PJN
ISSN 1680-5194

PAKISTAN JOURNAL OF NUTRITION

ANSInet
308 Lasani Town, Sargodha Road, Faisalabad - Pakistan
Mob: +92 300 3008585, Fax: +92 41 8815544
E-mail: editorpjn@gmail.com

Pakistan Journal of Nutrition 12 (9): 827-832, 2013
ISSN 1680-5194

Fermented Catfish Oil on Cognitive Function

Iskari Ngadiarti[1,2], Clara M. Kusharto[3], Dodik Briawan[3], Sri Anna Marliyati[3] and Dondin Sajuthi[4]
[1]Jurusan Gizi, Politeknik Kesehatan Kemenkes Jakarta 2, Hang Jebat 3, PO. Box. 8, Indonesia
[2]Program Studi Ilmu Gizi, Universitas Esa Unggul Jakarta, Terusan Arjuna, Jakarta, Barat, Indonesia
[3]Departemen Gizi Masyarakat, Institut Pertanian Bogor, Darmaga Campus, Bogor-16680, Indonesia
[4]Primate Research Centre, Bogor Agricultural University, Darmaga Campus, Bogor-16680, Indonesia

Abstract: The relationship between fatty acid composition with levels of amyloid beta and tau proteins in the cerebrospinal fluid is not widely known. The aim of this study was to assess the influence of catfish oil (CFO) and fermented catfish oil (FCFO) on cognitive functions (biology markers) aged female cynomolgus monkey (*Cynomolgus fascicularis*). Twelve aged female *Cynomolgus* were divided into 4 groups, each were fed with atherogenic iso calory with 0.2% cholesterol and 30% E (12% w/w), 3% from soybean oil, 9% from different fat sources, beeftallow (BFT), catfish oil (CFO), fermented cat fish oil (FCFO) and soybean oil (SBO). Cerebrospinal fluid was taken through suboccipital then kept at 20°C. Cognitive biology markers which were analyzed by using Tau and Aβ42ELISA kits. Changes in level of amyloid beta, tau protein and ratio of tau protein and amyloid beta were not statistically significant in the cynomolgus group four that were fed with BFT, FCFO, CFO and SBO, despite a trend toward increased levels of amyloid beta and decreased level of the tau protein / amyloid beta ratio were found in the group given with FCFO and CFO. In summary, FCFO and CFO intake capable to improve the cognitive function based on biological biomarkers.

Key words: Catfish oil, cognitive function, tau protein, amyloid beta

INTRODUCTION

Health is the main problem to elderly people, because it relates to the natural physical and physiological deterioration that occurs with age (Sikoki *et al*., 2011). Cognitive impairment is a major component of health problem and influences the individual ability to function independently (Quiles *et al*., 2006). Due to aging of the population, the prevalence of cognitive impairment is expected to increase. Alzheimer's disease (AD) is regarded as the most common cause of progressive cognitive impairments and dementia in aged human patient (Salmon *et al*., 2009).

Research for biochemical diagnosis signs that can be used for early diagnosis of AD have led to the concentration of tau-protein and amyloid-beta (Aβ42) in cerebrospinal fluid (CSF). Enforcement diagnosis is characterized by decrease levels of amyloid beta and an increase levels of tau protein concentration (Mulder *et al*., 2010).

Measurement of CSF-tau and Aβ42 have been suggested to improve the diagnosis of AD. As part of the clinical routine, the biomarkers have been found to be highly sensitive and specific. Sensitivity of CSF-tau in AD in some studies is quite high, even up to 80-90%. At the cynomolgus, the average level of Aβ42 in CSF was reported consistently decreased around 30-50% followed by an increase in CSFt-tau and p-tau in individuals with Alzheimer's type dementia (Darusman *et al*., 2013).

