Eduvest – Journal of Universal Studies
Volume 5 Number 10, October, 2025
p- ISSN 2775-3735- e-ISSN 2775-3727

Majejaitan Activity and High Serum BDNF Levels as Protective Factors Against Cognitive Impairment in the Elderly

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ABSTRACT
The aging process in the elderly affects not only physical capabilities but also cognitive function. Cognitive impairment in older adults is thought to be associated with physical activity and neurotrophic factors, particularly the serum level of Brain-Derived Neurotrophic Factor (BDNF). Majejaitan—a traditional form of activity involving fine motor coordination and repetitive hand movements—is hypothesized to exert a protective effect against cognitive impairment by increasing serum BDNF levels. This study aimed to examine the role of Majejaitan activity and elevated serum BDNF levels as potential protective factors against cognitive impairment in elderly individuals. An observational case-control study was conducted from November 2024 to January 2025 at the East Denpasar 1 Primary Health Care Center. The participants were women aged 50–60 years, divided equally into two groups: a case group (with cognitive impairment) and a control group (without cognitive impairment), each consisting of 19 participants. Cognitive impairment was assessed using the Indonesian version of the Montreal Cognitive Assessment (MoCA-Ina), with scores below 26 indicating impairment. Majejaitan activity was defined as performing the activity at least three times per week for 30–60 minutes, and participants were classified as either active or inactive. Serum BDNF levels were measured using a sandwich-type ELISA with the Human BDNF ELISA Kit (BT LAB) and were categorized as high or not high based on receiver operating characteristic (ROC) curve analysis.

KEYWORDS *Majejaitan Activity, Brain-Derived Neurotrophic Factor, Cognitive Dysfunction, Elderly*

INTRODUCTION

The capacity of tissues to regenerate and maintain normal, physiological form and function declines with age (Brunet, Goodell, & Rando, 2023; Rando & Jones, 2021). The biological phenomena that occur in the elderly involve multifactorial changes, affecting not only physical abilities but also cognitive functions such as memory, attention, language, and problem-solving abilities. The aging process is also accompanied by a decline in Brain-Derived Neurotrophic Factor (BDNF), a protein that plays a crucial role in neuroplasticity, brain cell regeneration, and maintaining neuronal health and function. BDNF levels can be preserved by maintaining physical activity throughout life (Campbell, Donoghue, Ghosh, Nelson, & Roth, 2022; Murawska-Ciałowicz et al., 2021; Vecchio et al., 2018). High serum BDNF levels are believed to protect against cognitive impairment, which often occurs with age. Changes resulting from cognitive impairment during the aging process have wide-ranging effects, including economic problems, disability, and emotional distress for sufferers, their families, and their communities. This, in turn, impacts overall quality of life and well-being.

In recent decades, there has been significant growth in the elderly population in Indonesia, defined as those aged 60 years and older. Indonesia's total elderly population ranks

fourth highest in the world. By 2023, the proportion of elderly people in Indonesia was predicted to reach 11.75% (Aprilyawan, Makrup, Wulandari, & Waspada, 2025; Azis, 2025; Riani, Wijayanto, & Rivai, 2024). Bali Province has the largest elderly population compared to other provinces, increasing from 11.30% in 2019 to 12.37% in 2022 (Buckley, 2022). Rising life expectancy, which now averages 73 years for women and 69 years for men, contributes to this growth (BPS, 2020). This rapid demographic shift creates significant challenges in the health, social, and economic sectors.

The World Health Organization (WHO) has predicted that the world must prepare for an aging society. The global population aged 60 years and older is expected to reach 2 billion by 2050, up from 1 billion in 2019 (Grinin, Grinin, & Korotayev, 2023; Gu, Andreev, & Dupre, 2021; Xi, Lin, & Hao, 2022). Cognitive impairment is one of the most common health problems in older adults. Currently, approximately 50 million people live with severe cognitive impairment, most of them in developing countries. The number of people with cognitive impairment will continue to rise in both developed and developing nations, with estimates predicting 82 million cases by 2030 and 152 million by 2050 (Liu & Geng, 2025; Memudu, Olukade, & Alex, 2024).

In Indonesia, the prevalence of cognitive impairment is also expected to increase. According to Alzheimer's Disease International, about 1.2 million people in Indonesia currently live with cognitive impairment, and this figure is projected to grow further by 2030 (Organization, 2021).

BDNF, a member of the neurotrophin family expressed in the central nervous system, functions as a regulator of normal brain growth, homeostasis, and plasticity. It is vital for brain development, neuronal survival, and cognitive processes such as learning and memory. Neurons secrete BDNF, which plays a key role in synaptic plasticity. In addition to being present in the brain, BDNF is also found in human platelets and megakaryocytes. It is released during blood coagulation and can be measured in serum, making serum BDNF a useful indicator of brain function. BDNF promotes survival and growth in dorsal root ganglion cells, hippocampal neurons, and cortical neurons, and it enhances synaptic transmission. This makes it critical for memory, learning, hippocampal atrophy prevention, and age-related cognitive maintenance. Low BDNF levels are associated with cognitive impairment, neurodegenerative diseases, and Alzheimer's disease (Budni, Bellettini-Santos, Mina, Garcez, & Zugno, 2015).

Evidence shows that high serum BDNF levels can provide a protective effect against cognitive impairment in the elderly. Thus, identifying modifiable factors that elevate BDNF levels remains an important strategy for preventing cognitive decline. Physical activities such as aerobic exercise and repetitive manual movements have been shown to increase serum BDNF levels, supporting cognitive health .

Bali, as a province rich in tradition and culture, has long-standing social activities within families and communities, one of which is *Majejaitan. Majejaitan* is a handicraft activity central to Hindu rituals, requiring precision, concentration, memory retention, and fine finger skills (Mohanapriya & Suriya, 2025). It is taught across generations—children, adolescents, adults, and the elderly—as a deeply rooted cultural heritage. This activity is commonly performed daily, either regularly or intermittently, and predominantly by women. The process produces ritual crafts with specific shapes and sizes, making it both repetitive and mentally engaging.

Studies have consistently demonstrated that older adults who regularly engage in physical activity have a lower risk of developing cognitive impairment compared to sedentary individuals (Cunningham, O'Sullivan, Caserotti, & Tully, 2020). Such activities have been linked to increased BDNF synthesis, which supports neuronal function and psychological well-being.

In the context of aging and cognitive decline, exploring the interaction between cultural physical activities like *Majejaitan,* serum BDNF levels, and cognitive health may provide valuable insights for designing effective interventions. Living in a rapidly changing society, where technological advancements often replace traditional activities, challenges older adults' adaptability and resilience. Nonetheless, evidence of lifelong brain plasticity highlights the importance of sustaining cognitively stimulating and culturally rooted activities to promote well-being, independence, and social participation among older adults.

To date, no study has examined the relationship between *Majejaitan* activity and elevated serum BDNF levels as protective factors against cognitive impairment in older adults in Bali or Indonesia, despite the potential link between culturally embedded skills and brain health. Therefore, this study aims to analyze the role of *Majejaitan* activity and high serum BDNF levels as protective factors against cognitive function disorders in the elderly population within the working area of the East Denpasar Health Center I. By identifying the relationship between this traditional cultural activity and biological markers of brain health, this research seeks to provide scientific evidence supporting the integration of local traditions into health promotion programs for aging populations. The anticipated benefits extend beyond enriching knowledge of culture-based, non-pharmacological interventions. They could also serve as the foundation for developing effective, affordable, and sustainable public health strategies to enhance the quality of life of the elderly in Indonesia.

