Iron and Cognitive Function


Effects of iron deficiency anemia on cognitive function in children.

Agaoglu L, Torun O, Unuvar E, Sefil Y, Demir D.

Department of Pediatrics, Istanbul Faculty of Medicine, Istanbul University, Capa, Istanbul, Turkey. leyla.agaoglu@gmail.com

OBJECTIVE: To examine the effects of iron deficiency anemia on cognitive function and intelligence in children. METHODS: Matched case-control study was carried out with 30 children (aged 6-12 years) with iron deficiency anemia (IDA) but without any chronic disease and with normal neuromotor development. The WISC-R intelligence test was performed before and after 4-6 months of iron/vitamin treatment (5 mg iron/kg/day as iron(III)-hydroxide polymaltose complex, IPC, and multivitamin preparation). Pre- and post-treatment IQ scores of the IDA group were evaluated and compared to the control group. RESULTS: Treatment and control groups were similar in terms of age and gender (mean age 9.1 +/- 1.9 years for IDA group, 8.8 +/- 1.5 years for controls, 37 % versus 40 % girls, respectively). Mean total IQ score of the IDA group was 12.9 points lower than that of the control group and this was statistically significant (p < 0.01). Although a highly significant increase of 4.8 points in total IQ was found after treatment with IPC in the IDA group (p < 0.01), post-treatment mean total IQ score of the IDA group was 8.2 points lower than that of the control group. However this difference of 8.2 points was not statistically significant (p > 0.05). There were significant differences in the subtests of WISC-R between the pre-treatment IDA group and the control group. A significant improvement was found especially in these subtests following treatment. CONCLUSION: Iron deficiency anemia in children can affect long-term cognitive function. The WISC-R intelligence test subsets and pre- and post-treatment IQ scores of the IDA group were significantly differing from control group.

PMID: 17691592 [PubMed - indexed for MEDLINE]

Iron and Cognitive Function
Sleep and neurofunctions throughout child development: lasting effects of early iron deficiency.


Sleep and Functional Neurobiology Laboratory, Institute of Nutrition and Food Technology (INTA), University of Chile, Santiago, Chile. ppeirano@inta.cl

Iron-deficiency anemia (IDA) continues to be the most common single nutrient deficiency in the world. Infants are at particular risk due to rapid growth and limited dietary sources of iron. An estimated 20% to 25% of the world's infants have IDA, with at least as many having iron deficiency without anemia. High prevalence is found primarily in developing countries, but also among poor, minority, and immigrant groups in developed ones. Infants with IDA test lower in mental and motor development assessments and show affective differences. After iron therapy, follow-up studies point to long-lasting differences in several domains. Neurofunctional studies showed slower neural transmission in the auditory system despite 1 year of iron therapy in IDA infants; they still had slower transmission in both the auditory and visual systems at preschool age. Different motor activity patterning in all sleep-waking states and several differences in sleep states organization were reported. Persistent sleep and neurofunctional effects could contribute to reduced potential for optimal behavioral and cognitive outcomes in children with a history of IDA.

Publication Types:

- Research Support, N.I.H., Extramural
- Research Support, Non-U.S. Gov't
- Review

PMID: 19214058 [PubMed - indexed for MEDLINE]
A history of iron deficiency anemia during infancy alters brain monoamine activity later in juvenile monkeys.

Coe CL, Lubach GR, Bianco L, Beard JL.

Harlow Center for Biological Psychology, University of Wisconsin, 22 North Charter Street, Madison, WI 53715, USA. ccoe@wisc.edu

Both during and after a period of iron deficiency (ID), iron-dependent neural processes are affected, which raises the potential concern that the anemia commonly experienced by many growing infants could have a protracted effect on the developing brain. To further investigate the effects of ID on the immature brain, 49 infant rhesus monkeys were evaluated across the first year of life. The mothers, and subsequently the infants after weaning, were maintained on a standardized diet containing 180 mg/kg of iron and were not provided other iron-rich foods as treats or supplements. As the infants grew, they were all screened with hematological tests, which documented that 16 (33.3%) became markedly ID between 4 and 8 months of age. During this anemic period and subsequently at 1 year of age, cerebrospinal fluid (CSF) specimens were collected to compare monoamine activity in the ID and iron-sufficient infants. Monoamine neurotransmitters and metabolite levels were normal at 4 and 8 months of age, but by 1 year the formerly anemic monkeys had significantly lower dopamine and significantly higher norepinephrine levels. These findings indicate that ID can affect the developmental trajectory of these two important neurotransmitter systems, which are associated with emotionality and behavioral performance, and further that the impact in the young monkey was most evident during the period of recovery. (c) 2009 Wiley Periodicals, Inc.

