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Correlation of Anaemia and Cognitive Functions Measured by the Complex Reactiometer Drenovac

Duška Petranović[1], Vladimir Takšić[2], Renata Dobrila-Dintinjana[3], Ika Rončević-Gržeta[4], Klementina Ružić[4], Sanja Janović[4], Iva Crnarić[1], Antica Duletić-Načinović[1] and Brankica Sinčić-Mijandrušić[3]

[1] Department of Hematology, School of Medicine, University of Rijeka, University Hospital Center, Internal Clinic, Rijeka, Croatia
[2] Faculty of Arts and Sciences, University of Rijeka, Rijeka, Croatia
[3] Department of Gastroenterology, School of Medicine, University of Rijeka, University Hospital Center, Internal Clinic, Rijeka, Croatia
[4] Department of Psychiatry, School of Medicine, University of Rijeka, University Hospital Center, Rijeka, Croatia

A B S T R A C T

Cognitive impairment impinges significantly on the quality of life. Previous research revealed that anaemia can have a major influence on cognitive functioningt. The article is a correlational study examining the relationship between anaemia levels and cognitive functioning in adult patients. Sixty-one patients (both inpatients and outpatients), among them 30 anemic and 31 non- anaemic, 33 female and 28 male, aged 32–60 (median 43) treated at the Dept. of Hematology, Clinical Hospital Center Rijeka, Croatia were analysed according to hemoglobin (Hb) level and cognitive ability. Assessment of cognition (convergent inductive thinking) was performed by the Complex reactiometer Drenovac (CRD). The results showed that anaemia significantly undermines cognitive functions in adult patients ($p<0.01$). Even in non-anaemic patients (Hb higher than 120 g/L), Hb level is related to better cognitive ability.

***Key words**: anaemia, cognition, complex reactiometer Drenovac, hemoglobin*

Introduction

The human species define themselves as the most intelligent creatures. For centures the possibility of influencing the human brain presented a challenge. We could go back to ancient Greece to find studies of cognition and seeking ways to improve it. In the last two decades, many interdisciplinary studies have been carried out to determine what factors influence cognition[1–3].

Given the importance of that research, the 21 st century has been recognized as the »century of the mind«. Cognitive functions in humans and animals can be altered by many diseases, nutritional, metabolic and hormonal changes, ageing, drugs etc.[3–6] Cognitive impairment impinges significantly on the quality of life in patients with cancer[7–14] and in some tumors cognitive decline can predispose an adverse clinical outcome[15,16].

One theory which is partially accepted is that anaemia via cerebral hypoxia and other possible mechanisms has a major influence on cognition[17,18]. Iron deficiency anaemia is the most common form of anaemia. About 20% women, 50% pregnant women, and 3% men are iron deficient[18]. The problem has been widely studied among school children[19,20,] students[21], women[22,23] (who are accepted as »normally anaemic«), the elderly[24,25], and with various illnesses from helminthiasis[26] to cancer[6,7,12–18,27–30]. Cancer related cognitive disfunctions may be caused by anaemia as well as other factors (cancer treatment, medication, infection, metabolic problems, nutritional deficiency and localisation of tumor)[31.] In the last few years, cognitive impairment connected with anaemia has been widely studied as impinging significantly on the quality of life in patients with cancer in whom cognitive disfunctions may be caused not only by anaemia but by other factors too (cancer treatment, medications, infection, metabolic problems, nutritional deficiency and localisation of tumor)[1–4]. In some tumors, cognition or anaemia, independently, were defined as predictors of survival[15].

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Oski and Honig in 1978[36]. suggested that iron deficient infants have behavioural abnormalities. Since then a lot of studies have been carried out in different cultures and countries, in various populations (infants[19–21], adults, pregnant, menstruating or menopausal women, the elderly) and in various illnesses (helminthiasis, Alzheimer disease, cancer etc).

Despite the limitations in study designs and various measurings of cognition, it has been proven that iron deficiency anaemia may cause cognitive impairment. Iron plays an important role in oxygen transport and storage as well as being a co-factor in enzymatic reactions in various biochemical processes, including mitochondrial electron transport, catecholamine metabolism and DNA synthesis so the consequences of iron depletion encompass practically the whole body including neurological functions.