Several dietary factors may affect the risk of cardiovascular disease so that it can be assumed that the diet is also affect the risk of dementia (Panza *et al*., 2004). Several recent studies have shown that dietary fatty acids are thought to play a role in the progression of cognitive decline which is associated with aging or dementia (Solfrizzi *et al*., 2005; Freeman, 2012). There are several biological mechanisms appropriate to the relationship between fatty acids and cognitive function, including through the mechanism of antioxidant compounds in food rich in fatty acids, through atherosclerosis and thrombosis, inflammation, accumulation of amyloid beta or through effect in maintaining the structural integrity of neuronal membranes (Solfrizzi *et al*., 2005).

Catfish oil of flouring *by product* can be used as an alternative fat source which is still not well utilized. Catfish oil has saturated fatty acids, unsaturated fatty acids, namely MUFA (monounsaturated fatty acids) and PUFAs (polyunsaturated fatty acids). This study aims to look at the effect of fish oil cat fish (CFO), fermented catfish oil (FCFO), beef tallow (BFT) and soybean oil (SBO) on cognitive function. Cognitive measures only seen from the Alzheimer biomarkers amyloid β and tau proteins in the cerebrospinal fluid (CSF).

MATERIALS AND METHODS

Materials and equipments: The materials that are used as raw materials to feed in this study is beef tallow

Corresponding Author: Iskari Ngadiarti, Jurusan Gizi, Politeknik Kesehatan Kemenkes Jakarta 2, Hang Jebat 3, PO. Box. 8, Bogor, Indonesia

(BFT), catfish oil (CFO), fermented catfish oil (FCFO) and soybean oil (SBO). Catfish oils obtained from PT. Carmelitha Lestari Bogor. Fish oil was fermented by Lactobacillus plantarum (Hidayati method, 2005). Beef tallow oil obtained from PT. Garuda Mas Lestari Bekasi and soybean oil is obtained from the PT. Indofood Jakarta.

Analysis of tau protein and amyloid beta using Invitrogen, Aβ42 ELISA Kit and ELISA Kit Tau. Materials used were standard reagent Hu Aβ42, Tau Hu standard, standard buffer (0.1% NaN_3), Tau Hu antibody detection, Aβ42 antibody detection, Tau Hu Antibody Coated Wells, Aβ42 Antibody Coated Wells, Anti-Rabbit IgG HRP, tetrametilbenzidin (TMB) and Stop Solution.

Subject: Subjects in this study were 12 female cynomolgus (*Cynomolgus fascicularis*) which aged over 10 years and have been ovariectomized which are obtained from PT IndiAnilab Bogor, Indonesia. The adaptation process had been done in advance before the intervention by using individual cages. For two months subjects had been given 100 g each per day of standard feeding of Purina Monkey Chow.

Subjects were divided into 4 groups, each group was given atherogenic feeding containing 0.2% cholesterol and isocaloric. The fat content in each 100 g is 12% (30% of total energy) which contain 3% SBO and 9% from different fat sources; which are beef tallow (BFT), catfish oil (CFO), fermented cat fish oil (FCFO) and soybean oil (SBO). CSF taken through sub occipital then inserted into the tube and kept at a temperature of -20°C to analyze the rate of tau protein and amyloid beta. Tau protein and amyloid beta are analyzed by using *in vitro* gen, Tau and Aβ42ELISA kit. Absorbance measured at a wavelength of 450 nm with correction at 540 and 570 nm. All duplicate samples tested and the intra-assay coefficient of variation was 3.9% forAβ42 assay and 4.1% forp-tau assay. All study procedures has been approved by the ethics committee and animal welfare of PT. Bimana Indomedical Bogor with No. ACUC p.03.12-IR.

Composition of animal feeding: Feeding and water were given daily for 12 weeks. The amount of feeding given was 60 g in the morning and 60 g in the afternoon. Composition of feeding was based on food composition list per 100 g containing approximately 400 Kcal, with fat content ranged from 30-31 and ±13% protein content. Table 1 and 2 illustrate the nutrient contain of the four of feeding. All diets were designed to have the same contain of nutrient such as protein, fat and CHO, but fatty acid composition are different between each other depend on type of oil given. All feeding has both saturated fatty acid (SFA),unsaturated fatty acids either monounsaturated fatty acids (MUFA) or poly unsaturated fatty acids (PUFA). Fatty Acids content in several types of feeding was illustrated in Table 3.

