Eur Arch Psychiatr Neurol Sci (1987) 237:8–15

European Archives of Psychiatry and Neurological Sciences

Platelet Monoamine Oxidase Activity and Schizophrenia – A Myth that Refuses to Die?

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Summary. Platelet monoamine oxidase (MAO) activity was determined using kynuramine as a substrate in a group of schizophrenic patients ($n = 107$), a group of healthy individuals ($n = 100$), and a group of psychiatric patients who were neither schizophrenics nor alcoholics ($n = 110$). No significant difference emerged between the schizophrenics and the other two groups, while a significant reduction in platelet MAO activity in a group of alcoholics ($n = 60$) was confirmed. Breaking down the schizophrenic group according to course of illness, phenomenology (paranoid-hallucinatory or not) and drug use did not lead to a significant deviation in platelet MAO activity in any of these subgroups. It can also be demonstrated from the literature that the results reached by most research teams question the usefulness of platelet MAO activity as a genetic marker for psychiatric illness.

Key words: Platelet monoamine oxidase – Schizophrenia

Introduction

Monoamine oxidase (MAO, EC 1.4.3.4) has played an important role in research on the relationship between brain metabolism and psychoses since reduced platelet MAO activity was reported in schizophrenics (Murphy and Wyatt 1972) and bipolar depressives (Murphy and Weiss 1972). The impact of MAO studies is apparent from the publications which have subsequently appeared, some 500 in all. Approximately 100 of these have been concerned with platelet MAO as a biochemical marker for genetic predisposition to schizophrenia. In spite of several cautious comments (Wyatt et al. 1979; Buchsbaum et al. 1980; Sandler et al. 1981; DeLisi et al. 1982), the enticing speculation that MAO dysfunction in the brain results in a disturbance of biogenic amine metabolism leading to increased production of abnormal metabolites with psychotoxic effects has stimulated numerous MAO studies, as has the hypothesis that platelets can serve as a model for analogous processes in the brain. Certain similarities between platelets and central serotonergic neurones as regards monoamine transport, storage, metabolism, receptor functions, and the occurrence of enzymes have been postulated (Stahl 1977), although some reserve seems warranted (Achee et al. 1977; Fowler et al. 1982). The fact that MAO activity deviation has almost never been convincingly demonstrated in the brains of deceased schizophrenics (Schwartz et al. 1974; Crow et al. 1979) tends to reduce the significance of low platelet MAO activity levels. Recent evidence indicates that there is no genuine loss of MAO molecules in the platelets of schizophrenic patients (Rose et al. 1986) but, for example, an elevation in platelet membrane contents of phosphatidylserine leading to MAO inhibition (Tachiki et al. 1986; Orologas et al. 1986). Some investigators were unable to find significant differences between schizophrenics and controls (Belmaker et al. 1976; Owen et al. 1976; White et al. 1976; Eckert et al. 1980; Reveley et al. 1980; Koide et al. 1981; Mann et al. 1981). We have compared two large control groups (healthy individuals and nonschizophrenic psychiatric patients) and a group of alcoholics with a large group of schizophrenic patients. For reasons of good practicability we used the assay system proposed by McEntire et al. (1979), with slight modifications in order to guarantee rep-

resentative platelet yields. Negative findings were confirmed in our study.

Methods

Three groups were examined in a comparison of platelet MAO activity, one consisting of schizophrenic patients (definitive in the sense of Feighner et al. 1972), a control group of normal healthy individuals (healthy control), and a second control group of various nonschizophrenic psychiatric patients (psychiatric control). No member of these three groups met the criteria for chronic alcoholism, i.e., a daily alcohol consumption of more than 100 g pure alcohol (comparison calculation according to Löffler et al. 1979) in the year prior to the index evaluation. With the conistent studies showing reduced platelet MAO activity in alcoholics in mind (Adler et al. 1980; Fowler et al. 1982), a further group consisting of chronic alcoholics who were not schizophrenic was included for comparison.

Given the well-documented lowering of MAO in apparently normal subjects (Adler et al. 1980), we took care to avoid special selection factors in our healthy control group. This group, which was composed of nearly equal numbers of subjects from academic and nonacademic backgrounds (51/49), was selected from those taking part in a study of the relations between catecholamine metabolism and emotionality (Schneider 1986). The evaluation of their personality questionnaires showed no peculiarities which would have made them unsuitable as a reference group. Great care was taken to ensure that no subject had undergone or was undergoing psychiatric treatment or suffered from any acute or chronic disease at the time of the study. Apart from contraceptives, no drugs were being regularly taken.

