

Relationships Between Iron Status and Academic Performance

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ABSTRACT

Adolescent females are susceptible to iron deficiency. Iron may be linked to cognition based on its contribution to central nervous system function. Effects of iron deficiency may be reflected in academic performance as measured by grades. The purpose of this study was to determine whether an association existed between iron status and academic performance. Participants were 14- to 16-year-old healthy female students in the 10th grade. Relationships between academic performance, vitamin B₁₂ and albumin were also examined. Blood parameters for 71 participants included: serum ferritin, hemoglobin (Hb), vitamin B₁₂, and albumin. Academic performance was assessed by school grades and included the following measures: Overall average, plus individual scores in, Math, Science, Physical Education, and English. The prevalence of iron deficiency (serum ferritin ≤ 20 $\mu\text{g/L}$) in the sample was 58%. One participant was iron deficient anemic (Hb < 120 g/L). Two participants were deficient in vitamin B₁₂ (≤ 150 pmol/L). No participants displayed low albumin levels (< 35 g/L). In a bivariate correlation, serum ferritin was negatively correlated ($p < 0.05$) with Grade Average and English. There was no relationship between vitamin B₁₂ and academic performance. Albumin was correlated ($p < 0.05$) with Grade Average, Physical Education, and English, and was a significant predictor of grades in multivariate analysis ($p < 0.05$). Between subject t-tests revealed no significant difference in grades between those who were iron deficient and those who were not. It was concluded that the presence of serum ferritin below 20 $\mu\text{g/L}$ does not pose a significant hazard to scholastic achievement.

LIST OF TABLES

Table 1. Studies Involving Iron Status and Academic/Cognitive Performance in Female Adolescents	39
Table 2. Descriptive Statistics for Serum Ferritin (SF), Hemoglobin (Hb), Vitamin B ₁₂ , Albumin, Measures of Academic Performance, and Body Mass Index (BMI)	50
Table 3. Correlations (r) Between Serum Ferritin, Hemoglobin and Measures of Academic Performance	51
Table 4. Partial Correlations Between Iron Status and Performance Variables Controlling for B ₁₂ and Albumin	51
Table 5. Correlations by Descending Values of Hemoglobin	52
Table 6. Correlations (r) Between Vitamin B ₁₂ , Albumin and Measures of Academic Performance	53
Table 7. Multiple Correlation. Predictors: Serum Ferritin (SF), Hemoglobin (Hb), B ₁₂ Albumin	54
Table 8. Between Subjects/Independent T-Test	55
Table 9. Relative Risk or Risk Ratios	56
Table 10. 3 Day Dietary Analysis Results	58

LIST OF FIGURES

Figure 1. Performance Model of Factors Affecting Academic Performance	20
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TABLE OF CONTENTS

Acknowledgements.....	i
Abstract.....	ii
List of Tables/List of Figures.....	iii
Chapter 1: INTRODUCTION.....	1
Purpose.....	4
Significance of Study.....	4
Definitions	5
Limitations.....	8
Delimitations.....	9
Chapter 2: REVIEW OF LITERATURE	10
Introduction.....	10
Iron Overview	10
Iron Assessment.....	13
Factors Affecting Academic Performance or Achievement	14
Iron Deficiency	21
Iron Cognition and Behaviour	25
Iron Status and Academic Performance in Adolescents	34
Summary.....	41
Chapter 3: METHODOLOGY.....	42
Participants.....	42
Procedure	43
Hematological Data Instruments.....	45
Statistical Analysis.....	46
Chapter 4: RESULTS.....	49
Chapter 5: DISCUSSION.....	59
Iron Status in Related Samples	59
Serum Ferritin	61
Hemoglobin.....	63
Vitamin B ₁₂	64
Albumin	64
Group Differences.....	67
Dietary Analysis.....	70

Chapter 6: SUMMARY and CONCLUSIONS	71
---	----

Conclusions.....	72
------------------	----

Recommendations for Future Research.....	72
--	----

REFERENCES	74
-------------------------	----

APPENDICIES

A. Participant Consent Form	85
-----------------------------------	----

B. Health Information/Physical Activity Participation Survey	87
--	----

C. Additional Questions	88
-------------------------------	----

D1. Food Intake Log.....	89
--------------------------	----

D2. Dietary Analysis Instructions.....	90
--	----

E. Scatter Plots of Serum Ferritin and Hemoglobin vs. Measures of Academic Performance	91
---	----

F. Macronutrient/RNI Percentages from 3 Day Dietary Analysis.....	96
---	----

G. Scatter Plot of Iron Status vs. % RNI.....	98
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CHAPTER 1

INTRODUCTION

Iron deficiency (ID) is the most prevalent nutritional deficiency in the world, representing a public health concern of extreme importance (Youdim, 2000). Iron deficiency is the main cause of anemia in infancy, childhood, and pregnancy, affecting more than two billion persons world wide (Peirano et al., 2001). Iron deficiency is prevalent in much of the developing world and is probably the only micronutrient deficiency of public health relevance in industrialized nations (Peirano et al., 2001). The most severe stage of the disorder occurs when iron deficiency is accompanied by anemia (IDA). It has been estimated that 20% of adult men, 35% of adult women, and 40% of children across the planet could be anemic with iron deficiency being the main contributing factor (DeMaeyer & Adiels-Tegman, 1986).

Certain groups are particularly vulnerable to iron deficiency. In developing countries, the prevalence is usually greatest in infants. In industrialized countries iron deficiency is found mainly in women (Peirano et al., 2001). The physiological changes of adolescence leave an individual prone to developing iron deficiency. The adolescent growth spurt increases iron demands during puberty (Weaver & Rajaram, 1992). Regular blood loss due to the start of menses increases the need for greater iron intake in adolescent females (Bothwell & Charlton, 1981). These increased needs continue until menopause (Bothwell & Charlton, 1981). Low iron intakes are often observed in adolescent females making them susceptible to iron deficiency (Houston, Summers, & Soltész, 1997). Adding to the risk, a society which pressures young women to look thin

can lead to adopting low kilocalorie diets and development of eating disorders which may result in them not getting the required amount of iron in their diet (Johnson, 1994).

There is a consistent body of data indicating that iron deficiency with or without anemia can no longer be considered a hematological condition (Peirano et al., 2001; Youdim, 2000). Iron deficiency can result in broader systemic effects related to behaviour, and cognition (Peirano et al., 2001). These effects can limit an individual's cognitive development (Peirano et al., 2001). With such possible consequences at stake, the importance of further investigating the relationship between iron status and academic performance becomes evident.

Physiologic rationales explaining how iron status may affect cognition and thus academic performance can be proposed. The major function of iron in the human body is oxygen transport via hemoglobin and to a lesser extent myoglobin. Oxygen transport requires approximately 74% of the body's iron (Krause & Mahan, 1979). A much smaller amount of iron, found in oxidative enzymes, is crucial to cellular energy production (Krause & Mahan, 1979). An iron deficient individual may display symptoms such as fatigue, lethargy, and irritability (Schoene et al., 1983). It can be argued that these symptoms strain the ability to study, interfere with learning, and consequently reduce academic performance. Specific to neural operation, Roncagliolo, Garrido, Walker, Peirano, and Lozoff, (1998), Peirano et al. (2001), and Walter (2003) have suggested that varying levels of iron deficiency can affect the brain's neurofunctional maturation and normal central nervous system function. They have found evidence of abnormal neurofunctional development in iron deficient individuals. It can be speculated that this abnormality could contribute to decreased academic performance. Iron is

important to the production and maintenance of myelin (a fat and protein substance which provides insulation and increases the transmission speed of electrical impulses throughout the central nervous system) (Carlson, 1997). Iron plays a role in the synthesis and function of dopamine and serotonin (brain chemicals) transmission systems (Peirano et al., 2001). Metabolic activity related to memory processing also requires iron (Larkin & Rao, 1990). As iron contributes to these biochemical processes it has been speculated that iron depletion may affect multiple cognitive functions reflected in impaired academic performance (Grein, 2001). The majority of related research has been dominated by standardized test assessments, which do have identified limitations. Much of the research is delimited to infants and children living outside of North America in less developed countries where iron deficiency is highly prevalent. In these populations variables such as other nutrient deficiencies, increased infections, and poor living conditions may have confounded results. Due to higher living standards, a Canadian study may potentially eliminate some of the socioeconomic factors present in developing countries.

Work by Lozoff, Jimenez, Hagen, Mollen, and Wolf (2000), suggests that children who were anemic at a young age continue to perform suboptimally as they grow up even after the deficiency is corrected. Most researchers using correlation to study the topic of iron deficiency and cognition find associations between iron deficiency and poor cognitive development (Grantham-McGregor & Ani, 2001). However, few investigators have focused on older age North American groups. This issue was confirmed in a review on the topic by DiSilvestro (2005). A gap in knowledge linking iron status to cognitive performance in teenaged populations currently exists.

Purpose of the study

The purpose of this study was to determine whether there is an association between iron status as measured by serum ferritin and hemoglobin, and academic performance as measured by overall average, plus individual scores in, Math, Science, Physical Education, and English, in adolescent females.

Significance of the Study

Few researchers have investigated the relationship between iron deficiency and cognition or academic performance in adolescent populations (Taras, 2005; DiSilvestro, 2005). To this author's knowledge, there are only four researchers that have studied the link between iron status and academic/cognitive performance including North American adolescent participants (Bruner, Joffe, Duggan, Casella, & Brandt, 1996; Groner, Holtzman, Charney, & Mellitis, 1986; Halterman, Kaczorowski, Aligne, Auinger, & Szilagyi, 2001; Murray-Kolb, Whitfield, & Beard, 2004). Groner et al. (1986) sampled pregnant participants. The Murray-Kolb et al. paper included 18- to 35-year-olds in their analysis and to this author's knowledge, has not been published in a peer reviewed journal. Bruner et al. (1996) and Halterman et al. (2001) measured cognitive achievement through analysis of various indexes of cognition, but neither attempted to obtain and correlate iron status parameters such as serum ferritin and hemoglobin with actual school grades. Neither of these investigators measured B₁₂ or albumin concentrations.

This researcher directionally hypothesizes that lower iron status will accompany lower academic performance. A significant correlational relationship between iron status

and all measures of academic performance should reveal a difference between iron deficient and iron sufficient groups regarding school grades. Positive relationships between iron status and academic performance may encourage support for research of a causal nature. Establishing a causal relationship would be a challenge, but the implications of such a study could have a large scale impact. Iron treatment programs could be initiated with the goal of improving an individual's and a society's developmental potential. These improvements could arguably boost national economies (Hunt, 2002). Non-significant or negative relationships may help investigators focus on different research objectives.

Conducting this study will add to a body of literature requiring more research, and demonstrates the willingness of this researcher to play a role in serving the community by providing direction for future health recommendations.

Definitions

Academic Performance: For the purposes of this study academic performance was defined as both average term grade and individual course grades in Math, Science, English, and Physical Education.

Albumin: Albumin is a blood plasma protein that is produced in the liver and forms a large proportion of all plasma protein. Albumin helps maintain osmotic pressure and transports substances such as thyroid and fat soluble hormones, and fatty acids. This protein competitively binds calcium and buffers pH. Albumin can be found in blood plasma or serum, muscle, the

whites of eggs, milk, and other animal substances and in many plant tissues and fluid (National Library of Medicine, 2006).

BMI: Body Mass Index. The ratio of the weight of the body in kilograms to the square of its height in meters. BMI is used as a practical marker to assess obesity. An indicator of optimal weight for health, BMI is different from lean mass or percent body fat calculations because it only considers height and weight (National Library of Medicine, 2006).

Ferritin: A crystalline iron-containing protein that functions in the storage of iron. Nearly all cells contain ferritin, although the bulk of body iron stores are found in the liver and spleen (National Library of Medicine, 2006).

Hemoglobin: An iron-containing respiratory pigment of red blood cells that functions primarily in the transport of oxygen from the lungs to the tissues of the body. Hemoglobin combines loosely and reversibly with oxygen in the lungs to form oxyhemoglobin and with carbon dioxide in the tissues to form carbhemoglobin. In women hemoglobin is present normally in blood to the extent of 12 to 16 grams per 100 milliliters and is determined in blood either colorimetrically or by quantitative estimation of the iron present (National Library of Medicine, 2006).

Operational Definitions of Iron Related Terms:

Subject Groups	Parameters
Group 1: Iron Sufficient	Serum Ferritin > 20 :g/L Hemoglobin: normal 120 to 160 g/L
Group 2: Iron Deficient not Anemic	Serum Ferritin ≤ 20 :g/L Hemoglobin: normal 120 to 160 g/L
Group 3: Iron Deficient Anemic	Serum Ferritin < 12 :g/L Hemoglobin < 120 g/L

Adapted from Tobin and Beard 1997

RNI: Recommended Nutrient Intake. “A dietary recommendation for nutrient intake. The Canadian RNI covers the needs of 98% of the healthy population, including those with higher than average nutrient requirements.” (Manore & Thompson, 2000, p.5).

Vitamin B₁₂: A complex cobalt-containing compound C₆₃H₈₈CoN₁₄O₁₄P that occurs especially in liver and is essential to normal blood formation, neural function, and growth, and is used especially in treating pernicious and related anemias – also called *cyanocobalamin* (National Library of Medicine, 2006).

Limitations

1. The only requirement for inclusion was being a healthy grade 10 female student. Participation from different subgroups (i.e., active vs. non-active or athlete vs. non-athlete) was not controlled which may affect generalizability of data.
2. Several interrelated factors affect academic performance. Socioeconomic status and specific environmental factors were not measured and could be considered possible confounders. Although, the likeliness of these variables to selectively alter the relationship of iron status to some academic subjects and not others can be speculated.
3. Serum ferritin is an acute phase reactant and may be falsely elevated by factors other than iron status such as exercise, acute inflammation or infection. These factors were monitored, but not statistically controlled. This is a common limitation identified in the field of study.
4. The extent of menstrual blood loss was not measured. Menstrual blood losses can effect iron status. Collecting menses data would have placed added burden on the participants, possibly decreasing their motivation to volunteer. Cyclic variations in iron status are a potential source of error when iron status is assessed in ovulating teenage females (Kim, Yetley, & Clavo, 1993). However timing of menstrual period and cycle phase were monitored and considered upon interpretation of results.

5. The dietary analyses were dependent upon the following: accuracy of the information recorded by each participant on whether the three days analyzed represented the true intakes, accuracy and consistency of the investigators' interpretations, and the accuracy of the nutrition software program Foodworks (version 1.0).

Delimitations

1. This study was delimited to grade 10 apparently healthy (no known health condition) menstruating females between the ages of 14 and 16 years residing in Thunder Bay, Ontario, Canada.
2. Blood assays were performed for serum ferritin, hemoglobin (Hb), vitamin B₁₂ and albumin. These parameters served as independent or predictor variables.
3. The dependent or criterion variables were the discrete scores achieved in Grade Average, Math, Science, Physical Education, and English. Collectively these scores were termed Academic Performance. Other measured variables included: height, (continuous), weight (continuous), and body mass index (continuous).

CHAPTER 2

REVIEW OF LITERATURE

Introduction

The literature relating iron, to cognition, and more specifically to academic performance is reported in this chapter. For organizational purposes, the literature is presented under the following topics: 1) Iron overview, 2) Iron assessment, 3) Factors affecting academic performance or achievement, 4) Iron deficiency, 5) Iron, cognition and behaviour, 6) Iron status and academic performance in female adolescents, and 7) Summary

Iron Overview

Iron (Fe) is considered a *minor* or *trace* mineral. Although present in small amounts in the human body, iron plays an essential role for hundreds of proteins and enzymes. Iron's functions in the body include the following: oxygen transport and storage, electron transport and energy metabolism, deoxyribonucleic acid (DNA) synthesis, erythropoiesis (red blood cell formation), and production and maintenance of myelin (Wardlaw, Hampl, & DiSilvestro, 2004). Iron is also important in the synthesis and function of dopaminergic, serotonergic, and catecholaminergic neurotransmission systems (Peirano et al., 2001; Youdim, 2000).

Approximately two thirds of the body's iron is found in hemoglobin, the iron-protein compound that increases the oxygen carrying capacity of blood by about 65 times (Bothwell, Charlton, Cook, & Finch, 1979). Smaller amounts of iron are also present in

myoglobin, a compound similar to hemoglobin that aids in oxygen transport within the muscle cells (Bothwell et al., 1979). The iron found in cytochromes, iron-protein electron carriers in the mitochondrion, helps facilitate energy production during exercise. The hemoglobin molecule consists of the protein *globin*, which is composed of four subunit polypeptide chains. Each of these polypeptides contains a single heme (iron containing) group with a single iron atom that acts as a magnet for binding oxygen. Hemoglobin gives blood its red colour (Wardlaw et al., 2004). There are about 280 million hemoglobin molecules packed into each of the 25 trillion red blood cells in the body (Wardlaw et al.). Hemoglobin also carries carbon dioxide away from the muscles to the lungs (Manore & Thompson, 2000).

In total there is normally between three and five grams of iron present in the human body (Bothwell et al., 1979). Eighty percent of this iron is found in the functionally active compounds hemoglobin, myoglobin, and cytochromes. The other 20% is not combined in functionally active compounds and make up the iron stores or reserves located in the liver, spleen, and bone marrow (Beard & Dawson, 1997). Iron is stored in the form of hemosiderin and ferritin. Hemosiderin is an insoluble form of stored iron that forms large concentrated clusters within the cell (Beard & Dawson, 1997). Ferritin is a protein that binds iron and stores it within the cells (Beard & Dawson, 1997). A small amount of it circulates in the blood. This circulating ferritin reflects the amount of iron stored in the body. A gender difference exists regarding iron storage. Males typically have about 1000 mg of stored iron whereas females store about 300 mg (DiSilvestro, 2005). The lower iron stores in women are mainly attributable to menstrual blood losses. Menstrual bleeding is a major factor increasing the risk for developing iron deficiency

(Manore & Thompson, 2000). Females usually lose between 5 and 45 mg of iron during menstruation (Haymes & Lamanca, 1989).

Dietary iron comes from two sources: *animal (heme)*, and *plant (non-heme)*. Both sources come from different foods and are absorbed at different rates. Between 2% and 10% of iron from plant sources is absorbed whereas 10% to 35% of animal iron is bioavailable (Beard & Dawson, 1997). Bioavailability refers to the proportion of any nutrient in food that is absorbed and utilized. The low bioavailability of non-heme iron puts people on vegetarian diets at risk for developing iron deficiency, particularly if these individuals are women.

Besides the source there are other factors which either enhance or inhibit iron absorption. Vitamin C promotes absorption of plant iron (Rossander, Hallberg, & Bjorn-Rasmussen, 1979). Any condition that increases demands for iron in the body such as pregnancy, high altitude, and exercise training, also increases its absorption. High gastric acid production, resulting in low stomach pH is another factor enhancing iron absorption (Yip, 2001). Factors that inhibit iron absorption include: decreased iron demand or good iron status, tea, coffee, oxalic acid, fiber, soy, mineral-mineral interactions that compete with iron for transport into intestinal cells (i.e., zinc, calcium, manganese), and high antacid use resulting in higher stomach pH (Yip, 2001). A decrease in iron intake or an increase in iron loss either through the blood, urine, feces, or sweat will first deplete iron stores and then may lead to iron deficiency with or without anemia (Weaver & Rajaram, 1992).

Iron Assessment

Traditionally the condition of iron deficiency anemia has been detected by a blood value called hematocrit (Ross, 2002). This value refers to the percent of blood volume taken up by red blood cells (Braunwald et al., 2001). Values beneath 34% to 37% are associated with iron deficiency (Braunwald et al., 2001). Clinical laboratories typically measure whole blood hemoglobin when assessing anemia (DiSilvestro, 2005). Iron deficiency is not the only cause of anemia, but it is a common cause (Ross, 2002). There are useful methods for testing iron status in the absence of anemia. Serum ferritin, which is proportional to iron stores, is one of these methods (Wardlaw et al., 2004; Ross, 2002). A downside to serum ferritin is that it can be affected by factors besides iron status such as inflammation and day-to-day variations within individuals (Lipschitz, Cook, & Finch, 1974). Iron status assessment is occasionally performed using serum iron. Drawbacks of this method include wide diurnal (having a daily cycle) variation and depression as a feedback response (Wardlaw et al., 2004; Ross, 2002). Serum iron values can drop due to blood loss, a pregnancy, or development of cancer (DiSilvestro, 2005). Another evaluation measurement is transferrin saturation, which is the ratio of serum iron to iron-binding capacity (Wardlaw et al., 2004; Ross, 2002). The obstacles with this method are the same as serum iron. An additional assessment is erythrocyte protoporphyrin (Wardlaw et al., 2004; Yip, 2001). This particular evaluation calls for only a few drops of blood and requires minimal technical experience. Values tend to be less subject to diurnal variations compared to other iron evaluation techniques. However, lead poisoning, and inflammation raises levels (Yip, 2001). Protoporphyrin has been used mainly in population surveys and not typically in clinical situations (DiSilvestro, 2005).

