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RESEARCH ARTICLE

The Relationship between Brain-derived Neurotrophic Factor (BDNF) Levels and Cognitive Function in the Elderly

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ABSTRACT

Human physiological function will decline with age, including a decline in cognitive function. Brain-derived neurotrophic factor (BDNF) is one of the neurotrophins of the neurotrophic group. BDNF is involved in synaptic development, plasticity, and cognitive function and is elevated in ischemic stroke. So, this study aims to analyze the relationship between BDNF levels and cognitive function in the elderly. This study was conducted in Gowa Regency, Indonesia. The cross-sectional research design involved 64 older adults aged 60 to 75. BDNF levels were measured by ELISA and cognitive function using the Indonesian version of the Montreal Cognitive Assessment (MoCA-INA) and were variables to be analyzed. Sex, age, education level and occupation affected cognitive function, and there was a strong correlation between BDNF levels and cognitive function. The cut-off level of BDNF ≤ 1.99 ng/mL had a sensitivity of 82.9% and a specificity of 85.7% as a marker of cognitive dysfunction. Serum BDNF levels are significant for cognitive function impairment in the elderly

INTRODUCTION

The increase in the number of elderly yearly will cause *an aging population*. When individuals enter old age, the brain's nerves begin to decline in the form of an inability to process new information and retrieve information from memory. Therefore, the decline in cognitive function causes several problems in older people (Prahasasgita and Lestari, 2023). There is an increase in the prevalence of cognitive disorders along with age, where the prevalence of cognitive disorders, namely *Mild Cognitive Impairment* (MCI) over the age of 60 years, is estimated to be around 42% worldwide (Hu et al., 2017). The incidence of cognitive impairment in patients aged 75-79 is 22.5 per 1000. The prevalence of Mild Cognitive Impairment in Asian countries reaches 17.1%, and in developing countries, it is predicted to increase to 100% between 2001 and 2040 (Gillis et al., 2019). A person is said to have a decline in cognitive function when showing three or more of the symptoms in the form of disturbances in terms including attention, memory, the orientation of place and time, construction and execution abilities (Klimova et al., 2017; Sheppard et al., 2020). The decline in cognitive function

can be influenced by various factors, both from the individual and the environment (Zainotto et al., 2018). Individual factors include age, gender, education level, genetic factors, and a history of diseases such as stroke (Zhang and Bi, 2020; Farokhi-Sisakht et al., 2019)

Various biomarkers have been widely developed to detect cognitive impairment due to degenerative processes as early as possible, one of which is brain-derived neurotrophic factor (BDNF) (Turana and Handayani, 2021). Currently, the study of BDNF is still being developed. It is in demand because BDNF has a vital role in long-term potentiation, a form of synaptic plasticity currently thought to be a long-term cellular model of memory (Cunha et al., 2010). Several clinical studies have shown a close link between BDNF and the presence of cognitive impairment. A significant decrease in peripheral BDNF levels due to aging is a predisposing factor for the clinical manifestation of dementia in old age (Dogliotti et al., 2010). Optimism using BDNF as a biomarker is increasingly popular because there is experimental evidence that BDNF can cross the blood-brain barrier so that peripheral BDNF levels are the same as BDNF levels in the brain (Laske et al., 2007; Komulainen et al., 2008).

RESEARCH METHOD

This type of observational analytical research using a cross-sectional study design was conducted in Bontosunggu Village, South Bontonompo District, Gowa Regency from August to December 2024. with the criteria of the elderly who are 60-75 years old, do not have mental disorders and can read and write.

The sociodemographic questionnaire and the Indonesian version of the Montreal Cognitive Assessment Instrument (MoCA-Ina) were used to collect data. The sociodemographic questionnaire includes age, gender, marital status, education level, occupation, and prayer activities. Cognitive function was assessed with MoCA-Ina. The instrument has eight dimensions with varying points: executive visuospatial examination (5 points), object naming (3 points), memory (0 points), attention (6 points), language ability (3 points), abstraction (2), and procrastination. Memory (5 points), and orientation (6 points). The maximum value is 30. A total score of > 25 is categorized as normal cognitive function. The result of CVI was 0.82, and Cronbach's alpha was 0.963 for reliability (Husein et al., 2010). BDNF levels were determined through venous blood sampling and measured using the Enzyme-Linked Immunosorbent Assay (ELISA) Method (Naegelin et al., 2018). The research began after receiving ethical approval from the Health Research Ethics Commission, Faculty of Medicine, Hasanuddin University with Letter No. 141/UN4.6.4.5.31/PP36/2023 and Protocol No. UH23020070. The results of the study were analyzed using Microsoft Excel and SPSS 24.0. The data is presented in the form of a cross-tabulation table.

