Functional Significance of Early-Life Iron Deficiency: Outcomes at 25 Years

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Objective To evaluate adulthood function following chronic iron deficiency in infancy.

Study design At 25 years, we compared 33 subjects with chronic iron deficiency in infancy to 89 who were iron-sufficient before and/or after iron therapy. Outcomes included education, employment, marital status, and physical and mental health.

Results Adjusting for sex and socioeconomic status, a higher proportion of the group with chronic iron deficiency did not complete secondary school (58.1% vs 19.8% in iron-sufficient group; Wald value = 8.74; $P = .003$), were not pursuing further education/training (76.1% vs 31.5%; Wald value = 3.01; $P = .08$; suggestive trend), and were single (83.9% vs 23.7%, Wald value = 4.49; $P = .03$). They reported poorer emotional health and more negative emotions and feelings of dissociation/detachment. Results were similar in secondary analyses comparing the chronic iron-deficient group with subjects in the iron-sufficient group who had been iron-deficient before treatment in infancy. Path analysis showed direct paths for chronic iron deficiency in infancy and being single and more detachment/dissociation at 25 years. There were indirect paths for chronic iron deficiency and not completing secondary school via poorer cognitive functioning in early adolescence and more negative emotions via behavior problems in adolescence, indicating a cascade of adverse outcomes.

Conclusion The observational nature of this study limits our ability to draw causal inference, even when controlling for background factors. Nonetheless, our results indicate substantial loss of human potential. There may be broader societal implications, considering that many adults worldwide had chronic iron deficiency in infancy. Iron deficiency can be prevented or treated before it becomes chronic or severe. *(J Pediatr 2013;163:1260-6)*.

See editorial, p 1242 and related article, p 1267

Iron deficiency is most prevalent in developing countries[1] but remains a problem worldwide, especially among infants and pregnant women.[2,3] Iron-deficiency anemia (or other indications of chronic severe iron deficiency) in infancy is associated with poorer cognitive, motor, social-emotional, and neurophysiologic outcomes.[4,5] Most studies report lower scores despite iron treatment and correction of anemia.[6,7] Available longitudinal studies find persisting differences.[5,8,9]

Most information on outcome beyond early childhood comes from our previous longitudinal study conducted in Costa Rica. By early adolescence, children with chronic, severe iron deficiency in infancy had not caught up in motor performance to their peers who were iron-sufficient before and/or after iron treatment in infancy.[10] More of them had repeated a grade in school and/or been referred for special services.[11] According to their mothers and teachers, they had more anxiety/depression, social problems, and inattention, along with a corresponding increase in summary measures of internalizing problems and total problems, compared with their iron-sufficient peers.[11] At age 19 years, they did worse on neurocognitive tests of executive function and recognition memory.[12] They did not catch up in overall cognitive performance; the gap in cognitive test scores was wider in subjects from families of lower socioeconomic status (SES).[13]

Here we report functional outcomes in these subjects at age 25 years related to educational attainment, employment, health, and close personal relationships. We expected that poorer adult outcomes would result from a cascade of effects, for example, disadvantaged background combined with chronic iron deficiency in infancy, to affect cognitive performance and socioemotional behavior in childhood and adolescence and subsequent functional outcomes in adulthood.[11,13,14]

Methods

Subjects

The original study was conducted in a predominantly working class urban community near San Jose, Costa Rica.[15] Enrollment (from July 1983 to February

HB	Hemoglobin
SES	Socioeconomic status

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1985) entailed door-to-door screening of all 12- to 23-month-old infants with birth weight ≥2.5 kg and uncomplicated term singleton birth who were free of acute or chronic medical problems and had normal physical examination findings.[15] Iron status varied from iron sufficiency to marked iron deficiency anemia (see below). All iron-deficient infants, regardless of hemoglobin (HB) concentration, and those with low ferritin levels received iron therapy (6 mg/kg/day) for 3 months.

The mean age of the subjects at study entry was 17 months. Iron deficiency was thus likely to have been of at least several months duration, especially because unmodified cow's milk was often introduced early. Of the 191 infants in the initial study group, 6 lacked information on iron status after iron therapy, resulting in a potential sample size of 185 infants. Subjects were reassessed at age 5 years,[16] early adolescence (11-14 years),[11] mid-adolescence (15-17 years),[13] and 19 years.[13] Subjects provided signed informed consent for the 25-year follow-up. The protocol was approved by the Ethics Committees of University of Michigan and Universidad Ciencias Médicas, Costa Rica.

