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CURRENT TOPIC

A Literature Review of the Relation Between Iron Deficiency Anaemia, Physical Activity and Cognitive Function in Adolescent Girls

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Abstract

Women, especially those young and/or pregnant, are at high risk of experiencing an iron deficiency. Low iron stores in the body can affect cognitive function and physical activity in adolescents, but the results of epidemiological studies about the effect of iron deficiency on cognitive function decline and physical activity in adolescents are not consistent. Therefore, it is necessary to review the literature on the relationship between iron deficiency, cognitive function and physical activity in women and girls. This study is an article review using sources from Google Scholar, PubMed and ProQuest database searches from 2014 to 2021. The keywords used were iron deficiency OR anaemia AND adolescent girls OR young women AND activity AND cognitive. By using review criteria, sources were limited to those in English that used a sample of adolescents or young women. In the initial search stage, 63 reviews were obtained and based on the predetermined criteria, 12 reviews were selected to be analysed. Eleven studies examined the relationship between iron deficiency and cognitive decline, there was one study that showed a non-significant relationship between the two; ten studies showed a significant effect of iron deficiency on cognitive decline in the domains of attention tasks, memory tasks and executive function. Three studies showed their effect on decline in adolescents by using different measuring tools. Lack of iron in the body caused a decrease in cognitive function, especially in the domain attention tasks, memory task domains and executive functions domains. In addition, iron deficiency can cause a decrease in physical activity in adolescents due to the low supply of oxygen to the blood and tissues. Therefore, it is necessary to research nutrition intervention programs to improve iron anaemia status in adolescent girls and prevent a decline in cognitive function and physical activity as a result of the impact of iron deficiency.

Key words: Iron deficiency; Adolescence; Activity; Cognitive.

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Introduction

Anaemia due to iron deficiency develops when body stores of iron drop too low to support normal red blood cell (RBC) production, indicated by low levels of haemoglobin. Iron deficiency (ID) is defined as a decrease in the total iron content in the body or having iron stores below normal for physiological status. There are many types of anaemia but anaemia due to iron deficiency is the most common type of anaemia.[1] Anaemia affects 1.62 billion people in the world, especially in developing and developed countries. Iron deficiency is the cause of 50 % of cases of anaemia worldwide and represents a global health problem.[2] Teenage girls or women of childbearing age often experience iron deficiency, which is at risk of anaemia; due to adolescents experience

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rapid growth, requiring high iron intake during puberty,[3-5] as well as loss of iron during menstruation.[6]

Adolescence is marked by physical growth and cognitive and socio-emotional development, which are the characteristics seen in adolescence and this period is strongly influenced by the social, cultural and economic environment.[7] Adequate nutrition in adolescence affects the future growth and health in adulthood. It will also have an effect on offspring, so adequate nutrition in adolescence has influence on the next generation.[8]

Anaemia due to iron deficiency can cause delays in individual psychological and physical development, cognitive dysfunction, low immune status, decreased physical capacity and performance and increased foetal morbidity and mortality. In addition, iron deficiency also causes reduced attention, decreased memory and school attendance, which in turn affects school achievement in adolescents.[9, 10]

Several preliminary studies have investigated the importance of iron in cognitive function and found a link between iron deficiency, diet and changes in psychological development and cognitive function.[11-13] Experimental studies in both animals and humans suggest that iron deficiency has the potential for cognitive impairment, with damage to brain mitochondria as the basis for these changes. Cognitive impairment, including those associated with impaired attention, intelligence and perception sensory, emotional and behavioural and generally, is associated with iron deficiency anaemia.[12]

Furthermore, there are very few studies on iron deficiency associated with decreased physical activity. Decreased physical activity is caused by a decrease in iron stores and haemoglobin concentration, which causes a reduction in the availability of oxygen to the tissues and work of the heart.[18] Although various studies on the effects of iron deficiency on decreased cognitive function and activity have been investigated, the results are still inconsistent, considering the relevance of iron deficiency problems to the development of cognitive function, relative changes that can last into adulthood as a result of iron deficiency in the body.[12]

This paper aimed to review the results of research from several existing observational studies and randomised controlled trials (RCTs) to determine the effect of iron deficiency on decreased cognitive function and physical activity in adolescent girls.

Methods

The article search process was based on three relevant databases (Google Scholar, ProQuest and PubMed). The search started from the year 2014 and ended in 2021. The studies included in this review met the following criteria: 1) focus on impaired cognitive function and decreased physical activity, 2) observational studies and RCTs, 3) articles in English, 4) sample of adolescents or young women. Exclusion criteria were 1) review articles, unpublished work and study protocols, 2) populations with nonspecific iron deficiency-related problems. Key terms used were: iron deficiency OR anaemia AND young women OR adolescent girls AND activity AND cognitive.