The group of schizophrenics was broken down into the following subgroups (see Table 2): (a) according to course of illness into subchronic (0.5–2 years since onset of symptoms) and chronic (more than 2 years since onset of symptoms), and (b) according to phenomenology into patients with and without paranoid hallucinatory symptoms by the ICD criteria, 9th revision. Patients were classified as paranoid hallucinatory if they predominantly produced delusions or hallucinations in the history of their illness (ICD 295.3). The patients of the psychiatric control, particularly neurotics, depressives, and psychopaths (see Table 3), did not show Feighner symptoms of schizophrenia (Feighner et al. 1972). All the patients were inpatients at the psychiatric university clinic, and diagnosis took place without reference to MAO activity levels.

Determining platelet MAO activity by the method of McEntire et al. (1979) involved measuring the amount of 4-hydroxychinoline formed from kynuramine by a fluorescent technique at 315 n*m* excitation and 380 n*m* emission. Platelets were obtained using a modified method as follows: fresh venous blood was collected in polyethylene tubes containing EDTA as anticoagulant. Platelet-rich plasma (PRP) was obtained following centrifugation at 260 *g* for 10 min at 4°C in a Sorvall RC 2B centrifuge (rotor HB 4) and processed immediately. Sodium borate buffer, pH 8.2 (1.6 ml 0.1 *M*) and 0.2 ml PRP were equilibrated at 37°C, then 0.2 ml 1.0 *M* kynuramine diHBr (Sigma Chemie GmbH, D-8024 Deisenhofen, FRG) was added and incubated for 1 h. In view of substrate inhibition, the employed concentration of kynuramine was not saturating, nevertheless it exceeded the average Km value of platelet MAO activity (about 0.03 m*M*) by more than three times.

The remaining PRP was stored at −20°C in portions of 0.2 ml. Samples from various patients and controls were reanalyzed by a second investigator within 3 months. This enabled the degree of precision of the method to be assessed.

Statistical evaluation was carried out using the Statistical Package for Social Sciences (Nie et al. 1975) and the Statistical Analysis System (1981, 1985).

Results

We found a very good correlation between the replicate assays of the same sample performed by two different personnel ($r = 0.97$). Table 1 confirms higher MAO activity in females compared with males. In addition a reduction in MAO activity in the groups consisting of patients was apparent when compared with the healthy controls. Variance analysis of the mean values in the first 3 groups indicated significant differences both in females ($P < 0.01$) and males ($P < 0.05$). Pairwise Scheffé comparisons, however, failed to show significant differences between the schizophrenics and the control groups, both for females and males. A significant difference could only be found between the two control groups.

The mean values of the alcoholics were significantly reduced compared with all other groups ($P < 0.05$). Female alcoholics showed a more marked divergence in MAO activity, reducing the otherwise significant difference between males and females from approximately 20% to approximately 10%.

The values for platelet MAO activity were skewed towards the lower range (Fig. 1), confirming results in the literature (Friedman et al. 1974; Propping et al. 1981).

A post hoc split of the schizophrenic group according to different relevant criteria (chronicity and phenomenology) did not yield significant differences of mean MAO activity between these subgroups (Table 2). The highly significant age difference of about 10 years between subchronic and chronic patients was explained by the selection criteria. Reclassification of the psychiatric controls into subgroups, based on ICD 9 diagnoses of the patients' records,

Table 1. Comparison of platelet monoamine oxidase (MAO) activity[a]

Group	Males			Females		
	n	Mean	SD	*n*	Mean	SD
Healthy controls	59	8.95	3.27	41	11.33	4.08
Schizophrenics	67	7.96	3.32	40	10.52	4.76
Psychiatric controls	59	7.35	3.00	51	8.70	3.55
Alcoholics	31	5.40	2.79	29	6.06	3.15

