

THE EFFECTS OF SHIFT WORK, NUTRITIONAL STATUS, AND STRESS LEVEL ON NURSE BRAIN-DERIVED NEUROTROPHIC FACTOR (BDNF) GENE LEVELS DURING THE COVID-19 PANDEMIC IN CENTRAL JAKARTA, INDONESIA

Atthariq¹, Suryani As'ad², Saidah Syamsuddin³, Mochammad Hatta⁴, Tria Astika Endah Permatasari^{5,*},
Yusminah Hala⁶, Ilhamjaya Patellongi⁷, Jumraini Tammase⁸, Rosdiana Natzir⁹,
Sri Ramadhany¹⁰, Andi Alfian Zainuddin¹¹

^{1,2,3,4,7,8,9,10,11} Faculty of Medicine, Universitas Hasanuddin, Makassar, Indonesia

⁵ Department of Nutrition, Faculty of Medicine and Health, Universitas Muhammadiyah Jakarta, Indonesia

⁶ Department of Biology, Faculty of Mathematics and Natural Science, Universitas Negeri Makassar, Indonesia

E-mail: tria.astika@umj.ac.id

ABSTRACT

Introduction: The study aimed was to analyze the decrease in BDNF gene levels in unit work, shift work, nutritional status, and stress levels of nurses during the Covid-19 pandemic. The number of patients confirmed by the Covid-19 virus receiving treatment at hospitals in Indonesia has increased significantly. This condition causes increased fatigue that can lead to higher stress on nurses. Low serum levels of brain-derived neurotrophic factor (BDNF) were found in workers with high-stress levels. This stress is triggered by several factors such as sleep disturbances, workload, and conflicts that occur in the workplace. **Method:** This research used an analytic observational method with a cross-sectional design during July-September 2020 at the Cempaka Putih Islamic Hospital Jakarta, in Central Jakarta, Indonesia. A sample of 89 nurses recruited by the purposive sampling technique who met the inclusion criteria obtained, namely not having a systemic disorder, not suffering from psychiatric disorders, not consuming alcohol, and not smoking. The data were collected using anthropometric measurements and intravenous blood collection to check BDNF gene mRNA expression using real-time PCR. **Results:** The results showed that the mean BDNF levels on respondents with low, medium, and high-stress levels were 11.68752, 8.65197, and 7.35583, respectively. There was a significant relationship between shift work (P-Value = 0.007) and stress levels (P-value = 0.000) of nurses and decreased BDNF gene's level during the Covid-19 pandemic. However, nutritional status was not significantly (P-Value = 0.163) related to BDNF gene's level.

Keywords: Brain-derived neurotrophic factor (BDNF) gene; nurse; nutritional status; shift work, stress work

I. INTRODUCTION

Health workers who are responsible for monitoring patients and often dealing with stressful conditions include nurses. Compared to other professions, nurses have an important role in improving health status and must perform more tasks. So those nurses are often exposed to various situations and conditions that have the potential to cause stress during work. (1,2) According to Indonesia's health profile, all nursing resources in Indonesia in 2019 total of 345,508 people, and 220,192 of whom were utilized in hospitals. (3)

Highley in Tom Cox et al (1996) said that naturally, nurses are a profession full of stress. Nurses are faced with various health problems for their patients. Many of the duties of nurses are unpleasant and stressful, often belittled, frightening, or even unappreciated. In the nursing profession, sources of stress are closely related to interactions with patients and other health professionals. (1,4) According to the study, there were 9 (nine) sources of stress identified in nurses who worked in the hospital as follows, were faced with death and dying; inadequate preparation for the emotional needs of patients and families; uncertainty about treatment; conflicts with doctors;

conflicts with other nurses and supervisors; lack of staff support; excess workload; workplace; and discrimination. (1,2)

Given the impact caused by COVID-19 at this time, nurses are at the forefront of services in hospitals that are prone to work stress due to excessive workloads, asymptomatic patients, and insufficient PPE equipment. (5). It was found that 25.6% of nurses with night work shifts suffered from disturbed sleep patterns due to shift work. The impact that occurs on night work shifts causes circadian rhythm disorders, lack of sleep, mood disorders, chronic anxiety, depression, and gastrointestinal disorders. (6–8). Nurses need nutritious intake to maintain a healthy body and to carry out daily activities, including in their work. It is reported that stress has contributed significantly to underweight and overweight status as well as energy and food consumed. (9).