METHOD

This study is an observational analytical study with a case-control design to understand the ratio of *Majejaitan* activity and high serum BDNF levels as protective factors for cognitive impairment in the elderly. The following is the study design used:

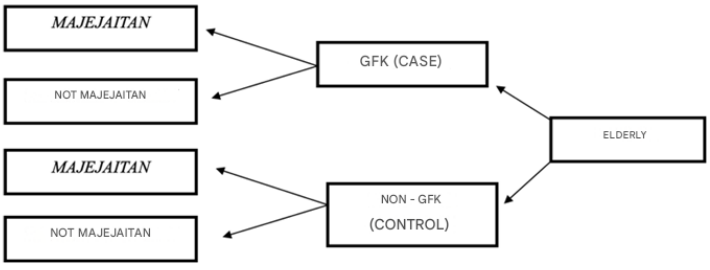

Figure 1. Research Design of Case-Control *Majejaitan* Activities
Source: Primary data, 2025

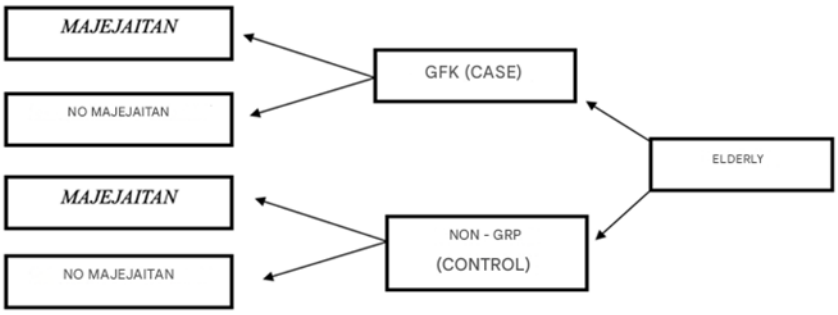

Figure 2. BDNF Level Research Design for Case-Control Patients
Source: Primary data, 2025

Sampling was conducted at the East Denpasar 1 Community Health Center, while serum BDNF levels were measured at the Integrated Biomedical Laboratory, Faculty of Medicine, Udayana University. The study was conducted from November 2024 to January 2025.

The target population for this study is all elderly people. The accessible population for this study is all elderly women aged 50-60 years in the East Denpasar 1 Community Health Center work area who visited the East Denpasar 1 Community Health Center in November 2023.

The research sample consists of study subjects drawn from the accessible population and who meet the inclusion criteria.

Inclusion criteria for the case group:

1. Elderly individuals aged 50-60 years
2. Female
3. Suffering from CFK (Moca-Ina score <26)
4. No mental disabilities
5. Able to read and write and cooperate
6. Willingness to participate in the research after the purpose and objectives of the research procedure have been explained and informed consent has been signed.

Inclusion criteria for the control group:

1. Elderly individuals aged 50-60 years
2. Female
3. Not suffering from CFK (Moca-Ina score 26-30)
4. No mental disabilities
5. Able to read and write and cooperate
6. Willingness to participate in the research after the purpose and objectives of the research procedure have been explained and informed consent has been signed.

Exclusion criteria for this study:

1. Stroke
2. Head trauma
3. Diabetes mellitus
4. Brain tumor
5. Parkinson's disease

6. Brain infection
7. Epilepsy
8. Autoimmune disease
9. Depression
10. Anxiety
11. Banten traders

The sample size in this study was calculated using the formula for unpaired categorical analytical research (Sastroasmoro & Ismael, 2011) as follows:

$$N_1N_2 = \left(\frac{(Z\alpha\sqrt{2PQ}+Z\beta.\sqrt{P1Q1+P2Q2})^2}{(P1-P2)^2}\right) \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (1)$$

N = sample size
Zα = Type 1 error, namely 1.96 (Significant level α = 5%)
Zβ = Type 2 error, namely 0.84 (Significant level β = 20%)
P1 = Proportion for the variable group whose values have been identified (GFK in the elderly is 12% (Eka et al., 2021).
P2 = Proportion of the dependent and independent variables as evaluated by the researcher 40% = 0.4
P = Total proportion of P1 and P2 = (P1 + P2)/2
Q1 = 1 – P1
Q2 = 1 – P2
P1-P2 = Minimum difference in proportions assumed to be significant

Based on the calculation results using this formula, the sample size for the control group and the case group are each at least 19 people, so the minimum sample size in this study is 38 people.

Sampling was conducted using consecutive sampling. All elderly people who visited the East Denpasar 1 Community Health Center and met the inclusion criteria were included in the study sample until the required number was reached.

Research Variables

1. Classification of Research Variables
2. Independent variables: *Majejaitan* activity, education level, occupation, and hypertension
3. Dependent variable: Cognitive dysfunction
4. Control variables: age, gender
5. Confounding variables: Stroke, head trauma, diabetes mellitus, brain tumor, brain infection, Parkinson's disease, depression, anxiety, and autoimmune disease

Operational Definition of Variables

1. *Majejaitan* activity refers to individuals who engage in *Majejaitan* activities ≥3 times a week or for ≥30-60 minutes (Agustana et al., 2023). This was determined based on interview questions, including how long they began engaging in *Majejaitan* activities, the frequency, intensity, duration, and type of *Majejaitan* performed. This is a categorical variable.

2. Brain-derived neurotrophic factor (BDNF) is a member of the neurotrophin family expressed in the central nervous system and functions as a regulator of normal brain growth, homeostasis, and plasticity. BDNF levels were measured in serum using an enzyme-linked immunosorbent assay (ELISA) laboratory test. The examination procedure was performed according to the RayBio® Human BDNF Elisa Kit ELH-BDNF-1 manual. This variable is categorized into high BDNF levels (≥3.91 ng/ml) and low BDNF levels (≥100 ng/ml). This variable is categorical.
3. Cognitive impairment (CFD) is a condition whereby one has difficulty remembering, focusing, learning new things, or making decisions that impact daily life. Cognitive impairment is determined based on the results of the MoCA-Ina test. Data are grouped on a nominal scale, namely a MoCA-Ina score <26 (CFD) and a MoCA-Ina score ≥26-30 (non-CFD) (Husein et al., 2010).
4. Subjects have reached the peak of their formal education by completing school. The following categories are classified according to the national scale: (1) did not complete elementary school, (2) elementary school, (3) middle school, (4) high school, and (5) diploma/college. Years of education are denoted as ≤12 with a high school diploma or higher education, and as >12 with a diploma/college degree. This variable is categorical.
5. Occupation is defined as an activity undertaken by a person or organization through exertion at a specific location and time, sometimes in exchange for money or other benefits, and sometimes out of a sense of social obligation rather than personal gain (Meisartika and Safrianto, 2021). The work performed by the subjects to earn a living is referred to as "occupation data" in this study, which is obtained from anamnesis. This variable is categorized into two groups: employed and unemployed. This variable is categorical.
6. Hypertension is a history of hypertension in the subjects obtained through interviews and medical records from the East Denpasar I Community Health Center. This variable is categorized into two groups: those with a history of hypertension and those without a history of hypertension. This variable is categorical.
7. More frequent and severe seizures are characteristic of epilepsy, a neurological disease with widespread effects on a person's brain, behavior, and social interactions. Epilepsy data, as collected from medical records, refers to the subject's history of epilepsy or seizures. This variable is categorized into two categories: having a history of epilepsy and not having a history of epilepsy. This variable is categorical.
8. Tumors that develop in or spread to the brain are collectively known as brain tumors. Information is collected through patient history, interviews, and necessary physical examinations. This variable is categorized into two groups: having a history of brain tumor and not having a history of brain tumor. This variable is categorical.
9. Anxiety, depression, and stress are assessed using the 21-item DASS-21 questionnaire. To determine depression, the Depression, Anxiety, and Stress Scale (DASS-21) is used. Each scale has three scores, each of which is then summed and interpreted as normal, mild, moderate, severe, and very severe (Indira, 2016). Data are obtained through interviews and/or medical records. This variable is categorized into two groups: having a history of anxiety, depression, and stress and not having a history of anxiety, depression, or stress. This variable is categorical.

