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Iron deficiency and the cognitive and psychomotor development of children: A pilot study with institutionalised children

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IRON DEFICIENCY is the most frequent form of nutritional deficiency in man, since it is observed in 10–20% of the general population. The frequency is higher among the low socio-economic class and particularly among children aged 1–3 years. Iron deficiency in infancy is particularly important because its consequences may be both serious and long-term. Cantwell (1974) states that 6–7-year-old children, who had suffered from iron deficiency during the 6th–18th month of life, show less ability to concentrate, are more clumsy and more hyperactive when compared to a group of children who did not have iron deficiency during the first two years of life. In recent years attention has been focussed on the behavioural disturbances which accompany iron deficiency. A considerable number of studies have shown that infants with iron deficiency have a lower developmental index, lack interest in their environment, have a shorter attention span and diminished cognitive ability (Judisch *et al.* 1966; Oski, 1978).

It has also been observed that older children suffering from iron deficiency have a lower IQ, poorer vocabulary, poor school

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performance, are irritable and have difficulty in concentrating, when compared to other children not suffering from anaemia (Sulzer *et al.*, 1973; Webb T.E., Oski F.A., 1973).

No study however has yet demonstrated whether the lower performance of those children is due exclusively to iron deficiency, or exclusively to anaemia, or whether it is the result of general nutritional disturbances since it is known that iron deficiency also affects the rate of physical development.

For that reason, the "METERA BABIES' CENTRE", in collaboration with the Institute of Child Health in Athens, has planned a study of all the babies that will enter the Centre during the next two years. The study will include thorough checking of their nutritional patterns, their physical and psychomotor development and their behaviour, from birth up to the age of 12 months.

In a previous study (Kyriazakou-Kosmopoulou, M. and Driva, A., 1972) it was observed that a high percentage of "METERA" babies develop anaemia during the first six months of life. It should be noted that the mothers of these babies belong, in general, to the lower socio-economic class and also that more than 50% of them suffered from iron deficiency towards the end of their pregnancy.

In a pilot investigation, it was found that METERA'S babies, aged between 2–24 months, have very low hematocrit (below 33) levels, as shown in Table I. METERA'S babies have very low hemoglobin levels (below 11) as well. In Table II, hemoglobin levels from a sample of infants of very similar socio-economic status are compared.

In view of the above, we were led to the hypothesis that institutionalisation is not the sole factor responsible for the lower rate of psychomotor development in these babies as compared to babies living with their families: anaemia and other nutritional disturbances may also be factors contributing to the above phenomenon.

TABLE I

Hematocrit levels distribution among 82 infants and toddlers of the Baby Center "Metera"

Hamatocrit (vol %)	n = 82	%
≤21	2	2.4
22–29	54	66
30–33	20	24.3
34–37	5	6.0
≥38	1	1.2

TABLE II

Hemoglobin levels distribution of 82 infants and toddlers of the Baby Center "Metera" in comparison to 160 infants 8–13 months from normal families in Florina County, Greece

	"METERA" (n = 82)	FLORINA (n = 160)
Hemoglobin (gr/dl)	%	%
≤10	57.2	16.6
10.1–11	29.2	16.5
11.1–12	10.9	20.5
>12.1	2.4	46.4

Measurements of Hb and Ht, however, are not sufficient for a diagnosis of iron deficiency. A more accurate index would be the level of serum ferritin defining the levels of iron stored in the body.

The aim of this pilot study was to define a model for the methods to be used and to solve certain technical problems. We assumed that the treatment of anaemia by the administration of iron would have a favourable effect on their psychomotor development.

SUBJECTS AND METHOD

The pilot study sample consisted of 48 children from the "METERA" babies' Centre, aged 3–25 months, suffering from iron deficiency. Of the 48 children, only 8 had Hg higher than 11 gr/dl, with an average of 11–11.4 although they were all suffering from iron deficiency (average level of serum ferritin 17.4). These children comprised Group C. The other 40 children, all of whose Hb was below 10.9 gr/dl (average 9.2–9.6) were divided into two random groups, A and B, each consisting of 20 children.