Table 1: Food intervention composition

Raw food material	BFT	CFO	FCFO	SBO
Flour (g)	38	38	38	38
Maizena (g)	10	10	10	10
Skim CFOk powder (g)	10	10	10	10
Fish powder (g)	7	7	7	7
Bungkil kedelai (g)	5.8	5.8	5.8	5.8
Dedak padi (g)	2	3	2	3
Sugar (g)	1	10	10	10
Soybean oil (g)	3	12	3	3
Beef tallow (g)	9	-	-	-
Catfish oil (g)			-	9
Fermented catfish oil (g)			9	-
Margarin (g)	1	-	2	-
Agar-agar (g)	1	1	0.5	1
CMC (g)	1	1	0.5	1
Mineral mix (g)	1	1	1	1
Mineral (g)	1	1	1	1
Cholesterol (g)	0.2	0.2	0.2	0.2
Total (g)	100	100	100	100

BFT: Beef tallow
CFO: Catfish oil
FCFO: Fermented catfish oil
SBO: Soybean oil

Table 2: Nutrition content in food

Komponen	BFT	SBO	CFO	FCFO
Energy	398	397	396	400
Fat	13.5	13.5	13.5	13.5
Protein	13.4	13.4	13.4	13.4
Carbohydrate	55.8	55.8	55.9	55.8
Protein to energy (%)	13.5	13.5	13.5	13.4
Fat to energy (%)	30.	30.1	30	30.8
CHO to energy (%)	56	56.4	56.5	53.8

Based on food composition table
BFT: Beef tallow
CFO: Catfish oil
FCFO: Fermented catfish oil
SBO: Soybean oil

Table 3: Fatty acid composition of BFT, CFO, FCFO and SBO in food (%) asam lemak

Fattty acid	BFT	CFO	FCFO	SBO
C8:0	-	-	0	-
C10:0	0	-	0	-
C12:0	0.1	0	0.	-
C14:0	0.5	0.2	0.3	0
C16:0	2.9	3	2.9	1.3
C18:0	3.4	0.7	1	0.4
ΣSFA	6.8	3.2	4.2	1.7
C14:1	0	0	-	-
C16:1	0.2	1.1	0.3	0
C18:n9c	2.7	3.0	4.2	2.7
ΣMUFA	2.9	4.1	4.5	2.7
C18:2n6c	1.9	4	2.6	6.6
C20:0	0	0	0	0
C18:3n3	0.2	0.3	0.3	0.8
C22:0	0.1	0.1	0.05	0.1
C22:1n9	0	0.	0.1	0
C20:4n6	0	0	0	-
C24:0	0	0	0	-
C20:5n3	0	0.1	0.1	-
C22:6n3	-	0.4	0.1	-
CLA	0.1	0	0.05	0
ΣPUFA	2.3	4.8	3.3	7.5
ΣMUFA+PUFA	5.2	8.9	7.8	10.2
ΣSFA+MUFA+PUFA	12	12.	12	11.9
P/S	0.3	1.5	0.8	4.4
W6:W3	-	15 : 1	13:1	9:1

BFT: Beef tallow
CFO: Catfish oil
FCFO: Fermented catfish oil
SBO: Soybean oil

Statistical analysis: The data obtained are presented in the form of the average and standard deviation. All data were analyzed with analysis of variance test at 5% level test. Duncan difference test is only done when a real treatment effect ($p<0.05$).

RESULTS

Amyloid beta levels: The increased levels of beta-amyloid is one indicator of impaired brain function of both cognitive and vascular cognitive Alzheimer's that it can become a biomarker of biological cognitive function. Results of changes of the levels of amyloid beta in Cynomolgus Monkey before and after the intervention are presented in Fig. 1.