Brain-derived neurotrophic factor (BDNF) is a neurotrophin that plays an important role in the survival, growth, and maintenance of neurons in the main brain circuits involved in emotional and cognitive function. BDNF levels decrease and have a substantial effect on stress. (10,11) In the brain the dominant neurotrophic is BDNF. (12) Research has found that the BDNF hormone plays an important role as a component of changes in the pathomechanism of stress and stress resistance. (13,14) The Hippocampus of the central nervous system in particular directly produces BDNF. Various studies have shown that BDNF levels may decrease due to stress and depression-related conditions. (15,16). This study aims to determine the comparison of BDNF gene levels in unit work, shift work, nutritional status, and stress levels of nurses.

II. MATERIAL AND METHODS

This research used an analytic observational method with a cross-sectional design. Conducted in July-September 2020 at the Cempaka Putih Islamic Hospital Jakarta, Indonesia. The population in this study were all nurses (IGD Unit, Inpatient, Operating Room, and ICU) who worked at the Jakarta Islamic Hospital (RSIJ) total of 120 peoples. The sample in this study were 89 people with the sampling technique using a purposive sampling technique. The sample inclusion criteria were willingness to fill out a questionnaire, not having a systemic disorder, not suffering from psychiatric disorders, not consuming alcohol, and not smoking. Data collection was done by selecting samples then weighing and measuring the height of the sample. Blood was drawn intravenously for an examination of BDNF gene mRNA expression with real-time PCR according to the previous research method. (17–23) Then the sample was asked to fill out a research questionnaire.

Data analysis in this study used univariate analysis to see the distribution of sample characteristics and bivariate analysis with ANOVA and T-test to determine the difference in the mean of the two groups and their relationship. This research has received an ethical approval recommendation issued by the Health Research Ethics Committee of RSPTN the Universitas Hasanuddin on July 9, 2020, with number 361/UN4.6.4.5.31/PP36/2020.

III. RESULTS

In **Table 1**, it can be seen from 89 respondents who met the research criteria as many as 76.4% were female, with a diploma education of 83.1%, a marital status of 82.0% of respondents were married, most of the respondents worked in inpatient units as many as 61, 8%, working on night shifts as much as 51.7%, most of the nutritional status is normal as much as 46.1% and the stress level of respondents is 42.7% in the moderate category. The average age of the respondents was 38.75 years old, the youngest respondent was 23 years old and the oldest was 55 years old. The average length of time for the respondents to work is 15.88 years, with a working age of at least 1 year and a maximum of 34 years. From the results of blood tests, it is known that the BDNF gene levels of respondents on average were 8.93 ng/ml with the lowest levels being 5.34 ng/ml and the highest levels being 13.43 ng/ml.

Table 1. Characteristics of Respondents (n = 89)

Characteristics	N	%
Sex		
Women	68	76.4
Men	21	23.6
Education level		
Diploma	74	83.1
Degree	15	16.9
Marital status		

Single	16	18.0
Married	73	82.0
Unit work		
IGD	11	12.4
Inpatient	55	61.8
Surgery room	7	7.9
ICU	16	18
Shift work		
Morning shift (8 am – 3 pm)	37	41.6
day shift (3 pm – 9 pm)	6	6.7
Night	46	51.7
Nutrition status		
Malnutrition (<18.5)	3	3.4
Normal (18.5-25)	41	46.1
Overweight (25.1-27)	24	27.0
Obesity (>27)	21	23.5
Stress level		
Low	21	23.6
Medium	38	42.7
High	30	33.7
Age	Mean : 38.75, SD 9.550 Median : 39 years Min-Max: 23 years -55 years	
Length of work	Mean : 15.88, SD 9.408 Median : 17 years Min-Max: 1 year -34 years	
BDNF Gene's levels	Mean : 8.93 ng/ml, SD 1.89 ng/ml Median : 8.63 ng/ml Min-Max: 5.34-13.43	

Based on **Table 2**, it is known that the work shift variable and the respondent's stress level are significantly related to the BDNF gene level with p-value <0.05). Meanwhile, work unit variables and nutritional status were not related to BDNF gene levels (p-value> 0.05).