[a] MAO activity as nmoles 4-hydroxychinoline/10^8 platelets per h

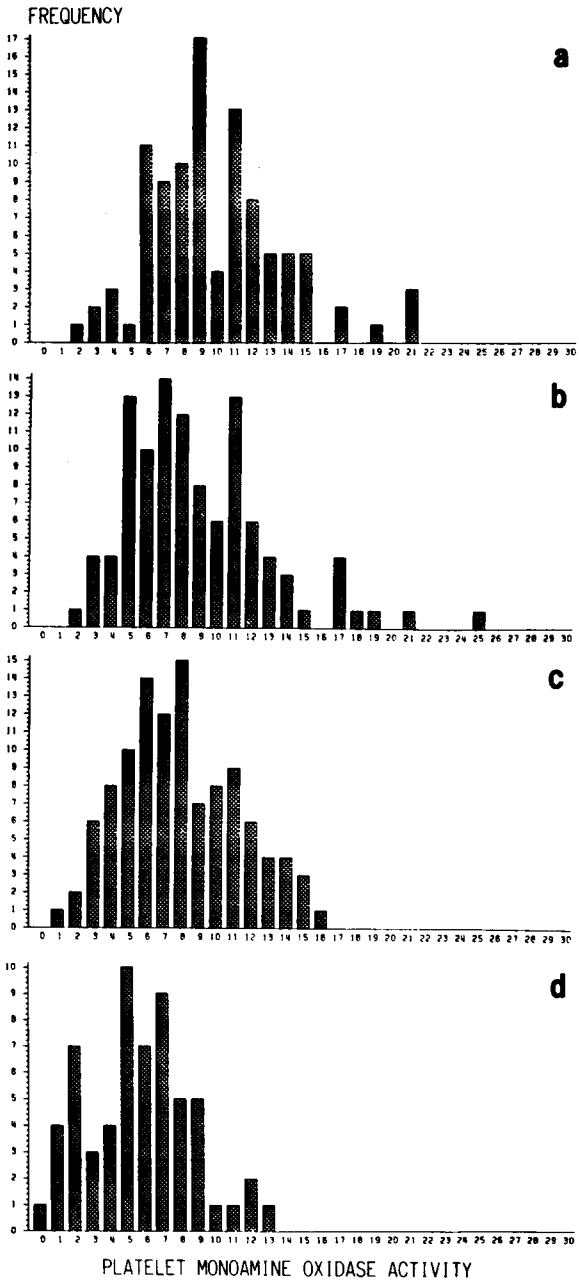

Fig. 1. Frequency distribution of platelet MAO activity **a** in healthy controls, **b** in schizophrenics, **c** in psychiatric controls, **d** in alcoholics. MAO activity is expressed as nmoles 4-hydroxychinoline/10^8 platelets per h

also did not lead to significant differences between these groups (Table 3).

Whereas age (means and standard deviations in parentheses) was comparable between schizophrenics (32.24 ± 11.14; see Table 2) and psychiatric controls (33.15 ± 11.06; see Table 3), it was lower in healthy controls (males: 28.56 ± 5.91; females: 25.17 ± 4.42) and higher in alcoholics (males: 37.71 ± 7.81; females: 41.41 ± 10.96). Within these groups correla-

Table 2. Platelet MAO activity[a] in subgroups of schizophrenics

Group	*n*	Age		MAO	
		Mean	SD	Mean	SD
Males					
(a) Chronicity					
Subchronic	50	27.44	7.71	8.31	3.30
Chronic	17	37.06	9.69	7.02	3.90
(b) Phenomenology					
Paranoid-hallucinatory	41	30.54	8.95	8.53	3.67
Without paranoid-hallucinatory symptoms	26	28.85	9.69	7.13	3.02
Females					
(a) Chronicity					
Subchronic	24	32.42	9.76	9.56	3.99
Chronic	16	41.88	15.31	12.03	5.61
(b) Phenomenology					
Paranoid-hallucinatory	26	35.42	13.09	10.73	4.97
Without paranoid-hallucinatory symptoms	14	37.64	13.11	10.21	4.62

[a] MAO activity as nmoles 4-hydroxychinoline/10^8 platelets per h

Table 3. Platelet MAO activity[a] in subgroups of psychiatric controls

Group	*n*	Age		MAO	
		Mean	SD	Mean	SD
Males					
Neurotics	14	30.64	8.82	6.93	2.96
Suicide attempts	7	31.86	10.56	7.36	3.16
Psychopaths	16	27.50	8.65	7.69	2.95
Bipolar depressives	8	40.88	7.88	5.47	1.83
Patients with organic cause	9	35.00	12.17	8.36	3.55
Patients with psychogenic reactions	5	33.80	18.32	8.64	3.28
Females					
Neurotics	16	30.31	7.52	9.00	3.82
Suicide attempts	13	35.38	12.99	8.84	4.10
Psychopaths	2	25.00	14.14	5.06	1.57
Bipolar depressives	7	39.14	7.52	8.98	3.11
Patients with organic cause	6	45.17	15.25	9.16	3.05
Patients with psychogenic reactions	4	33.50	6.81	9.27	3.81
Monopolar depressives	2	23.00	2.83	5.73	3.30
Puerperal psychosis	1	24		8.40	

[a] MAO activity as nmoles 4-hydroxychinoline/10^8 platelets per h

Table 4. Comparison of platelet MAO activity[a] in paralleled groups

Group	Males ($n = 11$)				Females ($n = 6$)			
	Age		MAO		Age		MAO	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Schizophrenics without neuroleptic medication	28.64	9.47	8.59	3.54	37.00	11.08	9.27	2.93
Schizophrenics with high neuroleptic dosage	27.82	8.67	10.39	4.52	31.67	8.19	10.99	4.10
Healthy controls	29.00	9.02	9.76	3.50	31.83	4.62	11.27	2.94

[a] MAO activity as nmoles 4-hydroxychinoline/10^8 platelets per h

tions between MAO activity and age were computed. None of the Pearson coefficients approached significance. Therefore the difference in age between groups was considered negligible.

