Iron Deficiency and Educational Deficiency

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Existing data suggest that iron deficiency anemia (IDA) is a risk factor for poor educational performance in schoolchildren. The synergistic effect of IDA in combination with other forms of malnutrition and other risk factors may affect educational performance more strongly. Thus, IDA and its effect on educational performance should be studied in the context of other risk factors.

Introduction

This paper addresses whether in low-income countries the formal educational progress of school-age children is placed at risk by the presence of iron deficiency anemia (IDA) . The data are drawn from three experimental studies and one correlational study. Conclusions and proposed directions for future research are offered. The author participated in these four studies.

Nutrition and psychology professionals generally believe that adverse effects of nutrition deficiencies become apparent most often in early childhood, particularly during the period of fast neuronal growth. Because effects in later life are usually trivialized, malnutrition among schoolchildren is not generally defined as a risk factor in the social and economic growth of either individuals or society. Additionally, investments made by governments or international agencies such as the World Bank in the education sector of low-income countries are usually targeted toward building more schools, providing training and better salaries for teachers, revising curricula, and increasing the availability of educational materials. Although well intentioned, these policies often do not work[1] because they fail to recognize that the quality of the educational experience cannot be improved without also investing in the health and well-being of the students.

The first of the four studies reviewed herein was conducted by Dr. A.G. Soemantri in Semarang, Indonesia,[2-4] and published in 1985. The second study took place in Chon Buri, Thailand,[5,6] under the direction of Drs. Aree Valyasevi and Phongjan Hathirat from Mahidol University. The study was implemented with the intent of replicating the findings from Indonesia. The third study, conducted in a semirural community in Egypt, was part of a much larger project that tested the effects of iron deficiency on cognitive performance, manual work productivity, and resistance to infection (Hussein et al., unpublished findings).[7] Although the complete results are unpublished, the psychological testing results were published in a letter to the editor of *The Lancet*.[7] The final study was a correlational study conducted in Guatemala; the data were presented at the 1993 International Congress on Nutrition in Australia (Pollitt et al., unpublished findings).

Because this paper focuses on school achievement, the studies in Indonesia and Thailand are particularly important because the outcomes included standardized tests developed by the respective governments to assess the educational progress of schoolchildren. It is also noteworthy that these two studies and the project in Egypt were based on randomized clinical trial designs.

Indonesia[2-4]

Location

The study site was Kalibawang, on the northern border of the Yogyakarta province in central Java, Indonesia. The epidemiology of iron deficiency in this area was unknown at that time; however, the tropical climate and prevalent low consumption of animal protein and heme iron were indicative of widespread iron anemia among children. Preliminary laboratory analysis showed that 10–20% of the population had hookworm infection with more than 2000 eggs per gram of stool.

Subjects

Criteria for case inclusion were (1) >80th percentile for weight and height and >85th percentile for midarm circumference of Indonesian growth standards; (2) negative parasite egg count after treatment of ancylostomiasis;* (3) no evidence of hematological diseases (i.e., thalassemia, malaria) or other severe

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* Before the administration of either ferrous sulfate or placebo, all parasite-positive children were treated with pyrantel pamoate (combination) at a dosage of 10 mg/kg/day for 2 days.

illnesses, physical handicap, or neurological abnormalities; (4) parental consent; and (5) IQ >75. In all there were 119 children ranging in age from 8.2 to 13 years.

Iron Status and Treatment

The definition of the iron classes were: iron anemia = hemoglobin (Hb) < 11 g/dL and transferrin saturation < 16%; nonanemia = Hb 12.0 g/dL and transferrin saturation > 20.0%. Once free of parasites, the subjects received either ferrous sulfate or a placebo. These two iron classes included 78 iron-anemic and 41 nonanemic children, whose average ages were 10.6 and 11.1 years, respectively. Ferrous sulfate, at a daily dose of 10 mg/kg (i.e., 2 g elemental iron), was given to 35 (49%) of the iron-anemic children and to 16 (39%) of the nonanemic children. The remaining subjects received a placebo tablet of saccharin and tapioca. The iron and placebo tablets were administered by school teachers and supervised by paramedical personnel every morning of the school session.