Iron status in infancy was based on venous HB concentration and 3 measures of iron status. Anemia was defined as HB ≤105 g/L and nonanemia as HB ≥120 g/L, with HB concentration 106-119 g/L considered intermediate.[15] Iron deficiency was defined as serum ferritin <12 ng/mL and free erythrocyte protoporphyrin ≥1.77 μmol/L (100 μg/dL) of red blood cells and/or transferrin saturation <10%.[15] After iron therapy, HB increased by an average of 37 g/L in the infants with iron-deficiency anemia.[15] None of the infants still had iron-deficiency anemia, although many had a measurable iron deficiency.[16]

Following the approach taken since the 5-year follow-up,[10-13,16] the chronic-iron deficiency group comprised subjects with marked iron deficiency anemia during infancy (HB ≤100 g/L) or iron deficiency with higher HB concentrations who did not become iron-sufficient after iron therapy. Their higher erythrocyte protoporphyrin concentrations indicated more chronic, severe iron deficiency.[16] The primary analyses compared subjects who had chronic, severe iron deficiency in infancy with those who were iron-sufficient before and/or after iron therapy, defined as absence of anemia and no more than 1 abnormal iron measurement.

No subject had iron deficiency anemia on subsequent blood testing (at age 5, 11-14, and 19 years)[11,13,16] with the exception of 4 women at age 19 years. Iron deficiency was present in <5% of subjects. Thus, dietary iron intake was apparently sufficient to correct iron measures that remained altered after treatment in infancy and to support subsequent good iron status.

Adult Assessment

The 25-year follow-up was planned as a 2-hour assessment. However, because of work obligations, only 51 subjects were able to come for testing between February 2007 and July 2008. Thus, we collected information on functional outcomes for the rest of the sample from February to June 2009 using the questions that could be answered in a 20- to 30-minute telephone interview. The information (in person or by telephone) was obtained by an experienced physician (S.G.) who had examined the subjects at age 19 years and remained unaware of their iron status or response to treatment in infancy.

Education and academic achievement were measured based on questions from the Status Questionnaire.[17] Employment was measured by questions from Monitoring the Future.[18] Questions from a SES measure that is sensitive to differences at the lower end of the spectrum in Latin American populations (Graffar Scale[19]) were used to assess the type of home and the material goods in the home. Close relationships were measured by portions of the Monitoring the Future survey.[18] Physical and mental health were measured by questions from the Status Questionnaire[17] and the Young Adult Health Survey.[20] Mental health was further assessed using the Beck Depression Inventory[21] and a short form of the State-Trait Anxiety Scale.[22] Life stressors were measured by a modified Social Readjustment Rating Scale.[23] Because our goal was to identify group differences in functional outcomes, we considered it reasonable to use these measures even though they had not been standardized in Costa Rica. The project's experienced psychologists and physicians deemed the questions to be relevant and appropriate in this context.

Statistical Analyses

Our initial comparisons of the chronic iron-deficient and iron-sufficient groups on each of the outcomes were made using *t* tests. We then tested each significant difference with covariates, using multiple regression for continuous outcomes and logistic regression for dichotomous outcomes and retaining covariates that contributed significantly to a given model. On conceptual grounds, we considered sex and SES of family of origin (based on parental education and occupation[24] and dichotomized as lower or middle class) as covariates. We also considered other preexisting group differences and disadvantages that often co-occur with iron deficiency, such as slightly lower birth weight, earlier weaning from breast milk, more father absence, less supportive home environment, and so on.[15] To consider these factors in a parsimonious fashion, we created a propensity score[10] and considered it as a covariate. A propensity score indexes the risk for having a condition of interest based on relevant preexisting factors and allows consideration of multiple factors in a single control variable in analyses of outcomes.[25] The other covariate considered was lead level (available only in infancy and early adolescence), given its well-established relationship with long-term cognitive and behavioral outcomes. Secondary analyses divided the iron-sufficient group, comparing the chronic iron-deficient subjects with subjects who became iron-sufficient after iron therapy during infancy (separate from those who were iron-sufficient at enrollment).