No correlation could be found between neuroleptic dosage and platelet MAO activity in our group of schizophrenic patients, using standardized figures for neuroleptic potency according to Haase (1972), Mason and Granacher (1980), and Langer and Heimann (1983). To establish a crucial test for the effect of neuroleptics, the existing group of drug-free schizophrenics (more than 4 weeks without neuroleptic medication, $n = 17$) was compared with a reduced group of schizophrenics receiving high dosage neuroleptic medication (1.75 ± 0.86 g equivalents of chlorpromazine per day, $n = 17$), and a healthy control group ($n = 17$), paralleled by age and sex (Table 4). These groups did not show any significant mean differences in MAO activity.

Discussion

The demonstration that females show some 20% more platelet MAO activity than males is probably the most consistent element in MAO research (Schooler et al. 1978; Fowler et al. 1982). Most authors express the view that platelet MAO activity is largely genetically determined (Nies et al. 1973; Friedl et al. 1981). Thus platelet MAO activity is a relatively constant factor in the individual, without measurable daily fluctuations (Wirz-Justice et al. 1975). It made no difference whether benzylamine (Belmaker et al. 1976; Owen et al. 1976; Bond et al. 1979; Mann and Thomas 1979; Duncavage et al. 1982; Jackman and Meltzer 1983), tryptamine (Shaskan and Becker 1975; Belmaker et al. 1976; White et al. 1976; Eckert et al. 1980; Mann et al. 1981), or tyramine (Owen et al. 1976; Bond et al. 1979; Mann and Thomas 1979) were used as substrate. As McEntire et al. (1979) have shown, measuring platelet MAO activity using kynuramine as a substrate gives almost identical results to those obtained using benzylamine.

In contrast to these generally confirmed findings, the claim that platelet MAO activity is decreased in schizophrenic patients has been contradicted by the results of numerous studies. Our investigation also failed, despite the large sample used, to find any significant difference between the schizophrenics and the control groups. Moreover, subclassification into subgroups did not lead to positive findings.

The idea that reduced MAO activity is only to be found in certain subgroups of schizophrenics has led to attempts to group the patients more uniformly according to their present symptoms. Lowered MAO activity was found by Schildkraut et al. (1976) particularly in schizophrenics with auditory hallucinations and/or delusions. Further publications have duplicated these findings (Orsulak et al. 1978; Adler et al. 1980), while Groshong et al. (1978) and Mann and Thomas (1979) were unable to confirm them. Similarly, a subgroup consisting of paranoid-hallucinating schizophrenics in our sample showed no significant reduction in MAO activity.

Berrettini et al. (1980) and Baron et al. (1981), on the other hand, claimed a genetic link between low MAO activity and patients with a family history of schizophrenia. This has been contradicted by the findings of several other groups (Belmaker et al. 1977; Propping and Friedl 1979; DeLisi et al. 1980; Duncavage et al. 1982). Baron et al. (1984) themselves treated their previous findings with more reservations when the sample was increased: "However, the considerable overlap in enzyme activity between affected and unaffected individuals limits the usefulness of low MAO activity as a major risk factor in schizophrenia."

In addition to the hypothesis of heterogenous subgroups, the discrepancies have also been attributed mainly to differences in the medication of patients. While some authors assert that neuroleptics at a dosage in the therapeutic range have no effect on MAO activity (Murphy and Wyatt 1972; Shaskan and Bekker 1975; Gruen et al. 1982), others maintain that neuroleptics reduce platelet MAO activity (Friedhoff et al. 1978; Jackman and Meltzer 1980; Robinson and

Nies 1980; Chojnacki et al. 1981; DeLisi et al. 1981; Owen et al. 1981; Rawat et al. 1981; Meltzer et al. 1982; Maj et al. 1984). While neuroleptics probably do influence MAO activity in the long-term, some additional factors must be involved, since many relatives of schizophrenics (Berrettini et al. 1980; Reveley et al. 1983) and several other psychiatric patients show low MAO activity levels without neuroleptic treatment.

Pursuing another line of investigation, we were also unsuccessful in our attempt, using the method of Berrettini and Vogel (1978), to establish the existence of an endogenous inhibitor in the blood plasma of several patients with low MAO activity (Fuisting 1983). Other authors have similarly failed to find any indication that such plasma caused a significant decrease in normal or higher MAO activity (Wise et al. 1979; Yu and Boulton 1979; Demisch et al. 1981).

