

CLINICAL VARIABLES AND PLATELET MAO IN SCHIZOPHRENIA¹

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SUMMARY

Platelet MAO activity was estimated in 60 male drug free schizophrenics and 26 controls matched for age. The paranoid group had significantly lower enzyme activity than the non-paranoid group and controls. Patients with premorbid schizoid personality had significantly lower enzyme activity than patients with non-schizoid premorbid personality and controls. A significant negative correlation between platelet MAO activity and severity and duration of illness was observed. Family history of schizophrenia, presence of auditory hallucinations and type and age of onset of illness were not related to platelet MAO activity.

It has been suggested that platelet monoamine oxidase (MAO) activity could be a genetic marker for vulnerability to schizophrenics (Wyatt et al., 1973). Most studies show reduced platelet MAO activity in chronic schizophrenic patients but the deviations from control values have varied from study to study (Wyatt et al., 1979). Although extraneous factors such as diet, hospitalization and hormonal status cannot adequately account for this variation, biological heterogeneity has been offered as a source of variability across studies (Wyatt et al., 1979).

A point of interest has been the evidence that certain clinical features of schizophrenia - auditory hallucinations, paranoid symptoms, intensity and duration of illness (Wyatt et al., 1979) and global prognostic score (Gruen et al., 1982) may be related to platelet MAO activity.

This study was undertaken to find out the relationship between clinical features - type and age of onset of illness, premorbid schizoid personality, family history of schizophrenia and duration and intensity of illness, and platelet MAO (MAO - B subtype) activity in schizophrenia.

Material and Methods

Patient group

60 male schizophrenics between 16-50 years of age (mean 27 ± 8.56), diagnosed as per DSM-III criteria (American Psychiatric

Association, 1980) independently by two psychiatrists, were selected from the out - patient section of the University Hospital, Banaras Hindu University, Varanasi. These patients had no history of drug intake in the past 2 weeks, of receiving ECT in the past 6 months or of drug addiction (alcohol, cannabis, opium etc.) and did not have any accompanying illness (neuro - psychiatric disorder, anaemia, hypertension, migraine or a physical illness requiring treatment). In addition, none of the patient had a past or family history in their first degree relatives of an affective or schizoaffective illness.

Control group

30 male, normal age matched (mean 27.57 ± 9.69 years) healthy volunteers were selected from the blood donors attending the Blood Bank of the University Hospital, B.H.U., Varanasi. These subjects did not have a history of drug addiction or a neuropsychiatric illness (schizophrenia, affective disorder, schizoaffective disorder, migraine, Huntington's chorea etc.) in themselves or their first degree relatives.

Procedure

The patients were hospitalized and kept drug free till the next day when blood was collected for enzyme estimation. Details of psychiatric history and mental status examination were recorded on a structured proforma within 2 days of hospitalization. Diagnosis of past and

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family history was made according to DSM - III criteria. Premorbid personality was assessed by the Schizoid - Non-schizoid scale of Gütelman - Klien and Klien (1969) and the patients were rated on the Brief Psychiatric Rating Scale (BPRS) (Overall and Gorham, 1962) for the severity of symptoms. Patients were categorised into paranoid and non-paranoid group according to the presence or absence of paranoid features (suspiciousness, grandiosity, persecutory delusions, hostility, rigidity and emotional distance).

20ml of fasting venous blood was collected between 9-11 AM from each subject through venepuncture in heparinized polypropylene tubes, and immediately placed in ice. Platelet protein was estimated by Lowery's method (Lowery et al., 1951). Finally, platelet MAO activity was estimated by Radio-Isotopic technique using ¹⁴C Tryptamine Bisuccinate as the substrate according to the procedure of Parvez and Parvez (1973). The method has been described in detail by Sharma et al. (1990).

All the estimations were done in duplicate and the mean taken. Enzyme activity was expressed in nanomoles/mg protein/hour (n mol/mg protein/h). The laboratory personnel were blind to the identity of the sample. Recent findings suggest that very low and very high platelet MAO activity is associated with personality profiles linked with vulnerability to various psychiatric disorders and the group with intermediate enzyme activity is presumably more normal (Schalling et al., 1987). Platelet MAO activity in the healthy control group ranged from 9.5-0.5 n mol/mg protein/h. The subjects with platelet MAO activity in the upper and lower decile were excluded so that 26 controls were available for final analysis. The data was analysed by student 't' test and analysis of variance.

Results

The mean platelet MAO activity in the patient group was 3.40 ± 2.06 (range 0.31 \pm 8.11) and that in the control subjects was 4.06 ± 1.16 (range 1.94 \pm 6.89) n mol/mg/protein/h. Although enzyme activity in the patients was lower than that in controls, the difference was not statistically significant

($t=1.68$; d.f.=84).