We conducted path analyses using Mplus (www.StatModel.com) to identify pathways to poorer adult outcome. We included factors from infancy (family SES

and iron status) and early adolescent behavior problems and cognitive function. Cognitive function was indexed by a composite of standardized cognitive test scores at age 11-14 years,[13] and behavior problems were indexed by the total problem score of the Child Behavior Checklist.[26] There was continuity in these measures between age 5 years and early adolescence, but the relationship between early adolescence and outcome at age 25 years was stronger than that between 5 years and 25 years; thus, we used data from adolescence in the path analyses.

As a preliminary step for depressive symptoms, we determined how Beck Depression Inventory items clustered together in this Costa Rican sample using principal components factor analysis with varimax rotation. Three factors emerged (*z*-scored), related to negative emotions, feelings of detachment or dissociation from normal activities, and physical symptoms of depression.

Results

Of the 185 potential subjects for longitudinal follow-up, 122 (65.9%) participated in the adult assessment. Two subjects declined, 3 were living outside Costa Rica, and the remaining 58 could not be located. The sole statistically significant background difference between subjects who participated at age 25 years and those who did not was a childhood home environment more supportive of child development ($P < .05$), as measured by the Home Observation for Measurement of the Environment-Revised.[27] Demographic characteristics of the sample are summarized in Table I. The mean age at assessment was 25 years (range, 22.8-27.0 years). Most of the subjects (n = 86; 70.5%) had participated in all previous assessments; an additional 29 (23.8%) had been part of the early adolescent assessment (at age 11-14 years) and at least 1 other follow-up before age 25 years. Males and females were roughly equally represented. Approximately 70% of the subjects were employed full-time in the previous year, one-third were pursuing higher education or further training, and one-third were married or engaged.

Of the 122 subjects in the follow-up, 33 (27.0%) had chronic iron deficiency as infants, and 89 (73.0%) had been iron-sufficient before and/or after iron therapy; 41 became iron-sufficient after treatment. There was no differential attrition; subjects with chronic iron deficiency in infancy represented 31.7% of those not assessed at the 25-year follow-up, compared with 27.0% of those assessed ($\chi^2 = 0.45$, $P = .50$). As in previous follow-ups, a higher proportion of the chronic iron-deficient group was male (69.7% vs 43.8% of the iron-sufficient group; $\chi^2 = 6.45$, $P = .01$). The age at assessment was similar (24.8 ± 1.0 years in the iron-deficient group vs 25.1 ± 1.0 years in the iron-sufficient group; $t = 1.03$, $P = .31$). There were no differences in the distribution of functional outcome responses obtained in person or by telephone, with the exception of being in school or obtaining further training. A higher proportion of subjects who were interviewed in person reported in the affirmative, regardless of iron status group in infancy, compared with those interviewed by telephone (52.0% vs 20.0%; $\chi^2 = 13.25$, $P < .001$).

Table II compares 25-year functional outcomes in the chronic iron-deficient and iron-sufficient groups. Propensity score and lead levels did not contribute significantly to the models relating iron status in infancy to adult outcomes and were not retained as covariates. However, sex and SES of family of origin were significant covariates for some outcomes and thus were considered in all comparisons.

Individuals with chronic iron deficiency in infancy completed 1 year less of schooling on average compared with the iron-sufficient group (11.5 ± 0.3 vs 12.5 ± 0.4 years; $t = 2.03$, $P = .04$). The year turned out to be critical for finishing secondary school and receiving a "bachillerato" (roughly equivalent to a US high school diploma). The proportions of subjects who did not complete secondary school and were not pursuing further education or training were significantly higher in the chronic iron-deficient group compared with the iron-sufficient group. Controlling for family SES and sex did not change the findings to any significant degree; the approximate 3-fold difference in secondary school completion remained statistically significant, and the approximate 2-fold difference in pursuit of further education/training still showed a suggestive trend (Table II). There were no differences in employment outcomes (working ≥20 hours/week in the previous month and working full-time at least 6 months in the previous year).

