

Platelet Monoamine Oxidase Activity in Children With Attention Deficit Hyperactivity Disorders

A. Mubarak, G. Shammah, A. El Dod, E. Gad, and A. Foda

Platelet monoamine oxidase "MAO" activity was studied in 20 children diagnosed as having attention deficit hyperactivity disorder (ADHD) and 15 healthy children as control.

The aim of this study was to find out any correlation between platelet MAO activity and symptomatology of ADHD which may help in evaluating the use of platelet MAO as an objective biochemical tool in the diagnosis of such common childhood psychiatric disorder.

Result: The results of this study demonstrated significantly lowered platelet MAO activity in children with ADHD than control cases. Also multiple regression analysis of the effect of symptoms and age on the platelet MAO "dependent variable" showed that the combination of age, impulsivity, overactivity and disturbing other children are of significant "though different" effect on the level of platelet MAO activity. These results raise the suspiciousness of the biochemical heterogeneity of these symptoms; a conclusion that should be confirmed by future studies.

(Egypt.J.Psychiat., 1996, 19:117 -128).

Introduction

Attention Deficit Hyperactivity Disorder (ADHD) is defined by Barkley (1982) as "significant deficiency in age appropriate attention, impulse control and role governed behaviour (compliance, self control and problem solving) that arises in infancy or early childhood. It is significantly pervasive in nature and is not the direct result of general intellectual retardation, severe language delay, emotional distractibility or gross sensory or motor impairment. So, ADHD include symptoms in three areas

"short attention span, impulsivity and hyperactivity"²

ADHD is a relatively common disorder of childhood. The prevalence of this disorder varies from 1-20% depending on the diagnostic criteria employed, the population of children studied, the methods of investigation and the source of information³. An Egyptian study reported 20% prevalence rate of the disorder among the psychiatric presentations to child psychiatry clinics within the school health system⁴.

Evidence accumulated within the last 25 years suggested that many neuropsychiatric disorders are related to metabolic abnormalities of the biogenic amines⁵.

Indirect biochemical observations suggested that monoaminergic mechanisms may relate to the pathogenesis of hyperkinesis of childhood⁶. Methylphen-

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idate and d-amphetamine medications (showing the most consistent effect on the symptoms of inattention and hyperactivity) both have significant noradrenergic activity and both decrease serum and urinary MHPG⁷. Also, desipramine a relatively potent noradrenergic uptake inhibitor has been determined to be useful in treatment of ADHD⁸.

Monoamine oxidase activity has been used as an indirect functional measure of monoaminergic neurotransmission⁹. The strong evidences that MAO could be under genetic control is encouraging to correlate it with behaviour and regarding its activity as an indicator of biological predisposition¹⁰.

Monoamine oxidase activity cannot be measured in the living intact brain; so the more accessible platelet MAO activity has been extensively studied in relation to psychosis, behavioural disorders and personality¹¹. Studies reported connections between brain MAO activity and platelet MAO activity, since the latter has been associated with behaviour in many studies¹².

Shekim et al.¹³ found that normal children with platelet MAO activity values in the high and low ends of the MAO distribution are more impulsive than children with platelet MAO values in the middle range. Also, Stoff et al. (1989) found that an elevated platelet MAO activity in children with disruptive behaviour disorders is correlated with more impulsivity than high MAO controls on some performance tasks.

Klein et al. (1980) reported that children with ADHD have low platelet MAO activity than in control children. Shekim et al. (1984) also found a significant correlation between low MAO activity & measures sensitive to impulsivity and inattention.

The aim of this study is to compare platelet MAO activity in children with

ADHD with that of the normal control and to find out any correlation between platelet MAO activity and symptomatology of ADHD which may help in evaluating the use of platelet MAO as an objective biochemical tool in the diagnosis of such common childhood psychiatric disorder.

Subjects and Methods

The subjects of this study included:

1-Twenty children from those attended Department of Neuropsychiatry of Tanta University Hospital and diagnosed as having Attention Deficit Hyperactivity Disorder (ADHD) according to diagnostic and Statistical manual of Mental Disorders, forth edition, (DSM-IV).

2-Fifteen healthy children (from those attended the hospital for any other reason and their parents agree to participate in the study) matched with the patients by age and sex.

Patients should fulfill the following criteria:

1-No gross clinical neurologic manifestation or epilepsy.

2-Intelligence quotient (IQ) should be 90 or more, so mentally subnormal children are excluded.

3-Anaemic cases were excluded.

4-Patients should be free of medications particularly the psychiatric medications and caffeine for at least fifteen days.