Figure 1 shows that there are changes in the levels of amyloid beta after a Cynomolgous was given BFT, CFO, FCFO and SBO intervention. Given before the intervention, amyloid beta in the group fed with BFT, CFO and FCFO are, respectively 299.86 ρg/mL, 361.16 ρg/mL and 340.36 ρg/mL. After 3 months of intervention, the levels of amyloid beta in the cynomolgous group fed with BFT, CFO and FCFO has increased, respectively to 422.86, 431.46 and 487.95 ρg/mL. The highest increase of amyloid beta was found in the group given with CFOT which was 43% that reach 147.6 ρg/mL. In contrast, in the group fed with SBO, the average levels of amyloid decreased slightly from 354.26 to 334.76 ρg/mL. ANOVA test results showed that there was no real difference between the group fed with BFT, CFO, FCFO and SBO with amyloid beta levels ($p>0:05$).

Tau protein levels: In addition to amyloid beta, tau protein levels are biomarkers that can be used in animals and human to see cognitive function. In this study, levels of tau protein of the cynomolgous monkeys were analyzed before and after the intervention. Figure 2 describes the differences between the levels of tau protein before and after the intervention.

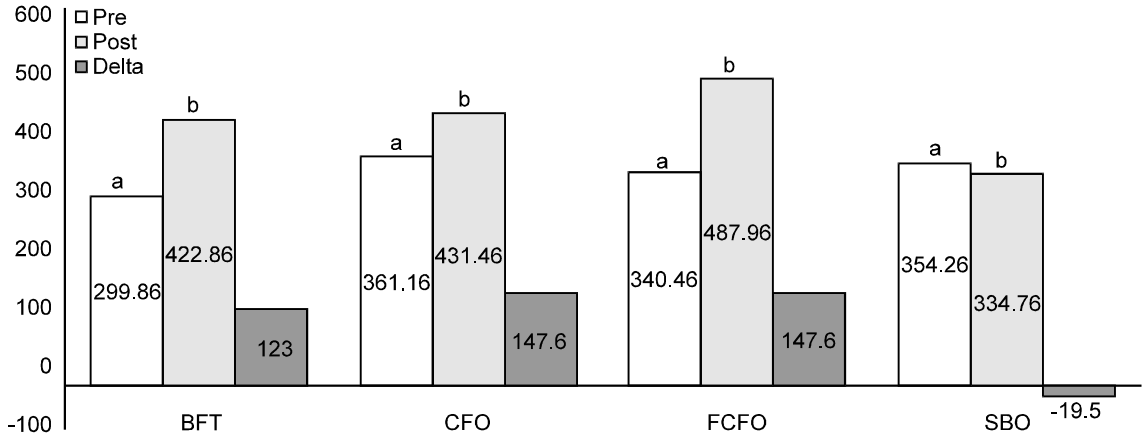

Fig. 1: Beta amyloid levels before and after intervention. Numbers follow with same color and alphabet show no significant difference ($p>0.05$)

