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Huffaz Have Higher BDNF Level and Better Memory Ability Than Administrative Workers in Same Age and Education

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Keywords *Huffaz, environmental enrichment, BDNF, cognitive, memory*

Abstract Cognitive function can be improved by environmental enrichment. Memorizing is a kind of environmental enrichment to build neuron structures. Huffaz is a person who serves his life to memorize and knows the Quran by heart in his daily activity.This study was aimed to investigate whether there is a difference in BDNF and cognitive abilities between group of huffaz and non-Huffaz. A cross sectional study with quota sampling was conducted to identify the serum BDNF level and cognitive abilities among adult Huffaz. A purposive sampling of 25 huffaz in Palembang was compare to 25 non-huffaz who has been consecutively selected among administrative workers, matched by age, sex, and education. Huffaz had higher level of BDNF level compare to administrative workers (301.9 ±50.6 µg/ml vs 236.3±69.9 µg/ml;$p<0.01$). Huffaz also had significant better memory ability ($p<0.05$). There were no differences of analogy, analytical reasoning, logical reasoning, and executive functions between Huffaz and administrative workers. In conclusion, Memorizing task of holly Quran could increase neurotrophic factors and improved memory ability as a basic component of cognitive function compare to daily administrative activities. However, this task had no better effects to improve cognitive functions that are influenced by complex learning process and multi-tasks experience.

1. INTRODUCTION

Cognitive process is a higher mental process in a form of perception, memory, language, problem solving and abstract thinking which really determines one's intellectual ability (Association/APA, 2013). Cognitive process highly depends on the maturation of histological structure and functional work of neuron cells in brain, which can be increased through environmental stimulation.(Kandel, 2001; McMorris, Tomporowski and Audiffren, 2009)Environmental stimulation in a form of experiential exposure and learning will trigger neuroplasticity. Neuroplasticity itself is a restructurisation process of neurons in a form of protein synthesis that leads to new sinaps connectivity.(Kandel, 2001; van Praag, 2009). Neuroplasticity plays a pivotal role in the development of neuron's structure and nervous system recovery. (Lou *et al.*, 2008)

The development of neuron's structure through a precussor in neuroplasticity depends on a group of protein that triggers the growth of neurons (neurotrophyn)(Ming and Song, 2011). There are four types of proteins that are classified into neurotrophyn. They are *Brain-Derived Neurotrophic Factor* (BDNF), *Nerve Growth Factor* (NGF), *neurotrophin-3* (NT-3) and*neurotrophin-4/5* (NT-4/5). Although each neutrophyn has its own spesific role in neuron cells, BDNF is the most active neutrophyn of all with the biggest role in neuroplasticity (Binder and Scharfman, 2004).

In humans, BDNF is mostly expressed in hippocampus, hipothalamus and cerebral cortex (Maisonpierre *et al.*, 1991). BDNF triggers neuronal differentiation, neuronal growth, and new sinaps development, thus leading to the increment of neuronal connectivity and maintaining current neuronal viability (Gottmann, Mittmann and Lessmann, 2009; Zoladz and Pilc, 2010).

BDNF has long been considered as the most important neurotrophyn in cognitive process, including the memory form, learning process and behaviour (Vaynman, Ying and Gomez-Pinilla, 2004; Lou *et al.*, 2008; Zoladz and Pilc, 2010). Decreasing level of BDNF is believed to play a role in the incidence ofneurodegenerative diseases such as Alzheimer and Parkinson (Zoladz and Pilc, 2010).

Many studies have revealed the effect of environmental stimulation towards the increment of BDNF level and cognitive function. However, most of the environmental stimulations are in a form of physical activity and formal education (Griffin *et al.*, 2011; Nagahara and Tuszynski, 2011; Fediani Y, Rita Dewi M, Irfannuddin M, Saleh MI, 2014). There are only few data regarding the impact of environmental stimulation related to religious activity towards BDNF level and cognitive process. One of the environmental stimulation-religious activity related that is being conducted consistently is memorizing The Holy Qur'an in Huffaz(Ludwig W. Adamec, 2009).This study wished to compare the BDNF serum level and cognitive function of Huffaz and administrative workers.