RESULTS

Table 1 shows the characteristics of respondents of the female gender who experience cognitive impairment based on the MoCA-Ina score of 24 people (38.1%) and four men (6.3), the age range of 66-70 years who experience cognitive impairment as many as 17 people (27.0%), marital status with the marriage category who experience cognitive function impairment as many as 25 people (39.7%), the education level of respondents with the elementary level who experience the most impairment cognitive function, namely 19 people (30.2%) and respondents with jobs as IRTs also experienced the most cognitive function impairment as many as 20 people (31.7%), then the average BDNF level of respondents was 2,473 $\pm$ 1,704 and the average MoCA-Ina score of respondents was 25.4 + 2.06. The statistical test results were obtained by gender, age, education and meaningful occupation with a decrease in the cognitive function of the elderly.

Table 1: Essential characteristics of respondents (n=64)

Characteristic	Cognitive Function		Total (%)	p-value
	Annoyed (%)	Normal (%)		
Gender				
Man	4 (6.3)	14 (21.9)	17 (28.1)	0.030*
Woman	24 (38.1)	22 (34.9)	46 (73.0)	
Age (Years)				
60-65	9 (14.3)	23 (36.5)	32 (50.8)	0.027*
66-70	17 (27.0)	10 (15.6)	26 (41.3)	
>71	2 (3.2)	3 (4.7)	5 (7.9)	
Marital status				
Marry	25 (39.1)	35 (54.7)	60(93.8)	0.193*
Not yet	3 (4.7)	1 (1.6)	4 (6.3)	
Education				
Elementary school	19 (30.2)	5 (7.9)	24 (38.1)	
Junior high school	7 (11.1)	18 (28.6)	25 (39.7)	0.001*
Senior high school	1 (1.6)	6 (9.3)	6 (10.9)	
Diploma	1 (1.6)	5 (7.9)	6 (9.5)	
Bachelor	0 (0.0)	2 (3.2)	2 (3.2)	
Job				
IRT	20 (31.7)	15 (23.8)	35 (55.5)	
Farmer	7 (11.1)	11 (17.2)	17 (28.3)	0.045*
Self-employed	1 (1.6)	7 (11.1)	8 (12.7)	
Retired	0 (0.0)	3 (4.8)	3 (4.8)	
BDNF (mean + SD)	**2.473 ± 1.704**			
MoCa-Ina Score	**25.4 ± 2.06**			

*Chi-Square Test

Table 2 shows that based on the statistical results, BDNF levels strongly correlate with cognitive function measured by MoCA-INA.

Table 2: Correlation of BDNF Levels with MoCA-INA Score

Variable	Cognitive Function	
	P	r
BDNF levels	0.000	0.757*

*Spearman correlation test

Figure 1 shows that based on the ROC curve analysis, the Cut Off BDNF level of ≤ 1.99 ng/mL has a sensitivity of 83.3% and a specificity of 85.7% as well as a positive prediction value of 89.4% and a negative prediction value of 83.4% with an AUC of 94.0%.