10. The metabolic condition known as Type 2 Diabetes Mellitus is defined by high blood sugar levels arising from problems with insulin production or action, or both. The presence of classic symptoms along with a fasting blood glucose level of 126 mg/dL or higher, or a random plasma glucose level of more than 200 mg/dL 2 hours after an oral glucose tolerance test (OGTT), can establish a diagnosis of diabetes mellitus (DM). Classic symptoms include polyuria, polydipsia, weight loss, and a random plasma glucose level. A random blood glucose level of 200 mg/dL or higher, or an HbA1C level of 6.5 mg/dL or lower, as determined by standard procedures (PERKENI, 2021). Interviews, additional examinations, and medical records were used to collect data. There are two categories for this variable: those with a history of DM and those without. This is a categorical variable.
11. Eosinophilic cytoplasmic inclusions, often known as Lewy bodies, and basal ganglia degeneration are pathological hallmarks of Parkinson's disease, a form of parkinsonism (PERDOSSI, 2018). Information was collected through interviews, additional tests, and medical records. This variable was categorized into two groups: those with a history of Parkinson's and those without a history of Parkinson's. This variable is a categorical variable.
12. Stroke is a history of stroke in subjects obtained through interviews and medical records from East Denpasar Community Health Center 1. This variable was categorized into two groups: those with a history of stroke and those without a history of stroke. This variable is a categorical variable.
13. Head trauma is characterized by injury to the scalp, skull, and brain caused by a blow or violent impact to the head, regardless of whether the victim is conscious or not. Information was collected through interviews, additional tests, and patient records. This variable was categorized into two groups: those with a history of head trauma and those without a history of head trauma. This variable is a categorical variable.
14. Head trauma is characterized by injury to the scalp, skull, and brain caused by a blow or violent impact to the head, regardless of whether the victim is conscious or not. Information was collected through interviews, additional tests, and patient records. This variable was categorized into two groups: those with a history of head trauma and those without a history of head trauma. This variable is a categorical variable.
15. In autoimmune diseases, the immune system mistakenly targets healthy tissues and organs, causing damage and disruption to normal body processes. The inflammation and damage characteristic of autoimmune diseases can manifest in any organ or tissue in the body. Various sources, including interviews, additional examinations, and medical records, were used to collect data. This variable was categorized into two groups: those with a history of autoimmune disease and those without a history of autoimmune disease. This variable is a categorical variable.

Research Preparation

The research preparation stage was carried out by submitting ethical clearance and obtaining permits to conduct the research at East Denpasar Community Health Center 1.

Research Sample Selection

1. Female subjects aged 50-60 years at Community Health Center I, East Denpasar, were immediately examined and treated by a community health center doctor.
2. The researcher explained the informed consent to the subject and her family and ensured that they understood the informed consent process. After participating in the study, the researcher asked the subject or family, along with a guardian or impartial witness, to sign the research consent document three times. The researcher then affixed their signatures three times to the research consent document. The next step was to collect consent from the subject, consisting of three copies: one copy to be kept in the medical record at Community Health Center I, East Denpasar, and the other copy to be kept by the researcher.
3. The researcher then matched the subject to the case and control inclusion criteria for the research sample. Subjects were used as the research sample if they met the inclusion requirements. Subjects were not used as the research sample unless they met the inclusion requirements.
4. The researcher then used the research sample exclusion criteria to determine whether the subject was suitable. Subjects were excluded from the study if they met the exclusion criteria. Subjects remained as research samples unless they did not meet the exclusion criteria.
5. Cognitive function measurements in the elderly were conducted using the MoCA-Ina questionnaire. The measurement results were categorized into subjects with GFK (+) if the MoCA-Ina score was <26 and those without GFK (-) if the MoCA-Ina score was ≥26-30.
6. Laboratory personnel took blood samples from patients for BDNF level testing. A 3 ml blood sample was drawn from a vein and stored in an EDTA vacutainer.
7. To test serum BDNF levels, prepare reagents and samples. All reagents were brought to room temperature before use. Prepare a vial tube and prepare a blank and standard solution at a ratio of 5 to 1. Dilute the wash buffer to produce 500 ml of wash buffer. Determine the number of strips needed. Store the remaining strips at 2-8°C after inserting the strips you intend to use. Fill the standard tube with 50 µL of standard solution. Mix 40 µL of sample with 10 µL of anti-BDNF antibody in a sample tube. Then, combine the sample tube with 50 µL of streptavidin-HRP in a standard tube. Mix thoroughly. Incubate at 37 degrees Celsius for 60 minutes after sealing the container with a lid or sealant. After removing the sealer, wash the plate five times using 300 µL of wash buffer, varying the duration between 30 seconds and 1 minute per wash. Add 50 µL of substrate solution A to each tube, followed by 50 µL of substrate solution B. Incubate the sealed plate in the dark. Add 50 µL of stop solution to each tube, turning the blue liquid yellow. Use a microplate reader to obtain the optical density of each tube. Add the stop solution and use a 450 nm microscope no later than 10 minutes later. Proceed with computer-assisted analysis.
8. Researchers enter and evaluate all data related to the study variables using SPSS software. The findings will then be shared.

Afterward, SPSS version 25 was used to statistically analyze the data in the following steps:

1. Descriptive analysis was conducted to gather information about the characteristics of the study participants and the distribution of all study variables. The results of the descriptive analysis were displayed in tabular format.
2. Bivariate analysis was conducted between the independent and dependent variables, using the unpaired categorical nominal scale, using the Chi-Square test. Differences in proportions were declared significant with a p-value <0.05. Furthermore, the odds ratio calculation was used in this study to measure the magnitude of risk by expressing a measure of strength, which is expected to have a value <1.
3. Multivariate analysis was conducted using the logistic regression method because this study's variables were categorical. The logistic regression test was conducted based on the results of the proportion difference test, which showed a significant difference in proportions.

RESULT AND DISCUSSION

This study, an observational analytical study with a case-control design, was conducted in January 2025 at the Denpasar Timur 1 Community Health Center, with a total of 38 subjects meeting inclusion and exclusion criteria. Data collection included assessing GFK conditions using the MoCA-INA questionnaire, interviewing participants regarding their vascular activity using a questionnaire, and drawing blood for measuring serum BDNF levels, which were then analyzed using the ELISA method. The study data were collected to determine vascular activity and serum BDNF levels as protective factors for GFK in the elderly.

Characteristics of Study Participants

Based on data collection, subjects were divided into two groups: 19 cases (GFK) and 19 controls (non-GFK). The average age of the GFK subjects was 55.53 + 3.422 years, while the average age of the non-GFK subjects was 55.26 + 3.3729 years. The mean serum BDNF level in the non-GFK group was higher at 7.494 ± 4.908 ng/mL compared to the GFK group, which had a mean BDNF level of 3.305 ± 0.759 ng/mL. Regarding cognitive function, as measured using the MoCA-InA, the mean score in the non-GFK group was higher at 26.78 ± 0.787, while the mean score in the GFK group was 21.15 ± 3.236.

