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Platelet monoamine oxidase activity and psychometric correlates in male violent offenders imprisoned for homicide or other violent acts

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Abstract Violent behavior has been associated with certain personality traits like poor impulse control, sensation seeking, and monotony avoidance, which predispose to increased risk for violent acts. Low platelet monoamine oxidase (MAO) activity has been found in subjects with such traits, as well as in imprisoned violent offenders. On the other hand, cigarette smoking is expected to inhibit MAO activity. We assessed impulse control, lifetime history of aggression, suicide risk, as well as platelet MAO activity in 82 male offenders (mean age 33.0 ± 10.7 years) imprisoned for homicide or other violent acts, and in 54 control male subjects (mean age 35.1 ± 6.6 years). General psychopathology was assessed by the Hopkins Symptom Check List (SCL-90) questionnaire. A high rate of smoking (89%), significantly higher than controls (63%), was observed in offenders, but there were no differences in MAO activities among nonsmokers, moderate, or heavy smokers in either group. Offenders showed significantly higher scores in Impulse Control, Past Feelings and Acts of Violence, Suicide Risk and SCL-90 scales. Offenders who had committed other violent acts than homicide had higher scores in the three psychometric scales and in the Depression, Obsessive-Compulsive, Hostility, and Anxiety subscales of the SCL-90, than offenders who had committed homicide. Platelet MAO activity was significantly lower (p = 0.01) in the offenders' group (38.1 ± 14.4) compared to controls (44.7 \pm 15.2). The difference could not be attributed to smoking, and seems to be related to personality traits and behaviors that characterize the offenders' group.

■ **Key words** platelet MAO · violence · homicide · personality · aggression

Introduction

Low platelet monoamine oxidase activity (MAO) has been connected with personality traits like impulsiveness, sensation seeking, monotony avoidance, and increased psychiatric morbidity (Buchsbaum et al. 1976; von Knorring et al. 1984; Schalling et al. 1987; Oreland and Hallman 1995; Stalenheim et al. 1997), which, on the other hand, seem to predispose for violent behavior and increased risk for antisocial and criminal acts. Indeed, low platelet MAO activities have been repeatedly reported in violent criminal offenders (Yu et al. 1984; Lidberg et al. 1985; Belfrage et al. 1992; Garpenstrand et al. 2002)

Since MAO is the main enzyme that catabolizes the biogenic amines noradrenaline, dopamine, and serotonin, it can be hypothesized that low MAO activity may be related to a dysregulation of these neurotransmitter systems. The general idea underlying the study of MAO activity in relation to violent behavior is that low MAO activity may result in an imbalance in central neurotransmitter systems that regulate aggression. This imbalance may cause changes in the regulation of hormone release or responses to stressors. Neurotransmitter turnover and hormone levels have been studied in this context. Lidberg et al. (2000) assessed the main metabolites of serotonin (5HIAA), dopamine (HVA), and noradrenaline (MHPG) in CSF of 35 males convicted for homicide. Their levels were not significantly different from those of age-matched controls, but subgroups of offenders with previous suicide attempts, and offenders with impulse control disorder had lower 5HIAA. The authors noticed that there was no association between self-

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Tel.: +30-21/72-89266 Fax: +30-21/72-42032 E-Mail: markian@otenet.gr reported impulsiveness and the diagnosis of impulse control disorder. No differences in 5HIAA were found between subjects who committed impulsive versus premeditated crime, as was reported earlier by Linnoila et al. (1983). The last group reported higher levels of recidivism in violent offenders who had low levels of CSF 5HIAA (Virkunnen et al. 1989).

Platelets contain only the B form of the enzyme. Although both MAOA and MAOB catabolize all three mentioned biogenic amines, the B-form has been more closely connected to serotonin, since there are indications for compartmentalization of MAOB within glial cells and serotonergic neurons in the primate brain (Westlund et al. 1985). In addition, platelet enzyme activity has been shown to correlate with cerebral MAOB activity, as measured in seven subjects in vivo using positron emission tomography after administration of a MAOB reversible inhibitor (Bench et al. 1991).