Cognitive Testing

Three psychological tests were administered to all subjects. The Raven Progressive Matrices,[8] a culture-free test that assesses nonverbal intelligence, was administered before the beginning of the trial only. The Educational Achievement Test, a revised, abbreviated version of the standard achievement test used by the Ministry of Education of the government of Indonesia, included questions in mathematics, biology, social science, and language and was administered both before and after the experimental intervention. The Bourden-Wisconsin test for concentration was also administered before and after the intervention.

Results

There were no significant differences at baseline between the iron-anemic and the nonanemic groups in any of the potentially confounding social and economic variables. Likewise, there were no differences in geohelminth infections as indicated by egg count. However, the nonanemic children were significantly heavier and taller ($p<0.05$) than the iron-anemic children.[4]

Hematology. The effects of the iron and placebo interventions are published elsewhere.[2,4] For illustrative purposes, the focus here is restricted to the effects on Hb. To test for these effects, we used an analysis of covariance (ANCOVA) that included iron class and type (Fe, placebo) of intervention as the independent variables and the baseline values as the covariates.

The main effect of treatment on delta (Δ) Hb was statistically significant; however, there was a statistically significant two-way interaction (treatment × Fe status). For the iron-anemic children, the difference between those who received Fe (mean =2.67 g/dL) and those who received the placebo (-1.17 g/dL) was statistically significant ($p<0.05$), whereas this result was not observed among the nonanemics. The initial difference in Hb between anemic and nonanemic children was not present in the posttreatment evaluation.

Cognition. At baseline, iron-anemic and nonanemic children did not differ markedly in the Raven Progressive Matrices IQ (97.7 versus 98.9). Performance on the Educational Achievement test was significantly better among the nonanemic (42.3, SD =10.8) than among the anemic children (31.8, SD =10.3). An ANCOVA showed a main effect of treatment ($p<0.05$) on the adjusted Δ (T2-T1) score (Fe = 1.67, placebo = 0.20) and a significant interaction between treatment and iron status. Among anemics, the Δ of the children treated with iron (3.64) was significantly larger than for those who received the placebo (-0.67). Conversely, among the nonanemics there were no significant differences between the Δ of the children who received iron (0.29) and those who received the placebo (0.28). However, the change in the achievement scores of the iron-anemic children who received iron was not large enough to erase the significant difference observed at baseline between them and the nonanemic children.

Thailand[5,6]

Location

This double-blind clinical trial involving 16 elementary schools in Chon Buri, Thailand, had the specific goal of replicating the results from the trial in central Java. The site was a rice-producing area on the eastern coast of Thailand, about 85 km from Bangkok. The 16 schools selected met the following criteria: (1) location in a nonmalarial area; (2) enrollment of ≥ 150 children; and (3) access to the main roads. A total of 2268 children were screened; this figure represented 23% of all children enrolled in grades 3 through 5 in the entire Chon Buri province (1980 statistics).[5]

Subjects

Criteria for case inclusion were (1) absence of AE Bart or hemoglobin (Hb) H disease, (2) absence of abnormal Hb E (hemoglobinopathy), and (3) age 9–12 years.

Iron Status and Treatment

The children were classified into one of three groups according to iron status: iron anemic, iron depleted, and iron replete. Iron anemia was defined as Hb < 12.0 g/dL plus two out of three of the following criteria: serum ferritin < 10 mg/L, transferrin saturation < 16%, and free erythrocyte protoporphyrin > 700 mg/L red blood cells. Iron depletion was defined by the same criteria except that Hb ≥ 12.0 g/dL. Iron repletion was also identified by a Hb ≥ 12.0 g/dL plus two of the following three criteria: serum ferritin ≥ 10 mg/L, transferrin saturation ≥ 16%, and free erythrocyte protoporphyrin ≥ 700 mg/L red blood cells. A total of 1358 children were classified, with 101 in the iron-anemic, 47 in the iron-depleted, and 1210 in the iron-replete groups. A total of 417 children did not meet these criteria and were therefore excluded. The 1775 children enrolled in the study were assigned to receive either the iron or the placebo before their iron status was known.

The iron treatment consisted of a 50-mg/day tablet of ferrous sulfate during the first 2 weeks (2 mg elemental Fe/kg/day) and a 100-mg/day tablet (4 mg/kg/day) during the remaining 14 weeks. The placebo was a tablet of sweet cassava powder with a color and appearance similar to those of the iron tablet. The tablets were distributed daily by the room teacher, who was supervised weekly by a field director. The teacher was blind to whether the tablet contained iron or cassava.