One intramuscular injection of 50 mg of iron was administered to each child, in all three groups. The difference between groups A and B was that the intra-muscular iron was given in group A right after the first developmental assessment. In group B (See Table III), the iron was given after the second developmental assessment 10 days later. Over a period of between 1–3 months after administration of the iron, blood tests were given to some of the children and the results may be regarded as indicative of the haematological improvement observed (Tables IV & V).

The mental and psychomotor development of each child, on Bayley's scales, were assessed, by the same investigator, on two or three occasions with a lapse of ten days between each test. Testing of the children from the three groups was carried out in such a way that neither the tester nor the nursery nurse who brought the child for testing knew the type of therapeutic intervention implemented in the case of child or when it had been implemented.

The Group A children were assessed three times on Bayley's scales and the therapeutic intervention took place immediately after the first assessment. The Group B children were also

TABLE III
Hemoglobin, Hematocrit and Ferritin levels in the anaemic children Group B before intromuscular administration of iron
Before iron administration (n = 20)

	Median	Range		
Hemoglobin (g/dl)	9.2	(8.4–10.6)	—	—
Hematocrit (vol. %)	30.0	(27–35)	—	—
Ferritin (mg/dl)	34.5	(12–320)	—	—

TABLE IV
Hemoglobin, Hematocrit and Serum Ferritin levels in the anaemic children in Group A before and after intramuscular administration of iron

	Before administration of iron (n = 20)		After administration of iron (n = 7)	
	Median	Range	Median	Range
Hemoglobin (g/dl)	9.6	(8–10.9)	11.2	(8.4–11.2)
Hematocrit (vol. %)	32.0	(29–35)	35.0	(34–37)
Ferritin (mg/dl)	27.0	(4.6–116)	48.5	(29–72)

TABLE V
Hemoglobin, Hematocrit and Serum Ferritin levels in the non-anaemic children (Group C) before and after intramuscular administration of iron

	Before administration of iron (n = 8)		After administration of iron (n = 8)	
	Median	Range	Median	Range
Hemoglobin (g/dl)	11.0	(11–11.4)	10.6	(10–11)
Hematocrit (Vol. %)	36.0	(33–38)	36.2	(35–40)
Ferritin (mg/dl)	17.4	(11.6–21)	37.0	(23–44)

assessed three times and the therapeutic intervention took place immediately after the second assessment. The Group C children were assessed twice and the therapeutic intervention took place immediately after the first assessment.

In this way, each group also constituted its own control, and group B was used as a control for group A during the first 10 days of the study.

RESULTS

Table VI shows the results of assessment on Bayley's scales for Psychomotor Development. No statistically significant differences were observed in the indices of psychomotor development, after the therapeutic intervention, in any of the three groups. On the other hand, a statistically significant differences was observed on the indices of mental development after the administration of iron (Table VII). In Group A, to which iron was administered immediately after the first assessment, there was an increase in the average Mental Development Index when the group was assessed for the second time, while no difference was observed between the second and third assessments.

TABLE VI
Mean scores of all three groups on Motor Development of the Bayley's Developmental Scales for infants

	First Assessment			Second Assessment			Third Assesment		
	n	Mean	S.D.	n	Mean	S.D.	n.	Mean	S.D.
Group A (Hgd ≤ 11g/dl)	20	84.8	12.72	20	85.6	14.54	11	87.70	16.20
Group B (Hgd ≤ 11g/dl)	20	89.7	18.69	20	93.2	17.12	20	99.65	14.89
Group C (Hgd > 11g/dl)	8	84.3	19.96	8	87.3	19.19	—	—	—

t = N.S.