Publication Types:
- Research Support, N.I.H., Extramural

PMID: 19194962 [PubMed - in process]

Early-life iron deficiency anemia alters neurotrophic factor expression and hippocampal neuron differentiation in male rats.

Tran PV, Carlson ES, Fretham SJ, Georgieff MK.

Department of Pediatrics, Center for Neurobehavioral Development, University of Minnesota, Minneapolis, MN 55455, USA.

Fetal-neonatal iron deficiency alters hippocampal neuronal morphology, reduces its volume, and is associated with acute and long-term learning impairments. However, neither the effects of early-life iron deficiency anemia on growth, differentiation, and survival of hippocampal neurons nor regulation of the neurotrophic factors that mediate these processes has been investigated. We compared hippocampal expression of neurotrophic factors in male rats made iron deficient (ID) from gestational d 2 to postnatal d (P) 7 to iron-sufficient controls at P7, 15, and 30 with quantitative RT-PCR, Western analysis, and immunohistology. Iron deficiency downregulated brain-derived neurotrophic factor (BDNF) expression in the hippocampus without compensatory upregulation of its specific receptor, tyrosine-receptor kinase B. Consistent with low overall BDNF activity, we found lower expression of early-growth response gene-1 and -2, transcriptional targets of BDNF signaling. Doublecortin expression, a marker of differentiating neurons, was reduced during peak iron deficiency, suggesting impaired neuronal differentiation in the ID hippocampus. In contrast, iron deficiency upregulated hippocampal nerve growth factor, epidermal growth factor, and glial-derived neurotrophic factor accompanied by an increase in neurotrophic receptor p75 expression. Our findings suggest that fetal-neonatal iron deficiency lowers BDNF function and impairs neuronal differentiation in the hippocampus.

Publication Types:

- Research Support, N.I.H., Extramural

PMID: 19022978 [PubMed - indexed for MEDLINE]
Brain iron deficiency and excess; cognitive impairment and neurodegeneration with involvement of striatum and hippocampus.

Youdim MB.

Eve Topf and USA National Parkinson Foundation, Centers of Excellence for Neurodegenerative Diseases Research and Department of Pharmacology, Rappaport Family Research Institute, Technion-Faculty of Medicine, Haifa, Israel. youdim@tx.technion.ac.il

While iron deficiency is not perceived as a life threatening disorder, it is the most prevalent nutritional abnormality in the world, and a better understanding of modes and sites of action, can help devise better treatment programs for those who suffer from it. Nowhere is this more important than in infants and children that make up the bulk of iron deficiency in society. Although the effects of iron deficiency have been extensively studied in systemic organs, until very recently little attention was paid to its effects on brain function. The studies of Oski at Johns Hopkin Medical School in 1974, demonstrating the impairment of learning in young school children with iron deficiency, prompted us to study its relevance to brain biochemistry and function in an animal model of iron deficiency. Indeed, rats made iron deficient have lowered brain iron and impaired behaviours including learning. This can become irreversible especially in newborns, even after long-term iron supplementation. We have shown that in this condition it is the brain striatal dopaminergic-opiate system which becomes defective, resulting in alterations in circadian behaviours, cognitive impairment and neurochemical changes closely associated with them. More recently we have extended these studies and have established that cognitive impairment may be closely associated with neuroanatomical damage and zinc metabolism in the hippocampus due to iron deficiency, and which may result from abnormal cholinergic function. The hippocampus is the focus of many studies today, since this brain structure has high zinc concentration and is highly involved in many forms of cognitive deficits as a consequence of cholinergic deficiency and has achieved prominence because of dementia in ageing and Alzheimer's disease. Thus, it is now apparent that cognitive impairment may not be attributed to a single neurotransmitter, but rather, alterations and interactions of several systems in different brain regions. In animal models of iron deficiency it is apparent that dopaminergic interaction with the opiate system and cholinergic neurotransmission may be defective.

PMID: 18790724 [PubMed - indexed for MEDLINE]
Iron deficiency alters expression of genes implicated in Alzheimer disease pathogenesis.

Carlson ES, Magid R, Petryk A, Georgieff MK.

