Correlation of physical activity with cognition and mental health in medical students

Yhusi Karina Riskawati[1], Faresa Aulia Rastramadhani[2], Henny Mulyani[2], Ridha Saniyyah[2], Muhammad Isa Mahendra[2], Christyaji Indradmojo[3], Aswaty Nur[1]
[1]Physiology Department, Faculty of Medicine, Universitas Brawijaya, Malang, Indonesia
[2]Faculty of Medicine, Universitas Brawijaya, Malang, Indonesia
[3]Faculty of Medical, Malik Maulana Ibrahim Islamic State University, Malang, Indonesia

Article Info

Article history:

Received Mar 12, 2023
Revised Mar 5, 2024
Accepted Apr 24, 2024

Keywords:

Anxiety
BDNF
Cognition
Cortisol
Depression
Physical activity
Sedentary behavior

ABSTRACT

Low physical activity increases the number of non-communicable diseases. This phenomenon occurs in medical students. This study aimed to determine the correlation between sedentary behavior and physical activity on cognition, mental health, cortisol, and brain derived neurotropic factor (BDNF). Using a cross-sectional design of observational study, eighty-six medical students were involved in this study. The subjects were interviewed to assess cognitive function and depression levels. Saliva was taken to measure cortisol and BDNF level. Bivariate analysis was performed using the Spearman test. Depression is the only variable that correlates significantly with habitual physical activity (p=0.025, r=-0.214). Sedentary behavior has a weak correlation with cognitive failure, anxiety, and depression ([p=0.046, r=0.216]; [p=0.039, r=0.223]; [p=0.011, r=0.273]). The results found that high physical activity improves mental health and cognition. This study suggested that physical activity can alleviate symptoms of depression and anxiety among medical students.

Corresponding Author:

Yhusi Karina Riskawati
Physiology Department, Faculty of Medicine, Universitas Brawijaya
Malang, Indonesia
Email: yhusi@ub.ac.id

1. INTRODUCTION

Modern world development has created changes in human physical activity. This condition results in sedentary behavior because people do their daily activities efficiently and do not move much. Decreased physical activity and increased sedentary behavior are global problems. About 41.5% of adults spend ≥4 hours daily sitting [1]. Low physical activity among medical students was higher than among non-medical students [2]. Medical students tend to spend a lot of time every day studying in class. This can be a problem, because physical activity can improve fitness, mental health, and cognitive function [3]. So if they are sedentary, they can get mental illness and cognitive decline that inhibit learning.

Someone who is physically active has a better cognitive function when compared to less active peers. Physical activity can also prevent cognitive decline. Most studies about the benefits of physical activity on cognitive function were conducted on the elderly, while studies on young people are still minimal [4]. A study on young populations is hoped to increase awareness about the importance of physical activity on cognitive function so that cognitive decline in old age can be prevented.

Sitting in front of a computer screen is a sedentary behavior practiced by many medical students. There is a significant relationship between prolonged sitting and moderate levels of psychological distress [5]. Low-intensity physical activity increases the risk of depressive symptoms and anxiety [6]. There are also cohort studies that report an association between sedentary behavior and the risk of mental disorders [7]. It is why sedentary behavior in medical students needs to be prevented, so there is no increase in mental illness.

Physical activity induces an increase in cortisol levels depending on the intensity [8]. Cortisol is a steroid hormone that is produced in response to stress. Medical students tend to experience more stress than students in non-medical programs. Cortisol can be measured using serum, urine, and saliva [9]. Salivary cortisol is non-invasive, and its uptake is convenient for the study subjects [10].

It is also widely known that physical activity affects brain derived neurotropic factor (BDNF) levels. BDNF is one of the neurotrophins involved in all important aspects of neuroplasticity [11]. Various literature also shows an increase in BDNF levels along with physical activity. In general, an increase in BDNF correlates with an increase in catabolic needs and reactive oxygen species (ROS) due to the increased activity of mitochondria, which mediates the effects of physical activity [12]. Much is known about the correlation between physical activity and BDNF. However, little is known about its relationship with sedentary behavior.

Based on the finding described above, it is necessary to determine the correlation between sedentary behavior and habitual physical activity with cognitive function, anxiety, depression, cortisol, and brain-derived neurotrophic factor level in medical students. The urgency of this research because medical students are young adults who will continue their lives to become doctors. As doctors, they must be mentally healthy and have good cognition. The benefit is to know the physical activity level of students, so that it can be evidence and reasons to prevent sedentary living.