Poor impulse control and increased aggressive and suicidal behavior characterize subjects who commit violent acts. In this study, we were interested to replicate the findings about platelet MAO activities in a population of imprisoned offenders after controlling for cigarette smoking, to search if there are differences between offenders who committed homicide from offenders who committed other violent acts, and to search for possible correlations of MAO activity to psychological measures. We used questionnaires to assess lifetime history of aggression, impulsivity, and suicide risk, as well as the SCL-90 questionnaire for a general evaluation of psychopathology.

Subjects

The offenders were males subjects, imprisoned because of homicide(s) or other violent crime (assault, robbery), in Koridallos Prison, in Athens, Greece. The consent of the prison administration was obtained for the study. Prisoners were recruited after their history of violent acts. They were informed in detail by a psychiatrist (M.S.) about the purpose of the study and its requirements, and a written consent was obtained from each participant. Eighty-two offenders (mean age = 33.0 years, SD = 10.7), of whom 47 had committed homicide and 35 other violent acts, agreed to participate in the study, while less than 10 percent of the offenders asked, refused to participate. The high participation rate was achieved, we think, because we chose to work with selffilling questionnaires and to avoid diagnostic interviews, which in the specific conditions of prison may have a negative impact on participation. The study was designed to relate a biological variable to psychometric data like impulse control, suicide risk, and intensity of violent behavior, independent of psychiatric diagnosis. In a study of 99 imprisoned criminal offenders, Garpenstrand et al. (2002) did not find any significant association of platelet MAO to any psychiatric diagnosis or specific personality disorder. For a general evaluation

of psychiatric symptomatology, we used the Hopkins Symptom Checklist (SCL-90) questionnaire (Derogatis et al. 1973), in which subjects report the frequency of experienced symptoms over the past week, with subscales for somatization, depression, anxiety, obsessive-compulsive symptoms, hostility, phobic anxiety, paranoid ideation, psychoticism, and interpersonal sensitivity.

Because of the possible influence of being in the restricted prison conditions on biological and psychometric variables of the study, we used two control groups, one consisting of prison personnel (29 subjects), and another of healthy subjects not connected to prison (25 subjects), in the same age range as the offenders (mean age of the 54 control subjects = 35.1 years, SD = 6.6).

In addition to the SCL-90 questionnaire, all offenders and control subjects filled in the Impulse Control Scale (ICS, Plutchik and van Praag 1989), the Past-Feelings and Acts of Violence Scale (PFAVS, Plutchik and van Praag 1990), and the Suicide Risk Scale (SRS, Plutchik et al. 1989).

Methods

For the estimation of MAO activity in platelets, a 10 ml blood sample was taken in tubes containing EDTA from all subjects of the study in the morning, between 8:00 and 10:00 am. Platelets were isolated by three consequent centrifugations of the blood and the platelet-rich plasma at 200 x g, precipitated by a fourth centrifugation at 2500 x g, washed with phosphate buffer 10 mM, pH 7.2, precipitated again by centrifugation, and kept frozen in the same buffer at -30 °C. MAO activity was assessed within three days using the method described by Eckert et al. (1980). In short, platelets were disrupted by sonication at 0 °C for 60 s and incubated for 20 min with [14C]tryptamine at a final concentration of 0.025 mM. The reaction was stopped by addition of HCl, the deaminated product extracted into toluene, and the radioactivity measured in a liquid scintillation counter. A blank was used for each estimation, where the reaction was stopped by adding HCl at zero time. Protein was estimated in the sonicated platelet aliquots by the Lowry method, using human albumin (Sigma Chemical Co.) as the standard, and the activity of the enzyme was expressed in pmol deaminated substrate per mg protein and minute. All estimations were done in duplicate, and the coefficients of variation were below 5%. Usually, samples from both cases and controls were estimated in the same bunch in order to reduce the influence of inter-assay variation on the results.

Statistics

We first searched for possible differences in MAO activity and the psychometric data of the two control groups and when no differences were found, the sum of the subjects was used as the comparison group to the offenders.

From the 82 offenders of the study, 45 did not take any drugs, while 37 subjects received tranquilizers and/or antidepressants and neuroleptics in various combinations to control their behavior. The possible influence of the drugs on platelet MAO activity was examined before comparisons to the control group. Moreover, 17 offenders were heroin users before imprisonment. Their measures were compared to non-users, and were included in the offenders' group after no differences in MAO activities were established. Twenty-seven offenders had attempted suicide while in prison, and their MAO activities were compared to the offenders without attempts.

