

Review

The role of iron and zinc in cognitive development of children

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Abstract: The effects of iron and zinc on cognitive, motor and behavioral development are on children is scientifically accepted and concentrates on the more recent work, some previous work and areas of controversy. There are well established associations with poor development and iron and zinc deficiency in food source but the deficiencies usually occur in disadvantaged circumstances and establishing causal relationships is not easy. The health and well being of children depend upon the interaction between their genetic potential and exogenous factors like adequacy of nutrition, safety of the environment, social interaction and other childhood activity. Both proteins-energy malnutrition and micronutrient deficiencies increase the risk of death from common diseases such as acute gastroenteritis, pneumonia and measles. Iron deficiency anemia, for example, is estimated to affect almost 25% of the world's population resulting in high economic cost by adding to the burden on health care services, affecting learning in school. Dietary practices frequently seen in children from both developed and developing countries, leading to frequent consumption of nutrient poor foods, may also put them at risk of micronutrient deficiencies.

Keywords: cognitive development; iron; zinc; child health and development; food sources

1. Introduction

UNICEF (1998) defined micronutrients as nutrients that are only needed by the body in minute amounts, which play leading roles in the production of enzymes, hormones and other substances, helping to regulate growth activity, cognitive development and the functioning of the immune and reproductive systems. There are well established associations with poor development and iron and zinc deficiency but the deficiencies usually occur in disadvantaged circumstances and establishing causal relationships is difficult (Grantham *et al.*, 1995). Micronutrients of known public health importance include the following: zinc, iodine, iron, selenium, copper, vitamins A, E, C, D, B₂, B₆ and folate. Deficiency of these micronutrients has a significant impact on children health and cognitive development as well as on the economic development of communities and nations. The full genetic potential of the child for physical growth and mental development may become compromised due to sub clinical deficiencies of micronutrients, which are commonly referred to as "hidden hunger". Children with these sub clinical deficiencies of micronutrients are more vulnerable to develop frequent and more severe common day-to-day infections thus triggering a vicious cycle of under nutrition and recurrent infections (Singh, 2004). According to Caballero, almost two thirds of the deaths of children around the world are directly or indirectly associated with nutritional deficiencies (Caballero, 2002).

According to Singh, vitamins and trace minerals are required for production of various enzymes, hormones, and biochemical mediators for regulation of biological processes. He further stated that micronutrients are required for energy production, synthesis of RNA and DNA and for providing protection against reactive oxygen-free

radicals. Micronutrients are also required for promotion of physical growth, sexual maturation and neuromotor development. They are recognized to boost both cell-mediated and humoral immune deficiencies of the body. Micronutrients play significant roles in the health of children. This paper therefore reviews the roles of the various micronutrients specifically iron and zinc in children as found in literature.

2. Cognitive development

Cognition is a complex construct and consists of a field of thought processes by which an individual registers, encodes, selects, maintains, transforms, stores and retrieves information (Shinjini and Sunita, 2001). This would extend to include visual and somato-sensory perception, thinking, memory, and learning. Memory helps to learn, retain and reproduce information. Another important aspect is attention; an integrated process by which the individual, from the time of infancy focuses on information that is essential for its growth and development (Ruff and Rauthbart, 1996). It includes a readiness to respond and an intact capacity to focus on one thing resisting other distracting stimuli. In the first year of life, the infant learns to construct mental structures, which is dependent on perceptions and body movements. It further develops its attention skills by exploring and concentrating on the novel aspects of its environment and extends it to focus on testing and organizing the information through the pre-school years. Activity and motor skills form an integral part of developing the attention system by increasing the responsiveness to the environment. A lethargic child with delayed motor activity would have fewer opportunities to explore and concentrate on specific objects or events. Activity would be directly related to motor activities at that particular age. Cognitive development continues as a period of concrete operations through school years as skills like thought, memory and language develop. During this period multiple stimuli are appreciated simultaneously and attention abilities increase with greater learning and memory. Full adult intelligence and hypothetical thinking evolve during adolescence. Assessment of cognitive development would include evaluation of perception, thought, attention, memory, language and activity (Shinjini and Sunita, 2001).