2. METHOD

This cross-sectional observational study, conducted at the Physiology Laboratory of the Faculty of Medicine, Universitas Brawijaya (FMUB) funded by grant from the Non-Tax State Revenue (Penerimaan Negara Bukan Pajak/PNBP) of FMUB, contract number 3969.2/4/UN10.F08/PN/2021, involving medical students from the second, third, and fourth years. Approval was obtained from the FMUB ethics committee (No.292/EC/KEPK-S1-PD/10/2021), and informed consent was obtained from all participants. The study targeted students willing to undergo direct sampling and interviews, excluding those with physical disabilities affecting movement, COVID-19 symptoms, diagnosed mental disorders, or ongoing therapy for mental or cognitive-function-related diseases, and used purposive sampling to yield a minimum of 85 participants.

The study employed a holistic research approach involving various assessment tools to comprehensively evaluate participants. The Sedentary Behavior Questionnaire measured the duration of nine activities, distinguishing between weekdays and weekends. The Baecke Habitual Physical Activity Questionnaire categorized participants into low, moderate, or high activity intensity based on their responses to 16 questions across three domains: work activities, sports activities, and leisure activities. Cognitive function was assessed through the mini-mental state examination (MMSE), which included 30 questions covering orientation, registration, attention, calculation, memory, language, and construction. The cognitive failure questionnaire (CFQ) evaluated cognitive function in the domains of perception, memory, and motor functions using 25 questions, providing insights into daily cognitive failures over the past six months. Mental Health were addressed with the Zung Self-Rating Anxiety Scale (SAS) and Hamilton Depression Rating Scale (HDRS). The SAS measured anxiety levels with 20 questions, categorized into normal, mild, moderate, and severe anxiety levels. The HDRS, comprising 17 items, categorized depression severity into normal, mild, moderate, and severe based on the reported symptoms in the past week.

Additionally, cortisol and brain-derived neurotrophic factor (BDNF) levels were assessed through saliva samples. Cortisol levels were measured using the DiaMetra® Competitive Immunoenzymatic Colorimetric Method, employing an enzyme-linked immunosorbent assay (ELISA) technique that determined cortisol concentration based on color intensity. BDNF levels were examined using a similar ELISA technique involving BDNF antibodies, biotinylated human BDNF antibody, Streptavidin-HRP, and a substrate solution, with absorbance measured at 450 nm. This multifaceted approach provided a comprehensive understanding of participants' physical, cognitive, and psychological well-being.

Normality tests of all numerical data were performed using the Kolmogorov–Smirnov test. Spearman correlation analysis was used to test the statistical significance of the correlation between sedentary behavior and habitual physical activity and the cognitive function, anxiety level, depression level, cortisol level, and BDNF level used a 95% confidence interval and a statistical significance of $p<0.05$.

3. RESULTS AND DISCUSSION

A total of 86 participants were included. Demographic characteristics can be seen in Table 1. This study includes both sex, and females outnumbered males with age range from 18-22 years old. Table 2 represents the frequency distribution of six categorical variables used in this study. Moderate habitual physical activity has the highest percentage of 61.6%. As many as 96.5% of subjects have a normal cognitive function. Most subjects have a high level of cognitive failure at 52.3%. The normal level of anxiety takes the most significant percentage at 62.8% of all subjects. Of five categories of depression in this study, mild depression predominates and makes up to 46.5% of all subjects. Salivary cortisol is categorized into normal and low levels. Most of the subjects had low salivary cortisol levels.

Table 1. Characteristics of participant (n=86)

Characteristics	Frequency	Percent
Gender		
Male	37	43%
Female	49	57%
Age		
18	5	5.8%
19	25	29.1%
20	38	44.2%
21	15	17.4%
22	3	3.5%
Year of study in medical school		
2	30	34.9%
3	43	50.0%
4	13	15.1%

Table 2. Distribution of physical activity, cognitive function, cognitive failure, anxiety, depression and cortisol level (n=86)

Variables	Frequency	Percent
Habitual physical activity		
Low	11	12.8%
Moderate	53	61.6%
High	22	25.6%
Cognitive function		
Normal	83	96.5%
Suspicious of cognitive Impairment	3	3.5%
Cognitive failure		
Low	37	43.0%
High	49	57.0%
Anxiety		
Normal	54	62.8%
Mild	26	30.2%
Moderate	5	5.8%
Severe	1	1.2%
Depression		
Normal	22	25.6%
Mild	40	46.5%
Moderate	17	19.8%
Severe	2	2.3%
Very severe	5	5.8%
Cortisol		
Normal	32	37.2%
Low	54	62.8%

The value of the sedentary behavior time spent, cortisol and BDNF levels, are shown in Table 3. The average time of sedentary behavior was 82.7 hours per week. The average salivary cortisol level is 0.5 mcg/dl. The average salivary BDNF level was 1.7 ng/ml. The BDNF level of the salivary subjects had a median value of 0.7 ng/ml.