In a recent publication Tachiki et al. (1986) presented evidence in favor of inhibition of platelet MAO in schizophrenics caused by an increased phosphatidylserine membrane content. Compared to healthy controls, a greater additional amount of phosphatidylserine was needed to achieve a halving of enzyme activity in schizophrenics, a fact that can be interpreted as evidence for a completely normal basal MAO activity in schiophrenics, which is merely reduced by preinhibition. Such a membrane-coupled inhibition factor could possibly explain the decreased MAO activity in females in the postovulatory period (Belmaker et al. 1974) as well as in males, and would fit the fact that plasma amine oxidase does not show sex differences (Murphy et al. 1976). According to this view, a stronger inhibitory influence should reduce the numerical sex difference, an expectation which is supported by the more pronounced platelet MAO reduction in female alcoholics. It follows that the molecular amount of MAO per platelet should not vary between groups to the same extent as suggested by MAO activity determination. Based on a novel radioimmunoassay (Fritz et al. 1986), Rose et al. (1986) did in fact find that the specific concentration of platelet MAO was not different between female schizophrenic patients and healthy women, whereas this specific concentration was even higher in male schizophrenics compared to healthy men, an effect that "may reflect a physiological adjustment to the decreased catalytic capacity of the enzyme in these individuals". These authors seemed to favor "the interpretation that a genetically determined deficiency in MAO B, possibly originating from a structural defect in the enzyme, could be one factor leading to vulnerability to schizophrenia". They quote the study of Reveley et al. (1983), and interpret its main result that "platelet MAO activity was found to be highly correlated between all twin pairs, and was significantly reduced in both schizophrenics and their normal twins..." as "...strong evidence for genetically controlled lowering of platelet MAO activity in schizophrenia...". Why not argue that the missing MAO activity difference between schizophrenics and their normal co-twins and the fact that many substances and various physiological conditions lead to a lowering of platelet MAO activity (Robinson and Nies 1980; Sullivan et al. 1980; Demisch et al. 1984) disproves any definite value of this parameter?

A progression into more complex systems of hypotheses must be accompanied by stricter criteria of verification and replication. If enzyme kinetic data are considered as an improvement in spite of interference from unforeseeable factors in unpurified probes, the complexity will be large enough to find data to support almost any interpretation. No wonder the conflicting results in the literature on MAO enzyme kinetics are not easy to explain (Mann et al. 1981). Under strictly controlled and reliable conditions no evidence of abnormal kinetic constants of MAO could be found in platelets from unmedicated schizophrenics (Jackman and Meltzer 1983).

After a careful analysis of nearly all the publications dealing with platelet MAO and schizophrenia, – and with full awareness of the limitation of such a global comparative synopsis concerning diagnostic criteria, laboratory methods, and other parameters – we reached the conclusion that only 5 out of 30 groups have reported significantly reduced MAO activity without reservations, while the majority either definitely did not find any significant reduction (8 groups) or found reduced activity only for specific conditions (17 groups). The latter is the case, for instance, in a series of more than 15 publications by Murphy et al. who restricted their positive findings to chronic schizophrenia. Remarkably, some members of this group have – albeit in a different context – recently presented a result with completely normal platelet MAO activity for untreated chronic schizophrenics (Karson et al. 1983). Because of limited space a detailed documentation and evaluation concerning psychiatrically relevant MAO research will be presented elsewhere (Fleissner and Seifert, in preparation).

Although there have always been critical reservations (Friedman et al. 1974; Belmaker et al. 1976; Mann and Thomas 1979), probably not enough attention has been paid to the danger of producing biochemical or epistemological artifacts in MAO research (Belmaker 1984; Murphy 1984; Demisch et al. 1985; Siever and Coursey 1985). In conclusion, the generally contradictory results leave the impression of complex and obscure interactions which suggest

that MAO when considered in isolation is unsuited as a pathochemical marker for schizophrenia. This general reservation also applies to all the many other research areas where the marker function of this enzyme for the hypothesized biochemical bases of behavioral traits or disturbances must also be seriously questioned.

Acknowledgements. The authors wish to express appreciation to Mrs. H. Appelt, Mrs. A. Finke-Khan, Mrs. H. Kloss, and Mrs. C. Koop for their excellent technical assistance. The help of Dr. B. Andresen in the revision of this paper is gratefully acknowledged.

References

Achee FM, Gabay S, Tipton KF (1977) Some aspects of monoamine oxidase activity in brain. Prog Neurobiol 8:325–348

Adler SA, Gottesman II, Orsulak PJ, Kizuka PP, Schildkraut JJ (1980) Platelet MAO activity: Relationship to clinical and psychometric variables. Schizophr Bull 6:226–231

Baron M, Levitt M, Perlman R (1981) Platelet monoamine oxidase values and genetic heterogeneity in schizophrenia research. J Am Med Assoc 246:1418–1421

Baron M, Levitt M, Gruen R, Kane J, Asnis L (1984) Platelet monoamine oxidase activity and genetic vulnerability to schizophrenia. Am J Psychiatry 141:836–842

Belmaker RH (1984) The lessons of platelet monoamine oxidase. Psychol Med 14:249–253

Belmaker RH, Murphy DL, Wyatt RJ, Loriaux DL (1974) Human platelet monoamine oxidase changes during the menstrual cycle. Arch Gen Psychiatry 31:553–556

Belmaker RH, Ebbesen K, Ebstein R, Rimon R (1976) Platelet monoamine oxidase in schizophrenia and manic-depressive illness. Br J Psychiatry 129:227–232