Based on the results of the *Majejaitan* activity questionnaire, both the elderly on GFK and non-GFK groups engaged in fairly active and regular *Majejaitan* activities. Of both groups, 94.7% of subjects in the non-GFK group and 84.2% of the GFK group had engaged in *Majejaitan* activities for ≥ 5 years. However, in terms of activity intensity (frequency, duration, and type of variation), varied results were found.

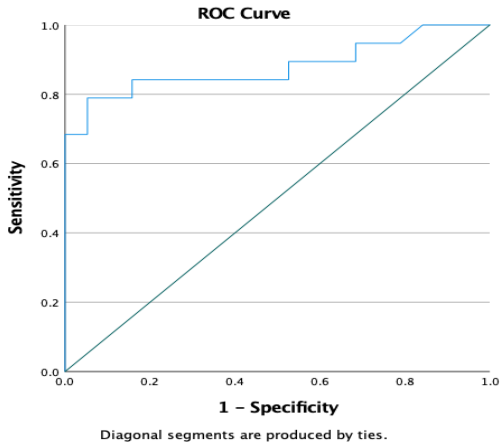

Figure 3 ROC Curve of BDNF Levels Against Cognitive Impairment

Source: Primary data, 2025

In this study, the cut-off serum BDNF level was 3.91 ng/mL, with a sensitivity of 84.2% and a specificity of 89.5%. The serum BDNF level data were divided into two categories: those with low serum BDNF levels (<3.91 ng/mL), and those with high serum BDNF levels (>3.91 ng/mL). The results of this study showed that 68.4% of the group with high serum BDNF levels had high serum BDNF levels, while 52.6% of the group with GFK had low serum BDNF levels.

5.2 Differences in Cognitive Function Domains of *Majejaitan* Activities in the Elderly.

The results of this study indicate significant differences in cognitive function domains between elderly individuals who engage in active and inactive *Majejaitan* activities. This shows that *Majejaitan* activities can play a role in maintaining visuospatial function, attention and orientation ($p<0.05$) in the elderly.

Bivariate Analysis of High Serum BDNF Levels and GFK in the Elderly

The analysis results showed a significant correlation between high serum BDNF levels and GFK ($p<0.05$) in the elderly. The OR value indicated that subjects with high serum BDNF levels had a 95.8% lower chance of developing GFK and was a protective factor for the development of GFK.

Bivariate Analysis of Age, Education, Occupation, and Hypertension with GFK in the Elderly

Elderly people with less than 12 years of education are at higher risk of developing GFK compared to those with more than 12 years of education. There was no significant association between age, occupation, and hypertension with GFK ($p>0.05$).

Multivariate Analysis

Multivariate analysis was conducted to evaluate the relationship between several independent variables and the dependent variable, namely GFK. Variables analyzed were those associated with GFK with a p-value <0.25. Serum BDNF levels, *Majejaitan* activity, and education, with p-values <0.25, indicated a correlation between these variables and GFK. Multivariate analysis was performed using backward logistic regression. Table 5.6 shows the results that serum BDNF levels have an independent relationship with GFK ($p <0.05$) and are

a protective factor (OR <1), whereas, religious activities and education do not have a statistically significant independent relationship with the occurrence of GFK in the elderly (p>0.05).

Characteristics of Research Subjects

Based on the results of this study, the average age of non-GFK subjects was 55.26 + 3.3729 years, while for the GFK group, the average age was 55.53 + 3.422 years for the GFK group. Research by Jefers et al. (2021) also showed that the 45-65 age group was most likely to have cognitive impairment. Cognitive impairment is related to changes in brain structure and function with age, making it more common in older adults than in younger adults. Aging causes atrophy, particularly in the prefrontal cortex, and a reduction in white matter volume, which plays a role in memory function (Petersen, 2016). Neuronal death is a cause of brain atrophy (Harada et al., 2013). Morphological changes that lead to decreased synaptic density are also factors contributing to brain atrophy. The mean BDNF level in the non-GFK group was 7.494 ± 4.908 ng/mL and in the GFK group it was 3.3054 + 0.759 ng/mL. These results are consistent with the study by Nicastri et al. (2021) which stated that increased BDNF levels are associated with better cognitive performance. However, a difference was found in the mean BDNF levels in this study compared to the study by Buchman et al. (2016), which was -0.16 ± 1.17. The difference in BDNF levels was due to the difference in age of the study subjects used in this study with the age matching method of 50-60 years, whereas, in the study by Buchman et al. (2016) the average age was 81 years old with a study method conducted through brain autopsy at the time of death not derived from the subject's blood serum.

BDNF levels can be measured using serum, blood, plasma, or cerebrospinal fluid samples. The efficacy of measuring peripheral BDNF concentrations has been supported by several studies, as BDNF has been shown to cross the blood-brain barrier. Among the various sample options, some studies prefer serum because BDNF levels in serum can be up to 100-fold higher than in plasma (Polacchini et al., 2015). Generally, serum BDNF levels are measured using the enzyme-linked immunosorbent assay (ELISA), a valid, sensitive, and reliable method with a sensitivity approaching 100% (Naegelin et al., 2018a; Polacchini et al., 2015).

BDNF concentration in plasma is significantly influenced by the blood sample handling process, as BDNF is stored in platelets, which require degranulation for secretion. Slight needle movement during blood draws, changes in room temperature, and the timing of the examination can trigger platelet degranulation, resulting in inconsistent measurement results and difficulty in repeating them by different operators (Piepmeier & Etnier, 2015; Polacchini et al., 2015). Furthermore, BDNF is not produced by megakaryocyte precursor cells but is actively taken up from circulating BDNF. Therefore, serum BDNF levels are considered a better representation of the amount of BDNF circulating systemically.

The normal range for BDNF levels varies depending on the measurement chosen and the population studied. This study found a serum BDNF level range of 0.544-22.52 ng/mL. Because there is no gold standard for determining normal serum BDNF levels, ROC analysis and AUC assessment were used to determine the relationship between serum BDNF levels and GFK. In this study, the cut-off for serum BDNF levels was 3.91 ng/mL, with a sensitivity of 84.2% and a specificity of 89.5%.

The mean score of the non-GFK group was higher with a score of 26.78 ± 0.787 compared to the GFK group with a score of 21.15 ± 3.236. The purpose of developing the MoCA-Ina is to identify MCI through screening (Wester et al., 2013). It takes approximately 10 minutes to evaluate various cognitive domains, such as attention, memory, language, visuoconstruction skills, conceptual thinking, calculation, and orientation. A total score of 30 points is considered normal, and a score below 26 indicates GFK. The eight stages of the MoCA-Ina assessment are as follows: visuospatial/executive ability (understanding dimensions and shapes), naming (naming pictures of animals), memory (measuring memory), attention (replaying numbers), language (forming sentences), abstraction (abstraction ability), noun similarity judgment, delayed recall (recalling words without prompts), and orientation (ability to orient oneself in understanding the year, month, day, date, place, and city) (Akbar et al., 2019). A total Kappa value of 0.820 was found in a validity test conducted in Indonesia for the MoCA. The MoCA-Ina test has been established as valid and can be administered by neurologists and general practitioners in accordance with transcultural validation standards (Husein et al., 2010). The trial results support the use of the MoCA-Ina evaluation as a first-line screening tool for people with cognitive impairment, as the instructions are clear and easy for general practitioners to follow.