The newest addition to assessment of iron status is serum transferrin receptors (Feelders, Kuiper-Kramer, & van Eijk, 1999). These receptors, found on cell membranes, make their way into the serum. In response to a dropping iron supply, even in mild instances, synthesis for transferrin receptors increases (Feelders et al., 1999; Takala et al, 2003; Beguin, 2003). Unlike values for serum ferritin or iron, serum ferritin receptor levels do not change with inflammation (Beguin, 2003). This assessment technique may be practical for identifying iron deficiency in the presence of chronic disease, as is found in elderly populations (DiSilvestro, 2005).

Factors Affecting Academic Performance or Achievement

Achievement in school is a topic of great practical concern to teachers and parents, and of great theoretical concern to researchers. Undoubtedly there are a multitude of coexisting and interrelated variables contributing to academic performance. Environmental, socioeconomical, personal/psychological, physical, and nutritional are all variables potentially affecting school achievement. Collectively, these variables combine to determine the degree of cognitive engagement responsible for attaining academic goals. Underlying this process are three influencing factors: attitude, motivational desire, and use of academic strategies or techniques (Tuckman, 1999). A condensed performance model of factors affecting academic performance is presented in Figure 1.

A student's academic performance may hinge on the education environment itself. Factors such as quality of instruction, classroom size, teacher training, teacher expectations (Rosenthal & Jacobsen, 1968) and availability of textbooks and other resources exert an enormous impact on student success (Peterson-Geierstanger, Amaral,

Mansour, & Walters, 2004). Social and environmental factors, such as socioeconomic status or household characteristics, play a key role in academic performance. These factors operate directly or indirectly by influencing student health status (Blum et al., 2000).

Personal/psychological factors also produce effects. Researchers have documented the influence of alcohol, tobacco, and other drug use (Blum et al., 2000; Hanson & Austin, 2003; Symons, Cinelli, James, & Groff, 1997; Glied & Pine, 2002; Klerman, 1996), emotional problems (Blum et al.; Glied & Pine; Klerman), diet (Hanson & Austin; Symons et al., 1997; Glied & Pine), intentional injuries (Blum et al.; Hanson & Austin; Symons et al.; Glied & Pine), physical illness (Bailey-Britton, 1987), self-esteem, sexual behavior (Symons et al., 1997), and health care utilization (Bailey-Britton, 1987) on academic performance. Research has indicated a relationship between resiliency, developmental assets, and academic performance (Scales & Roehlkepartain, 2003). School connectedness, the perception of closeness to school and school personnel, has been associated with improved academic standing (Hanson & Austin, 2003). School health programs such as school nursing, health education, counseling, psychological and social services, and nutrition programs often integrated with school based health centres can also play a role. Although, documenting clear and robust links between single events and academic outcomes is challenging. Following a literature review on the link between school nursing and academic performance, Maughan (2003) concluded that it is difficult to link any specific school performance outcome solely to one intervention by a school nurse, and controlling for extraneous variables over time makes the research design complex (Maughan, 2003).

Physical activity is another factor which may affect performance in school. Physical activity improves general circulation, increases blood flow to the brain, and raises levels of norepinephrine and endorphins (Fleshner, 2000). These physiologic changes may reduce stress, improve mood, induce a calming effect after exercise, and perhaps as a result improve academic achievement (Fleshner, 2000; Morgan, 1994). The structure of physical activity in schools provides social benefits that could result in academic outcomes. Children who learn to cooperate, share, and follow rules in a team setting where members function as a unit, and children who learn to test their physical boundaries in individual activities are likely to feel more connected to their school or community and want to challenge themselves (Taras, 2005). Physically active adolescents are less likely to attempt suicide, adopt risk-taking behaviors, and become pregnant. Reduction of these practices may be associated with better academic results (Brown & Blanton, 2002; Patel & Luckstead, 2000). Intimately linked to physical performance is another factor which can affect academic achievement – nutrition.

The possible effects of nutrition on academic performance can be summarized under the following topics: nutritional supplements and micronutrients, food insufficiency, and effects of eating breakfast (Taras, 2005).

Researchers in the United States and United Kingdom have investigated giving multivitamin and mineral supplements to healthy populations of school-age children to determine effects of these supplements on intelligence or school achievement. Results have varied. Upon review, it appears there are no effects of multivitamin supplementation on the intelligence or academic performance of most children (Taras, 2005). Non-verbal intelligence improvements in certain populations of children are

possible, but there are no predictable characteristics of these subpopulations.

Commentary has pointed to a possible fundamental shortcoming with the research. A theoretic foundation indicating how vitamins and minerals improve intelligence may be lacking (Smith, 2000). Conclusions are further limited due to the small number of researchers in the field and uncertainty about possible connections between the vitamin-mineral supplement industry and the research (Smith, 2000).

Food insufficiency (the limited availability of nutritionally adequate and safe food) is a serious problem affecting children's ability to learn. Of ten articles found, seven investigated populations outside North America. Effects on reported school performance have been discovered. Although, in some of the studies poverty and parasites confounded results. In two of three studies from the United States, food insufficiency was associated with decreased school attendance, or declining academic performance (Taras, 2005).

There are 18 studies identified describing the effects of eating or not eating breakfast on student academic performance. Less than half included North American participants. Findings suggest eating breakfast is an effective way to improve academic performance in undernourished populations (Taras, 2005). Eating breakfast versus fasting may improve scholastic performance on the morning eaten (Pollitt, Cueto, & Jacoby, 1998). The long term effects of eating breakfast on academic performance in students with no signs of malnourishment are less certain (Taras, 2005).

It has been proposed that attitude, motivational desire, and use of academic strategy or techniques are three underlying factors which drive and influence academic achievement (Tuckman, 1999). The attitude often used in combination with motivation

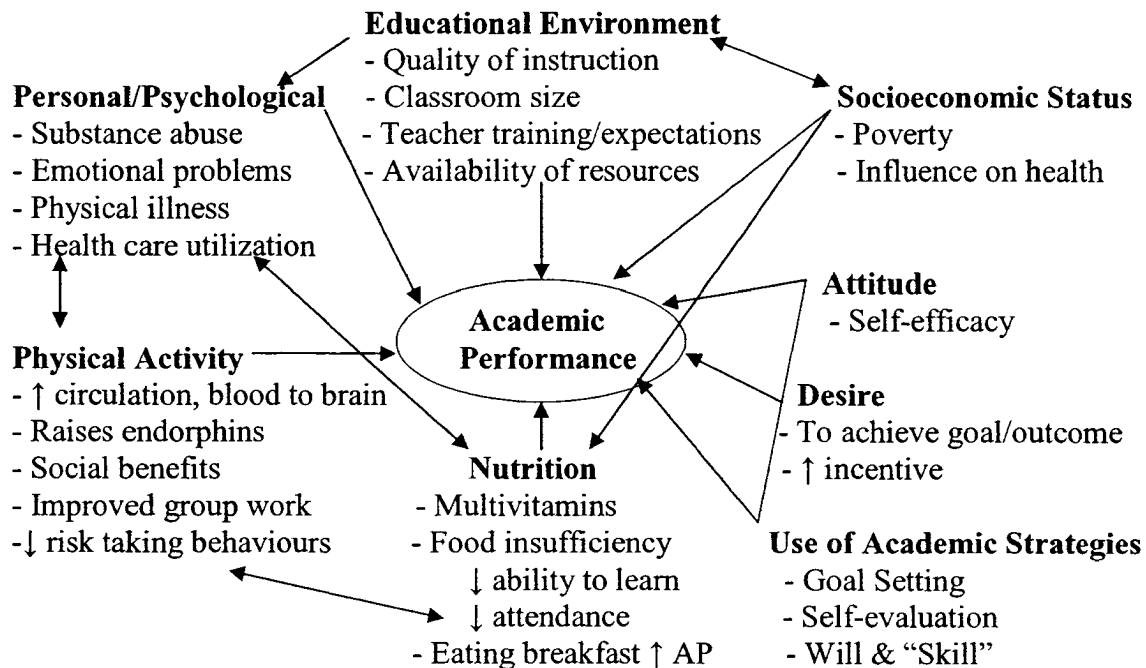
to achieve is self-efficacy, or how capable people judge themselves to be to perform a task successfully (Bandura, 1977). This author provided evidence that self-efficacy is an important factor in the extent to which people can bring about significant outcomes in their lives. Specifically, there is evidence that self-efficacy beliefs contribute to academic achievement by enhancing the motivation to achieve. Schunk (1989) has shown that children with the same level of intellectual capability differ in their performance due to their level of self-efficacy.

One potential source of the drive to perform is the incentive of producing the performance. Incentive theories of motivation suggest that people will perform an act when the result of the performance is likely to conclude with some outcome they desire, or that is important to them (Overmier & Lawry, 1979). For example, in anticipation of a scenario involving requisite performance, a person may expend considerable effort in preparation because of the desire to achieve success or avoid failure (Overmier & Lawry, 1979). This desire may provide incentive motivation for the person to expend the effort to achieve his/her goal (Tuckman, 1999). Other studies support the importance of drive or value using sources alternative to incentives as a factor related to achievement. Pintrich and De Groot (1990) found a significant negative correlation between test anxiety, often considered an expression of drive, and achievement among seventh graders. Zimmerman, Bandura and Martinez-Pons (1992) found a relationship between school achievement and an additional demonstration of value or drive - their high school student's grade goals.

Believing in one's personal competence to perform a task and possessing the desire to achieve a particular outcome can aid in reaching a goal. However, being able to carry

out specific strategies that support success, in a variety of fields including academics, appears critical (Zimmerman, 1998). Work has been done reflecting the connection between specific strategies and performance outcomes (Tuckman, 1999). Academic success is not determined only by will, but also by skill. Strategies that can impress upon achievement include: self-observing, self-judging, and self-reacting (i.e., goal setting, planning) (Tuckman, 1999). More additions to this list include: self-evaluation and monitoring, goal setting and strategic planning, strategy implementation and monitoring, and strategic outcome monitoring (Zimmerman, 1998).

Figure 1.
Performance Model of Factors Affecting Academic Performance.



Abbreviations and symbols: ↑ = increase in, ↓ = decrease in, ↕ = direction of affect, AP = academic performance.

Iron Deficiency

Iron deficiency is a major problem around the world and could be called the most common micronutrient deficiency worldwide (DiSilvestro, 2005). This deficiency occurs in both underdeveloped and industrialized nations. Specific populations have an increased risk of experiencing iron deficiency. In developing countries, the prevalence is usually greatest in infants, whereas in industrialized countries it is found mainly in women (Peirano et al., 2001). Infancy is considered the time of highest vulnerability for developing iron deficiency anemia (IDA) due to rapid growth and limited sources of dietary iron (Lozoff et al., 2000). Approximately 25% of all infants in the world have IDA and many more have iron deficiency without anemia (Lozoff et al., 2000). Iron deficiency in Canada has been reduced over the last two to three decades. This reduction is attributable to consumption of iron fortified foods and increased breast feeding (Feightner, 1994). It is currently estimated that only 5 to 7% of Canadian infants are iron deficient anemic (Health Canada, 2004). However, for some groups the cost of iron fortified food is beyond their means. Groups at risk include: minority children of low socioeconomic status, Chinese children, Aboriginal children, Mexican children, and infants of low birth weight (Lozoff et al., 2000). Prevalence statistics accurately reflecting Northern Ontario are difficult to pinpoint. Newhouse, Clement, Taunton, and Lai (1993) sampled 111 female participants from the Thunder Bay area and revealed iron depletion (serum ferritin < 20 µg/L) and iron deficiency anemia (hemoglobin < 120 g/L) rates of 39% and 3.6% respectively.

The fact that IDA is most prevalent during infancy has further implications for the future. Infancy is a time of high vulnerability for the central nervous system and the most critical period of brain growth (Lozoff et al., 2000). Infants affected by iron deficiency at this time have a developmental disadvantage and face the possibility of not reaching their developmental potential in society.

In addition to infancy adolescence is another time period, with physiological outcomes, predisposing an individual to acquire iron deficiency. The adolescent growth spurt and recurrent iron loss resulting from menstruation place an added burden on the iron status of women who already have lower iron stores than men (Bruner et al., 1996). Females with heavy menstrual blood losses are especially prone to iron deficiency (Marx, 1997). Compounding the issue, low energy intakes observed in some women cannot satisfy iron requirements. Therefore, the adolescent female is highly vulnerable to iron deficiency (Manore & Thompson, 2000). Low meat consumption, often observed in young adult women and teenaged females compared to their male counterparts, contributes to iron deficiency (Allen, 2002). Sociocultural demands on young women to be thin, pressuring them to engage in disordered eating behaviours (Johnson, 1994) may also have an effect.

Pregnant women are fortunate in the sense that they do not have to contend with menstrual blood losses, however iron levels are still an issue. Throughout pregnancy a large amount of iron goes into creating a new bloodstream and other body changes (Marx 1997; Wardlaw et al., 2004). Premature infants are susceptible to iron problems (O'Keeffe et al., 2002). Iron stores are supposed to support many baby needs in early stages following birth. The majority of these iron stores are generated during the last

trimester of pregnancy. A premature birth cuts short the iron storage period (Rao & Georgieff, 2002).

It has been reported in several studies and review articles that athletes, especially endurance athletes involved in heavy training, may be prone to iron deficiency (Clement Asmundson, & Medhurst, 1977; Clement & Sawchuck 1984; Manore & Thompson, 2000; Newhouse & Clement, 1988). It is generally agreed that low serum ferritin levels are frequently found in athletes, but there is no agreement as to the significance of these findings. Low serum ferritin may represent a true iron deficiency or a physiological adaptation to training (Eichner, 1992; Sherman & Kramer, 1990). Ehn, Carlmark, & Hoglund (1980) showed that iron absorption is lower in athletes than non-athletes, even when both have an ample supply of iron. This decrease in iron absorption might be because food tends to pass faster through the gastrointestinal tracts of athletes (Lampe, Salvin, & Apple, 1990). The highest risk of inadequate iron intake is found in athletes competing in gymnastics, ballet, or long-distance running (Otis, Drinkwater, Johnson, Loucks, & Wilmore, 1997). In these sports low body weight is an asset. Other risk factors applying to athletes involve high iron losses. Demanding bouts of exercise have been reported to result in iron losses from the gastrointestinal tract (Lampe et al., 1990; Weaver & Rajaram, 1992), in urination (Haymes & Lamanca, 1989; Jones, Newhouse, Jakobi, LaVoie, & Thayer, 2001), and in perspiration (Haymes & Lamanca, 1989; Lamanca, Haymes, Daly, Moffatt, & Waller, 1989). Although these losses may be short lived or transient, physical activity may provoke a negative iron balance due to increases in iron losses and requirements.

In the elderly, several researchers have found that iron status can become a problem due to low iron intake, development of chronic disease, and GI blood losses (Balducci, 2003; Beard, Richards, Smicklas-Wright, Bernardo, & Kordish, 1996; Bohmer, Fruhwald, & Lapin, 2003; Coban, Timuragaoglu, & Meric, 2003). In certain cases, anemia can take a mild form. Anemia left untreated can progress and contribute to escalation in mortality, poor health, fatigue, and functional dependence (Balducci, 2003). Increased risk of cardiovascular or neurological problems may result as well (Balducci, 2003). However, not all elderly populations show a high prevalence of iron deficiency. Fleming et al. (2001) showed that a large group of non-institutionalized U.S. elderly participants (n = 1016) displayed a low, three percent, incidence of low iron stores.

Vegetarians are prone to iron deficiency (Wardlaw et al., 2004; Marx, 1997). This group struggles to take in enough iron because they do not eat meat, which provides well-absorbed heme iron. Meat also promotes iron absorption from other foods. The high fiber or oxalic acid content of typical vegetarian diets can further depress iron absorption (DiSilvestro, 2005). Although, most vegetarian diets provide adequate amounts of vitamin C, which promotes iron absorption (Wardlaw et al., 2004).

As the evidence mounts it becomes apparent that iron deficiency is not only a hematological condition; there are significant systemic effects to consider (Peirano et al, 2001). Research has indicated that iron deficiency with or without anemia alters the behaviour of an individual in cognitive, motor and emotional frameworks. These changes likely interfere with optimal development. Such consequences hanging in the balance support the need to appraise the relationship between iron, cognition and behaviour.

Iron, Cognition and Behaviour

Within normal levels it is plausible that iron status may not be related to cognitive performance. In a spectral electroencephalographic study of 14 men aged 20 to 64 (mean \pm SD, 29.4 ± 10.6 years) and mean serum ferritin $78.1 \mu\text{g/L}$, Tucker and Sandstead (1981) noted that task performance measured by digit span forward and backward and tonal memory forward and backward was not significantly ($p > 0.05$) related to iron status (serum ferritin, serum iron). Electroencephalographic (EEG) correlates of iron status did reach highly significant values (i.e., Frequency of Peak Power on serum ferritin; $R\text{-square} = 0.92$; $p < 0.005$) although the clinical significance of these EEG results were raised based on the lack of any significant relationships observed between the iron status parameters and the performance tasks. However, impaired cognitive function appears to be associated with anemia (DiSilvestro, 2005).

Webb and Oski (1973) indicated a correlation between hemoglobin concentration and academic performance. These authors studied 12- to 14-year-old ($n = 193$) junior high students from an economically deprived community in Philadelphia. Anemia was present in 92 students with hemoglobin (Hb) values ranging from 100 g/L to 115 g/L . The other 101 students had Hb values from 140 g/L to 149 g/L and served as normal controls. The Iowa Test of Basic Skills was administered to all participants. Relationships of anemia, age, and sex with composite achievement scores were calculated by multifactor analysis of variance. Test scores were significantly lower in the anemic, presumably iron deficient students (5.08 ± 1.25 vs. 6.73 ± 2.07 ; $p < 0.025$). The magnitude of the derived correlation coefficient between iron status and test score was fairly strong ($r = 0.67$). However, potential confounding variables such as poverty and

race were not considered. Most correlational researchers find associations between iron deficiency anemia and poor cognitive development, motor development, and behavioural problems (Grantham-McGregor & Ani, 2001). Looking as far back as 1919, several studies can be identified noting significant associations between hemoglobin levels and measures of cognitive performance or school achievement (Agarwal, Upadhyay, & Tripathi, 1987; Clarke, Grantham-McGregor, & Powell, 1991; Florencio, 1988; Grindulis, Scott, Belton, & Wharton, 1986; Popkin & Lim-Ybanez, 1982; Waite & Neilson, 1919; Walker, Grantham-McGregor, Himes, Williams, & Duff, 1998; Webb & Oski, 1973). Correlational studies offer the opportunity to look for possible interactions between anemia and socioeconomic or medical conditions, but few have controlled for both and most had sample sizes insufficient for doing so. Besides hemoglobin some of the studies did not include other measures of iron status. The possibility exists that iron deficiency was not the sole cause of anemia.

The relationship between level of anemia and developmental decline has also been investigated. It appears that the level of anemia associated with declining development varies in different populations. In one study Walter, de Andraca, Chadud, and Perales (1989) compared development scales, of 196 children (birth to 15 months), with hemoglobin concentrations. Individuals with iron deficiency anemia ($Hb < 110$ g/L) were compared to iron deficient non-anemic ($Hb > 120$ g/L, serum ferritin ≤ 12 μ g/L) and control ($Hb > 120$ g/L, serum ferritin > 12 μ g/L) participants. The three groups were significantly different ($p < 0.001$; one-way ANOVA) from each other in both their motor (96.4 ± 1.3 vs. 103.4 ± 0.8 vs. 102.1 ± 1.8) and mental (90.0 ± 2.0 vs. 98.7 ± 1.0 vs. 101.2 ± 2.1) developmental indices (Bayley Scales of Infant Development).

