



TECHNICAL SUMMARY

HUMAN NUTRITION RESEARCH

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Beef's Nutrients and Cognition

Introduction

Cognition, or one's ability to perceive, think, and remember, is influenced by many factors, one of which is nutrition.¹ Protein-energy malnutrition, a multiple nutrient deficiency syndrome, is associated with a variety of cognitive and behavioral deficits. Among children, protein-energy malnutrition adversely impacts mental development and cognition.^{2,3} It also reduces children's interaction with the environment which, in turn, can lead to problems with attention, perception, motivation, motor control, physical activity, and responsiveness. Each of these behaviors may compromise children's ability to learn and their school performance. Among older adults, malnutrition may lead to cognitive deficits and reduce their ability to function independently.⁴ Even short-term nutritional deprivation, hunger, or skipping a meal can adversely affect cognitive development and performance.⁵

Deficiencies of specific nutrients, in particular iron and zinc, may be involved in many of the same effects ascribed to protein-energy malnutrition. Impaired cognitive function is one of several potential outcomes associated with deficiencies of iron, zinc, and some B vitamins.^{2,6,7} Given that beef is a good or excellent source of many nutrients (e.g., readily bioavailable iron, zinc, several B vitamins, etc.) involved in cognitive development, it is of particular interest to determine whether intake of red meat, such as beef, affects cognition.

When examining studies of nutrition and cognition, it is important to appreciate the difficulties in comparing findings across studies. These difficulties stem from differences in tests used to measure specific cognitive functions, the choice of the diagnostic criteria used to

define nutritional status, and potential confounding factors such as deficiencies of other nutrients and socioeconomic factors (e.g., poverty, quality of the care-giving environment).^{2,6,8,9} For example, supplementation with micronutrients in children at high risk for micronutrient deficiencies may improve cognitive performance, whereas micronutrient supplementation may have little beneficial effect on cognitive performance in healthy, well nourished children.²

Iron's Role in Cognition

Iron is an essential nutrient¹⁰ that has multiple structural and metabolic roles in the development and function of the human brain.¹¹ In addition to its role in oxygen transport and protection of cells from oxidative damage, iron is required by enzymes involved in specific brain functions, including myelination and synthesis of the neurotransmitters, serotonin and dopamine (a precursor of epinephrine and norepinephrine).¹¹

Findings from both experimental animal and human studies provide evidence for the role of iron in cognitive function.^{3,12} In laboratory animals, iron deficiency during gestation and lactation reduces iron in specific areas of the brain, which in turn impairs myelination of nerve cells and neurotransmitters, especially dopamine.¹¹ These changes could lead to alterations in the maturation and function of a variety of aspects of the central nervous system involved in specific behaviors. Iron deficiency in experimental animals could also affect cognitive behaviors by reducing animals' attentiveness and responsiveness to environmental stimuli. This, in turn, could lead to fewer learning experiences and less ability to obtain information. Research in experimental animals indicates that the timing

of iron deficiency (i.e., prenatally vs. postnatally) influences specific behavioral consequences.^{13,14} Experimental animal studies also point to potential mechanisms.¹⁵

Human studies indicate that adequate iron nutrition, from infancy through later adult years, is important to realize cognitive potential. Most of the research in this area has involved infants, preschoolers, and school-age children.^{8,11} Numerous observational studies consistently show that iron deficiency anemia, and possibly milder forms of iron deficiency, are associated with decreased cognitive development compared to that in iron sufficient subjects.^{8,11,16} Using data from more than 5,300 children aged 6 to 16 years from NHANES (National Health and Nutrition Examination Survey) III, researchers demonstrated that children with iron deficiency, with and without anemia, had lower test scores on a standardized mathematics test than did children with normal iron status.¹⁶ Iron deficient infants, preschoolers, and school-aged children are also described as being withdrawn, cautious, inattentive, and lethargic, which could interfere with their ability to interact with the environment and compromise their intellectual development.^{17,18} As reviewed by Lozoff¹⁵, almost every case-control study that has examined social-emotional behavior has found that iron deficient or anemic infants tend to be more wary, hesitant, and keep closer to their mothers than infants who are not iron deficient. Similarly preschool children with iron deficiency anemia demonstrate altered affective and behavioral effects compared to nonanemic preschoolers.¹⁸