Table 2. Relationship between Unit Work, Shift Work, Nutritional Status and Stress Level on BDNF gene levels

Variables	Mean	SD	95% CI		p-value
			Lower	Upper	
Unit work					
The emergency room	8.99809	1.355873	8.0872	9.90898	0.102
Inpatient room	8.60964	1.817556	8.11828	9.10099	
Surgery room	10.28600	2.505303	7.96898	12.60302	
Intensive care unit	9.39856	1.972006	8.34775	10.44937	
Shift work					
Morning shift (8 am – 3 pm) and day shift (3 pm – 9 pm)	8.94623	1.645348	-0.77318	0.83087	0.007*
Night shift (9 pm – 8 am)	8.91739	2.114105	-0.76686	0.82454	
Nutrition Status					
Malnutrition (<18.5 kg/m ²)	7.98100	1.242182	4.89525	11.06675	0.163
Normal (18.5-25 kg/m ²)	8.60363	1.842493	8.02207	9.1852	
Overweight (>25.1 kg/m ²)	9.29324	1.924489	8.71506	9.87142	
Stress level					
Low	11.68752	1.018085	11.2241	12.15095	0.000*
Medium	8.65197	0.810925	8.38543	8.91852	
High	7.35583	1.063881	6.95857	7.75309	

In this study, the number of female nurses is more than men, the education of nurses is dominated by diploma education, most of the nurses who work at the hospital are married and most of the nurses work in the inpatient unit. The distribution of schedules or shifts to keep nurses is almost the same in the morning and night. Most of the nurses have normal nutritional status. A nurse with good nutritional status will have better body immunity so that it can support the quality of work compared to nurses with less or more nutritional status. The stress level of nurses was slightly more in the medium category. Work demands and pressures cause stress to nurses. Based on

the results, it is known that the nurse work unit is not related to BDNF gene levels. This shows that each unit work has the same stress level so that there is no difference in the average BDNF level in each unit work.

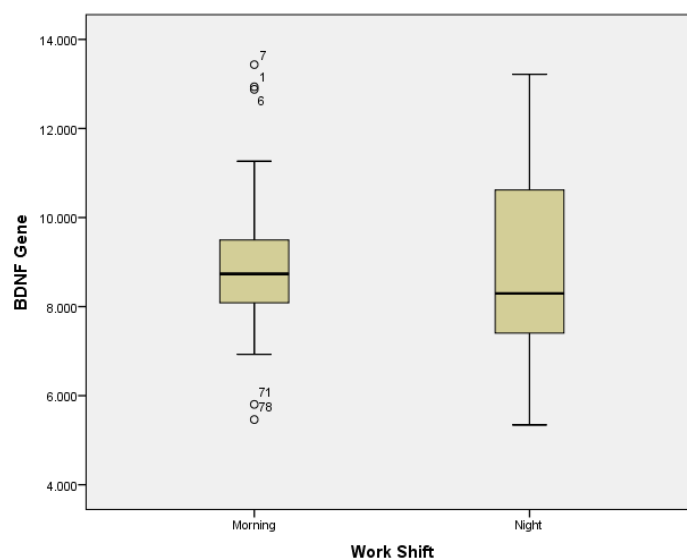


Figure 1. BDNF serum values. Box plot of serum BDNF concentration (ng/ml) in nurses according to work shift

IV. DISCUSSION

In this study found that the mean score of BDNF gene's level on the nurses who works in night shifts (work during 9 pm – 8 am) were lower (8.91739 ng/ml) than the nurses who works in morning and day shift (8.94623 ng/ml). There was a significant relationship between shift work and BDNF gene's levels on nurses. The nurses who get night shifts (work during 9 pm – 8 am) lower the BDNF gene levels in the blood because generally at night is a time of rest. Scientific evidence shows that nurses who work at night will affect sleep patterns. This condition is related to brain-derived neurotrophic factor (BDNF), possibly involved in sleep regulation. Study in a general hospital in Beijing among 244 health workers shows that there was serum BDNF levels related with sleep problems significantly (P -value < 0.05). Serum BDNF levels were significantly lower in subjects with Insomnia with short sleep duration (ISS) than in those without. Furthermore, the research also shows that the serum BDNF levels of insomniacs were significantly lower than those in non-insomniacs among health workers with short sleep duration (<6 h), whereas serum BDNF levels did not differ between insomniacs and non-insomniacs with normal sleep duration (6 h) (24). Another study showed that BDNF serum levels were significantly higher in the pulse pressure reduction group after an hour's rest in nurses working the night shift. (25) A previous study reported that there was an association between BDNF and insomnia and lack of sleep. (11) The interaction between stressful experiences and sleep perceptions affects the level of BDNF. (26) Nurses who served at night had less sleep time than nurses who served during the day, so this caused a decrease in BDNF levels.

