MONOAMINE OXIDASE ACTIVITY: A GENETIC MARKER OF SCHIZOPHRENIA?

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The results of pilot studies of the activities of platelet monoamine oxidase (MAO) and catechol-0-methyl transferase (COMT) in the blood of selected schizophrenics and the families of schizophrenics is presented.
No statistically significant difference was found between the blood COMT levels of 21 control subjects and 26 schizophrenics, whereas the values found for platelet MAO activity were significantly lower for the schizophrenic group than for the control group.
In one acutely disturbed first-admission schizophrenic the platelet MAO activity increased to a normal level in parallel with the clinical improvement, whereas in the relapsing schizophrenics the platelet MAO activity remained at its initial level although the clinical picture improved.
No consistent findings with regard to the platelet MAO activity emerged from the study of 3 families having a history of schizophrenia.

INTRODUCTION

Disturbances in catecholamine metabolism have often been suggested to occur in schizophrenia (Bourdillon and Ridges 1970). However, the nature of the disturbance and its relationship to the disease process are unclear, since many other factors, unassociated with schizophrenia, may be responsible for the observed differences, and control of all of these has not been possible.

In the course of our studies we have obtained evidence that in some forms of schizophrenia abnormally methylated catecholamines are excreted in the urine (Ridges et al. 1968). This has led us to investigate the activities of the enzymes involved in the metabolism of the catecholamines, namely, catechol-0-methyl transferase and monoamine oxidase.

This paper reports on pilot studies of enzyme activities in acutely disturbed schizophrenics and in the families of schizophrenics.

MATERIALS AND METHODS

Schizophrenics were using a modified form of the Iowa 500 rating scale (Morrison et al. 1972) in which patients without a six-month history were also included. They were all selected by the same psychiatrist.

Controls. Mentally normal individuals, with no known family history of psychiatric illness requiring treatment, served as controls. They were matched with the schizophrenics in the series for age and sex.

Catechol-O-methyl transferase (COMT) activity was measured in whole blood using a radiometric method which was essentially the same as that described by Axelrod and Cohn (1971).

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Monoamine oxidase (MAO) activity was studied in platelets by the method of Robinson et al. (1968) in which the radioactivity was studied in the products formed from C^{14} tyramine when it was incubated in the presence of the platelet preparation. The platelet preparation was made by differential centrifugation (Shulman et al. 1964), frozen and thawed twice, and the protein content assayed by the phenol reagent assay. Approximately 0.2 mg protein in 200 μl physiological saline were used per assay.

RESULTS AND DISCUSSION

COMT Activity

The COMT activity in the blood of 21 control subjects and 26 schizophrenics was measured. There was no statistically significant difference between the COMT activity of these two groups (Table 1).

TABLE 1

CATECHOL-O-METHYL TRANSFERASE ACTIVITY IN SCHIZOPHRENICS

	No. of subjects	Mean age	COMT activity (n. mol./ml. blood)
Controls	21 (18 males, 3 females)	40.1 ± 10.4	1.1 ± 0.7
Schizophrenics	26 (19 males, 7 females)	34.5 ± 11.0	1.0 ± 0.6 *ns*

MAO Activity

Figure 1 shows the activity of monoamine oxidase in the platelets of a group of controls and schizophrenics. The values found for the schizophrenic group were statistically significantly lower than for the control group (Table 2). This is in agreement with the findings of Murphy and Wyatt (1972) who, using a slightly different method, reported that MAO activity was reduced in the platelets of chronic schizophrenics. These workers reported that the platelet MAO activity remains constant in the same individual. It seems that this is probably true in the majority of schizophrenics (repeated determinations on 6 relapsing schizophrenics showed little or no alteration in MAO activity), but there are exceptions.

Figure 2 shows the change in MAO activity in relation to the clinical state of a first-admission schizophrenic who had not received treatment. The change in MAO activity paralleled the clinical improvement, particularly with regard to the severity of thought disorder and delusions. MAO activity in platelets, therefore, may be of value in certain instances as an indicator of prognosis; the prognosis is often good in this type of clinical presentation.

