PLATELET MONOAMINE OXIDASE TYPE B (MAO-B) ACTIVITY IN PSYCHOPATHY

by

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Abstract

Studies of platelet MAO-B activity have revealed a link between low platelet activity and psychiatric syndromes characterized by an inability to control impulses and to anticipate future consequences of behavior (Oreland, 1980; Gottfries, von Knorring, & Oreland, 1980). These characteristics are fundamental to the construct of psychopathy, and we might therefore expect that psychopathy is associated with low MAO activity. Indeed, some investigators have suggested that low platelet MAO-B activity is a potential marker for vulnerability to psychopathy (Schalling, Asberg, Edman, & Oreland, 1987). However, no study to date has directly examined the association between platelet MAO activity and psychometrically-sound indices of psychopathy. The present study measured platelet MAO-B activity in a sample of 54 male offenders, assessed with the Psychopathy Checklist-Revised (PCL-R; Hare, 1991). PCL-R scores were not significantly related to level of platelet MAO activity. The results are discussed in terms of methodological issues involved in conducting biochemical research.

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I. Introduction

Recent research has focussed on gaining a better understanding of the neurochemical bases of psychiatric disorder. Monoamine Oxidase (MAO), a mitochondrial enzyme responsible for the oxidative deamination of endogenous neurotransmitter amines as well as oxidative monoamines, seems to be largely under genetic control and stable over time. Human blood platelet MAO activity is more accessible for measurement than brain MAO. Because of its accessibility and relative stability over time, it has been studied extensively as a possible peripheral marker for constitutional vulnerability to psychopathology.

Two catalytically active forms of MAO activity have been distinguished, differing in their substrate specificity and inhibitor sensitivity. MAO-A displays greater affinity for amine neurotransmitters 5-hydroxytryptamine (5-HT) and norepinephrine, and is sensitive to inhibition by clorgyline. MAO-B oxidizes tryptamine, phenylethylamine and benzylamine, and is sensitive to inhibition by deprenyl and pargyline. Tyramine and dopamine are substrates for both forms (Brown, Powell, & Craig, 1980; Murphy, 1978, Edwards, 1980 for review). Human liver and brain express high levels of both MAO-A and MAO-B. MAO-B is localized in neuronal cell bodies in regions containing serotonergic neurons, including the raphe complex and the nucleus centralis superior. MAO-A is found in catecholamine-containing neurons

such as the nucleus locus coeruleus and cells scattered in the commissural and solitary nuclei. Platelets, lymphocytes and mononuclear leukocytes, all appear to contain MAO-B but no detectable MAO-A.

Human platelet MAO, like other tissue monoamine oxidases, appears to be primarily located in the mitochondria. Because of findings of an association between serotonin turnover and MAO activity in certain parts of the brain (Adolfsson et al, 1978), it has been speculated that both brain and platelet MAO activity, as well as serotonin turnover in the central nervous system (CNS), reflect some stable characteristic of the serotonin system, and that low serotonin turnover might be related to vulnerability to psychopathology. Some further support for a connection between platelet MAO activity and serotonergic turnover in the CNS comes from findings of positive correlations between platelet MAO activity and spinal fluid concentrations of dopamine and seratonin metabolites, homovanillic acid (HVA) and 5-HIAA, in normals (Oreland et al, 1981). The relation between platelet MAO activity and MAO activity in the mammalian brain has not been established (Fowler et al, 1982). It has been hypothesized that platelet and brain MAO activity and part of the central monoaminergic system is regulated by a common, possibly genetic factor (Oreland & Fowler, 1982).

Several studies have indicated that platelet MAO activity is at least in part under genetic control. Variation in activity

per unit platelet from blood samples taken from the same individuals over time appears to be relatively small and stable over short periods (1-2 weeks), and long periods (8-10 weeks) (Murphy et al, 1976; Fowler et al, 1982). Evidence from family (Pandey, Dorus, Shaughnessy, & Davis, 1979) and twin (Hussein, Sindarto, & Goedde, 1980) studies indicates that much of the stability in monoamine oxidase activity within individuals is genetically determined. Little is known about the genetics of MAO; however recent evidence indicates that the genes encoding monoamine oxidases-A and B are located in close proximity on the X chromosome (Pintar, 1981; Kochersperger, Parker, Siciliano, Darlington, & Denney, 1986).

II. Platelet MAO as a Marker Enzyme for Psychiatric Disorder

In humans, extremes in platelet MAO activity have been found in patterns of personality and behavior considered high risk for psychiatric dysfunction. Specifically, low platelet MAO activity may reflect some constitutional weakness of monoamine systems in the brain (Oreland, 1980). Studies of deviant platelet MAO-B activity have revealed a link between low platelet activity and psychiatric syndromes characterized by an inability to control impulses and to anticipate future consequences of behavior. Low levels of platelet MAO-B activity have been associated with: violent suicide attempts (Gottfries, von Knorring, & Oreland, 1980); attention deficit disorder and hyperactivity (Shekim et al, 1986); drug abuse in teenage boys (von Knorring et al, 1987); conduct disorder-undersocialized

type (Bowden, Deutsch, & Swanson, 1988); and "Type II" alcoholism (characterized by early age of onset, signs of social complications, aggressiveness when intoxicated, and tendency to abuse illegal drugs) (von Knorring et al, 1985). Low MAO activity is associated with sensation seeking (Murphy et al, 1977) and with several dimensions measured by the Karolinska Scales of Personality (KSP): impulsivity, monotony avoidance, verbal aggression, and indirect aggression (Klinteberg et al, 1987; A. von Knorring, Bohman, L. von Knorring, & Oreland, 1985; Perris, Eisemann, von Knorring, Oreland, & Perris, 1984). Mattsson et al (1980) have also observed, in young male delinquents, a pattern consisting of a high testosterone level, low MAO activity, and high sensation seeking.

In high-risk studies of male college students, low MAO activity is associated with a high frequency of psychiatric counselling, many convictions for legal offenses, and a high rate of suicides, and suicide attempts in their relatives (Murphy et al, 1977; Buchsbaum, Coursey, & Murphy, 1976).

Traits that appear common to the above studies include monotony avoidance, sensation seeking, and impulsivity. When measured against levels of MAO activity, the general finding is that individuals who high on these traits show a common pattern of low MAO activity (von Knorring et al, 1987, Shekim et al, 1986, Schalling et al, 1987, Schalling et al, 1983).

While the pattern of findings described above appears to be impressive, it is difficult to evaluate the consistency of the

obtained relationships. For example, in two studies Pliszka et al (1988a, 1988b) reported no differences in platelet MAO activity in conduct disordered youth. There were still no differences when the subjects were further subtyped as violent or nonviolent according to their arrest record. They did, however find an inverse relationship between MAO activity and score on the Lie Scale of the Revised Children's Manifest Anxiety Scale (RCMAS). From these findings it is assumed that inconsistencies do exist within the literature. Inconsistencies, however, are difficult to assess since negative findings are not usually published except in conjunction with other significant findings. Considering the relatively stable patterns of activity observed within individuals, MAO activity has been suggested as a biological marker, useful in identifying vulnerability to some forms of psychopathology (Schalling et al, 1987).