73.7% of the subjects in this study actively engaged in *Majejaitan* activities and did not experience GFK. This is consistent with research by Agustana et al. (2023), which found that activities that can stimulate increased BDNF levels and improve cognitive function are needed. The recommended frequency and duration is 30-60 minutes per session, three times per week. This recommendation provides stimulation without causing excessive fatigue, which can then lead to oxidative stress.

Differences in Cognitive Function Domains of *Majejaitan* Activities in the Elderly at East Denpasar Community Health Center 1

Based on cognitive function domains, *Majejaitan* activities were significantly correlated with visuospatial, attention, and orientation domains. Cognitive domains can be negatively affected by aging. There are many domains within cognitive function. Aging typically affects selective attention, divided attention, processing speed, executive control, short-term memory, working memory, episodic memory, and prospective memory (Mokhber et al., 2019).

The analysis of differences in cognitive function domains showed that visuospatial, attention, and orientation variables were significantly correlated with *Majejaitan* activities ($p<0.05$). These results are supported by several studies showing that activities involving manual dexterity and eye-hand coordination, such as *Majejaitan*, can help maintain and improve cognitive function in the elderly. Activities that stimulate connectivity between the inferior parietal lobe and the medial prefrontal cortex can help maintain visuospatial and executive function in the elderly. Furthermore, research by Murman (2015) revealed that activities requiring concentration and fine motor coordination can help maintain the integrity of white matter, which plays a crucial role in attention and orientation. Livingston et al. (2020) also emphasized that engaging in social and creative activities can reduce the risk of mild cognitive impairment (MCI) and slow age-related cognitive decline.

This is consistent with the fact that repetitive movements can stimulate brain neuroplasticity, thereby improving fine motor efficiency and accuracy (Fahlevi et al., 2023).

Majejaitan involves precise cutting, folding, and arranging materials. This involves intense hand-finger coordination, which strengthens small muscles and improves manual dexterity. Furthermore, this activity requires good hand-eye coordination to ensure each step is executed accurately according to the desired design, which in turn helps improve visual-motor coordination and reflexes, attention, and orientation skills, which are essential in daily life (Deniati et al., 2022). The complexity of *Majejaitan* activities and the high mental and emotional involvement required in *Majejaitan* require concentration and focus, which stimulate brain areas associated with cognitive functions such as memory and problem-solving (Phillips, 2017). This stimulates neuroplasticity and results in increased BDNF levels, which impact cognitive function.

6.3. Relationship between Serum BDNF Levels and GFK

Based on bivariate and multivariate analyses, this study demonstrated a significant association between high serum BDNF levels as a protective factor against GFK in the elderly. This further supports previous studies demonstrating the important role of BDNF levels in cognitive function.

These results align with research by Perkovic et al. (2023) that examined the relationship between BDNF and cognitive impairment in dementia patients, demonstrating a negative correlation between cognitive function and plasma BDNF concentrations, indicating lower BDNF levels in subjects with more pronounced cognitive decline. Similarly, Nicastri et al. (2022) examined BDNF, which mediates improvements in cognitive performance after computerized cognitive training in healthy older adults. Their results showed that increased BDNF levels were associated with improved cognitive function (Nicastri et al., 2022). However, these results differ from those of Nabih et al. (2023), who showed no statistically significant difference between BDNF and disease duration and cognitive function (Nabih et al., 2024). This may be due to the different study subjects. Furthermore, many factors can influence the relationship between BDNF and cognitive function, such as activity, age, and gender (Nicastri et al., 2022).

BDNF is a neurotrophin produced by neurons, endothelial cells, smooth muscle cells, and inflammatory cells that plays a crucial role not only in neurodevelopment and neuroprotection but also in synaptic plasticity, learning, and various cognitive functions (Nabih et al., 2024). As a family of proteins, neurotrophic factors, or "growth factors," are directly involved in neuronal and synaptic growth. The BDNF protein, in particular, is crucial for short-term cognitive performance and for long-term adaptations in brain morphology (e.g., plasticity). Much of the focus on BDNF's effects on cognitive performance has been on memory tasks (Piepmeier & Etnier, 2015). Inhibition of BDNF signaling can impair learning and long-term memory formation (Nabih et al., 2024). Serum BDNF levels are as a significant factor associated with the hippocampus and memory impairment (Utami, Effendy, & Amin, 2019). The hippocampus has been identified as a primary site of BDNF expression and is widely accepted as crucial for memory performance (Piepmeier & Etnier, 2015).

BDNF is highly expressed in the cerebral cortex and hippocampus. Extensive research has shown that BDNF enhances neural plasticity, facilitating synaptic transmission, dendritic modification, receptor movement, and long-term potentiation. Furthermore, BDNF is known to support neurogenesis and synaptic growth and repair (Nicastri et al., 2022). Through stimulation of the high-affinity receptor tropomyosin receptor kinase B (TrKB), BDNF

contributes to cell differentiation, cell survival, synaptic plasticity, and embryonic and adult neurogenesis in central nervous system neurons (Mariana et al., 2021).

6.4. Relationship between *Majejaitan* Activities and GFK

The results of this study's analysis show a significant correlation between *Majejaitan* activities and GFK ($p<0.001$) and a protective factor ($OR<1$) against GFK. To date, no studies have directly compared *Majejaitan* with GFK. However, one study examined the relationship between knitting and cognitive function. Knitting can improve health and quality of life and provide a creative outlet. Participants who knit frequently have better cognitive function, reporting clearer thinking and better concentration. The challenge of knitting or practicing new knitting skills can improve problem-solving abilities (Nordstrand et al., 2024; Riley et al., 2013). Creative activities that can improve concentration, hone motor skills through repetitive movements, and challenge problem-solving, such as *Majejaitan* activities and knitting, can increase synaptic connectivity and neuroplasticity, which in turn can slow the process of cognitive decline associated with aging. This may explain why *Majejaitan* is associated with improved cognitive function.

More severe declines in hand motor function are associated with cognitive impairment in the elderly. Patients with Alzheimer's disease experience impaired motor function, including fine motor skills, while patients with mild cognitive impairment (MCI) have less severe hand motor impairment than those with Alzheimer's. Furthermore, from a therapeutic perspective, hand motor activity can improve cognitive function, and rehabilitation programs consisting of multicomponent interventions to improve visuomotor and executive processes may have greater positive benefits (Rycroft et al., 2019). These results align with the findings of a study of active elderly people with *Majejaitan*, 73.7% of whom did not have CFK.

Motor activity has long been recognized as having numerous benefits for everyone. It can also produce significant cognitive and neuroprotective benefits, particularly in processes involving learning and memory. Investigations into the effects of motor activity on cognitive function have proposed several mechanisms that could explain this relationship. Motor activity can produce a series of biological and structural modifications and adaptations that enable brain cells to form new connections in various cortical areas. Motor activity, in fact, can trigger a cascade of neurochemical growth factors that can alter the entire structure of the brain. This reflects the brain's ability to adapt to the various cognitive challenges it faces (Latino & Tafuri, 2024; Thomas, 2012).

