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THE EFFECTS OF IRON DEFICIENCY ON COGNITIVE FUNCTION AND NEUROPHYSIOLOGICAL FUNCTION IN EARLY ADOLESCENT FEMALES

by

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The work described in this thesis was carried out by me under the supervision of Prof Kumudu Wijewardenena, Professor of Community Medicine, Faculty of Medical Sciences, University of Sri Jayewardenepura, Nugegoda, Sri Lanka; Professor Gunilla Lindmark, Department of Women's and Children's Health, Section for Women's and Children's' Health, University Hospital, Uppsala, Sweden and Professor Karin Edebol Eeg Olofsson, Department of Clinical Neurophysiology University Hospital, Uppsala, Sweden; and a report of this has not been submitted in whole or in part to any university or any other institution for another degree/diploma.

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29/11/2010

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Dedicated to the memory of

my dear parents

the late Mr. and Mrs. K. D. S. Wimalasekera

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ACD	Anaemia of chronic disease
Amp	Amplitude
BAEP	Auditory brain stem evoked potentials
BMI	Body Mass Index
CI	Confidence Interval
CNS	Central nervous system
Cz	Vertex
dB	Decibel
D Lat	Distal latency
ENG	Electroneurograph
F Lat	F latency
FSIQ	Full scale IQ
Hb	Haemoglobin
LO	Left-Occipital
MCH	Mean Corpuscular Haemoglobin
MCHC	Mean corpuscular haemoglobin concentration
MCV(fl)	Mean Corpuscular Volume
MCV	Motor Conduction Velocity
MO	Mid-Occipital
MP	MidParietal
ms	Milliseconds

mV	millivolt
n	Number
PCV	Packed Cell Volume
PRI	Perceptual Reasoning Index
PSI	Processing Speed Index
RBC	Red cell count
RDW	Red cell Distribution width
RO	Right-Occipital
SCV	Sensory conduction velocity
SF	Serum ferritin
SL	Sensory latency
SI	Serum Iron
TIBC	Total iron binding capacity
TONI	Test Of Nonverbal Intelligence
VCI	Verbal Comprehension Index
VEP	visual evoked potentials
WBC	White blood cell count
WBC/DC	White blood cell differential count
WHO	World Health Organisation
WMI	Working Memory Index

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ABSTRACT

Iron deficiency is the commonest micronutrient deficiency in adolescence. The WHO estimates that more than 53% of adolescents of 11- 15 years of age are iron deficient. Iron deficiency in infancy, has caused delays in psychomotor development and impaired intellectual capabilities in some populations. Adolescent females are at risk of iron deficiency due to the onset of puberty, menarche and menstruation.

The main objective of the study was to determine the iron status and its impact on cognitive and neurophysiological function in Sri Lankan female adolescents. The specific objectives were to assess the iron status among females in early adolescence; to assess cognitive function, visual evoked potentials (VEP), auditory brain stem evoked potentials (BAEP), peripheral sensory and motor nerve conduction in adolescence; to describe the association between iron status and cognitive function, VEP, BAEP, motor and sensory nerve function, in adolescent females and to determine the effect of iron supplementation of anaemic and iron deficient adolescent females on their iron status, cognitive function, VEP, BAEP, motor and sensory nerve function.

A descriptive interventional study was conducted on a study population of 11-14 yr old female adolescents from the Colombo District of Sri Lanka. Five hundred and thirty adolescents (n=530) were selected by stratified random sampling. The study instruments used were questionnaires to determine the socio-economic data, menstrual history and psychosocial adversity index; clinical examination to assess the health status and stage of puberty; venous blood examination to determine the haemoglobin level, iron profile (ie. serum iron, serum ferritin, serum total iron binding capacity and

serum transferrin) and serum albumin. In a subsample of 180 subjects (ie 60 iron deficient anaemic (IDA), 60 iron deficient (ID) and 60 non iron deficient non anaemic (NAN), cognitive function [using Wechsler Intelligence tests (WISC—IV)(Psychological Corporation, UK) and Tests of Non verbal intelligence (TONI–3)] and neurophysiological functions were assessed. The neurophysiological tests, [Visual evoked potentials (VEP), Brainsten auditory evoked potentials (BAEP), motor and sensory function of the lower limbs (MCV, F waves and SCV)] were assessed using standared measurement techniques on a Nihon Kohden Neuropack II, ENG/EMG machine (Nihon Kohden Inc, Japan).

The anaemic and iron deficient adolescents in the subsample were supplemented with iron for three months. The entire subsample was reassessed to determine the iron status, cognitive function and neurophysiological tests after three months of supplementation.

Two hundred and twenty (41.7%) adolescents aged 11- 14 years, were ID and of them 86 (16.3%) were anaemic (IDA). The mean scores of Perceptual Reasoning Index (PRI), mean scores of Working Memory Index (WMI), Verbal Comprehension Index (VCI), Processing Speed Index (PSI), and Full scale IQ (FSIQ) of anaemic adolescents and iron deficient adolescents were statistically significantly decreased when compared with the mean scores of non anaemic adolescents ($p < 0.05$). There was a significant positive correlation between iron parameters and the VCI, PRI, WMI, PSI, and the estimated FSIQ ($p < 0.05$); and the scores of Tests of Non verbal Intelligence (ToNI) ($p < 0.05$). There was poor correlation between the iron parameters (haemoglobin, serum

iron, serum total iron binding capacity, serum transferrin and serum ferritin) and the VEP among these adolescents ($p > 0.05$). There was a significant negative correlation between serum iron and waves I, II, III, IV, and V auditory brain stem evoked potentials (BAEP) of the right ear among the moderate anaemic group ($p < 0.05$). There was no significant difference in the motor and sensory nerve function between the three groups in this study.

There was a significant improvement in the VCI and the PSI in the IDA group after iron supplementation ($p < 0.05$). A significant improvement was observed in the VCI after iron supplementation in the ID group too ($p < 0.05$).

The study reveals that iron status is important for proper cognitive function development among female adolescents. There was a significant reduction in the VEP latencies, and BAEP latencies among the anaemic and iron deficient adolescents in this study. Iron supplementation for three months improved the iron status but did not completely reverse cognitive function test scores to normal. Neither were the VEP and BAEP latencies normalised by three months of iron supplementation although there was an improvement in the latencies with supplementation. The impairments seen in cognitive function and evoked potentials may be due to brain iron depletion having an effect on myelination of the central conducting pathways and maturation of iron and dopamine dependant neurotransmittors in the brain. There is an urgent need to educate parents on proper nutrition of adolescent females, since they will be the future mothers of the world.