III. Methodological Considerations

There are non-genetic factors that may affect platelet MAO activity. Factors that are known or suspected to influence measured platelet MAO activity levels include alcoholism, pharmacological treatment, smoking, hormones, diet, age, sex, race, platelet preparation, and assay methodology. Practical considerations may prohibit the ability of researchers to control for all of the potentially confounding variables that may affect platelet MAO activity. These factors require consideration, however, when researchers construct and interpret studies linking platelet MAO-B activity to psychopathology. Some

of the demographic/lifestyle factors known to affect platelet MAO-B activity will be discussed below.

A. Alcoholism: Most investigators confirm a link between low platelet MAO activity and alcoholism (Ghanshyam, et al, 1988, von Knorring et al, 1985, Wiberg, Gottfries, & Oreland, 1977) that is not related to iron deficiency. A stable level of reduced platelet MAO activity has been found in chronic alcoholics over a twelve month period (Sullivan, Stanfield, Schanberg, & Cavenar, 1978). Alcoholic patients studied acutely or months after abstinence showed significantly lower MAO activity than age and sex matched controls (Wiberg, Gottfries, & Oreland, 1977). Whether alcohol itself alters platelet MAO activity is still unclear. Robinson and Nies (1980) found no significant changes in plasma or platelet MAO after acute ethanol administration. In contrast, Tabakoff et al (1988) found inhibition of MAO activity in alcoholics when saturating concentrations of substrate were used in assaying enzyme activity. This effect in alcoholics may reflect a long term response to ethanol consumption or an inherent characteristic of persons with alcoholism. Given the strong and consistent link that has been drawn between low MAO activity and long term alcohol use, it is obviously an important factor to be accounted for in studies attempting to draw associations between MAO activity and psychopathology. However, in spite of the evidence, it appears to be a factor that has largely been ignored. For example, Zureick & Meltzer (1988) found that in approximately

half of studies investigating platelet MAO activity in schizophrenia, history or evidence of alcohol use was not reported.

B. Smoking Several studies suggest that smoking is associated with low MAO activity (Yu & Boulton, 1987; Norman et al, 1986; Oreland et al, 1981a). Whether smoking produces an inhibitor of MAO activity, decreases the synthesis of the enzyme, or whether individuals who have lower MAO activity are more likely to smoke, remains to be answered. Most authors ascribe findings of lowered activity in smokers to personality characteristics (e.g. Oreland et al, 1981a). The few studies that looked for changes in platelet MAO activity upon cessation of smoking have demonstrated mixed results. Oreland et al (1981a) found that platelet MAO activity for ex-smokers was not significantly different than MAO activity for smokers, while Norman, Chamberlain, and French (1986) found that one month after cessation of smoking MAO activity rose significantly. These differing results have been attributed to differences in definitions used to describe smoking behavior. Whereas in Oreland et al's (1981a) study self report data were used, Norman et al (1986) used plasma thiocyanate as an index of exposure to cigarette smoke. Whether cigarette smoke directly inhibits MAO activity, or MAO is a marker for personalities prone towards smoking behavior, cigarette smoking is clearly a factor that should be controlled in studies investigating the role of MAO activity in psychopathology.

C. Pharmacological Treatment The possibility that low platelet MAO activity might be an artifact of pharmacological treatment requires consideration. Tricyclic antidepressant drugs act as weak reversible inhibitors of the enzyme MAO in human cerebral cortex and platelets, with more potent inhibitory actions on MAO B than MAO A (Reid, Hill, & Murphy, 1988). Fluoxetine, desmethylclomipramine, desipramine, amitriptyline, and clomipramine all inhibit MAO B in human brain cortex and human platelet . Each drug appears to be a more potent inhibitor of human platelet than human cortex preparations ($p<.05$) (Reid, Hill & Murphy, 1988). An atypical biphasic response occurs in human platelet preparations with 10^{-4} M clomipramine and imipramine (Reid et al, 1988) when benzylamine, but not phenylethylamine is used as a substrate. Considering the different drug effects observed on MAO activity, depending on the substrate used in analysis, caution is recommended when comparing MAO B data using benzylamine versus phenylethylamine as substrates.

There is evidence that neuroleptic treatment can be associated with a drop in platelet MAO activity. This drop appears sufficient enough to produce a significant effect when comparisons are made between the platelet MAO activity of patient groups and normal controls. In a study that examined the effects of neuroleptic treatment on platelet MAO activity, Chojnacki et al (1981) found that mean MAO activity (as measured with both tryptamine and phenylethylamine substrates) was

decreased by an average of about 15% in schizophrenic patients receiving 3 weeks of treatment with haloperidol. The extent of decrease in platelet MAO activity in chronic patients treated with haloperidol was positively related to the mean plasma level of haloperidol. In patients receiving butaperazine, the decrease averaged 38.9% for both substrates (Chojnhacki et al, 1981). Similarily, Meltzer et al, 1982 found that platelet MAO activity significantly decreased in both men and women after treatment with either haloperidol or chlorpromazine. Patients with highest initial platelet MAO activity tend to have the largest decreases in platelet MAO activity during neuroleptic treatment (Meltzer et al, 1982). It has been suggested that at least some of the differences in platelet MAO activity reported in relation to the use of some drugs might be explained by changes in the rates of platelet formation, release, or degradation, which could in turn affect the average density of platelet populations sampled (Murphy, Costa, Shafer, & Corash, 1978). However, regardless of the mechanism by which these changes of activity occur, these findings underline the importance of monitoring history of pharmacological treatment in patients and controls. These results suggest that at least part of the decrease in MAO activity that has been observed in chronic schizophrenic patients (Wyatt et al, 1979) may be due to treatment with neuroleptic drugs. Findings of differences in platelet MAO activity based on subjects who have been treated pharmacologically must be interpreted with caution.

Low MAO activity has been associated with heavy marijuana use (Stillman, Wyatt, & Murphy, 1978). Benzodiazepines and barbituates do not appear to have a significant effect on MAO activity. Amphetamines appear to affect MAO activity only in extreme concentrations. Reports on the effect of lithium carbonate on MAO activity are contradictory (for review see Sullivan et al, 1980).

D. Age and Platelet MAO Activity The effect of age on MAO activity is disputed. A number of studies have found a significant positive correlation between age and MAO activity (Fowler, Wiberg, Oreland, Marcusson, & Winblad, 1980; Robinson & Nies, 1980). In these studies males tend to show a small, linear increase in MAO activity with age beginning at age 20. Females show a different trend, tending to be stable from the second until the fifth decade, with a sudden rise occurring after age 60 (Robinson, & Nies, 1980). In contrast, Murphy et al (1976) found no significant changes in platelet MAO activity in either males or females between the ages of 10 and 70 when MAO activity was measured per unit platelet. Sandler et al (1981) confirm this finding of no significant change with age.

