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The Correlation between Brain Derived Neurotrophic Factor (BDNF) Level and Motor Development of Children Aged Under 2 Years in Timor Tengah Selatan Nusa Tenggara Timur

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Abstract

BDNF is neurotrophin which widely distributed in the CNS that regulate axonal and dendritic growth, synaptic structure and plasticity, neurotransmitter release and long-term potentiation (LTP) related to the learning process. Motor development depends on the formation of the specific connections between corticospinal axonal and motor circuits in the contralateral of spinal cord. The aim of this study was to analyze the correlation between the level of BDNF and motor development of children aged under 2 years. This was a cross-sectional study in regency of Timor Tengah Selatan province of Nusa Tenggara Timur. Participants were 75 children aged 6 – 20 months who met the inclusion and exclusion criteria. On subjects performed BDNF levels test and measurement of motor development using a questionnaire for DDST (Denver Developmental Screening Test). Statistical analysis was performed using t-independent test. Results shown that by using t-independent test, there was a significant correlation between BDNF levels and motor development. Motor development obtained significantly better at BDNF levels 1,083±1,722 ng/ml in the category of normal motor development compared to BDNF levels 0,031±0,105 ng/ml in the category of caution motor development.

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In conclusions, there was a significant correlation between BDNF levels and motor development of children aged under 2 years.

***Keywords*:** BDNF; motor development.

1. Introduction

BDNF is a neurotrophin which involved in the mechanism of long-term synaptic plasticity, neurogenesis, motoneuron survival and neuron cell migration [1]. BDNF plays an important role in the initial growth of nerve tissue in the human brain. These proteins regulate axonal and dendritic growth, synaptic structure and plasticity, neurotransmitter release, and long-term potentiation (LTP) related to the learning process [2]. BDNF protein widely distributed in the CNS, with the highest levels found in the cerebral cortex, the basal part of the forebrain, striatum, hippocampus, hypothalamus, brain stem and cerebellum [3]. A study using olivocerebellar as an axonal injury model to investigate the effect of BDNF-induced by collateral reinnervation on cognitive function and motor complex concluded that BDNF can trigger reinnervation of transcommissural Cognitive Function in juvenile animals and is associated with improved cognitive function related to the function of motor skills, spatial learning and memory [4].

One important aspect in the growth and development of infants and children is motor development since the beginning of their social and emotional intelligence. Motor development reflects the increasing of the brain maturation that regulates the development of the nervous system and muscles (neuro-muscular) which allows the children more agile and active. Motor skills arises when the brain, nervous system and muscles work together to produce movement. Although no doubt that the incidence of motor behavior reflects the maturity of cognitive function, sensory and motor systems. Along with the maturity of the corticospinal system, adaptive motor behavior began to be expressed [5]. Motor control development depends on the formation of specific connections between corticospinal axons and motor circuits in the contralateral of spinal cord [6]. The objective of this study was to determine the correlation between the levels of BDNF and motor development of children aged under 2 years in the regency of Timor Tengah Selatan province. of Nusa Tenggara Timur.

2. Materials and Method

This was a cross-sectional study involve the 75 children aged under 2 years in the regency of Timor Tengah Selatan province of Nusa Tenggara Timur. Inclusion criteria were infants and children aged 6-20 months, and no objection was included in the study by signing the informed consent. Exclusion criteria were infants and children aged 6-20 months who have severe disease when the study was ongoing, children who have neurological and congenital disorders, and malnutrition. The level of serum BDNF was performed by using the Human BDNF by ELISA method, brand Komabiotech. Blood samples were taken from vein performed by a laboratory analyst from Airlangga University. Measurement of motor development of infants and children was performed by using a questionnaire for DDST (Denver Developmental Screening Test). Statistical was analysis using independent t-test. Data were analyzed using SPSS version 16.0. This study was approved by the Ethics Committee of Biomedical Research on Human, the Faculty of Medicine, University of Hasanuddin, Makassar.

3. Results

3.1 Demographic Characteristics

Overall subjects amounted 75 children aged under 2 years consisted of 44 (58.7%) boys and 31 (41.3%) girls. Children distribution according to the age groups are divided into the age of 6-8 months were 23 (30.7%) children, 9-11 months were 19 (25.3%) children, 12-17 months were 23 (30.7%) children, and 18-20 months were 10 (13.3%) children. Malnutrition status obtained 15 (20%) children, good nutritional status 60 (80%) children. Normal category of motor development obtained 64 (85.3%) children, and caution category 11 (14.7%) children (Table 1).

Table 1: Distribution of children aged under 2 years according to gender, age group, nutritional status and motor development

Demographic Characteristics	Number	
	n = 75	%
Sex		
Boys	44	58.7
Girls	31	41.3
Age groups		
6 – 8 month	23	30.7
9 – 11 month	19	25.3
12 – 17 month	23	30.7
18 – 20 month	10	13.3
Nutritional Status		
Poor nutrition	0	0
Under nutrition	15	20
Good nutrition	60	80
Over nutrition	0	0
Motor Development		
More	0	0
Normal	64	85.3
Caution	11	14.7

In Table 2 shows that father's occupation as a farmer is dominant, that is 54 (72%) subjects and mother's occupation as a housewife were 59 (78.7%) subjects. Majority the education of fathers and mothers are primary school level, 28 (37.3%) subjects, and 34 (45.3%) subjects, respectively. House ownership status was dominated by their own, that is 65 (86.7%) and most of the house constructions were made of the wood, that is 41 (54.7%). Location of defecation majority in the closed toilet were 39 (52%) followed by opened toilet were 29 (38.7%).

