2. BRAIN-DERIVED NEUROTROPHIC FACTOR (BDNF) SERUM AND INTELLIGENCE LEVELS OF ELEMENTARY SCHOOL CHILDREN IN RURAL AREAS, SELUMA REGENCY

by Rostika Flora

BRAIN-DERIVED NEUROTROPHIC FACTOR (BDNF) SERUM AND INTELLIGENCE LEVELS OF ELEMENTARY SCHOOL CHILDREN IN RURAL AREAS, SELUMA REGENCY

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ABSTRACT

Children living in rural areas are prone to nutritional deficiencies. Low-income levels impact people's purchasing power so that the intake of most nutrients comes from plant-based foods and consumes less animal food. Nutritional intake greatly affects the development of children's cognitive function. Brain-derived neurotrophic factor (BDNF) is a group of neurotrophins that contribute greatly to the learning process and memory. This study aims to analyze the relationship between levels of BDNF with the level of intelligence in elementary school children in rural areas of Seluma Regency. This was a cross-sectional study involving 70 elementary school children aged 9-12 years were taken by multi-stage random sampling, who came from 5 districts of Seluma Regency. Blood was collected for measurement of BDNF levels, and stool samples were examined to detect intestinal parasites. The data on respondent characteristics were derived from questionnaires. Data analysis were done by using the chi-square test. The results of BDNF measurements found 31 children (44.3%) had BDNF levels below the average (<3342.95ng / mL). The results of measuring intelligence level found that 54 children (77.1%) had a level of intelligence below the average. Chi-Square test results obtained p = 0.012 with a PR value of 7.538. There was a significant association between the BDNF level and intelligence level in elementary school students in the rural area. Elementary school children in rural areas with BDNF levels below the average risk of 7.538 times have below-average intelligence levels.

Keywords: Brain-derived neurotrophic factor, elementary school children, intelligence, rural areas

ABSTRAK

anak-anak yang tinggal di daerah pedesaan rentan mengalami kekurangan zat gizi. Tingkat pendapatan yang rendah mempengaruhi daya beli masyarakat, sehingga asupan zat gizi sebagian besar berasal dari sumber nabati dan lebih sedikit mengkonsumsi sumber hewani. Asupan gizi sangat mempengaruhi perkembangan fungsi kognitif anak. *Brain-derived neurotrophic factor* (BDNF) adalah sekelompok neurotrofin yang berkontribusi besar pada proses pembelajaran dan memori. Penelitian ini bertujuan untuk menganalisis hubungan antara kadar BDNF dengan tingkat kecerdasan pada anak sekolah dasar di daerah pedesaan, Kabupaten Seluma. penelitian ini merupakan penelitian potong lintang dengan melibatkan 70 anak sekolah dasar usia 9-12 tahun yang berasal dari 5 kecamatan di Kabupaten Seluma. Dilakukan pengambilan darah untuk pengukuran kadar BDNF, dan pengambilan sampel feses untuk mendeteksi infeksi kecacingan. Data karakteristik responden diperoleh dari kuesioner. Semua data kemudian dianalisis menggunakan uji *Chi-square*. hasil pengukuran kadar BDNF didapatkan bahwa, 31 anak (44,3%) memiliki kadar BDNF di bawah rata-rata (<3342,95ng / mL). Hasil pengukuran tingkat kecerdasan didapatkan bahwa, 54 anak (77,1%) memiliki tingkat kecerdasan dibawah rata-rata. Hasil uji *chi-square* diperoleh p = 0,012 dengan nilai PR=7,538. terdapat hubungan yang signifikan antara kadar BDNF dan tingkat kecerdasan pada anak sekolah dasar di daerah pedesaan. Anak sekolah dasar di daerah pedesaan dengan kadar BDNF di bawah rata-rata berisiko 7,538 kali memiliki tingkat kecerdasan di bawah rata-rata.