Cigarette smoking needs specific attention when evaluating platelet MAO activity, since there are several reports that smokers have lower MAO activities. We checked for differences in MAO activity between subgroups of smokers and non-smokers, both in the control and the offenders' groups, and more specifically, by dividing the groups into non-smokers, moderate smokers (up to 20 cigarettes per day), and heavy smokers (more than 20 cigarettes per day) (Fig. 1).

We performed a multiple regression analysis with dependent variable platelet MAO and independent variables smoking, violent acts (homicide or not), history of suicide attempt, and history of heroin use. We also calculated the mean values for the subgroups formed according to these criteria and evaluated each question per se. The same was done for the group of controls, with criteria being or not prison personnel, and smoking behavior.

After checking for these factors that may influence MAO activity, we compared the enzyme activities of the offenders' group as a whole, and of the subgroups of homicide and of other violent acts offenders to the control group, using analysis of variance (ANOVA), with covariates when appropriate. The same was done for the psychometric data of the groups. Correlations of the psychometric data to MAO activity were searched using the non-parametric Spearman correlation coefficient test.

Results

Platelet MAO activities in the group of 29 male prison personnel did not differ from that of the 25 males from general population (Table 1, p = 0.52), and the data of the two groups were merged for comparison with the of-

Fig. 1 Individual platelet MAO activities of the 82 violent offenders plotted versus their daily cigarette consumption. No differences in the enzyme activities exist between non-smokers, moderate, or heavy smokers (Spearman correlation coefficient Rs = 0.0107, p = 0.92)

90 80 70 PLATELET MAO ACTIVITY 8 Ö Ö 8 ò 50 8 40 8 80 Ò 30 6 800 Ò 20 0 10 Ò 0 0 10 20 30 50 60 70 -10 40 CIGARETTES PER DAY

Table 1 Evaluation of the differences in platelet MAO activities in subgroups of controls or offenders, according to being or not prison personnel for the controls group, smoking for both groups, and current drug treatment, history of heroin use before imprisonment, suicidal behavior in prison, and homicide for the offenders

Group	Dichotomy criterion	No		Yes	Yes			
		N	MAO	N	MAO	df	F	p
Controls	Prison personnel	25	46.2±13.4	29	43.5 ± 16.8	1.52	0.42	0.52
Controls	Smoking	20	48.2±15.5	34	42.5 ± 15.5	1.52	1.71	0.20
Offenders	Smoking	9	39.1±15.0	73	38.0 ± 14.3	1.80	0.05	0.83
Offenders	On Drugs now	37	40.5 ± 16.4	45	36.2 ± 12.3	1.80	1.92	0.17
Offenders	History of heroin use	65	37.8 ± 15.0	17	39.5 ± 11.9	1.80	0.20	0.66
Offenders	Suicide attempts	55	38.3 ± 15.1	27	37.8 ± 13.0	1.80	0.02	0.88
Offenders	Homicide	35	37.8±14.4	47	38.4±14.4	1.80	0.02	0.88

fenders' group. There were also no significant differences in the psychometric scores between these two subgroups.

There was no indication of a correlation between age and MAO activity. In the group of 54 control males, age range 25 to 51 years, the correlation coefficient was r = -0.0037, n. s. In the offenders' group, age range 18 to 60 years, the coefficient was r = 0.0249, n. s.

A multiple regression analysis with dependent variable platelet MAO and independent variables smoking, violent acts (homicide or not), history of suicide attempt, and history of heroin use, gave a multiple R=0.165, F=0.43, df=5,76, and p=0.83, showing that none of the independent variables exerts an influence on MAO activity. For the control group, using as independent variables being prison personnel or not, and smoking, the multiple R was 0.184, F=0.89, df=2,51, and p=0.42.

To evaluate each of these factors separately, subgroups of offenders were formed with the criteria present drug treatment, history of heroin use, and history of suicide attempt(s) in prison, and the MAO activities of the subgroups were compared. As expected from the results of the regression analyses, the differences were not significant (Table 1).