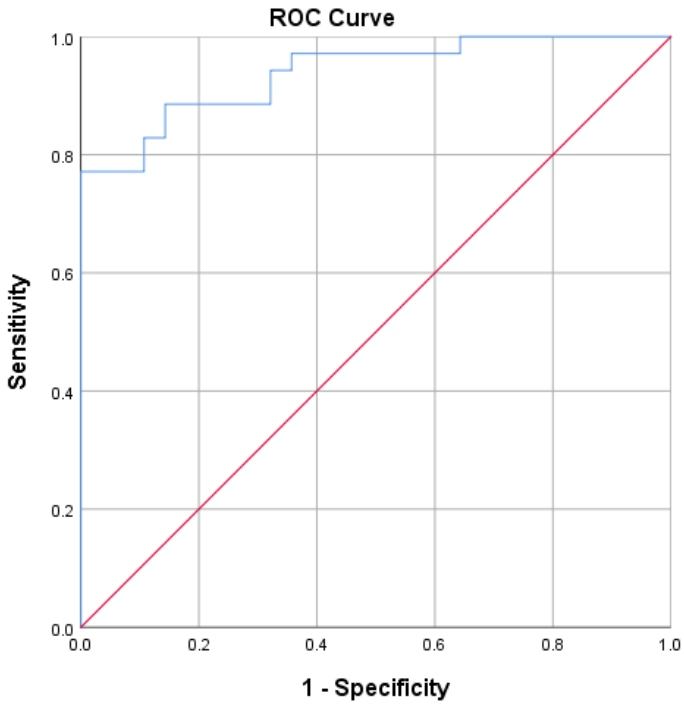

Figure 1: BDNF ROC Curve to MoCA-INA Score

Table 3 shows that based on the statistical test results, a P value of < 0.05 was obtained, which means that the cut-off of BDNF levels ≤ 1.99 ng/mL has a significant relationship with cognitive function impairment in the elderly.

Table 3: Cut-off relationship of BDNF levels with cognitive function in the elderly

BDNF Cut Off: 1.99 ng/mL	Cognitive Function				Total		p-value
	Annoyed		Normal				
	n	%	N	%	N	%	
≤ 1.99	25	89.4	6	16.6	31	48.4	0.000*
> 1.99	3	10.6	30	83.4	32	51.6	
Jumlah	28	100	36	100	64	100	

*Chi-Square Test

DISCUSSION

Naturally, human physiological functions, including cognitive function, decline with age. Of the 64 respondents based on age grouping, the age group of 66-70 years had the most cognitive function impairment (17.0%). Aging causes changes in brain size, blood vessels, and cognition. The brain shrinks with age, and changes occur at all levels, from molecules to morphology, which in itself can cause a decline in cognitive function (Peters, 2006). Various homeostatic reserves in the elderly begin to decrease. Therefore, there is a decrease in the supply of glucose and oxygen, which are the primary sources of nutrients for brain metabolism; this disrupts the brain's metabolic pathways, impacting cognitive function disorders (Sundariyati et al., 2015). The gender in this study was female

(73.0%). The results of the Central Statistics Agency (2022) in eight provinces in Indonesia that have entered the structure of the elderly population found that based on gender data, there are more elderly women than elderly men, namely 51.81% compared to 48.19%. Factors that affect a person's cognitive function are age, gender, education and socio-cultural status, psychosocial conditions, environment and occupation (Ardian and Nuraini, 2018). Women are more at risk of cognitive decline due to the role of endogenous sex hormone levels in changes in cognitive function. Estrogen receptors have been found in areas of the brain that play a role in learning and memory functions, such as the hippocampus. Low levels of estradiol in the body have been linked to decreased general cognitive function and verbal memory. Estradiol is thought to be neuroprotective and can limit damage due to oxidative stress and is seen as a neuronal protector against amyloid toxicity in Alzheimer's patients (Dong *et al*., 2010). In a study conducted in both men and women, it was suggested that BDNF was not associated with cognition in men. However, BDNF levels may indicate impairment of memory and general cognitive function in older women (Budni et al., 2015). As for the level of education, the respondents were more at the elementary education level (38.1%) and junior high school (39.7%). Education is a process of life experience and an intellectual stimulation process that affects a person's cognition. A low level of education means that mental experiences and the environment also have less impact on intellectual stimulation, which can result in poor cognition. The results of research conducted by Shiddieqy et al. (2022) showed that education affects cognitive function, where the elderly who do not go to school tend to experience cognitive function problems compared to those who are highly educated. Respondents' employment status was dominated by IRT, with a percentage (55.5%). Among people living in rural areas, there is a recognition that women are considered to not have a high work culture compared to men. Conditions like this are due to the prevailing customs and culture, where cultural values place women in domestic affairs in the household so that they cannot develop their potential. In addition to the prevailing cultural values, this condition is also caused by an educational pattern that does not lead them to become trained personnel. This study's results are from research conducted by Fazriana (2020) which showed that most elderly respondents working as IRTs have a lower cognitive category than retired seniors.

The results of this study obtained the average BDNF level of the respondents which was 2,473 ng/mL. And the average MoCA-Ina score of the respondents was 25.4 $\pm$ 2.06. This study found a significant relationship between BDNF levels and MoCA-INA scores. Based on previous research, higher levels of BDNF are associated with better cognitive test performance in healthy adults (Madeng et al., 2023). BDNF is a significant factor in hippocampus shrinkage and decreased memory function in the elderly (Erickson et al., 2010). Simultaneous improvements in cognitive function and serum levels of BDNF can also be found after regular physical exercise and high levels of BDNF correlate with improvements in cognitive function (Niimi et al., 2016; Ashcroft et al., 2022).