Kata Kunci: Brain-derived neurotrophic factor, anak sekolah dasar, kecerdasan, daerah pedesaan

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Introduction

Brain-derived neurotrophic factor (BDNF) is is a neurotrophine involved in synapsis development, synapsis plasticity and cognitive function.[1,2,3,4,5] BDNF is closely related to cognitive functions, including memory formation, learning process, and behavior.[6] Study by Yeom et al. (2016) and Rita et al (2015) found that BDNF level in children with good nutrition status is higher than those who has lower nutrition status (1.047 ± 1.735 ng/ml vs 0.458 ± 1.055 ng/m), there was a significant relationship between BDNF levels and intelligence levels in elementary school children aged 5–7.[7,8]

Children living in rural areas are prone to nutritional deficiencies. Low-income levels impact people's purchasing power so that the intake of most nutrients comes from plant-based foods and consumes less animal food. Nutritional intake greatly affects the development of children's cognitive function. Children with good nutritional status allow optimal cognitive development and vice versa. Children with insufficient nutritional intake will interfere with brain development, cause cognitive development to be inhibited, and ultimately lead to poor learning achievement.[9]

Seluma Regency is one of rural area and also one of the underdeveloped regencies in Bengkulu Province. Unhygienic environments, chronic poverty, and poor access to health services are underlying causes why children in Seluma Regency are vulnerable to worm infection and malnutrition.[10] Intelligence levels may be influenced by many factors such as genes, nutrition, and environment.[11] There is a significant correlation between nutritional status and cognitive functions; poor nutritional quality is correlated with low IQ levels.[12,13] This study analyzes the association between BDNF levels and intelligence levels of elementary school children in rural areas, Seluma Regency.

Methods

This study was cross-sectional design conducted in April 2019. The subject of this study was 70 elementary school children aged 9-12 years old. The subject's inclusion criteria were as follows: not transfer citizens from other sub-districts selected for this study, not infected with chronic diseases, and not having a period during the study.

The subject was collected using a multi-stage random sampling technique. The sampling process was started by determining the sub-districts of the Seluma Regency with the highest malarial incidences. From the total 14 sub-districts, 5 sub-districts were selected, i.e., Lubuk Sandi, Seluma Barat, Seluma Timur, Seluma Utara, and Talo Sub-Districts. From each of these sub-districts, 14 students were selected. The total of study subjects was 70. Blood sampling was carried out to examine BDNF levels, and stool samples were analyzed to detect intestinal parasites. Besides that, nutritional

status and intelligence levels (IQ) were also measured. Research Ethics Committee has approved this study of Public Health Faculty, Universitas Sriwijaya based on approval decree number 78/UN9.1.10/KKE/2019.

Measurement of BDNF Levels

To measure the level of the BDNF, two milliliters of venous blood were collected from study subjects. The blood was centrifuged at the speed of 3000 rpm for 15 minutes. The plasma portion from the centrifugation was removed and stored at 18°C. BDNF levels were determined using the enzyme-linked immunosorbent assay (ELISA) method with Human BDNF ELISA Kit (Cat. No. E-EL H0010, Elabsience; with specification: sensitivity: 18.75 pg/mL, detection range: 31.25-2000 pg/mL, specificity: This kit recognizes Human BDNF in samples, repeatability: coefficient of variation is < 10%.). The levels of BDNF were calculated to find out the cut-off point based on the average level. Finally, the BDNF levels obtained from this calculation were grouped into two categories, i.e., high average and low average.

Measurement of Intelligence Levels

The measurement of intelligence levels used culture fair intelligence test (CFIT) scale 2 for children aged 8-14. This research instrument consisted of two forms, and each of which contained 4 sub-tests. Time allocated for subtest 1: series is three minutes; subtest 2: classifications are four minutes; subtest 3: matrices is three minutes; and subtest 4: conditions is 2.5 minutes. The IQ scores obtained from the scale were classified as follows: genius (scores >170); very superior (140–169); superior (120–39); high average (110–119); average (90–109); low average (80–89); borderline (70–79); and mentally defective (< 70).

Measurement of Nutritional Status

Nutritional status was assessed based on indices of height and age (H/A). The body height was measured using *microtoice* hung on a vertical wall 2 meters away from the horizontal floor with no carpet. The respondents stood upright on a wall with both soles attached to the floor and wore no footwear, cap, or hair accessories. The assessments of nutritional status were classified into short (Z-score -3 SD - < -2 SD) and normal (Z-score -2 SD – 2 SD).

Determination of Intestinal Parasites

Direct microscopy of stool samples using *eosin 2%* was performed to determine intestinal helminths.

Statistic

The data analysis were done using the Chi-square test in SPSS version 19.0, to examine the association between serum BDNF levels and intelligence levels.