At the beginning of the trial, in addition to either the iron or the placebo, the children also received Albendazole, an anthelminthic drug. This schedule and combined treatment differed from those of the Indonesian study, where the anthelminthic intervention preceded the administration of iron and placebo. In Indonesia, a negative parasite egg count was one of the criteria for case inclusion.

Cognitive Testing

IQ, Thai language, and math tests were administered in group form in the classrooms after the children were informed of the nature and objectives of the study. The educational achievement tests for Thai language and mathematics (math) were adapted from the Thai government's Ministry of Education instruments used in the public school system. Each test was divided into two parallel forms based on the odd (O) and even (E) items of the original test forms. Half of the sample took the O form before treatment (T1) and the E form after treatment (T2), and the other half took the tests in the reverse sequence (E, O).

Results

Hematology. The Hb increment of the iron-deficient (ID) children treated with either iron (change of 2.9 ± 0.27 g/dL) or placebo (1.4 ± 0.14 g/dL) was statistically significant (p<0.0001). Likewise, the small change in the iron-depleted (0.53 ± 0.15 g/L) and iron-replete (0.15 ± 0.03 g/L) children treated with iron was statistically significant (p<0.0001). The fact that this later small Δ reached a statistical level of significance is explained by the large sample size (n=1210) and the relatively small standard error of the measure (0.3). The iron-replete children treated with a placebo had a negative Δ (-1.5 ± 0.03 g/L), which was also statistically significant (p<0.001). The change among the iron-depleted children on placebo (-0.2) was not significant.

Cognition. At baseline the mean IQ ([T1+T2]/2) of the iron-replete children (94.16 ± 0.29) was larger and significantly different (p=0.0008) from that of the iron-anemic children (90.77 ± 0.9). However, there were no differences between the mean IQ of the iron-depleted group and those of the other two groups. The mean Thai language score of the iron-replete (58.97 ± 0.45) children was also larger and significantly different from that of the anemic (55.92 ± 1.49, p<0.05) and the iron-depleted (51.76 ± 2.18, p<0.01) children. Moreover, the mean language scores of these two last groups were significantly different from each other. None of the differences in the math scores reached the conventional level of statistical significance (p<0.05); the p value for the difference between the anemic (51.03 ± 1.48) and the normal (53.74 ± 0.45) children was 0.08.

None of the two-way interactive terms of time by treatment or three-way interactions among time, iron status, and treatment were statistically significant. There were also no significant interactions of time and treatment with either school or grade. These findings were consistent when we placed the three iron classes together into the same ANCOVA as well as when the analyses were restricted solely to an iron class. Thus, there was no evidence that iron treatment had an effect on IQ or on either of the two educational achievement measures. Likewise, there was no evidence that the magnitude of the Δ (T2-T1) in any of the three outcome measures was associated with treatment.

The conclusion was that the data from Thailand did not replicate the findings from the Indonesian study.[2,3]

Egypt[7]

In Indonesia and Thailand the focus was on school achievement indicators, but the objective of the study in Egypt was to test the effects of iron anemia on the cognitive style of primary school children. Like the two previous studies, we used a randomized double-blind trial design.

Location

The site was Burtos, a village about 15 miles northwest of Cairo on the main road connecting the northern Nile Delta region with the capital of Egypt. At the time of the study Burtos had a population of approximately 13,000, living mostly in sun-dried or fired mud brick houses with dirt floors and wooden or thatched roofs. Most households had an average of seven family members sharing one or two bedrooms. In the study population, family size ranged from four to 11 members, with a maximum of seven families sharing a house. All homes had electricity and most had a radio, with a substantial number of families owning television sets and other electrical appliances.

Agriculture was the main economic activity, but community members also worked in nearby factories or in Cairo. The village had two public schools, one religious school, and one hospital staffed by at least two permanent medical residents and a dentist.

Subjects

The unit of analysis for the overall study was the family. Criteria for selection included the presence of the biological parents in the same household, with two children 4–7 and 8–11 years old. The present analysis is restricted to the older group, which initially included 203 children. Following the selection of the subjects according to the availability of iron data and iron status classification (defined below), the sample was restricted to 68 subjects: 28 classified as iron anemic and 40 as nonanemic (Table 1). Mean age for the iron-anemic group was 9.73 years and for the nonanemic group was 9.5 years.