Belmaker RH, Galon A, Perez L, Ebstein R (1977) Platelet MAO in schizophrenics with and without family history of schizophrenia. Br J Psychiatry 131:551–552

Berrettini WH, Vogel WH (1978) Evidence for an endogenous inhibitor of platelet MAO in chronic schizophrenia. Am J Psychiatry 135:605–607

Berrettini WH, Benfield TC, Schmidt AO, Ladman RK, Vogel WH (1980) Platelet monoamine oxidase in families of chronic schizophrenics. Schizophr Bull 6:235–237

Bond PA, Cundall RL, Falloon IRH (1979) Monoamine oxidase (MAO) of platelets, plasma, lymphocytes, and granulocytes in schizophrenia. Br J Psychiatry 134:360–365

Buchsbaum MS, Coursey RD, Murphy DL (1980) Schizophrenia and platelet monoamine oxidase: Research strategies. Schizophr Bull 6:375–384

Chojnacki M, Kralik P, Allen RH, Ho BT, Schoolar JC, Smith RC (1981) Neuroleptic-induced decrease in platelet MAO activity of schizophrenic patients. Am J Psychiatry 138:838–840

Crow TJ, Baker HF, Cross AJ, Joseph MH, Lofthouse R, Longden A, Owen F, Riley GJ, Glover V, Killpack WS (1979) Monoamine mechanisms in chronic schizophrenia: Post-mortem neurochemical findings. Br J Psychiatry 134:249–256

DeLisi LE, Wise CD, Potkin SG, Zalcman S, Phelps BH, Lovenberg W, Wyatt RJ (1980) Dopamine-β-hydroxylase, monoamine oxidase, and schizophrenia. Biol Psychiatry 15:899–908

DeLisi LE, Wise CD, Bridge TP, Rosenblatt JE, Wagner RL, Morihisa J, Karson C, Potkin SG, Wyatt RJ (1981) A probable neuroleptic effect on platelet monoamine oxidase in chronic schizophrenic patients. Psychiatr Res 4:95–107

DeLisi LE, Wise CD, Bridge TP, Phelps BH, Potkin SG, Wyatt RJ (1982) Monoamine oxidase and schizophrenia. In: Usdin E, Hanin I (eds) Biological markers in psychiatry and neurology. Pergamon, Oxford, pp 79–96

Demisch L, Gebhart P, Kaczmarczyk P, von der Mühlen H, Bochnik HJ (1981) Low platelet MAO activity in psychiatric patients and plasma factors: No evidence for inhibitory influences on MAO in the circulating platelet population. Biol Psychiatry 16:21–33

Demisch L, Gebhart P, Kaczmarczyk P, Roser M (1984) Factors that may regulate MAO activity. In: Tipton KF, Dostert P, Strolin Benedetti M (eds) Monoamine oxidase and disease. Academic Press, London, pp 253–263

Demisch L, Reinhuber F, Bochnik HJ (1985) The use of platelet monoamine oxidase in multifactorial research on endogenous psychoses. In: Beckmann H, Riederer P (eds) Pathochemical markers in major psychoses. Springer, Berlin Heidelberg New York, pp 96–109

Duncavage M, Luchins DJ, Meltzer HY (1982) Platelet MAO activity and family history of schizophrenia. Psychiatr Res 7:47–51

Eckert B, Gottfries C-G, von Knorring L, Oreland L, Wiberg A, Winblad B (1980) Brain and platelet monoamine oxidase in mental disorders: I. Schizophrenics and cycloid psychotics. Prog Neuro-Psychopharmacol 4:57–68

Feighner JP, Robins E, Guze SB, Woodruff RA, Winokur G, Munoz R (1972) Diagnostic criteria for use in psychiatric research. Arch Gen Psychiatry 26:57–63

Fowler CJ, Tipton KF, MacKay AVP, Youdim MBH (1982) Human platelet monoamine oxidase – A useful enzyme in the study of psychiatric disorders? Neuroscience 7:1577–1594

Friedhoff AJ, Miller JC, Weisenfreund J (1978) Human platelet MAO in drug-free and medicated schizophrenic patients. Am J Psychiatry 135:952–955

Friedl W, Krüger J, Propping P (1981) Intraindividual stability and extent of genetic determination of platelet monoamine oxidase activity. Pharmacopsychiatry 14:83–86

Friedman E, Shopsin B, Sathananthan G, Gershon S (1974) Blood platelet monoamine oxidase activity in psychiatric patients. Am J Psychiatry 131:1392–1394

Fritz RR, Abell CW, Denney RM, Denney CB, Bessman JD, Boeringa JA, Castellani S, Lankford DA, Malek-Ahmadi P, Rose RM (1986) Platelet MAO concentration and molecular activity: I. New methods using an MAO B-specific monoclonal antibody in a radioimmunoassay. Psychiatr Res 17:129–140