Both patients and control cases were subjected to:

1-Clinical study

a)Clinical psychiatric examination; using semistructured interview for patients and their families, interrater reliability among the authors was carried out. Agreement on both the final diagnosis and the symptoms was a must to include the patient in the study.

b) Neurological examination was carried out for patients and controls to exclude any gross neurologic signs.

2-Psychometric study

a) Wechsler intelligence scale for children (WISC) to assess the IQ and to exclude mentally subnormal children.

b) Conners Abbreviated rating scale which gives quantitative estimate of the symptoms of ADHD¹⁶, which is translated to Arabic by Professor Mohammed El-Defrawi (personal communication).

3-Biochemical study

Determination of platelet MAO activity¹⁷

Results

The age of children with ADHD ranged from 7.5 to 9.8 years with a mean of 8.63 ± 0.65 years, while that of control children ranged from 7.5 to 9.5 years with a mean of 8.31 ± 0.55 year. The age

difference of both groups is statistically non significant.

Sixteen (80%) of children with ADHD are males & 4 (20%) are females, in comparison to 12 (80%) of controls are males & 3 (20%) are females. No statistical difference between both groups ($P > 0.05$).

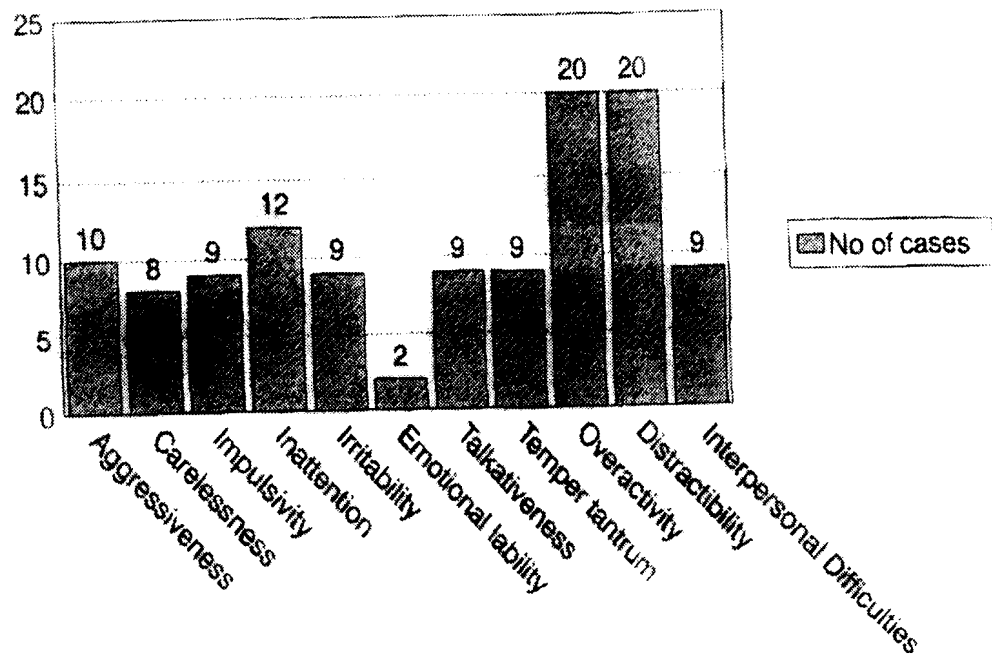
Clinical evaluation: Shows the wide range of symptoms that were present in children with ADHD:

(1) Overactivity in 100% of cases. 2- Distractibility in 100% of cases. 3- Inattention in 12% of cases. 4- Aggressiveness in 50% of cases. 5- Impulsivity in 45% of cases. 6- Irritability in 45% of cases. 7- Talkativeness in 45% of cases. 8- Temper tantrum in 45% of cases. 9- Difficulties in peer relationship in 45% of cases. 10- Emotional lability in 10% of cases. 11- Carelessness in 40% of cases. (Table 1).

Table (1)
Clinical Evaluation of the Studied Group

Symptom	No	%
Aggressiveness	10	50
Carelessness	8	40
Impulsivity	9	45
Inattention	12	60
Irritability	9	45
Emotional lability	2	10
Talkativeness	9	45
Temper tantrum	9	45
Overactivity	20	100
Distractibility	20	100
Difficulties in interpersonal relationship	9	45