Iron Status and Treatment

Hematological determinations included Hb, hematocrit (Hct), plasma ferritin, transferrin saturation, and free erythrocyte protoporphyrin (FEP). After completion of the field work, the children who had received either ferrous sulfate or the placebo were classified as either iron anemic or iron replete. In contrast to the usual procedure of selecting established cutoff points to discriminate between iron status categories, a discriminant function to maximize the sensitivity and specificity of the respective diagnostic classes was used. A discriminant function is a statistical technique for classification purposes that calculates a linear combination of variables that will maximally differentiate among a set of individuals on a particular criterion.

Table 1. Number of Iron-anemic and Nonanemic Children Who Received Either Ferrous Sulfate (Fe) or Placebo in Egypt

	Fe	Placebo	
Iron anemic *	18	10	28
Nonanemic **	19	21	40
Total	37	31	68

* Iron anemic: Hb < 11.5 g/dL, ferritin < 20 ng/mL, and/or transferring saturation < 25%.

** Nonanemic: Hb > 13 g/dL, ferritin > 20 ng/mL, and/or transferrin saturation > 25%.

A discriminant function analysis was calculated on the hematological data only of those 88 cases (43.1%) of the total sample with complete hematological records who had been treated with iron. At issue was the discrimination between iron-anemic and nonanemic children based on their Hb, transferrin saturation, and ferritin.

A first step was to classify the 88 children treated with iron as either iron anemic or nonanemic using the Hb response to the iron treatment as a criterion (Hb ≥ 1.0 g/dL). Forty-nine cases (55.6%) were anemic and the rest were nonanemic. Next, using this same group of 88 children, the discriminant function based on their respective values of Hb, ferritin, and transferrin saturation was calculated. The results showed that this procedure classified as anemic those children with Hb < 11.5 g/dL and either a transferrin saturation < 25% or a serum ferritin < 20 ng/mL. Nonanemia was defined as Hb ≥ 13 g/dL plus either a transferrin saturation 25% or a serum ferritin ≥ 20 ng/mL.

A cross-tabulation between the subjects classified on the basis of Hb response and the discriminant function showed that of the 49 subjects with Hb response $\Delta > 1$ g/dL, 38 (77.6%) were correctly classified as iron anemic by their discriminant scores. Thus, the discriminant function had a sensitivity of 78% and a specificity of 70%. The total percentage of group cases correctly classified was 74%. Finally, the discriminant function was used to classify all subjects: those who did and those who did not receive the ferrous sulfate. Twenty-eight were defined as iron anemic and 40 as nonanemic.

Oral ferrous sulfate (50 mg; about 2 mg elemental iron) and placebo were administered randomly to all participating children 6 consecutive days per week for 4 months.

Cognitive Testing

The battery included the Continuous Performance

Test (CPT), an Egyptian adaptation of the Peabody Picture Vocabulary Test (PPVT) and the Matching Familiar Figure Test (MFFT). The CPT is a test of vigilance and attention widely used in studies of neuropsychology, particularly in research on attention deficit disorders. The PPVT is a popular test of verbal development that in the United States maintains a correlation of about 0.75 with IQ tests such as the Stanford Binet and the Wechsler Intelligence Scale for Children (WISC). For this study, the PPVT was adapted to Egyptian culture and language.

The MFFT taps the child's capacity to focus on and select visual information for problem solving.[9] Performance on the MFFT is assessed in terms of speed and accuracy. Each test problem includes two cards, one with a figure or probe (e.g., chicken) and the other with five variants and one perfect match of the probe. The child was instructed to identify the match. A correct response was followed by the next problem, whereas an incorrect response led to a second presentation of the same problem. Two scores were obtained from the test: mean latency (time) to first response, and total errors across problems. Latency was interpreted as motivation or strategy to perform, and accuracy was defined as the capacity to discriminate or choose between useful and worthless visual cues. For the purpose of the study, the classification developed by Salkind and Wright[10] was used to discriminate between cognitive strategies that combine latency and accuracy. Impulsivity was defined as a dimension of individual differences ranging from fast-inaccurate to slow-accurate, and efficiency was defined as a dimension conceptually independent of (orthogonal to) impulsivity along a performance scale ranging from slow-inaccurate to fast-accurate.

