

**Brain Derived Neurotrophic Growth Factor
In Children With Iron Deficiency Anemia And
Its Relation To Their Cognitive Function**

Thesis

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List of Abbreviations

IDA	Iron deficiency anemia
S.S	Social state
WT%	Weight percentage for the median of age
HT%	Height percentage for the median of age
HC	Head circumference
B.M.I	Body mass index
I.Q.R	Interquartile range
CBC	Complete blood count
H.B	Hemoglobin concentration
M.C.V	Mean corpuscular volume
FL	Femtoliter
pg/ ml	Picogram per milliter
M.C.H	Mean corpuscular hemoglobin
R.D.W	Red cell distribution width
CNS	Central nervous system
PNS	Peripheral nervous system
S.D	Standard déviation
BDNF	Brain derived neurotrophic growth factor
I.Q	Intelligence quation

Introduction

Many diseases, different nutritional, metabolic, hormonal changes 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 (IDA) the most common form of anemia, has been suggested to result in cognitive deterioration and alteration of neurological functions. We suggest a significant influence of iron deficiency anemia on dynamic properties and functional features of the central nervous system (CNS) activity. Cognitive achievement is strongly related to hemoglobin level and could be expected in all patients that higher hemoglobin level results in better CNS function (*Petranovic et al., 2008*).

Iron deficiency anemia (IDA) cause reduced work capacity in adults and impact motor and mental development in children and adolescents. There is evidence that iron deficiency without anemia affects cognition in adolescent girls. IDA may affect visual and auditory functioning in children (*Verdon et al., 2003*).

Although the vast majority of neurons in the mammalian brain are formed prenatally, parts of the adult brain retain the ability to grow new neurons from neural stem cells in a process

known as neurogenesis. Neurotrophins are chemicals that help to stimulate and control neurogenesis, brain derived neurotrophic growth factors (BDNF) being one of the most active (*Zigova et al., 2001*).

Brain derived neurotrophic growth factors (BDNF) acts on certain neurons of the central nervous system and the peripheral nervous system, helping to support the survival of existing neurons and encourage the growth and differentiation of new neurons and synapses (*Acheson et al., 2001*).

In the brain, it is active in the hippocampus, cortex, and basal forebrain-areas vital to learning, memory, and higher thinking (*Yamada et al., 2003*).

Aim of the Work

The aim of this study was to estimate the level of B.D.N.F in IDA children and its correlation with their cognitive function.

Iron Deficiency Anemia

Introduction:

Anemia is one of the most extensive pandemics, affecting mostly developing countries. About 3.5 billion persons are affected by anemia in developing countries. In most cases anemia is caused by iron deficiency, although a smaller proportion is due to deficiencies of other micronutrients such as folate and B12 (*Iyengar, 2000*).

The presence of anemia in children under five years of age is of particular relevance because it negatively impacts mental development and future social performance. Children suffering from iron deficiency anemia during their first two years of life have slower cognitive development and poorer school performance and work capacity in later years (*Sayed et al., 1999*).

Iron deficiency anemia has also been associated with a diminished ability to fight infections by impairing cell-mediated immunity, resulting in greater rates of morbidity due to acute infection (*Freire, 1998*).

Linear growth and physical work capacity, especially endurance exercise, are also negatively affected by iron deficiency anemia (*Beard et al., 2000*).

The extent of the infant iron stores at birth is inversely

proportional to the degree of maternal iron deficiency during pregnancy. Thus, maternal iron stores are associated with earlier development of anemia during infancy, frequently around 4 months of age (*Menéndez et al., 1994*).

Definition:

Iron deficiency anemia (IDA): is that anemia resulting from lack of sufficient iron for synthesis of hemoglobin (*Behram, 1992*).

characterized by decreased or absent iron stores, low serum iron concentrations, low transferrin saturations, and low hemoglobin concentrations or hematocrit values, is the most advanced stage of iron deficiency (*Beutler et al., 2001*).

Prevalence:

Iron deficiency affects at least a third of the world's population, or two billion persons, and is, therefore, second only to hunger as a major, world wide nutritional problem (*Beutler et al., 2001*).