Longitudinal follow up studies linking iron status to cognition and behaviour have also been conducted. In longitudinal study of participants with IDA (n = 48) ten years after treatment, Lozoff et al. (2000) observed statistically significant differences in components of the Wide Range Achievement Test (reading: 121.6 ± 2.4 vs. 126.9 ± 1.5 ; $p < 0.01$), (writing: 93.2 ± 1.9 vs. 98.6 ± 1.2 ; $p < 0.01$), (math: 88.8 ± 2.2 vs. 95.7 ± 1.4 ; $p < 0.01$), and Bruininks-Oseretksy Motor Proficiency Test (motor/spatial function: 42.4 ± 1.8 vs. 48.0 ± 1.1 ; $p < 0.05$) compared to non-anemic controls (n = 114). Analysis of covariance was the primary statistical approach. Covariates included sex and mother's IQ. Observed dropout from the study was 13%. The linking of hemoglobin levels to cognitive development or school achievement in early childhood versus later childhood and adolescence has been assessed by the following investigators using longitudinal analyses: (Cantwell 1974; de Andraca et al., 1990; Dommergues et al., 1989; Hurtado, Claussen, & Scott, 1999; Lozoff, Jimenez, & Smith, 2006; Lozoff, Jimenez, & Wolf, 1991; Lozoff et al., 2000; Palti, Pevsner, & Adler, 1983; Palti, Meijer, & Adler, 1985; Wasserman et al., 1992 and 1994). Collectively the initial age of the samples was under two years of age, except for Hurtado et al. (1999), who included children between birth and five years of age. On follow up the oldest participants ranged from 4 to 19. Sample sizes ranged from 21 to 148 children excluding Hurtado et al. who retrieved public records (n = 5411). All of these studies demonstrated that children with IDA as infants continued to have poorer cognition, and school achievement along with more behavioural problems into middle childhood or adolescence. In appraising these longitudinal investigations along with other studies of foreign participants it should be kept in mind

that results may have been confounded by poor socioeconomic status. Whether there was adequate control for social background is debatable.

North American studies of iron's link to cognition and behaviour have less problems with socioeconomic confounders. Oski, Honig, and Helu (1983) examined 38 non-anemic U.S. infants (9 to 12 months old). Iron supplementation impacted Mental Development Index Scores (paired t-test: 84.6 ± 19.0 vs. 106 ± 15.3 ; $p < 0.05$) in iron deficient participants. No effect was seen for infants with good iron status. Tucker, Sandstead, Swenson, Sawler, and Penland (1982) found no correlation ($p > 0.05$) between iron status (serum ferritin) and cognitive task performance (Work fluency, Imagery) in a longitudinal study of seven male university students that focused on Electroencephalographic (EEG) power and Event-Related Potentials (ERP'S). Correlations were not presented however those based on such a small number of participants should be interpreted with caution. Tucker, Sandstead, Penland, Dawson, and Milne (1984) noted that iron status (serum ferritin, serum iron) was not significantly related to 4 of 6 cognitive performance tasks in a larger university sample ($n = 69$). Covariation between iron measures and the measures of cognitive performance were assessed with zero-order Pearson correlations. Iron status was significantly related to tonal memory backward ($r = -0.30$, $p < 0.05$), associated with poorer performance and word fluency ($r = -0.30$, $p < 0.05$), associated with better performance. Gender differences were controlled. Quantitative EEG measures were also examined. In a study conducted at a Pennsylvania state college Murrari-Kolb et al. (2004) sampled 183 women between the ages of 18 and 35 years (mean age 21 years) in the attempt to demonstrate iron deficiency and iron deficient anemia in young women alters cognitive

performance affecting attentional, memory, and learning processes. The subjects were placed in three groups (iron sufficient, iron deficient, iron deficient anemia) and completed tasks from the Detterman's Cognitive Abilities Test (CAT), a computerized battery administered by a video monitor with a touch screen. Following supplementation (blinded, placebo-controlled) results by Analysis of Variance (ANOVA) showed that iron deficient women in the lowest quintile of plasma ferritin (1.1-6.5 $\mu\text{g/L}$), performed significantly ($p < 0.05$) worse in memory, assessed by mean reaction time (1,250 msec vs. 1,050 msec) learning, mean trial time (17,000 msec vs. 11,000 msec) and attention tests, and mean decision time (100 msec vs. 250 msec) than healthy women. Iron deficient women also had more anger and anxiety ($p < 0.05$). The authors concluded that iron status was related to performance on attentional, memory, and learning tasks in young women. The authors suggested that cognitive variables were altered in young women as a result of iron deficiency even in the absence of anemia. These findings agreed with those published by Bruner et al. (1996) who showed that iron had an impact on verbal learning and memory in iron deficient adolescent females without anemia.

Study of the link between iron and cognitive ability has occurred mostly through youth populations living outside North America. In a double-blinded study of 48 male children (8 to 15 years) in India, matched for age and hemoglobin, Seshadri and Gopaldas (1989) showed that iron supplementation improved overall cognitive function measured by visual recall tests (7.25 ± 0.25 vs. 5.75 ± 0.26), digit span (4.21 ± 0.49 vs. 3.16 ± 0.46), maze cognitive function test (6.90 ± 0.20 vs. 5.77 ± 0.40), and visual discrimination/ perception (6.39 ± 0.40 vs. 6.48 ± 0.21) compared to a placebo group ($n = 16$) (paired t-test; $p < 0.05$). In a separate study these authors matched 65 pairs of 8- to

15-year-old female subjects for age, hemoglobin, and cognitive function and found that supplementation improved performance on the same cognitive tests (paired t-test; $p < 0.05$). Hutchinson, Powell, Walker, Chang, and Grantham-McGregor (1997) assessed 800 male ($n = 417$) and female ($n = 383$) Jamaican fifth graders aged 9-13 years using a cross-sectional design. Participants were randomly selected from 16 schools.

Hemoglobin was used to determine iron status in relation to school achievement (WRAT). Stool specimens were analyzed for parasites. By correlation, children with iron deficiency anemia ($Hb < 110$ g/L) had lower achievement scores in reading ($r = 0.13$; $p < 0.001$) and spelling ($r = 0.12$; $p < 0.01$). Anemia predicted poor school attendance in multivariate analysis ($B = - 4.40$; $p < 0.01$). Soemantri, Pollitt, and Kim (1985) sampled 119 participants from Indonesia aged 8 to 13 years. Psychological tests included: The Ravens Progressive Matrices, The Educational Achievement Test, and The Bourden-Wisconsin test for concentration. Analysis of covariance (ANCOVA) showed that children with iron deficiency anemia performed significantly poorer in the achievement tests than those not anemic (31.8 ± 10.3 vs. 42.3 ± 10.8 ; $p < 0.05$). Pollitt (1997) assessed the correlation between iron deficiency without anemia and iron replete Guatemalan subjects ($n = 1203$) on cognitive test performance. Participants ranged from 9 to 27 years. Iron-deficient ($Hb < 120$ g/L; serum ferritin < 10 μ g/L) and iron replete ($Hb > 120$ g/L; serum ferritin > 10 μ g/L) groups were similar in all but one test. Iron replete participants responded faster in Sternberg's memory task ($p < 0.05$). Serum ferritin was not strongly associated with scores on any cognitive tests ($R = 0.06$ to 0.07). In summary Pollitt suggested that the absence of a significant correlation between iron deficiency (without anemia) and poor cognitive test performance raises skepticism as to

whether a modest degree of iron deficiency affects cognition. Evidence supporting this claim was provided by Sungthong, Mo-suwan, and Chongsuvivatwong (2002). These researchers examined the effects of hemoglobin and serum ferritin on cognitive function. Participants were school children from socioeconomically deprived communities in Thailand (n = 427). The ratio of males to females was 1:1. The average age was 9.6 years. Cognitive function was measured using the Test of Nonverbal Intelligence (TONI II), which was converted to IQ, and school performance (average Thai language and Math scores). Hemoglobin and serum ferritin were used to determine iron status. The low serum ferritin cutoff was $\leq 20 \mu\text{g/L}$. Cutoffs for anemia were (Hb $< 115 \text{ g/L}$; 5- to 11-year-olds, Hb $< 120 \text{ g/L}$; 12- to 13-year-olds). One eighth (13%) of participants had low serum ferritin. Prevalence of IDA was 4.2%. Linear regression models were used in statistical analysis. The highest scoring group included children with normal hemoglobin but low serum ferritin. Using a group of exclusively serum ferritin $> 20 \mu\text{g/L}$ participants as the reference, the investigators found significantly higher IQ (86.5 ± 3.6 ; $p = 0.03$), Thai Language (0.8 ± 0.3 ; $p < 0.01$), and Math scores (1.1 ± 0.3 ; $p < 0.01$) in children with normal hemoglobin but low serum ferritin (Test for trend, STATA statistical software version 6). A suggested reason for this unexpected finding was that if hemoglobin is high enough, increasing iron levels may have some adverse effect on cognition (Sungthong et al. 2002). To gain further insight, iron's association to cognition and behaviour has also been expanded to studies of learning disorders.

Iron status may be linked to attention deficit hyperactivity disorder (ADHD). ADHD is a behavioural syndrome characterized by an inappropriate degree of inattention, impulsiveness and hyperactivity (American Psychiatric Association, 1994). Individuals

with ADHD have can have low levels of magnesium, zinc, copper and iron (Kozielec, Starbart, & Herhelin, 1994). ADHD can be alleviated by dopamine releasers (i.e., psychostimulants, amphetamine and methylphenidate). Hypoactivity of the brain dopaminergic system may be associated in the pathophysiology of ADHD (Shaywitz, Cohen, & Bowers, 1977). Iron is important in dopaminergic regulation (Youdim & Yehuda, 1985).

Relationships between iron status and ADHD represent a developing area of study. Mixed results have been observed. Studies showing opposite effects and no effects will now be presented. Konofal, Lecendreux, Arnulf and Mouren (2004) investigated the relationship between iron stores and ADHD. Iron stores were determined by serum ferritin. Other measures of iron status included hemoglobin, hematocrit, and serum iron. ADHD was determined by the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) evaluation. Fifty-three participants with ADHD ranged in age from 4 to 14 years (mean \pm SD, 9.2 ± 2.2 years). Forty-five participants were boys. Eight were girls. Twenty-seven control participants were matched for age (mean \pm SD, 9.5 ± 2.2 years) and gender. Participants were from France. Between-group statistical analyses were performed using t-tests and χ^2 . Pearson correlations were used to test the relationship between iron stores (serum ferritin) and severity of ADHD symptoms (Connors Parent Rating Scale). Results showed that 84% of ADHD participants and 18% of controls had low serum ferritin (Hb < 30 $\mu\text{g/L}$). No participants were anemic. Serum ferritin was lower in ADHD participants versus controls (23 ± 13 $\mu\text{g/L}$ vs. 44 ± 22 $\mu\text{g/L}$; $p < 0.01$). In correlation, low serum ferritin was significantly related to severity of ADHD symptoms (Connors' Parent Rating Scale) and greater cognitive impairment ($r = -0.34$; p

< 0.02 , $r = -0.38$; $p < 0.01$). These results suggest that low serum ferritin (iron stores) has a role in ADHD. Conversely, Millichap, Yee, and Davidson (2006) noted no effect regarding the association between serum ferritin and severity or frequency of ADHD. Serum ferritin was measured as part of a laboratory assessment in American ADHD participants ($n = 68$) between 5 and 16 years of age. Male ($n = 54$) and female ($n = 14$) participants were included and compared to controls ($n = 27$) and U.S. national data. The name of the tool used to confirm the diagnosis of ADHD was not reported, although the study's setting was an established clinic in Chicago (Children's Memorial Hospital). Prevalence of low serum ferritin was presented at different cutoff values. Results showed that the percent of participants below $30 \mu\text{g/L}$, $20 \mu\text{g/L}$, and $12 \mu\text{g/L}$ were 44%, 18%, and 7% respectively. Anemia was not observed. Average serum ferritin in ADHD patients ($39.9 \pm 40.6 \mu\text{g/L}$) compared to controls ($44 \pm 22 \mu\text{g/L}$) was not statistically different ($t = 0.86$; $p > 0.20$). Evaluating the clinical characteristics of 12 participants in the lowest category of serum ferritin values versus 12 in the highest category ($< 20 \mu\text{g/L}$ vs. $> 60 \mu\text{g/L}$) revealed no significant difference in severity of comorbid symptoms or frequency of ADHD. The authors concluded that in this participant cohort, low serum ferritin cannot be confirmed as a cause of ADHD. Adding a different outcome, Antalis et al. (2006) recently noted higher serum ferritin levels in ADHD participants compared to controls ($113.54 \pm 49.35 \mu\text{g/L}$ vs. $71.13 \pm 44.89 \mu\text{g/L}$; $p < 0.04$). There was no difference between any other measures of iron status and ADHD. The primary objective of Antalis et al. was to assess Omega-3 fatty acid status in attention-deficit/hyperactivity disorder. ADHD ($n = 35$) and control ($n = 112$) participants were American adults in their twenties (ADHD: 24.1 ± 3.4 years; control: 23.1 ± 3.4 years). Diagnosis of ADHD

was provided by the staff at Counseling and Psychological Services (CAPS) at Purdue University. Hemoglobin, hematocrit, mean corpuscular volume and serum ferritin were used to assess iron status. Other measured variables included: antioxidants, oxidative stress, inflammation, and fatty acid profiles. Gender, age, body mass index, smoking, and ethnicity were controlled. Statistical analyses included: Fisher's Exact Test, Shapiro-Wilk Test, Student's two-tailed t-test, Kruskal-Wallis Test, Pearson and Spearman correlations.

It appears severe iron deficiency early in the lifespan has debilitating effects on cognitive and behavioural development. Effects in older populations and ADHD patients are not as clear. Studies of late childhood and adolescent populations are limited. Such a reality underlines the importance of further investigation of the relationship between iron status and academic performance in teenage populations.

Iron Status and Academic Performance in Female Adolescents

Studies presented in this section are grouped by number of indicators used to determine iron status. In screening for iron deficiency, it is not uncommon that only one or two parameters are used as cost and convenience are important factors to consider. Sensitivity and specificity are critical when using just one or two parameters. Hemoglobin remains a key screening measure as it can detect the most severe stage of iron deficiency associated with the majority of clinical symptoms. By combining hemoglobin with serum ferritin measurements, sensitivity and specificity are greatly improved (Cook, Baynes, & Skikne, 1992).

To gain further insight into the area of iron status and academic performance or cognitive ability in adolescents, Walker et al. (1998) assessed 452 eighth grade Jamaican girls between the ages of 13 and 14 years. Hemoglobin was the only indicator of iron status among other nutritional status measures including weight and height for age. School performance was measured using the Wide Range Achievement Test (WRAT). Using a multiple regression analysis, girls with iron deficiency anemia were significantly ($p < 0.001$) more likely to have poor academic achievement in reading (R-square = 0.21) and spelling (R-square = 0.26). Walker et al. relied on hemoglobin as the only marker for iron status. Students with iron deficiency but not anemia were not identified. Similarly, in a random sample of 800 Saudi girls and boys between the ages of 9 to 21 years Abalkhail and Shawky (2002) measured iron status with hemoglobin. Of the 800 participants, 84 were surveyed for nutritional habits. Academic performance was measured by actual school tests. Proportions and 95% confidence intervals were calculated. Differences between proportions were considered significant if the 95% confidence intervals (CI) did not overlap. Results showed that iron deficiency anemia was significantly more prevalent among those who failed school exams compared to those with excellent achievement (33.8%; CI: 23.0 to 44.6 vs. 17.2%; CI: 12.6 to 21.8). A failure included a mark of zero to 70% while excellence was defined by a mark greater or equal to 90%. Again, hemoglobin was the only measure of iron status.

The addition of serum ferritin as a marker of iron status allows consideration of larger iron status ranges and helps identify more subtle effects of iron deficiency (Cook et al., 1992). Lynn and Harland (1998) studied two matched (age, sex, IQ) groups of 208 and 205 participants (12 to 16 years) from the United Kingdom. Academic performance

was measured by IQ using the Ravens Progressive Matrixes. Hemoglobin and serum ferritin were measures of iron status. The initial correlation between hemoglobin and IQ ($r = 0.17$, $p = 0.01$) was small, but statistically significant. The correlation between ferritin and IQ was not significant. Participants were then grouped into three sub groups of low, medium, and high iron levels. Between group tests showed that iron treatment improved IQ performance significantly (IQ gain: 5.8 points, $t = 2.34$; $p = 0.02$) in those with low iron stores (serum ferritin ≤ 12 $\mu\text{g/L}$) compared to the placebo group. The results of this study included non-adolescent participants and both genders. Generalizing findings to females alone is difficult. Bruner et al. (1996) sampled 98 adolescent American girls between the ages of 13 and 18 years who displayed iron deficiency without anemia. Serum ferritin and hemoglobin were used to determine iron status. Academic performance was determined by the following standardized tests: Brief Test of Attention (BTA), Symbol Digits Modalities (SDMT), Visual Search and Attention (VSAT), and the Hopkins Verbal Learning Test (HVLT). Ferritin level was not correlated with test performance prior to intervention. Stepwise regression analysis assessing the effect of iron treatment on postintervention test scores, adjusted for baseline scores, showed that the group who took iron ($n = 37$) improved significantly compared to controls ($n = 36$) in a test (HVLT) of verbal learning and memory ($R\text{-square} = 0.25$, $R\text{-square change} = 0.07$, Baseline score: 1.79; $p < 0.02$). Bruner et al. acknowledged that further research is needed to assess whether cognitive effects are limited to standardized neuropsychological measures or are also evident in academic performance.

Using multiple markers of iron status Groner et al. (1986) studied 38 (at risk due to poverty) 14- to 24-year-old pregnant American females. Serum ferritin, hemoglobin,

hematocrit, and mean corpuscular volume were included as measures of iron status in this supplementation study. Academic performance was assessed by a battery of standardized tests for short term memory and attention. There was no correlation between iron status and psychometric test score initially or after one month. Iron treated participants significantly improved on the Digit Symbol test ($p < 0.005$, paired t-test) and Consonant Trigrams ($p < 0.05$; paired t-test). The change in Digit Symbol score was greater for the experimental group compared to their untreated counterparts, but did not reach statistical significance (experimental: 1.3 ± 1.5 vs. control: 0.3 ± 1.7 ; $p < 0.08$). The change in Consonant Trigrams was significantly greater for the experimental group (experimental: 1.1 ± 2.5 vs. control: -0.7 ± 2.4 ; $p < 0.05$). There was a large ($n = 10$) loss from the control group, leaving only 9 participants. Because participants were pregnant, the author admitted that findings cannot be generalized to other groups and similar investigations should be performed among non-pregnant teenagers and young adults. Using multiple indicators of iron status, Halterman et al. (2001), investigated a group of 6- to 16-year-old American children and adolescents ($n = 5398$). This national representative sample included 2731 girls. Data were taken from the National Health and Nutrition Examination Survey III. Serum ferritin, hemoglobin, transferrin saturation, and free erythrocyte protoporphyrin were measured in different age groups. One group was females between 12-16 years ($n = 1114$). Academic performance was measured by standardized test scores on the Wechsler Intelligence Scale for Children (WISC-2) and the Wide Range Achievement Test (WRAT- reading and math). Results showed that average math scores were lower for iron deficient participants, with anemia (86.4; $p < 0.05$) and without anemia (87.4; $p < 0.05$) compared to those with normal iron status

(93.7). Iron deficient participants had more than twice the risk of scoring lower in Math compared to those who had normal iron status (odds ratio: 2.3; 95% confidence interval, 1.1 to 4.4). Average test scores were compared using t-test statistics for means and χ^2 for proportions. Logistic regression was used for multivariate analysis. For organizational purposes the studies of iron status and academic performance in female adolescents are presented in Table 1.

Table 1.
Studies Involving Iron Status and Academic/Cognitive Performance in Female Adolescents.