Figure (1) Symptom Cluster in the Studied Group



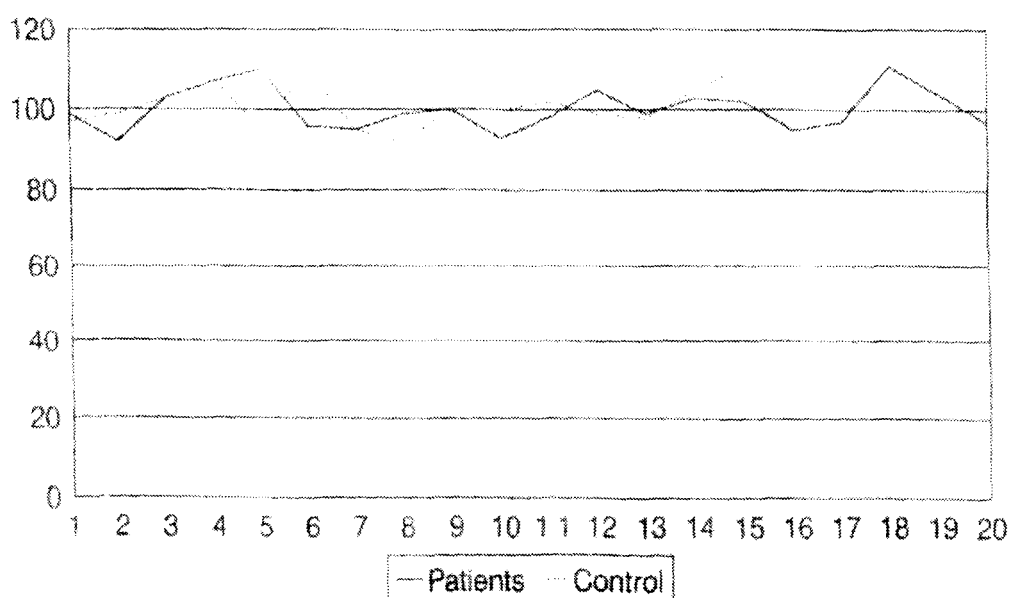
Psychometric evaluation

The results of WISC showed that children with ADHD had IQ which ranged from 92 to 115 with a mean of 100.6 ± 6.44 in comparison to controls who had IQ which ranged from 92 to 111 with a mean of 100.87 ± 5.51 . The difference between both groups is statistically not significant ($t = 0.133$, $p > 0.05$).

Table (2)
Intelligence Quotient (IQ) of Children
with ADHD in Comparison to Control

I.Q	Patients	Control
Range	92-115	92-111
Mean	100.6	100.87
SD	± 6.44	± 5.51
SE	1.44	1.42
t	0.133	
P	> 0.05 non significant	

Figure (2) IQ in Patients and Control Cases



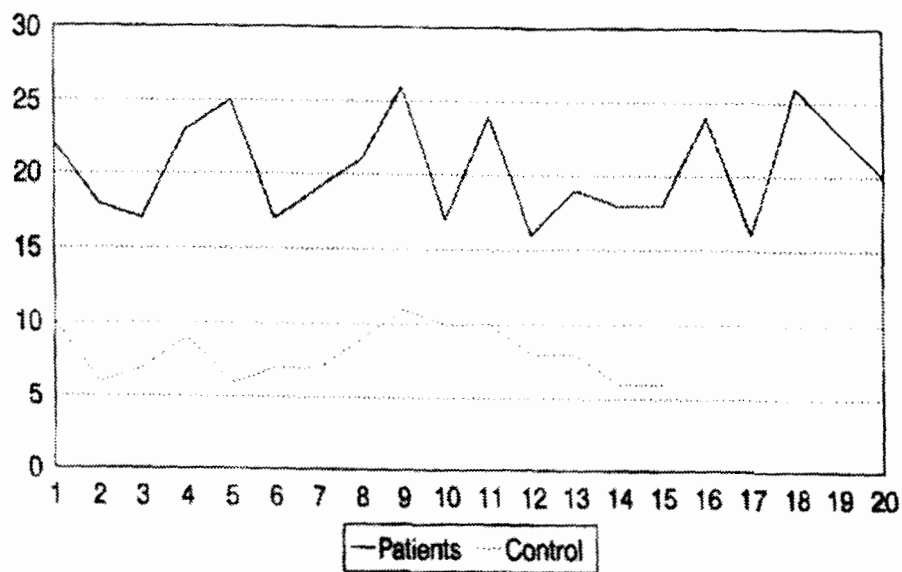
Results of Conners rating scales (Table "3" Fig. "3")

Children with ADHD had scores which ranged from 16 to 26 with a mean of 20.45 ± 3.41 in comparison to controls who had scores which ranged from 6 to 11 with a mean of 8 ± 1.73 . The difference between both groups is statistically significant ($t = 14.10$, $P < .05$).

