Platelet MAO Activity: Relationships to Clinical and Psychometric Variables

by Stephanie A. Adler, Irving I. Gottesman, Paul J. Orsulak, Patricia Platz Kizuka, and Joseph J. Schildkraut

Abstract

Platelet monoamine oxidase (MAO) activity was measured in a group of hospitalized male psychiatric patients. The findings of this study confirm previous reports of: (1) reduced platelet MAO activity in patients with auditory hallucinations, (2) reduced platelet MAO activity in patients with alcoholism, and (3) a positive correlation between platelet MAO activity and a psychometric index of social introversion.

Reduced or elevated levels of platelet monoamine oxidase activity have been found to occur in a wide range of psychiatric disorders including some types of schizophrenias, some types of affective disorders, and alcoholism as well as in apparently normal subjects. It has also been suggested that high or low levels of platelet MAO activity may be associated with vulnerability to various forms of psychopathology in "normal" college students (Buchsbaum, Coursey, and Murphy 1976; Haier et al. 1980). Additionally, a number of studies have reported a positive relationship between platelet MAO activity and measures of social introversion and extraversion.

Many studies have found reduced levels of MAO activity in platelets of at least some types of schizophrenic subjects, but not all studies concur. However, since the initial report from this laboratory of reduced platelet MAO activity in schizophrenic subjects with auditory hallucinations (Schildkraut et al. 1976), the relationship of auditory hallucinations to lower levels of platelet MAO activity among schizophrenics has been confirmed by a number of other investigators (Becker and Shaskan 1977; Demisch et al. 1977; Meltzer 1979). However, Groshong et al. (1978) and Mann and Thomas (1979) did not find such a relationship, and although Bond, Cundall, and Falloon (1979) reported that schizophrenics with auditory hallucinations had significantly lower levels of MAO activity in platelets and lymphocytes than did nonhallucinating schizophrenics, the levels in the schizophrenics with hallucinations were not significantly different from control values.

Most studies examining platelet MAO activity in alcoholic subjects have reported reduced levels of enzyme activity (Schildkraut et al. 1976; Takahashi, Tani, and Yamane 1976; Brown 1977; Wiberg, Gottfries, and Orelend 1977; Major and Murphy 1978; Sullivan et al. 1978b, 1979). However, the trait-state nature of reduced platelet MAO activity in alcoholic patients has not been resolved.

A behavioral dimension, potentially relevant to psychopathology, social introversion and extraversion, has also been shown to be related to platelet MAO activity in a number of different populations, including nonpsychiatric subjects, depressed patients, and even nonhuman primates. For example, Murphy et al. (1977), Schoo ler et al. (1978), and Coursey, Buchsbaum, and Murphy (1979) have reported an inverse relationship between platelet MAO activity, stimulus seeking, and extraversion in nonpsychiatric subjects. This is consistent with the earlier findings of low platelet MAO activity in bipolar patients as reported by Murphy and Weiss (1972). On the other end of the dimension, Schildkraut and

Reprint requests should be addressed to Dr. Adler at Massachusetts Mental Health Center, 74 Fenwood Rd., Boston, MA 02115.
his colleagues (1978) have found elevated levels of platelet MAO activity in depressed patients with histories of chronic asocial behavior. Furthermore, Redmond, Murphy, and Baulu (1979) have recently reported a strong positive correlation between platelet MAO activity and time spent alone for a group of rhesus monkeys.

Thus, increasing evidence suggests that low or high levels of platelet MAO activity may not be specific to any one type of psychopathology, but rather that the extremes of MAO activity may be found in a number of clinical conditions. One interpretation may be that platelet MAO is associated with one or more specific dimensions or clinical characteristics which may interact with other variables (whether biological, genetic, or environmental) to produce a final clinical expression of some psychopathology.