Department of Pediatrics, University of Minnesota School of Medicine, 420 Delaware Street SE, Minneapolis, MN 55455, USA.

Neonatal brain iron deficiency occurs after insufficient maternal dietary iron intake, maternal hypertension, and maternal diabetes mellitus and results in short and long-term neurologic and behavioral deficits. Early iron deficiency affects the genomic profile of the developing hippocampus that persists despite iron repletion. The purpose of the present study was threefold: 1) quantitative PCR confirmation of our previous microarray results, demonstrating upregulation of a network of genes leading to beta-amyloid production and implicated in Alzheimer disease etiology in iron-deficient anemic rat pups at the time of hippocampal differentiation; 2) investigation of the potential contributions of iron deficiency anemia and iron treatment to this differential gene expression in the hippocampus; and 3) investigation of these genes over a developmental time course in a mouse model where iron deficiency is limited to hippocampus, is not accompanied by anemia and is not repletable. Quantitative PCR confirmed altered regulation in 6 of 7 Alzheimer-related genes (Apbb1, C1qa, Clu, App, Cst3, Fn1, Htatip) in iron-deficient rats relative to iron-sufficient controls at P15. Comparison of untreated to treated iron-deficient animals at this age suggested the strong role of iron deficiency, not treatment, in the upregulation of this gene network. The non-anemic hippocampal iron-deficient mouse demonstrated upregulation of all 7 genes in this pathway from P5 to P25. Our results suggest a role for neonatal iron deficiency in dysregulation of genes that may set the stage for long-term neurodegenerative disease and that this may occur through a histone modification mechanism.

PMID: 18723004 [PubMed - indexed for MEDLINE]

PMCID: PMC2605272 [Available on 2009/10/27]
Iron states and cognitive abilities in young adults: 
neuropsychological and neurophysiological assessment.

Khedr E, Hamed SA, Elbeih E, El-Shereef H, Ahmad Y, Ahmed S.

Department of Neurology and Psychiatry, Assiut University Hospital, P.O. Box 71516, Assiut, Egypt.

Many investigators found that iron deficiency anemia (IDA) had a great influence on cognitive functions in infants and children. However, studies of such topic in adults are few and controversial. We prospectively assessed the possible influence of IDA and iron supplementation (for 3 months) on cognitive function and intelligence of 28 young adults with IDA. We used group of hematological, cognitive, neurophysiological tests for assessment including: mini-mental state examination (MMSE), Wechsler memory scale-revised (WMS-R), Wechsler adult intelligence scale-revised (WAIS-R), event-related potentials (ERPs), and electroencephalography (EEG). Compared to controls, patients demonstrated lower scores of different cognitive tests (MMSE, WMS-R, and WAIS-R), which showed significant improvement after treatment. Prolongation of ERPs latencies (N200 and P300) and reduction in their amplitudes (P200 and P300) were identified with significant increase in amplitude occurred after treatment. EEG abnormalities were observed in 55% of patients which showed improvement in 35% after treatment. Positive correlation was identified before and after treatment between hemoglobin levels and MMSE (P=0.01, 0.05), total verbal (P=0.04) and performance (P=0.05, 0.04) IQ scores. Negative correlation was identified between before and after treatment between P300 latency and total IQ of WAIS-R (P=0.03, 0.008) and hemoglobin level (P=0.4, 0.01). Positive correlation was found before and after treatment between P300 amplitude and total IQ (P=0.028, 0.01) and serum iron (P=0.01, 0.001). In conclusion, IDA is a significant factor in cognitive performance in adult population, which can be partially reversed by treatment.

Publication Types:

- Clinical Trial

PMID: 18574611 [PubMed - indexed for MEDLINE]

Quantitative EEG and cognitive evoked potentials in anemia.

Kececi H, Degirmenci Y.

Department of Neurology, Duzce University Medical Faculty, Duzce, Turkey. hulusikececi@dtip.edu.tr

OBJECTIVE: The anemic status may alter brain functions and electrogensis, as reflected by EEG and cognitive EPs (CEPs). This study aims to evaluate CEPs and EEG power spectra in adult patients with iron-deficiency anemia and to determine the effects of appropriate iron therapy on electrodiagnostic findings.