The group of offenders with other violent acts than

homicide showed the highest scores in the SCL-90 scale (Fig. 2). It is of interest that in this group, the number of cigarettes smoked daily gave high correlations to the scores in the SCL-90 subscales, except the Hostility score, which is the only one that gives a significant correlation in the homicide group (Table 2). No such correlations exist in the group of controls.

The difference in platelet MAO activities between offenders and controls was significant (F = 6.58, df = 1,134, p = 0.01), with the offenders' group having 14% lower (mean) activities (Table 3). The percentage of smokers in the offenders group is significantly higher than in controls. Nevertheless, when we used Smoking as a covariate in the ANOVA, the difference in MAO activities between controls and offenders remained significant (df = 1,133, F = 4.01, p = 0.047). No differences in the enzyme activities were found between the homicide sub-

Fig. 2 Mean values of the scores in the subscales of the SCL-90 questionnaire of the groups of controls (n = 54), offenders who committed homicide (HOM-YES, N = 47), and offenders who committed other violent acts (HOM-NO, N = 37)

group and the subgroup of subjects who had committed violent acts other than homicide (mean values \pm SD 38.4 ± 14.4 and 37.8 ± 14.4 , p = 0.88).

Platelet MAO activities did not correlate with the scores of Impulse Control, Past Feelings and Acts of Violence, or Suicide Risk Scales, either in the controls or in the offenders groups. A marginal negative correlation was observed only in the homicide group of 47 subjects for the PFAV score, with r = -0.2497, and p = 0.09. Regarding Impulse Control, it has to be mentioned that Lidberg et al. (2000) did not find an association between self-reported impulsiveness and a diagnosis of impulse control disorder.

Offenders who had committed violent acts other than homicide scored significantly higher in the Depression, Obsessive Compulsive, Hostility, and Anxiety subscales of the SCL-90, while offenders who had com-

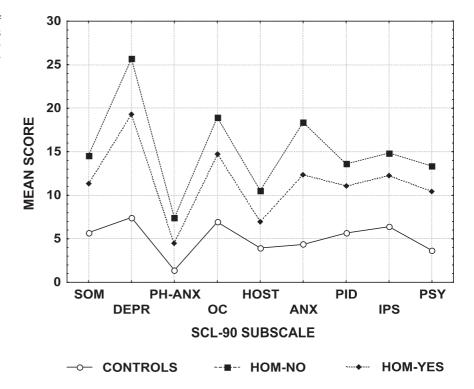


Table 2 Spearman correlation coefficients between number of cigarettes smoked per day and the score in the subscales of the SCL-90 general psychopathology questionnaire, for controls (n=54), offenders who had committed homicide (N=47), and offenders who had committed other violent acts (N=35). Significant correlations are found for the third group. The correlation to the Hostility score is the only significant correlation for the Homicide group, and the only non-significant correlation for the Other Violent Acts group

SCL-90	Controls	Controls		Homicide		Other violent acts	
	Rs	p	Rs	р	Rs	р	
Total	-0.047	0.73	0.201	0.18	0.597	0.0001	
Somatization	0.063	0.65	0.271	0.06	0.592	0.0002	
Depression	-0.024	0.86	0.178	0.23	0.601	0.0002	
Phobic anxiety	0.039	0.77	0.178	0.23	0.498	0.0001	
Obsessive-compulsive	-0.126	0.36	0.090	0.54	0.485	0.003	
Hostility	-0.146	0.29	0.368	0.01	0.135	0.44	
Anxiety	-0.134	0.33	0.200	0.18	0.583	0.0002	
Paranoid ideation	0.027	0.85	0.061	0.68	0.280	0.10	
Interpersonal sensitivity	-0.007	0.96	0.212	0.15	0.626	0.0001	
Psychoticism	-0.180	0.19	0.104	0.48	0.507	0.002	

Table 3 Mean values (\pm SD) of platelet monoamine oxidase activity (MAO) and psychometric scores of controls and violent imprisoned offenders. *PFAV* Past Feelings and Acts of Violence; *ICS* Impulse Control Scale; *SRS* Suicide Risk Scale. Evaluation of the differences by ANOVA. Controls vs offenders, df = 1,134. Homicide-no vs. homicide-yes df = 1,80. Age was used as covariate in the comparison of MAO activity between the homicide subgroups (df = 1,79)