Table 2. Mean (and Standard Error) Values of Hemoglobin Before and After Treatment of Anemic and Nonanemic Subjects

	Anemic		Nonanemic	
	Fe	Placebo	Fe	Placebo
Pretreatment	10.8 (1.01)	10.6 (0.96)	14.4 (1.30)	13.8 (1.18)
Posttreatment	13.0 (1.31)	11.7 (1.12)	14.5 (1.12)	12.9 (1.17)

Note: Within anemic and nonanemic groups, values with the same superscript are significantly different ($p<0.05$) from each other.

Table 3. Mean (and Standard Error) Values of Serum Ferritin (μg/L) Before and After Treatment of Anemic and Nonanemic Subjects in Egypt

	Anemic		Nonanemic	
	Fe	Placebo	Fe	Placebo
Pretreatment	21.0 (6.09)	16.7 (5.20)	33.5 (6.91)	30.6 (6.20)
Posttreatment	13.5 (8.05)	24.2 (5.49)	39.9 (9.45)	29.0 (6.04)

Table 4. Mean (and Standard Error) Values of Transferrin Saturation (%) Before and After Treatment of Anemic and Nonanemic Subjects in Egypt

	Anemic		Nonanemic	
	Fe	Placebo	Fe	Placebo
Pretreatment	20.5 (1.90)	18.4 (1.86)	24.6 (1.88)	24.7 (1.74)
Posttreatment	30.4 (2.54)	24.9 (2.19)	22.0 (3.65)	24.1 (1.12)

Results

Hematology. The hematological values are presented in Tables 2–4. An analysis of covariance (ANCOVA), with iron status and treatment as independent variables and the baseline hematological values as covariates, showed a statistically significant effect of treatment on hemoglobin (Table 2). However, the interaction between treatment and iron status was not statistically significant (>0.05 p <0.10). On the one hand, the Hb values increased (T2-T1) in the anemic group independent of treatment; on the other hand, among the nonanemic children, ferrous sulfate resulted in a negligible change, whereas Hb values for the placebo-treated group decreased from 13.8 to 12.9. The means for the iron- and placebo-treated groups were 13.7 and 12.3 g/dL, respectively (F=11.2, $p<0.01$).

There was a statistically significant effect of treatment (F=13.7, $p<0.001$) on ferritin, but neither the other main effects nor the interactive terms were statistically significant (Table 3). Regarding ferritin, a peculiar finding was the small magnitude of the response to the administration of the ferrous sulfate in the iron-anemic children, particularly because the Hb responses were relatively large. For example, among the iron-anemic children the ferritin change was 10 μg/L whereas the Hb response was about 2.5 g/dL. By contrast, among the Indonesian children described above,[2,4] the ferritin response among the iron-anemic subjects was 59.1 μg/L with a Hb change of 2.8 g/dL.

Cognition. There were no significant differences between the iron-anemic and nonanemic subjects in the CPT and the PPVT. However, after controlling for age in an ANCOVA, there was a statistically significant effect of iron status on the number of errors in the MFFT at baseline; the mean numbers of errors for the anemic and nonanemic children were

Table 5. Mean Number of Errors on Matching Familiar Figures Test for Iron-Anemic and Nonanemic Children in Egypt Before and After Treatment

	Anemic		Nonanemic	
	Fe	Placebo	Fe	Placebo
Pretreatment	26.2	22.6	21.8	19.6
Posttreatment	19.4	23.6	22.5	21.2

Table 6. Mean Efficiency Scores on Matching Familiar Figures Test for Iron-Anemic and Nonanemic Children in Egypt Before and After Treatment

	Anemic		Nonanemic	
	Fe	Placebo	Fe	Placebo
Pretreatment	0.39	-0.16	-0.30	-0.30
Posttreatment	-0.30	0.24	-0.23	0.09

Note: Negative scores indicate higher efficiency.

24.1 and 20.7 (F=6.7, p<0.001), respectively (Table 5). There were no other main effects or statistically significant interactive terms. Moreover, the ferrous sulfate did not have a significant effect on the change in scores from the baseline to the second evaluation in either diagnostic group.