Results

Demographic characteristics

The demographic data characteristics found in subjects based on sex and age found that most children (55.7%) were female and aged 9–10 years old (65.7%). The measurements of nutritional status found that 30% of children were stunted. From the clinical history of helminthiasis, 30% had ever had the infection, and microscopic examination found 31.4% of the respondents were positive with helminthiasis (Figure 1). On the other hand, the demographic characteristics of parents based on education and occupation showed that most fathers graduated from senior high school (32.9%) and worked as farmers/labors (64.3%). Most mothers graduated from junior high school (32.9%) and worked as a housewife (61.4%) (Figure 2).
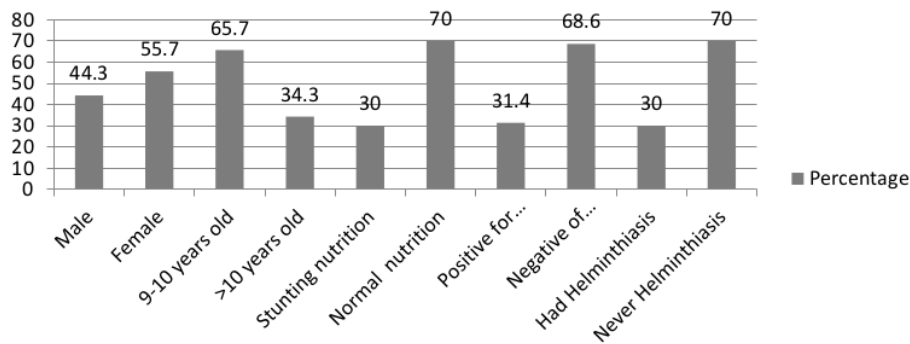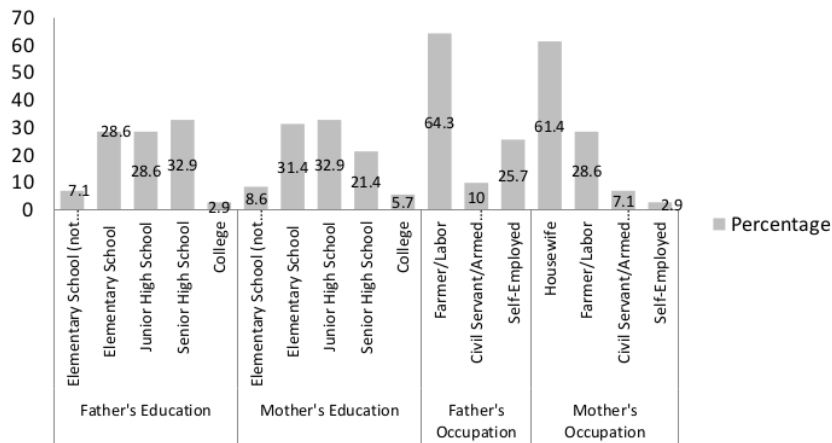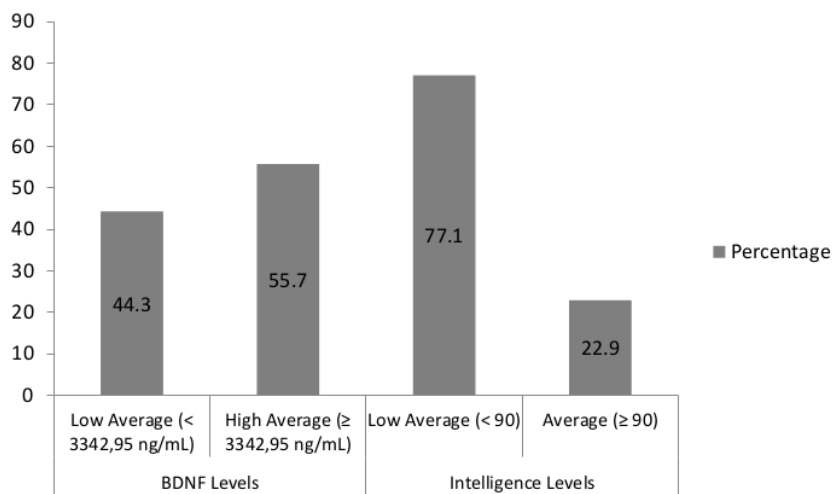

Figure 1. Frequency distribution of respondent based on sex, age, nutritional status and helminthiasis (n= 70)

Figure 2. Frequency distribution of respondent based on parental education and occupation
(n = 70)

From the measurement of serum BDNF levels as seen in Figure 3, it was found that 55.7% of children had high-average BDNF levels (> 3342.95 ng/mL). From the measurement of intelligence levels (Figure 3), it was found that 77.1% of the children had intelligence levels in a low-average category.