E. Sex Differences in Mao Activity Studies have consistently shown that women have significantly higher mean platelet and plasma MAO activity than men (Robinson & Nies, 1980, Robinson et al, 1971; Murphy et al, 1976).

F. Diet Riboflavin deficiency is associated with decreased MAO activity (Sullivan et al, 1980; Sourkes, 1983). This

decrease in activity can be reversed by the introduction of riboflavin into the deficient diet.

Iron deficiencies have been reported to result in a decrease in MAO activity (Sourkes, 1983). However, platelet MAO activity apparently returns to normal when iron-deficient subjects are treated with iron. Youdim et al (1975) have shown that serum iron levels are positively related to MAO activity. It is unclear to what extent moderate variations in the intake of these nutritional factors affect MAO activity.

The influence of caffeine is a factor that has been largely neglected in the literature. In a single study that addressed caffeine as a potential confound, Giller et al (1984) found no significant correlation between platelet MAO and number of cups of coffee consumed per day.

G. Race Although racial effects would appear to be an important factor to consider in studies of platelet MAO activity in psychopathology, the influence of race on MAO activity has been largely neglected in literature. Groshong et al (1978) found platelet MAO activity to be significantly lower in blacks than whites. Meltzer (1988) reports a complex interaction between race, subtype of schizophrenia, symptoms, and platelet MAO activity, whereby black paranoid schizophrenics with auditory hallucinations had lower platelet MAO activity than white patients of the same type. No studies to date have addressed differences in MAO activity between white, Asian, or native Indian populations.

IV. Platelet MAO Activity and Psychopathy

The emerging relationships between platelet MAO-B activity and vulnerability to psychopathology, are of considerable interest to the study of the psychiatric syndrome of psychopathy. Psychopathy is a personality disorder. Like all personality disorders, it has an early onset and characterizes the individual's long-term functioning, resulting in social and interpersonal dysfunction (American Psychiatric Association, 1987; Millon, 1981). Symptoms of psychopathy are usually evident by middle to late childhood, and can be assessed reliably in adolescence (Forth, Hart, & Hare, 1990; Robins, 1966). The disorder is chronic and persists well into adulthood, although there may be some changes in its symptom pattern after age 45 or so (Cleckley, 1976; Hare, McPherson, & Forth, 1988; Harpur & Hare, 1990b; Robins, 1966). The pattern of personality variables associated with low MAO activity in the current literature, shows striking similarities to the psychopathic personality. Impulsivity, unreliability, proneness to boredom, lack of insight, irresponsibility, violence, and aggressive behaviour are personality and behavioural characteristics considered to be core elements of the psychopathic personality (Cleckley, 1976; Hare & McPherson, 1984a). Psychopathy is associated with unstable interpersonal relations, poor occupational functioning, and increased risk of involvement in criminal activity (Cleckley, 1976; Hare et al., 1988; Hart, Kropp, & Hare, 1988; Kosson, Smith, & Newman, 1990; Woodruff, Guze, & Clayton, 1980).

Psychopathy can be differentiated from other personality disorders on the basis of its characteristic pattern of interpersonal, affective, and behavioral symptoms. Interpersonally, psychopaths are grandiose, egocentric, manipulative, dominant, forceful, and cold-hearted. Affectively, they display shallow and labile emotions, are unable to form long-lasting bonds to people, principles, or goals, and are lacking in empathy, anxiety, and genuine guilt or remorse. Behaviorally, psychopaths are impulsive and sensation-seeking, and tend to violate social norms; the most obvious expressions of these predispositions involve criminality, substance abuse, and a failure to fulfill social obligations and responsibilities. It is their disproportionate involvement in crime, particularly violent crime, that makes them of particular concern to the criminal justice system, and to society in general.

While the concept of psychopathy has long held a prominent position in psychiatry and clinical research, there is a dearth of literature addressing possible links between biochemistry and psychopathy. Only two studies to date have attempted to examine the relationship between psychopathy and platelet MAO activity.

Lidberg, Modin, Oreland, Tuck and Gillner (1985)

Lidberg et al. (1985) examined MAO levels in a sample of 37 men admitted to a Forensic Psychiatric Clinic for psychiatric examination by court appointment. Patients were diagnosed as either schizophrenic, psychopathic (according to global ratings

based on descriptions by Cleckley [1976]), or "other" (i.e. no schizophrenic or psychopathic diagnosis). Two control groups were included; they were a group of construction workers and male staff in the clinic. Substance use was assessed via blood assay and reported to be negligible. Smoking habits did not differ between the groups. There was a tendency for the "psychopathic" group to have low MAO activity. While this finding of differences between the groups is interesting, these results should be interpreted with caution. The method for diagnosing psychopathy was inadequate: Information on how the diagnoses were made, and evidence for the reliability and validity of the diagnoses, was absent.

Yu, Davis, Gordon, Reid, Green, and Boulton (1985)

Yu et al (1985) examined MAO levels in 125 male inmates in a Canadian Federal Penitentiary. Inmates were categorized into violent, semi- violent, and non- violent groups according to court records and institutional behavior. They were also assessed for verbal and non-verbal aggression. MAO activity varied inversely and significantly with dimensions of anger, hostility, and depression proneness. Platelet MAO activity was not found to be significantly different in "aggressive psychopaths". Details concerning their procedures for classifying psychopaths were not given. It appears that psychopathy was not formally assessed, but rather inferred based upon court records and institutional behavior. They did, however find an inverse relationship between MAO activity and anger and

hostility, consistent with previous patterns that have been observed. However, without valid psychopathy assessments, the findings are difficult to interpret in relation to the concept of psychopathy.

These findings suggest that further investigation in platelet MAO-B activity, in search of a better biochemical understanding of psychopathy, may be fruitful. However, reliable and valid assessment procedures are essential if neurochemical correlates of psychopathy are to be uncovered. Most importantly, investigations concerning biochemical underpinnings of psychopathy have long term implications in terms of diagnosis and treatment of psychopaths in the mental health and criminal justice system. These practical implications underscore the need for valid and reliable assessment of psychopathy, if biochemical studies of psychopathy are to be useful.

V. The Revised Psychopathy Checklist (PCL-R)

The Revised Psychopathy Checklist (PCL-R; Hare, 1991; Hare et al., 1990) is a 20-item rating scale designed to assess the traditional clinical construct of psychopathy, perhaps best exemplified in the work of Cleckley (1976). The PCL-R is the basis for one of the four criteria sets being evaluated in the DSM-IV field trials for antisocial personality disorder (Hare, Hart, & Harpur, 1991).