Additional support for a causal link between iron status and cognitive development comes from studies of iron supplementation.^{8,19} As stated in a review by Grantham-McGregor and Ani,⁸ “the evidence for a beneficial effect of iron treatment on cognition in anemic older children is reasonably convincing, but it would be helpful to run one or two more rigorous RCT (randomized controlled trials) with detailed reporting of the results.” More recently, Sachdev and coworkers¹⁹ concluded that “iron supplementation improves mental development score modestly. This effect is particularly apparent for intelligence tests above 7 years of age and in initially anemic or iron-deficient anemic subjects.” However, according to a number of controlled iron intervention trials, there is insufficient evidence to conclude that correction of anemia and possibly less severe forms of iron deficiency in children less than 2 years of age improves cognitive development.^{8,15,19} Long-term studies that evaluated the effects of early iron deficiency have demonstrated that children with iron deficiency anemia,

chronic severe iron deficiency, or anemia in infancy continue to perform less well on tests of overall mental, motor, and social/emotional functioning and on specific neurocognitive tests from preschool to adolescence.¹⁵ Moreover, the adverse consequences of early iron deficiency are particularly marked for children from more disadvantaged families.²⁰ These findings support the importance of preventing iron deficiency during the first two years of life.

The effects of iron deficiency on cognition may not be limited to the developing brain. A recent blinded, placebocontrolled intervention study in women of reproductive age (18 to 35 years) demonstrated that iron status influenced cognitive performance.²¹ At baseline, the iron-sufficient women performed better and completed the cognitive performance tasks faster than did the iron-deficient anemic women. At the end of the 16 week period of iron supplementation (60 mg/day), a significant improvement in iron status was associated with a five- to seven- fold improvement in cognitive performance.²¹

Relatively little information is available on the cognitive effects of iron = nutrition in older adults. However, there is some evidence that iron deficiency in older adults is associated with subtle alterations in electroencephalograms, indicative of neuropathologic changes in the aged brain, and with poor scores on selected tests of cognitive function.^{4,22}

Zinc's Role in Cognition

Zinc is an essential nutrient¹⁰ that has multiple structural and metabolic roles in the development and function of the human brain.^{12,23} Experimental animal studies suggest a biological role for zinc in central nervous system development and cognitive function. Also, behavioral problems have been described in zinc deficient animals.^{24,25} In a series of studies in rhesus monkeys, zinc deficiency during prenatal, early postnatal, and adolescent/puberty years altered cognitive behavior, evidenced by decreased motor activity and attention, abnormalities in short-term memory, and difficulties solving problems.^{24,25}

Compared to iron, relatively few studies have examined zinc's role in human cognitive performance. Nevertheless, emerging research suggests a beneficial role for zinc in cognitive development and functioning especially in malnourished children or children with poor zinc status.^{12,26-28} As reviewed by Penland²⁷, motor development, attention, responsiveness, and activity improved in zinc-deficient infants who received 10 mg zinc/day. A randomized, double-blind trial in

undernourished Jamaican children aged 9 to 30 months showed that zinc supplementation (10 mg/day) in combination with psychosocial stimulation for six months improved cognitive development (i.e., hand eye coordination, hearing and speech, and performance).²⁹ Although zinc supplementation alone did not have a major influence on cognitive development in this study, there was a positive interaction between zinc and stimulation on cognitive development. Findings from a preliminary study in 42 children aged 3 to 5 years from low-income families suggest that sufficient zinc or iron protects against lead absorption and the negative effects of lead on cognition.³⁰