Reference	Participants	Measures of Academic or Cognitive Performance	Indicators of Iron Status and Cutoff Values Used	Outcome
Walker et al. (1998)	452 (8th grade) Jamaican girls aged 13 to 14 years.	WRAT	Anemia:Hb < 115 g/L	Anemic girls more likely ($p < 0.001$) to have poor AA in reading ($R^2 = 0.21$) & spelling ($R^2 = 0.26$) (MR).
Abalkhail & Shawky (2002)	800 Saudi boys and girls aged 9 to 21 (mean 14).	School grades expressed as percent of marks. Individual courses (i.e., math) not presented. No standardized tests.	Anemia: Hb < 115 g/L for 5-11 year old boys and girls; < 120 g/L for 12-14 year old boys and girls; < 120 g/L for 15+ girls; < 130 g/L for 15+ boys.	Anemia was more prevalent among those who failed school exams compared to those with excellent achievement (33.8%; CI: 23.0 to 44.6 vs. 17.2%; CI: 12.6 to 21.8). Failure (mark of zero to 70%); Excellence (mark $\geq 90\%$)
Lynn & Harland (1998)	208 participants (12 to 16 years of age) matched with 205 controls for age, sex, and IQ. Treated group received iron and ascorbic acid for 16 weeks.	IQ using Ravens Progressive Matrixes.	Hb below normal: < 120 g/L; low SF: $\leq 12 \mu\text{g/L}$.	Initial corr. b/w Hb and IQ ($r = 0.17$, $p = 0.01$) was small, but statistically significant. The corr. b/w SF and IQ was not significant. Fe treatment group with low iron stores (SF $\leq 12 \mu\text{g/L}$) improved IQ performance significantly (IQ gain: 5.8 points, $t = 2.34$; $p = 0.02$) compared to the placebo group.

Table. 1 (continued)

Bruner et al. (1996)	98 adolescent American girls 13 to 18 years of age with non-anemic ID. Anemic participants excluded. Double blind placebo controlled for 8 weeks.	By the following standardized tests: BTA, SDMT, VSAT, HVLТ	Anemia: Hb < 115 g/L for African Americans; Hb < 120 g/L for white girls. Non-anemic ID defined as SF < 12 µg/L with normal Hb.	SF no corr. with CTP prior to intervention. Fe group (n = 37) improved significantly (SR) vs. controls (n = 36) in HVLТ (R ² = 0.25, R ² change = 0.07, Baseline score: 1.79; p < 0.02).
Groner et al. (1986)	38 (at risk due to poverty) 14- to 24-year-old pregnant American females. Double blind randomized for 1 month.	By the following standardized tests measuring short-term memory and attention: Digit Span, Digit Symbol, Arithmetic, Vocabulary (WAIS) and Consonant Trigrams, RAVLT	SF, Hb, hematocrit, and mean corpuscular volume. No reference to cutoffs.	No corr. b/w Fe status and CTP initially or after one month. Fe treated improved on DS test (p < 0.005, paired t-test) and CT (p < .05; paired t-test). CT change greater for the ex. group (ex.: 1.1 ± 2.5 vs. control: -0.7 ± 2.4; p < 0.05).
Halterman et al. (2001)	5398 American children and adolescents 6 to 16 years of age. One group was 1114 females b/w 12-16 years of age.	By the following standardized tests: WISC-2 and WRAT (reading and math).	Anemia: Hb < 120 g/L; low SF : < 12 µg/L; erythrocyte protoporphyrin: > 1.24 :mol/L; transferrin saturation: < 14%. Individual considered ID if 2 of 3 values abnormal (not including Hb)	Ave. Math scores lower for ID with anemia (86.4; p < 0.05) and without anemia (87.4; p < 0.05) vs. those with normal Fe status (93.7). ID had more than twice the risk of scoring lower in Math vs. normal. Fe status (OR: 2.3; 95% CI, 1.1 to 4.4). Ave. test scores compared by t-test (means), Π ² (proportions). LR used for MA.

Abbreviations: AA = academic achievement, Ave = Average, BTA = Brief Test of Attention, b/w = between, CI = confidence interval, corr. = correlation, CT = Consonant Trigrams, CTP = cognitive test performance, ex. = experimental, Fe = iron, DS = Digit Symbol, Hb = Hemoglobin, HVLТ = Hopkins Verbal Learning Test, ID = iron deficient, IDA = iron deficient anemic, IQ = intelligence quotient, LR = linear regression, MA = multivariate analysis, MR = multiple regression, OR = odds ratio, RAVLT = Rey Auditory Verbal Learning Test, SDMT = Symbol Digit Modalities Test, SF = serum ferritin, SR = step-wise regression, vs. = versus, VSAT = Visual search and Attention Test, WAIS = Wechsler Adult Intelligence Scale, WISC = Wechsler Intelligence Scale for Children, WRAT = Wide Range Achievement Test.

Summary

Iron deficiency is a very prevalent health problem in the world today. The fact that iron deficiency is so far reaching provides justification for its study. Impaired cognitive function appears to be associated with anemia. Children who were anemic as infants seem to have poorer school achievement and more behaviour problems progressing into middle childhood. There is a noticeable knowledge gap in the literature regarding iron deficiency in adolescents. The number of studies in the field is small. Heterogeneous populations have been investigated. Knowledge regarding the link between iron deficiency and school achievement or cognitive ability has been derived primarily from observations of individuals living outside North America. Some researchers have based results on data that included both genders. Other investigators have mixed non-teenagers with teenaged participants in their analyses. Studies have been geographically scattered, ranging from third world developing countries, which present several confounding methodological challenges, to developed nations, making generalizations difficult. Reports specifically linking iron deficiency to academic performance are even more limited in number. There are few published articles to justify any definitive conclusions. Further research is required. A study investigating the link between iron status and academic performance using actual school grades and not standardized measures of cognitive performance, in a North American adolescent population, has not been produced.

CHAPTER 3

METHODOLOGY

Participants

Following approval from the Lakehead University ethics review committee, seventy-one healthy female participants were recruited for the study. Participants were 10th grade female students attending public high schools in Thunder Bay. Student populations in these urban schools were demographically similar. With one exception (n = 600) number of students ranged from 1000 to 1300 individuals per school. The recruitment process was initiated by the Lakehead Public School Board. The Board notified public secondary school principals, by email, that the study had passed university and school board ethics review. This researcher arranged meetings at each school to inform the principals about the nature of the study and was permitted to conduct short recruitment/orientation presentations in each grade ten classroom. The potential risks of the study were explained. Informed consent and assent (Appendix A) forms for students and legal guardians were distributed to potential participants. Participants represented a non-probability sample. All measures of academic performance were converted to standard scores (z-scores) to achieve comparability of grades between schools. The Ontario educational system follows a strict guideline of high school curriculum that is delivered, in a uniform manner, by each department. All students receive very similar instruction. The choice of 10th grade students ensured participants received a similar standard of teaching in the year prior (9th grade) to the investigation. Sampling a single grade limited the confounding influence of maturation. Participants completed a survey (Appendix B)

which identified pertinent health information. Individuals whose health status could complicate testing procedure or interpretation of results, as identified by the literature, were excluded. Criteria for exclusion included: use of contraceptives, pregnancy, and use of any medication causing acute or chronic blood loss from the gastrointestinal tract as a published side effect. Besides this exclusion criteria, no requirement for participation was imposed.

Procedure

Following arrangements between the researcher and school principals, blood/data collection commenced, on separate days, at each secondary educational institution between 9:30 and 11:30 am. Participants were asked to report to testing in an overnight fasted state, having avoided strenuous physical activity in the preceding 24 hours. On the day of the test, participants were instructed to meet at the room designated for testing. Participants were asked to fill out the health survey (Appendix B) and additional questions sheet (Appendix C) if they had not already done so. Participants were seated together in the room. They were called one at a time to enter an enclosed area where blood samples were taken. A certified phlebotomist collected the blood samples in two 3 mL Vacutainer tubes (Vacutainer plus Plasma Separator Tube {PST} containing lithium heparin and plasma separator gel with hemogard, and Becton Dickinson {BD} Vacutainer K2 containing the anticoagulant salt of ethylene diamine tetra-acetic acid {EDTA}), by antecubital venipuncture. Participants were allowed to remain seated to monitor any side effects on the body following blood extraction (i.e., dizziness, fainting). All single use needles were disposed using a Vacutainer sharps collector. Blood samples

were immediately taken to the Thunder Bay Regional Health Science Centre. These samples were stored at a refrigeration temperature of 2°- 8°C, and analyzed for levels of serum ferritin, hemoglobin, vitamin B₁₂, and albumin.

Vitamin B₁₂, and albumin served as statistical controls. Their effect on academic performance was removed by partial correlation. Vitamin B₁₂ is found exclusively in foods of animal origin. The rationale for its measurement in the study is that B₁₂ plays a role in red blood cell formation (Hebert, 1996). A deficiency in vitamin B₁₂ can lead to impaired DNA synthesis and development of abnormal red blood cells (Savage & Lindenbaum, 1995). Individuals deficient in this nutrient can develop anemia (pernicious anemia) not related to poor iron status (Savage & Lindenbaum, 1995). Albumin is a blood plasma protein that is produced in the liver and forms a large proportion of all plasma protein. Albumin helps maintain osmotic pressure and transports substances such as thyroid and fat soluble hormones, and fatty acids (National Library of Medicine, 2006). Bulow and Madsen (1986) showed low levels of albumin can signal episodes of malnutrition or high blood loss, both would contribute to altered iron status.

With permission from school officials and the school board, transcripts of the grade 10 students were obtained. Individual courses and most recent term grade averages were used in subsequent data analysis.

A 3-day dietary analysis (one weekend day included) performed one time at the onset of the investigation was used as an indicator of participant diet. Basiotis, Welsh, Cronin, Kelsay, and Mertz (1987) found that energy intake can be reasonably assessed over three days. As participants were inexperienced in dietary analysis procedures the decision to monitor diets for a short 3-day period seemed likely to maintain participant enthusiasm

and motivation to produce accurate reports. Diet assessment was based on the Canadian Recommended Nutrient Intake (RNI). The RNI for each nutrient is set at an amount substantially higher than what the average person requires taking into account the variation in needs for most individuals in the population. With this added safety margin, the RNI covers the needs of 98% of the healthy population, including those with higher than average nutrient requirements. The average healthy person can consume about 67 to 70% of their recommended nutrient and still be adequately nourished (Lombardi, 1997). Participants recorded all foods and beverages consumed in a food intake log (Appendix D1) over three consecutive days. Participants were briefed on the correct way of recording food intake amounts and were provided instructions with examples for improved clarification (Appendix D2). Subjects were instructed to make no changes in their typical diet. The data were analyzed using Foodworks college edition computer software (version 1.0). Body Mass Indexes (BMI) were calculated to acquire data pertaining to general health. BMI calculations were based on participant self reported height and weight obtained at the time of the dietary analyses.

Hematological data instruments

Blood collection equipment included: Eclipse blood collection needles, a sharps collector, and two 3 mL blood collection tubes (Becton Dickinson Canada Inc., Oakville ON). Hemoglobin assessment was assayed using the Coulter Counter instrument (Coulter Electronics, Hialeah FL). Serum ferritin concentrations were determined by the Quantimmune ferritin immunoradiometric assay (Bio-Rad Laboratories, Mississauga, Ontario). Vitamin B₁₂ level was determined by radioisotopic assay (Becton Dickinson,

Oakville ON). Albumin level was measured using colorimetric assay (BioAssay Systems, Hayward CA). Assays performed conformed to the internal methodologies in use by the Thunder Bay Regional Health Science Centre. These measured parameters determined the iron status and identification of students into one of three groups: 1. Iron sufficient 2. Iron deficient not anemic 3. Iron deficient anemic.

Statistical Analysis

The basic correlational research design was employed. Two scores were obtained for each member (case) of the sample – one score for each variable of interest. The paired scores were then correlated. The result was expressed as a correlation coefficient that indicated the degree or strength of relationship between the two variables.

Bivariate Pearson correlations (r) were used to assess the strength of the relationship between the variables serum ferritin and, hemoglobin, versus the measures of academic performance (Grade Average, Math, Science, Physical Education, and English). These relationships were initially examined using scatter plots to obtain a visual appreciation of the data. Partial correlations (X) were also calculated to statistically control for vitamin B₁₂ and albumin. Correlations were flagged as significant if the 0.05 probability level was reached. Secondary to the main focus of this study, vitamin B₁₂ and albumin were correlated with all measures of academic performance. All variables identified were quantitative. Hematological parameters represented continuous independent or predictor variables. Measures of academic performance represented discrete dependent or criterion variables.

$$r = \frac{E(Z_x Z_y)}{N}, \quad X = a_x + b_x A$$

Multiple correlation was used to test the relationship between overall Grade Average and statistical models including serum ferritin, hemoglobin, vitamin B₁₂, and albumin.

$$\sqrt{R^2_{YX_1X_2}}$$

In order to assess if iron deficient participants were performing at a significantly different level academically, as a group, a between-subjects/independent t-test was used to compare their grade averages to the iron sufficient participants. This analysis served as an additional means of exploring the relationship between iron status and academic performance. The use of a dichotomy is common practice in the field and allowed comparison across similar populations to be made.

$$t_{X_1 - X_2} = \frac{(X_1 - X_2) - \mu_{X_1 - X_2}}{\sigma_{X_1 - X_2}}$$

Risk ratios were calculated to quantify the potential excess risk of a participant to score below the provincial academic standard (level 3/B average) based on the event of being iron deficient (ferritin ≤ 20 $\mu\text{g/L}$) or iron sufficient (ferritin > 20 $\mu\text{g/L}$).

	Below "B" (provincial standard)	Above "B" (provincial standard)
Iron Deficient	a	b
Iron Sufficient	c	d

$$RR = \frac{a/(a+b)}{c/(c+d)}$$

All data was inputted and analyzed using SPSS (Statistical Package for the Social Sciences) 10.0 for Windows. It should be noted that the statistical methods selected are similar analyses, however their presentation should appeal to different types of academics including teachers, school administrators, researchers and clinicians.

CHAPTER 4

RESULTS

Signed consent forms were obtained from 71 of 200 female students who expressed interest in the study after initial recruitment at six public Thunder Bay high schools {Hammarskjold (n = 24), Hillcrest (n = 9), Port Arthur Collegiate Institute (n = 11), Churchill (n = 14), Fort William Collegiate Institute (n = 7), and Westgate (n = 6)}. All 71 females were subsequently blood tested for levels of serum ferritin, hemoglobin, vitamin B₁₂, and albumin. With permission from school principals official grades were obtained. No participants dropped out upon entering the study.

Race and ethnicity can influence the prevalence of iron deficiency (Feightner, 1994; Lozoff et al., 2000). Ninety-two percent (n = 65) of the participants were white, 4% (n = 3) were Aboriginal, 1% (n = 1) was White/Aboriginal, 1% (n = 1) was African Canadian, and 1% (n = 1) was of Chinese descent (these percentages add to 99% due to rounding). The average age of the females was 15.4 ± 0.56 years.

Of the 71 females, fifty-eight percent (n = 42) were iron deficient (serum ferritin \leq 20 $\mu\text{g/L}$). Only one participant was identified as anemic (hemoglobin <120 g/L). The average values, as a group, for serum ferritin and hemoglobin were 19.8 $\mu\text{g/L}$ and 136.2 g/L respectively. Two participants were deficient in vitamin B₁₂. Levels \leq 150 pmol/L were considered B₁₂ deficient. The serum ferritin and hemoglobin values for these two participants fell within the normal range. No participants displayed low albumin levels (< 35 g/L). Body Mass Index (BMI) calculations were performed to gather more information on the health of participants. These indexes suggested that 85% of

participants had an optimal BMI (18.6 to 24.9) while 8% were overweight (25 to 29.9), 3% were obese (BMI \geq 30) and 3% were underweight (BMI \leq 18.5) (Canadian Physical Activity, Fitness and Lifestyle Approach, 2003) (above percentages add to 99% due to rounding). Group descriptive statistics are listed in table 2.

Table 2.
Descriptive Statistics for Serum Ferritin (SF), Hemoglobin (Hb), Vitamin B₁₂, Albumin, Measures of Academic Performance, and Body Mass Index (BMI).

Parameter	Means \pm SD	Min	Max	Range	Normal Levels
Age (yrs)	15.4 \pm 0.56	14	16	2	
Height (cm)	162.6 \pm 2.4	147.3	177.8	30.5	
Weight (kg)	26.5 \pm 8.5	44.5	90.9	21.0	
Serum Ferritin (μ g/L)	19.8 \pm 9.8	4.3	49.4	45.1	20-150
Hemoglobin (g/L)	136.2 \pm 7.2	120.0	153.0	33.0	120-160
Vitamin B ₁₂ (pmol/L)	355.9 \pm 129.8	148	658	510	151-900
Albumin (g/L)	43.7 \pm 2.5	37.4	49.5	12.1	35-50
Grade Ave (%)	75.8 \pm 11.2	42.4	94.4	52.0	
Math (%)	70.8 \pm 16.6	33	100	67	
Science (%)	70.3 \pm 15.4	14	97	83	
Phys Ed. (%)	80.4 \pm 9.4	34	93	59	
English (%)	76.1 \pm 12.2	41	96	55	
BMI	21.9 \pm 3.0	17.83	33.4	15.52	18.6-24.9

Bivariate Pearson correlations were conducted to assess the strength of the relationship between the variables serum ferritin and, hemoglobin, versus the measures of academic performance (Grade Average, Math, Science, Physical Education, and English) (table 3). To statistically control for B₁₂ and albumin partial correlations were calculated (table 4). Correlations were flagged as significant if the 0.05 probability level was

reached. Correlations were first examined by scatter plot graph to aid in the interpretation of relationships (Appendix E).

Table 3.
Correlations (r) Between Serum Ferritin, Hemoglobin and Measures of Academic Performance.

	Grade Ave.	Math	Science	Phys. Ed.	English
Serum Ferritin	$r = -0.259^*$	$r = -0.212$	$r = -0.185$	$r = -0.127$	$r = -0.259^*$
Hemoglobin	$r = +0.015$	$r = +0.005$	$r = +0.093$	$r = +0.112$	$r = +0.042$

Note:* indicates significance at the 0.05 level.

Table 4.
Partial Correlations Between Iron Status and Performance Variables Controlling for B₁₂ and Albumin.

	Grade Ave.	Math	Science	Phys. Ed.	English
Serum Ferritin	$r = -0.298^{**}$	$r = -0.230$	$r = -0.224$	$r = -0.172$	$r = -0.304^{**}$
Hemoglobin	$r = -0.045$	$r = -0.025$	$r = +0.037$	$r = +0.044$	$r = -0.024$

Note:* indicates significance at the 0.05 level.

**indicates significance at the 0.01 level.

The correlations between serum ferritin and all measures of academic performance resulted in correlational coefficients in the negative direction. Magnitudes reached significance ($p < 0.05$) with Grade Average ($r = -0.259$) and English ($r = -0.259$). In partial correlation the same pattern was observed although the magnitude of the

relationship did increase: Grade Average ($r = -0.298$, $p < 0.01$) and English ($r = -0.304$, $p < 0.01$) (table 4). Presence of outliers in the data can inflate or deflate correlations (Diekhoff, 1992). These radically different cases, with residuals greater than three standard deviations, were removed from the iron status and academic performance variables. Outliers were identified using the casewise diagnostics function of SPSS. Correlations were recomputed. Again ferritin produced correlational coefficients in the negative direction in relation to all measures of academic performance, reaching statistical significance ($p < 0.05$) with Grade Average ($r = -0.268$) and English ($r = -0.259$).

None of the initial (table 3) or partial (table 4) correlations involving hemoglobin and academic performance reached statistical significance. This was true when outliers were present or when they were identified and removed from the calculation.

Although statistical significance with hemoglobin correlations was not achieved, an observation noted was that correlational direction between hemoglobin and Grade Average, Math, and Science became increasingly positive as hemoglobin dropped, reaching a peak when $Hb < 130$ g/L. Notably, the correlation with Math displayed positive direction and moderate strength ($r = 0.459$, $p < 0.10$) but, was not beyond the play of chance (table 5).

Table 5.
Correlations by Descending Values of Hemoglobin (Hb).