10 patients had received neuroleptic medication for variable periods (3 month - 1¹/₂ yr) but were drug free at the time of their inclusion in the study. There was no significant difference ($t=0.73$, df=58) in the platelet MAO activity of treated (N=10; 3.79 ± 2.2 n mol/mg protein/h) and untreated patients (N=50; 3.21 ± 2.04 n mol/mg protein/h).

Platelet MAO activity in chronic schizophrenics (N=13; 2.75 ± 1.99 n mol/mg/protein/h) was significantly lower ($t=2.19$; $p < 0.05$; d.f.=37) than enzyme activity in control subjects. Although platelet MAO activity was lower in the chronic schizophrenics compared to sub-chronic schizophrenics (N=47, 3.58 ± 2.07 n mol/mg protein/h), the difference was not statistically significant.

Enzyme activity did not differ significantly ($F=2.79$; N.S.) between patients with family history of schizophrenia (N=9; 2.40 ± 1.15 n mol/mg protein/h), patients without family history of schizophrenia (N=51, 3.58 ± 2.15 n mol/mg portein/h) and controls.

14 patients presented with auditory hallucinations and 46 patients did not present with these symptoms. The enzyme activity did not differ ($F=2.52$, N.S.) between the hallucinatory (2.71 ± 1.53 n mol/mg protein/h) and non-hallucinatory groups (3.77 ± 2.68 n mol/mg protein/h) and controls.

The paranoid group had significantly lower enzyme activity than the non-paranoid group and controls (Table-1).

Schizophrenics with premorbid schizoid personality had significantly lower enzyme activity than those with non-schizoid premorbid personality and controls (Table-2).

Table-1 Platelet MAO activity in paranoid and non-paranoid groups of schizophrenia

	Paranoid (n=17)	Non-Paranoid (n=45)	Control (n=26)
Platelet MAO activity			
Mean	2.25	3.85	4.06
S.D.	1.097	2.19	1.16

$F=6.38, p<0.01$

Paranoid vs Non-Paranoid : $t=2.85$, df=58; $p<0.01$
 Paranoid vs Control : $t=5.73$, df=41, $p<0.001$
 Non-paranoid vs Control : $t=0.11$, df=67, $p>N.S.$

Table-2 Comparison of MAO activity in patients with schizoid/non-schizoid premorbid personality

	Schizoid PMP (n=37)	Non-schizoid PMP (n=23)	Controls (n=26)
Platelet MAO activity			
Mean	2.96	4.12	4.06
S.D.	1.76	2.35	1.16

F=4.14, p<0.025

Schiz. vs Non-schizoid : t=4.31; df=58, p<.001
 Schiz. vs Controls : t=2.76; df=61, p<0.01
 Non-schiz. vs Controls : t=0.08; df=47; N.S.

Table-3 Correlation between platelet MAO activity with intensity of symptoms and duration of illness

Variables	r	r ²
Platelet MAO in patients (Mean=3.40; S.D.=2.06)		
BPRS of schiz. patient (Mean=46.43; S.D.=6.55)	-0.60**	0.36
Duration of illness (Yrs) (Mean=1.76; S.D.=2.22)	-0.32*	0.10

[*p<.05, **p<.001]

The severity of illness, measured by the total BPRS score, and duration of illness in the patients (range 6 mon-11 yrs) correlated negatively with platelet MAO activity (Table-3).

Table-4 Comparison of paranoid and non-paranoid groups on schizoid/non-schizoid premorbid personality and intensity and duration of illness

	Paranoid group (N=17)	Non-paranoid group (N=43)
Premorbid personality		
Schizoid	11	26
Non-schizoid	6	17
	χ ² =0.08, d.f.=1, N.S.	
Intensity of illness (Total B.P.R.S. score)	48± 6.14	45.95± 6.84
	t=1.07, d.f.=58, N.S.	
Duration of illness (in Yrs)	1.85± 1.88	1.72± 2.36
	t=0.2, d.f.=58, N.S.	

There was no significant difference between

the paranoid and non-paranoid groups with regard to schizoid premorbid personality, intensity and duration of symptoms (Table-4).

Discussion

The present investigation was an attempt to clarify the relationship between platelet MAO activity and certain clinical features of schizophrenia. Platelet MAO activity was observed to be lower in the paranoid group when compared to the nonparanoid group and controls. The two groups of patients were comparable on clinical variables. Schizoid premorbid personality, intensity and duration of illness were found to be related with enzyme activity. These observations are in conformity to several reports (Schildkraut et al., 1975; Sullivan et al., 1978) and suggest that the paranoid patients may form a sub-group with low platelet MAO activity. Some investigators could not find a significant difference between paranoid and non-paranoid schizophrenics (Berger et al., 1978 ; Freidhoff et al., 1978 ; Trivedi et al., 1987).