Studies using imaging techniques have shown that movement can stimulate angiogenesis, the development of new blood vessels from existing ones; neurogenesis, the presence of undifferentiated nerve cells that can renew themselves and differentiate into various neural pathways; and increase synaptic plasticity, the ability of the nervous system to alter the efficiency of interneuron connections, eliminating some and building new ones. Therefore, consistent and regular motor activity can positively influence cognitive processes, such as:

1. Facilitating neural development;
2. Increasing the concentration of synapses between neurons;
3. Improving vascular circulation in the cerebral cortex;
4. Increases neurotransmitter synthesis and neurotrophy, which triggers neurogenesis, angiogenesis, and neuroplasticity (Latino & Tafuri, 2024; Xian et al., 2024).

Although there was a significant association in the bivariate analysis, the logistic regression analysis did not find a direct effect of *Majejaitan* activity on GFK. This difference was attributed to the logistic regression analysis factor comparing other variables in the study.

The Relationship between Age, Education, Occupation, and Hypertension with GFK in the Elderly

The results of this study show no significant correlation between age and GFK in the elderly. This is inconsistent with existing literature, as is the research of Khare et al. (2022), which showed that age is associated with cognitive function. As people age, they change in various ways—both biologically and psychologically. Some of these changes may be for the better, while others may not. Aging occurs with a gradual decline in cognitive abilities related to changes in the cortex and hippocampus, two brain regions involved in memory and learning. BDNF helps protect neurons from damage caused by infection or injury. Therefore, a decrease in BDNF can also lead to a decline in cognitive function (Mudjihartini, 2021). This finding may be due to the age range used in the matching method (50-60 years), which is still too early for BDNF levels to decline.

Brain aging appears to follow an anterior-posterior continuum, with anterior regions being highly susceptible to aging and posterior regions less so. However, the hippocampus and surrounding structures in the medial temporal cortex also undergo changes with age. Volumetric MRI studies have shown a significant decrease in medial temporal volume with age; although some researchers have suggested that different structures may decline at different rates (e.g., the hippocampus compared to the entorhinal cortex), a clear consensus has not emerged. Finally, the striatum is also affected. The striatum is closely interconnected with the prefrontal cortex and medial temporal regions and also exhibits significant structural and functional decline with age. Interest in the striatum's role in cognitive aging has been fueled by the suggestion that the cognitive profile of normal aging resembles Parkinson's disease.

Research has shown a significant correlation between education and GFK in the elderly. Consistent with Goncalves et al. (2023), a significant correlation between education and GFK in the elderly ($p<0.001$) has been demonstrated. Several mechanisms have been proposed to explain the benefits of education on cognitive function. It has been suggested that education contributes to increased resistance to neurodegenerative processes (i.e., brain preservation). However, this does not explain why individuals with higher levels of education demonstrate better cognitive performance despite the same level of neuropathology or exhibit a relatively greater neuropathological burden in clinical samples (Soldan, Pettigrew, & Albert, 2021; Stern, 2013). It has been hypothesized that education facilitates cognitive function by increasing cognitive reserve. Cognitive reserve refers to the ability to compensate for the detrimental effects of neuropathological processes through recruitment of existing neural networks and/or compensatory processes through alternative networks. However, the contribution of education to cognitive reserve remains debated (Jansen et al., 2021).

This study also showed no significant correlation between occupation and GFK in older adults. The relationship between occupation and GFK remains unclear. It has been hypothesized that sedentary or unemployed work, combined with poor diet and lack of physical activity, can lead to various health problems, such as cardiovascular disorders, which can lead to cognitive impairment, but the impact remains unclear. However, there is also evidence that

exposure to occupational stress has a significant detrimental effect on cognitive performance and accelerates cognitive decline (Bufano et al., 2024).

Several studies have shown a significant association between hypertension and cognitive impairment (CFD). Research by Han et al. (2022) revealed that hypertension is closely associated with cognitive decline in the elderly. However, the results of the bivariate analysis in this study showed no significant association between hypertension and CFD, which is consistent with research by Riasari et al. (2022), who reported no significant association between hypertension and cognitive decline. This difference in findings is likely influenced by the duration of hypertension experienced by individuals. According to Walker et al. (2017) and Tadic et al. (2016), long-term hypertension can cause reduced blood flow to the brain, leading to a decrease in the number of capillaries in the cerebral cortex, fibrosis, necrosis, and nerve cell death. This damage primarily occurs in the frontal cortex, which plays a role in executive function and information processing. In the elderly, cognitive changes can include decreased intellectual ability, slowed thinking, and cognitive decline.

CONCLUSION

The study concludes that high serum BDNF levels serve as an independent protective factor against impaired cognitive function (GFK) in the elderly, while *majejaitan* activity demonstrates a significant protective effect though not independently after controlling for other variables. These findings highlight both the biological importance of BDNF and the potential contribution of traditional cultural practices in preventing cognitive decline, reinforcing the value of integrating cultural and biological perspectives in public health strategies. Future research is suggested to explore the neuroplasticity mechanisms involved, develop standardized culture-based interventions, and conduct longitudinal studies to establish causal relationships and assess the effectiveness of their integration into public health policies.

REFERENCES

Agustana, R. S., Suparto, T. A., Sumartini, S., Purwandari, A., Puspita, W., Keperawatan, D., Olahraga, P., & Kesehatan, D. (2023). Pengaruh aktivitas fisik terhadap fungsi kognitif pada lanjut usia: Kajian literatur. *Jurnal Ilmiah Ners Indonesia*, *4*(1). https://www.onlinejournal.unja.ac.id/JINI

Akbar, N. L., Effendy, E., & Camellia, V. (2019). The Indonesian version of Montreal Cognitive Assessment (MoCA-Ina): The difference scores between male schizophrenia prescribed by risperidone and adjunctive of donepezil in Public Hospital of Dr Pirngadi Medan, Indonesia. *Open Access Macedonian Journal of Medical Sciences*, *7*(11), 1762–1767. https://doi.org/10.3889/oamjms.2019.461

Aprilyawan, G., Makrup, M., Wulandari, E., & Waspada, E. (2025). The effect of balance exercise on muscle strength in the elderly at UPT Panti Sosial Tresna Werdha Glenmore. *Open Access Health Scientific Journal*, *6*(2), 223–229.

Azis, A. N. A. (2025). Physical activity, muscle mass, and bone mineral density in older adults: A cross-sectional study. *Majalah Ilmiah Fisioterapi Indonesia*, *13*(3), 580–585.

Badan Pusat Statistik. (2020). *Statistik penduduk lanjut usia 2020*. Badan Pusat Statistik Lanjut Usia.

Brunet, A., Goodell, M. A., & Rando, T. A. (2023). Ageing and rejuvenation of tissue stem cells and their niches. *Nature Reviews Molecular Cell Biology*, *24*(1), 45–62.

Buchman, A. S., Yu, L., Boyle, P. A., Schneider, J. A., De Jager, P. L., & Bennett, D. A. (2016). Higher brain BDNF gene expression is associated with slower cognitive decline in older adults. *Neurology*, *86*(8), 735–741. https://doi.org/10.1212/WNL.0000000000002387

Buckley, K. L. (2022). *Aucanquilcha volcanic cluster magma evolution and magma plumbing system architecture during the Gordo stage (6-4 Ma)* [Doctoral dissertation].

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.

Bufano, P., Di Tecco, C., Fattori, A., Barnini, T., Comotti, A., Ciocan, C., Russo, S., Ghelli, M., Mensi, C., Bonzini, M., & Iavicoli, S. (2024). The effects of work on cognitive functions: A systematic review. *Frontiers in Psychology*, *15*, Article 1351625. https://doi.org/10.3389/fpsyg.2024.1351625

Campbell, T. S., Donoghue, K. M., Ghosh, U., Nelson, C. M., & Roth, T. L. (2022). Early life stress affects Bdnf regulation: A role for exercise interventions. *International Journal of Molecular Sciences*, *23*(19), Article 11729.