Table 2: Demographic characteristics according to household data

Characteristics	Total	
	n	%
Parent Characteristics		
Father's Occupation		
Farmer	54	72
Seller	1	1.3
Labour	5	6.7
Private	2	2.7
Fisher	1	1.3
Driver	5	6.7
Others	7	9.3
Mother's Occupation		
Farmer	8	10.7
Private	1	1.3
Household	59	78.7
Others	7	9.3
Father's education		
Not school	10	13.3
Primary school	28	37.3
Junior high school	17	22.7
Senior high school	17	22.7
University	3	4
Mother's education		
Not school	9	12
Primary school	34	45.3
Junior high school	14	18.7
Senior high school	15	20
University	3	4
Household characteristics		
House ownerships status		
Private ownerships	65	86.7
Rental	1	1.3
Family ownerships	9	12
House construction		
Permanent	13	17.3

Semi permanent	20	26.7
Wooden house	41	54.7
Others	1	1.3
Toilets Type		
Closed toilet	39	52
Opened toilet	29	38.7
Others	7	9.3

3.2 Sample characteristics

3.2.1 BDNF (Brain derived neurotrophic factor)

Table 3 shows the concentration average of BDNF in boys were (0.658 ± 1.197) ng / ml lower than girls (1.313 ± 2.064) ng / ml. *p* values = 0.087 ($p > 0.05$), there is no difference in BDNF levels between boys and girls. The highest average of BDNF levels obtained in the age group 12-17 months (1.052 ± 1.749) ng / ml and the lowest were in the age group 6-8 months (0.774 ± 1.535) ng / ml, *p* value = 0.945 ($p > 0.05$), there is no difference between the levels of BDNF in the age groups of children aged under 2 years.

Table 3: The mean concentration of BDNF by sex and age group

Sample characteristics	**Number**	**BDNF (ng/ml)**	***p***
	n = 75 (%)	**MEAN ± SD**	
Sex			
Boys	44 (58.7)	0.658 ± 1.197	0.087
Girls	31 (41.3)	1.3130 ± 2.06420	
Age groups			
6 – 8 Month	23 (30.7)	0.774 ± 1.535	0.945
9 – 11 Month	19 (25.3)	0.907 ± 1.595	
12 – 17 Month	23 (30.7)	1.052 ± 1.749	
18 – 23 Month	10 (13.3)	1.041 ± 1.867	

3.2.2 Motor development

Motor development was measured using the DDST significantly better at 1.083 ± 1.722 ng / ml of the BDNF levels in the normal category of motor development compared to 0.031 ± 0.105 ng / ml of the BDNF levels in the caution category of motor development with *p* value = 0.04 ($p < 0,05$) (Table 4).

Table 4: The correlation between mean of the BDNF concentration and motor development of children aged under 2 years

Motor Development (DDST)	Number n = 75(%)	BDNF (ng/ml) MEAN ± SD	*P*
Advanced	0	0	
Normal	64 (85.3)	1.083 ± 1.722	0.04
Caution	11 (14.7)	0.031 ± 0.105	

3.2.3 Nutritional Status

Nutritional status measured by the z-score has shown that in good nutritional status has the higher BDNF levels (1.047 ± 1.735) ng / ml compared to the BDNF levels of undernutrition status 0.458 ± 1.055 ng / ml, *p* value = 0.079 ($p > 0.05$), there is no significant association between nutritional status and BDNF levels (Table 5).

Table 5: The correlation between mean of BDNF concentration and nutritional status

Nutritional Status	Number n = 75(%)	BDNF (ng/ml) MEAN ± SD	*p*
Under nutrition	15 (20)	0.458 ± 1.055	
Good nutrition	60 (80)	1.047 ± 1.735	0.079
Over nutrition	0	0	

3.2.4 Nutritional Status and Motor Development

Of 15 children aged under 2 years with under nutrition status, obtained 12 (16%) children have normal category of motor development and 3 (4%) children in the category of caution. Of 60 children with good nutritional status, obtained 52 (69.3%) have normal category of motor development and 8 (10.7%) children in the category of caution. According to the statistical analyze results there is no significant association between nutritional status and motor development $p = 0.514$ ($p > 0.05$) (Table 6).