METHODS: Fifty-one patients with iron-deficiency anemia underwent CEP and EEG recording. All patients were re-assessed after three months of oral-iron therapy. RESULTS: All patients had recovered from their anemia through the three-month iron therapy. Central N1 amplitude and parietal P2 amplitude was increased. N2 latencies were shortened in frontal and central regions. P3 latencies were shortened in frontal, central and parietal areas and P3 amplitude was increased in the parietal region. Except in the gamma-band, all pretreatment and post-treatment mean-power values were significantly lower at the temporal, parietal and occipital regions. CONCLUSIONS: This study indicates that in iron-deficiency anemia, appropriate iron therapy can improve brain electrogensis, as reflected by P300 and EEG power spectra.

PMID: 18423335 [PubMed - indexed for MEDLINE]
Selective impairment of cognitive performance in the young monkey following recovery from iron deficiency.

Lubach GR, Coe CL.

Harlow Center for Biological Psychology, Department of Psychology, University of Wisconsin, Madison, Wisconsin 53715, USA. grlubach@wisc.edu

OBJECTIVE: While poor nutrition during development is an obvious concern, the magnitude and duration of the neural and cognitive deficits that occur after moderate iron deficiency in infancy have remained controversial. A nonhuman primate model of infancy anemia was refined to investigate the effects on cognitive performance. METHODS: Young rhesus monkeys that experienced a delimited period of iron deficiency were tested on a series of cognitive tasks following normalization of their hematological status. Beginning at 8 to 9 months of age, 2 months after weaning from their mothers and consumption of solid food, the previously iron-deficient (ID) monkeys (n = 17) were compared to age- and gender-matched, iron-sufficient (IS) (n = 27) monkeys on a series of three tests of cognitive performance. Using the Wisconsin General Testing Apparatus, a Black/White Discrimination task was followed by acquisition of Black/White Reversal (BWR). RESULTS: ID monkeys were significantly slower at mastering the BWR task (p < .04), which required reversing and inhibiting the previously learned response. In addition, ID infants were significantly less object oriented (p < .017) and more distractible (p < .018). However, on two subsequent tests, the Concurrent Object Discrimination and Delayed Non-Match-to-Sample, there were no differences in acquisition, performance, or behavioral reactivity.

CONCLUSIONS: The initial cognitive and behavioral deficits are similar to those seen in follow-up evaluations of anemic children, but the limited extent of the impairment after this moderate iron deficiency that involved a select nutrient deficiency is encouraging for the benefits attainable through early identification and iron supplementation.

Publication Types:

- Research Support, N.I.H., Extramural

PMID: 18300719 [PubMed - indexed for MEDLINE]
The role of iron in neurodevelopment: fetal iron deficiency and the developing hippocampus.

Georgieff MK.

Department of Pediatrics, Division of Neonatology, University of Minnesota School of Medicine, Minneapolis, MN 55455, USA. georg001@umn.edu

Iron is a ubiquitous nutrient that is necessary for normal neurodevelopment. Gestational conditions that compromise fetal iron status include maternal iron deficiency, smoking, diabetes mellitus and hypertension. The iron-deficient neonate has altered recognition memory function and temperament while iron-deficient. The memory deficits persist even after iron repletion. Animal models demonstrate that early iron deficiency affects neuronal and glial energy metabolism, monoamine metabolism and myelination, consistent with behavioural findings in human infants. Of particular recent interest are genomic changes in transcripts coding for signal transduction, dendritic structure and energy metabolism induced by early iron deficiency that last well into adulthood in spite of iron treatment. Early iron sufficiency is critical for long-term neurological health.

Publication Types:

- [Research Support, N.I.H., Extramural]
- [Review]

PMID: 19021538 [PubMed - indexed for MEDLINE]
The role of iron dysregulation in the pathogenesis of multiple sclerosis: an Egyptian study.

Abo-Krysha N, Rashed L.