3. Nutritional needs for mental development during late pregnancy and the first two years of life

During the last three months of gestation and early infancy, the brain is a site of high activity, where cells divide and differentiate into neurons and accessory cells. During this period of growth, proteins, lipids and energy supply is needed. Micronutrients, which serve as cofactors for many metabolic and signaling processes, are essential as well. These nutrients are normally brought prenatally by placental transfer to the fetus, and postnatally by breastfeeding (Piaget, 1997).

3.1. Iron

It is to keep in mind that iron is always prioritized to red blood cells over any other organ; including the brain (Denis and Denis, 2005): iron deficiency can be pathologic even before iron deficiency anemia (IDA). In other words, iron homeostasis mechanisms are made in a way which first, ensures production of red blood cells. Particularly, iron deficiency induces irreversible effects on the brain of children if occurring during pregnancy or the first year of life. One of the most important features of iron is its role in energy utilization in the respiratory chain of mitochondria (Lozoff, 2000). Studies in the rat model by De Ungria and colleagues demonstrated that iron deficiency was associated with a decreased energy metabolism in the hippocampus, a region involved in cognition and memory. This might explain the observations that iron deficiency in human neonates are associated with electrophysiological evidence of reduced recognition memory at birth (De Ungria *et al.*, 2000). Second, iron is essential for myelin production because it is a co-factor for lipid biosynthesis. As a consequence, IDA has been shown to be associated with myelin defects and slower transmission through the auditory and visual systems (Georgieff and Innis, 2005). This phenomenon is not reversible and persists despite treatment for IDA with iron supplementation. Finally, iron plays a role in the metabolism of monoamines, which constitute a group of neurotransmitters and neuromodulators, particularly dopamine (Algarín *et al.*, 2003). In several studies, iron deficiencies and moderate anemia occurring during infancy were shown to affect cognitive performance at school. These studies were controlled for socio-economical background of children (UN Children Fund, 2011). In addition, iron supplementation is not always able to revert the low cognitive abilities of those children: mental development seems to occur in a “window -period” during life, inside which damages can be irreversible.

3.2. Zinc

Zinc is found in all human tissues but it is found at high concentrations in the brain. It is essential for the activity of a large number of metalloenzymes: the cellular functions are as wide as RNA and DNA synthesis, cellular

growth, differentiation and metabolism. Early development –when cell activity is the highest- may be particularly sensitive to zinc deficiency. In some studies, it has been associated with reduced neuronal growth and brain volume. In addition, zinc deficiency has been shown to compromise activity, cognitive development and attention (UN Children Fund, 2011; Lozoff *et al.*, 2000]. In some studies, zinc levels have also been correlated with reading ability and academic performances. Finally, zinc supplementation studies have shown an effect on reasoning abilities (UN Children Fund, 2011). Zinc is known to be essential for the normal growth and development of the fetus. A deficiency of this nutrient in pregnant animals has been shown to result in malformations and abnormal development and functioning of the central nervous system of the offspring (Frederickson, 1989). So malnutrition in pregnant women may affect child cognition through its effects on fetal development (Maureen, 2003). Zinc is of particular concern during pregnancy because of its potential effect on fetal brain development (Shinjini and Sunita, 2001) and birth outcomes. Fluid cognitive deficits and impaired working memory have been associated with the hippocampus (Tsunenobu Tamura *et al.*, 2003) that has a role in spatial memory and has been suggested to be sensitive to zinc deficiency (Stoecker, 2009).