The current study was undertaken to explore the specific personality or clinical variables which might be associated with platelet MAO activity in a psychiatric population unselected for specific clinical diagnosis. Although many variables were examined (Adler 1979), this article presents findings on several specific variables that have been previously reported to have a relationship to platelet MAO activity. In particular, data are reported on the relationship of MAO activity to auditory hallucinations, alcohol abuse, and social introversion in 60 male patients between the ages of 18 and 45 who were admitted consecutively to the Massachusetts Mental Health Center in Boston. Patients were included regardless of race, ethnic background, or initial psychiatric diagnosis, as long as they were admitted to the hospital on a voluntary basis, were English speaking, and gave their informed consent to participate in the study. Patients with major medical or neurological disorders, and patients who were currently being treated with monoamine oxidase inhibitors were excluded.1

All subjects were interviewed by one of the investigators (S.A.) using the Schedule for Affective Disorders and Schizophrenia—SADS (Endicott and Spitzer 1977), and a diagnosis for each subject was obtained using the Research Diagnostic Criteria—RDC (Spitzer et al. 1977). A second diagnosis for each patient was also established by obtaining the official hospital discharge diagnosis which was based on DSM-II criteria (American Psychiatric Association 1968).

Most subjects were given the Minnesota Multiphasic Personality Inventory (MMPI; Dahlstrom, Welsh, and Dahlstrom 1972). Subjects were also given the Zuckerman Sensation Seeking Scale (Zuckerman 1974) and were rated on the Hamilton Depression Rating Scale (Hamilton 1960). Subjects were rated for alcoholism according to the RDC. Each subject was also rated on a 20-point scale of alcohol abuse generated from the probe questions used in the SADS. The SADS interview and information from hospital records were used to generate ratings for each subject on a number of clinical variables of interest such as history of auditory hallucinations, delusions, paranoia, and schizotypal features.

Auditory hallucinations were rated as definite, questionable, or not present. To be rated as "definite," hallucinations either had to be acknowledged by the patients during the SADS interview, or must have been well documented in hospital charts. The group of patients designated as having "no" hallucinations had no evidence of auditory hallucinations at any time. Patients for whom there was some doubt as to the authenticity of the report of hallucinations were rated as having "questionable" hallucinations.2

Platelet MAO activity was measured using tryptamine as substrate following the procedures described by Orsulak et al. (1978) and was expressed in nanomoles of tryptamine deaminated/hr/mg of platelet protein. All biochemical determinations were performed by laboratory personnel who were blind to clinical data, and all clinical interviewing and ratings were done blind to biochemistry.

Although most of the men in the group tended to show schizophrenic-like illnesses, characterized by a great deal of psychotic symptomatology, only about half of the sample received an RDC diagnosis of definite or probable schizophrenia. There was virtually no difference in platelet MAO activity when values were compared in the 17 patients with definite or probable schizophrenia and in the 31 patients who did not receive such a diagnosis. The respective group means ± SEM were 3.65 ± 0.43 and 3.64 ± 0.23 nanomoles deaminated/hr/mg of protein.

Official hospital diagnoses tended to vary from the RDC diagnoses,

---

1 Because of increasing evidence that tricyclic antidepressants and lithium may alter platelet MAO activity (Sullivan et al. 1978a; Bockar, Roth, and Heninger 1975), an additional 12 subjects being treated with these medications were also excluded from the data analysis, leaving a total of 48 patients.

2 One subject on whom there was inadequate information for past episodes was dropped from the analysis at this stage. He was described as having several drug-induced psychotic episodes in the past, but refused permission for his past hospital records to be requested.
with more patients receiving diagnoses of schizophrenia \((n = 28)\) in the former system. However, as with the RDC system, there was no significant difference in platelet MAO activity in the schizophrenic subjects \((3.76 \pm 0.31 \text{ nanomoles deaminated/hr/mg protein})\) and the nonschizophrenic subjects \((3.48 \pm 0.24 \text{ nanomoles deaminated/hr/mg of protein})\).

Only eight patients in the entire sample showed no evidence of auditory hallucinations at any time. None of these eight patients received an RDC diagnosis of schizophrenia, although two were given DSM-II diagnoses of schizophrenia.

Platelet MAO activity was examined in three groups of patients: those with “definite” hallucinations (that is, with auditory hallucinations that were either endorsed by patients in the SADS interview, or that were well documented in the hospital records for the current or for past hospitalizations); those with “no” history of auditory hallucinations; and those with “questionable” hallucinations, i.e., cases in which there was some doubt as to the authenticity of the report of hallucinations.