Department of Neurology, Cairo University, Cairo, Egypt. nhtaha@yahoo.com

BACKGROUND: Iron is essential for virtually all types of cells and organisms. The significance of iron for brain function is reflected by the presence of receptors for transferrin on brain capillary endothelial cells. Iron imbalance is associated with proinflammatory cytokines and oxidative stress, which have been implicated in the pathogenesis of multiple sclerosis (MS). Transferrin receptor (TfR) is the major mediator of iron uptake. Its expression is increased to facilitate iron entrance into the cell. The increased serum level of soluble transferrin receptor (sTfR) may indicate an abnormal intracellular distribution of iron and a decrease in the cytoplasmic compartment. OBJECTIVE: Our objective is to assess the possible role of iron metabolism dysfunction in the pathogenesis of MS. METHODS: Thirty subjects were selected from the Neurology Department of Kasr El-Aini hospital, Cairo University: 20 MS patients, where nine patients were relapsing and progressive (secondary progressive (SP) of which six were secondary progressive active (SP-A) and three were secondary progressive stable (SP-S)), seven were relapsing-remitting active (RR-A) and four were primary progressive (PP); and 10 control subjects matched in age and sex. Each patient was subjected to a thorough general medical and neurological examination, Kurtzke MS rating scales, laboratory assessment, neuro-imaging, evoked potentials and quantitative determination of the indices of iron metabolism, such as serum iron and sTfR. RESULTS: The serum level of sTfR was significantly higher in our MS patients compared with the control group (p = 0.0001). The levels were significantly higher in SP-A (p = 0.001), SP-S (p = 0.01), RR-A (p = 0.0001) and PP (p = 0.003) patients than in controls. Iron values were within normal limits in all patients. The increased serum sTfR level in non-anemic MS patients with active disease reflects the increased iron turnover. The elevation of sTfR levels in stable patients may indicate active inflammation with ongoing oxidative damage that is not detectable by history or examination. CONCLUSIONS: Iron overload and upregulation of iron-handling proteins, such as TfR, in the MS brain can contribute to pathogenesis of Multiple Sclerosis and iron imbalance is associated with a pro-oxidative stress and a proinflammatory environment, this suggest that iron could be a target for MS therapy to improve neuronal iron metabolism.

PMID: 18408021 [PubMed - indexed for MEDLINE]
Iron deficiency and infant motor development.

**Shafir T, Angulo-Barroso R, Jing Y, Angelilli ML, Jacobson SW, Lozoff B.**

Center for Human Growth and Development, University of Michigan, Ann Arbor, Michigan 48109-5406, USA.

BACKGROUND: Iron deficiency (ID) during early development impairs myelination and basal ganglia function in animal models. AIMS: To examine the effects of iron deficiency anemia (IDA) and iron deficiency (ID) without anemia on infant motor skills that are likely related to myelination and basal ganglia function. STUDY DESIGN: Observational study. SUBJECTS: Full-term inner-city African-American 9- to 10-month-old infants who were free of acute or chronic health problems with iron status indicators ranging from IDA to iron sufficiency (n=106). Criteria for final iron status classification were met by 77 of these infants: 28 IDA, 28 non-anemic iron-deficient (NA ID), and 21 iron-sufficient (IS). OUTCOME MEASURES: Gross motor developmental milestones, Peabody Developmental Motor Scale, Infant Neurological International Battery (INFANIB), motor quality factor of the Bayley Behavioral Rating Scale, and a sequential/bi-manual coordination toy retrieval task. General linear model analyses tested for linear effects of iron status group and thresholds for effects. RESULTS: There were linear effects of iron status on developmental milestones, Peabody gross motor (suggestive trend), INFANIB standing item, motor quality, and toy retrieval. The threshold for effects was ID with or without anemia for developmental milestones, INFANIB standing item, and motor quality and IDA for toy retrieval. CONCLUSIONS: Using a comprehensive and sensitive assessment of motor development, this study found poorer motor function in ID infants with and without anemia. Poorer motor function among non-anemic ID infants is particularly concerning, since ID without anemia is not detected by common screening procedures and is more widespread than IDA.

Publication Types:
- Research Support, N.I.H., Extramural
- Research Support, Non-U.S. Gov't

PMID: 18272298 [PubMed - indexed for MEDLINE]
Cellular iron concentrations directly affect the expression levels of norepinephrine transporter in PC12 cells and rat brain tissue.

**Beard JL, Wiesinger JA, Jones BC**

Department of Nutritional Science, S-128 Henderson South Building, The Pennsylvania State University, University Park, PA 16802, USA. jbeard@psu.edu