	Hb \geq 140 g/L	<140 Hb \geq 130 g/L	Hb < 130 g/L
Grade Average	$r = -.203$	$r = -.023$	$r = +.176$; $p = 0.57$
Science	$r = -.134$	$r = -.089$	$r = +.003$; $p = 0.99$
Math	$r = -.253$	$r = +.065$	$r = +.459$; $p = 0.09$

Secondary to the main focus of this study, the relationship between vitamin B₁₂, albumin and academic performance was assessed by correlation. B₁₂ showed no significant correlations (table 6) with or without outliers present in the calculations ($p > 0.05$). On the other hand, albumin correlations showed significance with Grade Average ($r = + 0.250$; $p < 0.05$), Science ($r = + 0.273$; $p < 0.05$), Physical Education ($r = + 0.325$; $p < 0.01$), and English ($r = + 0.280$; $p < 0.05$) (table 5). Outliers were present in Science and Physical Education data. When these outliers were removed, the correlation with Science was no longer significant ($r = + 0.193$; $p > 0.05$). The correlation with Physical Education lost strength but remained significant at the 0.05 level ($r = + 0.262$; $p < 0.05$) (table 6).

Table 6.
Correlations (r) Between Vitamin B₁₂, Albumin and Measures of Academic Performance.

	Grade Ave.	Math	Science	Phys. Ed.	English
B₁₂	$r = + 0.147$	$r = + 0.053$	$r = + 0.131$	$r = + 0.172$	$r = + 0.163$
Albumin	$r = + 0.250^*$	$r = + 0.145$	$r = + 0.273^*$	$r = + 0.352^{**}$	$r = + 0.280^*$
Albumin (with outliers removed)	$r = + 0.250^*$	$r = + 0.145$	$r = + 0.193$	$r = + 0.262^*$	$r = + 0.280^*$

Note: *indicates significance at the 0.05 level.

**indicates significance at the 0.01 level.

A multiple correlation was calculated to test the relationship between overall Grade Average and iron status. Serum ferritin and hemoglobin were entered in the model. The relationship ($R = 0.269$, $\text{Adj. } R^2 = 0.045$, $\text{df} [2, 68]$, $F = 2.64$; $p = 0.078$) was not statistically significant. The additions of B₁₂ and albumin to the model boosted the proportion of variance explained in grades ($R = .349$, $F \text{ Change} = 3.03$; $p = 0.024$) to a

significant level with medium (Cohen's $f^2 = 0.18$) effect size (table 7). Serum ferritin ($p = 0.01$) and albumin ($p = 0.03$) were significant contributors to the model (table 7).

Table 7.
Multiple Correlation. Predictors: Serum Ferritin (SF), Hemoglobin (Hb), B₁₂, Albumin.

Predictors of Grade Ave.	R	R Square	Adjusted R square	df	F	P level	Cohen's f^2
SF/Hb/ B ₁₂ / albumin	0.394	0.155	0.104	4, 66	3.03	0.024*	0.18
Coefficients	B	t	Sig.				
Serum Ferritin	-0.335	-2.51	0.014*				
Hemoglobin	0.002	0.112	0.911				
B ₁₂	0.0008	0.827	0.411				
Albumin	1.16	2.21	0.030*				

Note: B = regression coefficient.

* indicates significance at the .05 level.

To assess whether iron deficient participants ($n = 42$) were significantly different academically, as a group, between-subjects/independent t-tests were used to compare their Grade Averages, Math, Science, Physical Education, and English marks to iron sufficient participants ($n = 29$). The differences were not statistically significant (table 8).

Table 8.
Between Subjects/Independent T-Test.

	Iron deficient Group (n = 42) (Means \pm SD)	Iron Sufficient Group (n = 29) (Means \pm SD)	t-test
Grade Average	77.4 \pm 10.7	73.5 \pm 11.7	t ₍₆₉₎ = -1.41, p = 0.15
Math	72.8 \pm 17.1	67.9 \pm 15.7	t ₍₆₉₎ = -1.23, p = 0.22
Science	71.9 \pm 16.4	68.1 \pm 13.8	t ₍₆₉₎ = -1.01, p = 0.31
Phys ed.	81.1 \pm 9.4	79.4 \pm 9.4	t ₍₆₉₎ = -0.74, p = 0.46
English	77.5 \pm 11.6	74.1 \pm 12.9	t ₍₆₉₎ = -1.17, p = 0.25

Risk ratios were calculated to quantify the potential excess risk of a participant to score below the provincial academic standard (level 3/B average) based on the event of being iron deficient (ferritin \leq 20 μ g/L) or iron sufficient (ferritin $>$ 20 μ g/L). Iron status did not result in any excess risk to academic performance. The magnitudes of risk associated with Grade Average (risk ratio: 1.5; 95% confidence interval: 0.9 to 2.5), Math (risk ratio: 1.5; 95% confidence interval: 0.9 to 2.6), Science (risk ratio: 1.8; 95% confidence interval: 1.0 to 3.1), Physical Education (risk ratio: 1.1; 95% confidence interval: 0.8 to 1.4), and English (risk ratio: 1.1; 95% confidence interval: 0.7 to 1.7) were statistically non-significant. Corresponding confidence intervals captured the value of no effect (RR = 1.0) (table 9).

Table 9.
Relative Risk or Risk Ratios.

	Grade Average	
	Below "B" (provincial standard)	Above "B" (provincial standard)
Iron Deficient	n = 18	n = 24
Iron Sufficient	n = 17	n = 11

	Math	
	Below "B" (provincial standard)	Above "B" (provincial standard)
Iron Deficient	n = 17	n = 24
Iron Sufficient	n = 18	n = 11

	Science	
	Below "B" (provincial standard)	Above "B" (provincial standard)
Iron Deficient	n = 16	n = 25
Iron Sufficient	n = 19	n = 10

	Physical Education	
	Below "B" (provincial standard)	Above "B" (provincial standard)
Iron Deficient	n = 8	n = 34
Iron Sufficient	n = 7	n = 22

	English	
	Below "B" (provincial standard)	Above "B" (provincial standard)
Iron Deficient	n = 20	n = 22
Iron Sufficient	n = 15	n = 14

Menstrual phase can affect iron status (Kim et al., 1993). Dates of menses were recorded to monitor menstrual phase. Of forty-two iron deficient participants, ten were in the menstruation phase of their cycle at the time blood was drawn. Five of twenty-nine iron sufficient participants were tested during the menstruation phase.

Participants were asked to complete a 3-day dietary analysis. Nutrient intakes were monitored to assess the relationship between iron intake and iron status. Several subjects

did not submit their food diaries. Of the forty-one who completed this task, 73% (n = 30) were iron deficient (serum ferritin ≤ 20 $\mu\text{g/L}$). Ten percent (n = 4) reported iron intakes less than 70% of the daily Canadian recommended nutrient intake (RNI). Sixty-six percent (n = 27) reached the RNI for iron. Fifteen percent (n = 6) reported energy intakes less than 70% of the RNI. Fifty-four percent (n = 22) met of the RNI for kilocalories. Forty-four percent (n = 18) met the RNI for both kilocalories and iron. Most major health organizations recommend fat intake should not exceed 30% of the total daily energy intake. Sixty-one percent (n = 25) met this recommendation, while 39% (n = 16) did not. Recommendations based on fat breakdown reveals that saturated fat should be limited to 10% of total energy intake. Forty-four percent of respondents (n = 18), satisfied this requirement. No participants met the requirement that unsaturated fats (monounsaturated and polyunsaturated combined), should make up at least 70% of the overall fat intake. Macronutrient and RNI percentages achieved for kilocalories and iron are listed in (Appendix F). A summary of descriptive statistics is presented in table 10.

Table 10.
3 Day Dietary Analysis Results.

	RNI	Min	Max	Range
Iron Mean \pm SD = 15.7 \pm 5.9 mg/day	15 mg	4.5 mg	30.8 mg	26.3
Carbohydrates	50%-70% of daily intake	42%	70%	28
Protein	0.8 g/kg	8%	24%	16
Fat	< 30% of daily intake	21%	38%	17

In order to assess the relationship between reported iron intake and iron status a correlation between dietary iron (mg) and serum ferritin was calculated. The result ($r = 0.062$, $p = 0.70$) was not statistically significant.

CHAPTER 5

DISCUSSION

Within the scope of this study, the presence of serum ferritin below 20 $\mu\text{g/L}$ did not pose a significant hazard to academic achievement. There was no significant difference ($p > 0.05$) in grades between girls who were iron deficient (serum ferritin $\leq 20 \mu\text{g/L}$) and those who were not. Furthermore, iron deficient participants did not show an increased risk of performing below the standard of their iron sufficient counterparts.

Correlational coefficients (bivariate and multiple) between the measures iron status and academic performance did not achieve significance in the positive direction. Oddly, small negative correlations were observed between serum ferritin and Grade Average and English. Significant ($p < 0.05$) correlations between albumin and Grade Average ($r = + 0.250$), Physical Education ($r = + 0.262$) and English ($r = + 0.280$) were discovered and may warrant attention in future study. Separate sections will be dedicated to discussion of serum ferritin and albumin in comparison to previous research. All notable findings are presented under subheadings.

Iron Status in Related Samples

The volume of research linking iron status to academic performance in adolescents is limited. Knowledge regarding the link between iron deficiency and school achievement has been derived primarily from observations of populations living outside North America. Three published researchers investigating the link between iron deficiency and academic achievement including North American adolescent participants have been

identified (Bruner et al., 1996; Groner et al., 1986; Halterman et al., 2001), and only two of those (Bruner et al.; Halterman et al.) included non-pregnant adolescent females. Neither of these studies measured vitamin B₁₂ or albumin. In this study 58% of the sample was iron deficient ($\leq 20 \mu\text{g/L}$). Bruner et al. and Halterman et al. used a cutoff of $12 \mu\text{g/L}$ to describe their iron deficient subjects. A definitive cutoff for serum ferritin has not been established. Both values have been employed in related studies of iron deficiency (Manore & Thompson, 2000). Using a $12 \mu\text{g/L}$ cutoff there is still a 25% prevalence of iron deficiency in the present study. This figure is considerably higher than the rates observed in similar populations by Bruner et al. (16%), and Halterman et al. (8.7%). In the present investigation, a self-selection bias perhaps reflected recruitment of concerned volunteers with special interest in iron assessment. Bruner et al. specifically recruited non-anemic iron deficient participants. Halterman et al. sampled data from a previously completed national survey. The low incidence of anemia in this study (1.4%) was very similar to the 1.5% and 1.9% observed by Halterman et al. and Bruner et al. respectively. All are lower than the 5% to 8% prevalence of adolescent iron deficiency anemia in the Western world cited by Morad (2005). Discrepancy in anemia rates may be due to age. Participants ranged from 15 to 18 years in the three North American studies. The majority of participants were between 15 and 16 years. Therefore, participants in the upper teens were not considered in the prevalence statistics. Anemia as a consequence of iron deficiency may become more prevalent if a negative iron balance prevails over time.

Serum ferritin

In this investigation serum ferritin displayed negative correlation coefficients with all measures of academic performance. Statistical significance ($p < 0.05$) was reached with Grade Average and English after controlling for B₁₂ and albumin. In multivariate analysis serum ferritin made a significant contribution, in the negative direction, to the model ($B = - 0.335, p = 0.01$). In contrast Bruner et al. (1996) and Halterman et al. (2001) did not observe such negative associations in their investigations. After removing outliers (cases with residuals greater than 3 standard deviations) to avoid inflated relationships, significant correlations between serum ferritin and Grade Average ($r = - 0.268, p < 0.05$) and English ($r = - 0.259, p < 0.05$) remained. These associations reached significance in the negative direction, but should be interpreted with caution. Relationship strengths were quite low accounting for 7% and 6% respectively, of the variance in grades. These magnitudes do not suggest a perfect correlation. As ferritin dropped, grade average did not increase in a linear fashion. Inspection of the corresponding scatter plot graphs (Appendix E) provide visual support. The finding of non-significant group differences (iron deficient vs. iron sufficient) also casts doubt on the practical significance of the negative relationships.

In a larger sample ($n = 427$) with different characteristics than the present study (deprived children {mean age 9.6 years} from Thailand) similar negative relationships were noted by Sungthong, Mo-suwan and Chongsuvivatwong (2002). These researchers observed the highest IQ, Thai language, and math scores in participants displaying normal hemoglobin but low serum ferritin. We observed similar negative relationships with Grade Average and English. As in the present study, the low serum ferritin cutoff

selected by Sungthong et al. (2002) was $\leq 20 \mu\text{g/L}$. Prevalence rates of low serum ferritin and iron deficiency anemia ($\text{Hb} < 120 \text{ g/L}$) were 13% and 4.2%. Using the same cutoff values in this study revealed rates of 58% and 1.4%. Although we observed a much greater rate of iron deficiency than Sungthong et al. results of both studies suggest that systemic abnormalities of iron may not be related to brain function (Youdim, 2000). Alternatively, when hemoglobin is high enough, increasing iron levels may have some adverse effect on cognition (Sungthong et al., 2002).

The potential of serum ferritin to be a good predictor of academic performance can also be brought into question. As ferritin is an acute phase reactant, its serum levels may be falsely elevated in the presence of infection, inflammation or malignancy (Lipschitz, Cook, & Finch, 1974). This limitation is common in iron research. Serum ferritin is a reliable and sensitive parameter for iron store assessment in healthy subjects (Jacobs, 1977). Serum ferritin is widely used in clinical practice and population screening (DiSilvestro, 2005). However, other fields of research have shown that conclusions based solely on this parameter should be approached with skepticism. Investigation of serum ferritin and exercise performance in non anemic iron deficient participants has produced results indicating that low serum ferritin ($< 20 \mu\text{g/L}$) does not affect exercise performance (Beard & Tobin 2000; Newhouse, Clement, Taunton, & McKenzie, 1989). A recent review on this topic by DiSilvestro (2005) highlights both positive and negative results. The debate is not resolved.

Hemoglobin

In bivariate correlation hemoglobin produced correlational coefficients in the positive direction with all measures of academic performance. No bivariate correlations observed with hemoglobin achieved statistical significance ($p < 0.05$) in this study. In partial correlation, controlling for B_{12} and albumin, the direction of hemoglobin's relationship with Grade Average ($r = -0.045$), Math ($r = -0.025$), and English ($r = -0.024$) became negative. The magnitudes of these relationships were small and do not suggest a strong relationship. Other relationships were also pursued. When iron status parameters were sorted in descending order and grouped into thirds, the correlational coefficients between hemoglobin and several measures of academic performance (Grade Average, Math, and Science) became more positive as hemoglobin values dropped. The peak strength of the positive coefficients was reached in the lowest third of hemoglobin values ($Hb < 130$ g/L) but, none of these magnitudes reached statistical significance. Considering hemoglobin's insignificant predictive ability in multivariate analysis ($B = 0.002$, $p = 0.91$) it is possible that any relationship with descending hemoglobin values represented a spurious pattern.

The rationale for using tertiles should be discussed. In correlational analyses, considering the data in its entirety can result in different correlations than if researchers impose a restriction (Diekhoff, 1992). Iron deficiency has different stages and breaking down the participants into three groups helped the researchers look for patterns in non-anemic levels of iron deficiency. Participants with hemoglobin less than 130 g/L ($n = 15$) represented 21% of the sample. Although the number of participants in the bottom third was small ($n < 30$) and corresponding scatter plots did not show a robust trend, this

pattern generates speculation about clinical importance. From a clinical perspective, it is interesting that this pattern was observed starting at 130 g/L, a value above the 120 g/L cutoff for anemia.

Vitamin B₁₂

Vitamin B₁₂ levels were measured as a control ruling out the possibility of B₁₂ deficiency leading to anemia (Pernicious anemia) rather than iron deficiency. Only two participants were B₁₂ deficient. Both displayed normal iron status. The one case of anemia (Hb < 120 g/L) displayed normal B₁₂ levels ruling out the possibility of Pernicious anemia. There were no statistically significant correlations between vitamin B₁₂ and any measure of academic performance. In multivariate analysis B₁₂ was not a significant predictor of academic performance ($B = 0.008$, $p = 0.41$). Vitamin B₁₂ was not measured in comparable studies by Bruner et al. (1996) and Halterman et al. (2001). It will be interesting to note whether or not vitamin B₁₂ is included as a variable of interest in subsequent studies of iron status and academic performance. Further observation of no effect might imply that this micronutrient be excluded from such investigations.

Albumin

Albumin levels were measured to gain insight into participant health and assist interpretation of results. Low levels of this plasma protein have been shown to signal periods of malnutrition or high blood loss (Bulow & Madsen, 1986). Both conditions would alter iron status. No participants displayed low albumin. Therefore, there was no

indication of abnormally high blood loss or state of malnutrition leading researchers to speculate whether albumin would have any statistical influence on the outcome of the study. An indication of abnormally high blood loss or malnutrition would definitely affect iron status. In light of this reasoning it very interesting to note that when albumin was used in bivariate correlation with the measures of academic performance, four out of a possible five correlations reached significance ($p < 0.05$). These included correlations with Grade Average, Science, Physical Education, and English. Removal of outliers (standardized residual > 3) did affect the outcome. When outliers were removed three of five measures remained significant (Grade Average: $r = + 0.250$; $p < 0.05$, Physical Education: $r = + 0.262$; $p < 0.05$, English: $r = + 0.280$; $p < 0.05$). The correlation with Science was no longer significant. The significance level with Physical Education dropped from the 0.01 level to 0.05. Albumin also made a significant ($p = 0.03$) contribution to the model explaining grades in multivariate analysis. Albumin displayed the highest regression coefficient ($B = 1.16$; $p = 0.03$) versus the other predictors entered (serum ferritin, hemoglobin, B_{12}), meaning for every one-unit increase in albumin there was a statistically significant 1.16 unit increase in grades. Albumin was involved in the highest number of significant correlations discovered in this study and displayed significant predictive ability, perhaps leading to further speculation as to the link between albumin and academic performance.

Corsonello et al. (2001) also noted a relationship between albumin and cognition. The focus of the study was on the link between serum magnesium and cognitive impairment however, low albumin (< 35 g/L) was significantly associated with cognitive impairment (Hodkinson Abbreviated Mental Test). Their sample was larger, older, and

not as healthy as ours. These investigators studied 1058 Italian patients (mean age 70.7 ± 12.2 years) with hypertension. Comparing these results to the present study is interesting considering the relationships we observed occurred within the normal range of albumin levels. Albumin transports many small molecules in the blood (i.e., bilirubin, calcium, progesterone, fat soluble hormones, free fatty acids, and drugs). It is of prime importance in maintaining the oncotic pressure of the blood (keeping the fluid from leaking into the tissues) (Stone, 2005). As no participants displayed low albumin, none of the related functions of this protein should have been impaired making it difficult to pinpoint a likely explanation for the significant correlations. Perhaps a link to academic performance could exist with one of albumin's transported substances and not with albumin itself. Albumin has not been considered as a variable of interest in any previous studies relating or linking iron status to academic performance in an adolescent female population. This observation was made after critically appraising studies for this thesis and confirmed following inspection of a review on the topic by Taras (2005). The reproduction of this result may represent a point of interest in directing future research.

Statistically combining serum ferritin and hemoglobin in a multiple correlation showed no significance ($R = 0.269$, $p = 0.078$). The statistical combination of serum ferritin and hemoglobin was not strongly related to or able to strongly predict grade average. This model could not explain a significant proportion of the variance in grades. However, when albumin was included with serum ferritin and hemoglobin in the model, predictive ability increased to a statistically significant level ($B = 1.16$, $p = 0.030$). Adding B_{12} as a predictor increased the magnitude of the multiple correlation coefficient further ($R = 0.394$, $p = 0.024$). This model of nutritional predictors was able to explain a

statistically significant 10.4% ($\text{Adj. } R^2 = 0.104$) of the variance in grades corresponding to a medium effect size ($f^2 = 0.18$). By convention, effect sizes of 0.02, 0.15, and 0.35 are considered small, medium, and large, respectively (Cohen, 1988). It appears that when more blood parameters were available to the researchers, increased predictive ability in grades resulted. This suggests that the addition of more vitamin/mineral variables in future studies could potentially increase the percentage of variance in academic performance explained by nutritional factors. At the same time, significant predictor variables (i.e., albumin) could be identified for inclusion in subsequent related research. A multivariate approach emphasizes the challenge of focusing on single variables (i.e., iron status) and their influence on academic performance. Developing multivariate statistical models that consistently identify significant physiological or nutritive predictors of academic performance in adolescents represents a noteworthy goal for future researchers. We were not able to locate such a model in the published literature.