The PCL-R measures behaviors and inferred personality traits considered fundamental to the clinical construct of psychopathy. Each item is scored on a 3-point scale, where 0

indicates that it definitely does not apply, 1 that it applies somewhat or only in a limited sense, and 2 that it definitely does apply, to the individual. The information needed to score the items is obtained from a semi-structured interview and institutional files. Detailed instructions for scoring the items are contained in the manual for the PCL-R (Hare, 1990). Although clinical judgment and inference are required, the items are not difficult to score.

PCL-R Total scores can range from 0 to 40. In most samples, the distribution of scores is approximately normal, with a slight negative skew. Although the Total scores are dimensional, they have been used to provide a categorical diagnosis of psychopathy. A cutoff score of 30 has proven useful for this purpose. Mean Total scores are relatively consistent across samples of prison inmates, and across forensic patients, from different institutions and countries. Hare et al. (in press) reported that the mean Total score for six samples of male prison inmates (N = 1065) was 23.37 (SD = 7.96), and that the mean score for four samples of male forensic patients (N = 440) was 20.56 (SD = 7.79). Total scores in these samples had high interrater reliability and internal consistency. Thus, for the prison and forensic psychiatric samples pooled, the intraclass correlation was .83 for a single rating and .92 for the average of two ratings. Coefficient alpha was .87, and the mean inter-item correlation was .25.

Although it meets the statistical criteria for a homogeneous, unidimensional scale, there is very strong evidence

that two oblique factors underlie the PCL-R (Hare et al., in press; Harpur et al., 1988). The correlation between the factors is about the same in samples of prison inmates (.56 on average) as it is in samples of forensic patients (.53 on average). Factor 1 reflects interpersonal and affective characteristics, such as egocentricity, lack of remorse, and callousness, considered fundamental to clinical conceptions of psychopathy. In spite of the relatively small number (8) of items involved, Factor 1 scores, obtained by summing the individual item scores, are reliable in samples of prison inmates and forensic patients. Evidence presented elsewhere (Hare, 1990; Harpur et al., 1989; Hart & Hare, 1989) indicates that Factor 1 is most closely correlated with classic clinical descriptions of psychopathy, prototypicality ratings of narcissistic personality disorder, and with self-report measures of machiavellianism, narcissism, empathy, and anxiety. Factor 2 reflects those aspects of psychopathy related to impulsivity, antisocial behavior, and an unstable lifestyle. Factor 2 is most strongly correlated with diagnoses of Antisocial Personality Disorder, criminal behaviors, socioeconomic background, and self-report measures of socialization and antisocial behavior. In addition, recent evidence indicates that Factor 2 is much more strongly related to substance abuse than is Factor 1 (Hart & Hare, 1989; Smith & Newman, 1990).

The reliability and the validity of the PCL-R are well established. With respect to concurrent validity, the PCL is

positively correlated with prototypicality ratings of psychopathy and antisocial personality disorder and with diagnoses of antisocial personality disorder (APD) made according to DSM-III criteria (Hare, 1985b; Harpur et al., 1989; Hart & Hare, 1989). Second, with respect to convergent and discriminant validity, Hart and Hare (1989) found that PCL ratings were either uncorrelated or negatively correlated with most DSM-III Axis I disorders; positively correlated with histrionic, narcissistic, and antisocal personality disorder; and either uncorrelated or negatively correlated with the remaining personality disorders. Several studies indicate that the PCL is positively associated with both symptoms and diagnoses of substance use disorders (Hart & Hare, 1989; Hemphill, Hart, & Hare, 1990; Smith & Newman, in press). Third, with respect to predictive validity, PCL scores are related to conditional release violations (Hart, Kropp, & Hare, 1988; Serin, Barbaree, & Peters, 1987), poor response in institutional treatment programs (Ogloff & Wong, in press; Rice & Harris, 1988), and violent recidivism (Forth, Hart, & Hare, in press; Rice & Harris, 1988). Finally, with respect to other aspects of construct validity, PCL scores are related in theoretically meaningful ways to performance on a variety of psychophysiological, cognitive, and linguistic tasks (Gillstrom & Hare, 1988; Hare, Williamson, & Harpur, 1988) and to criminal behaviors (Hare & McPherson, 1984; Hare, McPherson, & Forth, 1989; Williamson, Hare, & Wong, 1987).

VI. Purpose of the Present Study

To date, no study has measured platelet MAO-B activity in well-defined groups of psychopaths under carefully controlled conditions. In this study, differences in platelet MAO activity were examined in a group of male offenders, assessed for psychopathy according to Hare's Psychopathy Checklist (PCL, Hare, 1991). The Psychopathy Checklist (PCL), scored from interview and case-history information, is an explicit, reliable, and valid procedure for the assessment of psychopathy in prison populations. Finally, as previously discussed, there is some evidence that platelet MAO-B activity may be influenced by a number of variables, including age (Persky, Smith, & Basu, 1971), alcoholism (Pandey et al, 1988, von Knorring et al, 1985, Wiberg, Gottfries, & Oreland, 1977), smoking (eg. Yu & Boulton, 1987); heavy marijuana use (Stillman, Wyatt, & Murphy, 1978); and pharmacological treatment (Reid, Hill & Murphy, 1988). These factors were determined via self-reports and institutional files; the effects of these variables were statistically controlled through regression analyses. If psychopathy is negatively associated with platelet MAO-B activity, as suggested in the literature thus far, it may be expected that high PCL scores, would correlate negatively with levels of MAO activity.

VII. Method

A. Subjects

Subjects were male inmates from Matsqui Institution, a medium security Canadian federal institution in Abbotsford,

B.C., who volunteered to participate in the present study. All were serving sentences for two years or longer, mostly for violent crimes. Participants provided informed consent and permission to inspect their institutional files. Anonymity was assured through a data coding system, and the inmates were assured that study results would not be released to the staff or administration of the institution. Subjects were assured that blood analyses were not performed for the purposes of AIDS testing. Subjects were paid a total of $25.00, deposited directly into their institutional accounts, for participation. Ethical approval was obtained from the University of British Columbia Ethics Committee. The study was approved by both the research committee and the inmate committee at Matsqui Institution. Information regarding age, race, history of alcohol and substance abuse, smoking, and pharmacological treatment was coded according to file information and self report.

Blood samples were obtained from sixty inmates. Of these, six were excluded for the following reasons: two subjects were transferred before psychopathy assessments could be made, one subject ate prior to the blood draw, and three samples were dropped due to difficulties with biochemical assays. Data from the remaining 54 male subjects, ranging from ages 18-53 years (M = 27.35, SD = 6.18) were used to complete the study. The racial composition of the sample was 74% White, 22% Native American Indian, and 4% other.

B. Procedure

1. Assessment of Psychopathy:

A crucial requirement of research with psychopathological populations is that the procedures for the diagnosis and selection of subjects have demonstrated reliability and validity. The assessment procedure that was used in the present study was the Revised Psychopathy Checklist (PCL-R; Hare, 1990; Hare et al., 1990), an instrument that has proven remarkably successful in generating a consistent body of findings on psychopathy. Briefly, the PCL-R is a 20-item rating scale designed to assess the traditional clinical construct of psychopathy, perhaps best exemplified in the work of Cleckley (1976). The PCL-R measures both personality- and behavior-related characteristics of psychopathy; it can be used to obtain both dimensional and categorical scores; it is scored on the basis of both present-state and historical information.