Neurological development and functioning are adversely affected by iron deficiency in early life. Iron-deficient rats are known to have elevations in extracellular DA and NE, suggesting alterations in reuptake of these monoamines. To explore possible mechanisms by which cellular iron concentrations may alter NE transporter functioning, we utilized NET expressing PC12 cells and iron-deficient rats to explore the relationship between NET protein and mRNA expression patterns and iron concentrations. Treatment of PC12 with the iron chelator, desferrioxamine mesylate (DFO, 50 microM for 24 h), significantly decreased [3H] NE uptake by more than 35% with no apparent change in Km. PC12 cells exposed to increasing concentrations of DFO (25-100 microM) exhibited a dose response decrease in [3H] NE uptake within 24 h (38-73% of control) that paralleled a decrease in cellular NET protein content. Inhibition of protein synthesis with cycloheximide resulted in NET disappearance rates from DFO-treated cells greatly exceeding the rate of loss from control cells. RT-PCR analysis revealed only a modest decrease in NET mRNA levels. Rat brain locus ceruleus and thalamus NET mRNA levels were also only modestly decreased (10-15%) despite a 40% reduction in regional brain iron. In contrast, NET proteins levels in thalamus and locus ceruleus were strongly affected by regional iron deficiency with high correlations with iron concentrations (r > 0.94 and r > 0.80 respectively). The present findings demonstrate that NET protein concentrations and functioning are dramatically reduced with iron deficiency; the modest effect on mRNA levels suggests a stronger influence on NET trafficking and degradation than on protein synthesis.

Publication Types:

- Research Support, N.I.H., Extramural

PMID: 16650837 [PubMed - indexed for MEDLINE]
Iron deficiency alters expression of genes implicated in Alzheimer disease pathogenesis.

Carlson ES, Magid R, Petryk A, Georgieff MK.

Department of Pediatrics, University of Minnesota School of Medicine, 420 Delaware Street SE, Minneapolis, MN 55455, USA.

Neonatal brain iron deficiency occurs after insufficient maternal dietary iron intake, maternal hypertension, and maternal diabetes mellitus and results in short and long-term neurologic and behavioral deficits. Early iron deficiency affects the genomic profile of the developing hippocampus that persists despite iron repletion. The purpose of the present study was threefold: 1) quantitative PCR confirmation of our previous microarray results, demonstrating upregulation of a network of genes leading to beta-amyloid production and implicated in Alzheimer disease etiology in iron-deficient anemic rat pups at the time of hippocampal differentiation; 2) investigation of the potential contributions of iron deficiency anemia and iron treatment to this differential gene expression in the hippocampus; and 3) investigation of these genes over a developmental time course in a mouse model where iron deficiency is limited to hippocampus, is not accompanied by anemia and is not repletable. Quantitative PCR confirmed altered regulation in 6 of 7 Alzheimer-related genes (Apbb1, C1qa, Clu, App, Cst3, Fn1, Htatip) in iron-deficient rats relative to iron-sufficient controls at P15. Comparison of untreated to treated iron-deficient animals at this age suggested the strong role of iron deficiency, not treatment, in the upregulation of this gene network. The non-anemic hippocampal iron-deficient mouse demonstrated upregulation of all 7 genes in this pathway from P5 to P25. Our results suggest a role for neonatal iron deficiency in dysregulation of genes that may set the stage for long-term neurodegenerative disease and that this may occur through a histone modification mechanism.

Publication Types:

- Research Support, N.I.H., Extramural
- Research Support, Non-U.S. Gov't

PMID: 18723004 [PubMed - indexed for MEDLINE]

PMCID: PMC2605272 [Available on 2009/10/27]
Iron treatment normalizes cognitive functioning in young women.

Murray-Kolb LE, Beard JL.

Department of Nutritional Sciences, The Pennsylvania State University, University Park, PA, USA. lmurrayk@jhsph.edu

BACKGROUND: Evidence suggests that brain iron deficiency at any time in life may disrupt metabolic processes and subsequently change cognitive and behavioral functioning. Women of reproductive age are among those most vulnerable to iron deficiency and may be at high risk for cognitive alterations due to iron deficiency. OBJECTIVE: We aimed to examine the relation between iron status and cognitive abilities in young women. DESIGN: A blinded, placebo-controlled, stratified intervention study was conducted in women aged 18-35 y of varied iron status who were randomly assigned to receive iron supplements or a placebo. Cognition was assessed by using 8 cognitive performance tasks (from Detterman's Cognitive Abilities Test) at baseline (n = 149) and after 16 wk of treatment (n = 113). RESULTS: At baseline, the iron-sufficient women (n = 42) performed better on cognitive tasks (P = 0.011) and completed them faster (P = 0.038) than did the women with iron deficiency anemia (n = 34). Factors representing performance accuracy and the time needed to complete the tasks by the iron-deficient but nonanemic women (n = 73) were intermediate between the 2 extremes of iron status. After treatment, a significant improvement in serum ferritin was associated with a 5-7-fold improvement in cognitive performance, whereas a significant improvement in hemoglobin was related to improved speed in completing the cognitive tasks. CONCLUSIONS: Iron status is a significant factor in cognitive performance in women of reproductive age. Severity of anemia primarily affects processing speed, and severity of iron deficiency affects accuracy of cognitive function over a broad range of tasks. Thus, the effects of iron deficiency on cognition are not limited to the developing brain.