More than 80% of the chronic iron-deficient group was single (ie, never married or engaged), compared with only approximately 24% of the iron-sufficient group (Table II). There was no effect of sex or SES of family of origin. There were no between-group differences in the proportion of subjects with children. The chronic iron-deficient group self-rated their emotional health[17] as worse compared with the iron-sufficient group and reported more symptoms than the iron-sufficient group for 2 factors derived from the Beck Depression Inventory, negative emotions and feelings of detachment/ dissociation. There were no between-group differences in self-reported anxiety, physical symptoms of depression, or problems related to substance abuse, physical health, or life stresses. We did not have anthropometric data at age 25 years, because most

Table I. Characteristics of the 122 subjects at the 25-year follow-up

Characteristic	Value
Female, % (n)	49.2 (60)
Chronic iron deficiency in infancy, % (n)	27.0 (33)
Did not complete secondary school, % (n)	41.8 (51)
Not currently enrolled in school or training, % (n)	67.5 (81)
Not employed ≥ 20 hours/week in previous month, %, (n)	30.4 (34)
Not employed full time for ≥6 months in previous year, %, (n)	29.8 (28)
Single, %, (n)	65.5 (76)
Has children, %, (n)	39.0 (46)
Age at testing, y, mean (SE)	25.0 (1.0)

The number of subjects with data varies slightly depending on the variable.

Table II. Functional outcomes at age 25 years by iron status in infancy

Outcome	Chronic iron-deficient*	Iron-sufficient*	Log OR (95% CI)	Test statistic†	*P* value
Did not complete secondary school	66.7 (22)	19.2 (17)	−1.44 (−2.34, −0.54)	10.21	.001
Adjusted for sex and SES	58.1 (19)	19.8 (17)	−1.40 (−2.35, −0.45)	8.74	.003
Not currently enrolled in school or training	83.9 (28)	27.4 (24)	−1.12 (−2.20, −0.04)	4.29	.04
Adjusted for sex and SES	76.1 (25)	31.5 (28)	−0.88 (−1.90, 0.14)	3.01	.08
Not employed ≥20 hours/week in past month	21.9 (7)	39.0 (35)	0.58 (−0.40, 1.46)	1.41	.24
Not employed full time ≥6 months in past year	26.9 (9)	31.9 (28)	0.17 (−0.85, 1.19)	0.11	.74
Single	83.3 (27)	22.5 (20)	−1.27 (−2.35, −0.19)	5.55	.02
Adjusted for sex and SES	83.9 (28)	23.7 (21)	−1.17 (−2.27, −0.07)	4.49	.03
Has children	32.3 (11)	47.3 (42)	0.38 (−0.48, 1.24)	0.79	.37
Beck Depression Inventory, total score‡	8.25 (1.42)	6.12 (0.75)	2.13 (−1.15, 5.41)	1.65	.20
Negative emotions, *z*-score	0.53 (0.25)	−0.12 (0.08)	0.65 (0.23, 1.07)	9.62	.002
Adjusted for sex and SES	0.52 (0.19)	−0.20 (0.11)	0.72 (0.29, 1.16)	9.3	.003
Detached/dissociated, *z*-score	0.68 (0.22)	−0.20 (0.09)	0.88 (0.49, 1.26)	9.06	.004
Adjusted for sex and SES	0.62 (0.19)	−0.20 (0.11)	0.82 (0.39, 1.26)	9.69	.002
Physical symptoms of depression, *z*-score	0.05 (0.18)	−0.01 (0.11)	0.06 (−0.37, 0.48)	0.10	.75
Self-rating of emotional health, *z*-score	−0.36 (0.22)	0.15 (0.09)	−0.51 (−0.91, −0.11)	4.58	.04
Adjusted for sex and SES	−0.41 (0.18)	0.19 (0.11)	−0.59 (−1.02, −0.17)	4.41	.04
Self-rating of overall health, *z*-score	−0.04 (0.17)	0.02 (0.11)	−0.06 (−0.48, 0.36)	0.09	.79
Self-reported physical health problems, *z*-score	−0.09 (0.19)	0.01 (0.11)	−0.10 (−0.52, 0.31)	0.22	.64
Anxiety (State-Trait Anxiety Inventory)§	13.49 (1.02)	12.87 (0.53)	0.62 (−1.52, 2.76)	0.33	.59
Number of life stressors in past year¶	2.15 (0.41)	2.69 (0.23)	−0.54 (−1.43, 0.36)	1.39	.24
Housing and material goods**	16.21 (0.81)	17.36 (0.42)	−1.15 (−2.85, 0.55)	1.58	.22

