Brief Report

Platelet Monoamine Oxidase Activity in a Nonhuman Primate Model of Type 2 Excessive Alcohol Consumption

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Objective: Low platelet monoamine oxidase (MAO) activity is associated with "type 2 alcoholism." MAO activity is also affected by cigarette smoking. Since most alcoholics are smokers, it is difficult to evaluate the possible effect of platelet MAO activity on alcoholism independently of the effects of smoking. The authors investigated the relationship between platelet MAO activity and excessive alcohol consumption in rhesus macaques.

Method: Platelet MAO activity and CSF metabolite concentrations were measured. The authors also investigated level of voluntary alcohol intake and social dominance rank.

Results: Subjects with low platelet MAO activity consumed alcohol to excess, had low CSF 5-hydroxyindoleacetic acid concentrations, and were less competent socially.

Conclusions: These findings show that nonhuman primates that exhibit type 2-like alcohol features display low platelet MAO activity and support the notion that platelet MAO activity is a biologic marker for central serotonergic activity. The results also challenge the hypothesis that low platelet MAO activity in type 2 alcoholism is simply an artifact of smoking.

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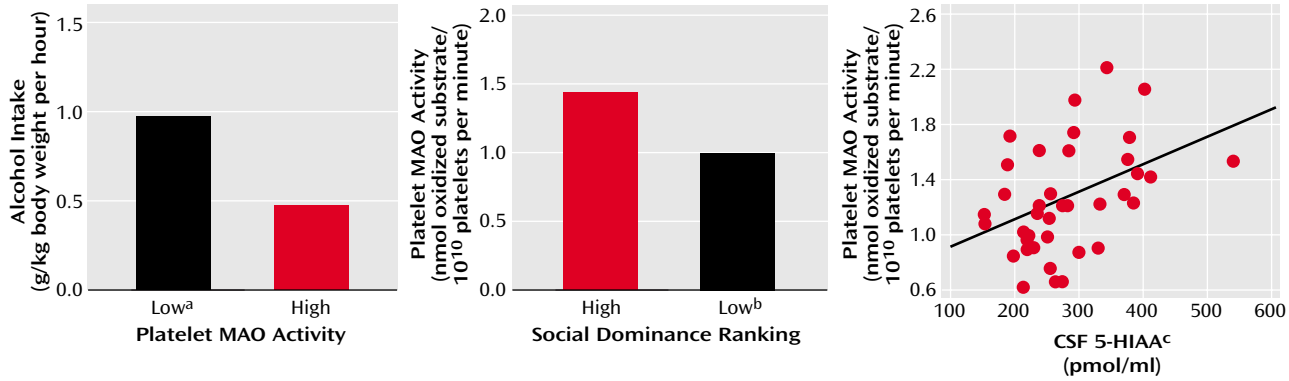
Low platelet monoamine oxidase (MAO) activity is associated with specific personality traits as well as alcoholism. Therefore, low platelet MAO activity has been proposed as a biological marker for alcoholism, especially "type 2 alcoholism," which is characterized by personality characteristics such as impulsiveness and sensation seeking (1). Alcohol intake itself does not affect platelet MAO activity.

One problem regarding the relationship between platelet MAO activity and type 2 alcoholism has been the possible effect of tobacco smoking, since type 2 alcoholics are usually heavy smokers. Independent of alcohol consumption, individuals that smoke display lower platelet MAO activity relative to nonsmokers, and cigarette smoke possesses MAO activity-inhibiting properties (1).

FIGURE 1. Association of Platelet MAO Activity With Alcohol Intake, Social Dominance Ranking, and CSF 5-HIAA in 38 Rhesus Macaques



[a] Significantly greater alcohol intake in subjects with low platelet MAO activity (t=2.68, df=36, p<0.01).
[b] Significantly lower platelet MAO activity in subjects with low social dominance ranking (t=2.48, df=27, p<0.02).
[c] Significant positive correlation with platelet MAO activity (r=0.41, df=36, p<0.02).

There are numerous similarities between human and nonhuman primates with respect to type 2-like alcohol abuse and associated behaviors (2). Rhesus monkeys that engage in excessive alcohol consumption have reduced CNS serotonin function as measured by low levels of CSF 5-hydroxyindoleacetic acid (5-HIAA) and also exhibit impaired social competence as well as severe aggression (2). We investigated the relationship between platelet MAO activity and alcohol consumption in nonhuman primates, in which any effect of smoking can be excluded for natural reasons. In addition, assessment of CSF 5-HIAA and homovanillic acid (HVA) concentrations and social competence were performed.