Table (3)
Score of Conners Scale in 20
Patients & 15 Control Cases

Conners scale	Patients	Control
Range	16-26	6-11
Mean	20.45	8
SD	± 3.41	± 1.73
SE	0.76	0.45
t	14.10	
p	<0.05	

Figure (3) Results of Conner's scale



Biochemical study (Table "4", Fig. "4"):

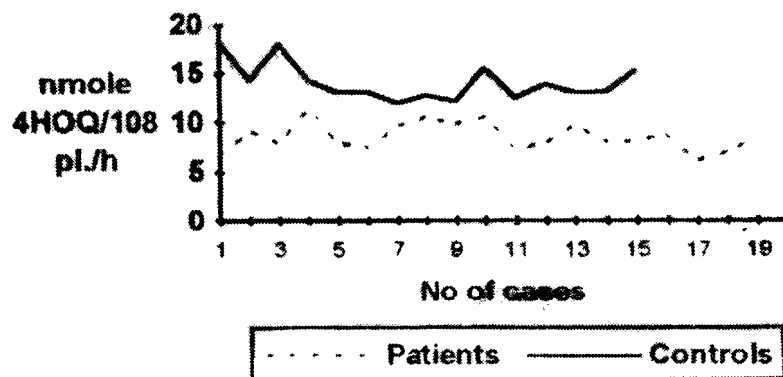
Platelet MAO activity in children with ADHD ranged from 6.50 to 11.30 with a mean of 8.59 ± 1.41 in comparison to control group which ranged from 11.86 to 18.28 with a mean of 13.95 ± 2.02 . The difference between both groups is statistically significant ($t = 8.90$, $P < 0.05$).

Platelet count in children with ADHD ranged from 2.2 to 4.8 with a mean of 3.92 ± 0.64 , in comparison to control group which ranged from 2.6 to 4.5 with a mean of 3.59 ± 0.6 . The difference between platelet count in both groups is statistically non significant ($t = 1.50$, $p > 0.05$).

Table (4)
 Platelet MAO Activity in Children with
 ADHD in Comparison to Control Group
 (Expressed as Nmoles 4 HO Q/10⁸ Platelet/Hour)

Platelet MAO activity	Cases	Control
Range	6.50-11.30	11.86-18.28
Mean	8.59	13.98
SD	±1.41	±2.02
SE	0.31	0.52
t	8.90	
p	<0.05	

Figure (4) Platelet MAO Activity in Patients and Control



Statistical analysis

Correlating platelet MAO activity with the clinical symptoms shows that there was no significant statistical difference in platelet MAO activity between those with and those without any of the symptoms of ADHD ($P > 0.05$).

Table (5)
Relation Between Platelet MAO Activity and Symptomatology

Symptom	Platelet MAO Activity							
		No	%	Mean	SD	SE	t	P
Aggressiveness	Absent	10	50%	8.9070	±1.289	0.407	1.00	.330
	Present	10	50%	8.2760	±1.518	0.480		
Carelessness	Absent	12	60%	8.9100	±1.424	0.411	-1.26	.225
	Present	8	40%	8.1138	±1.326	0.469		
Impulsivity	Absent	11	55%	8.8318	±1.240	0.374	-0.84	0.413
	Present	9	45%	8.2978	±1.616	0.239		
Inattention	Absent	8	40%	8.9912	±1.040	0.368	-1.04	.313
	Present	12	60%	8.3250	±1.594	0.460		
Irritability	Absent	11	55%	8.9082	±1.548	0.467	1.12	.278
	Present	9	45%	8.2044	±1.185	0.395		
Emotional lability	Absent	18	90%	6.6478	±1.458	0.344	-0.53	0.605
	Present	2	10	8.0850	±0.983	0.695		
Talkativeness	Absent	11	55%	8.6645	±1.337	0.403	-.25	.805
	Present	9	45%	8.5022	±1.567	0.522		
Temper tantrum	Absent	11	55%	8.5509	±1.510	0.455	.14	.891
	Present	9	45%	8.6411	±1.361	0.454		

Correlating platelet MAO activity with the results of Conners scale shows that there was no significant correlation between platelet MAO activity & neither any of the subitems nor the total score of Conners scale at 0.05 level; item 1,2 showed significance at 0.01 level (Table 6).

Table (6)
Spearman's Correlation Coefficient (r) Between Scores of Subitems of Conners Scale and Platelet MAO Activity in Children with ADHD

Subitems of Conners scale	r
Restless or overactive	0.3000
Excitable, impulsive	0.3974
Disturbs other children	-0.1734
Fails to finish things he starts, short attention span	-.0087
Constantly fidgeting	0.1892
Inattentive, easily distracted	0.0610
Demands must be met immediately, easily frustrated	0.0065
Cries often and easily	0.1313
Mood changes quickly and drastically	0.0565
Temper outbursts, explosive and unpredictable behavior	0.0345
Total score	.1058

** P < 0.05 * P < 0.1

Stepwise multiple regression analysis using platelet MAO activity as dependent variable while age, IQ and subitems of Conners scale as independent variables showed that the combination of overactivity, impulsivity & disturbing other children in addition to age have a significant effect on platelet MAO activity as shown in the following table.

