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Platelet monoamine oxidase B activity in Parkinsonian patients

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Abstract

Monoamine oxidase B (MAO B) plays a pivotal role in N-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) induced Parkinsonism. An increased MAO B activity in platelets of patients with idiopathic Parkinson's disease (PD) is reported in this study. The possibility that high MAO B activity may represent a trait of vulnerability for PD by enhancing the neurotoxic effects of environmental compounds is discussed.

Human blood platelets may be regarded as a reliable model of monoaminergic synaptosome because of their specific biochemical mechanisms for uptake, storage, metabolism and release of several amines.[1] Platelets and nerve cells both have monoamine oxidase B (MAO B),[2] which inhibits arylalkylamine dependent serotonin (5HT) release in platelets, thus enhancing its storage.[3]

Basing their investigation on different substrate affinity, Zeller *et al*[4] reported a qualitative difference in platelet MAO B activity between PD patients and controls, but Mann *et al*[5] noticed no change. Moreover, Danielczyc *et al*[6] reported platelet MAO B activity in PD patients treated with levodopa-benserazide and amantadine which was higher than in controls; the effect of the combination of these drugs, however, on MAO B activity is not completely known. Recently it has been suggested that platelet MAO B activity may be a good peripheral marker to evaluate the time course of l-deprenyl MAO B inhibitory action in PD,[7] but the study in question was unfortunately not concerned with the possible differences in platelet MAO activity between PD patients and normal controls.

MAO B is necessary for bioactivation of N-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP),[8] a toxin causing selective degeneration of dopaminergic nigrostriatal neurons in humans.[9] On the other hand, several studies suggest a correspondence between 3H MPTP binding sites and MAO B within the brain[10] and in human platelets.[11]

Since unequivocal data on platelet MAO B activity in PD patients cannot be drawn from these studies and because of its importance in MPTP-induced nigrostriatal neural degeneration, we studied platelet MAO B activity in a group of PD patients.

Subjects and methods

The group of patients consisted of 18 subjects, 11 males and seven females (mean age (SD) 61·3 (10·6) years, with idiopathic PD mean illness duration 10·1 (6·5) months. None of the patients were on drugs at the time of the study and none had ever been treated with l-deprenyl. Eleven patients had never received any anti-Parkinsonian drugs, while the others had suspended taking their drugs (bromocriptine and/or orphenadrine) at least one month before the study. Severity of illness was evaluated according to the Hoehn and Yahr criteria[12]: ten patients were stage II and eight stage I. None showed signs of mental impairment on the Mini Mental State,[13] depression on the Hamilton rating scale,[14] thyroid or blood diseases.

The control group was made up of 20 healthy subjects (nine males and 11 females; mean age 65·4 (4·8 years). None of the patients or controls were smokers.

Thirty ml of venous blood was taken from patients and controls at the same time, and processed together for the entire procedure. Blood was centrifuged to obtain a platelet pellet, then frozen at −70°C. MAO B assay was performed according to the modified radiometric method by Belmaker *et al*[15] using 14-C-Benzylamine as substrate.

After 30 minutes incubation at 37°C enzyme reaction was stopped by HCl 3N; extraction was performed using toluene. Radioactivity of 2 ml organic layer was determined by means of liquid scintillation counter. Protein were evaluated according to the method by Lowry *et al*.[16] Enzyme activity was expressed in nmols of product/mg of platelet protein/hour (nmol/mg prot/h). Statistical analysis was carried out using 2-tailed *t* test for heterogeneous variances or Pearson's r correlation coefficient calculation.

Results

Platelet MAO B activity in PD patients was significantly higher ($p < 0.01$) than in control subjects: 39·48 (15·22) versus 26·28 (4·26) nmol/mg prot/h (fig).

Male patients showed a mean (SD) activity of 37·77 (15·77) nmol/mg prot/h, significantly higher ($p < 0.001$) than that of male controls, 25·58 (3·99). For female subjects, the mean value in patients was 46·90 (11·72) nmol/mg prot/h, significantly greater ($p < 0.001$) than the control mean 29·50 (2·04). We observed no significant differences between male and female MAO activity in PD group or in the control group.

No correlation was found between platelet enzyme activity and severity or length of illness.

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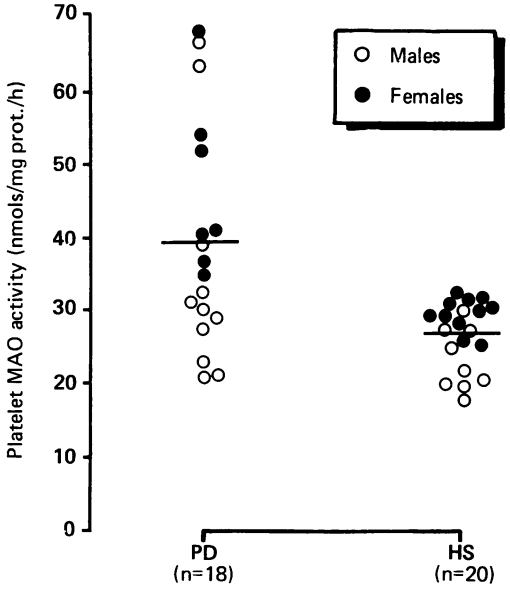

Figure Platelet MAO activity in Parkinsonian patients (PD) was higher ($p < 0.01$) than in control subjects (HS).

Discussion

This study reports a significantly increased platelet MAO B activity in PD patients and this differs from the findings of Zeller *et al*[4] and Mann *et al*,[5] who observed no quantitative differences in platelet MAO B activity between patients and controls. However, Zeller *et al* did not report their subjects' smoking habits, which may be a factor in decreasing platelet MAO B activity.[17] The patients in the study by Mann *et al* had suspended their pharmacological treatments only two weeks before the study: such a short period may not be sufficient to eliminate possible drug influences on enzyme activity.

The increase in platelet MAO B activity noted in PD patients might be considered as a trait of vulnerability for this disease even if not specific: high MAO B activity levels might represent a facilitating factor for the onset of PD by enhancing the neurotoxic effects of some endogenous or environmental compounds. However, it is difficult to evaluate to what extent peripheral biochemical changes parallel those in the brain.

Lloyd *et al*[18] studying striatum, and Yong and Perry,[17] studying only frontal cortex and substantia nigra, did not find any difference in MAO activity between PD patients and controls in brains at necropsy. Konradi *et al*,[19] using an immunocytochemical method, localised MAO B in 5HT-containing neurons of dorsal raphe and other nuclei of the human brain, but not in dopaminergic cell bodies which proved to be rich in MAO A, suggesting that MAO B is related to 5HT systems. Substantial damage to 5HT neurons has been reported in patients with idiopathic PD,[20] but to our knowledge, MAO B activity has not yet been studied in 5HTergic brain nuclei of PD patients.

The clinical usefulness of this abnormally high platelet MAO B activity as a biological marker of PD is debatable, because the same feature has been observed in other neurodegenerative disorders such as Amyotrophic lateral sclerosis (ALS)[21] and Alzheimer's disease (AD).[22] PD, AD and ALS are regarded by some authors[23] as degenerative processes resulting from an interaction between genetic factors, such as MAO B activity, and environmental toxins. Multifactorial expression of these postulated genetic factors or different types of xenobiotics could eventually lead to the appearance of these different diseases, generally occurring alone, rarely in combination.

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