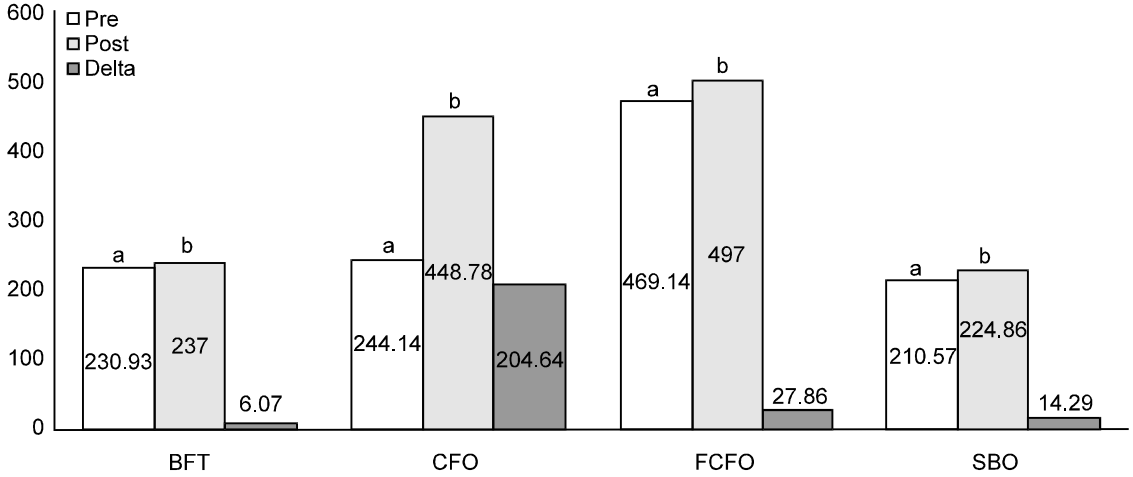

Fig. 2: Tau protein levels before and after intervention. Numbers follow with same color and alphabet show no significant difference ($p>0.05$)

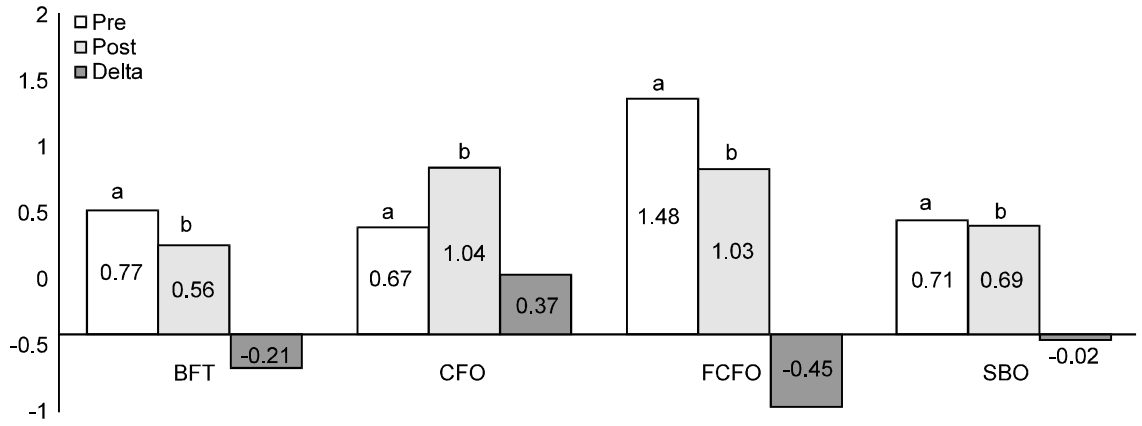

Fig. 3: Tau protein to beta amyloid ratio before and after intervention. Numbers follow with same color and alphabet show no significant difference (p>0.05)

Graph of the average levels of tau protein which can be seen in Fig. 2 shows that the intervention for 3 months by giving BFT, CFO, FCFO and the SBO can increase levels of tau protein of the cynomolgous. Before the intervention, levels of tauprotein of cynomolgous group that were given BFT, CFO, FCFO and SBO are, respectively 230.93, 256.644, 469.14 and 210.57 ρg/mL. The increased levels of tauprotein in the 3rd month are 237.00 ρg/mL (BFT), 282.71 ρg/mL (CFO), 497 ρg/mL (FCFO) and 224.86 ρg/mL (SBO). It means that all groups suffered an increase in very small so as likely to say constant between before and after intervention. By statistically, there was no significant difference between the levels of tauprotein in every treatment (p>0.05).

Tau protein dan amyloid beta ratio: The rasio of CSF tau protein to amylioid beta has allowed for better discrimination of AD patients from healthy controls, non Alzheimer dementias and other neurological disorders than any of these markers alone (Maddalena *et al*., 2003). Ratio of tau protein and beta amylioid of subject group before and after intervention is presented in Fig. 3.

The graph in Fig. 3 shows the change in the ratio of tau protein and amyloid beta after cynomolgous was given the intervention. In the group fed with BFT, FCFO and SBO it can be seen that the ratio of tau protein and amyloid beta had decreased. Highest ratio decline was seen in the group fed with FCFO while the other group got only slight change.