The distribution of values of platelet MAO activity was compared in patients with definite hallucinations and patients with no hallucinations using a chi-square analysis based on a median split of platelet MAO activity. The distributions of MAO values in the two groups were significantly different with hallucinating patients showing lower values \((\text{chi-square} = 4.26; p < .05)\).

Mean platelet MAO activity in the various groups was also compared. As can be seen in table 1, patients with definite hallucinations had significantly lower mean MAO activity than did patients with no history of hallucinations. Mean MAO activity in the group of patients with “questionable” hallucinations was slightly, but not significantly, lower than in patients without hallucinations (table 1).

As many investigators have reported reduced platelet MAO activity in subjects with alcoholism, this relationship was also examined in the present study. In the sample, there were six patients rated as definite alcoholics and three as probable alcoholics according to the RDC. As can be seen in table 2, patients who were rated as currently (definite or probable) alcoholics according to the RDC had mean MAO activity that was significantly lower than MAO activity in subjects rated as not alcoholic according to the RDC. We also found a statistically significant inverse correlation between platelet MAO activity and scores on the 20-point scale of alcohol abuse based on the SADS probe items for alcoholism in the entire sample \((r = -.37; p < .01)\). Former alcoholics, that is, subjects who had been alcoholic in the past but were not currently, had slightly lower mean MAO activity than nonalcoholic subjects (table 2).

In order to separate the possible confounding effects of alcohol abuse and auditory hallucinations on platelet MAO activity, the relationship between auditory hallucinations and MAO activity was examined in the nonalcoholic subjects. Again, subjects with definite hallucinations had lower mean MAO activity than did subjects with no history of hallucinations, although this difference did not quite reach statistical significance \((p = .08)\).

Since a number of previous studies have suggested that the dimension of social introversion and extraversion may be related to platelet MAO activity, in this study platelet MAO activity was also examined in relation to measures of social introversion. One of the MMPI research scales, Wiggins’ SOC (Social Maladjustment),³

³ A slightly abbreviated form of this scale (consisting of 24 out of the original 27 items) was used in this study. High correlations between the “short” and “long” forms of the scale have been reported (Cohler, Weiss, and Grunebaum 1974).
Table 2. Platelet MAO activity and alcohol abuse

<table>
<thead>
<tr>
<th>Alcohol abuse</th>
<th>n</th>
<th>Platelet MAO activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td>28</td>
<td>3.96 ± 0.29</td>
</tr>
<tr>
<td>Former</td>
<td>11</td>
<td>3.46 ± 0.41</td>
</tr>
<tr>
<td>Current</td>
<td>9</td>
<td>2.76 ± 0.30 *</td>
</tr>
</tbody>
</table>

Platelet MAO activity was compared in psychiatric patients who were diagnosed as currently alcoholic, formerly alcoholic, or never alcoholic according to the RDC. Platelet MAO activity is expressed as means ± SEM in nanomoles/hr/mg protein.

\*p < .05 for difference from values in patients who were never alcoholic using a one-tailed Student's t test.

showed a significant positive correlation with MAO activity (r = .32; p < .025). This scale has been described by Wiggins as roughly measuring the popular concept of introversion-extraversion, with high scorers being characterized as socially bashful, shy, embarrassed, self-conscious, and socially reserved (Wiggins 1966). The main MMPI scale Social Introversion (SI) showed a positive correlation to MAO in this sample, but this correlation (r = .13) failed to reach statistical significance.

Diagnosis, as determined either by the RDC or by official DSM-II hospital discharge diagnoses, was not demonstrated to be related to platelet MAO activity in this sample. There were virtually no differences in MAO activity between schizophrenic and nonschizophrenic subjects using either diagnostic system. An analysis of variance between five different RDC diagnostic groups also showed no significant difference in levels of platelet MAO activity. However, this may be largely due to the lack of diagnostic variance in this sample as well as to the diagnostic systems used.

The results of this study did confirm the presence of lower levels of platelet MAO activity in subjects with a history of alcohol abuse. A clear and statistically significant negative relationship was demonstrated using either the RDC criteria or the SADS. MAO activity is indicated.