Patients with premorbid schizoid personality were observed to have significantly lower activity than those who were premorbidly non-schizoid. A positive correlation between prognostic score and platelet MAO activity in chronic schizophrenics has been reported (Gruen et al., 1982). Patients with premorbid schizoid personality were poor prognosis cases as schizoid personality has been reported to be a poor prognostic indicator (Slater and Roth, 1980). Thus, lowered enzyme activity in this group is understandable. There is a need to prospectively validate the prognostic utility of the platelet MAO levels in schizophrenia, using follow up studies.

Of particular interest was the finding of an inverse relationship between severity of illness, as measured by the BPRS, and platelet MAO activity (p<0.001). The former accounted for 36% of the variation in enzyme activity (r²0.36). There have been reports (Wyatt et al., 1973; Becker and Shaskan, 1977; Cookson et al., 1975) in which similar observations have been made. Cookson et al. (1975) observed changes in platelet MAO activity which paralleled the mental state in a patient of schizophreniform psychosis.

Much more variability in platelet MAO

activity has been reported in studies of acute than of chronic schizophrenic patients (Wyatt et al., 1972), suggesting that chronicity of illness was observed to be a significant variable accounting for 10% ($r^2=0.10$) of the variance in enzyme activity of patients. A few workers (Mann and Thomas, 1979; Trivedi et al., 1987), however, did not observe a relation between severity and duration of illness and platelet MAO activity in chronic schizophrenics.

Although chronicity may be associated with drug intake, it may be pointed out that the MAO values in medicated and unmedicated patients did not differ significantly. This finding reduces the likelihood that the results of the present investigation are largely drug related. Even though neuroleptic-induced reduction in enzyme activity has been reported (Takahashi et al., 1975; Friedhoff et al., 1978) the weight of evidence suggests that phenothiazines and butyrophenones, have, if anything, a tendency to increase platelet MAO activity (Wyatt et al., 1979). Furthermore, as the life span of platelet is about 9.9 days (Harker and Finch, 1969) it seems that a 2 week drug free period is sufficient for a study of platelet MAO activity.

It would have been desirable to analyse MAO activity in relation to dose and different medications. However, the medicated subjects had been treated with different combinations and doses of neuroleptic drugs for variable periods of time. The variability did not allow a meaningful analysis of differential drug effects on enzyme activity.

The findings of the present study are at variance with some others, possibly because of differences in diagnostic criteria (Schildkraut et al., 1976; Becker and Shaskan, 1977; Potkin et al., 1978; Berger et al., 1978; Friedhoff et al., 1978; Bond et al., 1979; Trivedi et al., 1987) and assay procedures (Potkin et al., 1978; Bond et al., 1979; Trivedi et al., 1987). Whereas some investigators studied chronic schizophrenics (Berger et al., 1978; Trivedi et al., 1987) diagnosed as per RDC or DSM-II criteria, others investigated acute schizophrenics (Bond et al., 1979) or mixed populations of patients (Potkin et al., 1978; Friedhoff et al., 1978). Patients of the present study were diagnosed according to DSM-III criteria which includes sub-chronic

and chronic forms of schizophrenia.

The work of Berger and co-workers (Berger et al., 1978) involved the study of chronic schizophrenics, most of them receiving neuroleptics for long periods and hospitalized for over a year. Others have relied on hospital records (Schildkraut et al., 1976; Berger et al., 1978), a less reliable source of data.

Platelet MAO activity has been reported to be higher in females and to fluctuate during the pre and post-ovulatory phases (Wyatt et al., 1979). Thus, the findings reported by some workers (Friedhoff et al., 1978; Bond et al., 1979) are questionable since they involved small samples with patients of both sexes and did not control for the phase of menstrual cycle. The population of this study hence was restricted to male patients.

In the presence of biological heterogeneity (Wyatt et al., 1979; Baron et al., 1984), the discrepant results across studies may represent a variable representation of genetic (i.e. low MAO values) versus non-genetic (i.e. normal MAO values) types of schizophrenia. The findings reported should be regarded as tentative. It would be necessary to replicate the work on female patients as well.

The present data show that specific clinical features of the schizophrenic illness, severity and duration of illness, presence of paranoid features and premorbid schizoid personality may be related to platelet MAO activity and can account, in part, for the discrepant results obtained across studies. There are indications that the relationship between platelet MAO activity and schizophrenia is complex. Further work should involve the study of other factors in relation to platelet MAO activity, particularly those that have been shown to have prognostic significance.

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