Before the intervention, levels of tauprotein/beta amyloid ratio of cynomolgous group that were given BFT, CFO, FCFO and SBO are, respectively 0.77, 0.71,1.48 and 0.71 and after intervention in the 3rd month are 0.56 (BFT), 0.66 (CFO), 1.03 (FCFO) and 0.69 (SBO). Comparing between the CFO and FCFO seems that decreased FCFO higher than the CFO, although statistically not significant.

DISCUSSION

Cognitive impairments such as Alzheimer's dementias or vascular cognitive impairment are influenced by many risk factors such as age, genetics and lifestyle. They are also affected by vascular diseases such as stroke, hypertension, diabetes, dyslipidimia, obesity and atherosclerosis. The biomaker used to measure cognitive impairment in this study is measure of microtubule-associated protein tau (MAP-tau) and amyloid-â-protein (Aβ42) in Cerebrospinal fluid (CSF). CSF is the clear fluid that surrounds the spinal cord and brain and acts as shock absorber. The main function of CSF is to supply nutrients to nervous system tissue and to remove waste products from cerebral metabolism. Cerebrospinal fluid containing dissolved glucose, proteins, salt and some lymphocytes (Clayman, l989).

Descriptively can be seen that the cynomolgous groups given FCFO, CFO and BF increased the levels of amyloid beta, while another group given SBO decreased levels of amyloid beta. There are several assumption about increasing of amiloid beta in CSF such as a decreased deposition of amyloid beta in brain; decreased clearance of amyloid-β-protein from brain and disturbance in the metabolism of APP and A-β leading to a neuronal dysfunction which brings on the CSF Aβ42 levels reduction (Sobow *et al*., 2004). The result also showed that concentration of tau protein was relative constant. It means there was no changes abnormal conformation and the phoosphorilation on formation of Paired helical filaments (PHF) in microtubule cynomolgous.

Thus a diet containing FCFO and CFO proved to have a real ability to improve cognitive cynomolgous which can be seen from biological biomarkers. Darusman *et al*. (2013) stated that there is a positive relationship between levels of amyloid beta with the behavioral tests on the cynomolgus. If there is an increase levels of amyloid beta, it will be followed by improvement of behavioral test.

Many recent studies emphasize different fat intake with cognitive function. Intake of saturated fatty acids or SFA and cholesterol is associated with vascular dementia and dementia Alzaimer and cognitive decline, whereas mono unsaturated fatty acids (MUFA) seems to protect the decline of cognitive. In this study, dietary FCFO consist of MUFA>SFA>PUFA while CFO consist of PUFA>MUFA>SFA.

This result is consistent with the results of Arsenault *et al.* (2012) who suggested that the administration of a normal fat diet (30% E) for 6 months with its main source of fatty acids derived from MUFA significantly improve and maintain cognitive function, especially in nerve enthorthinal cortex and hippocampus.

Hwang *et al.* (2011) reported that PUFA instead of SFA in phospholipid membranes is a critical targets of ROS such as hydroxyl radicals and superoxide anions. Increased ROS production associated with linoleic acid> oleic acid>stearic acid. Oleic acid is less potent than linoleic acid in stimulating the production of ROS in human lymphocytes. Protection mechanisms caused by the SFA and MUFA. PUFA concentration in the liver decreased so that the availability of substrate for lipid peroxidation decreased as well. Another mechanism is that oleic acid provides an antioxidant effect by increasing the delay before the rapid oxidation of LDL isolated.

Fatty acid supplementation with stearic acid, oleic acid and do not linolenic alpha acid provide protection against H_2O_2 that cause cytotoxicity, such as ROS, lipid hydroperoxide production and release of lactate dehydrogenase (LDH), so that eventually led to oxidized LDL and finally endothelial dysfunction occur in porcine aortic endothelial cells (PAEC). Diniz *et al.* (2004) also reported that there was no difference in LDH in rats given SFA and MUFA diet for 5 weeks, but given PUFA diet showed level of myocardial lipoperoxides and lipid are increased but activity of superoxide dismutase and catalase are decreased.