Cunningham, C., O'Sullivan, R., Caserotti, P., & Tully, M. A. (2020). Consequences of physical inactivity in older adults: A systematic review of reviews and meta-analyses. *Scandinavian Journal of Medicine & Science in Sports*, *30*(5), 816–827.

Deniati, G. A. S., Anadhi, I. M. G., & Putra, I. B. K. S. (2022). Implementasi majejaitan untuk meningkatkan kemampuan motorik halus anak usia 5-6 tahun. *Jurnal Kumara Cendekia*, *10*(3), 232–242.

Eka, N., Riskiana, P. N., & Mandagi, A. M. (2021). Tingkat pendidikan dengan fungsi kognitif pada lansia dalam periode aging population. *Preventif: Jurnal Kesehatan Masyaarakat*, *12*(2), 256–268. http://jurnal.fkm.untad.ac.id/index.php/preventif

Fahlevi, R., Diwyarthi, N. D. M. S., Anurogo, D., Anwari, M., Herlambang, H. A., Hidayati, S. A., Nurdahlia, D. U., Pramudito, A. A., Aji, R., & Putri, G. A. (2023). *Gerontologi*.

Gonçalves, N. G., Avila, J. C., Bertola, L., Obregón, A. M., Ferri, C. P., Wong, R., & Suemoto, C. K. (2023). Education and cognitive function among older adults in Brazil and Mexico. *Alzheimer's and Dementia: Diagnosis, Assessment and Disease Monitoring*, *15*(3), Article e12470. https://doi.org/10.1002/dad2.12470

Grinin, L., Grinin, A., & Korotayev, A. (2023). Global aging: An integral problem of the future. How to turn a problem into a development driver? In *Reconsidering the limits to growth: A report to the Russian association of the Club of Rome* (pp. 117–135). Springer.

Gu, D., Andreev, K., & Dupre, M. E. (2021). Major trends in population growth around the world. *China CDC Weekly*, *3*(28), 604–613.

Han, F., Luo, C., Lv, D., Tian, L., & Qu, C. (2022). Risk factors affecting cognitive impairment of the elderly aged 65 and over: A cross-sectional study. *Frontiers in Aging Neuroscience*, *14*, Article 903794. https://doi.org/10.3389/fnagi.2022.903794

Harada, C. N., Natelson Love, M. C., & Triebel, K. L. (2013). Normal cognitive aging. *Clinics in Geriatric Medicine*, *29*(4), 737–752.

Husein, N., Lumempouw, S., Ramli, Y., & Herqutanto. (2010). Uji validitas dan reliabilitas Montreal Cognitive Assessment versi Indonesia (MoCA-Ina) untuk skrining gangguan fungsi kognitif. *Neurona*, *27*(4), 15–22.

Indira, L. (2016). *Gambaran tingkat depresi, ansietas, dan stres pada mahasiswa fakultas kedokteran Universitas Sumatera Utara* [Skripsi, Universitas Sumatera Utara].

Jansen, M. G., Geerligs, L., Claassen, J. A. H. R., Overdorp, E. J., Brazil, I. A., Kessels, R. P. C., & Oosterman, J. M. (2021). Positive effects of education on cognitive functioning depend on clinical status and neuropathological severity. *Frontiers in Human Neuroscience*, *15*, Article 723728. https://doi.org/10.3389/fnhum.2021.723728

Jeffers, E. M., Bouldin, E. D., McGuire, L. C., Knapp, K. A., Patel, R., Guglielmo, D., Armour, B. S., & Croft, J. B. (2021). Prevalence and characteristics of subjective cognitive decline among unpaid caregivers aged ≥45 years—22 states, 2015–2019. *MMWR. Morbidity and Mortality Weekly Report*, *70*(46), 1591–1596. https://doi.org/10.15585/mmwr.mm7046a1

Khare, C., Mueser, K. T., & McGurk, S. R. (2022). The relationship between cognitive functioning, age and employment in people with severe mental illnesses in an urban area in India: A longitudinal study. *Schizophrenia Research: Cognition*, *29*, Article 100255. https://doi.org/10.1016/j.scog.2022.100255

Latino, F., & Tafuri, F. (2024). Physical activity and cognitive functioning. *Medicina*, *60*(2), Article 216. https://doi.org/10.3390/medicina60020216

Liu, S., & Geng, D. (2025). A systematic analysis for disease burden, risk factors, and trend projection of Alzheimer's disease and other dementias in China and globally. *PLOS ONE*, *20*(5), Article e0322574.

Livingston, G., Huntley, J., Sommerlad, A., Ames, D., Ballard, C., Banerjee, S., Brayne, C., Burns, A., Cohen-Mansfield, J., Cooper, C., Costafreda, S. G., Dias, A., Fox, N., Gitlin, L. N., Howard, R., Kales, H. C., Kivimäki, M., Larson, E. B., Ogunniyi, A., ... Mukadam, N. (2020). Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. *The Lancet*, *396*(10248), 413–446.

Mariana, A. P., Anneken, J. H., & Kuhn, D. M. (2021). The role of brain-derived neurotrophic factor in the pathophysiology of psychiatric and neurological disorders. *Journal of Psychiatry and Psychiatric Disorders*, *1*(5), 1–12. https://doi.org/10.26502/jppd.2572-519X0024

Meisartika, & Safrianto. (2021). *Konsep dasar keperawatan komunitas*. Deepublish.

Memudu, A. E., Olukade, B. A., & Alex, G. S. (2024). Neurodegenerative diseases: Alzheimer's disease. In *Integrating neuroimaging, computational neuroscience, and artificial intelligence* (pp. 128–147).

Mohanapriya, B., & Suriya, M. (2025). *Indian knowledge systems: Principles and practices*. SSS Publications.

Mokhber, N., Avan, A., Azarpazhooh, M. R., & Chaimowitz, G. (2019). Ageing and cognitive function: A mini-review. *Archives of Neuroscience*, *6*(4), Article e84726.

Mudjihartini, N. (2021). Brain-derived neurotrophic factor (BDNF) dan proses penuaan: Sebuah tinjauan. *Jurnal Biomedika dan Kesehatan*, *4*(3), 117–122. https://doi.org/10.18051/JBiomedKes.2021

Murawska-Ciałowicz, E., Wiatr, M., Ciałowicz, M., Gomes de Assis, G., Borowicz, W., Rocha-Rodrigues, S., Paprocka-Borowicz, M., & Marques, A. (2021). BDNF impact on biological markers of depression—Role of physical exercise and training. *International Journal of Environmental Research and Public Health*, *18*(14), Article 7553.

Murman, D. L. (2015). The impact of age on cognition. *Seminars in Hearing*, *36*(3), 111–121. https://doi.org/10.1055/s-0035-1555115

Nabih, M. I., Khalil, N. M., Shaker, O., Ghanema, M., & Hassan, S. A. (2024). Cognitive dysfunction, depression and serum level of brain-derived neurotrophic factor (BDNF) in Egyptian patients with rheumatoid arthritis. *Reumatologia Clinica*, *20*(4), 175–180. https://doi.org/10.1016/j.reuma.2023.12.003

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), Article ENEURO.0419-17.2018. https://doi.org/10.1523/ENEURO.0419-17.2018

Nicastri, C. M., McFeeley, B. M., Odom, J., Mosher, C., Vörös, S., Ledreux, A., Håkansson, K., Mohammed, A. H., Granholm, A. C., & Daffner, K. R. (2021). BDNF mediates

cognitive improvement following a 6-month multi-domain intervention among healthy older adults. *Innovation in Aging*, *5*(Suppl 1), 869–870.

