LETTERS TO THE EDITORS

ALCOHOL-DEPENDENT PATIENTS WITH NEUROENDOCRINE EVIDENCE FOR REDUCED DOPAMINE D₂ RECEPTOR FUNCTION HAVE DECREASED PLATELET MONOAMINE OXIDASE-B ACTIVITY

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This letter is a report of a re-evaluation of the results obtained in an earlier study of ours (Balldin et al., 1994) of platelet monoamine oxidase (MAO)-B activity in alcoholics with reduced dopamine (DA) D₂ receptor function, as assessed by the growth hormone (GH) response to the D₁/D₂ agonist apomorphine (APO), which was published in this journal. The reason for the re-evaluation of the results in our study is a Letter to the Editors of this journal by Farren and Dinan (1996) reporting on platelet MAO-B activity in alcoholics with reduced DA D₂ receptor function, as assessed by the GH response to the D₂/D₂ receptor agonist apomorphine. In the report by Farren and Dinan (1996), four of eight alcoholics had no increase in GH above baseline, whereas all eight subjects in the control group had the expected GH response to bromocriptine. The authors compared platelet MAO-B activity in the four alcoholic subjects who had no increase in GH above baseline to that in the four alcoholics who had a significant increase in GH after bromocriptine. They found no significant difference in platelet MAO-B activity between these two groups and thus no evidence for altered platelet MAO-B activity in alcoholics with reduced DA D₂ receptor function.

In their Letter to the Editors, Farren and Dinan (1996) made a very valuable comment with regard to our earlier study (Balldin et al., 1994). We then reported that platelet MAO-B activity in alcoholics with reduced DA D₂ receptor function, as assessed by the GH response to the D₂/D₂ receptor agonist APO, was not different from that in controls. Eleven out of 14 alcoholics had blunted GH response to APO (an increase in GH above baseline of less than 8 mU/l), in comparison to three out of 12 in the control group. Farren and Dinan (1996) correctly pointed out that we did not compare platelet MAO-B activity in the alcoholics with blunted GH response (n = 11) to those with non-blunted GH response (n = 3). This comment by Farren and Dinan (1996) thus prompted us to re-evaluate the results in our earlier study.

When defining blunted GH response in a neuroendocrine challenge test, two criteria for bluntness have been proposed: (1) an increase in GH less than 8 mU/l (Hunt et al., 1986) or (2) less than 2 mU/l (Nutt, 1989). Taking into account that, in the report by Farren and Dinan (1996), comparison of platelet MAO-B activity was made between alcoholics who had no increase in GH above baseline to those who had, we also used the lower criteria for bluntness of 2 mU/l in our re-evaluation.

The subjects were 14 male patients with a mean ± SD age of 45 ± 9 years. They all fulfilled the diagnostic criteria for alcohol dependence according to DSM III-R (American Psychiatric Association, 1987). The total reported length of their alcoholism was 20 ± 8 years. The length of the last period of continuous alcohol intake prior to investigation was 157 ± 222 days with an estimated daily alcohol consumption of 377 ± 163 g of pure ethanol. All patients had earlier been admitted to psychiatric hospitals (16 ± 23 times) and 10 had also been treated in hospitals for alcohol-related medical disorders. Eleven patients had experienced hallucinosis and six of those had also had delirium tremens during earlier withdrawal episodes. During a 2-month period prior to the investigation, all patients were carefully controlled for sobriety by staff members at a treatment unit and also with the aid of repeated tests for liver function. Twelve male subjects (age 46 ± 10 years) were recruited as controls. Based on an interview, they were all considered physically and psychiatrically healthy. Results of routine laboratory analyses were all within the laboratory reference ranges. All of them were light social drinkers with a reported alcohol consumption of less than 100 g of pure ethanol weekly. In the statistics, an unpaired t-test was used for comparisons between groups, since the data on MAO-B activity appeared to have normal distributions.