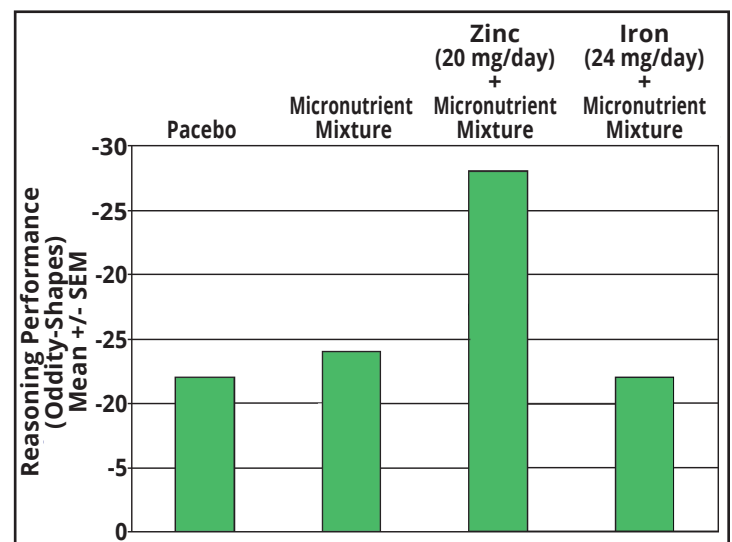
Among school-age children, increasing zinc intake has been demonstrated to improve cognitive performance, particularly when deficiencies of other micronutrients are corrected.^{26-28, 31, 32} In a 10-week, double-blind, randomized, controlled trial involving 740 urban and 540 rural Chinese children aged 6 to 9 years, recognition memory, reasoning, psychomotor function, and attention improved more in the children receiving a micronutrient mixture including 20 mg zinc/day than in those fed the micronutrient mixture alone.³¹ A beneficial effect of zinc and a micronutrient mixture on cognition was also demonstrated in a study of 240 low-income Mexican-American children aged 6 to 9 years at risk of zinc deficiency because their high phytate diets.^{26,27} The children received a micronutrient mixture, 20 mg zinc/day plus the micronutrient mixture, 24 mg iron/day plus the micronutrient mixture, or a placebo five days/week for 10 weeks in a double-blind, controlled trial. Cognitive and psychomotor function (i.e., attention, perception, memory, reasoning, motor and spatial skills) were determined before and after treatment. Posttreatment measures were expressed as a percentage of pre-treatment measures for analysis. Significantly greater improvements in reasoning (i.e., fewer trials to learn simple concepts) were found in the group receiving zinc plus the micronutrient mixture compared to the other treatments or placebo (Figure 1).

When the effect of zinc supplementation (0, 10 or 20 mg zinc) provided each school day for 10 weeks on cognitive performance was examined in 209 children in 7th grade, researchers found that fortification with 20 mg zinc improved cognitive performance compared to the placebo group.³² Reviews of zinc and cognition have concluded that, although zinc deficiency has been linked to decreased activity and depressed motor development

in nutritionally at-risk children, associations with cognitive development are unclear and may be limited to specific neuropsychological processes.^{6, 28}

There are few experimental studies of zinc intake or zinc status and cognition in adults. In a study of mildly deficient women aged 19 to 41 years, zinc supplementation improved tests of cognitive function beyond the addition of micronutrients alone, or supplemental iron.³³ In adults aged 65 to 90 years living in Spain, a positive association between dietary zinc intake and cognitive function was found.⁴ Clearly, well-controlled, randomized trials are needed to clarify zinc's role in human cognition.

Figure 1. Effect of Zinc, Iron, and Micronutrient Supplementation on Reasoning Performance of Mexican-American Children ²⁷



Other Nutrients in Beef and Cognition

Other nutrients in beef such as B-vitamins, protein, selenium, and choline have been investigated for their role in cognition.

B Vitamins and Cognition

B vitamins such as vitamin B₁₂, vitamin B₆, and folic acid have been demonstrated to reduce blood levels of the amino acid, homocysteine.³⁴ Elevated blood levels of homocysteine are positively associated with cognitive impairment, dementia and Alzheimer's disease.^{35, 36} A number of observational studies provide evidence for a positive association between specific B vitamins or combinations of B vitamins and cognitive functioning or reduced risk of dementia and Alzheimer's disease.^{7, 36, 37} For example, high homocysteine levels were associated with a greater risk of dementia or cognitive impairment,

and higher blood levels of vitamin B₁₂ reduced the risk of homocysteine-associated dementia or cognitive impairment in a longitudinal study of 1779 Mexican-American older adults.³⁶ Likewise, when 321 older men were followed for three years, lower plasma homocysteine and higher folate, vitamin B₆, and vitamin B₁₂ concentrations were associated with improved cognitive performance.³⁷ However, a recent systematic review of 24 observational studies of B vitamins and cognitive function, including Alzheimer's disease, in older adults concluded that differences among studies and the lack of good quality studies limit conclusions related to the association between folate, vitamin B₆, and vitamin B₁₂ and cognitive function.³⁸ Findings from dietary intervention trials that have examined the effects of B vitamins on cognitive performance also are inconclusive.³⁹ A systematic review of 14 randomized trials using approximately 50 different cognitive function tests concluded that the effect of vitamin B₆, vitamin B₁₂, or folic acid supplementation alone or in combination on cognitive performance remains to be firmly established, although folic acid supplementation may be beneficial for some population groups.³⁹ It has been convincingly demonstrated that adequate intake of folic acid, vitamin B₆, and vitamin B₁₂ is necessary to maintain optimum concentrations of blood homocysteine levels³⁴, but data from long-term intervention studies with healthy individuals are needed to conclusively determine whether the maintenance of vitamin B status will benefit cognitive performance.