Initial search results obtained 63 references. These references were included in the Mendeley library and filtered by title and abstract. Furthermore, an analysis was carried out based on the full text of the selected references. Finally, based on the exclusion criteria, 12 articles were analysed.

Results

Twelve published journal articles were found and the source of each article was checked (Table 1). The first study was conducted in Peshawar, Pakistan.[14] The second research was conducted in the city of Rwanda, France with the subjects being university students.[15] The third study was conducted at Idaho University, Moscow with female students who were not anaemic.[16] The fourth study was conducted in urban areas on non-anaemic women of reproductive age,[6] the fifth study was conducted in metropolitan (Sydney) and regional/rural (Bathurst) areas in the state of New South Wales in Australia.[17] The sixth study was conducted at the Pennsylvania State University with the subjects being female students.[18] The 7th and 8th study were conducted in India[19] and Newcastle University, Australia,[20] while the ninth study was conducted in Maharashtra, India with the subjects being female students aged 12–16 years.[21] The tenth study was conducted in El Minya province, Upper Egypt with the subjects being female teenagers.[22] Eleventh and twelfth studies were conducted in Jintan, China[23] and India,[24] respectively. There were three journals that discuss research output on physical activity.[6, 14, 19]

Table 1: The relationship between iron deficiency and decreased cognitive function and physical activity in adolescents

N	Author (year)	Study participant	Study design	Outcome Measure/Tools	Findings
1	Abbas Khan et al (2019)	Teenage girl, 10-14 years old; N = 100	Cross-sectional. Study duration: 6 weeks	Physical work capacity up and down stairs (Modified Harvard's Steep)	Anaemic girls had significantly lower physical work capacity than non-anaemic girls.
				Coloured progressive cognitive functions (Raven Matrix)	Anaemic girls had significantly lower cognitive function compared to non-anaemic girls.[14]
2	Laura et al (2017)	Female aged 10-27 years; N = 150	RCT. Study duration: 18 weeks	Cognitive function (computerised MJW and DMDX program) with 5 domains: ATN, SRT, GNG, CRT, SMS.	Iron biofortified nuts consumed for 18 weeks can improve iron status and cognitive function, especially ANT and SMS in young adult women.[15]
3	Blanton C (2014)	Non-anaemic women aged 18-30 years; N = 42	RCT. Study duration: 16 weeks	Cognitive function (CANTAB) with 5 areas: 1. Motor screening test; 2. Verbal recognition memory; 3. SWM; 4. One touch stocking; 5. Rapid visual information processing.	Iron in the body was significantly associated with cognitive function of SWM and One touch stockings of Cambridge (OTS) speed.[16]
4	Dziembowska et al (2019)	Healthy women aged 20 – 32 years; N = 23	Cross-sectional	Physical activity energy expenditure units per week (IPAQ);	Low levels of iron and ferritin caused decreased activity and perceived endurance.
				Cognitive function intelligence test - APM Raven.	Raven's APM cognitive scores in iron-deficient women were not significantly different from iron-enough women, but iron-deficient women needed more time to complete a given task compared to iron-enough women.[6]
5	Rebecca et al (2017)	Healthy young woman aged 18-35 years; N = 300	Cross-sectional	Cognitive function (computerised Integneuro, brain resource) with 5 cognitive domains: 1. GNG; 2. Attention; 3. The switching of attention test; 4. The memory recognition; 5. EF.	Women with IDA obtained significantly lower cognitive scores in the attention domain than women with ID, but cognitive function in the other four domains was not significant.[17]
6	Samuel et al (2015)	Female 18-35 years old; N = 127	Cross-sectional	Cognitive functions (PEBL platform computing, through 5 tasks): 1. GNG; 2. ANT; 3. SMS task; 4. EF; 5. Card sorting.	Adequate iron in the body can give a better performance on ANT cognitive function and executive function planning ability.[18]
7	Laura et al (2021)	12–16-year-old school children; N = 130	RCT	Light, moderate and strong physical activity (Accelerometer)	Children who consumed iron biofortified pearl millet had 22.3 minutes more LPA than children who did not consume pearl millet.[19]