Group	N	Age	MAO	SCL-90	PFAV	ICS	SRS
Controls	54	35.1±6.6	44.7±15.2	50±30	3.8±1.7	15.4±5.3	1.3±1.5
Offenders	82	33.0 ± 10.7	38.1 ± 14.4	129±74	12.1±7.3	18.0 ± 8.1	7.1 ± 4.4
F		1.56	6.58	55.54	65.78	4.48	88.38
р		0.21	0.011	0.0001	0.0001	0.036	0.0001
Homicide-no	35	30.1±8.6	37.8±14.4	150±74	14.7±7.3	19.8±7.0	8.4±4.7
Homicide-yes	47	35.2 ± 11.6	38.4 ± 14.4	113 ± 70	10.1 ± 6.8	16.6±8.6	6.2 ± 4.0
df		1.80	1.79	1.80	1.80	1.80	1.80
F		4.74	0.01	5.52	8.68	3.27	5.19
р		0.032	0.91	0.02	0.004	0.07	0.025

mitted homicide scored higher in the Phobic Anxiety subscale. The two offenders' subgroups did not differ regarding their scores in the subscales for Somatization, Paranoid Ideation (p = 0.09), Interpersonal Sensitivity, or Psychoticism (Table 4).

Discussion

Platelet MAO activity did not correlate with age in our sample of controls (age range 20 to 51 years) or offenders (age range 18 to 60 years). Reports of increases in MAO activity with age include subjects older than 60 years, and usually the increases begin after that age. Fowler et al. (1997) calculated MAOB concentrations in brain regions of living humans using positron emission tomography and [11C]L-deprenyl as the ligand, and found a positive correlation with age. They studied 12 men and 9 women in the age range of 23 to 86 years, and the activities of the four subjects over 70 years are responsible for the correlation. Unfortunately, they do not mention possible differences between males and females, and use the data of the entire sample for correlations to age. For platelet MAO activities, several groups have found no correlation to age (i.e., Gattaz et al. 1981; Wahlund et al. 1995; Blanco et al. 1996). No correlation of platelet MAO to age was also reported by Garpenstrand et al. (2002), who studied 99 imprisoned criminal offenders, in the age range 19 to 64 years.

Regarding cigarette smoking, no significant differences in platelet MAO activity could be detected in the

samples of controls or offenders. In the group of controls, the mean value of MAO of the smokers is 12% lower than that of the non-smokers, and the mean activity of the heavy smokers 14% lower than in non-smokers, a difference on the same order as reported in some other studies, i.e. a 15% reduction reported by von Knorring and Oreland (1985), but the difference is far from being significant (Table 5). Similar results, i. e., no significant differences in platelet MAO activity between smokers and non-smokers in male normal volunteers, have also been reported by Norman et al. (1982). In the offenders' group, the mean values of MAO in smokers and non-smokers were very close (Table 5).

Possible reversible MAO inhibitors present in tobacco or tobacco smoke that circulate in the blood and are attached to the enzyme at the time of blood sampling are expected to be removed during the platelet isolation procedure. As described in the Methods, platelets are precipitated from platelet-rich plasma by high-speed centrifugation, washed by suspension in buffer, precipitated again, the supernatant discarded and taken up in fresh buffer. The wash up and the further dilution for the incubation makes it impossible that such inhibitors may be present in concentrations that can influence MAO activity. Snell et al. (2002) estimated both platelet MAOB activity and platelet MAOB protein using a selective polyclonal antibody. They found that heavy smokers had significantly lower MAO activity than non-smokers, but platelet MAOB protein concentrations did not differ significantly between smokers and non-smokers. Affinity labeling by a selective MAOB antagonist correlated with

Table 4 Mean scores in the SCL-90 subscales of the control group, and the offenders' homicide subgroups. The scores of both subgroups are all significantly higher compared to controls, thus only the p value of the differences between the offenders' subgroups are mentioned (ANOVA, Tukey test)