Multiple R ,99214
R Square ,98434
Adjusted R Square ,98042
Standard Error 1,21732

Analysis of Variance

	DF	Sum of Squares	Mean Square
Regression	4	1490,23241	372,55810
Residual	16	23,70969	1,48186
F =	251,41318	Signif F = , 0000	

Variables in the Equation

Variable	B	SEB	Beta	T	Sig T
Age	,495440	,212752	,492458	2,329	,0333**
Disturbs other children	-1,026042	,582264	-,300665	-1,762	,971*

* P < 0.1

** P < 0.05

Discussion

The study examined the relationship of platelet MAO activity to ADHD on many levels:

Comparing platelet MAO activity in patients with that of control cases revealed significantly low activity in patients which is going with the results of previous authors¹⁸. The function of MAO is to convert the monoamines to their metabolites (figure 4). This lowered platelet MAO could be an expression of either increased level of monoamines or decrease in their metabolites, which could be an underlying mechanism of the disease, a conclusion that still needs confirmation by studying the behaviour of the monoamines in relation to the disease process.

Studying the relation between platelet MAO and either the presence of the symptom (as evaluated clinically) or the severity of the symptom (as measured by Conners scale) could not find statistically significant linear relation between platelet MAO activity and any of the individual symptom. However; testing the items of Conners scale in addition to IQ and age of the patient against platelet MAO activity using stepwise multiple regression analysis (Table 7 a, b,c) revealed that the combination of overactivity (item 1 of Conners scale), impulsivity (item 3 of Conners scale) in addition to age has a significant positive relation to the level of MAO activity while disturbing other children (item 2 of Conners scale) showed significant negative relation i.e. lowered platelet MAO activity. This controversies in the relation between MAO activity and different could be explained by the assumption that the symptoms of this disorder could be originated by different biological mechanisms which indicate the heterogeneity of the syndrome. This stimulate the research to look for the relation of different types of

MAO and symptomatology and the relation of different symptoms to other biochemical substrates specially the biological amines.

To conclude

The lowered platelet MAO activity could be a biological indication of the disease state; however its correlation with the symptomatology reveals the biological heterogeneity of symptoms of ADHD this conclusion needs more confirmation by replication of the study on a large scale of patients and also studies on the relation of each monoamine and their metabolites with the symptomatology.

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L'étude de l'activité de l'enzyme oxidase qui se trouve au sang chez les enfants ayant le diagnostic de déficit de l'attention et hyperactivité

Cette étude souligne qu'il ya une relation signifiante autre l'activité de cette enzyme elles symptoms qui se trouvent chez ses enfants, et les résultats a démontré qu'il ya diminuation signifiante à l'activité de l'enzyme (MAO) chez ses enfants.

دراسة نشاط مؤكسد أحادى الأمين فى الصفائح الدموية للأطفال ذوى قصور الإنتباه وفرط النشاط

تمت دراسة نشاط مؤكسد أحادى الأمين فى الصفائح الدموية فى عشرين طفلا مصابا باضطراب قصور الإنتباه وفرط النشاط، وكذلك فى ١٥ طفلا صحيحا كعينة ضابطة، حيث كان هدف الدراسة هو البحث عن علاقة بين مؤكسد أحادى الأمين فى الصفائح الدموية وأعراض اضطراب قصور الإنتباه وفرط النشاط مما قد يساعد فى تقييم استخدام مؤكسد أحادى الأمين فى الصفائح الدموية كوسيلة بيولوجية موضوعية فى تشخيص هذا الاضطراب الشائع.

وقد أسفرت النتائج عن نقص (نو دلالة إحصائية) لمؤكسد أحادى الأمين فى الصفائح الدموية فى الاضطراب عنه فى العينة الضابطة. كما أسفرت النتائج عن أن عوامل العمر والإندفاعية مع فرط النشاط وإزعاج الآخرين لهم تأثير ملحوظ، ولكنه متباين على نسبة مؤكسد أحادى الأمين فى الصفائح الدموية للمرضى مما يثير الشك حول تباين الأسس البيوكيميائية لهذه الأعراض وهو شك يحتاج لمزيد من الدراسات فى المستقبل لإثباته.