Age is a strong predictor of degenerative factors in the brain. Changes in brain structure in older people include a decrease in brain volume, although it does not occur in all parts of the brain. The parts of the brain most affected by aging are the frontal and hippocampus. The hippocampus is involved in learning and memory processes and in the modulation of emotional control (Hölzel et al., 2011). BDNF is widely expressed in brain regions with high levels of plasticity, namely in the hippocampus, hypothalamus, and cortex. BDNF also regulates synaptic transmission and expression changes regulated by neuronal activity (Arancio and Chao, 2007). The expression of BDNF in the central nervous system is influenced by various factors in the brain, such as seizures, stress, ischemia, and hypoglycemia. Changes in its expression can lead to several pathological conditions, such as depression, Alzheimer's, Parkinson's disease, and epilepsy (Lima Giacobbo et al., 2019).

In the brain, BDNF is active in the hippocampus, cortex, and forebrain, which have functions in long-term thinking and memory processes. In addition to the brain, BDNF is also expressed in the retina, motor neurons, kidneys, saliva, and prostate (Mandel et al., 2009). BDNF plays a role in central nervous system neurons to support the presence of neurons, aid in the growth and differentiation of

new neurons, increase synaptogenesis, play a role in neurogenesis, and are able to protect *Neural Stem Cells* (NSCs) and *Neural Precursor Cells* (NPCs) (Pansri et al., 2021).

In this study, the sensitivity and specificity values of BDNF levels in the prediction of cognitive function of the elderly were obtained. This study obtained a sensitivity of 82.9% and a specificity of 85.7% and was meaningful. The Receiver Operating Characteristic (ROC) analysis shows that a cut-off serum BDNF level of ≤ 1.99 ng/mL can predict cognitive impairment based on the MoCA-Ina score. This condition allows the serum BDNF examination to predict outcomes in the elderly and prevent cognitive function disorders

CONCLUSION

High levels of BDNF are significantly associated with good cognitive function in the elderly. As we age, BDNF levels may decrease. There was a meaningful relationship between BDNF rates and cognitive function measured using MoCA-INA in the elderly. BDNF can be used as a predictor of cognitive function in the elderly. These findings are short-term, so measurements are needed over a more extended period, more comprehensive coverage, and a larger population.

Author's contribution

HP, ELS, KAE, and VH developed the idea, researched, and wrote the manuscript together. N and RA determined the research design and assisted in discussing the research results, and JT evaluated molecular genetic studies and AAZ as statistical analysis. All authors have read and approved this final manuscript for publication.

Limitation

Some unmeasured factors that may influence the study's findings, such as this study, do not fully account for the potential confounding variables that can affect BDNF levels and cognitive function. Factors such as comorbidities, dietary habits, smoking habits, medication consumption, and physical activity levels may affect the results but are not adequately measured in the analysis. External factors such as stress and health conditions may affect BDNF levels and are not adequately considered in the study design or analysis. This initial study focuses more on the relationship between BDNF levels and cognitive function of the elderly, so it is necessary to explore more widely in future research.

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REFERENCES

Arancio, O., & Chao, M. V. (2007). Neurotrophins, synaptic plasticity and dementia. *Current opinion in neurobiology*, *17*(3), 325–330. https://doi.org/10.1016/j.conb.2007.03.013

Ardian, I., & Nuraini, N. (2018). The Effectiveness of Brain Gym and Brain Vitalization Gym in Increasing Cognitive Function of The Elderly in Pucang Gading Social Rehabilitation Unit of Semarang. *NurseLine Journal, 3*(1), 38-45. https://doi.org/10.19184/nlj.v3i1.7001

Ashcroft, S. K., Ironside, D. D., Johnson, L., Kuys, S. S., & Thompson-Butel, A. G. (2022). Effect of Exercise on Brain-Derived Neurotrophic Factor in Stroke Survivors: A Systematic Review and Meta-Analysis. *Stroke*, *53*(12), 3706–3716. https://doi.org/10.1161/STROKEAHA.122.039919

Badan Pusat Statistik. 2021. Statistik Penduduk Lanjut Usia 2021. BPS. Jakarta. https://www.bps.go.id/id/publication/2021/12/21/c3fd9f27372f6ddcf7462006/statistik-penduduk-lanjut-usia-2021.html