Nicastri, C. M., McFeeley, B. M., Simon, S. S., Ledreux, A., Håkansson, K., Granholm, A., Mohammed, A. H., & Daffner, K. R. (2022). BDNF mediates improvement in cognitive performance after computerized cognitive training in healthy older adults. *Alzheimer's & Dementia: Translational Research & Clinical Interventions*, *8*(1), Article e12337. https://doi.org/10.1002/trc2.12337

Nordstrand, J., Gunnarsson, A. B., & Häggblom-Kronlöf, G. (2024). Promoting health through yarncraft: Experiences of an online knitting group living with mental illness. *Journal of Occupational Science*, *31*(4), 504–515. https://doi.org/10.1080/14427591.2023.2292281

Perkatan Endokrinologi Indonesia (PERKENI). (2021). *Pedoman pengelolaan dan pencegahan diabetes melitus tipe 2 dewasa di Indonesia 2021*. PB PERKENI.

Perkovic, M. N., Borovecki, F., Filipcic, I., Vuic, B., Milos, T., Nedic Erjavec, G., Konjevod, M., Tudor, L., Mimica, N., Uzun, S., Kozumplik, O., Svob Strac, D., & Pivac, N. (2023). Relationship between brain-derived neurotrophic factor and cognitive decline in patients with mild cognitive impairment and dementia. *Biomolecules*, *13*(3), Article 570. https://doi.org/10.3390/biom13030570

Perhimpunan Dokter Spesialis Saraf Indonesia (PERDOSSI). (2018). *Panduan praktik klinis neurologi*. PERDOSSI.

Petersen, R. C. (2016). Mild cognitive impairment. *CONTINUUM: Lifelong Learning in Neurology*, *22*(2), 404–418.

Phillips, C. (2017). Lifestyle modulators of neuroplasticity: How physical activity, mental engagement, and diet promote cognitive health during aging. *Neural Plasticity*, *2017*, Article 3589271. https://doi.org/10.1155/2017/3589271

Piepmeier, A. T., & Etnier, J. L. (2015). Brain-derived neurotrophic factor (BDNF) as a potential mechanism of the effects of acute exercise on cognitive performance. *Journal of Sport and Health Science*, *4*(1), 14–23. https://doi.org/10.1016/j.jshs.2014.11.001

Polacchini, A., Metelli, G., Francavilla, R., Baj, G., Florean, M., Mascaretti, L. G., & Tongiorgi, E. (2015). A method for reproducible measurements of serum BDNF: Comparison of the performance of six commercial assays. *Scientific Reports*, *5*, Article 17989. https://doi.org/10.1038/srep17989

Rando, T. A., & Jones, D. L. (2021). Regeneration, rejuvenation, and replacement: Turning back the clock on tissue aging. *Cold Spring Harbor Perspectives in Biology*, *13*(9), Article a040907.

Riani, E., Wijayanto, A. W., & Rivai, A. (2024). An analysis of employment participation and its determinants among older adults in Jambi Province, Indonesia. *Jurnal Perspektif Pembiayaan dan Pembangunan Daerah*, *12*(4), 371–382.

Riasari, H., Saraswati, L. D., & Adi, M. S. (2022). Faktor-faktor yang berhubungan dengan penurunan fungsi kognitif pada lansia. *Jurnal Kesehatan Masyarakat*, *10*(4), 467–475.

Riley, J., Corkhill, B., & Morris, C. (2013). The benefits of knitting for personal and social wellbeing in adulthood: Findings from an international survey. *British Journal of Occupational Therapy*, *76*(2), 50–57. https://doi.org/10.4276/030802213X13603244419077

Rycroft, S. S., Quach, L. T., Ward, R. E., Pedersen, M. M., Grande, L., & Bean, J. F. (2019). The relationship between cognitive impairment and upper extremity function in older primary care patients. *The Journals of Gerontology: Series A*, *74*(4), 568–574. https://doi.org/10.1093/gerona/gly246

Sastroasmoro, S., & Ismael, S. (2011). *Dasar-dasar metodologi penelitian klinis* (Edisi ke-4). Sagung Seto.

Soldan, A., Pettigrew, C., & Albert, M. (2021). Cognitive reserve from the perspective of preclinical Alzheimer disease: 2020 update. *Clinics in Geriatric Medicine*, *36*(2), 247–263. https://doi.org/10.1016/j.cger.2019.11.006

Stern, Y. (2013). Cognitive reserve in ageing. *The Lancet Neurology*, *11*(11), 1006–1012. https://doi.org/10.1016/S1474-4422(12)70191-6

Tadic, M., Cuspidi, C., & Hering, D. (2016). Hypertension and cognitive dysfunction in elderly: Blood pressure management for this global burden. *BMC Cardiovascular Disorders*, *16*(1), Article 208.

Thomas, M. (2012). The effect of different movement exercises on cognitive and motor abilities. *Advances in Physical Education*, *2*(4), 172–178. https://doi.org/10.4236/ape.2012.24030

Utami, N., Effendy, E., & Amin, M. (2019). The relation of brain-derived neurotropic factor (BDNF) serum level to sub-domain cognitive functions of Indonesian schizophrenia patients measured by MoCA-Ina. *Open Access Macedonian Journal of Medical Sciences*, *7*(23), 4053–4058. https://doi.org/10.3889/oamjms.2019.705

Vecchio, L. M., Meng, Y., Xhima, K., Lipsman, N., Hamani, C., & Aubert, I. (2018). The neuroprotective effects of exercise: Maintaining a healthy brain throughout aging. *Brain Plasticity*, *4*(1), 17–52.

Walker, K. A., Power, M. C., & Gottesman, R. F. (2017). Defining the relationship between hypertension, cognitive decline, and dementia: A review. *Current Hypertension Reports*, *19*(3), Article 24.

Wester, A., Dunki, R. M. J., Kaschel, R., Kessels, R. P. C., & Egerhazi, A. (2013). The Montreal Cognitive Assessment (MoCA): A brief screening tool for mild cognitive impairment in the elderly. *Orvosi Hetilap*, *154*(34), 1316–1323.

World Health Organization. (2021). *Global status report on the public health response to dementia*. World Health Organization.

Xian, G., Chai, Y., Gong, Y., He, W., Ma, C., Zhang, X., Ren, X., Zhang, Y., Liu, M., & Ma, Y. (2024). The relationship between healthy lifestyles and cognitive function in Chinese older adults: The mediating effect of depressive symptoms. *BMC Geriatrics*, *24*(1), Article 387. https://doi.org/10.1186/s12877-024-04922-5

Xi, J. Y., Lin, X., & Hao, Y. T. (2022). Measurement and projection of the burden of disease attributable to population aging in 188 countries, 1990-2050: A population-based study. *Journal of Global Health*, *12*, Article 04093.

Zhang, J., Zhao, Y. J., Wang, J. Y., Cui, H., Li, S., Meng, X., Cai, R. Y., Xie, J., Sun, S. Y., Yao, Y., & Li, J. (2024). Comprehensive assessment of fine motor movement and cognitive function among older adults in China: A cross-sectional study. *BMC Geriatrics*, *24*(1), Article 167. https://doi.org/10.1186/s12877-024-04725-8