Some studies showed that at a critical period of brain growth IDA in young children may produce irreversible abnormalities (Walter 1989, Lozoff 1987, 1991). Several possible mechanisms link iron deficiency anaemia to altered cognition. Anaemic children tend to move around and explore their environment less than children without anaemia, which may lead to developmental delays. Conduction of auditory and optic nerve impulses to the brain has been found to be slower in children with iron deficiency anaemia. This effect could be associated with changes in nerve , which have been observed in iron deficient animals. synthesis may also be sensitive to iron deficiency. Significant differences in intellectual performance between anaemic and non-anaemic children and adolescents were noticed by Anderson et al. 1994, while in adults clear evidence of an association between anaemia and cognitive function is sparse and non-conclusive (Tucker et al. 1984). Fordy and Benton,1994.[37] examined British university students aged 17–27 years and found no relation between iron status and psychometric test scores.

Anaemia and its functional consequences are extremely interesting because they are easily treatable. Stivelman[1] showed the benefits of anaemia treatment on cognitive functions in patients on dialysis. Treatment for intestinal helminth infection is known to have effects on cognitive performance in children (Dickson[32]). Young women who took iron supplementation for 16 weeks significantly improved their attention span, short-term and long-term memory, and their performance on cognitive tasks, even though many were not considered to be anaemic when the study began, according to researchers at .

The challenge is greater if we know that anaemia, in most cases, is readily treatable. Some trials showed that correction of anaemia improved cognitive abilities but that the level of improvement depended on the duration of anaemia, which emphasises the importance of early detection and treatment[1,18,32].

One of the most complex problems in previous studies was how to measure cognition.

Some of the tests used in clinical practice are not sufficiently sensitive for very fine or minimal functional changes in otherwise healthy persons (i.e. Folstein Minimental state exam)[16] and some of them are too expensive and sophisticated to be used in everyday work (i.e. average signals by Functional Color Magnet Resonance, PET)[33].

We therefore used a system of psychodiagnostic equipment different from the standard set of instruments used in psychological practice and scientific research. A Complex Reactiometer Drenovac (CRD) test item series is a PC based psychodiagnostic laboratory for determination of mental and psychomotor functions. It is based on the chronometric approach to the examination of dynamic properties and functional features of the activity of the central nervous system (CNS). The basic assumption of chronometry in psychology is that the time (duration) needed for a certain psychological activity contains information about the complexity of its structure and indicates the structure and validity of the functioning of neuropsychological mechanisms through which such activity is realized.

Technically, CRD consists of 4 electronic instruments (of the reactiometer sort) with 54 signal control devices and accompanying accessories (pedals, earphones) enabling presentation of the CRD series. CRD measures:

1. Perceptive abilities: detection, identification, visual orientation, spatial visualisation
2. Memory: short-term memory, maze learning, actualisation of memorised contents
3. Thinking: operative thinking, problem solution, convergent thinking
4. Psychomotor reactions (simple and complex)
5. Dynamic features of CNS function: excitability, agility, stability, balance, endurance, reliability
6. Attention: attention span, concentration,vigilance
7. Functional disturbances: rigidity, agitation, perseverance, regression

Up until now, CRD has been used mainly in professional medicine, medical research and occupational health (in areas such as industry, education, traffic, military, police, sport and elsewhere)[5,34,35]. As far as we know, this is the first application of CRD in clinical work with patients in everyday clinical hematological practice. Observations of performance on individual tests from the CRD series make it possible to determine with high sensitivity the dynamic features of the CNS functions and the functional qualities of cognition[5,34,35].

Because some previous research was not conclusive about the effect of anaemia on cognitive functions, we hypothesised that with a very sensitive apparatus like CRD, we could measure an adverse influence of anaemia on cognitive functions. For this purpose, we used CRD 11 test (operative thinking, problem solution, convergent thinking). We presented only this one indicator of cognitive functioning because previous research revealed that this test was correlated mostly with IQ (factor G) with a high impact (saturation 0,831). For clarity and shortness of text, we presented our results as numeric IQ. It is obvi-

ous that only numbers and seconds to perform some task are insufficient to express a person's intelligence, but for our study we found it very illustrative. In this place also we have not presented the results of all other psychodiagnostic tests which patients performed at the same time during 20-30 minute sessions.

Patients and Methods

The study was designed as a correlational study examining the relationship between anaemia levels and cognitive functioning.We examined 61 patients, among them 30 anemic and 31 non-anemic, 33 female and 28 male, aged 32–60 (median 43).