Nutrition can induce brain-derived neurotrophic factor (BDNF) which is a mediator of neural plasticity. Excess daily food intake continuously can lead to excess body weight which can increase BDNF gene levels (27). In this study, a half of the 89 nurses were overweight, namely overweight and obese, 27.0% and 23.5%, respectively. However, the analysis results show that the nutritional status of the nurses did not correlate with BDNF gene's levels. But, there was a tendency that nurses with overnutrition had higher levels of BDNF gene (9.29324 ng/ml) than nurses with normal nutritional status (8.60363 ng / ml) and nurses with undernutrition (7.98100 ng/ml). In similar, ther studies have shown that no significant association has been found between psychological stress and Body Mass Index (BMI), body composition, and another metabolism. (28).

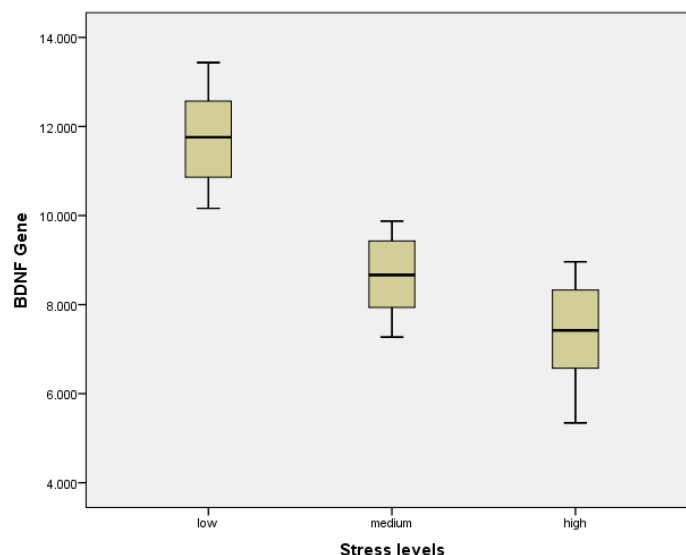


Figure 2. BDNF serum values. Box plot of serum BDNF concentration (ng/ml) in nurses according to stress levels

Based on the results, it was found that there was a significant relationship between stress levels and BDNF gene levels in nurses. This shows that the higher the stress level of the nurse, the lower the BDNF gene levels in the blood. BDNF levels decreased and had a substantial effect on stress. (10,11) Research conducted by Giese et al (2013), showed that there was a relationship between stress and BDNF in subjects without insomnia. (26) A case-control study conducted for 4 years was found. That there was a decrease in serum BDNF levels in major depressive disorders and minor depressive disorders with major depressive disorder history. (29-33) There was also a decrease in serum BDNF levels in schizophrenia patients. (34-35)

V. CONCLUSION

The results of this study indicate that work shifts and stress levels of nurses are associated with decreased levels of BDNF. From these results, we can conduct further research on the relationship between demography, genetic background, and the environment with decreased levels of the BDNF gene.

ACKNOWLEDGMENT

The author would like to express our gratitude and high appreciation for the support of the Faculty of Medicine and Health, Universitas Muhammadiyah Jakarta and the Faculty of Medicine, Universitas Hasanuddin, Makassar in the success of this research. The author would like to thank laboratory assistant for their excellent technical laboratory work in the Laboratory Faculty of Medicine, Universitas Hasanuddin, Makassar, Indonesia. Furthermore, the author would like to appreciate all nurses at the Cempaka Putih Islamic Hospital Jakarta, in Central Jakarta, Indonesia who are respondents in this study.

DISCLOSURE OF INTEREST

The authors declare that they have no conflicts of interest concerning this article.

FUNDING SOURCE

The source of financial support in this research is the Faculty of Medicine and Health, Universitas Muhammadiyah Jakarta.