Group Differences

When the teenaged participants were grouped by iron status as either iron deficient or iron sufficient, there was no significant difference (between subjects/independent t-test) in how the groups were performing academically. This result seems to match the weak/small bivariate correlational strength between serum ferritin, hemoglobin and the measures of academic performance (strength ranged from 0.024 to 0.304 after controlling for B₁₂ and albumin) and the few statistically significant relationships they produced (after removing outliers 2 of 10 correlations were significant; serum ferritin vs. Grade

Average, $r = -0.268$ and serum ferritin vs. English, $r = -0.259$). A non-significant difference between the groups in any measure of academic performance agrees with the non-significant results of Bruner et al. (1996). In the Bruner et al. study a group of iron deficient American teenage girls ($n = 36$) did not score significantly different than a matched group ($n = 37$) with improved iron status on three measures of attention. Bruner et al. did find a significant difference between the groups in verbal learning and memory. The present study showed no significant difference between groups on any academic measure. Our results conflict with Halterman et al. (2001) regarding math findings. In a large sample of teenage American females ($n = 1114$), Halterman et al. found a significant difference between an iron deficient group and a normal iron status group in math scores. Iron deficient females scored significantly lower in the math component of the Wide Range Achievement Test – Revised. Our study showed no difference between the groups in math. Halterman et al. did note no difference between the groups in reading, block design, and digit span. Comparison across these studies is difficult because the previous investigations utilized standardized cognitive tests whereas this study used actual school grades.

In terms of relative risk, participants in this study were not at an increased risk of scoring below the provincial standard or “B” level for all measures of academic performance based on the event of being iron deficient or iron sufficient. All confidence intervals included the value of no effect (1.0). Such a finding was not expected. One might argue that if an individual is proven to be nutrient deficient then it would be expected to see a greater chance of impaired academic performance - unless the deficiency and academic performance are not related. The low correlational strength and

lack of group difference (iron deficient vs. iron sufficient) we observed support this argument. However, considering iron's physiologic role in neural and brain function and revisiting the rational linking iron status to academic performance established at the onset of this investigation, a more plausible explanation for these relative risks, and results as a whole can be stated. The effect of iron deficiency on cognitive function may be subtle. Without the development of anemia statistical conclusions based on iron deficient groups must be interpreted carefully. Additionally, when studying female participants menstrual cycles should be considered.

We did not want to pose a threat to privacy and avoided intrusive menstrual evaluation. In turn reducing participant burden likely aided the recruitment process. However, the potential limitation imposed by varying individual menstrual cycles warrants discussion. Women show variation in iron parameters during their menstrual cycles. Kim et al. (1993) noted that during the monthly cycle, hemoglobin values varied from 130 g/L to 133 g/L and serum ferritin from 17.2 $\mu\text{g/L}$ to 24.0 $\mu\text{g/L}$ (menstruation to luteal/late luteal). There is evidence that the low point for blood iron occurs as the menstruation phase, accompanied by maximum cumulative blood loss, is completed (Kim et al., 1993). The menstruation phase usually lasts three to five days. Menstrual cycles of the participants identified as iron deficient (ID), $n = 42$, were evaluated. We did not have the equipment to intricately differentiate between cycle phases. For example, progressing from the *ovulation phase* to the *luteal phase* is marked by a body temperature increase of 1/4 to 1/2 degree Celsius (Milman, Clausen, & Byg, 1998). Instead we relied on the onset of bleeding as recollected by participants to identify day 1 of the menstrual phase. Of the forty-two iron deficient participants, ten were in the menstruation phase of

their cycle when blood was drawn. Five of the twenty-nine iron sufficient participants were also tested during the menstruation phase. Iron status varied from good to poor regardless of cycle phase. Statistical analysis was not attempted with this data. Our menstrual analysis was fairly rudimentary, although attempting to control the menstrual cycle might be practically unrealistic. The sample would become less representative of the population. External validity of the findings may be reduced. Clearly the association between iron status and academic performance is complex and further research is needed.

Dietary Analysis

Dietary analyses were performed to assess whether iron status was linked to iron intake. Forty-one individuals completed their dietary analyses. The correlation between iron intake and iron status ($r = 0.062$; $p = 0.70$) was small and not significant. Iron intake was not strongly related to iron status. This lack of relationship was clear after inspecting the scatter plot graph (Appendix G). These results support the fact that predisposition to absorb iron varies across otherwise similar individuals (DiSilvestro, 2005). Such large variation leads to speculation about inaccurate under or over-reporting on food records.

CHAPTER 6

SUMMARY AND CONCLUSIONS

The purpose of this study was to determine whether an association existed between iron status and academic performance. Participants were 14- to 16-year-old apparently healthy female students in the 10th grade. A rationale for why such an association may exist focused on the established role of iron in neurotransmission, neurofunctional maturation, and overall efficacy of the central nervous system. Assays for serum ferritin, hemoglobin, vitamin B₁₂, and albumin were performed. At the onset of the study, this researcher hypothesized that lower iron status would accompany lower academic performance and that a significant correlation between iron status and all measures of academic performance would reveal a difference between iron deficient and iron sufficient individuals regarding school grades. Following data analysis, a significant positive relationship was not found between iron status and academic performance. The relationship (correlation) between serum ferritin and academic performance was in the negative direction, achieving significance with Grade Average and English. However, a difference between iron deficient and iron sufficient groups was not observed in any measure. Consequently, the hypothesis cannot be supported. Noteworthy findings included: statistically significant relationships between albumin and several academic performance measures. These findings support albumin as a variable of interest in future research related to academic performance. This iron study was unique in that it was the first to assess vitamin B₁₂ and albumin in a teenage sample from a developed country. It

was the first to use actual school grades rather than standardized tests as the measure of cognitive ability in such a sample.

Within the limitations of this study the following conclusions are warranted:

1. A significant positive correlation did not exist between iron status (serum ferritin, hemoglobin) and academic performance (Grade Average, Math, Science, Physical Education, English).
2. In this sample, menstruating teenage females between the ages of 14 and 16 years were a high risk group, vulnerable to iron deficiency.
3. Lower levels of albumin were associated with poorer academic performance.

The following recommendations are made for future research:

1. Studies using diverse methodological and statistical strategies (i.e., expanded multivariate models) investigating the relationship between iron status and academic performance in adolescents should be performed. There are presently few published studies examining this population from which to draw any definitive conclusions.

2. These findings regarding the statistically significant correlations between albumin and academic performance should be replicated and explored further. More research should be conducted to investigate albumin's possible link to academic performance.

3. More research should be done with larger samples to determine if cognitive performance decrements are consistent with hemoglobin values between 130 g/L and 120 g/L. The clinical implications of such an event, in the absence of anemia, would suggest further investigations of non-anemic iron deficiency are needed. Increased screening, and iron supplementation programs among those without anemia may be warranted.

REFERENCES

- Abalkhail, B., and Shawky, S. (2002). Prevalence of daily breakfast intake, iron deficiency Anaemia, and awareness of being anaemic among Saudi school students. *Int J Food Sci Nutr*, 53: 519-528.
- Agarwal, D., Upadhyay, S., Tripathi A., and Agarwal K. (1987). Nutritional Status, Physical Work Capacity and Mental Function in School Children. *Indian Pediatr*, 24: 703-712.
- Allen, L. (2002). Iron supplements: scientific issues concerning efficacy and implications for Research and programs. *J. Nutr*, 132: 813-814.
- American Psychiatric Association. (1994). *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.). Washington DC: American Psychiatric Association.
- Antalis, C., Stevens, L., Campbell, M., Pazdro, R., Ericson, K., and Burgess, J. (2006). Omega-3 fatty acid status in attention-deficit/hyperactivity disorder. *Prostaglandins, Leukot, Essent Fatty Acids*, 75: 299-308.
- Bailey-Britton A. (1987). The relationship between health and academic performance in school-age children. *Issues Compr Pediatr Nurs*, 10: 273-289.
- Balducci, L. (2003). Epidemiology of anemia in the elderly: information on diagnostic evaluation. *J Am Geriatr Soc*, 51:S2.
- Bandura, A. (1977). Self Efficacy: Toward a unifying theory of behavioural change. *Pshchol Rev*, 84:191-215.
- Basiotis, P., Welsh, S., Cronin, F., Kelsay, J., and Mertz, W. (1987). Number of days of food intake records required to estimate individual and group nutrient intakes with defined confidence. *J Nutr*, 117:1638-1641.
- Beard, J., and Dawson, H. (1997). Iron. In O'Dell, B., and Sunde, R. (Eds.), *Handbook of Nutritionally Essential Mineral Elements*, Marcel Dekker: New York, chpt 9.
- Beard, J., Richards, R., Smicklas-Wright, H., Bernardo, V., and Kordish, S. (1996). Iron nutrition in rural home bound elderly persons. *J Nutr Elder*, 15: 3-4.
- Beard, J., and Tobin, B. (2000). Iron status and exercise. *Am J Clin Nutr*, 72: 594-597.
- Beguin, Y. (2003). Soluble transferrin receptor for the evaluation of erythropoiesis and iron status, *Clin Chim Acta*, 329: 9-13.

- Blum, R., Beuhring, T., Shew, M., Bearinger, L., Sieving, R., and Resnick, M. (2000). The effects of race/ethnicity, income, and family structure on adolescent risk behaviors. *Am J Public Health*, 90:1879-1884.
- Bohmer, F., Fruhwald, T., and Lapin, A. (2003). Soluble transferrin receptor and iron status in elderly patients, *Wien Med Wochenschr*, 153: 232-233.
- Bothwell, T., and Charlton, R. (1981). Iron deficiency in women: A report of the international nutritional anemia consultative group.
- Bothwell, T., Charlton, R., Cook, J., and Finch, C. (1979). Iron metabolism in man. Boston, Blackwell Scientific Publications.
- Braunwald, E., Fauci, A., Kasper, D., Hauser, S., Longo, D., and Jameson L. (2001). *Harrison's Principles of Internal Medicine*, 15th ed.
- Brown D., and Blanton, C. (2002). Physical activity, sports participation, and suicidal behavior among college students. *Med Sci Sports Exerc*, 34:1087-1096.
- Bruner, A., Joffe, A., Duggan, A., Casella, J., and Brandt, J. (1996). Randomized study of cognitive effects of iron supplementation in non-anemic iron deficient adolescent girls. *The Lancet*, 348: 992-996.
- Bulow, J., and Madsen, J. (1986). Regulation of fatty acid mobilization from adipose tissue during exercise. *Scand J Sports Sci*, 8:19-26.
- Canadian Physical Activity, Fitness & Lifestyle Approach (CPAFLA): CSEP-Health & Fitness Program's Health-Related Appraisal and Counselling Strategy (2003). Canadian Society for Exercise Physiology, Ottawa Ontario.
- Cantwell, R. (1974). The long term neurological sequelae of anemia in infancy. *Pediatr Res*, 342:68-70.
- Carlson, N. (1997). *Psychology: The Science of Behaviour*. Allyn and Bacon
- Clement, D., Asmundson, R., and Medhurst, C. (1977). Hemoglobin values: comparative survey of the 1976 Canadian Olympic team. *Can Med Assoc J*, 117: 614-616.
- Clement, D., and Sawchuck, L. (1984). Iron status and Sports performance. *Sports Med*, 1: 65-74.
- Clarke, N., Grantham-McGregor, S., and Powell, C. (1991). Nutrition and health predictors of school failure in Jamaican children. *Ecol Food Nutr*, 26:1-11.
- Clarkson, P. (1991). Minerals: exercise performance and supplementation in athletes. *J Sports Sci*, 9:91-93.

- Coban, E., Timuragaoglu, A., and Meric, M. (2003). Iron deficiency anemia in the elderly: prevalence and endoscopic evaluation of the gastrointestinal tract in outpatients. *Acta Haematol*, 110: 25-27.
- Cohen, J. (1988). *Statistical power analysis for the behavioural sciences* (2nd ed.). Erlbaum: Hillsdale, N.J.
- Cook, J., Baynes, R., and Skikne, B. (1992). Iron deficiency and the measurement of iron status. *Nutr Res Rev*, 5: 189-202.
- Corsonello, A., Pedone, C., Pahor, M., Malara, A., Carosella, L., Mazzei, B., Onder, G., Corsonello, F., Carbonin, P., and Corica, F. (2001). Serum magnesium levels and cognitive impairment in hospitalized hypertensive patients. *Magnes Res*, 14: 273-282.
- De Andraca, I., Walter, T., Castillo, M., Pino, P., Rivera, P., and Cobo, C. (1990). Iron deficiency anemia and its effects upon psychological development at pre-school age: a longitudinal study. Nestle Foundation Lausanne, Switzerland, 53-62.
- De Maeyer, E., and Adiels-Tegman, M. (1986). The prevalence of anemia in the world. *World Health Statistics Quartely*, 38:302-316.
- Diekhoff, G. (1992). *Statistics for the social and behavioral sciences: univariate, bivariate multivariate*. Midwestern State University. Brown Publisher. United States of America.
- DiSilvestro, R. (2005). *Handbook of minerals as nutritional supplements*. Boca Raton, FL CRC Press.
- Dommergues, M., Archambeaud, B., Ducot, Y., Gerval, Y., Hiard, C., Rossignol, C., and Tchernia, G. (1989). Carence en fer et tests de developpement psychomoteur: etude ongitudinale entre l'age de 10 mois et l'age de 4 ans. *Arch Fr Pediatr*, 46: 487-490.
- Ehn, L., Carlmark, B., and Hoglund, S. (1980). Iron status in athletes involved in intense physical activity. *Med Sci Sports Exerc*, 12: 61-64.
- Eichner, E. (1992). Sports anemia, iron supplements, and blood doping. *Med Sci Sports Exrc*, 24: 315-318.
- Feelders, R., Kuiper-Kramer, E., and van Eijk, H. (1999). Structure, function and clinical significance of transferrin receptors. *Clin Chem Lab Med*, 37: 1-5.
- Feightner, J. (1994). Prevention of iron deficiency anemia in infants. *Canadian Task Force on Preventive Health Care*.

- Flemming, D., Jacques, P., Tucker, K., Massaro, J., D'Agostino, R., Sr., Wilson, P., and Wood, R. (2001). Iron status of the free-living elderly, Framingham Heart Study cohort: An iron-replete population with a high prevalence of elevated iron stores. *Am J Clin Nutr*, 73: 638-641.
- Fleshner, M. (2000). Exercise and neuroendocrine regulation of antibody production: protective effect of physical activity on stress-induced suppression of the specific antibody response. *Int J Sports Med*. 21:S14-S19.
- Florencio, C. (1988). Nutrition, health and other determinants of academic achievement and school-related behavior of grades one to six pupils. University of the Philippines Quezan City, Philippines.
- Glied, S., and Pine, D. (2002). Consequences and correlates of adolescent depression. *Arch Pediatr Adolesc Med*, 156:1009-1014.
- Grantham-McGregor, S., and Ani, C. (2001). A review of studies on the effect of iron deficiency on cognitive development in children. *J Nutr*, 131: 649S-668S.
- Grindulis, H., Scott, P., Belton, N., and Wharton, B. (1986). Combined deficiency of iron and vitamin D in Asian toddlers. *Arch Dis Child*, 61: 843-848.
- Grein, J. (2001). The cognitive effects of iron deficiency in non-anemic children. *Nutr Noteworthy*, 4: 1-5.
- Groner, J., Holtzman, N., Charney, E., and Mellitis, E. (1986). A randomized trial of oral iron on tests of short-term memory and attention span in young pregnant women. *J Adolesc Health Care*, 7: 44-48.
- Halterman, J., Kaczorowski, J., Aligne, A., Auinger, P., and Szilagyi, P. (2001). Iron deficiency and cognitive achievement among school aged children and adolescents in the United States. *Pediatrics*, 107: 1381-1385.
- Hanson, T., and Austin G. (2003). Student Health Risks, Resilience, and Academic Performance in California: Year 2 Report, Longitudinal Analyses. Los Alamitos, Calif. WestEd..
- Haymes, E., and Lamanca, J. (1989). Iron loss in runners during exercise: Implications and recommendations. *Sports Med*, 7: 277-285.
- Health Canada. (2004). www.healthcanada.ca [On-line].
http://www.hc-sc.gc.ca/index_e.html
- Hebert, V. (1996). Vitamin B-12. In Ziegler, E., and Filer, L. (Eds.), *Present knowledge in nutrition*. Washington, DC: ILSI Press, 191-205.

- Houston, M., Summers, S., and Soltesz, K. (1997). Lifestyle and dietary practices influencing iron status in university women. *Nutr Res*, 17: 9-22.
- Hunt, J. (2002). Reversing productivity losses from iron deficiency: the economic case. *J Nutr*, 132: 794S-800S.
- Hurtado, E., Claussen, A., and Scott, K. (1999). Early childhood anemia and mild or moderate mental retardation, *Am J Clin Nutr*, 69: 116-119.
- Hutchinson, S., Powell, C., Walker, S., Chang, S., Grantham-McGregor, S. (1997). Nutrition, anemia, geohelminth infections, and school achievement in rural Jamaican primary school children. *Eur J Clin Nutr*, 51: 729-735.
- Jacobs, A. (1977). Serum ferritin and iron stores. *Fed Proc*, 36:2024-2027.
- Johnson, M. (1994). Disordered eating in active and athletic women. *Clin Sports Med*, 13: 355-369.
- Jones, G., Newhouse, I., Jakobi, J., LaVoie, N., and Thayer, R., (2001). The incidence of hematuria in middle distance track running. *Can J Appl Physiol*, 26:336-349.
- Kim, I., Yetley, E., and Clavo, M. (1993). Variations in iron status measures during the menstrual cycle. *Am J Clin Nutr*, 58: 705-709.
- Klerman, L. (1996). Can school-based health services reduce absenteeism and dropping out of school? *Adolesc Med*, 7: 249-260.
- Konofal, E., Lecendreux, M., Arnulf, I., and Mouren, M. (2004). Iron deficiency in children with attention-deficit hyperactivity disorder. *Arch Pediatr Adolesc Med*, 158: 1113-1115.
- Kozielec, T., Starbart, E., and Herhelin, B. (1994). Deficiency of certain trace elements in children with hyperactivity. *Pol J Psychiatry*, 28: 345-353.
- Krause, M., and Mahan, L. (1979). Food, Nutrition and Diet Therapy. Saunders Company, Philadelphia.
- Lamanca, J., Haymes, E., Daly, J., Moffatt, R., Waller, M. (1988). Sweat iron loss of male and female runners during exercise. *Int J Sports Med*, 9: 52-55.
- Lampe, J., Salvin, J., and Apple, F. (1990). Iron status of active women and the effect of running a marathon on bowel function and gastrointestinal blood loss. *Int J Sports Med*, 12: 173-179.

- Larkin, E., and Rao, G. (1990). Importance of fetal and neonatal iron: Adequacy for normal development of CNS. In Dobbing, J. (Ed.), *Brain, behaviour, and iron in the infant diet*. London: Springer-Verlag, 43-62.
- Lipschitz, D., Cook, J., and Finch, A. (1974). A clinical evaluation of serum ferritin as an index of iron stores. *N Eng J Med*, 290: 1213-1216.
- Lombardi, J. (1997). A report on food consumption in Canada and the diet-health-environment connection. McGill University.
- Lozoff, B., Jimenez, E., Hagen, J., Mollen, E., and Wolf, A. (2000). Poorer behavioural and developmental outcome more than 10 years after treatment for iron deficiency. *Pediatrics*, 105: E51.
- Lozoff, B., Jimenez, E., & Smith, J. (2006). Double burden of iron deficiency in infancy and low socioeconomic status: a longitudinal analysis of cognitive test scores to age 19 years. *Arch Pediatr Adolesc Med*, 160: 1108-1113.
- Lozoff, B., Jimenez, E., and Wolf, A. (1991). Long-term developmental outcome of infants with iron deficiency. *N Engl J Med*, 325:687-694.
- Lynn, R., Harland, P. (1998). A positive effect of iron supplementation on the IQs of iron deficient children. *Pers Individ Dif*, 24: 883-885.
- Manore, M., and Thompson, J. (2000). Sport nutrition for health and performance. Human Kinetics: United States of America.
- Maughan, E. (2003). The impact of school nursing on school performance: a research synthesis. *J Sch Nurs*, 3:163-171.
- Marx, J. (1997). Iron deficiency in developed countries: prevalence, influence of lifestyle factors and hazards of prevention. *Eur J Clin Nutr*, 51: 491-495.
- McArdle, W., Katch, F., and Katch, L. (2001). Exercise physiology (5th ed.). Williams & Wilkins: United States of America.
- Millichap, G., Yee, M., and Davidson, S. (2006). Serum ferritin in children with attention deficit hyperactivity disorder. *Pediatr Neurol*, 34: 200-203.
- Milman, N., Clausen, J., and Byg, K. (1998). Iron status in 268 Danish women aged 18 – 30 years: influence of menstruation, contraceptive method, and iron supplementation. *Ann Hematol*, 77: 13–19.