Furthermore, iron deficiency remains the most common cause of anemia. Globally, 30% of the estimated world population of almost 4.5 billion are anemic, and 500 million people are believed to have iron deficiency anemia (*Hoffman,*

2001). Its prevalence depends mainly on age, being higher in infancy and adolescence (***Panagiotou and Douros, 2004***).

Studies have shown that in US and UK children aged from one to two years, prevalence rates are greater than 10% and 30% for IDA and iron deficiency, respectively (***Eden ,2005***).

The prevalence of iron intakes likely to be inadequate to prevent anemia was estimated as 35% in Egypt, 13% in Kenya, and 43% in Mexico. The prevalence of zinc intakes likely to be inadequate to meet basal requirements was estimated as 57% and 25% in Kenya and Mexico, respectively (***Allen, 2003***).

In Egypt, particularly in rural areas, the prevalence of IDA is relatively high. According to 1993 study by the Egyptian nutrition institute the prevalence of IDA was between 23% and 30% in rural population group the study also found that the population group were primarily affected were the children under five years of age and the pregnant and lactating women (***Walid et al., 1994***).

Causes:

Generally speaking, iron deficiency may occur as a result of:

- 1- Chronic blood loss.
- 2- Inadequate dietary iron intake.

- 3- Malabsorption of iron.
- 4- Parasitic infestations.
- 5- Intravascular hemolysis with hemoglobinuria, or a combination of these factors.
- 6- Low birth weight and significant perinatal hemorrhage may be associated with decreases in neonatal hemoglobin mass and stores of iron (*Beutler et al., 2001*).

Anemia caused solely by inadequate dietary iron is unusual during the first four to six months but becomes more frequent after 9 to 24 months of age. Thereafter, it is relatively infrequent. Besides, blood loss must be considered a possible cause in every case of iron deficiency anemia, particularly in older children (*Behram, 1992*).

Clinical picture of IDA:

Patients with iron deficiency may present (1) with no signs or symptoms, when anemia develops slowly, (2) with the features of the underlying disorder responsible for the development of iron deficiency, or (3) with the manifestations common to anemia (*Hoffman, 2001*).

There is a poor correlation between the severity of symptoms and the blood hemoglobin concentration. Pallor is

the most important clue to iron deficiency. But in mild to moderate iron deficiency, compensatory mechanisms may be so effective that few symptoms of anemia are noted. In more severe iron deficiency, pallor, fatigue, irritability, anorexia and delayed motor development are common. Tachycardia and cardiac dilatation occur, and systolic murmurs are often present. The spleen is palpably enlarged in 10% to 15% of patients and in long-standing cases, widening of the diploe of the skull may occur (**Behram, 1992**).

Children whose iron deficiency is due in part to ingestion of unfortified cow's milk may be fat and floppy, with poor muscle tone. A history of pica is common (**Hay, 2001**).

Iron deficiency may also have effects on neurologic and intellectual function. A number of reports suggest that iron deficiency anemia affects attention span, alertness, and learning of both infants and adolescents (**Behram, 1992**).

Biochemical Indicators:

Table (1): Biochemical Indicators for diagnosis of IDA.

Indicator	*Diagnostic Range **	Stages of Iron Deficiency
Stainable bone marrow iron	Absent	Stage 1 Depletion of iron stores
Total iron binding capacity	> 400 µg/dL	
Serum ferritin concentration	< 12 µg/L or <20 µg/L + low Hb or Hct indicates iron deficiency	
Transferrin saturation	< 16%	Stage 2 Early functional iron deficiency
Free erythrocyte protoporphyrin	> 70 µg/dL erythrocyte	
Serum transferrin receptor	> 8.5 mg/L	
Hemoglobin concentration	< 12 g/dL	Stage 3 Iron deficiency anemia
Mean cell volume	< 80 fL	

*Laboratory cutoff value is instrument specific and may not apply in all laboratories.

** Collection techniques can impact results.

(Institute of Medicine, 2001).