Protein and Cognition

Some data indicate that a high protein meal results in better overall cognitive performance than that achieved from foods higher in carbohydrate⁴⁰, but other investigations have not confirmed these observations.⁴¹ Although the role of dietary protein on cognitive function has yet to be conclusively established, beef protein may indirectly affect cognition by its ability to enhance iron and zinc absorption from other dietary sources.⁴²

Selenium and Cognition

Selenium, an essential trace element that serves as a natural antioxidant⁴³, may protect against cognitive decline. Emerging observations from epidemiological studies indicate that selenium may play an important role in slowing the age-related decline in cognition.^{44, 45} Studies in elderly Chinese people living in the People's Republic of China⁴⁴ and in elderly French adults⁴⁵ linked low selenium

status with lower cognitive function after adjusting for confounding factors.

Choline and Cognition

Emerging scientific findings, primarily from experimental animal and limited human studies, suggest a role for choline in cognition.^{34, 46, 47} Choline is a precursor of the neurotransmitter, acetylcholine, which is used in the transmission of impulses between nerves, muscles, and organs and is important in brain functions such as memory.^{34, 46} In experimental animals, the availability of choline during gestation and perinatal development is linked to improved neurological function or performance of offspring in cognitive and behavioral tests.^{46, 47} Some studies in experimental animals suggest that adequate intake of choline during pregnancy and lactation may enhance the offspring's lifelong cognition and memory.⁴⁶ In a study in humans receiving long-term total parenteral nutrition, choline intake improved both verbal and visual memory.⁴⁸ Choline and its metabolite, betaine, may also help prevent degenerative diseases such as Alzheimer's disease in the elderly.⁴⁹ An epidemiological study involving 1,960 participants in the Framingham Offspring Study found that high intakes of dietary choline and betaine were associated with lower blood levels of homocysteine.⁴⁹ In this study, red meat was the primary source of choline.⁴⁹

Beef Intake and Cognition

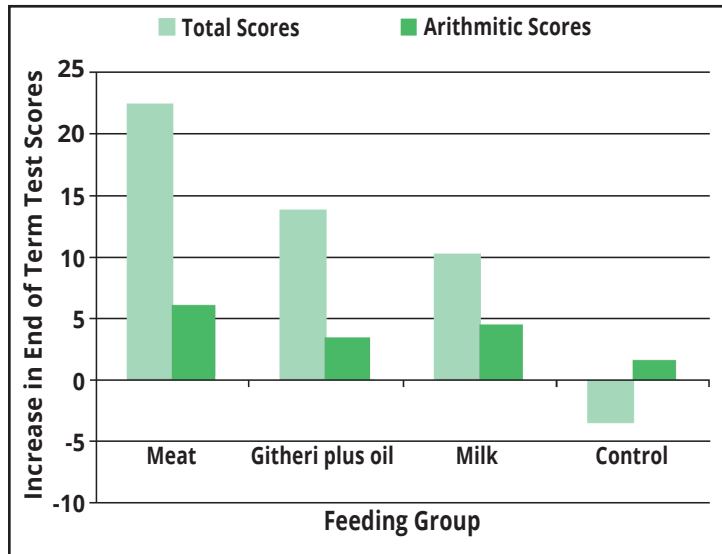
Considering the potentially beneficial effects of iron, zinc, and other nutrients on cognitive performance, it is of practical interest to determine whether food sources of these nutrients, such as red meat (e.g., beef), improve cognition.

Studies in developing countries have shown that meat, including beef, improves cognitive development among malnourished school-aged children.⁵⁰⁻⁵² A randomized controlled school feeding study involving 900 children aged 6 to 14 years in a rural area of Kenya showed that meat (beef) supplementation was positively associated with several functional outcomes including improved cognitive performance.⁵² Twelve schools were randomly assigned to three intervention feeding groups and a control group that received no feedings. Children in the intervention schools received a local plant-based dish, githeri, as a mid-morning snack supplemented with meat (finely ground beef with 10-12% fat), milk, or fat to equalize the caloric content of the feedings. Cognitive status using a

variety of tests was assessed at baseline and longitudinally over the 2¼ year study.