Anaemia was defined according to a Hb level less than 120 g/L in both sexes as it is standard value in the majority of similar studies. Laboratory measurement of Hb level was made in the Hematologic Laboratory of the Clinical Hospital Center Rijeka, using the methodology of computerized performance on the TEHNICON H3 machine produced by Bayer. The method is a modification of manual cyanmethemoglobin methodology developed by the International Committee for Standardisation in Hematology.

Every patient was clinically examined by a Hematologist and evaluated for ethyology of anaemia. Only patients with iron deficiency anaemia (IDA) and no other anaemias were tested.

Other exclusion criteria were: malignant disease (solid and hematologic malignancies), diabetes, acute bleeding, acute infectious diseases, cardiocirculatory disorders, hypertension, neurological diseases including history of stroke or signs of dementia (tested by Folstein Mini Mental State Exam), Karnoffsky performance state less than 80%. Variables such as age, education and gender were independently analysed because of their possible influence on cognition.

Cognition was assessed by the Complex reactiometer Drenovac (CRD). Original psychodiagnostic tests (UNITS CRD1, CRD2, CRD3, CRD4) on IBM PC 486

Data analysis

Correlations between cognition i.e. numeric IQ (NIQ) which was measured by CRD test 11, hemoglobin level (Hb) and other sociodemographic variables were tested. The examined variables were: sex, age, education, hemoglobin level and IQ. We then analysed the significance of Hb as a dependent variable after controlling the effect of gender, age and education, using beta weights, proportion of explained variance, semi-partial correlations.

Multiple regression analysis was used to test dependence of cognition and Hb level.

Distribution of all results of cognitive ability score depending on Hb level is presented in the diagram.

Results

Analysis of correlation among all variables shows that cognitive functions are related to gender, age, education and hemoglobin level (Table 1).

TABLE 1
CORRELATIONS BETWEEN COGNITIVE FUNCTIONS AND SOCIODEMOGRAPHIC VARIABLES N=61

	Hemoglobin level (g/L)	Numeric IQ
Gender	–0.48	0.24
Age	–0.19	0.47
Education	0.06	0.38
Numeric IQ	–0.39	1

r=0.26, p=0.05, r=0.33, p=0.01

When statistically partialized, the effects of gender, age, education and hemoglobin level showed the Hb level as the most effective variable on cognition analysed by beta weights. We could say that anaemia has a 10,5% influence on IQ, tested by CRD (Table 2).

TABLE 2
BETA-PONDERS, PROPORTION OF EXPLAINED VARIANCE, SEMI-PARTIAL CORRELATIONS AND THE SIGNIFICANCE OF HB AS A DEPENDENT VARIABLE AFTER CONTROLLING THE EFFECT OF GENDER, AGE AND EDUCATION

	R	Beta	Beta*r	Semipar	t(60)	p-level
NIQ/Hb	–0.39	–0.27	0.105	–0.23	–2.46	0.017

Figure 1 represents the influence of Hemoglobin level (degree of anaemia) on cognitive functions in all patients. Patients with a higher Hb level had better performance on cognitive test CRD-11, and cognition was impaired as the level of Hb dropped.

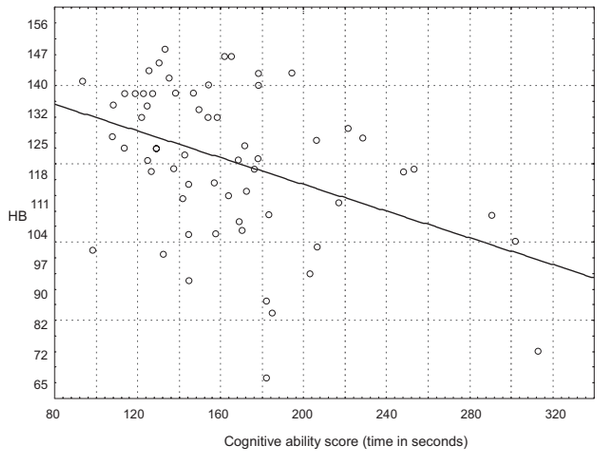

Fig. 1. Influence of hemoglobin (Hb) level on cognitive ability score presented as time in seconds to perform CRD-11 test. Cogntive functions correlated to hemoglobin (HB) level.