The previously reported negative relationship between low platelet MAO activity and auditory hallucinations was also confirmed by the present findings. Patients with definite auditory hallucinations had significantly lower mean MAO activity than did patients with no evidence of auditory hallucinations. That the lower levels of MAO activity in the hallucinating patients were not due to the use of more alcohol in that group than in the group of nonhallucinating patients was supported by the finding of a negative relationship between platelet MAO activity and hallucinations in the nonalcoholic subjects.

Antipsychotic medication is unlikely to be contributing to the relationship between low platelet MAO activity and auditory hallucinations, as there was no overall correlation between average daily dose of neuroleptics (expressed as chlorpromazine equivalents) during the current admission and platelet MAO activity. Furthermore, five of the eight patients with no evidence of hallucinations were currently being treated with antipsychotic medication in doses comparable to those given to the majority of patients with hallucinations.

Finally, the relationship between platelet MAO activity and social introversion, as suggested by previous studies in human subjects and in nonhuman primates, was also confirmed by the finding of a significant positive correlation between MAO activity and scores on the Wiggins' SOC scale. Wiggins, Goldberg, and Appelbaum (1971) have demonstrated in a normal population a very high correlation between the SOC scale and the main MMPI scale which measures social introversion (SI) (r = .90). However, in the current sample, SI, while showing a positive correlation to MAO activity, failed to reach statistical significance. This main scale is not as homogeneous as Wiggins' SOC, and has been shown by factor analysis to be composed of a number of different clusters of items: personal discomfort and inferiority, discomfort with others, personal rigidity, hypersensitivity, distrust, and somatic concerns (Graham, Schroeder, and Lilly 1971). Of all the factors of the SI, Wiggins' SOC shares most items (11 out of 27) with the cluster dealing specifically with introversion, shyness, and avoidance of social contact (i.e., personal discomfort and inferiority). Further exploration of the specific aspects of the concept of social maladjustment and introversion that may be relevant to platelet MAO activity is indicated.

In summary, these findings in a group of hospitalized psychiatric patients confirm previous reports of: (1) reduced platelet MAO activity in patients with auditory hallucinations; (2) reduced platelet MAO activity in patients with alcoholism; and (3) a positive correlation between platelet...
MAO activity and a psychometric index of social introversion—perhaps similar to Meehl's (1962) concept of interpersonal aversiveness. The results of this study suggest that focusing on particular symptoms, or symptom clusters, such as auditory hallucinations or social withdrawal, may be an important complement to traditional approaches in biological psychiatry which have relied heavily on clinical diagnoses.

References


Bockar, J.; Roth, R.; and Heninger, G. Increased human platelet monoamine oxidase activity during lithium carbonate therapy. Life Sciences, 15:2109-2118, 1975.


Murphy, D.L.; Belmaker, R.H.; Buchsbaum, M.S.; Martin, N.F.; Ciaramello, R.; and Wyatt, R.J. Biogenic amine-related enzymes and personality variations in normals. Psychological Medicine, 7:149-157, 1977.


Spitzer, R.L.; Endicott, J.; and Roberts, E. Manual for the Research Diag-


Acknowledgments

This work was supported in part by an Alcohol, Drug Abuse, and Mental Health Administration grant from the National Institute of Mental Health (MH 15413) and by a grant-in-aid of research from Sigma Xi awarded to Stephanie A. Adler.

The Authors

Stephanie A. Adler, Ph.D., is Staff Psychologist, Massachusetts Mental Health Center, and Instructor, Department of Psychiatry, Harvard Medical School. Irving I. Gottesman, Ph.D., is Professor of Psychology and Director, Behavior Genetics Center, University of Minnesota. Paul J. Orsulak, Ph.D., is Associate Director, Neuropsychopharmacology Laboratory, Massachusetts Mental Health Center, and Assistant Professor, Department of Psychiatry, Harvard Medical School. Patricia Platz Kizuka, B.S., is Chemist, Neuropsychopharmacology Laboratory, Massachusetts Mental Health Center, and Research Assistant, Department of Psychiatry, Harvard Medical School. Joseph J. Schildkraut, M.D., is Director, Neuropsychopharmacology Laboratory, Massachusetts Mental Health Center, and Professor of Psychiatry, Harvard Medical School.