Table 3. Sedentary behavior time, cortisol and BDNF levels

Variables	Mean±SD
Sedentary behavior (hour/week)	82.78±34.35
Cortisol (mcg/dl)	0.50±0.35
BDNF (ng/ml)	1.73±2.96

Table 4 contains a bivariate analysis of Spearman's correlation between habitual physical activity and sedentary behavior to the other variables. Habitual physical activity is only significantly correlated with depression. The two variables' correlation is weak and in the negative direction (p=0.025, r=-0.214). In contrast, other variables found no correlation. Analysis of sedentary behavior shows a significant correlation only with three variables: cognitive failure, anxiety, and depression. All three are weakly correlated and unidirectional ([p=0.046, r=0.216]; [p=0.039, r=0.223]; [p=0.011, r=0.273]).

Table 4. Correlation between physical activity to cognition, mental health, cortisol and BDNF Level

Dependent variables	Habitual physical activity		Sedentary behavior	
	p-value	r	p-value	r
Cognitive function	0.571	0.062	0.536	0.068
Cognitive failure	0.065	-0.200	0.046	0.216*
Anxiety	0.654	-0.049	0.039	0.223*
Depression	0.025	-0.241*	0.011	0.273*
Cortisol	0.265	0.121	0.357	-0.101
BDNF	0.822	-0.025	0.712	0.040

*Correlation is significant at the 0.05 level (2-tailed)

3.1. Cognition: cognitive function and cognitive failure

This study's results indicate no correlation between habitual physical activity and sedentary behavior with cognitive function. These results are supported by research on adolescent [13]–[15] and adult [16], [17] subjects where there is no association between various types of sedentary behavior and cognitive function. It is not related because cognitive function can be influenced by several factors other than physical activity, such as age, genetics, smoking habits, physical/mental disorders, and lack of social support.

In previous studies on adolescent subjects, measurements of cognitive function used instruments covering various cognitive areas such as inhibitory control, planning, and cognitive flexibility. While for sedentary behavior, an accelerometer was used [18]. Although the accelerometer measures sedentary time objectively, it cannot distinguish the type of sedentary behavior. The inability of the accelerometer to distinguish the type of sedentary behavior makes it possible to find no association between sedentary behavior and cognitive function, where children and adolescents can engage in sedentary behavior that benefits cognitive development, such as reading and learning [19].

Research on adult subjects was similar to that of children and adolescents, except that in adult subjects, a questionnaire was added to measure sedentary behavior other than using only the accelerometer [16], [17]. However, the International physical activity questionnaire, physical activity readiness questionnaire, occupational sitting and physical activity questionnaire used in previous studies could not distinguish the type of sedentary behavior in research subjects such as the Sedentary Behavior Questionnaire [20].

Nonetheless, other studies found a positive and negative association between sedentary behavior and cognitive function [21]. The difference is possible because this research instrument cannot measure cognitive areas in depth and specifically, so it cannot determine the relationship between various sedentary behavior domains and one area of cognitive function. It is supported by previous research, which shows that the domain of sedentary behavior that requires cognition will have a positive relationship with cognitive function. However the domain and total of this sedentary behavior can differ between populations [21], [22].

Meanwhile, decreased cognitive function is associated with sedentary behavior and changes gradually in adulthood, which can be detected at 60 [23]–[25]. Which is responsible for the negative association of BDNF with the sedentary level and the changes that occur at the cellular and systemic levels [26], [27]. This is supported by other findings, which state that higher sedentary time is associated with hyperintensity of white matter volume. In contrast, biomarkers are associated with an increased risk of cognitive decline [28].

It was found that there was a significant and unidirectional relationship between sedentary behavior and the level of cognitive failure. Based on previous studies, the relationship between the two variables varies [25], [29]. One systematic review concluded that sedentary behavior is associated with lower cognitive performance. One study in that systematic review only found a significant relationship between the two variables in self-report sedentary time measurements but not in objective measurements [25]. The same results were found in other studies. One study found no relationship between overall sedentary time and perceived cognitive ability. However, when viewed at the within-person level, the results varied. Self-report sedentary time measurements show a significant negative relationship, while measurements with the accelerometer show no relationship [30].