Budni, J., Bellettini-Santos, T., Mina, F., Garcez, M. L., & Zugno, A. I. (2015). The involvement of BDNF, NGF and GDNF in aging and Alzheimer's disease. *Aging and disease*, *6*(5), 331–341. https://doi.org/10.14336/AD.2015.0825

Cunha, C., Brambilla, R., & Thomas, K. L. (2010). A simple role for BDNF in learning and memory?. *Frontiers in molecular neuroscience*, *3*, 1. https://doi.org/10.3389/neuro.02.001.2010

Dogliotti, G., Galliera, E., Licastro, F., & Corsi, M. M. (2010). Age-related changes in plasma levels of BDNF in Down syndrome patients. *Immunity & ageing : I & A*, *7*, 2. https://doi.org/10.1186/1742-4933-7-2

Dong, X., Wilson, R. S., Mendes de Leon, C. F., & Evans, D. A. (2010). Self-neglect and cognitive function among community-dwelling older persons. *International journal of geriatric psychiatry*, *25*(8), 798–806. https://doi.org/10.1002/gps.2420

Erickson, K. I., Prakash, R. S., Voss, M. W., Chaddock, L., Heo, S., McLaren, M., Pence, B. D., Martin, S. A., Vieira, V. J., Woods, J. A., McAuley, E., & Kramer, A. F. (2010). Brain-derived neurotrophic factor is associated with age-related decline in hippocampal volume. *The Journal of neuroscience : the official journal of the Society for Neuroscience*, *30*(15), 5368–5375. https://doi.org/10.1523/JNEUROSCI.6251-09.2010

Farokhi-Sisakht, F., Farhoudi, M., Sadigh-Eteghad, S., Mahmoudi, J., & Mohaddes, G. (2019). Cognitive Rehabilitation Improves Ischemic Stroke-Induced Cognitive Impairment: Role of Growth Factors. *Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association*, *28*(10), 104299. https://doi.org/10.1016/j.jstrokecerebrovasdis.2019.07.015

Fazriana, E. (2020). Profil Fungsi Kognitif Berdasarkan Karakteristik Lansia Binaan Sahabat Lansia. *Jurnal Keperawatan Silampari*, *4*(1), 314-321.

Gillis, C., Mirzaei, F., Potashman, M., Ikram, M. A., & Maserejian, N. (2019). The incidence of mild cognitive impairment: A systematic review and data synthesis. *Alzheimer's & dementia (Amsterdam, Netherlands)*, *11*, 248–256. https://doi.org/10.1016/j.dadm.2019.01.004

Hölzel, B. K., Carmody, J., Vangel, M., Congleton, C., Yerramsetti, S. M., Gard, T., & Lazar, S. W. (2011). Mindfulness practice leads to increases in regional brain gray matter density. *Psychiatry research*, *191*(1), 36–43. https://doi.org/10.1016/j.pscychresns.2010.08.006

Hu, C., Yu, D., Sun, X., Zhang, M., Wang, L., & Qin, H. (2017). The prevalence and progression of mild cognitive impairment among clinic and community populations: a systematic review and meta-analysis. *International psychogeriatrics*, *29*(10), 1595–1608. https://doi.org/10.1017/S1041610217000473

Husein, N., Lumempouw, S. F., Ramli, Y., & Herqutanto (2010). Montreal cognitive assessment versi Indonesia MoCAIna untuk skrining gangguan fungsi kognitif. *Neurona*.

Klimova, B., Valis, M., & Kuca, K. (2017). Cognitive decline in normal aging and its prevention: a review on non-pharmacological lifestyle strategies. *Clinical interventions in aging*, *12*, 903–910. https://doi.org/10.2147/CIA.S132963

Komulainen, P., Pedersen, M., Hänninen, T., Bruunsgaard, H., Lakka, T. A., Kivipelto, M., Hassinen, M., Rauramaa, T. H., Pedersen, B. K., & Rauramaa, R. (2008). BDNF is a novel marker of cognitive function in ageing women: the DR's EXTRA Study. *Neurobiology of learning and memory*, *90*(4), 596–603. https://doi.org/10.1016/j.nlm.2008.07.014

Laske, C., Stransky, E., Leyhe, T., Eschweiler, G. W., Maetzler, W., Wittorf, A., Soekadar, S., Richartz, E., Koehler, N., Bartels, M., Buchkremer, G., & Schott, K. (2007). BDNF serum and CSF concentrations in Alzheimer's disease, normal pressure hydrocephalus and healthy controls. *Journal of psychiatric research*, *41*(5), 387–394. https://doi.org/10.1016/j.jpsychires.2006.01.014