- Morgan, W. (1994). Physical activity, fitness, and depression. In Shephard, R., and Stephens, T. (Eds.). *Physical activity, fitness, and health: International proceedings and consensus statement*. Bouchard Champaign, Ill: Human Kinetics Publishers, 851-867.
- Morad, M. (2005). Iron deficiency anemia in adolescence. *Int J Adolesc Med Health*, 17: 96-97.
- Murray-Kolb, L., Whitfield, K., and Beard. J. (2004). *Iron status alters cognitive functioning in women during reproductive years*. Paper presented at the federation of American societies for experimental biology, Washington, D.C.
- Newhouse, D. (2003). The effects of iron deficiency and iron supplementation on cognition. *Unpublished manuscript*.
- Newhouse, I., and Clement, D. (1988). Iron status in athletes: An update. *Sports Med*, 5: 337-352.
- Newhouse, I., Clement, D., Taunton, J., and McKenzie, D. (1989). The effects of prelatent/latent iron deficiency on physical work capacity. *Med Sci Sports Exerc*, 21: 263-268.
- Newhouse, I., Clement, D., Taunton, J., and Lai, C. (1993). Effects of iron supplementation and discontinuation on serum copper, calcium, and magnesium levels in women. *Med Sci Sports Exerc*, 25: 562-571.
- O'Keeffe, M., O'Callaghan, M., Cowley, D., Tudehope, D., Gray, P., Burns, Y., and Mohay, H., (2002). Non-anemic iron deficiency identified by ZPP test in extremely premature infants: prevalence, dietary risk factors, and association with neurodevelopmental problems, *Early Hum Dev*, 70: 73-76.
- Oski, F., Honig, A., and Helu, B. (1983). Effect of iron therapy on behaviour performance in nonanemic iron deficient infants. *Pediatrics*. 71: 877-880.
- Otis, C., Drinkwater, B., Johnson, M., Loucks, A., and Wilmore, J. (1997). The female athlete triad. *Med Sci Sports Exerc*, 29: 1-9.
- Overmier, J., and Lawry, J. (1979). Conditioning and the mediation of behavior. In Bower, G. (Ed.), *The psychology of learning and motivation*. New York: Academic Press, 13: 1-55.
- Palti, H., Pevsner, B., and Adler, B. (1983). Does anemia in infancy affect achievement on developmental and intelligence tests?. *Hum Biol*, 55:183-194
- Palti, H., Meijer, A., and Adler, B.(1985). Learning achievement and behavior at school of anemic and non-anemic infants. *Early Hum Dev*, 10: 217-223.

- Patel, D., and Luckstead, E. (2000). Sport participation, risk taking, and health risk behaviors. *Adolesc Med*, 11:141-155.
- Peirano, P., Algarin, C., Garrido, M., Pizarro, F., Roncagliolo, M., and Lozoff, B. (2001). Interaction of iron deficiency anemia and neurofunctions in cognitive development. *Nutr Brain*, 5: 19-39.
- Peterson-Geierstanger, S., Amaral, R., Mansour, M., and Walters, S. (2004). School-based health centers and academic performance: Research, challenges, and recommendations. *J Sch Health*, 74; 347-353.
- Pintrich, P., and De Groot, E. (1990). Motivational and self-regulated learning components of classroom academic performance. *J Edu Psychol*, 82: 33-40.
- Pollitt, E. (1997). Iron Deficiency and educational deficiency. *Nutr Rev*, 55: 133-141.
- Pollitt, E., Cueto, S., Jacoby, E. (1998). Fasting and cognition in well and undernourished school children: a review of three experimental studies. *Am J Clin Nutr*, 67: 779-784.
- Popkin, B., and Lim-Ybanez, M. (1982). Nutrition and school achievement. *Soc Sci Med*, 16: 53-61.
- Rao, R., and Georgieff, M. (2002). Perinatal aspects of iron metabolism. *Acta Paediatr Suppl*, 91: 124-127.
- Roncagliolo, M., Garrido, M., Walter, T., Peirano, P., and Lozoff, B. (1998). Evidence of altered central nervous system development in young iron-deficient anemic infants: delayed maturation of auditory brainstem responses. *Am J Clin Nutr*, 68:683-690.
- Rosenthal, R., and Jacobsen, L. (1968). *Pygmalion in the classroom: Teacher expectation and pupils' intellectual development*. New York: Rinehart & Winston.
- Ross, E. (2002). Evaluation and treatment of iron deficiency in adults, *Nutr Clin Care*, 5:220-222.
- Rossander, L., Hallberg, L., and Bjorn-Rasmussen, E. (1979). Absorption of iron from breakfast meals. *Am J Clin Nutr*, 32: 2484-2488.
- Savage, D., and Lindenbaum, J. (1995). Folate-cobalamin interactions. In Bailey, L. (Ed.), *Folate in health and disease*. New York: Marcel Dekker, 237-285.
- Scales, P., and Roehlkepartain, E. (2003). Boosting student achievement: new research on the power of developmental assets. *Search Inst Insight Eviden*, 1:1-10.

- Schoene, R., Escourrov, H., and Robertson. (1983). Iron repletion decreases maximal exercise lactate concentrations in female athletes with minimal iron-deficiency anemia. *J Lab Clin Med*, 102: 306-309.
- Schunk, D. (1989). Self efficacy and cognitive skill learning. In. Ames, C., and Ames, R. (Eds.), *Research on motivation in education goals and cognitions*. San Diego: Academic Press, 13-44.
- Seshadri, S., and Gopaldas, T. (1989). Impact of iron supplementation on cognitive functions in preschool and school-aged children: the Indian experience. *Am J Clin Nutr*, 50: 675-686.
- Shaywitz, B., Cohen, D., and Bowers, M. (1977). CSF monoamine metabolites in children with minimal brain dysfunction: Evidence for alteration of brain dopamine. *J Pediatr*, 90: 67-71.
- Sherman, A., and Kramer, B. Iron nutrition and exercise. (1990). In. Hickson, J., and Wolinsky, I. (Eds.), *Nutr Exerc Sports*, Boca Raton: CRC Press, 291-300.
- Smith, W. (2000). Commentary on Schoenthaler et al: vitamin and mineral supplements – is the methodology sufficient to support the conclusions? *J Altern Complement Med*, 6: 31-35.
- Soemantri, A., Pollitt, E., and Kim, I. (1985). Iron deficiency anemia and educational achievement. *Am J Clin Nutr*, 42: 1221-1228.
- Statistics Canada. (2006). www.statcan.ca [On-line].
<http://statcan.ca/english/studies/index.htm>
- Stone, C. (2005). VeriMed Healthcare Network. Division of Gastroenterology, Washington University in St. Louis School of Medicine, St. Louis, MO.
- Sunghong, R., Mo-suwan, L., and Chongsuvivatwong, V. (2002). Effects of haemoglobin and serum ferritin on cognitive function in school children. *Asia Pacific J Clin Nutr*, 11: 117-122.
- Symons, C., Cinelli, B., James, T., Groff, P. (1997). Bridging student health risks and academic achievement through comprehensive school health programs. *J Sch Health*, 67: 220-227.
- Takala, T., Suominen, P., Lehtonen-Veromaa, M., Mottonen, T., Viikari, J., Raja-maki, A. and Irjala, K. (2003). Increased serum soluble transferrin receptor concentration detects subclinical iron deficiency in healthy adolescent girls, *Clin. Chem. Lab Med*, 41: 203-209.

- Taras, H. (2005). Nutrition and Student Performance at School. *J Sch Health*, 75: 199-213.
- Taras, H. (2005). Physical Activity and Student Performance at School. *J Sch Health*, 75: 214-219.
- Tobin, B., and Beard, J. (1997). Iron. In Wolinsky I, and Driskell J. (Eds.), *Sports Nutrition: vitamins and trace elements*. Boca Ranton, FL: CRC Press: 137-156.
- Tortora, G. (1999). Principles of Human Anatomy (8th ed.). Benjamin/Cummings Science Publishing: California.
- Tucker, D., and Sandstead, H., (1981). Spectral electroencephalographic correlates of iron status: Tired blood revisited. *PhysiolBehav*, 26: 439-449.
- Tucker, D., Sandstead, H., Swenson, R., Sawler, B., and Penland, J. (1982). Longitudinal study of brain function and depletion of iron stores in individual subjects. *Physio Behav*, 29: 737-740.
- Tucker, D., Sandstead, H., Penland, J., Dawson, S., and Milne, D. (1984). Iron status and brain function: serum ferritin levels associated with asymmetries of cortical electrophysiology and cognitive performance. *Am J Clin Nutr*, 39: 105-113.
- Tuckman, B. (1999). A Tripartite Model of Motivation for Achievement: Attitude/Drive/Strategy. Ohio State University. Presented in the Symposium: Motivational Factors Affecting Student Achievement – Current Perspectives. Annual Meeting of the American Psychological Association, Boston,
- United States National library of Medicine. (2006). National Institutes of Health.
- Waite, J., and Neilson, I. (1919). Study of the effects of hookworm infection upon the mental development of North Queensland school children. *Med J Austr*, 1:1-8.
- Walker, S., Grantham-McGregor, S., Himes, J., Williams, S., and Duff, E. (1998). School performance in adolescent Jamaican girls: associations with health, social and behavioural characteristics, and risk factors for dropouts. *J Adolesc Health*, 21: 109-122.
- Walter, T. (2003). Effect of iron-deficiency anemia on cognitive skills and neuromaturation in infancy and childhood. *Food Nutr Bull*, 4: 104-110.
- Walter, T., de Andraca, I., Chadud, P., and Perales, C. (1989). Iron deficiency anemia: adverse effects on infant psychomotor development. *Pediatrics*. 84: 7-17.
- Wardlaw, G., Hampl, J., and DiSilvestro, R. (2004). Perspectives in nutrition (6th ed.). McGraw-Hill Education: Madison, chap. 12.

- Wasserman, G., Graziano, J., Factor-Litvak, P., Popovac, D., Morina, N., Musabegovic, A., Vrenezi, N., Capuni-Paracka, S., Lekic, V., Preteni-Redjepi, E., Hadzialjevic, S., Slavkovich, V., Kline, J., Shrout, P., and Stein, Z. (1992). Independent effects of lead exposure and iron deficiency anemia on developmental outcome at age 2 years. *J Pediatr*, 121: 695-703.
- Wasserman, G., Graziano, J., Factor Litvak, P., Popovac, D., Morina, N., Musabegovic, A., Vrenezi, N., Capuni Paracka, S., Lekic, V., Preteni Redjepi, E., Hadzialjevic, S., Slavkovich, V., Kline, J., Shrout, P., and Stein, Z. (1994). Consequences of lead exposure and iron supplementation on childhood development at age 4 years. *Neurotoxicol Teratol*, 16: 233-240.
- Weaver, C., and Rajaram, S. (1992). Exercise and iron status. *J Nutr*, 122: 782-787.
- Webb, T., and Oski, F.(1973). Iron deficiency anemia and scholastic achievement in young adolescents. *J Pediatr*, 82: 827-830.
- Yip, R. (2001). Iron. In *Present Knowledge in Nutrition* (8th ed.). Bowman , B., and Russell, R. (Eds.), ILSI Press: Washington, chap. 30.
- Youdim, H. (2000). Nutrient deprivation and brain function: iron. *Nutrition*, 16: 504-508.
- Youdim, M., and Yehuda, S. (1985). Iron deficiency induces several dopamine dependent circadian cycles: Differential response to d-amphetamine and TRH. *Peptides*. 6: 851-855.
- Zimmerman, B. (1998). Academic studying and the development of personal skill: A self-regulatory perspective. *Educ Psychol*, 33: 73-86.
- Zimmerman, B., Bandura, A., and Martinez-Pons, M. (1992). Self motivation for academic attainment: the role of self-efficacy beliefs and personal goal setting. *Am Educ Res J*, 29: 663-676.
- Zlotkin, S. (2003). The role of nutrition in the prevention of iron deficiency anemia in infants, children and adolescents. *Can Med Assoc J*, 168: 59-63.

Appendix A – Participant Consent Form

Dear Potential Participant and Parent/Guardian:

Thank you for volunteering to participate in a study concerning Relationships between Iron Status, and Academic Performance.

Dr. Ian Newhouse, Dean of Professional Schools, Dr. Jim McAuliffe, Dr. Michel Bedard, and Donna Newhouse of Lakehead University along with Dr. Chris Lai are collaborating on and conducting a promising study regarding relationships between Iron Status and Academic Performance.

The purpose of this study is to determine whether or not an association exists between iron status and academic performance, of 14 to 16 year old apparently healthy female students. Through your participation in this research you will help identify groups at risk to iron deficiency in the Thunder Bay area. Iron deficiency is the most common mineral deficiency world wide affecting as many as 60 to 80% of people. You will also help in providing data that may provide direction for future health recommendations. Most importantly, your own health will be investigated and ultimately improved which will help you achieve your greatest potential as a student.

As a participant you will undergo the following:

1. One blood test; samples will be measured for serum ferritin, hemoglobin, vitamin B₁₂, and albumin.
2. Three cognitive tasks involving reaction time key pressing on a computer and pencil/paper tests (don't worry you will not have to study!); 30-45min. in total.
3. Record of what you ate over a 3 day period.
4. You may also be asked/chosen to participate in other research being developed during this study. Such participation is entirely your choice

In addition, your grades will be accessed and compared to the data you provide. All testing will be conducted by skilled and trained individuals. There are no side effects associated with this type of research and very little risk involved. All data you provide will remain confidential and securely stored at Lakehead University for seven years and no individual will be identified in any report of the results. However, the findings of this project will be made available to you at your request upon the completion of the project. As a volunteer you have the right to withdraw from the study at any time.

If you have any questions concerning the study, we can be reached at 345-9728.

Sincerely,

Appendix B -
HEALTH INFORMATION/PHYSICAL ACTIVITY PARTICIPATION SURVEY

Name: _____ Grade: _____ Age: _____

Please answer questions by checking "yes" or "no" and fill in blanks when applicable.

- | | Yes | No |
|--|-------|-------|
| • Are you currently pregnant? | _____ | _____ |
| • Are you presently taking any contraceptives (birth control medications)? | _____ | _____ |
| • At what age did you begin to menstruate (have periods)? _____ | | |
| • When was the date of your last period? _____ | | |
| • If you are on any medications can you please list them:
_____ | | |
| • If you are physically active can you describe the type of exercise you perform? i.e. running.
_____ | | |

Check off the answer that best applies to you.

Frequency:

Over a typical seven-day period (one week), how many times do you engage in physical activity that is sufficiently prolonged and intense to cause sweating and a rapid heart beat?

- At least three times
- Normally once or twice
- Rarely or never

Intensity:

When you engage in physical activity, do you have the impression that you:

- Make an intense effort
- Make a moderate effort
- Make a light effort

Perceived Fitness:

In a general fashion, would you say that your current physical fitness is:

- Very Good
- Good
- Average
- Poor
- Very Poor

Appendix D1 – Food Intake Log

FOOD INTAKE: Name: _____ Weight: _____ Height: _____ Age: _____

Day 1	
Breakfast	
<i>snacks</i>	
Lunch	
<i>snacks</i>	
Dinner	
<i>dessert</i>	
Day 2	
Breakfast	
<i>snacks</i>	
Lunch	
<i>snacks</i>	
Dinner	
<i>dessert</i>	
Day 3	
Breakfast	
<i>snacks</i>	
Lunch	
<i>snacks</i>	
Dinner	
<i>dessert</i>	

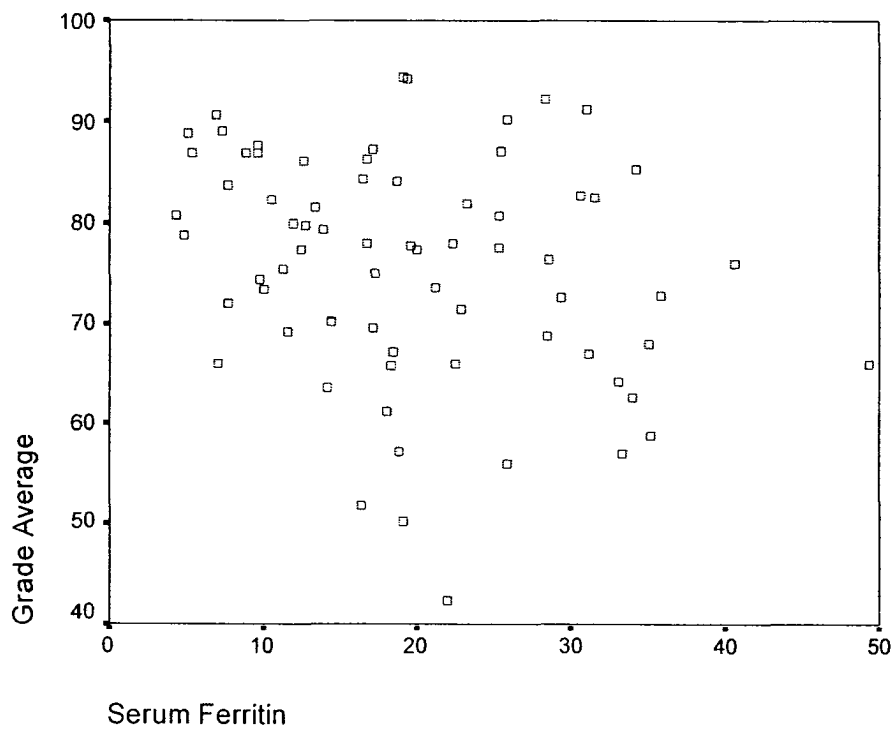
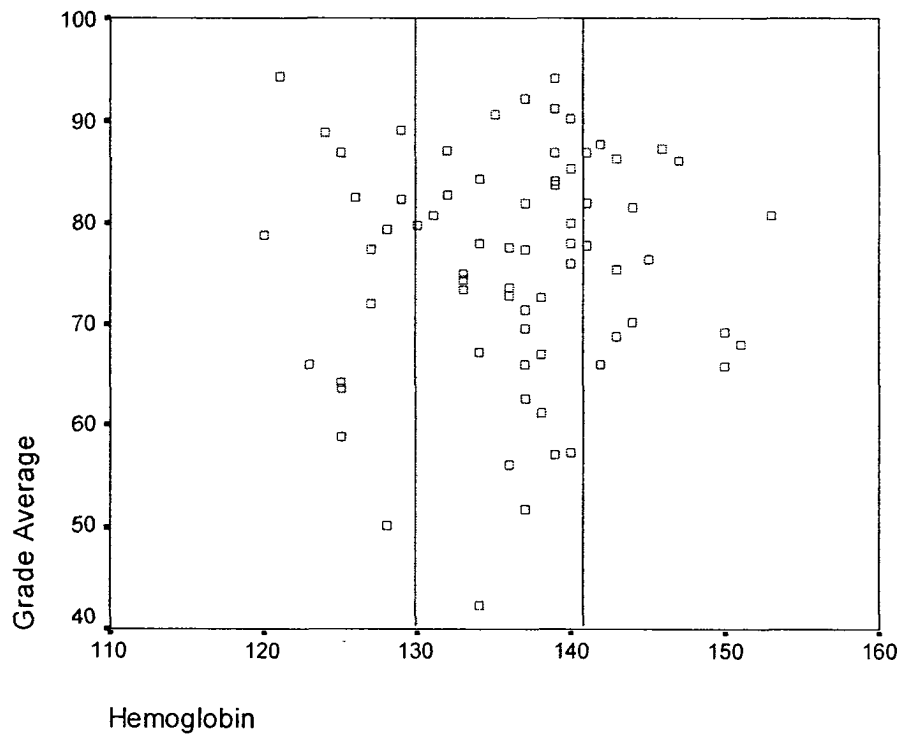
Appendix D2 - Dietary Analysis Instructions