In this study, no significant relationship was found between habitual physical activity and the level of cognitive failure. Similar results were also found in previous studies. Based on research by Loprinzi [31], it was found that physical activity has no direct relationship with both prospective and retrospective memory but that there is a possibility of an indirect relationship between variables through their influence on depressive symptoms. Most subjects in this study also have depression which can affect cognitive performance [32]. A possible explanation is that depressed people have chronic neuroinflammation triggered by various pro-inflammatory cytokines and oxidative stress. Neuroinflammation can cause damage to deoxyribonucleic acid (DNA), ribonucleic acid (RNA), lipids, proteins, and synapses in various brain regions [33].

3.2. Mental health: anxiety and depression

This study's results indicate a correlation between sedentary behavior and anxiety in medical students. This result follows the findings of other studies which show a relationship. This finding is similar to a study conducted by Wang *et al.* [34], who found sedentary behavior to be significantly associated with an increased risk of anxiety symptoms among young Indonesians. However, a study by Wang *et al.* [35] found no relationship between sedentary behavior and anxiety.

Psychological stress affects various psychiatric conditions, including anxiety and stress-related disorders. Stressors can activate the hypothalamus–pituitary–adrenal (HPA) axis [36]. The HPA axis causes an increase in cortisol secretion in the adrenal cortex. It then causes an increase in salivary cortisol. When this happens, individuals can experience increased anxiety levels [37]. Anxiety occurs concomitantly with the activation of the stress response that is not anticipated or prolonged in the HPA axis. This response causes hypervigilance, fear, and sympathetic dysregulation [38]. A study shows that regular physical activity decreases HPA axis reactivity. Physical activity alters the release of corticotropin-releasing factor (CRF) from the hypothalamus and adrenocorticotropic hormone (ACTH) from the anterior pituitary [39]. It shows that physical activity causes changes in the HPA axis which affects stress and anxiety reactivity in humans so that it can cause anxiolytic effects. This explanation suggests that medical students' regular physical activity or low levels of sedentary behavior can reduce anxiety. This study proves that there is a correlation between sedentary behavior and anxiety. However, the correlation between habitual physical activity and anxiety in this study is unrelated, possibly because the etiology of anxiety is multifactorial (stress, physical condition, genetics, and environmental factors).

This study's results indicate a correlation between habitual physical activity and sedentary behavior with depression. From a total of 86 respondents, the majority of respondents had a mild level of depression, which was 46.5%. Alshahrani *et al.* [40] described that medical students have a higher prevalence of depression. It is evident from the prevalence of depression among medical students. Medical students have the potential to experience depression due to a high study load, a dense curriculum and the obligation to do assignments or outside of lectures, such as student activities which can be a trigger factor for the emergence of depression in medical students.

Based on further analysis, the relationship between habitual physical activity and depression levels was examined through the Spearman correlation test with correlation value was -0.241, so it can be concluded that habitual physical activity has a significant negative (inverse) relationship to the level of depression. Many factors influence the onset of depression in medical students, such as gender, socio-economic and cultural factors, and a dense medical education curriculum. Women are two times more affected by depression than men due to hormonal differences. Socio-economic and cultural factors include a new environment, new friends, and higher tuition fees than other faculties. The medical curriculum uses a competency-based curriculum with a problem base learning approach, which requires students to study independently, with reduction in study time [40].

Research by Hadeel Halaweh at the Al-Quds University of Palestine shows that physical activity can help prevent a decrease in Health-Related Quality of Life (HRQoL). Adult individuals who are physically active have the opportunity able to carry out daily functional activities better and more integrated [41]. Mahindru's research review also shows that physical activity positively impacts and benefits mental health. Low physical activity level in children is associated with an increased risk of depression as adults [42].

3.3. Cortisol and BDNF level

This study's results indicate no correlation between habitual physical activity and sedentary behavior of medical students with salivary cortisol levels. This finding is similar to a study conducted by Teychenne *et al.* [43], which stated that there was no relationship between sedentary behavior and salivary cortisol levels. Meanwhile, Roberts [44] showed that salivary cortisol levels differed between groups with low cortisol levels in high-activity and high in low-activity groups. The possible reason for no correlation between these variables is that cortisol fluctuates due to the circadian cycle. Research shows cortisol levels can indicate stress levels. Medical students often deal with academic stress [45]. So, this exposure can affect cortisol levels as well.