4. Discussion

The study involved 75 children aged under 2 years as subjects, consisting of 44 (58.7%) boys and 31 (41.3%) girls. The largest age group was found in the age group of 6-8 months and 12-17 months, respectively of 23

(30.7%) children (Table 1). There were no specific criteria for gender and age group in the recruitment process. In this study, good nutritional status was found in 60 (80%) children and undernutrition in 15 (20%) children (Table 1). The results have shown a high prevalence of the undernutrition status. Data from UNHCR 2011 showed the issue of nutrition in infants is still a public health problem if the prevalence of underweight (wasting)> 5%, stunting > 20%, and undernutrition (underweight) > 15% [7].

Table 6: The correlation between nutritional status and motor development

Nutritional Status	Motor development			n = 75 (%)	*p*
	Advanced n (%)	Normal n (%)	Caution n (%)		
Under nutrition	0	12 (16)	3 (4)	15(20)	
Good nutrition	0	52 (69.3)	8 (10.7)	60 (80)	0.514
Over nutrition	0	0	0	0	

A population survey showed that undernutrition in children aged under five years is still a public health problem in NTT province with a prevalence of 20.4% and is one of the highest in Indonesia [8]. Data from Riskesda 2013 showed the proportion of children aged under five years with undernutrition in NTT province amounted to 34.6%. Overall, in Indonesia, the prevalence of underweight were 12.1%, stunting 37.2%, and undernutrition 19.6% [9]. The prevalence of underweight, stunting and undernutrition in the world commonly become a public health problem because of its prevalence is still 8%, 20%, and 16%, respectively [10] Regional district of Timor Tengah Selatan in the province of NTT, which has limited natural resources, high levels of poverty and difficult living circumstances will be the foundation of serious malnutrition among the population. Many factors affect the nutritional status of children, among them nutritional intake. Nutritional intake itself is determined by food security in the household, baby and children's dietary habit and the availability of health facilities in community [11].

Motor development in this study is dominated by normal criteria of 64 (85.3%) children followed by caution criteria of 11 (14.7%) children (Table 1). Differences in the proportion of motor development can be affected by factors of which the nutritional intake of children; maternal nutrition during pregnancy; genetic; maturity; birth trauma; and stimulation, and the opportunity to move all parts of the body. According to UNICEF (1993), the factors that influence the development of motor is a potential of resource, economic structures, political and ideological; the food insecurity of family, nurture for mother and child, and the utilization of environmental sanitation; and the adequacy of the food and health conditions [12].

In this study, statistical analyze significantly showed that a mean value of BDNF concentrations were higher in normal criteria of motor development (1.083 ± 1.722) ng / ml compared to caution criteria of motor development (0.031 ± 0.105) ng / ml with *p* value = 0.04 ($p < 0.05$). These results are not much different from a

study which concluded that BDNF can trigger transcommissural reinnervation Cognitive Function in juvenile animals and is associated with increased of cognitive function related to the function of motor skills, spatial learning and memory [4]. Another study found that BDNF levels significantly higher in infants who received breast milk and positively associated with the outcome of BSID-II (Bayley scales of infant development-second edition). Increased the levels of serum BDNF is associated with the increased of cognitive function [13]. Cognitive function improvement is associated with motor skills enhancement where BDNF is involved in mediating the motor learning-related plasticity.

The study also explored the relationship of BDNF levels and children aged under 2 years nutritional status; then observed the relationship of nutritional status and motor development. This study has shown that the average value of BDNF concentration were higher in good nutritional status (1.047 ± 1.735) ng / ml compared to under nutritional status (0.458 ± 1.055) ng / ml. Although the average value of the BDNF concentration was found higher in good nutritional status, but the statistical analyze results was not significant. Wang L, et al. 2007 conducted a study on the effects of perinatal protein malnutrition on the BDNF concentration in the brain of young mice models. They found that the perinatal protein malnutrition condition showed an adverse effect on the concentration of BDNF in mice. A decrease in BDNF concentration in the hippocampus area may partly lead to poor learning and memory performance in mice with protein deficiency [14]. Disruption to learning and memory performance can contribute to disturbances in the achievement of motor development milestones.

This study results, mostly children with good nutritional status have normal category of motor development, that is 52 (69.3%) children compared to under nutritional status, which amounted to 12 (16%) children. This suggests that the good nutritional status and under nutrition status have a different motor development. Whereas good nutritional status has a better motor development compared to under nutritional status, but statistically, there was no significant difference ($p > 0.05$). This results appropriate to the study showed that the children of a certain age, with a higher nutritional status can reach a certain stage of development compared to children with lower nutritional status [15]. Other researchers found that malnutrition negatively correlated with gross motor development in children aged 6-18 months [16]. This suggests the importance of an integrated approach to helping malnourished children, including monitoring the motor development. Another study investigated children aged 36-54 months and found that children with protein energy malnutrition have a lower cognitive function and motor ability compared to normal children [17]. The difference in the nutritional status of children has a different effect on each motor development. Malnourished children will provide an impact on limitation of growth and development, prone to infection and subsequently inhibit the development of motor compared to the children with good nutritional status.

5. Conclusion

In this study there is a significant correlation between the levels of BDNF and motor development of children aged under 2 years. There were no significant correlation between the levels of BDNF and nutritional status of children aged under 2 years. There is also no significant association between nutritional status and motor development of children aged under 2 years.

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