PCL ratings are usually made on the basis of both file and interview information, although they can be made on the basis of file information alone if the files are sufficiently detailed (Hart, 1987; Wong, 1988). The information needed to score the items is obtained from a 90-180 minute semi-structured interview and institutional files. Each item is scored on a 3 point scale: 2 indicates that the item definitely applies, 1 that it may or may not apply, and 0 that it definitely does not apply, to the subject. Items are summed to yield a total score that can range from 0 to 40. Factor 1 scores are obtained by summing the scores on items 1, 2, 4, 5, 6, 7, 8, and 16; Factor 2 scores by summing the scores on items 3, 9, 10, 12, 13, 14, 15, 18, and 19.

Interrater reliability (intraclass correlation coefficient, or ICC1) for the PCL-R was determined on twenty subjects by independent raters, using the videotaped interviews and institutional files. The ICC for PCL-R ratings was .83.

The total mean checklist score sample was 26.5 (SD = 6.71), a score that is slightly higher that obtained with much larger samples of inmates (Hare, 1991). The Total scores were used to form groups of Psychopaths (Total score > 30; n=20, M=33.3, SD=2.6), and Nonpsychopaths (Total score < 30, n=34, M=22.5 SD=5.8).

2. Biochemical Assays

Preparation of the Blood

At least two measurements on different days are required for data to be reliable (Davis, 1989). Two blood samples were taken per subject (one week apart), between 0700 and 0900 hrs, before breakfast. Blood was collected into 4.5 ml vacuum blood collection tubes containing sodium citrate as anticoagulant. Platelets and plasma levels were prepared by differential centrifugation. The literature indicates that time and gravity force should be held constant for all samples so that the type and density of the platelet obtained in the final pellet is constant (for review, see Wise et al, 1980). Briefly, a registered medical technician collected 20 ml blood samples from each of sixty subjects. Blood was then transferred into two 12-15 ml plastic tubes. Blood was centrifuged at 2000 g for thirty minutes. Red blood cells were discarded, and the platelet rich

plasma was transferred to a clean plastic tube and centrifuged again at 2000 g for 10 minutes. The platelet pellet was suspended in cold .32 M sucrose solution and centrifuged again at 2000 to 3000 g for ten minutes. Supernatant was discarded. The washed platelet preparations were labelled, packed in dry ice, and sent to a -70 C freezer outside of the institution, and within one week was sent packed in dry ice in a light proof box for air freight to the Neuropsychiatry Research Unit (NRU) at the University of Saskatchewan, where they were analyzed under the direction of Dr. A. Boulton, director of NRU Saskatchewan, Dr. B. Davis, and Dr. P. Yu. All biochemical determinations were performed by personnel who were blind to clinical data, and all clinical interviewing and ratings were done blind to biochemistry.

Assay of Platelet MAO-B Activity

MAO activity was determined radioenzymatically as described in Yu (1986; see appendix a), using 14C labelled p-[1- C] tyramine (1 10 -4 M), as the substrate, and toluene: ethylacetate (1:1) as the extraction solvent.

Intraindividual stability of platelet MAO-B activity intraclass correlation coefficient (ICC), established in the present study for the average of the two samples taken one week apart, was .79. Reliability between two assays, using p-tyramine as a substrate, has previously been reported to be somewhat higher ($r = .88$, $p < .01$, Yu. et al, 1982) in healthly controls. Mean platelet MAO-B activity for the entire sample was 17.27

nmol/hr/mg protein, SD = 8.31. Mean platelet MAO-B activity for the psychopathic group was 16.3, SD=7.2. Mean platelet activity for the nonpsychopathic group was 17.8, SD=8.9.

3. Alcohol Use Ratings

Information regarding alcohol, substance abuse, and smoking habits was coded according to file information and self report. A five-point global rating for history of alcohol abuse was made for each subject (1=No Use, 5=Chronic Problematic Use). Each alcohol abuse rating was made according to (a) descriptions obtained according to DSM-III-R criteria (b) medical and file information indicating history of alcohol abuse (c) self report information regarding history of alcohol use. Interrater reliability was established for history of alcohol use on a sample of twenty subjects. Characteristics of the present sample in terms of alcohol and substance use are detailed in Table 1. Interrater reliability was determined on twenty subjects by independent raters using institutional file information along with self report. The ICC-1 for alcohol abuse ratings was .85.

4. Substance Use Ratings

A five-point global rating for history of substance abuse was made using the same five-point scale. Ratings were made based on information obtained from (a) descriptions according to DSM-III-R criteria (b) medical and file information indicating history of alcohol abuse (c) self report information. Interrater reliability was established for history of substance abuse on a sample of twenty subjects. The ICC-1 for substance use ratings was .85.

Self report, file, and interview information indicated that a wide variety of prescription and non-prescription drugs was currently being used and transferred among inmates. In light of the variety of drugs used by the present sample, and in view of the practical difficulty of estimating amount of drug intake without the aid of blood assay or urinalysis to detect the presence of specific drugs, a mixed substance use rating was made. For the mixed substance use rating, inmates were rated according to the types of drugs taken over the last one month period. Subjects were given one point for each category of drug reported to have been taken over the last month. Total number of points was used as a rating for the mixed substance use category. The categories were: Narcotics (heroin, morphine, demerol); Amphetamine like substances; Cocaine; Sedatives, hypnotics, tranquilizers, valium, Cannabis derivatives (marijuana, hashish); Hallucinogens (LSD, Mescaline); Solvents; Non prescription drugs, antipsychotic and antidepressant medication, and alcohol.

Finally, subjects were separated according to history of alcohol and/or substance use, to investigate the proportion of subjects with either a substance use history, alcohol history, or both.

5. Other Lifestyle Factors

Information on several lifestyle variables was obtained using the PCL-R interview, as well as a questionnaire that was constructed specifically for the present study. These included:

smoking, coffee consumption, and exercise habits over the previous 24 hours, two week, and one month period (see appendix b). Using this information, daily and monthly lifestyle habits were estimated on each of the variables.

6. Data Analysis.

The key data analyses included: (a) calculation of correlations between PCL-R scores and biochemical variables, (b) hierarchical multiple regression procedures in order to statistically control for history and current substance use, smoking, age, and race.