Gu *et al.* (2012) state that, a diet high in omega-3 is associated with decreased plasma amyloid beta levels or increased levels of CSF amyloid beta. This profile is associated with reduced incidence Alzhaimer disease and slow cognitive decline. Lim *et al.* (2005) also stated that the dietary intake of omega-3 has relationship with the increased levels of CSF amyloid beta. Data from transgenic animal model of Alzheimer's disease have consistently shown giving the DHA-enriched diet significantly reduced insoluble amyloid beta detergent total more than 70% compared with low DHA diet or a standard diet.

Research Hooijman *et al.* (2007) in rats given a diet high in fat, 1% cholesterol and enriched with DHA for 12 months, showing at the cerebral blood volume increases. As a result of the circulation in the brain occurs that causes vasodilation occurs so that the amount of beta amyloid in nerve membrane decreases and the value of beta amyloid in the CSF increased. Other studies have reported in different way that omega-3 supelementasion for 6 months in human patients with mild and moderate Alzheimer's showed no effect on the elevated levels of beta amyloid (Aβ42) CSF. However, from the results of a cohort study reported that high levels of beta amyloid in serum and low levels of beta amyloid in CSF associated with a reduced risk of incident AD and cognitive decline.

These results support that particularly dietary fat source of MUFA or PUFA associated with increased levels of amyloid beta in the CSF which is a marker for improvement of cognitive function. Solfrizzi *et al.* (2005) stated that the epidemiologic evidence showed that n-3 PUFA could be expected to play a role in maintaining cognitive function in pre dementia symptoms, but does not apply at the time that Alzheimer's already suffered. Therefore, because there are many results that have not aligned relationship with cognitive fatty acids, the recommendation as to consume fish, unsaturated fatty acids, saturated fatty acids in relation to risk of cognitive decline has not been established.

Conclusion: ANOVA test results showed that there was no real difference between the intervention of each feeding (BFT, CFO, FCFO and SBO) with amyloid beta levels (p>0:05), tau protein and ratio tau and amyloid beta. However, the intervention with CFO and FCFO seems to influence the elevated level of amyloid beta in the CSF and the decreased ratio tau protein to amyloid beta. The result also showed that FCFO role in terms of increasing amiloid beta and decreasing tau protein/amiloid beta ratio seem higher than CFO.

Suggestion: To see the effect of diet on cognitive function research should be performed with a relatively longer period of minimal 1 year. In addition, examination of fatty acid level in each organ should be done so that it can be seen where the decline of fat begins.

ACKNOWLEDGEMENTS

We thank to PT Carmelitha Lestari dan PT. IndoAnilab Bogor, Indonesia for providing the sample and ingredients of this study. The authors are grateful to Dr. Irma suprapto and staff at the primate research Center Bogor Agricultural University and Dr. Nengah Budiarsa as Director of PT. Bimana Indomedical Bogor and staff for their technical assistance in research preparation.

REFFERENCES

Arsenault, D., C. Julien, C.T. Chen, R.P. Bazinet and F. Calon, 2012. Dietary intake of unsaturated fatty acids modulates physiological properties of entorhinal cortex neurons in mice. J. Neurochem., 122: 427-443.

Clayman, B. Charles, 1989. Encyclopedia of Medicine. The Am. Med. Assoc., p: 249.

Darusman, H.S., D. Sayuthi, O. Kalliokoshi, K.R. Jacobsen, J. Call, S.J. Schapiro, A. Gjedde, K.S.P. Abelson and J. Hau, 2013. Correlation between serum levels of amyloid beta, cerebrospinal levels of tau and phosphor tau and delayed response tasks in young and aged cynomolgous monkeys (*Cynomolgus fascicularis*). J. Med. Primatol., 42: 137-146.

