Causes of Iron and Zinc Deficiencies and Their Effects on Brain

Harold H. Sandstead

Division of Human Nutrition, Department of Preventive Medicine and Community Health, The University of Texas Medical Branch, Galveston, TX 77555-1109

ABSTRACT

Low consumption of foods rich in bioavailable iron (Fe) and zinc (Zn) such as meat, particularly red meat, and high consumption of foods rich in inhibitors of Fe and Zn absorption, such as phytate, certain dietary fibers and calcium, cause Fe and Zn deficiencies. Neuropsychologic impairment is one of several potential outcomes of these deficiencies. J. Nutr. 130: 347S–349S, 2000.

KEY WORDS: • iron • zinc • cognition • brain • diet • humans

Fe deficiency affects >2 billion people (Viteri 1998), and Zn deficiency is also common (Gibson 1994, Sandstead 1995). Because Fe and Zn are most bioavailable from many of the same foods and their absorption is inhibited by many of the same dietary substances, Fe and Zn deficiencies may occur simultaneously (Sandstead and Smith 1996).

The National Health and Nutrition Examination Survey (NHANES)-III found that 16% of black and 20% of Mexican-American women, aged 20–49 y in the United States were Fe deficient (Looker et al. 1997). Women who were poor (~17%), less educated (<12 y; ~15%), and high gravidity (≥4; ~21%), girls ages 12–19 y (9–11%) and toddlers (~9%) were especially affected. Thus, in the U.S., ~7.8 million women and 700,000 toddlers are Fe deficient and ~3.3 million women and 240,000 toddlers have Fe deficiency anemia.

Consumption data (Alaimo et al. 1994) and factorial estimates of requirements (Sandstead and Smith 1996) suggest that mild Zn deficiency is also common in the U.S. NHANES-III found median Zn intakes less than the RDA in almost all groups. For example, Zn intakes of females, aged 12–19 y, were 53–78% of the 1989 RDA (NRC 1989).

With the exception of some fortified foods, beef is the richest common dietary source of both Fe and Zn. The 1989–1991 USDA Continuing Survey of Food Intakes of Individuals (U.S. Department of Agriculture 1995) found that ready-to-eat cereals and yeast bread were the major sources of Fe (18.6 and 13.6%, respectively) and that beef was the major source of Zn (25.7%) for U.S. adults (Subar et al. 1998a and 1998b).

Food Fe occurs in two forms, heme-Fe and nonheme-Fe. Nearly 50% of the Fe in meat is heme-Fe (Fe-protoporphyrin); it is 15–35% bioavailable (Monsen 1988). With the exception of calcium (Ca), dietary inhibitors that impair nonheme-Fe absorption do not impair heme-Fe absorption (Hallberg et al. 1991). Most Fe in the diet is nonheme-Fe. Its absorption ranges from 2 to 20% (Monsen 1988), depending on the person’s Fe status and the presence in the diet of facilitators and inhibitors of absorption. Facilitators of nonheme-Fe include meat (Hulten et al. 1995) and ascorbic acid (Hallberg et al. 1989). Zn absorption is facilitated by meat (Hunt et al. 1995). Ascorbic acid has no beneficial effect on Zn retention (Sandstrom and Cederblad 1987).

Phytates (5 and 6 phosphate inositol) in cereal products, legumes and nuts inhibit Fe and Zn absorption. Humans are unable to compensate for the inhibitory effects of phytate (Brune et al. 1989). High phytate:Zn and phytate × Ca:Zn molar ratios increase the risk of Zn deficiency (Gibson et al. 1991, Gibson and Huddle 1998). The phytate content of foods is not currently listed in publicly available USDA databases (Food Nutrition Information Service 1998).

Other nondigestible ligands that inhibit absorption of nonheme-Fe and Zn include some dietary fibers (Brune et al. 1992, Krudsen et al. 1996), lignins (Fernandez and Phillips 1982), and products of nonenzymatic Maillard browning (Lykken et al. 1986, Rehner and Walter 1991). Phenolic polymers inhibit nonheme-Fe absorption (Tuntawiroon et al. 1991) but have little effect on Zn (Ganjii and Kies 1994).