As shown in Fig. 1, when the criterion for bluntness of a GH response to APO of less than 8 mU/l was used, the platelet MAO-B activity was 3.8 ± 1.2 (mean ± SD) µkat/kg protein in the patients with blunted GH responses (n = 11), 5.7 ± 0.6 µkat/kg protein in the patients with non-blunted GH responses (n = 3), and 5.2 ± 1.6 µkat/kg protein in the controls (n = 12). The platelet MAO-B activity was therefore significantly lower (P < 0.05) in the patients with blunted GH responses in comparison both to patients with non-blunted GH responses and to controls. When the lower criterion for bluntness of 2 mU/l was used the platelet MAO-B activity was 3.6 ± 1.2 µkat/kg protein in the patients with blunted GH responses (n = 9) and 5.3 ± 0.7 µkat/kg protein with non-blunted GH responses (n = 5). Platelet MAO-B activity was thus significantly lower in the patients with blunted GH responses in comparison to patients with non-blunted GH responses and to controls (P < 0.02 and P < 0.05, respectively).

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Furthermore, when platelet MAO-B activity was correlated with the GH response to APO, a significant correlation was obtained in the patients when using either Pearson’s product moment correlation ($r = 0.58$, $P < 0.05$) or Spearman’s rank correlation ($r = 0.72$, $P < 0.01$); the latter probably being more appropriate, since the GH data appeared to have an abnormal distribution. That is, low platelet MAO-B activity was found in patients with low GH response to APO. There was no correlation between platelet MAO-B activity and GH response to APO in the controls.

Thus, in our study, patients with alcohol-dependence with reduced DA D$_2$ receptor function, as assessed by the GH response to APO, did have significantly lower platelet MAO-B activity in comparison to those patients with normal DA D$_2$ receptor function. This finding is, however, in disagreement with the report by Farren and Dinan (1996) in which, as mentioned earlier, no difference was found between alcoholics with blunted and non-blunted GH responses to bromocriptine. The reason(s) for this discrepancy is unknown. There have been numerous studies of platelet MAO-B activity in alcoholics or in subtypes of alcoholics and the results of these studies have been contradictory. Platelet MAO-B activity has been shown to be either decreased in alcoholics or no different from that in controls (see e.g. Anthenelli et al., 1998).

In the recent study by Anthenelli et al. (1998), it was reported that cigarette smoking, but not alcohol dependence, is associated with decreased platelet MAO-B activity, and it was thus concluded that decreased platelet MAO-B activity is not a trait marker for alcoholism or its subtypes, but rather a state marker of cigarette smoking. This is not in agreement with the results from the present study, where platelet MAO-B activity did not differ between smokers ($4.9 \pm 0.8 \mu$kat/kg protein; $n = 5$) and non-smokers ($4.0 \pm 1.6 \mu$kat/kg protein; $n = 9$). The present report therefore suggests that alcoholics with reduced DA D$_2$ receptor function may be the subgroup of alcohol-dependent individuals who have low platelet MAO-B activity.

Finally, from a neurobiological point of view, it is of interest that platelet MAO-B activity and the GH response to DA D$_2$ receptor agonists are two methods for assessment of DA function in alcoholics, as mentioned by Farren and Dinan (1996). Platelet MAO-B activity has been reported to be highly correlated with brain MAO-B activity in humans (Bench et al., 1991). Since MAO-B activity is involved in the metabolism of DA in the presynaptic neuron, it is tempting to speculate on the possibility that the reduced platelet MAO-B activity, which reflects brain MAO-B activity, represents an adaptive mechanism to the reduced postsynaptic DA D$_2$ receptor function. Thus, the presynaptic DA neuron reduces the metabolism of DA in order to increase the amount of the neurotransmitter available for release, in order to compensate for the downregulated postsynaptic DA D$_2$ receptor function and thereby maintain a normal level of central DA neurotransmission.

**REFERENCES**