8	Alecia et al (2014)	Healthy women aged 18-35 years; N = 84	RCT	Cognitive Function (Battery of Integneuro Cognitive Test) includes 7 domains: 1. Memory; 2. Response speed; 3. GNG; 4. Attention; 5. Information processing; 6. EF; 7. Emotion identification.	Women who were given iron supplements had higher changes in cognitive scores for the impulsivity (GNG) and attention domains than women who were not given iron supplements.[20]
9	Samuel et al (2018)	Children aged 12-16 years; N = 140	RCT	Cognitive Functions (DMDX Program MJW Software Computing) includes 5 cognitive tasks: 1. SRT; 2. GNG; 3. ANT; 4. CRT; 5. CFE.	Iron biofortified pearl millet consumed by children can improve cognitive function on attention tasks (STR, GNG and ANT and memory tasks (CFE and CRT).[21]
10	Suzan et al (2016)	Teenage girls 12-15 years old; N = 151	Cross-sectional	Cognitive functions mathematical score (Stanford Binet intelligence scale V edition)	Adolescents with iron deficiency anaemia had significantly lower math scores than iron-deficient adolescents and also lower than adolescents who were not anaemic.[22]
11	Xiaopeng et al (2017)	Teenagers aged 11-14 years; N = 428	Longitudinal study	Neuro cognitive function (CNB), with 4 domains: 1. EC; 2. EM; 3. CC; 4. SS.	Iron deficiency leaded to decreased spatial processing ability, reflecting CC function and decreased abstraction reflecting EC function in adolescents.[23]
12	Shaik et al (2019)	18–22-year-old students; N = 100	Cross-sectional	Mental health cognitive function, MMSE and MoCA	There were significant differences between students with anaemia and non-anaemia in the values of Hb, MCV, MCH and MCHC, and MMSE and MoCA cognitive scores.[24]

RCT: Randomised controlled trial; ANT: Attentional network task; SRT: Simple reaction; GNG: Go no go (GNG); CRT: Cued recognition task; SMS: Sternberg memory search task; SWM: Spatial working memory; OTS: One touch stockings of Cambridge; IPAQ: Physical activity energy expenditure units per week; APM: advanced progressive matrix; EF: Executive functions; IDA: iron deficiency anaemia; ID: iron deficiency; LPA: light activity per day; CFE: Composite face effect; CNB: computerised neurocognitive battery; EC: executive control; EM: Episodic memory; CC: Complex cognition; SS: Sensorimotor speed; MMSE: Mini mental state examination; MoCA: Montreal cognitive assessment; Hb: haemoglobin, MCV: mean corpuscular volume; MCH: mean corpuscular haemoglobin; MCHC: mean corpuscular haemoglobin concentration;

Subject characteristics and study designs of the twelve studies found were labelled according to when they were conducted and published (Table 1). In general, the samples in the study were school age young women and female students of childbearing age up to 35 years of age. There were three types of initial sample conditions, (1) Anaemic adolescent girls or women (studies number 2, 7 and 9), (2) healthy women (study numbers 3-6, 8) and (3) a combination of anaemic and healthy women (study numbers 1, 11 and 12). There were six studies with a cross-sectional study design and six studies conducted with a randomised, double-blind, controlled design.

The 11 studies used different cognitive function instruments with different domains to give different results as a result of iron deficiency on cognitive decline. As reported in the study above, some of the individual tests used were: Modified Harvard's Steep,[14] CANTAB,[15] computerised neurocognitive battery (CNB),[20, 23] Stanford-Binet Scale,[22, 23] Raven Matrix,[6, 18] MJW and DMDX programs,[15, 21] IntegNeuro, Brain Resources[17] and Mini mental state examination (MMSE) Questionnaire, Montreal cognitive assessment (MoCA).[24]

Three studies described the relationship between iron deficiency and physical activity in adolescents and young women, using different measuring instruments. The three studies showed a significant relationship between iron deficiency and physical activity, including decreased work activity in children,[14] decreased activity, endurance and performance in completing tasks[6] and light activities (LPA) with less time per day compared to children who had enough iron in their bodies.[19]

Discussion

Relationship of iron deficiency with decreased cognitive function

An important component of heme, which is required for the synthesis of haemoglobin, is iron; iron deficiency can lead to low haemoglobin levels. Iron that comes from food in the form of ferric ions is reduced to ferrous ions before being absorbed. This ferrous form is then absorbed by the mucosal cells of the small intestine and undergoes oxidation to form ferric ions again. A small portion of ferric ions form ferritin and most of them are reduced to ferrous ions which are released into the bloodstream and ferrous ions are re-oxidised to form ferric ions which then bind to transferrin and are stored as reserves in the liver, spleen and bone marrow in the form of ferritin.[25, 26]

Iron is an essential component for brain development and is needed for cell differentiation, protein synthesis, haemoglobin synthesis, neurotransmitter production and energy metabolism.[27] Iron deficiency can cause abnormalities in three brain domains, namely a decrease in dendritic structure and an increase in glutamate in the hippocampus, nerve hypomyelination and changes in the metabolism of the neurotransmitter dopamine.[28, 29] Changes in dopamine metabolism can reduce the ability of the striatum and amygdala to regulate motivation. This decrease in motivation can reduce learning abilities and can reduce children's cognitive function.[30]