Publication Types:
- Randomized Controlled Trial
- Research Support, N.I.H., Extramural
- Research Support, U.S. Gov't, Non-P.H.S.

PMID: 17344500 [PubMed - indexed for MEDLINE]
Acquisition of visuomotor abilities and intellectual quotient in children aged 4-10 years: relationship with micronutrient nutritional status.


Instituto de Desarrollo e Investigaciones Pediátricas, Centro Asociado a la Comisión de Investigaciones Científicas de la Provincia de Buenos Aires, Hospital de Niños Sor María Ludovica, La Plata, Argentina. horaciofgonzalez@gmail.com

Lethargy, poor attention, and the high rate and severity of infections in malnourished children affect their educational achievement. We therefore studied the association between visuomotor abilities and intelligence quotient (IQ) and their relationship with iron, zinc, and copper. A cross-sectional study was carried out on a sample of 89 healthy children (age range, 4-10 years). Evaluations of visuomotor ability and IQ were performed with the Developmental Test of Visual Motor Integration (VMI) and the Scale for Measurement of Intelligence for children aged 3-18 years, respectively. Nutritional status was assessed using anthropometry and biochemical assessments, which included serum ferritin, zinc and copper levels, and Hb. The sample was classified as having low or normal VMI scores: 47 children (52.8%, mean age 7 +/- 1.5 years) had low VMI, and 42 (47.2%, mean age 7 +/- 2.06 years) had normal VMI. There were no statistically significant differences in socioeconomic and cultural condition between both groups. We found significantly higher serum copper and ferritin levels in normal as compared to low VMI, but we did not find any differences with zinc. IQ was significantly higher in normal vs low VMI children. The fact that children with abnormal VMI presented low mean serum copper and ferritin concentrations could indicate that copper and iron deficiencies in this sample could be related with visuomotor abilities.

Publication Types:

- Research Support, Non-U.S. Gov't

PMID: 17916959 [PubMed - indexed for MEDLINE]
Once-weekly and 5-days a week iron supplementation differentially affect cognitive function but not school performance in Thai children.

Sungthong R, Mo-suwan L, Chongsuvivatwong V, Geater AF.

Epidemiology Unit, Faculty of Medicine, Prince of Songkla University, Songkla 90110, Thailand. rassamee@ratree.psu.ac.th

Many studies have reported comparable hemoglobin response in subjects given intermittent and daily iron supplements. However, the effect of intermittent iron supplementation on impaired cognitive function, one of the serious consequences of iron deficiency among children, has not been studied. We investigated the effects of 1 d/wk (weekly) and 5 d/wk (daily) iron supplementation on changes in results of intelligence quotient (IQ), Thai language, and mathematics tests among Thai primary schoolchildren. A double-blind, randomized, placebo-controlled trial was conducted. Primary schoolchildren (n = 397) were randomly assigned to receive iron supplements daily or weekly or placebo. Ferrous sulfate (300 mg) or placebo tablets were given under direct observation by the researcher for 16 wk. Changes in IQ, and Thai language and mathematics scores were then compared. The increases in hemoglobin concentration were comparable in the weekly and daily iron supplementation groups but serum ferritin increased more in the children supplemented daily. Children receiving daily iron supplements, however, had a significantly lower increase in IQ (3 +/- 12 points) than those receiving the supplement weekly (6 +/- 12 points) or placebo (6 +/- 12 points), whereas the last-mentioned two groups did not differ. Z-scores of Thai language and mathematics test results did not differ among the groups. We conclude that weekly iron supplementation is the regimen of choice in this study community.

Publication Types:

- Clinical Trial
- Randomized Controlled Trial
- Research Support, Non-U.S. Gov't

PMID: 15333727 [PubMed - indexed for MEDLINE]
Effect of iron supplementation on cognition in Greek preschoolers.

Metallinos-Katsaras E, Valassi-Adam E, Dewey KG, Lönnerdal B, Stamoulakatou A, Pollitt E.