*Values are % (n) for categorical variables and mean (SE) for continuous variables. The number of subjects with data varies slightly depending on the variable.
†Test statistics are Wald values for dichotomous variables and *F* values for continuous variables.
‡Maximum possible score, 63; higher values indicate more symptoms of depression.
§Maximum possible score, 40; higher values indicate more symptoms of anxiety.
¶A total of 29 possible stressors.
**Maximum possible score, 24; higher values indicate better housing and more material goods.

information was collected by telephone. However, at age 19 years there were no between-group differences in body mass index (25.8 ± 6.6 in the chronic iron-deficient group vs 23.8 ± 4.1 years in the iron-sufficient group; $t = 1.54$, $P = .13$).

Secondary analyses that considered subjects who became iron-sufficient after treatment separate from those who were iron-sufficient at enrollment yielded the same statistically significant and suggestive differences compared with the chronic iron-deficient group. For instance, similar to the entire iron-sufficient group (Table II), among those who became iron-sufficient, 24.4% did not complete secondary school, 33.8% were not in school or pursuing further training, and 23.7% were single, again controlling for SES and sex, compared with 58.1%, 76.1%, and 83.9%, respectively, in the chronic iron-deficient group. Details of the secondary analyses are available on request.

To determine whether the major adult outcomes that demonstrated differences depending on infant iron status were interrelated, we examined the correlations among them. We found only 1 statistically significant correlation: not completing secondary school was negatively correlated with self-reported emotional health ($r = -.29$; $P = .001$).

Our analyses that considered pathways leading to poorer adult outcomes focused on educational attainment, marital status, and mental health (Figures 1 and 2). The path analysis for low educational attainment (ie, not completing secondary school) showed indirect paths for chronic iron deficiency in infancy via lower cognitive functioning and a suggestive trend toward more behavior problems in early adolescence. In contrast, for being single, there was only a direct path for iron deficiency in infancy. In the path analyses for mental health outcomes, there was a direct path between iron deficiency in infancy and feelings of detachment/dissociation and a suggestive trend for an indirect path via early adolescent behavior problems. There was an indirect path for iron deficiency in infancy and negative emotions via early adolescent behavior problems and suggestive trends for a direct path and another indirect path via early adolescent cognitive test scores (negative relation).

Discussion

In this long-term follow-up study, subjects who had chronic iron deficiency during infancy had indications of poorer adult functioning in all domains assessed except physical health and employment, partially supporting our framework of cascading effects. In path analyses, previous cognitive test scores and behavior problems contributed to some outcomes. Not completing secondary school was the sole outcome for which an indirect path for chronic iron deficiency via early adolescent outcomes was stronger than the direct effect for iron deficiency in infancy. However, contrary to our expectations, there were no direct or indirect paths for SES of family of origin. For secondary school graduation or further training, this result seems to conflict with our previous report of effects of both SES and iron deficiency in infancy on later cognitive test scores.[13] However, the studies had different foci—moderating effects in the longitudinal

