

Platelet monoamine oxidase activity in epilepsy

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SUMMARY The platelet monoamine oxidase activity (MAO) of 33 patients with epilepsy was compared with a group of neurological patients and a group of normal control subjects. We found that the MAO activity was increased significantly in the epileptic group when compared with the normal. This was not related to anticonvulsant medication. These results could be explained by the effect of epilepsy or anticonvulsant medication on the maturation of platelets.

The role of CNS monoamines in the aetiology of epilepsy is not clear. The incidence of seizures in susceptible individuals when they take tricyclic antidepressants¹ or when they are treated with monoamine oxidase inhibitors² is strong evidence for such an involvement. The observation that oral tyramine can activate pre-existing episodic EEG abnormalities in epileptic patients³, further indicates a possible monoaminergic involvement in this condition. Tyramine is a substance with well-defined indirect sympathomimetic activity, in that it can cause the release and block the re-uptake of noradrenaline and other amines⁴. Tyramine is also a good substrate for monoamine oxidase (MAO),⁵ an enzyme found in platelets which are a readily accessible source of the enzyme in man. One possible explanation of the findings of Swash *et al*³ is that tyramine metabolism is abnormal in patients with epilepsy, so we have studied MAO activity in platelets from such patients.

Patients and methods

Three groups were studied. The first group contained 33 patients with epilepsy (16 men and 17 women), average age 35 years. The second group included 22 control neurological patients (11 men and 11 women), average age 31 years. Finally, 19 normal control subjects (nine men and 10 women) with an average age of 35 years were studied. The patients with epilepsy all had a long-

standing seizure disorder mainly arising in the temporal lobe.

Eight millilitres of venous blood were collected from each subject into tubes treated with EDTA. The blood was then mixed with 8 ml of a solution containing 9 g/l of NaCl and 20 g/l of EDTA. The mixture was centrifuged at 1000 g for 15 min and the platelet rich plasma was carefully removed, avoiding contamination with red blood cells. This plasma was then centrifuged at 2400 g for 15 min and the supernatant was discarded. The platelets were then resuspended in 1 ml 0.3M sucrose and centrifuged again at 2400 g for 15 min. The supernatant was carefully aspirated and discarded, and the platelets resuspended in 1 ml 0.3M sucrose, and stored at -20°C. The identity of the source of the blood samples was known only to one of us (DFS) who collected them but who did not take part in the purification of the platelets, or in the measurement of enzyme activity.

Platelet MAO activity was measured using kynuramine as substrate^{6,7}. The platelets were gently thawed, and then suspended using a Potter-Elvehjem tissue homogeniser. Duplicate 100 µl samples were used for determination of enzyme activity and protein.⁸ The results are expressed as nmoles of product (4-hydroxyquinoline) formed/mg of protein/30 min incubation period.

Results

The MAO activity of platelets from patients with epilepsy was found to be significantly increased compared with that of normal subjects, and this

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was the case for both men and women (table 1). However, in the epileptic groups as a whole, there were no significant differences in platelet MAO activity when five other parameters were

Table 1 Human platelet MAO activity from male and female subjects. Results are expressed as mean MAO activity (nmoles 4-hydroxyquinoline formed/mg protein/30 min) \pm SE of mean. Number of observations in brackets. Level of significance were assessed using Student's *t* test.

	All subjects	Women	Men
Epileptic patients	496.5 \pm 44.3(33)*	583.0 \pm 65(16)‡	415.0 \pm 55.1(17)
Neurological control patients	440.3 \pm 50.8(20)	373.5 \pm 68(11)	522.0 \pm 72.1(9)
Normal control subjects	367.1 \pm 36.2(20)	444.0 \pm 62.4(10)	290.2 \pm 18.2(10)‡†

* *P* < 0.05 when compared with normal subjects

† *P* < 0.05 when compared with normal women

‡ *P* < 0.05 when compared with neurological control women

§ *P* < 0.05 when compared with neurological control men

examined. The severity of epilepsy, the degree of EEG abnormality, the time since the last fit, or whether high or low levels of anticonvulsant drug were being taken did not seem to be important (table 2).

Table 2 Influences of clinical factors on platelet MAO activity in patients with epilepsy. Results expressed as in table 1

Clinical factors	Platelet MAO activity
Severe epilepsy	421.9 \pm 112.5 (7)
More than one seizure/week	}
Mild epilepsy	
Less than one seizure/week	516.5 \pm 47.9 (26) NS
Marked EEG abnormality	433.5 \pm 77.4 (9)
Minimal EEG abnormality	520.0 \pm 53.7 (24) NS
Recent fit (with 24 h blood collection)	479.0 \pm 87.7 (11)
No recent fit	489.4 \pm 58.5 (21) NS
High daily anticonvulsant dose (6 units or more)	492.1 \pm 56.2 (21)
Low daily anticonvulsant dose (5 units or less)	}
All taking anticonvulsants	
Not taking anticonvulsants	481.4 \pm 77.8 (12) NS
	489.3 \pm 43.6 (33)
	403.4 \pm 31.4 (41) NS

Anticonvulsant dosage expressed in units⁹

Considering the patients with neurological conditions other than epilepsy, we found that MAO activity was significantly less than that of epileptic women, though not significantly different from normal women whose enzyme activity was intermediate between the epileptic and neurological groups, but not significantly different from either group.

Platelet MAO was significantly increased in men with neurological conditions other than epilepsy when compared with normal men, which contrasts with similar female groups between whom there was no significant difference. The MAO activity in blood platelets of normal women was significantly greater than that of normal men, who form a particularly homogeneous group.

Discussion

The importance of increased platelet MAO activity in epileptic patients compared with control subjects is not immediately obvious, especially as the clinical features of the condition do not relate to MAO activity. Our results contrast with those of Shohnori *et al*¹⁰ who found reduced platelet MAO activity in a small number of epileptic patients, but are in agreement as to the lack of association between changes in enzyme activity and seizure intensity, seizure frequency, proximity of last fit, and degree of EEG abnormality. There is no relationship between MAO activity and either the type of anticonvulsant drug used or the dose administered.

The results might be explained in terms of the influence of epilepsy or drugs on either platelet numbers or protein concentration within platelets, as Friedhoff *et al*¹¹ have shown that variations in human platelet MAO activity may arise because of non-genetically determined variations in these parameters. An alternative explanation might lie in different rates of maturation of platelets or turnover of MAO within platelets, which may occur in epilepsy or as a result of anticonvulsant drugs. Murphy *et al*¹² found that platelet MAO activity varied in different density gradient fractions of platelets, suggesting that size and MAO activity of platelets decrease with age. If it could be shown that epilepsy or anticonvulsant drugs affected the rate of maturation of the platelets, their proteins, or MAO then an explanation of our observations would be at hand.

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