TABLE 1

Group Comparisons on Demographic/Lifestyle Measures

	Group NonPsychopaths (N=34)	Psychopaths (N=20)
History Chronic Alcohol Abuse	27%	74%
History Chronic Substance Abuse	41%	59%
History Alcohol &/or Substance Abuse	85%	94%
# Cigarettes** Per Day	M=17.7 SD=17.6	M=17.6 SD=8.9
# Days aerobic** exercise/week	M=3.1 SD=2.6	M=2.2 SD=2.8
# Cups coffee/ Day*	M=11.1 SD=16.9	M=7.9 SD=7.6

**estimated over month prior to first blood sample
None of the differences between groups was significant

VIII. Results

A. PCL-R, Demographic, and Lifestyle Factors

There were no significant differences between psychopaths and nonpsychopaths with respect to age, smoking and exercise habits, coffee consumption, history of problematic and chronic alcohol and/or drug abuse, or in the variety of drugs used (see Table 1).

There was a significant between-groups difference in racial composition: 91.5% of psychopaths were white, compared to 65% of nonpsychopaths, $\underline{X}^2 = 4.20$, $\underline{p} < .05$. Thirty-one percent of the nonpsychopaths were Natives, and because there are no data on MAO levels in Natives the practical significance, for MAO levels, of a high proportion of Natives in the nonpsychopathic group is unknown. The disproportionate number of Natives in the nonpsychopathic group is unusual; in most samples obtained from Canadian prison populations there is little difference in the racial composition of psychopathic and nonpsychopathic groups (Hare, 1991). In any case, the confound between psychopathy and race was taken into account in the regression analyses described below.

B. PCL-R and Platelet MAO Activity

1. Correlational Analyses

Both platelet MAO activity and PCL-R scores were normally distributed in the present sample. Pearson correlations were computed as a liberal approach towards examining the relationships among platelet MAO activity, PCL-R ratings, and

demographic/lifestyle variables. The results are presented in Table 2; none of the correlations was significant.

2. Multiple Regression Analyses

Multiple regression analyses were also used in order to statistically control for potentially confounding demographic/lifestyle variables and to determine if combinations of variables were related to MAO activity. In each analysis, the dependent variable was platelet MAO-B activity and the predictor variables were demographic/lifestyle measures (current use and history of alcohol, substance abuse smoking, age, race) and psychopathy measures (see table 3). In one analysis, demographic/lifestyle variables were forced into the predictive equation and psychopathy measures were allowed to enter only if they had significant incremental validity (i.e., if they significantly improved the R^2 of the regression equation). In a second analysis, the psychopathy measures were forced in first, and demographic/lifestyle measures allowed to enter only if they have significant incremental validity.

An additional set of regression analyses evaluated the influence on MAO activity of other demographic/lifestyle variables: estimated coffee consumption and days of aerobic exercise over the last month. Nothing of significance emerged from these analyses.

Table 2

Correlations Among PCL-R Total Scores, Factor 1 Scores, Factor 2 Scores, Demographic/Lifestyle Variables, and Platelet MAO Activity

Variables:	MAO1	Alcohol Use	Substance Use	Mixed Drug Use2	Cigarette /Day2	Age
PCL-R	-.13	.01	.17	.00	.01	.04
FACTOR 1	.03	-.02	-.01	-.12	.10	-.02
FACTOR 2	-.15	.03	.19	.10	-.07	.04
MAO	1.00	-.07	.11	.03	.12	-.01

1 MAO activity (expressed in nmol/hr/mg protein); p-tyramine as substrate

2 estimated over one month prior to blood collection

* $p < .05$

Table 3

Multiple Regression/ Stepwise

Platelet MAO Activity

	Beta1
PCL-R	-.153
Alcohol Use	-.067
Substance Use	.132
Mixed Substance Use	-.005
Age	-.003
Cigarettes/day	.118
Race	.169

1 none of the values are significant

IX. Discussion

The correlational analyses did not reveal a significant relationship between platelet MAO activity and psychopathy. This result does not appear to be due to low statistical power. Previous studies investigating the association between platelet MAO activity, extraversion, monotony avoidance, and verbal aggression, have obtained correlations within the -.17 to -.38 range (Perris et al, 1984; af Klinteberg et al, 1988). With a sample size of 54, a correlation of only -.23 is required for significance at the .05 level.

Variables known or strongly suspected to influence MAO activity were recorded. None of these variables, including alcoholism, history of substance use, estimated mixed drug use over the last month, age, smoking, race, or estimates of aerobic activity, were associated with MAO activity. Dietary variables, including riboflavin and iron deficiency, are associated with decreased platelet MAO activity (Sullivan et al, 1980; Sourkes, 1983; Murphy et al, 1976). It was not possible to monitor these variables, and they may have had a confounding effect on the results. However, there is no reason to suspect that dietary deficiencies related to MAO activity are also related to psychopathy.

The lack of relationship between platelet MAO and alcohol or substance abuse was somewhat surprising; previous research indicates that platelet MAO activity and alcohol abuse, are consistently related to one another (e.g. Wiberg, 1979;

Ghanshyam, 1988; Giller et al, 1984). One possible explanation for this negative finding may have been the high level of both alcohol and substance use in the present sample: 94% of the psychopaths and 85% of nonpsychopaths had a prominent history of one year or more of severe alcohol and/or substance use. Group differences in MAO activity may have been overwhelmed by the high base rate for substance use.

Previous research investigating platelet MAO activity in psychiatric disorders has been plagued by unreliable psychiatric assessment. This does not appear to have been a problem in the present study. The reliability and the validity of the PCL-R are well established. Similarly, a standard method for the estimation of platelet MAO activity (Yu, 1986) was used.

Enzyme activites were expressed relative to protein per sample (nnmol/hr/mg protein). Using this method, values should not be affected by total platelet count because relative recoveries of plasma protein and MAO activity should remain constant across subjects. An alternative method would be to express platelet MAO activity in terms of platelet count. Estimations of platelet MAO activity using the platelet count are highly correlated with estimations using the platelet protein method (r =.85, p<.001; Murphy, 1978).

Previous studies have used a variety of substrates in their determinations of platelet MAO activity (e.g. p-tyramine, B-phenylethylamine, and tryptamine). Platelet MAO activity determinations, based on these substrates are highly correlated

in healthy individuals (Yu et al, 1982). It appears, therefore that substrate specificity for healthy subjects is quite homogenous. In chronic schizophrenics, however, correlations among substrates are somewhat lower (ranging from r = .64 to .81, $p < .05$), possibly due to long-term administration of neuroleptic drugs (Yu et al, 1982). Whether or not substrate specificity was compromized by the high base rate of drug and alcohol use in the present sample cannot be determined. This may limit the extent to which the present results can be compared to results obtained in other studies which, like this one, use tyramine as a substrate. Extraction efficiency depends on the substrates and solvents employed. Approximate recoveries, using 14C labelled p-[1- C] tyramine (1 10 -4 M) and toluene: ethylacetate (1:1), is high, estimated at 96% (Yu, 1986). Overall, intra-individual reliability and extraction efficiency, using radioenzymatic method of assay and p-tyramine as substrate, appear to be high relative to other methods employed for the determination of platelet MAO-B activity. All blood samples were treated and analyzed in the same manner. There is no obvious reason why assay methodology should have had differential effects on individual subjects or groups in this study.