Diversity cognitive function tests are grouped into different domains, multiple construct measurement tests and a variety of tests to evaluate specific cognitive domains. There is currently no consensus on the classification of cognitive tests and domains,[31] which may explain some of the differences between studies. The classification of the executive function domain includes attention and impulsive action; the working memory domain, which measures multiple constructs, includes information processing, memory and executive function planning.[31, 32] Continuous performance tests that measure sustained attention and capacity to inhibit impulsive responses over time, were used to assess the attention domain.[32]

Of the 11 studies that examined the relationship between iron deficiency and decreased cognitive function, there was one study that showed a non-significant relationship between iron deficiency and cognitive decline and there were ten studies that showed a significant relationship between iron deficiency and cognitive decline in children. Different domains were different. Five studies used cognitive function instruments with five domains, one study used four domains, one study used seven domains and three studies used cognitive function instruments with a total score. Several studies used the same cognitive function domain, including the impulsivity task domain (GNG), attention network task domain (ANT), memory task domain, simple reaction time task domain (SRT) and executive function domain.

Regional developmental requirements for iron differ across specific brain systems and it is likely that this underlying mechanism is still unclear across cognitive domains. The domains of cognitive function are related to different brain systems; therefore, the domains of cognitive function may vary in their sensitivity to iron deficiency or excess.[33]

The mechanism underlying changes in brain activity in relation to iron status may involve disturbances in neuroendocrine function. The enzymes that synthesize catecholamines, serotonin and thyroid hormones require an iron cofactor for their activity; changes in enzyme levels and activity are seen in iron-deficient animals and humans.[34] Iron deficiency and iron anaemia lead to lower intelligence and performance scores, disturbances in attention span and sensory perception functions, as well as functions related to emotion and behaviour, which are critical to school achievement in adolescents.[35, 37]

The effect of iron deficiency on physical activity

Iron is an important mineral that the body needs to produce one of the components of red blood cells, namely haemoglobin. Haemoglobin is a protein that functions to transport oxygen to be distributed throughout the body's tissues. When there is an iron deficiency, the body cannot produce enough haemoglobin. Lack of haemoglobin production reduces the oxygen supply in the blood so that the body does not get enough oxygen. This is what causes iron deficiency anaemia sufferers to become easily tired, weak, even short of breath and affect their physical activity.[38]

Anaemia due to iron deficiency can reduce the performance of young women in activities due to the low amount of oxygen supplied to tissues and cells.[14] A study reported that adolescent girls who were anaemic had significantly higher pulse rates immediately after one to two minutes of activity compared to adolescents who were not anemic,[39] this was due to the low supply of oxygen to the blood and tissues.[39, 40] Giving iron supplementation to adolescent girls can significantly reduce perceived fatigue.[41] The iron-dependent serotoninergic and dopaminergic reuptake systems function seems to be partially demonstrated by the activity.[42-47] Women who are iron deficient have decreased activity due to the changes in the brain system.[14]

Iron deficiency causes decreased energy levels and cognitive capacity due to changes in dopamine and serotonin levels that are felt in the body.[42-44] Increased sensitivity due to iron deficiency can cause difficulty in concentrating attention on tasks and cause feelings of frustration or irritability. More attention is concentrated on sensory processing. However, these results still require a more in-depth study in terms of theoretical approaches to sensitivity. Iron reduces the level of stimuli required for cognitive functioning and protects the nervous system from overstimulation .[6]

There is a relationship between haemoglobin levels and maximum oxygen volume (VO_2max), it is proven that an athlete who has high haemoglobin levels has good endurance or VO_2max. When the haemoglobin level is below normal, the oxygen level in the blood is also lower and *vice versa*. Normal haemoglobin levels make the process of transporting oxygen into the tissues more optimal.[48] A review of research has provided evidence that high-intensity exercise has a positive effect on oxygen levels. The mechanism of high intensity exercise is that the heart, lungs and muscular system are forced to work hard and one of the effects is an increase in the maximum amount of oxygen. A decrease in physical activity will affect a person's cardiorespiratory endurance in carrying out daily activities. The need for continuous oxygen supplementation can influence a 6-minute walking activity test in respondents.[49]

Conclusion

Lack of iron in the body causes a decrease in cognitive function, especially in the domain attention tasks, memory task domains and executive functions domains. In addition, iron deficiency can also cause a reduction of physical activity in adolescents due to the low amount of oxygen supplied to the blood, cells and tissues. Therefore, research is needed on nutritional intervention programs to improve iron anaemia status in adolescent girls and prevent a decline in cognitive function and physical activity due to iron deficiency.

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Conflict of interest

None.

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