REFERENCES

1. French S, Lenton R, Waltes V, Eyles J. An Empirical Evaluation of an Expanded Nursing Stress Scale. *J Nurs Meas.* 2000;8(2):161–78.
2. Moustaka E. Sources and effects of work-related stress in nursing. *Heal Sci J.* 2011;4:210–6.
3. Kemenkes RI. Profil Kesehatan Indonesia Tahun 2019. Kementerian Kesehatan RI. 2020.
4. Cox T, Griffiths A. Work-related stress in nursing: Controlling the risk to health University of Nottingham with Professor Sue Cox Loughborough University of Technology. 1996. 49 hal.
5. Dhriyasa C, Prasathkumar M, Becky R, Anisha S, Sadhasivam S, Essa MM, et al. Social and Biological Parameters Involved in Suicide Ideation During the COVID-19 Pandemic: A Narrative Review. *Int J Tryptophan Res.* 2020;13(December).
6. Permatasari, T. A. E., Rizqiya, F., Kusumaningati, W., Suryaalamshah, I. I., & Hermiwahyoeni, Z. (2021). The effect of nutrition and reproductive health education of pregnant women in Indonesia using quasi experimental study. *BMC Pregnancy and Childbirth*, 21(1), 1-15.
7. Haile KK, Asnakew S, Waja T, Kerbih HB. Shift work sleep disorders and associated factors among nurses at federal government hospitals in Ethiopia: A cross-sectional study. *BMJ Open.* 2019;9(8):1–8.