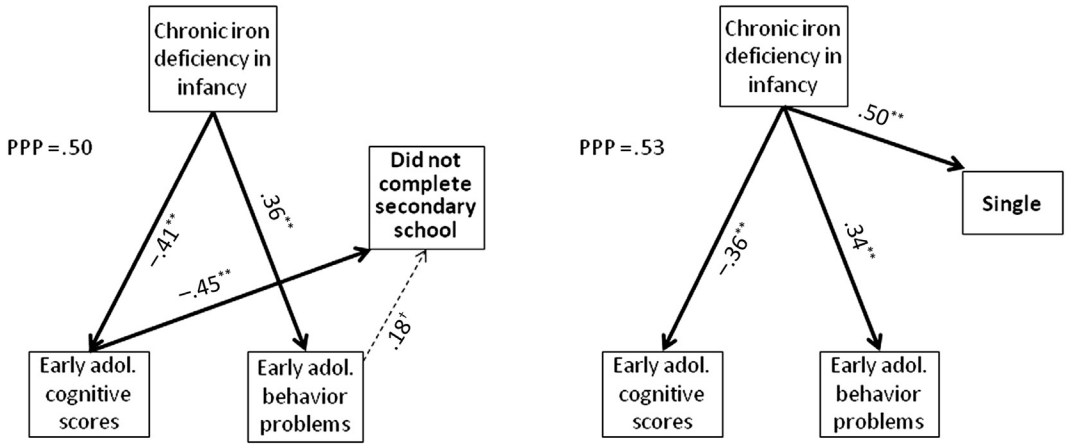

Figure 1. Path analyses for not completing secondary school and being single. Goodness of fit under the Bayesian modeling was assessed by the PPP; values close to .50 in either direction are considered to indicate a good fit, whereas values <.10 or >.90 indicate a poor fit. The path coefficients are provided for all statistically significant or suggestive paths. The strongest paths are shown as *thick lines*, other significant ones as *regular lines*, and those with suggestive trends as *dashed lines*. **P* < .05; ***P* < .01; †*P* < .10. *PPP*, posterior predictive *P* value.

analysis of cognitive scores[13] and mediators of functional outcome in the present study.

As for other early insults, the mechanisms by which chronic iron deficiency in infancy contribute to adverse adult outcomes are undoubtedly complex. Studies of animal models have found that iron deficiency early in life has an adverse impact on the developing brain. Short- and long-term effects include impaired myelination and dendritogenesis; altered neurotransmitter function; changes in neurometabolism in important brain regions, such as the hippocampus, striatum, and cortex; and altered gene and protein profiles, with associated behavioral changes.[8] Neurophysiological and behavioral alterations in human infants are consistent with the central nervous system effects in demonstrated animal models.[5,8,28]

Cascading effects seem likely, regardless of our limited ability to characterize them. For example, early brain effects of chronic severe iron deficiency in infancy may disrupt fundamental neural processes underlying sensory, cognitive, socioemotional, and motor development and contribute to diverging developmental trajectories. Early behavioral differences, such as wariness, hesitance, and lack of positive affect,[14,28] might contribute to long-lasting effects through their impact on caregivers. The chronically iron-deficient infant "might be less likely to seek, receive, or benefit from developmentally supportive interactions with the physical and social environment."[29] Our findings of more feelings of detachment and dissociation in adulthood seem particularly relevant in light of the pattern of behavioral differences in infancy[14] and more internalizing problems in early adolescence.[11]

It is noteworthy that adult functional outcomes were good in subjects with HB >100 g/L and iron deficiency in infancy who became iron-sufficient after 3 months of iron therapy. This finding suggests that poor long-term outcomes, at least on measures of overall functioning, may be prevented if iron treatment is provided before iron deficiency becomes chronic and severe. Good functional outcomes in individuals who became iron-sufficient after treatment during infancy also means that potential adverse effects of iron therapy[30] are not likely a factor in the poor outcomes in individuals with chronic iron deficiency during infancy. This is a consideration, given that the dose of iron was at the high end of the currently recommended range. Subsequent iron deficiency is also unlikely to be a major contributor to outcome, with <5% of subjects classified as iron-deficient at the childhood and adolescent follow-ups.[11,13,16]

Although limited by its small sample size, this Costa Rican study provides data on adult outcomes after iron deficiency in infancy. Like any other observational study, it cannot support causal inferences, despite the control for family SES and consideration of other background differences. Another limitation is the lack of information on the mothers' iron status during pregnancy; moreover, infant iron status was determined at 12-23 months postnatal age, and infant iron deficiency could have started prenatally or in the first year of life. Consequently, this study cannot address the issue of differential effects of iron deficiency depending on its time of occurrence during early development. However, the circumstances of this Costa Rican study are similar to those in many settings worldwide, where programs of iron supplementation in pregnancy and infancy are either absent or less than optimal and infants may be exposed to insufficient iron prenatally and/or postnatally. Thus, the findings may pertain to the real-life experiences of many infants. Other limitations include attrition and interview method. Although there was no differential attrition based on iron status in infancy or almost all background characteristics, one-third of the original cohort could not be located at age 25 years. Obtaining information from subjects in person yielded a higher