2. METHODS

This is a cross sectional study with quota sampling in two subjects groups. Huffaz (plural form of hafiz), aged 20-40 years old, were purposive selected among 25 students of The Quran Institute of Al-Ithifaqiyah in Palembang, South Sumatra. They were involved in this study if they have ability to memorize text of Quran for at least 10 juz (chapter). Huffaz group is compared with 25 administrative workers in Sriwijaya University that have been consecutively chosen with matching age, sex, and educational level. Age matching was done with tolerant level of one year difference. All subjects were known to not routinely do any kinds of physical exercise. None of them were suffered from hypertension, Diabetes Mellitus, Cerebrovascular disease, deafness and mental disorder.

BDNF serum level was measured using enzyme-linked immunosorbent assay (ELISA) in Molecular Biology Laboratory in Faculty of Medicine Sriwijaya University. Blood samples were obtained from the subjects in a resting condition in the morning. It then contained in micro tubebefore being centrifugated with 3000 rpm for 20 minutes in order to get the supernatan layer. Solid phase sandwich ELISA (Human BDNF ELISA kit, Sunlong Biotech® was used to analyze the BDNF level). Samples were put on a plate where it was added with standard before it was incubated in 37°C temperature for 90 minutes without being washed. Biotinylated antibodies were later added and the plates were being incubated again in 37°C temperature for 60 minutes. The plates were then washed for three times with PBS 0.001 M and were added with ABC working solution before it was having another incubation for 30 minutes in 37°C temperature. Plate was then washed 5 times using PBS 0.01 M and was added by TMB color developing agent. Plate then was incubated in 37°C temperature for 20 minutes in dark before it was added with TMB stop solution and Optical Density (OD) absorbance reading in 450 nm wave length in microplate reader. Standard curve was plotted as OD 450nm in each standard solution compared with standard solution concentration. The concentration of human BDNF samples were interpolated from standard curve. Resulting data was in a form of numerical data (in microgram/militer or µg/ml).(Sunlong, 2016)

Both groups were also undergoing a cognitive process evaluation consisted of various assessment methods. Memory ability was tested using the digit memory test which consisted of digit forward and digit backward. This test is used to assess the storage and recall capacity of short term memory (Soylu F, 2010). Subjects were asked to re-write all the numbers that have been mentioned by the examiner with the same sequence from the beginning to the end (digit forward) and vice versa (digit backward). Score was determined based on the correct answer from both test before it was converted to a raw score based on adult age criteria. Resulting data was in numerical form (Dyslexia-International, 2004; Lewis and Lewis, 2012).

Executive function ability is a mental ability of cognitive function that controls memory, planning, thinking, and decision making. Instrument that was used is a 'Draw A Person' test that was referred from Reynolds and Hickman 2004 (Reynolds CR, 2004). Drawing task can be an indicator to assess planning ability in executive function (Faria, Alves and Charchat-Fichman, 2015). Subjects were asked to draw a complete self image. Subjects were then asked to make a note about who was and what the person in their drawings were doing. Drawings were analyzed using a check list and the resulting data is in numerical form as well.

Analogy ability, analitical and logical thinking were assessed from self-questionnare based on Academic Potential Test Instrumen constructed by Saputra(Saputra E, 2013). The instrument is referred to Standard for Academic Potential Test from

National Development Planning Agency of Indonesia.Subjects were asked to answer amultiple choice questionnaire (MCQ). The answers were evaluated based on the answer key. Raw score was in numerical form.

Data analysis were done using SPSS software version 16.0. Comparison between the proportion of sex and educational level was tested using Chi-square test. Comparison of the difference between average age of the two subjects groups and average BDNF serum level was tested using independent-T test. Difference of numerical numbers in cognitive ability in both groups was tested using Mann-Whitney.

