Reduction of platelet monoamine oxidase activity in iron deficiency anaemia

S. CALLENDER, D.G. GRAHAME-SMITH, H.F. WOODS & M.B.H. YOUDIM*

MRC Unit of Clinical Pharmacology and Nuffield Department of Medicine, Radcliffe Infirmary, Oxford OX2 6HE, U.K.

Monoamine oxidase (MAO) oxidatively deaminates noradrenaline, dopamine, 5-hydroxytryptamine, phenylethylamine and certain other primary and secondary amines occurring naturally in mammals. The purified enzyme contains sulphydryl groups; covalently bound FAD is a co-factor and two moles of iron are present per mole of enzyme protein in the rat liver enzyme (Youdim & Sourkes, 1966; Youdim, 1974).

In vitro studies have shown a significant decrease in MAO activity in liver tissue from iron deficient rats (Symes, Sourkes, Youdim, Gregoriadis & Birnbaum, 1969) and experiments *in vivo* have confirmed this (Symes, Missala & Sourkes, 1971). These studies suggest that iron is important for MAO activity.

We have measured MAO activity in platelets obtained from patients with and without iron deficiency anaemia. Platelets were harvested from platelet rich citrated plasma and after centrifugation and washing the platelet plug was suspended in 0.3 M sucrose solution by means of low energy sonication. The MAO activity of the platelet suspension was measured using the procedure described by Robinson, Lovenberg, Keiser & Sjoerdsma (1968). The substrates (0.2 mmol/l final concentration) were [^{14}C]-tyramine, [^{14}C]-dopamine, [^{14}C]-5-hydroxytryptamine and [^{14}C]-phenylethylamine.

When compared with the normal controls the MAO activity in platelets from iron deficient patients was markedly lowered (see Table 1). The activity with tyramine as substrate was lowered by 39%, with dopamine by 46%, with 5-hydroxytryptamine by 52% and with phenylethylamine by 37%. These changes were significant ($P < 0.001$) for all substrates except phenylethylamine.

Following treatment with oral iron the platelet MAO activity returned to normal in those patients in whom serum iron was restored to within normal limits.

Serum iron and its effect on MAO activity will have to be taken into account in the interpretation of studies of platelet MAO activity in other conditions such as schizophrenia (Murphy & Wyatt, 1972) and depression (Murphy & Weiss, 1972).

Table 1 The effect of iron deficiency on MAO activity in human platelets

Subjects	Hb (g/100 ml)	MCV (cu μ)	Serum iron (μg/100 ml)	Platelet MAO activity (dpm/mg platelet protein, 30 min incubation)			
				Tyramine	Dopamine	5-Hydroxytryptamine	Phenylethylamine
Normals (20)	13.9 ± 0.40	92.5 ± 1.80	126.5 ± 12.50	2256 ± 260	2508 ± 189	3033 ± 314	1289 ± 199
Iron deficient (16)	8.79 ± 0.24	64.5 ± 1.36	21.67 ± 1.80	1386 ± 206	1385 ± 162	1448 ± 207	818 ± 180
P value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.05

The results are expressed as mean ± s.e.

The precise role which iron plays in the activity of MAO is not yet known. It may be necessary either for the synthesis of MAO protein or it may act as a co-factor.

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Dihydropteridine reductase: enzyme characteristics, regional distribution and ontogenetic development

S. ALGERI*, M. BONATI, F. PONZIO & A.J. TURNER

Istituto di Ricerche Farmacologiche 'Mario Negri', Milan, Italy

The hydroxylation of tyrosine to dihydroxyphenylalanine (DOPA) is considered the rate limiting step in catecholamine synthesis. Tyrosine hydroxylase (TH) is the enzyme which catalyzes this reaction, and it requires the presence of a reduced pterine cofactor (PtH_2). The regeneration of the reduced pterine is accomplished by means of a pyridine nucleotide-dependent enzyme, quinoid dihydropteridine reductase (DHPR).

Dihydropteridine reductase has been detected in rat brain and it has been suggested that DHPR, and hence the level of reduced pterine, may be a controlling factor in catecholamine synthesis. Some of the characteristics of this enzyme, its regional distribution in rat brain, and the changes in its activity during brain development and aging will be described.

Dihydropteridine reductase is a NADH-dependent enzyme (Km 13 μM). It is inhibited by methotrexate *in vitro* but not *in vivo*. Its activity is 10^3 times higher than TH activity. Its regional distribution in the brain does not parallel the distribution of TH.

The brains of rats that have been sympathectomized by 6 OH dopamine treatment have DHPR activity unchanged. This finding, together with the regional distribution data, indicates that the enzyme is not located in the adrenergic nerve terminals.

The brains of rat fetuses after 13 days of gestation present DHPR activity that is around 20% of the activity found in adult rat brain. At birth the DHPR activity is increased to 60% of the adults and remains constant up to 20 days of age. This development is similar to the one known for tyrosine hydroxylase.

In another experiment we compared DHPR and TH activity using 3 month old and 24 month old rats. While there was no difference between the two groups in TH activity, the group of 24 month old rats showed a DHPR activity two times higher than the 3 month old group.

Part of this work was carried out while A.J.T. was receiving a Royal Society European Fellowship at the Mario Negri Institute. His present address is: Department of Biochemistry, University of Leeds, Leeds LS2 GLS, England.