There were also no main effects or statistically significant interactive terms in response time at baseline. However, as observed in Table 6, an analysis of test efficiency showed that the iron-replete children performed significantly better than the iron-depleted children (-0.30 versus 12, F=4.5, p<0.05). The nonanemic children thus made better use of their time than the anemic children.

The Δ analysis showed that the differences at baseline between diagnostic groups in the number of errors were no longer present. In fact, this ANCOVA failed to yield any statistically significant findings. Among the anemic children, those treated with iron were able to select information faster and with fewer errors (t=2.08 with pooled variance estimated; p<0.05) than were those who received the placebo. This same comparison yielded no statistically significant findings among the iron-replete children.

Guatemala

This study was restricted to assessing the associations between iron deficiency without anemia and cognitive test performance and the correlation between ferritin and cognitive testing among iron-replete subjects. The data reported here are part of a larger study that tested the effects of protein and energy supplementation on the growth and development of nutritionally at-risk children living in four rural villages in the department of El Progreso, Guatemala.[8] There were two periods of data collection: a longitudinal period spanning 1969 to 1977 and a follow-up conducted in 1988. This second part included the assessment of body iron because it was considered a potential confounder in the detection of effects of the supplement on cognitive test performance. The methodology and principal results from the follow-up are detailed elsewhere.[11]

Initially the criteria for the selection of villages were social isolation (distance of 35–150 km), small population (between 500 and 1000 inhabitants), low level of education, and high prevalence of protein and calorie malnutrition. Seven villages were selected initially, but three were later dropped because of budgetary constraints.

The single criterion for case inclusion of the subjects from the four villages in the original study was participation in the longitudinal study. Among the subjects in the three villages originally excluded, case inclusion was limited to those subjects who matched the criteria of the longitudinal study and were living in the villages during the follow-up. Of 1704 potential participants, 1545 were residing in the villages. Of these, 1203 were included in the iron determinations.

Subjects

The subjects were classified into one of three iron status categories. Iron replete was defined as Hb > 120 g/L plus two of the following criteria: serum ferritin (SF) > 10 μg/L; transferrin saturation (TS) > 16%; erythrocyte protoporphyrin (EP) < 70 μg/dL. The classification of iron deficiency without anemia included the same Hb criterion as that of iron replete plus two of the following criteria: SF < 10 μg/L; TS < 16%; or EP > 70 μg/dL. The definition of iron deficiency with anemia included Hb < 120 g/L and the same criteria as those of iron deficiency for SF, TS, and EP.

The prevalence of iron deficiency was 3.16 (n=38), whereas that for IDA was 1.58% (n=19). Among males, prevalence of iron deficiency remained relatively stable across age classes. Among females, prevalence increased with age; in the youngest group (9–11 years), the iron deficiency prevalence was 2.27%, whereas in the 18–27-year group, iron deficiency prevalence rose to 6.67%.

Cognitive Testing

The test battery contained two sets of psychological tests. One assessed complex mental abilities (e.g., arithmetic and reading comprehension) that depend on the subject's formal and informal education. The second set included tests of elementary cognitive processes (e.g., simple reaction time, short-term memory) that reflect some of the neurophysiological underpinnings of cognition. The results from these tests reflect only a modest, if any, influence of schooling and informal education on attention and memory. These are more likely to be influenced by nutritional or other biological factors.

The psychoeducational set also included a non-verbal IQ test (Raven's Progressive Matrices) and tests of literacy, numeracy, and general knowledge, as well as two standardized tests (reading and vocabulary) successfully used in Guatemala. The second set included simple and choice reaction time, a Sternberg's memory task, and a paired-associates task. A detailed description of the tests, their psychometric properties, and procedures for administration have been reported in Pollitt et al. (1993).[8]

Social and Economic Background

As socioeconomic variables, we used measures of housing quality, father's occupation, and maternal education. The only difference of note between iron status groups was that iron-replete subjects had a higher mean housing quality than did iron-depleted subjects ($p=0.068$).

The schooling variables considered here are age at first enrollment in school and maximum grade attained at the time of the follow-up. There were no significant differences between the iron-replete and iron-depleted groups for maximum grade attained. However, the iron-depleted group entered school later on average than did the iron-replete group ($p< 0.05$). The iron-depleted group began school at an average age of 8.6 years compared with an average age of 8.0 years for the iron-replete group.

