic defect[1-8]. The casual relationship between the reduction/inhibition of β-galactosidase activity and the clinical manifestations of the diseases is not known. Therapy along the lines of 'restoration' of β-galactosidase activity should be considered only when the above correlation is clearly demonstrated. If such therapy is required, chloride ions (administered for example as a saline infusion) should be chosen as they are relatively innocuous compared to the alternatives suggested[3].

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MAE WAN HO
Department of Biochemistry,
Queen Elizabeth College,
University of London,
London W8 7AH, UK
ARVAN FLUHARTY
Pacific State Hospital,
Pomona, California

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