Ca (dietary or supplemental) impairs absorption of heme- and nonheme-Fe in a dose-dependent manner and independently of other dietary factors (Gleerup et al. 1995). Ca supplements may (Wood and Zheng 1997) or may not (Dawson-Hughes et al. 1986) inhibit Zn absorption.

Impaired neuropsychologic function is one of the adverse effects of severe Fe and Zn deficiencies (Henkin et al. 1975, Pollitt 1993). Less severe deficiencies also impair performance (Pollitt 1993, Sandstead et al. 1998).

Fe is highly localized in dopaminergic-peptidergic regions, such as the globus pallidus, substantia nigra, red nucleus,
thalamus, caudate nucleus and nucleus accumbens (Youdim and Ben-Shachar 1987). Nonheme-Fe concentrations in brain and the number of dopamine D2 receptors are decreased by Fe deficiency in experimental animals, and learning is decreased. The neuropsychologic effects of Fe deficiency with or without anemia have been studied in infants and children (Pollitt 1993). Some studies found Fe repletion improved function, whereas others did not. Some studies found that Fe deficiency during brain development resulted in residual abnormalities (Roncagliolo et al. 1998). The role of simultaneous deficiencies of other nutrients such as Zn in these phenomena is unclear (Hallberg 1989).

Research on the effects of Fe nutriture on cognition of adolescents and adults has been limited. In college students (n = 68), serum ferritin concentrations were related directly to characteristics of the electroencephalogram (EEG) and cognitive performance (Tucker et al. 1984). A study of nonanemic Fe-deficient high school girls found improved verbal learning and memory after Fe repletion (Bruner et al. 1996). A cross-sectional study in the elderly (n = 28) found that Fe status was associated with characteristics of the EEG (Tucker et al. 1990).

Concentrations of Zn in brain are highest in telencephalon and gray matter of cerebral cortex (Hu and Fiede 1968). Severe Zn deficiency caused increases in brain norepinephrine concentrations in rats (Wallwork et al. 1982), but had no effect on Zn concentrations in hippocampus or cortex (Wallwork et al. 1982). In contrast, mild Zn deficiency had no effect on whole-brain catecholamines (Halas et al. 1982). A special class of glutaminergic neurons has Zn-containing vesicles in its axon terminals (Frederickson and Moncrieff 1994). Vesicle Zn released during neurotransmission modulates postsynaptic N-methyl-D-aspartate receptors for glutamate (Westbrook and Mayer 1987), including calcium-channels (Browning and O’Dell 1995). In vitro findings indicate that oxidation of metallothionein by oxidized glutathione or analogous selenium compounds releases Zn to specific ligands. Glutathione and ATP facilitate this process (Jacob et al. 1998; Jiang et al. 1998). Zn-ATP is necessary for synthesis of pyridoxal-5-phosphate (Churchich et al. 1989) and flavin adenine dinucleotide (Yamada et al. 1990), coenzymes essential for biogenic-amino acid synthesis (Dakshinamurti et al. 1990) and monamine oxidase metabolism (Hsu et al. 1988).


Relationships between Zn-nutrition and brain function of humans have been reported. In Egyptian women, consumption of foods derived from animals rich in Zn during pregnancy was associated with their infants having higher attention scores on the Brazelton Neonatal Development Assessment Scale (Kirksey et al. 1991). At 6 mo of age, motor performance on the Bayley Scales of Infant Development was inversely related to maternal intakes of low bioavailable Zn from plants, phytate and fiber (Kirksey et al. 1994). Low hair Zn concentration, an indicator of low Zn status, was associated with poor reading performance and decreased EEG coherence in the frontal lobe (Thatcher et al. 1984). Two 10-21 double-blind, randomized controlled trials found improved neuropsychologic function in 740 Chinese (Sandstead et al. 1998) and 240 Mexican-American 6- to 9-y-old children (Penland et al. 1999) who were repleted simultaneously with 20 mg Zn/d and other potentially limiting micronutrients. A postmortem study of 12 elderly women found a negative association between plasma Zn 1 y before death and the number of senile and diffuse plaques in their brains (Tully et al. 1995).

**SUMMARY**

Fe and Zn deficiencies are common and can occur simultaneously. Mild-to-moderate deficiencies impair neuropsychologic function.

**LITERATURE CITED**