Lima Giacobbo, B., Doorduin, J., Klein, H. C., Dierckx, R. A. J. O., Bromberg, E., & de Vries, E. F. J. (2019). Brain-Derived Neurotrophic Factor in Brain Disorders: Focus on Neuroinflammation. *Molecular neurobiology*, *56*(5), 3295–3312. https://doi.org/10.1007/s12035-018-1283-6

Madeng, A. A. M., Bahar, A., Akbar, M., Zainuddin, A. A., Bintang, A. K., & Kaelan, C. (2023). Hubungan Kadar Brain-Derived Neurotrophic Factor (BDNF) Serum Dengan Fungsi Kognitif Penderita Stroke Iskemik. *Molucca Medica*, *16*(2), 169-176.

Mandel, A. L., Ozdener, H., & Utermohlen, V. (2009). Identification of pro-and mature brain-derived neurotrophic factor in human saliva. *Archives of oral biology*, *54*(7), 689–695. https://doi.org/10.1016/j.archoralbio.2009.04.005

Naegelin, Y., Dingsdale, H., Säuberli, K., Schädelin, S., Kappos, L., & Barde, Y. A. (2018). Measuring and Validating the Levels of Brain-Derived Neurotrophic Factor in Human Serum. *eNeuro*, *5*(2), ENEURO.0419-17.2018. https://doi.org/10.1523/ENEURO.0419-17.2018

Niimi, M., Hashimoto, K., Kakuda, W., Miyano, S., Momosaki, R., Ishima, T., & Abo, M. (2016). Role of Brain-Derived Neurotrophic Factor in Beneficial Effects of Repetitive Transcranial Magnetic Stimulation for Upper Limb Hemiparesis after Stroke. *PloS one*, *11*(3), e0152241. https://doi.org/10.1371/journal.pone.0152241

Pansri, P., Phanthong, P., Suthprasertporn, N., Kitiyanant, Y., Tubsuwan, A., Dinnyes, A., Kobolak, J., & Kitiyanant, N. (2021). Brain-derived neurotrophic factor increases cell number of neural progenitor cells derived from human induced pluripotent stem cells. *PeerJ*, *9*, e11388. https://doi.org/10.7717/peerj.11388

Peters R. (2006). Ageing and the brain. *Postgraduate medical journal*, *82*(964), 84–88. https://doi.org/10.1136/pgmj.2005.036665

Prahasasgita, M., & Lestari, M. (2023). Stimulasi Fungsi Kognitif Pada Lanjut Usia Di Indonesia: Tinjauan Literatur. *Buletin Psikologi, 31*(2), 247--264. doi:https://doi.org/10.22146/buletinpsikologi.80371

Sheppard, D. P., Matchanova, A., Sullivan, K. L., Kazimi, S. I., & Woods, S. P. (2020). Prospective memory partially mediates the association between aging and everyday functioning. *The Clinical neuropsychologist*, *34*(4), 755–774. https://doi.org/10.1080/13854046.2019.1637461

Shiddieqy, A., Zulfitri, R., & Elita, V. (2022). Analisis Faktor Risiko Yang Berhubungan Dengan Fungsi Kognitif Pada Lansia Suku Melayu. *JKEP*, *7*(1), 12-26. https://doi.org/10.32668/jkep.v7i1.775

Sundariyati, H., Ratep, N., & Westa, W. (2015). Gambaran faktor-faktor yang mempengaruhi status kognitif pada lansia di wilayah kerja puskesmas kubu II, Januari-Februari 2014. *E-Jurnal Med Udayana*, *4*(1).

Turana, Y., & Handayani, Y. S. (2021). Pengaruh Kadar Brain Derived Neurotrophic Factor Pada Hendaya Kognitif Ringan Tipe Amnestik. *NEURONA*, *38*(4).

Zaninotto, P., Batty, G. D., Allerhand, M., & Deary, I. J. (2018). Cognitive function trajectories and their determinants in older people: 8 years of follow-up in the English Longitudinal Study of Ageing. *Journal of epidemiology and community health*, *72*(8), 685–694. https://doi.org/10.1136/jech-2017-210116

Zhang, X., & Bi, X. (2020). Post-Stroke Cognitive Impairment: A Review Focusing on Molecular Biomarkers. *Journal of molecular neuroscience: MN*, *70*(8), 1244–1254. https://doi.org/10.1007/s12031-020-01533-8