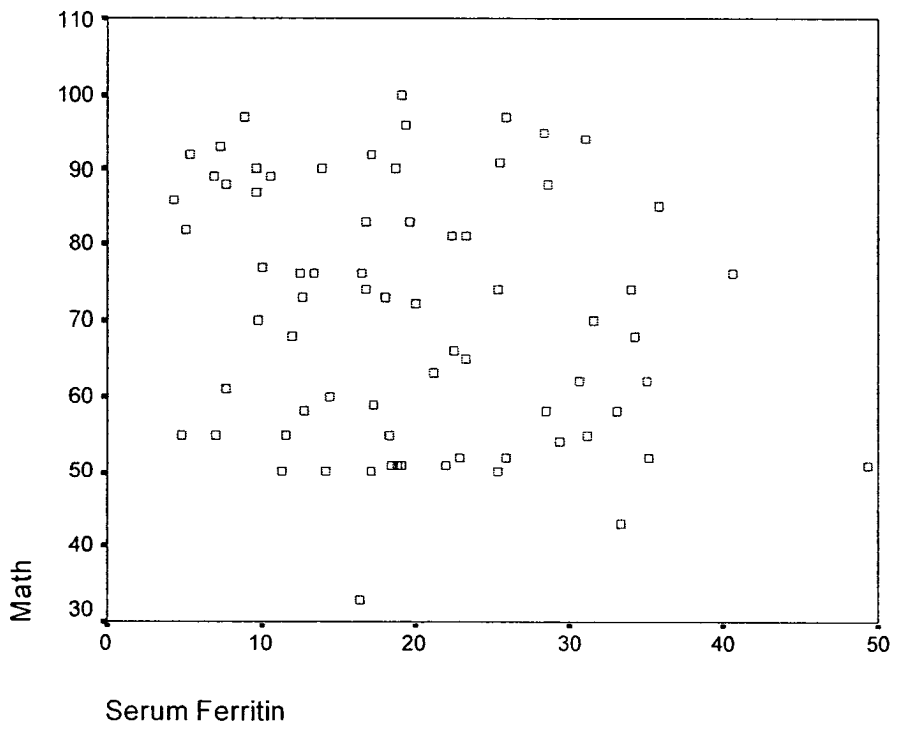
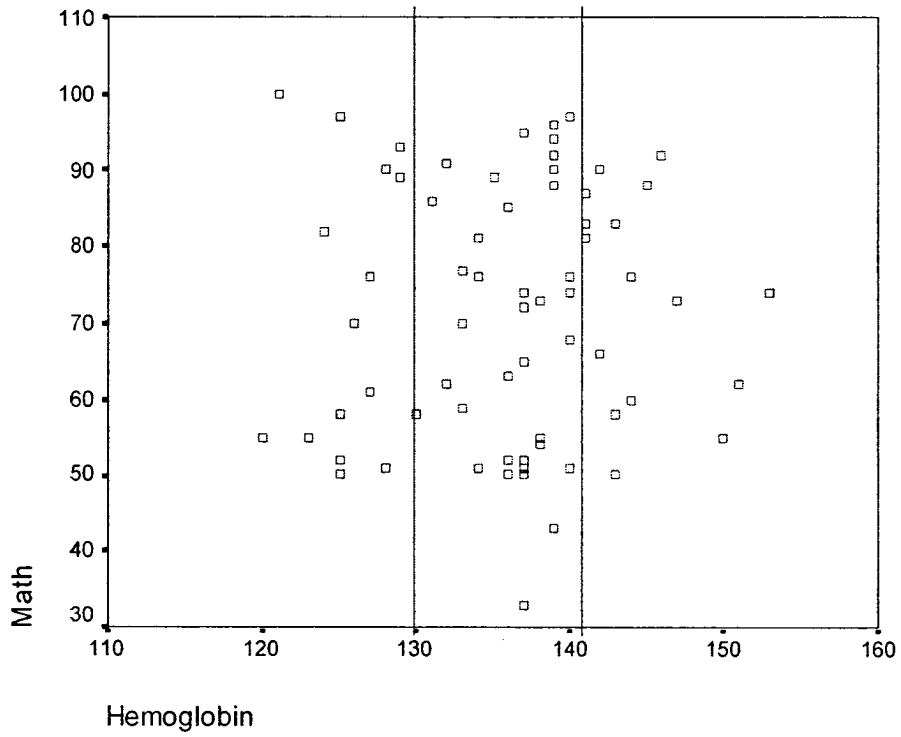
- Please record everything you eat over a consecutive 3 day period using the FOOD INTAKE form provided.
- Be sure to record honestly and please include one weekend day as one of the 3 days i.e. Wed, Thurs, Fri or Sun, Mon, Tues.
- Enter food items as accurately as possible using specific names and amounts i.e. McDonalds or 1 cup of Cheerios etc.
- For drinks specify: glass, juice box, can of pop, or when drinking a bottle (i.e. water) enter the amount i.e. 500 ml.
- SEE SAMPLE BELOW AS AN EXAMPLE TO HELP YOU OUT!!
- Don't worry about recording in servings!

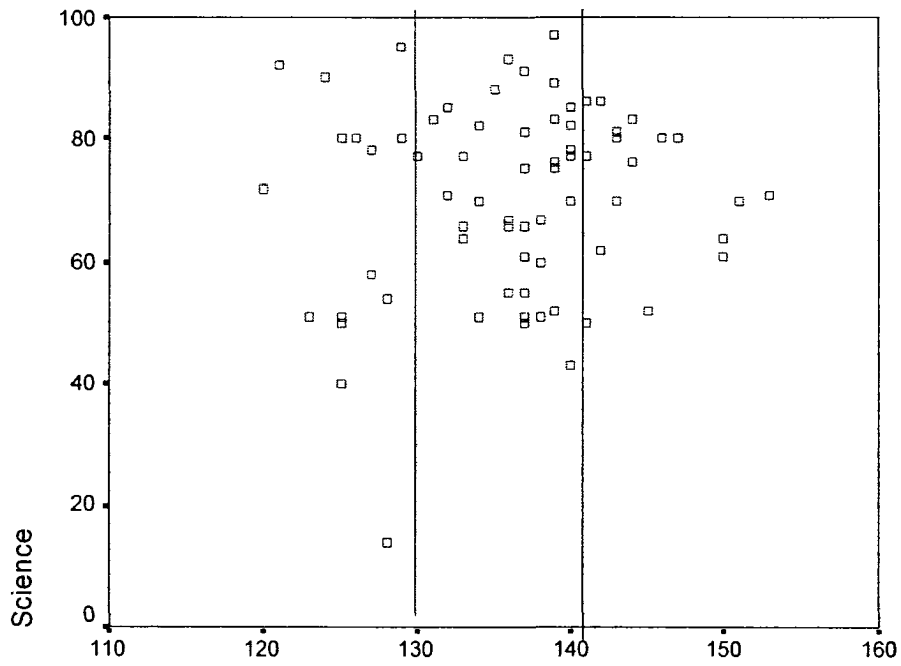
FOOD INTAKE: Name: Jane Doe Weight: 110 lbs Height: 5'4" Age: 15

Day 1	
Breakfast	1 bowl (2 cups) Honey Nut Cheerios, 1 cup milk (2%), 1 slice rye bread with peanut butter, 1 glass orange juice, 1 glass chocolate milk (1%)
<i>snacks</i>	Potato chips (1 small bag sour cream & onion)
Lunch	1 apple, submarine sandwich (cold cut), 1 can diet Pepsi
<i>snacks</i>	Chocolate chip granola bar
Dinner	Big Mac (McDonalds), 1 plate Pasta and Meatballs in tomato sauce (2 cups spaghetti, 1 cup meatballs) 1 bottle water (500 ml), 1 glass apple juice
<i>dessert</i>	Ice cream cone (Dairy Queen), hot fudge sundae (McDonalds)

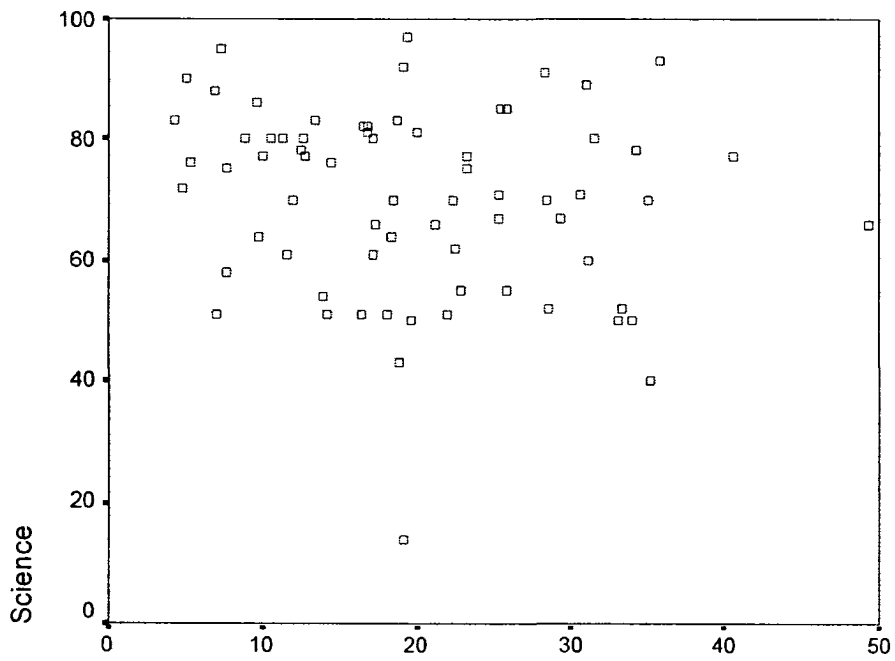
Appendix E – Scatter Plots: Serum Ferritin and Hemoglobin vs. Measures of Academic Performance



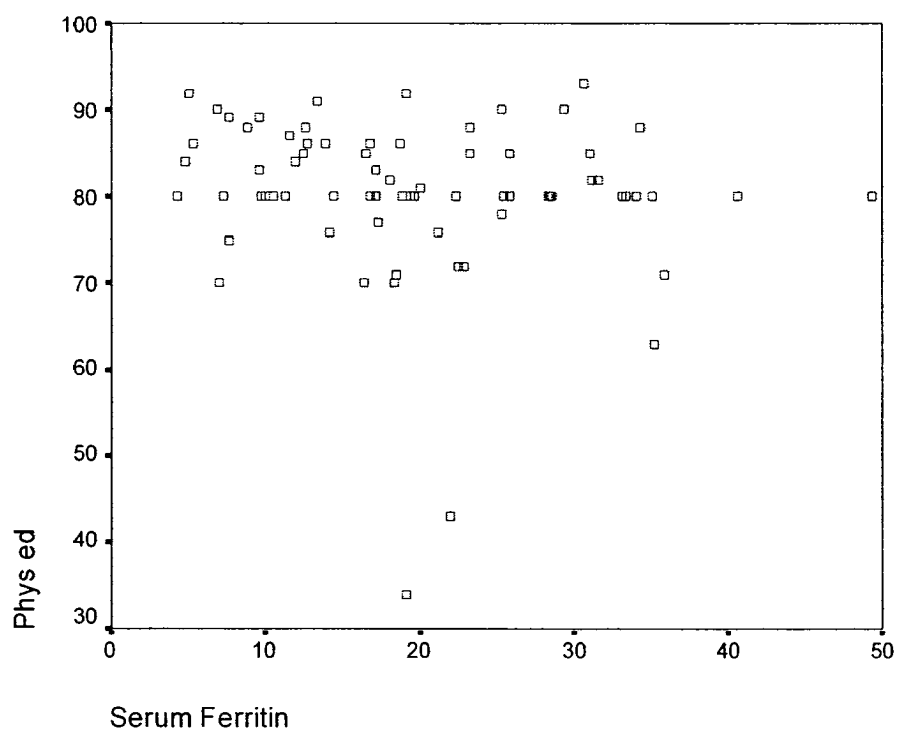
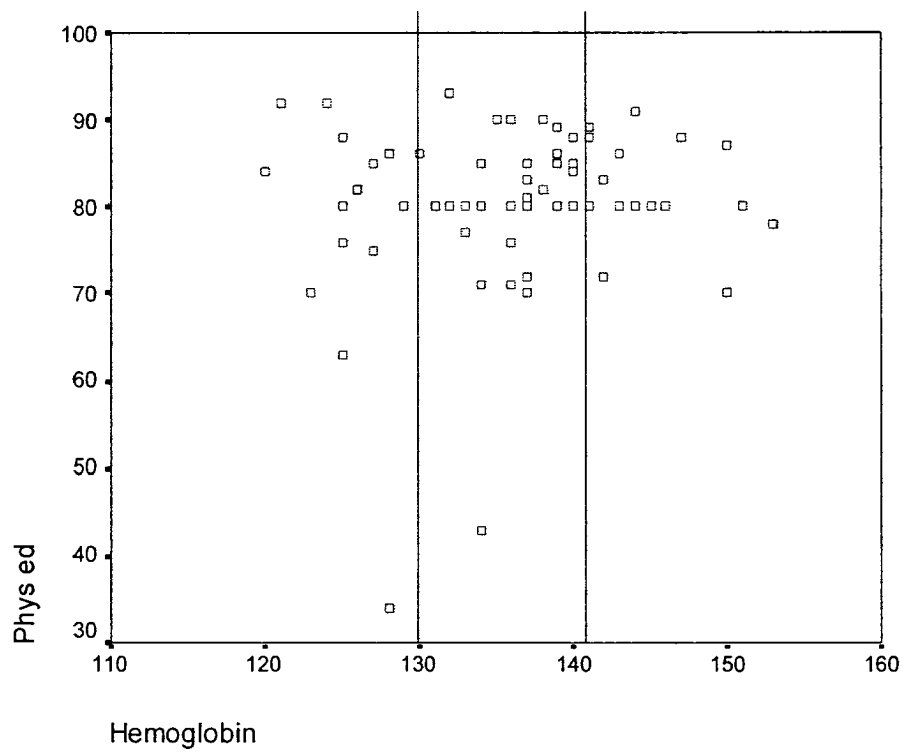


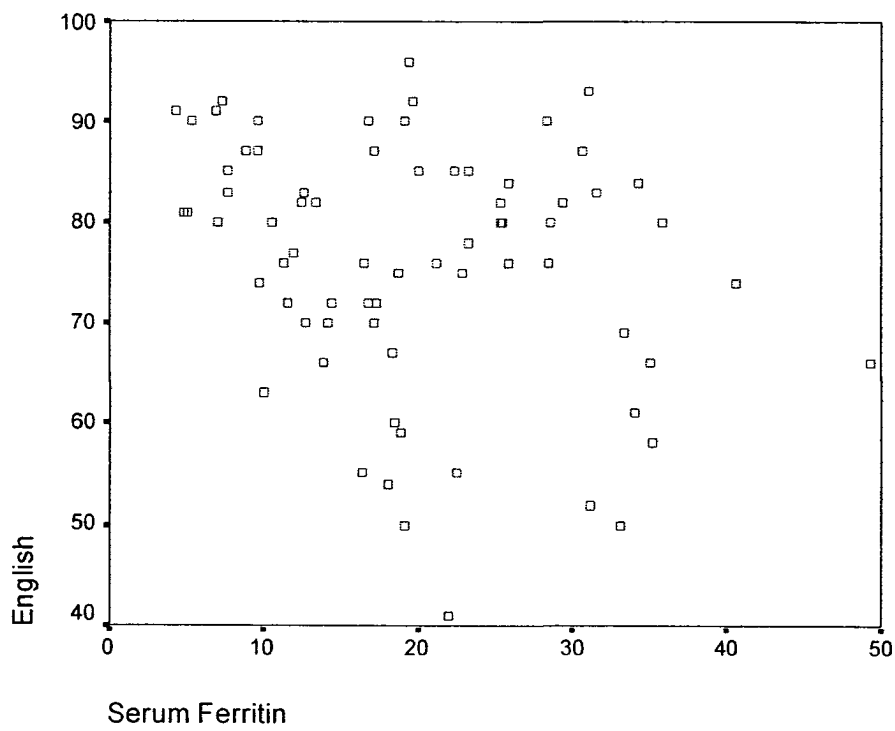
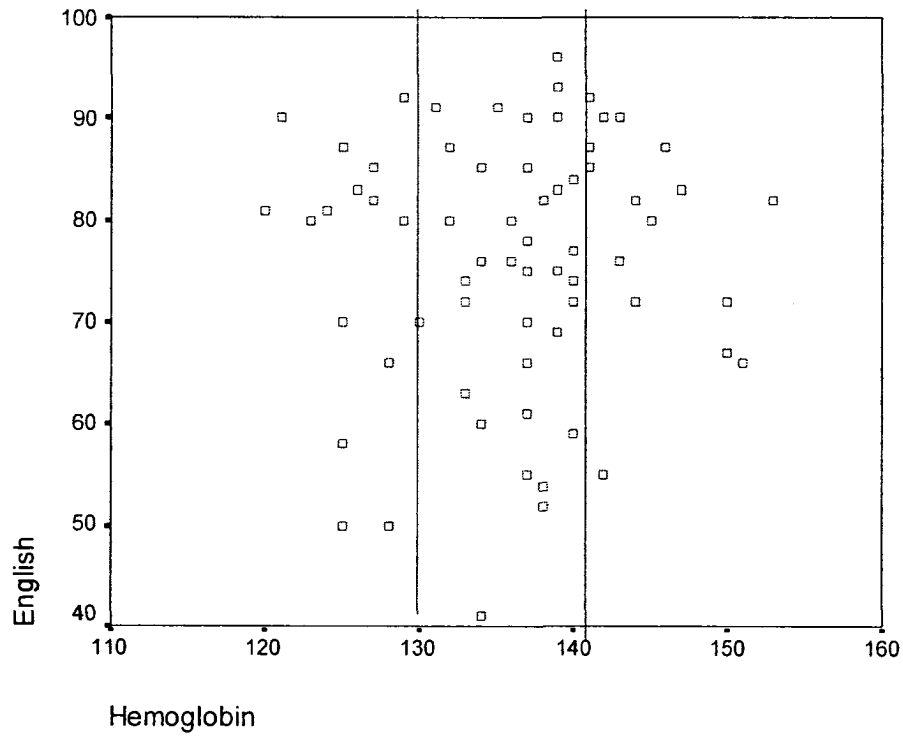


Hemoglobin



Serum Ferritin





Appendix F - Macronutrient/RNI Percentages From 3 Day Dietary Analysis

Participant #	% CHO	% PRO	% FAT	% Sat (of total)	% Unsat (of fat)	% RNI achieved (kcal)	% RNI achieved (iron)
1	59	13	28	10	32	104	76
2	48	13	29	14	42	143	108
3	53	15	32	14	36	137	169
7	49	15	38	15	52	87	120
10	60	13	28	15	38	127	121
11	55	16	29	8	31	131	158
15	56	16	28	10	54	90	149
16	49	16	33	14	52	100	85
17	52	17	31	12	44	137	153
19	66	13	21	11	41	93	164
21	57	11	32	10	51	126	195
24	57	17	27	11	37	97	193
26	52	16	32	13	50	97	151
27	59	13	28	9	59	97	172
28	63	11	27	10	42	150	257
29	50	15	35	12	49	35	35
30	51	12	37	12	55	99	109
32	42	24	37	12	51	60	91
33	63	10	27	8	50	138	197
34	53	13	35	12	52	145	219
35	56	15	29	8	45	137	103
36	63	13	24	11	45	120	162
37	53	13	34	12	53	140	188
41	55	14	31	9	64	64	90
42	50	23	26	14	55	43	55
43	53	12	35	10	48	115	112
45	54	16	30	11	53	33	36
46	53	15	32	12	36	111	112
49	70	9	21	7	55	101	150
51	65	13	23	8	56	81	69
55	56	14	30	11	32	99	98
56	55	17	28	11	50	92	116
59	61	14	26	11	48	112	93
62	70	9	22	6	47	79	92
63	52	16	33	11	57	124	132
64	52	21	27	8	56	60	86
66	65	8	27	8	47	113	72

68	61	12	28	9	53	113	166
69	58	12	31	10	41	109	108
70	52	21	28	9	51	92	126
71	58	11	30	12	53	75	95
N = 41							

Appendix G – Scatter Plot of Iron Status vs. % RNI