In the relapsing schizophrenics the platelet MAO activity remained at its initial level although the clinical picture improved. In these instances, measurement of platelet MAO may be of value in diagnosis and, in addition, it may serve as a genetic marker in individuals predisposed to schizophrenia. This has been borne out in the studies of monozygotic twins dis-

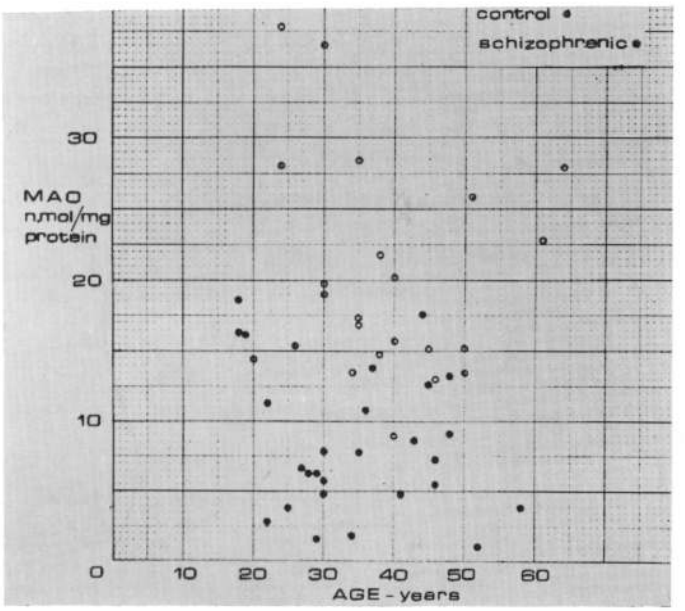

Fig. 1. Monoamine oxidase activity in schizophrenics.

cordant for schizophrenia (Wyatt et al. 1973). If there is low activity of platelet MAO in identical twins discordant for schizophrenia as compared with normals, then it should follow, from the genetic evidence to date (Shields 1968), that unaffected siblings may also have reduced MAO activity.

We have investigated this possibility in three families having a history of schizophrenia. No consistent findings with regard to the platelet MAO activity emerged from these studies. Figure 3 summarizes the data obtained. In this data it is noteworthy that two unaffected siblings (families 1 and 3) were found to have a greatly reduced platelet MAO activity; the relatively high values for platelet MAO activity in the remaining unaffected siblings may be

TABLE 2

MONOAMINE OXIDASE ACTIVITY IN SCHIZOPHRENICS

	No. of subjects	Mean age	MAO activity n. mol./mg. protein
Controls	23 (19 males, 4 females)	38.5 ± 11.2	20.1 ± 7.4
			$P < 0.001$
Schizophrenics	27 (20 males, 7 females)	34.8 ± 10.9	8.4 ± 5.0

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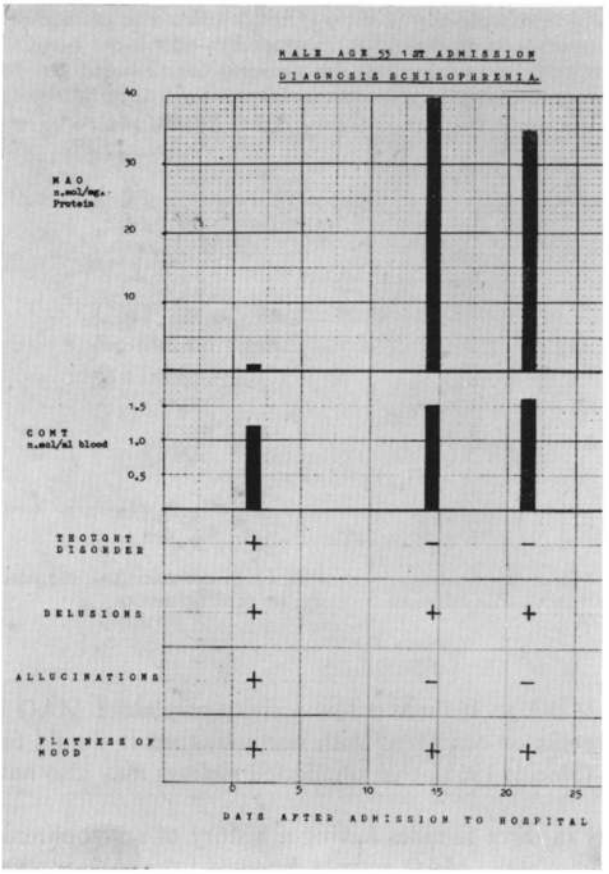


Fig. 2. Monoamine oxidase activity in relation to clinical state in an untreated first-admission schizophrenic.