Simmons College, Boston, MA 02132, USA. metallin@simmons.edu

OBJECTIVE: To examine effects of iron supplementation on vigilance, attention and conceptual learning in preschool children in Greece. DESIGN: Randomized Double-Blind Placebo Controlled trial of iron. Randomization stratified by iron status and day care center (DCC). SETTING: Nine public DCCs in Athens, Greece. SUBJECTS: In all, 49 3-4-y olds (21 anemic, 28 good iron status) with birth weight not less than 2500 g, currently healthy; benign past medical history, IQ > or =1 s.d. below the age-adjusted mean, serum Pb < or =200 ppb (none exceeded 50 ppb), and height, weight and head circumference for age > or =10th percentile. Anemia defined as: (1) pretreatment Hgb <112 g/l and TS <16% and ferritin <12 microg/L OR (2) Hgb rise of >10 g/l (T2-T0) with iron supplementation. Good iron status was defined as baseline levels of Hgb >120 g/l and either TS >20% or serum ferritin >12 microg/l. INTERVENTION: The intervention consisted of a 2-month supplementation of 15 mg iron (and MV) vs placebo (MV alone). RESULTS: After iron treatment, the anemic subjects made significantly fewer errors of commission (14% higher specificity, P<0.05), exhibited 8% higher accuracy (P<0.05) and were significantly more efficient (mean difference=1.09, P<0.05) than those given placebo. These effects of iron were not found among preschoolers with good iron status. No effects of iron treatment were found on the Oddity Learning task. CONCLUSIONS: This study demonstrated that iron supplementation of iron-deficient anemic preschoolers results in an improvement in discrimination, specifically selective attention.
Effects of haemoglobin and serum ferritin on cognitive function in school children.

Sungthong R, Mo-suwan L, Chongsuvivatwong V.

Epidemiology Unit, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand. sburapat@medicine.psu.ac.th

The association between iron deficiency anaemia and cognitive function impairment has been widely reported in young children, but whether the impairment is a result of iron deficiency per se or a combination of iron deficiency and anaemia, and how these conditions interact, is still questionable. Four hundred and twenty-seven school children from two schools in socioeconomically deprived communities were selected in southern Thailand. Iron status was determined by haemoglobin and serum ferritin concentrations. Cognitive function in this study was measured by IQ test and school performance, including Thai language and mathematics scores, using z-scores based on distributions within the same grade and school. Data on demography and socioeconomic status were collected by questionnaire answered by the parents. Linear regression models were used to investigate the effect of anaemia and iron deficiency, reflected by haemoglobin and serum ferritin concentration, on cognitive function and school performance. We found that cognitive function increased with increased haemoglobin concentration in children with iron deficiency, but did not change with haemoglobin concentration in children with normal serum ferritin level. Children with iron deficiency anaemia had consistently the poorest cognitive function (IQ, 74.6 points; Thai language score, 0.3 SD below average; and mathematics score, 0.5 SD below average). Children with non-anaemic iron deficiency but with high haemoglobin levels had significantly high cognitive function (IQ, 86.5 points; Thai language score, 0.8 SD above average; and mathematics score, 1.1 SD above average). This study found a dose-response relationship between haemoglobin and cognitive function in children with iron deficiency, whereas no similar evidence was found in iron sufficient children.

Publication Types:

- Research Support, Non-U.S. Gov't

PMID: 12074177 [PubMed - indexed for MEDLINE]
Iron deficiency anaemia influences cognitive functions.

Petranovic D, Batinac T, Petranovic D, Ruzic A, Ruzic T.

Department of Hematology, Rijeka University Hospital, Kresimirova 42, 51000 Rijeka, Croatia.

Many diseases, different nutritional, metabolic and hormonal changes, ageing and drugs can alter cognitive functions. Anemia via cerebral hypoxia and other possible mechanisms has been suggested to have a great influence on cognition. Iron deficiency anemia, the most common form of anemia, has been suggested to result in cognitive deterioration and alteration of neurological functions. Previous studies resulted in significant discrepancies considering correlation between anemia and cognitive achievement mainly because different or not sensitive enough tests used to measure cognition. We suggest a significant influence of iron deficiency anemia on dynamic properties and functional features of the central nervous system activity. Cognitive achievement is strongly related to hemoglobin level and could be expected in all patients. Higher hemoglobin level results in better CNS function. As a first step in confirming or refuting our hypotheses we suggest standardization of the method used to measure cognition, such as a very sensitive apparatus like Complex reactivity Drenovac (CRD).

PMID: 17574345 [PubMed - indexed for MEDLINE]