This study was approved by the Ethics Committee of Bioethics and Humaniora Unit Universitas Sriwijaya, Palembang, Indonesia.

3. RESULTS

Huffaz and administrative workers have the same age, sex and educational level distribution. Most of them are having a Bachelor's degree.

Table 1. Characteristic Distribution of Huffaz and administrative workers' groups

	Huffaz	Administrative Workers	Ind-t test
Mean age (years)	26,98 ± 5,5	27,08±4,7	t= -0.083*
	(N)	(N)	χ^2
Sex			
Male	14	14	0,000**
Female	11	11	
Education			
Graduate	18	18	
Diploma	1	1	0,000**
12th grade school	6	6	

*p=0.934; **p=1.000

Huffaz group have a significantly higher BDNF serum level compared to administrative workers' group, as it can be seen on figure 1 (301,9±50,6 µg/ml compared with 236,3±69,9 µg/ml). Huffaz group have a significantly better memory ability, while forother cognitive abilities showed no differences between the two groups, as it can be seen on figure 1.

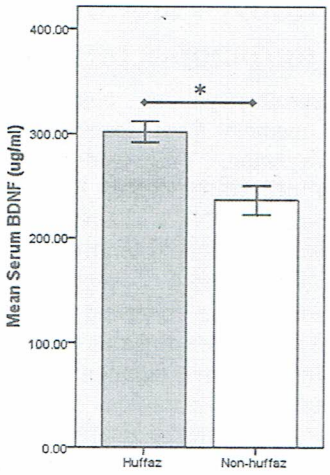

Figure 1. Serum BDNF level among huffaz and administrative workers. Independent-t test. *p<0.01

Table 2. Median value of cognitive abilities Among Huffaz and administrative workers

Cognitive Abilities	Huffaz (n=25)	Administrative Workers (n=25)	Mann-Whiteney U
Memory	108 (90-125)	86 (79-125)	90.0*
Analogy	17 (9-21)	17(8-22)	288.5**
Analytical Reasoning	11 (5-21)	10 (4-14)	276.5**
Logical Reasoning	8 (2-14)	6 (4-14)	257.5**
Executive Function	42 (25-51)	41 (28-43)	240.5**

*p<0.01; **p>0.05

4. DISCUSSION

Few studies have proven that neuroplasticity is affected by various factors like aging, stress, cerebrovascular diseases, diabetes mellitus, educational level and environmental stimulation like exercise(Lou *et al.*, 2008; Sanchez R, 2009; van Praag, 2009; Erickson *et al.*, 2011; Um *et al.*, 2011; Radak *et al.*, 2013).In this study, the distribution of age, sex, and educational level are equalized to minimize the confounding factors. Apart from that, both groups are known not to have suffered from metabolic and cerebrovascular diseases. Both groups are also known not to do a regular physical exercises.

BDNF level from subjects were taken from serum. The measurement of BDNF serum level was chosen because the measurement of BDNF level in

brain is not possible to be conducted. BDNF can be detected inside of plasma, serum, or inside trombocyte(Binder and Scharfman, 2004). BDNF serum level is 200 times higher than in plasma(Knaepen *et al.*, 2010). BDNF can go through blood brain barrier. It can also circulate in peripheral blood vessels in high saturation capacity, hence BDNF serum level can be considered as a reflection of BDNF level in brain and vice versa(Zoladz and Pilc, 2010).

Huffaz group has a higher BDNF serum level than administrative workers. Previous studies only focused on physical exercise as an enrichment environmental effort towards BDNF level. Aerobic exercise in animal models were proven to increase BDNF production and neuron viability in brain tissue(Vaynman, Ying and Gomez-Pinilla, 2004; Adlard, Perreau and Cotman, 2005; van Praag, 2009; Ferreira *et al.*, 2011). Aerobic exercises like ergocycle, running and gymnastics could increase BDNF level in serum, plasma and urine, and also improve the cognitive abilities of human start on children, young adult and elderly(Knaepen *et al.*, 2010; Erickson *et al.*, 2011; Griffin *et al.*, 2011; Fediani Y, Rita Dewi M, Irfannuddin M, Saleh MI, 2014).This study has proved that environment enrichment in the field of religious in form of hifz has related to the higher rate of neurotrophin to support neuroplasticity. Hifz is the activity of memorizing Holy Quran by heart. When doing hifz, a hafiz is encoding, storing and retrieving the text of Quran by practicing and reciting it in their daily activities. A research has been proved the Hifz significant increases the academic achievement and improve of education and socio-cultural life among huffaz (Nawaz and Jahangir, 2015).