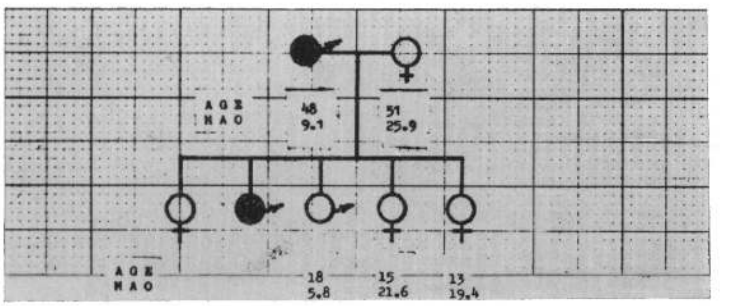
an age effect. Although data for this age group is not available, the work of Robinson et al. (1971) indicates that MAO activity declines as age increases from 25-35 years, so that it may be highest during the 'teens.

The two low values found might well represent two unaffected individuals who are at risk to schizophrenia. No such low values were found in the controls who were selected with the knowledge that there was no known history of schizophrenia in their family.

The significance of a low MAO activity in platelets remains to be established. However, Wyatt et al. (1973) claim that there is a relationship between the severity of illness and the extent of the lowering of platelet MAO activity as compared with normal individuals.

It is generally believed that the term schizophrenia, as it is used at present, refers to not one but a group of illnesses. Low platelet MAO activity has not been found in all of the schizophrenics which we have investigated; it may, therefore, be a feature of certain forms of schizophrenia only.

Our studies to date lead us to believe that the reduced platelet MAO activity in schizophre-



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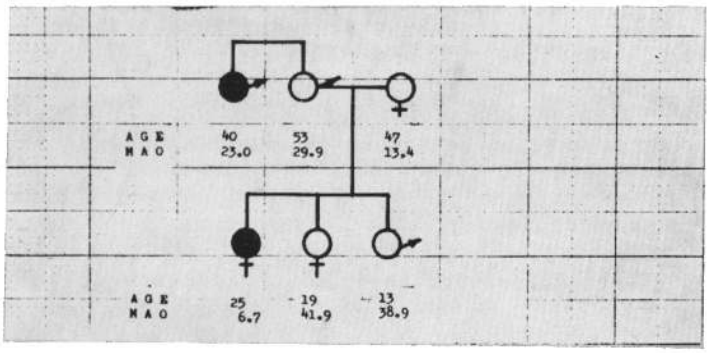

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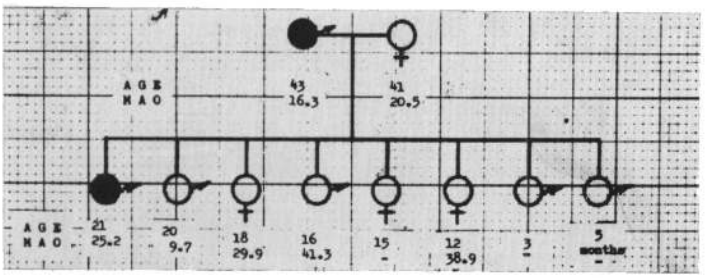

FAMILY 3

Fig. 3. Monoamine oxidase levels in platelets of individuals with a family history of schizophrenia.

nia may be due to the presence of endogenously produced inhibitor substances rather than an altered production of the enzyme.

Much further experimentation will be required to elucidate some of the points which these preliminary studies have raised, particularly with regard to the nature of the MAO isoenzymes and their activity in platelets and brain and the factors which modify MAO activity.

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