Fuisting B (1983) Untersuchungen zur Existenz eines MAO-Inhibitors im Blutsplasma Schizophrener mit negativem Ergebnis. Medizinische Dissertation Universität Hamburg

Groshong R, Baldessarini RJ, Gibson DA, Lipinski JF, Axelrod D, Pope A (1978) Activities of types A and B MAO and catechol-O-methyltransferase in blood cells and skin fibroblasts of normal and chronic schizophrenic subjects. Arch Gen Psychiatry 35:1198–1205

Gruen R, Baron M, Levitt M, Asnis L (1982) Platelet MAO activity and schizophrenic prognosis. Am J Psychiatry 139:240–241

Haase H-J (1972) Therapie mit Psychopharmaka und anderen psychotropen Medikamenten. 3. Aufl. Schattauer, Stuttgart

Jackman HL, Meltzer HY (1980) Factors affecting determination of platelet monoamine oxidase activity. Schizophr Bull 6:259–266

Jackman HL, Meltzer HY (1983) Kinetic constants of platelet monoamine oxidase in schizophrenia. Am J Psychiatry 140:1044–1047

Karson CN, Kleinman JE, Berman KF, Phelps BH, Wise CD, DeLisi LE, Jeste DV (1983) An inverse correlation between spontaneous eye-blink rate and platelet monoamine oxidase activity. Br J Psychiatry 142:43–46

Koide Y, Eberhard G, Sääf J, Ross SB, Wahlund L-O, Wetterberg L (1981) Kinetic aspects of monoamine oxidase activity in twins with psychoses. Clin Genet 19:395–400

Langer G, Heimann H (1983) Psychopharmaka. Grundlagen und Therapie. Springer, Wien

Löffler G, Petrides PE, Weiss L, Harper HA (1979) Physiologische Chemie. 2. Aufl. Springer, Berlin Heidelberg New York

Maj M, Ariano MG, Pirozzi R, Salvati A, Kemali D (1984) Platelet monoamine oxidase activity in schizophrenia: Relationship to family history of the illness and neuroleptic treatment. J Psychiatr Res 18:131–137

Mann J, Thomas KM (1979) Platelet monoamine oxidase activity in schizophrenia: Relationship to disease, treatment, institutionalization and outcome. Br J Psychiatry 134:366–371

Mann JJ, Kaplan RD, Georgotas A, Friedman E, Branchey M, Gershon S (1981) Monoamine oxidase activity and enzyme kinetics in three subpopulations of density-fractionated platelets in chronic paranoid schizophrenics. Psychopharmacology 74:344–348

Mason AS, Granacher RP (1980) Clinical handbook of antipsychotic drug therapy. Brunner/Mazel, New York

McEntire JE, Buchok SJ, Papermaster BW (1979) Determination of platelet monoamine oxidase activity in human platelet-rich plasma – A new microfluorescent assay utilizing kynuramine as substrate. Biochem Pharmacol 28:2345–2347

Meltzer HY, Duncavage MB, Jackman H, Arora RC, Tricou BJ, Young M (1982) Effect of neuroleptic drugs on platelet monoamine oxidase in psychiatric patients. Am J Psychiatry 139:1242–1248

Murphy DL (1984) Are there diseases attributable to monoamine oxidase abnormalities? In: Tipton KF, Dostert P, Strolin Benedetti M (eds) Monoamine oxidase and disease. Academic Press, London, pp 321–332

Murphy DL, Weiss R (1972) Reduced monoamine oxidase activity in blood platelets from bipolar depressed patients. Am J Psychiatry 128:1351–1357

Murphy DL, Wyatt RJ (1972) Reduced monoamine oxidase activity in blood platelets from schizophrenic patients. Nature 238:225–226

Murphy DL, Wright C, Buchsbaum MS, Nichols A, Costa JL, Wyatt RJ (1976) Platelet and plasma amine oxidase activity in 680 normals: Sex and age differences and stability over time. Biochem Med 16:254–265

Nie NH, Hull CH, Jenkins JG, Steinbrenner K, Bent DH (1975) SPSS. Statistical package for the social sciences. McGraw Hill, New York

Nies A, Robinson DS, Lamborn KR, Lambert RP (1973) Genetic control of platelet and plasma monoamine oxidase activity. Arch Gen Psychiatry 28:834–838

Orologas AG, Buckman TD, Eiduson S (1986) A comparison of platelet monoamine oxidase activity and phosphatidylserine content between chronic paranoid schizophrenics and normal controls. Neurosci Lett 68:293–298

Orsulak PJ, Schildkraut JJ, Schatzberg AF, Herzog JM (1978) Differences in platelet monoamine oxidase activity in subgroups of schizophrenic and depressive disorders. Biol Psychiatry 13:637–647

Owen F, Bourne R, Crow TJ, Johnstone EC, Bailey AR, Hershon HI (1976) Platelet monoamine oxidase in schizophrenia: An investigation in drug-free chronic hospitalized patients. Arch Gen Psychiatry 33:1370–1373