8. Koh SJ, Kim M, Oh DY, Kim BG, Lee KL, Kim JW. Psychosocial stress in nurses with shift work schedule is associated with functional gastrointestinal disorders. *J Neurogastroenterol Motil.* 2014;20(4):516–22.
9. Azmi NASM, Juliana N, Teng NIMF, Azmani S, Das S, Effendy N. Consequences of circadian disruption in shift workers on chrononutrition and their psychosocial well-being. *Int J Environ Res Public Health.* 2020;17(6).
10. Sanlier N, Unusan N. The relationship between body weight and stress and nutritional status in Turkish women. *Pakistan J Nutr.* 2007;6(4):339–44.
11. Phillips C. Brain-Derived Neurotrophic Factor, Depression, and Physical Activity: Making the Neuroplastic Connection. *Neural Plast.* 2017;2017.
12. Schmitt K, Holsboer-Trachslers E, Eckert A. BDNF in sleep, insomnia, and sleep deprivation. *Ann Med.* 2016;48(1–2):42–51.
13. Pezet S, Malsangio M. Brain-derived neurotrophic factor as a drug target for CNS disorders. *Expert Opin Ther Targets.* Oktober 2004;8(5):391–9.
14. Nowacka M, Obuchowicz E. BDNF and VEGF in the pathogenesis of stress-induced affective diseases: An insight from experimental studies. *Pharmacol Reports.* 2013;65(3):535–46.
15. Taliaz D, Loya A, Gersner R, Haramati S, Chen A, Zangen A. Resilience to chronic stress is mediated by hippocampal brain-derived neurotrophic factor. *J Neurosci.* 2011;31(12):4475–83.
16. Muller M. Brain-derived Neurotrophic Factor (BDNF): A New Marker to Estimate Stress Effects on Neuronal Plasticity. *MVZ Labor Ravensbg.* 2016;1–2.
17. Zhang J, Yao W, Hashimoto K. Brain-derived Neurotrophic Factor (BDNF)-TrkB Signaling in Inflammation-related Depression and Potential Therapeutic Targets. *Curr Neuropharmacol.* 2016;14:721–31.
18. Surachmanto EE, Hatta M, Islam AA, Wahid S. Association between asthma control and Interleukin-17F expression levels in adult patients with atopic asthma. *Saudi Med J.* Juli 2018;39(7):662–7.
19. Purnamanita, Budu, Hatta M, Massi MN, Natzir R, Ichsan AM, et al. The effectiveness of triamcinolone injection on risk of postoperative operations with the conjunctiva autograft technique and its association with change of VEGF mRNA Expression. *Biomed Pharmacol J.* 2020;13(2):543–9.
20. Wibisono JJ, Rauf S, Hatta M, Natsir R, Massi MN, Husni Cangara M, et al. Yin Yang 1 (YY1) and P53 Gene Expression Analysis in Cervical Cancer and Its Relationship with Cancer Staging. *Biomed Pharmacol J.* 2020;13(3):1095–101.
21. Mariana N, Asadul Isl A, Hatta M, Fransiscus H. IL23 mRNA Expression in Hirschsprung-Associated Enterocolitis. *J Med Sci.* 2020;20(2):39–43.
22. Gunawan I, Hatta M, Benyamin AF, Islam AA. The Hypoxic Response Expression as a Survival Biomarkers in Treatment-Naive Advanced Breast Cancer. *Asian Pac J Cancer Prev.* Maret 2020;21(3):629–37.
23. Mas Rusyati LM, Hatta M, Widiiana IGR, Adiguna MS, Wardana M, Dwiyantri R, et al. Higher Treg FoxP3 and TGF- β mRNA Expression in Type 2 Reaction ENL (Erythema Nodosum Leprosum) Patients in Mycobacterium leprae Infection. *Open Microbiol J.* 2020;14(1):304–9.
24. Farsida, Hatta M, Patellongi I, Prihantono, Shabariyah R, Larasati Laras RA, et al. The correlation of Foxp3 + gene and regulatory T cells with scar BCG formation among children with Tuberculosis. *J Clin Tuberc other Mycobact Dis.* Desember 2020;21:100202.
25. He SC, Wu S, Wang C, Du XD, Yin G, Jia Q, et al. Interaction between job stress and the BDNF Val66Met polymorphism affects depressive symptoms in Chinese healthcare workers. *J Affect Disord.* 2018;236(August):157–63.
26. Lee I Te, Sheu WHH, Lee WJ, Chen DY. Serum brain-derived neurotrophic factor predicting reduction in pulse pressure after a one-hour rest in nurses working night shifts. *Sci Rep.* 2018;8(1):1–10.
27. Giese M, Unternaehrer E, Brand S, Calabrese P, Holsboer-Trachslers E, Eckert A. The Interplay of Stress and Sleep Impacts BDNF Level. *PLoS One.* 2013;8(10).
28. Permatasari, T.A.E., Widjajanti, W., Sunarto, A., Andriyani., Ramadhan, A.I. (2020). Factors Related to the Granting of Colostrum in Newborn Baby with Caesarean Section in Hospital Government at Banten, Indonesia. *Food Science and Technology,* 8(3), 61-72.
29. Hansen SL, Lorentzen J, Pedersen LT, Hendrich FL, Jorsal M, Pingel J, et al. Suboptimal nutrition and low physical activity are observed together with reduced plasma brain-derived neurotrophic factor (BDNF) concentration in children with severe cerebral palsy (CP). *Nutrients.* 2019;11(3).
30. Permatasari, T. A. E., Sartika, R. A. D., Achadi, E. L., Purwono, U., Irawati, A., Ocviyanti, D., & Martha, E. (2018). Exclusive breastfeeding intention among pregnant women. *Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal),* 12(3), 134-141
31. Syafruddin, A., Permatasari, T.A.E., Ramadhan, A.I. (2020) Analysing the relationship of mini student oral case analysis (soca) test and mini objective structured clinical examination (osce) with the national doctor professional competency test in Indonesia. *International Journal of Innovation, Creativity and Change,* 11(12), pp. 668–674
32. Riffer F, Sprung M, Münch H, Kaiser E, Streibl L, Heneis K, et al. Relationship between psychological stress and metabolism in morbidly obese individuals. *Wien Klin Wochenschr.* 2020;132(5):139–49.
33. Ihara K, Yoshida H, Jones PB, Hashizume M, Suzuki Y, Ishijima H, et al. Serum BDNF levels before and after the development of mood disorders: A case–control study in a population cohort. *Transl Psychiatry.* 2016;6(4):e782-7.
34. Carlino D, Leone E, Di Cola F, Baj G, Marin R, Dinelli G, et al. Low serum truncated-BDNF isoform correlates with higher cognitive impairment in schizophrenia. *J Psychiatr Res.* 2011;45(2):273–9.
35. Permatasari, T. A. E., & Sudiartini, N. W. (2020). Do Health Workers Play a Role in Exclusive Breastfeeding among Working Mothers in Industrial Area?. *Journal of nutritional science and vitaminology,* 66(Supplement), S94-S98.