Discussion

Cognitive impairment impinges significantly on the quality of life. For centuries the possibility of influencing cognitive functions has been a challenge. Anaemia, which is easily treatable, was connected theoretically with possible cognitive deterioration. As iron plays an important role in oxygen transport and storage as well as being a co-factor in multi-organ enzymatic reactions, it is logical that iron depletion could affect neurological functions. Previous research attempted to examine such correlation between anaemia and cognitive ability. Some previously well structured studies were not conclusive and authors themselves stated that probably the reason for this lay in the lack of tests sufficiently sensitive to detect minimal changes. [15,16] So, seeking new instruments for measuring cognitive abilities has become a pressing problem in modern medicine.[16]

We used CRD, as far as we know, for the first time in medical clinical practice in evaluation of cognitive changes according to hemoglobin level. Previous studies with CRD in industry, military, sports etc. defined CRD as very sensitive in detection of minimal changes in cognitive functions among various groups or after various experimental situations (diving, flying...). We therefore used CRD instead of other assessment tools.

The article is a correlational study examining the relationship between anemia levels and cognitive functioning in 61 adult patients treated at the Clinical Hospital Center Rijeka, Croatia, Hematology Dpt.. The patients were analysed according to hemoglobin level and cognitive ability. Assessment of cognition (convergent inductive thinking) was performed by a Complex reactiometer Drenovac (CRD) test CRD 11 (presented as numeric IQ).

Our results showed a strong correlation between hemoglobin level and cognitive tasks. Our confirmed results were due to very sensitive psychometric testing by CRD. NIQ measured by CRD tests significantly correlated with Hb level. So we concluded that anaemia has a major influence on dynamic properties and functional features of the activity of the central nervous system (CNS).When we tested and eliminated other possible factors which could influence cognition (sex, age, education...) anaemia was shown to be a major factor connected with cognition.

Cognitive ability was strongly related to the Hb level, and, what is surprising, it was registered in all patients (so-called anaemic and non-anaemic persons). It means that the cut off point for Hb level which defines somebody anaemic is arbitrary and artificially made. A higher Hb means better CNS function.

The challenge in the future is to research the possibility of improving cognitive functions by correction of anaemia, which were approved in a few previous trials in children, in patients on hemodyalysis and in patients with cancer.

Conclusion

We tested the correlation between anaemia (Hb level) and cognitive functions (NIQ) using CRD for the first time in clinical medical practice (on Hematology Dpt.). CRD was shown to be a very sensitive computerized psychometric testing, applicable in everyday clinical practice, simple to use for the researcher and with good patient compliance. Using CRD, we detected significant differences in cognitive functions in correlation with anaemia. Anaemia was the most important factor (more than sex, age or education) influencing cognition.

As a matter of fact, we observed a strong correlation of Hb level and NIQ in all patients (regardless of whether they matched or not the criteria for anaemia – Hb level 120 g/L)). It is our opinion that the cut off point for Hb level, which defines somebody anaemic or non-anaemic is arbitrary and artificially made and that a higher Hb means better CNS function.

These findings are basic for our future research as part of a systemic program on a larger group of patients with repeated tests during correction of anaemia. We hope to prove that correction of anaemia could enhance cognitive functioning.

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D. Petranović

Department of Hematology, University Hospital Center, Hreljin 231, 51226 Hreljin, Croatia
e-mail: petranovic@vip.hr

KORELACIJA ANEMIJE I KOGNITIVNIH FUNKCIJA MJERENIH KOMPLEKSNIM REAKCIOMETROM DRENOVAC

S A Ž E T A K

Kognicija je vrlo važan segment kvalitete života. Prethodna istraživanja pokazala su da anemija utječe na kognitivne funkcije. Rad je korelacijska studija koja ispituje odnos stupnja anemije i kognitivnih sposobnosti ovisno o nivou hemoglobina (Hb). U istraživanje je uključeno 61 bolničkih i vanbolničkih bolesnika obrađenih na Hematološkom odjelu, u Kliničkom bolničkom centru Rijeka, Hrvatska. Za procjenu kognicije (konvergentno induktivno mišljenje) korišten je Kompleksni reakciometar Drenovac (CRD). Rezultati pokazuju da anemija značajno smanjuje kognitivne funkcije odraslih ($p<0,01$). Čak i u osoba koje nisu anemične (vrijednost Hb preko 120 g/L), viši nivo Hb korelira s boljim kognitivnim postignućem.