4. Role of iron

Iron is one of the trace minerals that play a vital role in the body. The whole body contains about 4 g of iron. Three-fourth of this is found in association with the protein, hemoglobin. In foods, iron occurs in two forms ferrous and ferric but the absorption form of iron is only in the ferrous state. The function of iron in the body cannot be overlooked as it is involved in the synthesis of other compounds in the body. Iron is important in reactions involving energy release in the body (oxidation and reduction reactions). It is a component of oxygen carrying compounds e.g. hemoglobin, myoglobin. Iron deficiency anemia is the most common micronutrient problem in the world as it affects more than 2 billion people globally (Black, 2003). Iron deficiency among children is common, especially in less developed countries and affects psychomotor development (Black, 2003). Infants and young children are the most adversely affected by iron deficiency because they are growing and developing at such a fast rate (Onyezili *et al.*, 1993). If iron deficiency is not corrected, it leads to anemia, which is the most common nutritional disorder in the world. The association of iron deficiency anemia with lower mental and motor developmental test scores in early childhood is well described and has recently been reviewed (Sally and Cornelius, 2001). Draper further stated that iron deficiency anemia is a major problem affecting more than 2 billion people – more than one-third of the entire world population (Onyezili *et al.*, 1993). The World Health Organization (WHO) also estimated that 51% of children under 4 years old in developing countries are anemic as a result of iron deficiency. According to Draper iron deficiency anemia is more common in situations of:

1. Social disadvantage (e.g. poverty, poor housing and overcrowding, and low levels of parental education),
2. Psychological disadvantage (e.g. lack of stimulation), and
3. Biological disadvantage (e.g. low birth weight, high infection rates, and other nutritional deficiencies) (Onyezili *et al.*, 1993).

The main nutritional causes of iron deficiency anemia are diets that provide too little iron, poor absorption of most dietary iron, and the presence of other dietary factors that inhibit iron absorption. Although an inadequate iron diet is by far the major cause of anemia, it also can occur as a result of parasitic infections, inherited disorders, and deficiencies of other nutrients. Parasitic infections include malaria and helminthes (notably, hookworm). Malaria causes the destruction of red blood cells and hookworms cause blood loss: Inherited disorders that can leave an individual vulnerable to anemia include sickle cell anemia. A much less common cause for anemia results from deficiencies of other nutrients, such as folate (a B-complex vitamin) (Onyezili *et al.*, 1993). Draper also observed that iron deficiency anemia is associated with impaired development of mental and physical coordination skills and impaired school achievement in older children (Draper, 1996). It lowers resistance to disease and weakens a child's learning ability and physical stamina. It also slows mental and motor development and reduces work performance (UNICEF, 2001).

There is evidence that iron deficiency anemia alters the emotional state of infants so that they are more withdrawn, cautious and hesitant, and maintain closer contact with their mothers. These types of behavior could hinder an infant's ability to interact with and learn from his or her environment thereby contributing to poor intellectual development. In school achievement two studies had robust designs and adequate sample sizes and examined school achievement, which has obvious policy implications (Pollitt, 1993). Children showed a clear improvement with treatment Iron deficiency anemia can be prevented in children by food fortification such as the addition of iron to food over and above that naturally found in food. Naturally iron-containing foods should not be neglected. Mothers should be encouraged to feed their infants and young children meat and foods rich in vitamin C, such as fruits, and to avoid foods and drinks that inhibit iron absorption, such as tea, during and 2

hours before and after mealtime. Traditional food practices such as germination and/or fermentation can also improve the availability of iron in the diet. Intake of iron supplement can as well help in reducing the prevalence of iron deficiency anemia. Iron supplements should be initiated as close to 6 months of age as possible, and supplements should be given for 6 months. Supplementation of longer duration, to 15 months of age is likely to be more beneficial (Onyezili *et al.*, 1993). A number of public health activities can lower the risk of iron deficiency anemia. For example, in areas where malaria is endemic, the use of bed nets should be promoted.

5. Role of zinc

Zinc is widely recognized as an essential micronutrient with a catalytic role in over 100 specific metabolic enzymes in human metabolism (Pollitt, 1993). It is one of the most ubiquitous of all trace elements involved in human metabolism and plays multiple roles in the perpetuation of genetic materials including transcription of DNA, translation of RNA, and ultimately in cellular division (Eugene and Robert, 2005). Zinc is a trace mineral that is involved with RNA and DNA synthesis and is critical to cellular growth, differentiation and metabolism (Ozgur *et al.*, 2004). Zinc deficiency can interfere with multiple organ systems particularly when it occurs during a time of rapid growth and development, such as infancy, when nutritional demands are high. Interest in zinc was stimulated when zinc supplements given to short children and failure to thrive infants in the U.S. city of Denver improved growth (Jill *et al.*, 2001). Collective Ability reported that zinc is found virtually in every tissue in the body and is particularly important for the correct functioning of the immune system, growth and development and the antioxidant system (Maureen, 1998). The major source of zinc intake is through diet and when the supply of dietary zinc is insufficient, biochemical abnormalities and clinical signs may develop (Allen, 2001). The following are the major functions of zinc:

- a) Zinc plays significant roles in the metabolism of proteins, carbohydrates, and lipids. It is incorporated into the active sites of many metalloenzymes (Lee *et al.*, 2007) and probably is used in the central nervous system (CNS) as a neurotransmitter or neuromodulator (Zulfiqar and Husein, 2004).
- b) As zinc is a constituent of metalloenzymes so, it is involved in a large number of biological processes related to child motor development.
- c) Zinc is essential for the metabolism of vitamin A.
- d) Zinc is involved in the synthesis of DNA and RNA without which cells cannot reproduce themselves and growth and development would be impossible.
- e) Zinc is needed for cell replication and is thus essential for regeneration of the intestinal mucosa.
- f) Zinc is essential for the healing of wounds and the turnover of epithelial cells necessary to maintain healthy skin.

Zinc is found in a wide range of foods; the richest sources are animal protein (meat, eggs and dairy products) shellfish, pulses, nuts and whole meal grains. White flour is a poor source of zinc because the zinc is mainly found in the outer layers of the grain and because the fiber in grain contains phytates, which inhibits the absorption of minerals. Zinc plays an important role in the promotion of normal growth and development and is an element in the enzymes that work with red blood cells, which move CO₂ from tissues to lungs. It also helps to maintain an effective immune system. Zinc deficiency in malnourished children contributes to growth failure and susceptibility to infections. It is also associated with complications of child birth. This deficiency usually occurs where malnutrition is prevalent (UNICEF, 2001). Medium-to-severe zinc deficiency disturbs several biological functions such as gene expression, protein synthesis, immunity, skeletal growth and maturation, gonad development and pregnancy outcomes, including taste perception and appetite (Onyezili *et al.*, 1993). According to Penny severe zinc deficiency is responsible for dwarfism and failure to mature in young Iranian and Egyptian youths eating a diet consisting largely of whole meal bread. Penny observed that lesser degrees of zinc deficiency are more common now than was appreciated and the sub clinical deficiency of zinc contributes to an increased incidence and severity of common but important infections such as diarrhea and pneumonia. Diarrhea is associated with an increased loss of zinc in feces. (Onyezili *et al.*, 1993) also stated that zinc deficiency increases the risk of mortality from diarrhea, pneumonia and malaria by 13 to 21 percent and unlike other micronutrients of public health importance has often subtle rather than dramatic clinical features.

Despite the widespread presence of zinc in common foods, dietary deficiency is common because bioavailability of zinc is reduced by the co-existence of inhibitory substances such as fiber and phytate in foods of vegetable origin. These substances inhibit the absorption of zinc. The diets of the poorest populations often lack zinc being dependent on vegetable staples with little access to animal products especially flesh products such as meat, fish and offal which are the richest sources of easily assimilated zinc. Children in poor communities do not manifest obvious signs of zinc deficiency but have often been found to have low plasma zinc levels compatible with sub-clinical zinc deficiency. Zinc supplements helped blunt the most severe malaria

cases in children. The deficiency of Zinc can be prevented by intake of zinc supplement and foods rich in protein.

6. Child health and development

Evidence suggests that micronutrient deficiencies may be associated with problems in early development and behavior. Iron deficiency is the most common nutritional deficiency in the world and a major cause of anemia particularly during infancy and toddlerhood when there is rapid growth and a high nutritional demand (Blair, 2006). Less is known about the prevalence of zinc deficiency, but supplementation trials in developing countries suggest low zinc intake among infants and toddlers (Takeda, 2001), which leads to the consensus that both iron and zinc deficiency are major public health problems (Stoltzfus, 2001; Hotz, 2001). In low-income societies (like Bangladesh), where dietary resources are inadequate to meet children’s requirements for iron and zinc, micronutrient supplementation or fortification may be necessary (UNICEF, 2011). To identify the dietary information related to child’s cognitive, health and development process-A cognitive processing model has been demonstrated (Black, 2004).