Huffaz is also having a better memory ability than administrative workers. The increment of memory ability is probably linked with the storage of BDNF, since BDNF is mostly expressed in hippocampus as memory storage(Tulving and Markowitsch, 1998; Zoladz and Pilc, 2010; Bear, M; Connors, B; Paradiso, 2014). Studies in various regions of animal models' brains showed that mRNA BDNF is mostly expressed in hippocampus, mostly in area CA1 and CA4. Studies have also proven that BDNF expression has a significant correlation with spatial memory (Neeper *et al.*, 1996).

A hafiz trains their memory ability by reciting Quran verses time and time. Long term memorywill be formedby experience or learning that stimulates the brain repeatedly through long term potentiating (LTP) mechanism. Repeated stimulation triggers the developments of neuron structure in pre and post sinaps. End stage of LTP will stimulate the translation in nucleus and begin the protein synthesis. The beginnning of protein synthesis build the structure of neuronal membrane and also create new synaps along with the increasing of synaps connectivity. (Touzani, Puthanveettil and Kandel, 2007)

This study finds no differences on analogy, reasoning and executive functions on both groups. This finding shows that memorizing Quran is not enough to train more complex cognitive ability. That cognitive ability has to be trained through learning exposure and multitasking experience. Huffaz and administrative are probably having the same environmental enrichment while doing their daily tasks. Analogy ability, reasoning and executive functions are a more complex cognitive ability that involves memory consolidation and multitasking thinking (Elliott, 2003). Executive function is a cognitive process that involves logic, planning, problem solving and decision making (Lezak *et al.*, 2004; Strauss, Sherman and Spreen, 2006). Analogy and reasoning is a process that connect or compare one idea with another idea (Elliott, 2003). Analogy and logic needs a complex involvement of various semantic memory that was gained gradually (Becker and Morris, 1999).

A multitasking cognitive process involves not only hippocampus region, but also other brain regions. Executive function is mediated by dorsolateral prefrontal cortex and subcortical structure.(Hofgren C, 2009). Studies in mice stated that in relational spatial memory, which is a more complex cognitive memory involving consolidations between memories in order to solve problems, a de novo protein synthesis in prefrontal cerebral cortex is needed (Touzani, Puthanveettil and Kandel, 2007). The mice that were tested with schema paired associative ability –an ability which requires a systematical consolidation between old information and the new one- need regulation in particular genes resided in prefrontal medial cerebral cortex and prelimbic (Tse *et al.*, 2011).

Hifz might be conducted as an effective method to prevent the decline of cognitive function, ranging from Mild Cognitive Impairment (MCI) to Alzheimer. MCI and dementia manifested in a form of memory decline as a basic component of cognitive function due to hippocampus disconnection with cerebral cortex(Stoub *et al.*, 2006; Alzheimer's Disease International, 2013). Those diseases are also strongly related with a low BDNF level(Antunes-Lopes *et al.*, 2011). Hifz of

Quran is expected to not only memorizing the text daily, but also to repeat, rehearse and recall the memories every day (Nawaz and Jahangir, 2015). This stimulation activity is hoped to be a method to maintain and stimulate neuroplasticity of many brain components that are related with memory function. Nevertheless, this recommendation needs to be supported with adequate scientiffic evidence. Thus a further longitudinal study that focuses on the effectivity of environment enrichment in a form of memorizing Quran in people with memory disfunction is suggested.

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