Results

There was only one difference of note between the iron-depleted and iron-replete groups among the 13 comparisons that were calculated. On average, the subjects in the iron-replete group responded faster than did those in the iron-depleted group on the memory test.

This was true after adjusting for sex, age, maternal education, father's occupation, and housing quality. After accounting for the effects of these confounders, the difference in reaction time on the memory test prevailed ($p< 0.05$).

Serum ferritin was not strongly associated with scores on any of the cognitive tests included in the psychoeducational and information-processing battery for iron-replete subjects. The highest correlations were with scores on Raven's Progressive Matrices ($R=0.07$, $p<0.05$), the test of general knowledge ($R=0.06$, $p=0.0711$), and specificity for memory test ($R=0.06$, $p=0.0936$). None of these correlations remained significant after accounting for the effects of school achievement.

The present findings suggest that the difference in scores on a language test between the iron-depleted and iron-replete schoolchildren for the Thailand study cited earlier was not due to differences in iron status.

Discussion

The study in Indonesia showed that nonanemic children performed significantly better on educational achievement tests than did iron-anemic children. It also showed that the administration of ferrous sulfate for a period of 3 months improved performance for the anemic children. However, the treatment did not succeed in boosting their performance to the level of the nonanemic children.

The association between iron anemia in Indonesia and comparatively poor performance on educational achievement tests was replicated in Chon Buri, Thailand. These findings were extended to include an association of comparatively low achievement scores among nonanemic children. However, in contrast to the findings in Indonesia, the iron treatment in Thailand had no effect on the three psychoeducational tests administered.

As noted earlier, the designs in Indonesia and Thailand differed in one critical feature: whereas the subjects in central Java were enrolled in the iron intervention after treatment for ancylostomiasis, the treatments in Thailand for geohelminth infection and for iron deficiency were introduced simultaneously. Although the effect of Albendazole on iron status was not as strong as that of the combination of Albendazole and ferrous sulfate, the anthelminthic drug alone did have a significant effect on anemia. Before the intervention, 7.2% and 2.8% of those who received the Albendazole ($n=880$) were classified as iron anemic and iron depleted, respectively; after the intervention the numbers dropped to 2.8% and 0.5%. It is therefore plausible that the lack of posttreatment differences in performance on the achievement tests was due to the similar benefits that resulted from the administration of Albendazole and ferrous sulfate.

However, this explanation is questionable. In Thailand the intragroup improvements in test scores were negligible, whereas in Indonesia the change in test performance among the iron-anemic children treated with iron was comparatively large and statistically significant. We must consider the possibility that although the classification of IDA was probably correct in most of the cases in both studies, there may have been other nutritional and/or clinical differences between the children included in the two studies. The external validity of studies such as those in Indonesia and Thailand is limited because of the particular features of the ecological settings. The challenge lies in identifying the particular features of the ecology that modify the effects of conditions such as iron anemia.

In Egypt, corroborating evidence exists that iron anemia affects cognition among school-age children. This study showed that anemic subjects committed more errors and were less efficient in the MFFT than were the nonanemic subjects. Moreover, the anemic subjects treated for iron anemia reduced their errors and improved their efficiency scores from the pre- to the posttreatment evaluation.

There are, however, unresolved methodological and substantive questions worth mentioning. First, the extent to which the relatively low sensitivity (78%) and specificity of the diagnostic criteria affected the findings is unknown. An answer to such a question would require a much larger sample size than what is available. Second, there is no obvious reason for the unexpected low ferritin response to the treatment. It is noteworthy that the cognitive tests were administered individually and not in group form, as in Thailand.

The absence of a significant correlation between iron deficiency without anemia and the poor performance on cognitive tests observed in Guatemala, in my view, raises skepticism as to whether this modest degree of iron deficiency affects cognition. Most studies that focused on this issue in early childhood[12] found results similar to the Guatemala findings.

Conclusion

Although the data presented may not be definitive and may indicate the need for further research, the task at hand is not additional testing for the main effects of iron anemia on school performance. Rather, the challenge lies in defining the role of iron deficiency and other forms of malnutrition in combination with other risk factors in determining educational efficiency. New information on developmental psychology strongly suggests that the additive and synergistic interactions among risk factors, rather than any single risk factor, have a much greater influence on school performance.

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