A cognitive-processing model has been demonstrated to be useful in understanding self-reports of other behaviors. Figure 1 graphically presents a simple representation of cognitive processing about food intake and questioning about that intake (Shaffer, 1985). This model was adapted from Shaffer and has three structural elements: a sensory register, short-term memory (STM), and long-term memory (LTM). The sensory register is a boundary structure that screens the information to which children attend. When information in the environment is perceived, it is used in STM, also known as working memory. All conscious intellectual activity is believed to occur in STM, however, most people can hold few items of information in STM (perhaps about five) at any one time. Some portion of the information in STM is transferred to storage for later

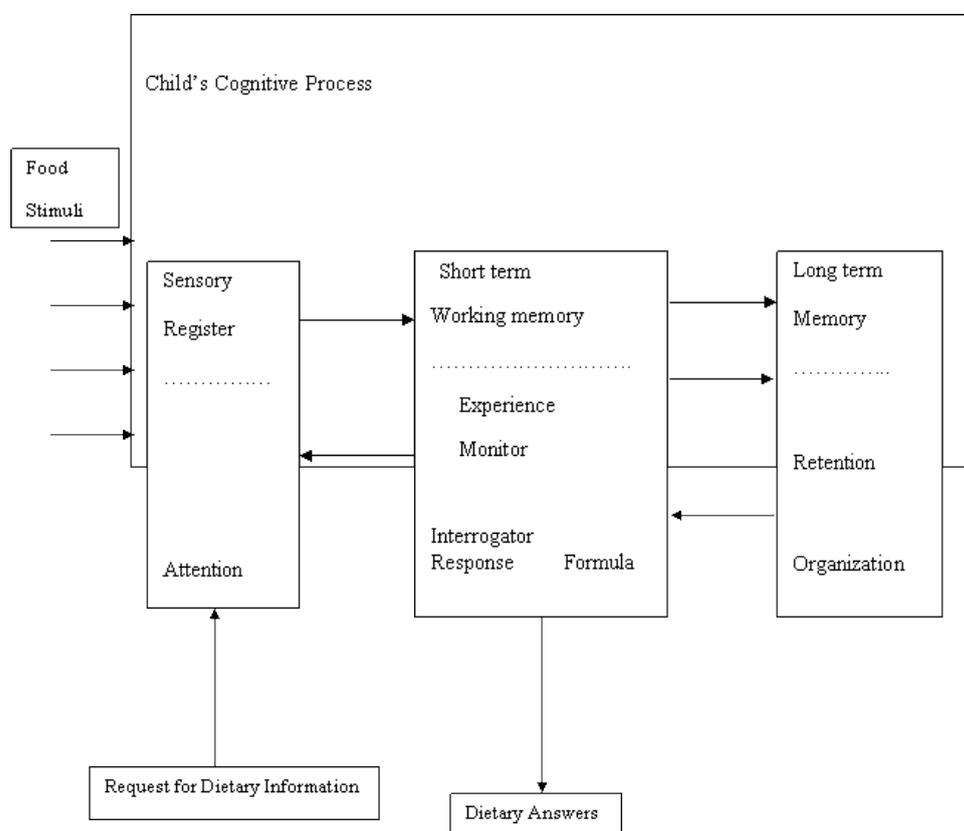


Figure 1. A model of a child’s cognitive processing of food information.

7. Conclusions

All efforts should be made that children take a well balanced nutritious food by encouraging them to consume green leafy vegetables, soy beans, seasonal fruits, milk and dairy products, fish, eggs, chicken and other food stuff. However, the prevailing dogma in nutritional science that a balanced diet is sufficient to meet all the nutritional requirements has been challenged (Singh M, 2004). According to the recommendations of United

Nations Sub-committee on Nutrition, it is not possible to meet the requirements of 100 percent recommended dietary allowance (RDA) of micronutrients from dietary sources alone (Jill *et al.*, 2001). Nutritional supplements are thus mandatory to improve physical growth and mental development and prevent occurrence of common day-today infections. Healthy children do provide a solid foundation to the society in order to ensure optimal resource development of a country.

Conflict of interest

None to declare.

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