Platelet MAO activity is measured in terms of rate of reaction per minute, rather than in absolute terms. Within laboratories, researchers standardize their techniques for measuring MAO activity, thereby reducing intra-laboratory noise

in platelet preparation and assay procedures. However, there is no universally accepted procedure for measuring platelet MAO activity. Because of this, there is a wide range of enzyme rates reported among researchers and studies. Due to the lack of standardized procedures across researchers, there is a lack of normative data against which to compare observed results. Studies conducted from the same biochemical laboratory have yielded estimations of platelet MAO activity ranging from 1.68 nmol/mg/hr for schizophrenic group to 3.17 nmol/mg/hour for institutional controls (Davis, Yu, Carlson, O'Sullivan, & Boulton, 1982). The large discrepency between these results and the present findings (the mean platelet MAO activity for the present sample was 17.27 nmol/hr/mg protein, SD = 8.31) is difficult to interpret. While it is not generally meaningful to compare the rates of platelet MAO activity among samples in which there are even minor variations in procedures, in light of the large differences in estimated platelet MAO activity between these two studies, conclusions based upon these findings should be made with caution.

There are several steps in platelet preparation and assay where variability may be introduced. Some of the steps that might contribute to variability include: (1) The determination of platelet protein concentration when estimating MAO activity per mg protein, when other plasma protein and non-protein substances are included in the platelet pellet during the centrifugation of platelet rich plasma; (2) Choice of

anticoagulant and substrate; and (3) Factors such as temperature, plasma proteins, gravity force, and variability in the distribution and platelet density between individuals that interact with differential centrifugation methods to yield variable results (for reviews see Jackman & Meltzer, 1980; Murphy, Costa, Shafer & Corash, 1978; Wise et al, 1980; Brown, Powell, & Craig, 1980). Procedures were standardized in order to minimize these potential sources of artifact. Samples were collected from psychopaths and nonpsychopaths in random fashion, using the same centrifuge, and holding constant the gravity force and time factor.

The reliability of the platelet MAO samples was somewhat lower than has been previously reported using similar methods--.79 averaged across samples in the present study versus .88 previously reported (Yu, 1982). Due to lack of facilities, samples were shipped on dry ice from the institution to a minus 70-degree freezer in a Vancouver hospital. When all samples had been collected, over a two-week period, they were shipped to Saskatoon for analysis. It is possible that during transportation there was some decomposition of the samples, resulting in an increase in error associated with the assays; this would have compromized the validity of the measurements of platelet MAO activity.

The results of the present study lend no support to the hypothesis of low platelet MAO activity in criminal psychopaths. This is an interesting finding in its own right, particularily

because of previous findings of significant relationships between platelet MAO activity and personality traits commonly associated with the construct of psychopathy (eg. Schalling, Edman, & Asberg, 1983; Lidberg et al, 1985; Schalling et al, 1987). These personality traits were not assessed in this study. It is possible that platelet MAO is more strongly related to specific personality traits (e.g impulsivity, extraversion, monotony avoidance) than to the constellation of symptoms that form the construct of psychopathy.

In addition, the inmate population from which the sample was derived no doubt had a high base rate for these personality traits, relative to the general population. A high rate of impulsivity, monotony avoidance, extraversion, and verbal aggression in the sample as a whole may override an association between platelet MAO activity and psychopathy. In future research the PCL-R should be used along with measures of personality known to vary with MAO activity (e.g. KSP scale of monotony avoidance, impulsiveness, extraversion), in order to compare the relationship between platelet MAO and psychopathy in the context of other personality measures, where differences are known to exist in normal populations.

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APPENDIX A

Radioenzymatic Assay Procedure

Enzyme Preparation

Crude tissue homogenates (tissues homogenized in 0.32*M* sucrose or 0.11*M* KCl), partially purified mitochondrial membrane fragments (see below), fractions prepared by solubilization in detergents, as well as enzymes that have been purified to different degrees of purity can all be used.

Reagents

1. Phosphate buffer (0.2 mol/L)
2. Substrate solution: This depends on which substrate is being utilized and the purpose of the study (often the final concentration of the substrate can be set at twice its K_m value)
3. ^{14}C-Labeled substrates: specific activity approximately 50 mCi/mmol, concentration 100 μCi/mL
4. Citric acid, 2*N*
5. Extraction solvent, i.e., toluene:ethylacetate (1:1)
6. Scintillation cocktail

Assay Procedure

The following incubation mixture (200 μL) is prepared in conical glass centrifuge tubes in an icebath.

	Volume, μL	Final concentration
Enzyme (suitably diluted)	50	—
Phosphate buffer (0.2*M*, pH 7.4)	50	$5 \times 10^{-2}M$
Substrate ($8–20 \times 10^{-4}M$)	49	$2–5 \times 10^{-4}M$
^{14}C-substrate (premixed with the nonlabeled substrate)	1	0.1 μCi
H_2O	50	—

In the incubation mixture used to obtain blank values, the MAO inhibitor pargyline (0.1 m*M*) is included. The incubation is carried out at 37°C for 30 min and terminated by adding 200 μL 2*N* citric acid and 1 mL extraction solvent. After vigorous mixing on a Vortex mixer, the mixtures are centrifuged at 3000*g* for 5 min in a clinical centrifuge. An aliquot (0.5 mL) of the organic phase is then transferred to a counting vial, toluene-based scintillation fluid (10 mL) is added, and the mixture is subsequently counted in a liquid scintillation counter.

Calculation

If the scintillation counter is not equipped with automatic quenching compensation, the counting efficiency (%) (or quenching correction) must be determined as described by Peng (1970).

$$\text{Specific MAO activity (nmoles/min/mg)} =$$

$$(\text{Exp–blank})\ \text{dpm} \times \frac{1}{\text{Specific radioactivity}} \times \frac{1}{\text{Time of incubation (min)}} \times$$

$$\text{Extraction coefficient} \times \frac{1.0}{0.6} \times \frac{1}{\text{protein (mg)}}$$

Extraction of Product

It has generally been considered (although it may not be true for some substrates) that the aldehydes formed in the above incubation conditions are unstable and are rapidly oxidized in air to their corresponding acids or alcohols in the presence of aldehyde reductase and NADH or NADPH. The extraction conditions are such that the amine substrates remain associated with the aqueous phase and the acidic or neutral metabolites (i.e., acids, alcohols, or aldehydes) extract into the organic solvent phase. Ion-exchange resins and liquid ion exchangers have also been used to separate the reaction products from the substrates. Comparisons of these various methods indicate that they are all rather similar in their efficiency of extraction (Anderson, 1983), and it is a fact that they are relatively easy to perform and apparently suitable for measuring both low and high MAO activity.