Diniz, Y.S., A.C. Cicogna, C.R. Padovani, L.S. Santana, L.A. Faine and E.I. Novelli, 2004; Diets rich in saturated and polyunsaturated fatty acids: Metabolic shiffing and cardiac health. Nutr., 20: 230-234.

Freeman, L.R. and A.C. Granholm, 2012. Vascular changes in rat hippocampus following a high saturated fat and cholesterol diet. J. Cereb Blood Metab., 32: 643-653.

Hwang, J., Y.Y. Chang, J.H. Park, S.Y. Kim., H. Chung, E. Shim and H.J. dan Hwang, 2011. Dietary saturated and monounsaturated fats protect against acute acetaminophen hepatotoxicity by altering fatty acid composition of liver microsomal membrane in rats. Lipids in Health and Dis., 10: 184.

Gu, Y., N. Schupf and Cosentino, 2012. Neurology, Am. Acad. of Neurology. p:1832-1840.

Hidayati, D., 2005. Pembentukan conjugated linoleic acid (CLA) oelh bakteri asam laktat pada fermentasi susu kedelai (thesis). Yogyakarta (ID): Universitas Gajah Mada.

Hooijman, C.R., F. Rutters and P.J. Dederen, 2007. Changes in cerebral blood volume and amyloid pathology in aged Alzheimer APP mice on docosahexaenoic acid (DHA) diet or cholesterol enriched typical western diet. Neurobiol Dis., 28: 16-29.

Lim, G.P., F. Calon, T. Morihara, F. Yang, B. Teter, O. Ubeda , N. Salem Jr., S.A. Frautschy and G.M. Cole, 2005. A diet enriched with the omega-3 fatty acid docosahexaenoic acid reduces amyloid burden in an aged Alzheimer mouse model. J. Neuro Sci., 25: 3032-3040.

Maddalena, A., A. Papassotiropoulos, B. Muller-Tillmanns, H.H. Jung, T. Hegi, R.M. Nitch and C. Hock, 2003. Biochemical diagnosis of Alzhaimer disease by measuring the cerebrospinal fluid ratio of phosphorylated tau proteon to B-amyloid peptide 42. Arch. Neurol., 60: 1202-1206.

Mulder, C., N.A. Vervey, W.M. Van der Flier, F.H. Bouwman, A. Kok, E.J. Van Elk, P. Scheltens and M.A. Blankenstein, 2010. Amyloid-β (1-42), Total Tau and Phosphorylated Tau as Cerebrospinal Fluid Biomarkers for the Diagnosis of Alzheimer Disease. Clin. Chem., 56: 248-253.

Panza, F., V. Solfrizzi, A.M. Colacicco, A. D'Introno, C. Capurso, F. Torres, A. Del Parigi, S. Capurso and A. Capurso, 2004. Mediterranean and cognitive decline. Pub. Health Nutr., 7: 959-963.

Quiles, J.L., G. Barja, M. Battino, J. Mataix and V. Solfrizzi, 2006. Role of olive oil and monounsaturated fatty acids in mitochondrial oxidative stress and aging. Nutr. Rev., 64: 31-39.

Salmon, D.P. and M.W. Bondi, 2009. Neuropsychological assesment of dementia. Annu. Rev. Psychol., 60: 257-282.

Sobow, T., M. Flirski and P.P. Liberski, 2004. Amyloid-beta and tau proteins as biochemical markers of Alzheimer's disease. Acta Neurobiol. Exp., 64: 53-70.

Solfrizzi, V., A.M. Colacicco, A. D'Introno, C. Capurso, F. Torres, C. Rizzo, A. Capurso and F. Panza, 2005. Dietary inake of unsaturated fatty acids and age-related cofnitive decline: a 8.5-year-follow-up of the Italian longitudonal study on aging. Neurobiol Aging., 27: 1694-1704.

Sikoki, B., Y. Kim, J. Strauss and F. Witoelar, 2011. Well being and support for the elderly in Indonesia: a challenge to policy for elderly, international conference on the population aging explosion: opportunities and challenges. Bali (ID).