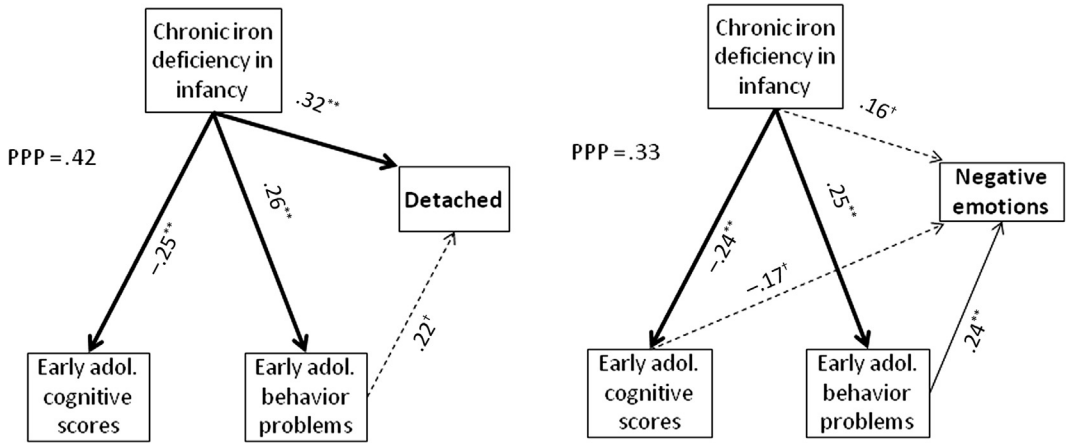

Figure 2. Path analyses for mental health outcomes (negative emotions, feelings of detachment/dissociation). Goodness of fit under the Bayesian modeling was assessed by the PPP; values close to .50 in either direction are considered to indicate a good fit, whereas values <.10 or >.90 indicate a poor fit. The path coefficients are provided for all statistically significant or suggestive paths. The strongest paths are shown as *thick lines*, other significant ones as *regular lines*, and those with suggestive trends as *dashed lines*. $^{*}P < .05$; $^{**}P < .01$; $^{\dagger}P < .10$.

proportion reporting further training/education compared with telephone interviews. These subjects might have had more flexible schedules, allowing them to come in person, or face-to-face contact might have facilitated more detailed responses. Although the higher proportion reporting further training was observed regardless of iron status group and thus does not appear to have affected the findings, uniform in-person data collection would have been stronger.

The Costa Rican sample comprised healthy infants who were growing normally by US standards. The observed outcomes might not generalize to settings where infectious diseases and growth faltering are common. The results also might not pertain to developed countries. However, before the widespread use of iron-fortified infant products in the 1970s iron-deficiency anemia was common in US infants, much like what we observed in the Costa Rica sample. Thus, many adults aged >40 years in the US today are likely to have had iron deficiency anemia during infancy. The situation is similar in Europe and Canada. Because iron therapy in clinical settings is often provided for a shorter period and under less careful supervision than in the Costa Rican study, iron deficiency likely was not fully corrected in many such infants in North America and Europe; thus, our findings may be relevant to these individuals in adulthood.

The adverse effects that we observed in adulthood are substantial. Outcomes such as not completing secondary school or pursuing further training or education may provide a good foundation for estimating the economic impact of early-life iron deficiency, because they are likely to influence career paths and income over time. However, whether long-term outcomes would be as problematic had iron deficiency been detected and treated earlier is unclear.

Compared with individuals who had been iron-sufficient in infancy, adults who had chronic iron deficiency as infants were less likely to complete secondary school or pursue further training and more likely to be single, experience negative emotions, and feel detached or dissociated. If replicated in larger samples, these adverse outcomes represent a substantial loss of human potential that is sad for the individual and detrimental for society. Nonetheless, the fact that subjects with less chronic iron deficiency (with or without anemia) who became iron-sufficient with iron therapy in infancy were functioning well is a reason for optimism. Our findings may help guide practice and policy to prevent or treat iron deficiency before it becomes chronic or severe. ■

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