Unfortunately, extraction with solvents is never 100% effective, and, indeed, the extraction efficiency depends on the substrates and solvents used (Tipton and Youdim, 1983). A number of different solvents have been employed (Wurtman and Axelrod, 1963; Otsuka and Kobayashi, 1964; McCaman et al., 1965; Southgate and Collins, 1969; Jain et al., 1973; Callingham and Laverty, 1973; Tipton and Youdim, 1976; Fowler and Oreland, 1980). To illustrate the point, approximate recoveries with different solvents for 5-HT, β-phenylethylamine, and *p*-TA are listed in Table 4. It is clear, therefore, that the extraction coefficients must be established for each substrate and solvent before proceeding to finalize any MAO activities.

Validation of Method

This radioenzymatic method is highly sensitive, specific, reproducible, relatively simple, and convenient because a wide variety of radioactively labeled amine substrates are commercially available. There are, however, several sources of error that may produce misleading results.

Although tritium-labeled amine substrates are commercially available and offer much higher specific radioactivities, their use in the radioenzymatic assay for MAO is not recommended. First, the

Table 4
Extraction of Different Amine Metabolites by Different Solvents[a]

Substrate used	Recovery of metabolite (%)	
	Toluene:ethyl acetate (1:1)	Benzene:ethyl acetate (1:1)
5-Hydroxytryptamine	74	91
β-Phenylethylamine	92	—
p-Tyramine	96	65
Dopamine	54	18

[a]Data from Otsuka and Kobayashi (1964), Tipton and Youdim (1976), and Fowler and Oreland (1980).

dpm values obtained after extraction are unreliable because of exchange of the isotope in water, even in the absence of enzyme (May, 1980). Second, it has recently been observed that when the label is on the α-carbon position, a significant isotope effect occurs during the enzyme reaction (Yu et al., 1981, 1982b). It has been shown, for example, that the rates of enzymatic deamination of those amines in which the α-side chain hydrogens had been replaced by deuterium were much slower (approximately one-third) than those exhibited with unlabeled amines. Compounds labeled with tritium would probably exhibit an even more pronounced isotope effect since the carbon-tritium bond is even stronger.

A further disadvantage of this method is the fact that it is a discontinuous procedure, i.e., incubation is carried out for 20–30 min and then the reaction is stopped. It is also necessary to establish the time course in order to ensure that the reaction is linear. Often the linearity disappears when a proportion of substrate has been consumed. It is also dependent on the amount of substrate added and the amount of enzyme present in the incubation mixture.

Finally, an additional criterion relates to substrate purity for both unlabeled and labeled substrates. Some contaminants are potent MAO inhibitors and frequently appear as substrate inhibitors in kinetic studies. Impurities in the radioactive amines often cause high background errors in the calculation of enzyme activity. In such cases the substrate should be purified by recrystallization, extraction with solvents, or appropriate chromatography.

Purification of MAO-B From Human Platelet

Human platelets contain exclusively type B MAO. A procedure has been developed to isolate homogenous MAO-B from them (Ansari et al., 1983).

The washed platelet suspension is frozen at –20°C overnight, thawed, and centrifuged at 35,000*g* for 60 min. The pellets are then suspended in 0.05*M* phosphate buffer at pH 8.0 containing 0.1% Triton X-100 at 4°C for 60 min. They are then recentrifuged at 35,000*g* for 30 min. The pellets, after suspension in the same buffer containing 0.5% Triton, are stirred for 60 min at 4°C and centrifuged at 150,000*g* for 60 min. The supernatant containing solubilized MAO is dialyzed against 0.01*M* phosphate buffer at pH 8.0. The MAO-B in the dialysate is then fractionated on a DEAE-Sephacel (Pharmacia) column that has been previously equilibrated with 0.01*M* phosphate buffer at pH 8.0. The column is

developed by stepwise elution with 0.01*M*, 0.1*M* phosphate buffer (pH 8.0), and 0.1*M* phosphate buffer (pH 8.0) containing 0.25% Triton X-100. The collected enzyme fractions are precipitated by addition of ammonium sulfate to 50% saturation. The precipitate that floats to the surface is dissolved in 0.05*M* phosphate buffer (pH 8.0) containing 1% octylglucoside and dialyzed against 0.025*M* Tris-acetate buffer at pH 7.4. Solid octylglucoside is then added to the dialyzed solution to a final concentration of 1%. This preparation is then further fractionated on a Polybuffer Exchanger 94 (Pharmacia) chromato-focusing column according to the instructions provided by Pharmacia Fine Chemicals. Diluted (1:8) Polybuffer 7.4 (Pharmacia) pH 4 (adjusted with 1*N* HCl) containing 1% octylglucoside is used to elute the enzyme. Those fractions exhibiting high MAO-B activity (i.e., near pH 5.3) are pooled and concentrated by ammonium sulfate precipitation. The floating precipitate is collected, dissolved in 0.05*M* phosphate buffer at pH 7.4 containing 1% octylglucoside and dialyzed against pH 7.4 buffer, and then subjected to HPLC separation performed on a Synchropah AX-300 column in 0.1*M* phosphate buffer (pH 7.4), followed by a gradient (0–1%) of octylglucoside in the same buffer. The MAO-B active fractions are pooled, dialyzed, and lyophilized. This method yields a 43-fold purification, but only a 0.25% recovery.

BIOCHEMICAL MEASURES OF BEHAVIOR

DATE:

SUBJECT I.D.

These are a few questions about your activities in the last 24 hours

**********ALL ANSWERS WILL BE KEPT STRICTLY CONFIDENTIAL**********

1. How many cigarettes have you smoked in the past 24 hours?_____

2. How many cups of coffee have you had in the past 24 hours? _____

3. Have you consumed any alcohol in the past 24 hours? _____

   If so, how much?_____

4. Have you taken any prescription drugs in the past 24 hours?_____

   If so, what kind of medication?_____

5. Have you taken any non-prescription drugs in the past 24 hours? _____

   If so, what kind of drugs?_____

6. Have you had any physical fights in the last 24 hours?_____

   If so, when? _____

7. Have you had any arguments in the last 24 hours?_____

   If so, when?_____

8. Have you done any physical exercises in the last 24 hours?_____

   If so, when?_____

BIOCHEMICAL MEASURES OF BEHAVIOR

DATE:

SUBJECT I.D.

These are a few questions about your activities in the last 2 weeks and 1 month period.

**********ALL ANSWERS WILL BE KEPT STRICTLY CONFIDENTIAL**********

1. Over the last 2 weeks how many cigarettes/ packages have you smoked per day?

   _____ Over the last month?_____

2. Over the last 2 weeks, approximately how many cups of coffee do you drink per day?

   _____ Over the last month?_____

3. Over the last 2 weeks, approximately how much alcohol have you consumed?

   _____ Over the last month?_____

4. Over the last 2 weeks have you taken any prescription drugs?

   If so, what _____ Over the last month?_____

   when_____ Over the last month?_____

5. Over the last 2 weeks have you taken any non-prescription drugs?

   If so, what _____ Over the last month?_____

   when_____ Over the last month?_____

6. Do you follow a regular exercise routine?_____

   If so, what_____

   How often in the last two weeks?_____

   How often in the last month?_____