Figure 3. Frequency distribution of respondent based on average levels of BDNF serum and
intelligence levels (n = 70)

The chi-square test results (Table 1) indicated that children with low-average serum BDNF levels had the risk of 7.538 times to have low-average intelligence levels compared with those with high-average serum BDNF levels.

Table 1. Association Between BDNF Levels And Intelligence Levels

Variable	Intelligence levels		PR (CI)	p
	Low : n (%)	Average : n (%)		
BDNF				
Low	29 (41.4)	2 (2.9)	7.538 (1.561–36.410)	0.012
High	25 (35.7)	14 (20)		

Discussion

The serum BDNF levels measurement showed that 55.7% of the children had high-average BDNF levels (> 3342.95 ng/mL). However, the measurement of intelligence levels found that 77.1% of the children had intelligence levels in the low-average category. This emphasized that children's intelligence levels were influenced by BDNF levels and the mother's education and parenting style.

According to research data characteristics, most mothers in this present study had lower education (72.9%) and worked as housewives (61.4%). Nurmaliza's study in 2018 indicated an association between a mother's education level and knowledge and nutritional status.[14] Mother's knowledge levels on nutrition highly influenced their parenting style. The higher the knowledge they have, the better the food they give to their children.[15] Mothers with sufficient knowledge levels have children with good nutritional status as well.[16] So, it can be stated that the level of a mother's knowledge affects the intelligence levels of their children.

The results of this present study also showed that there was an association between serum BDNF levels and intelligence levels (p = 0.012). Children with low-average BDNF levels had a higher risk of having low-average intelligence levels than those with high-average BDNF levels. This evidence showed that the decrease of BDNF levels was correlated with the reduction of cognitive functions.

Intelligence level is a part of cognitive functions. Cognitive functions are highly influenced by histological structure maturation and the functional performance of neurons in the brain. Quality development of the neuron system in childhood will affect the adult phase's quality of cognitive functions.[17]

Neuron development occurs through neurogenesis, a process of generating functional neurons from precursors.[18] Neurogenesis process highly depends on neurotrophin, a protein group that enforces the growth, development, plasticity, and endurance of neurons. One of the neurotrophins is

BDNF.[3] BDNF is a common growth factor in the central nerve system (CNS), which is essential for the development of CNS and neuronal plasticity.[19]

BDNF plays a key role in memory and learning processes.[1-5] Therefore, BDNF is closely related to cognitive functions such as memory formation, learning process, and behavior.[6] Thus, activity-dependent BDNF expression in the hippocampus and prefrontal cortex (PFC) may contribute to cognitive and behavioral flexibility.[21] Microglia promotes learning-related synapse formation through BDNF signaling to serve important physiological functions in learning and memory.[22]

This study's results were in line with those of Yoem et al. (2016), who stated that serum BDNF level in children aged 6-7 years is higher than in children aged 5-6 years. The serum BDNF level was negatively correlated with the Full-Scale IQ ($r = -0.39$, $p = 0.04$) and Verbal IQ ($r = -0.50$, $p = 0.01$), but not with the Performance IQ ($r = -0.12$, $p = 0.56$) [7]. Another similar study by Rita et al. found that children's motoric development is better on those with average BDNF levels of 1.083 ± 1.722 ng/mL compared with those with BDNF levels of $0.031 \pm 0,105$ ng/mL. The increase of cognitive functions is correlated with the increase of motor skills and BDNF as a mediator learning motorik related to plasticity. [8]

Conclusion

In conclusion, There was a significant association between the BDNF level and intelligence level in elementary school students in the rural area. Elementary school children living in rural areas with low-average BDNF levels had a risk of 7.538 times to have low-average intelligence levels.

Acknowledgment

Funding

Conflicts of Interest

There is no conflicts of interest in this study.

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