Subscale	Controls	Homicide-no	Homicide-yes	p (no/yes)
Somatization	5.7±4.9	14.6±10.8	11.3±10.8	0.24
Depression	7.4±5.1	25.7±12.6	19.3 ± 11.6	0.011
Phobic anxiety	1.4±1.9	7.4±5.8	19.3 ± 4.8	0.006
Obsessive compulsive	6.9±5.1	18.9±9.3	14.8±7.9	0.03
Hostility	3.9±3.5	10.5±6.8	7.0 ± 6.5	0.013
Anxiety	4.4±4.7	18.4 ± 10.8	12.4±11.4	0.009
Paranoid ideation	5.7 ± 4.1	13.6±5.9	11.1±5.9	0.087
Interpersonal sensitivity	6.4±3.4	14.8 ± 8.4	12.2 ± 6.7	0.15
Psychotisism	3.6±3.0	13.3 ± 8.2	10.4±8.2	0.12

Table 5 Evaluation of differences in platelet MAO activity in the control and offenders samples between non-smokers, moderate smokers (up to 20 cigarettes per day), and heavy smokers (more than 20 cigarettes per day)

	Contro	Controls		ers	
Smoking	N	MAO	N N	MAO	
No	20	48.2±15.1	9	39.1±15.0	
Moderate	21	43.9 ± 16.2	41	37.6±14.6	
Heavy	13	40.3 ± 14.6	32	38.6±14.1	
df		2.51		2.79	
F		1.07		0.06	
р		0.35		0.94	

MAO activity. The authors suggest that the differences in MAO activity found in heavy smokers is the result of an inhibitor contained in cigarette smoke, bound at the catalytic site of the enzyme.

It seems that while some smoke constituents may inhibit MAO activity in vivo, the expression of the enzyme is not affected by smoking. The differences observed in the ex vivo activity of the enzyme in platelets between smokers and non-smokers may be the result of irreversible inhibitors that have been accumulated especially in heavy smokers, and are not removed during the platelet isolation procedure. Our finding that in offenders there were no significant differences regarding smoking, but lower activities compared to controls, disagrees with the notion that smoking may explain the association of MAO activity to personality traits (Oreland et al. 2002), and rather supports the opposite, that when differences are found in MAO activity between smokers and non-smokers, they should be attributed to personality traits and behaviors that are connected to smoking. A multiple regression analysis with dependent variable MAO activity and independent variables Group (controls or offenders) and Smoking, gives an R = 0.227, df = 2,133, F = 3.63, p = 0.029, with a significant beta value of -0.186, p = 0.036 for Group, and a non-significant for Smoking (beta = -0.089, p = 0.31), attributing the lower MAO activities to the group rather than smok-

In our sample of 54 control subjects, 34 were smokers, i. e. 63 %, a number that is very close to that of the official statistics: The percentage of male population who are daily cigarette smokers in Greece is around 60% for the age range of 25 to 54 years (Eurostat Yearbook 2001) edition). In contrast, the percentage of cigarette smokers in the offenders' sample is 89 %, the difference from controls being highly significant (chi square = 13.18, p = 0.0003). It is of interest that Garpenstrand et al. (2002) reported a similar high rate of smokers (84%) in their sample of 99 imprisoned criminal offenders. A higher frequency of smoking has been reported for several populations, among them patients with depression, schizophrenia, anxiety disorders, conduct disorders, attention deficit hyperactivity disorder (Hughes et al. 1986; Glassman 1993; Upadhyaya et al. 2002). To this list, violent offenders can be added, as it seems that their character traits – and low platelet MAO activity? – predispose them to that behavior.

Conclusion

Low platelet MAO activity was found in the group of criminal offenders in this study, in agreement with previous studies mentioned in the Introduction. Smoking does not seem to explain this finding. Low MAO activity is much more connected to personality traits and behaviors that characterize the offenders' group, and this is in agreement with the conclusion of Garpenstrand et al. (2002). The enzyme activities did not correlate with the self-reported scores in the Impulse Control, Past Feelings and Acts of Violence, or Suicide Risk scales. These scores, as well as the scores in the SCL-90 scale, were higher than controls in the group of offenders who committed homicide, and even higher in the group of subjects who committed criminal acts other than homicide.

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