TABLE VII
Mean scores of all three groups on Mental Development of the Bayley's Developmental Scales for infants

	First Assessment			Second Assessment			Third Assessment		
	n	Mean	S.D.	n	Mean	S.D.	n	Mean	S.D.
Group A (Hgd ≤ 11g/dl)	20	90.2*	14.53	20	97.2*	17.37	11	97.4	19.11
Group B (Hgd ≤ 11g/dl)	20	95.2	17.43	20	98.0*	16.17	20	104.6*	18.31
Group C (Hgd > 11g/dl)	8	106.5	26.30	8	108.7	28.17	—	—	—

*$p \leq 0.01$
Group A t (between first & second assessment) = 3.128
Group B t (between second & third assessment) = 3.259

In Group B, to which iron was administered after the second assessment, an increase in the average Mental Development Index was observed when the children were tested for the third time. In Group C, no statistically significant difference in the Mental Development Indices was observed after the administration of iron.

CONCLUSIONS

1. It would appear that the improvement observed on Bayley's scales is largely due to the administration of iron, given that the

statistically significant increase was observed *only* after iron had been administered.

2. The learning effect, in view of repetition of testing, would not seem to have been a factor, as improvement when the test was repeated was only observed where iron had been previously administered.

3. Improved performance after the administration of iron seems to remain stable for at least ten days.

DISCUSSION

During the last ten years, quite a number of studies have been published concerning iron deficiency anaemia, especially in infants and pre-school children. These studies have shown improvement in the psychomotor development and the behaviour of these children very shortly after the intramuscular administration of iron. Thus, children with iron deficiency anaemia, who are described as irritable and lacking interest in their environment, with reduced ability to concentrate, and limited I.Q. and cognitive ability, improve significantly soon after treatment with iron (Oski F.A., Honig A., 1978; Oski, 1979; Finch C.A. and Huebers H., 1982).

However, the cause of the disturbed physical and psychomotor development which accompanies iron deficiency anaemia in infants is not yet known. We do not know whether the reduction in the rate of physical development is a result of malnutrition or poor apppetite, of disturbances in the metabolism and in DNA and RNA composition, or the malabsorption of iron from the intestinal mucosa of the small intestine (Schubert W.K., Lahey, M.E., 1959; Hoag *et al.*, 1961; Woodruff C.W., Clark J.L., 1972).

The biochemical connection between iron deficiency anaemia and cognitive, emotional and psychomotor development is also

unknown, despite the fact that previous studies have demonstrated relationships to disturbances in the metabolism of neurotransmitters. This hypothesis was originally based on the observations of Symes *et al.* (1969), who found that the level of the enzyme monoamino oxidase, which is normally present in the brains of rats, fell when the rats suffered from iron deficiency anaemia, returning to normal one week after the administration of iron.

Low levels of monoamino oxidase have also been found in the platelets of human patients suffering from iron deficiency anaemia. Administration of iron improved the enzyme levels (Youdim *et al.*, 1975).

Infants with iron deficiency anaemia have also been observed to secrete increased amounts of norepinephrine, possibly as a result of a deficiency in monoamino oxidase (Oski, 1979). Five days after the administration of iron in these cases, the norepinephrine level returns to normal, while similar changes in the norepinephrine secretion have not been observed in anaemic infants not suffering from iron deficiency. Other investigators have found low levels of aldehyde oxidase, (in the brains of rats suffering from iron deficiency) this being a basic enzyme for the breaking-down of synaptic serotonine (Finch C.A. and Huebers H., 1982).

It follows that the immediate improvement observed after the administration of iron may be caused by enzyme action.

The results of our pilot study are in complete agreement with those of previous research. Our results showed a statistically significant increase in Mental Development Indices only ten days after intramuscular administration of iron, although no improvement in the Psychomotor Development Indices was observed. Psychomotor improvement has been cited in only one study in which the investigators themselves regarded it as a chance finding. It would appear that the disturbances caused by iron deficiency in infancy subside soon after treatment with iron, but it is not yet known whether it continues to be possible to rectify them when the iron deficiency extends beyond infancy, nor whether the improvement is permanent. However, institutions that care for infants need to become alert to iron deficiency as a potential source for developmental delays and behavioural deficits in some of the infants in care.

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