As shown in Figure 2, children in the Meat group experienced the greatest percentage increases in school performance, as measured by end-of-term test scores, and arithmetic subtest scores, both of which were statistically significant. This first randomized, controlled feeding intervention study indicating that meat supplementation improves cognitive function in malnourished children also showed that meat supplementation was positively associated with increased physical activity, initiative and leadership behaviors, and mid-upper arm muscle area (an indicator of lean body mass).⁵² The researchers support the use of food, rather than single or multinutrient supplements, to improve children’s learning and school performance.⁵² They also suggest that the functional benefits attributed to meat (i.e., beef) in this study may be due to the higher intake of vitamin B₁₂ and more available iron and zinc from meat, which increases iron and zinc absorption from fiber and phytate-rich plant staples.⁵² An extension of this study identified a high prevalence of low plasma vitamin B₁₂ in the rural Kenyan school children which was improved by increasing intake of animal source foods such as beef.⁵³ Although studies from developing countries have shown that meat, including beef, improves cognitive development among school-aged children with malnutrition, additional data are needed to determine beef’s effect on cognitive development/function among children who are deficient in iron or zinc, but are not suffering from general malnutrition.

Figure 2. Beef Supplementation Improves Kenyan Children’s School Performance and Arithmetic Scores (Adapted from Neumann, C.G., et. al.⁵²)



Beef: Meeting Needs for Iron, Zinc, and Other Nutrients Involved in Cognition

Beef is an excellent or good source of many of the nutrients necessary for cognitive development/function. A 3-ounce serving of lean beef supplies more than 20% (excellent source) of the Daily Value for protein (51%), zinc (38%), vitamin B₁₂ (37%), and selenium (26%), and more than 10% (good source) of vitamin B₆ (15%) and iron (14%).^{54,55} Also, beef is a good source of choline.^{55,56}

According to dietary recall data from USDA’s 1989-91 Continuing Survey of Food Intake by Individuals, beef is the number one source of protein, vitamin B₁₂, and zinc in the diets of U.S. adults 19 years and older.⁵⁷ Also, beef is among the top five leading sources of vitamin B₆, iron, and selenium in this population.⁵⁷

In addition to being an important dietary source of many nutrients, beef contains nutrients such as iron and zinc in a readily bioavailable form.¹⁰ The majority of iron in beef is heme iron, which is more readily absorbed than non-heme iron found in plant-based and iron-fortified foods. Also, the absorption of non-heme iron is enhanced by beef’s “meat factor.” Recent data from a study which examined iron and zinc absorption from meals differing only in their protein source (i.e., beef or a low-phytate soy protein concentrate) found that iron and zinc absorption from a beef meal was greater than from a soy meal among 4 to 8-year-old children.⁴²

Providing bioavailable food sources of iron and zinc, such as beef, is particularly important for older infants and toddlers considering the apparent irreversible effects of deficiencies of these nutrients during these early years on cognitive development. Guidelines from the American Academy of Pediatrics⁵⁸ advise that foods other than human milk or infant formula be introduced to healthy infants at 4 to 6 months of age. Krebs and coworkers⁵⁹ found that pureed beef was well tolerated as the first complementary food among 88 exclusively breastfed infants. This study compared the effects of feeding either meat (pureed beef) or iron-fortified infant cereal as the first solid food. At 5 and 7 months of age, infants in the meat group had significantly higher zinc and protein intakes, while infants in the cereal group had significantly higher iron intakes at 7 months.⁵⁹ By 9 months (i.e., 2 months after the intervention ended), no differences in iron and zinc intakes were found, but protein intake was somewhat higher for the meat group. Recognizing that a high proportion of infants and toddlers

have marginal zinc and iron status, the researchers suggest that offering meat as a first complementary food for breastfed infants may help them meet their needs for both iron and zinc.⁵⁹ Other studies have shown that including beef in the diet of children deficient in multiple nutrients substantially improves their nutrient adequacy, including that for zinc, iron, and vitamin B₁₂.^{50, 51, 60}

Summary

Considering the potentially beneficial role of iron, zinc, and other nutrients in cognition, meeting needs for these nutrients is important at all ages. This is particularly true during the early years when the brain and its subsequent

function are developing and during later years to help maintain cognition. Animal products are a primary source of bioavailable iron and zinc in the U.S. diet and provide other essential nutrients potentially important for cognition. USDA's MyPyramid⁶¹, an interactive food guidance system, recommends that healthy Americans consume 5.5 ounces (based on a 2,000 calorie diet) of foods from the Meat & Beans group. Higher or lower amounts from this food group are recommended depending on caloric intake. Within this food group, beef is an excellent example of a naturally rich food that provides several key nutrients important for cognitive development and function.

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