Method

The subjects of the present study were female (N=21) and male (N=17) rhesus macaques *(Macaca mulatta)*, which were members of an ongoing longitudinal study investigating genetic and environmental influences on neurobiology, behavior, and alcohol consumption (2). This research protocol was approved by the National Institutes of Health (Bethesda, Md.) in accordance with the Animal Welfare Act.

When the subjects were at 3 years of age, social dominance rank was obtained by using competition-elicited behaviors, a well-established method of assessing social dominance ranking in nonhuman primate groups (3).

At 50 months of age, subjects were tested for voluntary consumption of an 8.5% alcohol solution. The procedure used to train the subjects to consume alcohol and the methods of data collection are described elsewhere (4).

Blood and CSF samples were collected within 20 minutes after administration of ketamine (15 mg/kg). Biochemical measures were not correlated with time to capture the subjects, time from ketamine injection until the samples were obtained, or time of sampling.

Platelet MAO activity was analyzed by a modified radiometric assay with 2-phenylethylamine as substrate (5). CSF monoamine metabolite concentrations were determined by high-performance liquid chromatography on one 2-ml sample collected from the cisterna magna (3). Intra- and interassay coefficients of variation were <10%.

Student's t test was used for comparisons between continuous variables and subgroups. MAO activity and CSF metabolite concentrations were compared by use of simple linear regression analysis. Multiple linear regression analyses were used to investigate the relationship between variables on the effect on alcohol consumption.

Results

There was no difference in platelet MAO activity between the genders (male subjects: mean=1.24, SD=0.46; female subjects: mean=1.30, SD=0.36). Thus, the genders were combined for the analyses. As seen in Figure 1, subjects with low platelet MAO activity, as determined by a median split, drank significantly more alcohol than those with high MAO activity. Figure 1 also shows that animals low in social dominance rank exhibited significantly lower platelet MAO activity compared with high-ranking subjects. Moreover, platelet MAO activity was positively correlated with levels of CSF 5-HIAA. However, platelet MAO activity was not correlated with CSF HVA concentrations (r=0.24, df=36, p<0.15). When values for CSF 5-HIAA concentrations and MAO activity were entered simultaneously as independent variables, the results of the multiple regression showed a strong overall effect between alcohol consumption and the predictors (r=0.55, df=36, p<0.01). Thus, MAO activity was the strongest predictor of alcohol consumption (t=3.26, df=37, p<0.01), whereas CSF 5-HIAA concentration was less important (t=0.43, df=37, p<0.90).

Discussion

The current results provide support for the hypothesis that nonhuman primate subjects that exhibit type 2-like alcohol consumption indeed have lower platelet MAO activity. MAO in platelets has the same amino acid sequence as brain MAO-B; however, brain and platelet MAO-B do not seem to be significantly correlated (6). We did not observe any difference between male and female monkeys

regarding MAO activity, which is in agreement with previous results (7). Interindividual differences in platelet enzyme levels are stable throughout life, and a strong genetic influence on platelet MAO activity has been observed in humans as well as in rhesus monkeys (1, 8).

Several studies have reported that personality traits in smokers are similar to those found in subjects with low platelet MAO activity (e.g., reference 9). Thus, in humans it has been difficult to separately analyze the relationship of platelet MAO activity, smoking, and personality traits. It is interesting that in a previous study on monkeys, significant correlations were observed between platelet MAO activity and behavior (7), which mainly supports the findings on the enzyme and personality in humans.

There is a significant correlation between CSF 5-HIAA concentrations and platelet MAO activity in healthy human individuals (1). Men with a tendency for aggressive behavior have low concentrations of 5-HIAA in the CSF, and low levels of CSF 5-HIAA have also been connected with type 2 alcoholism (10). Together, these and other findings have formed the hypothesis that platelet MAO activity in some way is correlated with CNS serotonin turnover, i.e., that individuals with low platelet MAO activity have a less well developed central serotonin system, rendering them more vulnerable for psychopathology (e.g., alcoholism and impulsive control disorders). The results of the current study clearly support the notion that platelet MAO activity is a biologic marker for central serotonergic activity.

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