Owen F, Bourne RC, Crow TJ, Fadhli AA, Johnstone EC (1981) Platelet monoamine oxidase activity in acute schizophrenia: Relationship to symptomatology and neuroleptic medication. Br J Psychiatry 139:16–22

Propping P, Friedl W (1979) Platelet monoamine oxidase activity in first-degree relatives of schizophrenic patients. Psychopharmacology 65:265–272

Propping P, Rey E-R, Friedl W, Beckmann H (1981) Platelet monoamine oxidase in healthy subjects: The "biochemical high risk paradigm" revisited. Arch Psychiatr Nervenkr 230:209–219

Rawat AK, Raab E, Kokott W (1981) Human platelet monoamine oxidase activity in subgroups of schizophrenic disorder. Res Commun Psychol Psychiatr Behav 6:9–20

Reveley MA, Gurling HMD, Glass I, Glover V, Sandler M (1980) Platelet gamma-aminobutyricacid-aminotransferase and monoamine oxidase in schizophrenia. Neuropharmacology 19:1249–1250

Reveley MA, Reveley AM, Clifford CA, Murray RM (1983) Genetics of platelet MAO activity in discordant schizophrenic and normal twins. Br J Psychiatry 142:560–565

Robinson DS, Nies A (1980) Demographic, biologic, and other variables affecting monoamine oxidase activity. Schizophr Bull 6:298–307

Rose RM, Castellani S, Boeringa JA, Malek-Ahmadi P, Lankford DA, Bessman JD, Fritz RR, Denney CB, Denney RM, Abell CW (1986) Platelet MAO concentration and molecular activity: II. Comparison of normal and schizophrenic populations. Psychiatr Res 17:141–151

Sandler M, Reveley MA, Glover V (1981) Human platelet monoamine oxidase activity in health and disease: A review. J Clin Pathol 34:292–302

Schildkraut JJ, Herzog JM, Orsulak PJ, Edelman SE, Shein HM, Frazier SH (1976) Reduced platelet monoamine oxidase activity in a subgroup of schizophrenic patients. Am J Psychiatry 133:438–440

Schneider K (1986) Wissenschaftshistorische Perspektiven und Grundzüge einer biochemischen Psychoseforschung dargestellt im Rahmen einer empirischen Untersuchung zum Zusammenhang zwischen Katecholaminstoffwechsel und Emotionalität. Philosophische Dissertation Universität Hamburg

Schooler C, Zahn TP, Murphy DL, Buchsbaum MS (1978) Psychological correlates of monoamine oxidase activity in normals. J Nerv Ment Dis 166:177–186

Schwartz MA, Wyatt RJ, Yang H-YT, Neff NH (1974) Multiple forms of brain monoamine oxidase in schizophrenic and normal individuals. Arch Gen Psychiatry 31:557–560

Shaskan EG, Becker RE (1975) Platelet monoamine oxidase in schizophrenics. Nature 253:659–660

Siever LJ, Coursey RD (1985) Biological markers for schizophrenia and the biological high-risk approach. J Nerv Ment Dis 173:4–16

Stahl SM (1977) The human platelet. A diagnostic and research tool for the study of biogenic amines in psychiatric and neurologic disorders. Arch Gen Psychiatry 34:509–516

Statistical Analysis System (1981) Graph user's guide. SAS Institute, Cary, North Carolina

Statistical Analysis System (1985) User's guide. Basics. 5th edn. SAS Institute, Cary, North Carolina

Sullivan JL, Coffey CE, DeRemer Sullivan P, Taska R, Mahorney S, Cavenar JO (1980) Metabolic factors affecting monoamine oxidase activity. Schizophr Bull 6:308–313

Tachiki KH, Buckman TD, Eiduson S, Kling AS, Hullett J (1986) Phosphatidylserine inhibition of monoamine oxidase in platelets of chronic schizophrenics. Biol Psychiatry 21:59–68

White HL, McLeod MN, Davidson JRT (1976) Platelet monoamine oxidase activity in schizophrenia. Am J Psychiatry 133:1191–1193

Wirz-Justice A, Pühringer W, Hole G, Menzi R (1975) Monoamine oxidase and free tryptophan in human plasma: Normal variations and their implications for biochemical research in affective disorders. Pharmakopsychiatrie 8:310–317

Wise CD, Potkin S, Bridge P, Wyatt RJ (1979) An endogenous inhibitor of platelet MAO activity in chronic schizophrenia: Failure to replicate. Am J Psychiatry 136:1336–1337

Wyatt RJ, Potkin SG, Murphy DL (1979) Platelet monoamine oxidase activity in schizophrenia: A review of the data. Am J Psychiatry 136:377–385

Yu PH, Boulton AA (1979) Activation of platelet monoamine oxidase by plasma in the human. Life Sci 25:31–36

Received September 10, 1986