Based on the results of Spearman's analysis, it was found that there was no relationship between the level of habitual physical activity and salivary BDNF levels. The study conducted by Moreira *et al.* also found no significant correlation between the two variables, and the basal salivary BDNF levels of athletes were higher than sedentary individuals [46]. In comparison, Portilla *et al.* [47] found a significant correlation between variables with lower basal serum BDNF levels in people who routinely do physical activity. The differences in study results could be due to various factors, such as variations in the single nucleotide polymorphism (SNP) and neuropsychiatric states between individuals, duration, timing, and sampling technique [48].

While it was concluded that there was no relationship between sedentary behavior and peripheral BDNF levels in the study subjects. This study supported by other studies conducted by Ullrich *et al.* [49], Segundo *et al.* [50], Mora-Gonzalez *et al.* [14], where no association was found between sedentary behavior and BDNF levels in children and young adult subjects. However, when measuring sedentary behavior using an accelerometer, an association was found between sedentary behavior and peripheral BDNF levels, where negative associations were found in women. In contrast, positive associations were found in men. In addition, the type of sedentary behavior has more influence on health problems and further studies are needed to explain the potential effect of sedentary behavior on peripheral BDNF levels [50].

Single-time completion of questionnaires may introduce recall bias, despite the questionnaire's assessed reliability, validity, and ease of administration. Salivary cortisol and BDNF levels were measured only once, overlooking potential variations in secretion rhythms. This study lacks control over variables influencing the outcomes, posing a significant limitation.

4. CONCLUSION

This study discovered that medical students exhibit moderate physical activity and high sedentary behavior for 82.7 hours weekly. Despite the known negative impact of high sedentary behavior and low physical activity on cognitive function, the subjects demonstrated good cognitive function. Surprisingly, sedentary and physical activity were not associated with salivary cortisol and BDNF, challenging previous expectations. The study emphasizes that physical activity alone doesn't solely influence cortisol and BDNF levels; these are also impacted by various factors which require further investigation.

ACKNOWLEDGEMENTS

We would like to express our gratitude for the funding provided by the Competitive Beginner Lecturer grant from the PNBP FMUB, contract number 3969.2/4/UN10.F08/PN/2021. Special thanks are extended to all the participants in this study and to bachelor students thesis co-advisors: Badrul Munir, Neuro.; Taufiq A.S., Anesth.; Seskoati P., Ophth.; and Novita T.H., Neuro., for their guidance and suggestions. A heartfelt appreciation goes to Endang Sriwayhuni, MD, MS., Retty Ratnawaty, MD, MSc. and all our Senior Physiologist, for their continuous support.

REFERENCES

[1] C. Zheng, W. Y. Huang, S. Sheridan, C. H.-P. Sit, X.-K. Chen, and S. H.-S. Wong, "COVID-19 pandemic brings a sedentary lifestyle in young adults: a cross-sectional and longitudinal study," *International Journal of Environmental Research and Public Health*, vol. 17, no. 17, Aug. 2020, doi: 10.3390/ijerph17176035.

[2] K. C. de Souza *et al.*, "Medical students show lower physical activity levels and higher anxiety than physical education students: a cross-sectional study during the COVID-19 pandemic," *Frontiers in Psychiatry*, vol. 12, p. 804967, 2021, doi: 10.3389/fpsyt.2021.804967.

[3] World Health Organization, WHO guidelines on physical activity and sedentary behaviour, web annex, evidence profiles. World Health Organization, 2020. [Online]. Available: https://iris.who.int/handle/10665/336657

[4] B. Klimova and R. Dostalova, "The impact of physical activities on cognitive performance among healthy older individuals," *Brain Sciences*, vol. 10, no. 6, Jun. 2020, doi: 10.3390/brainsci10060377.

[5] Y. Owari, "Relationship between psychological distress and prolonged sedentary bouts in the elderly: four period analysis," *Healthcare (Switzerland)*, vol. 9, no. 6, Jun. 2021, doi: 10.3390/healthcare9060676.

[6] P. Morga, B. Cieślik, M. Sekułowicz, M. Bujnowska-Fedak, I. Drower, and J. Szczepańska-Gieracha, "Low-Intensity exercise as a modifier of depressive symptoms and self-perceived stress level in women with metabolic syndrome," *Journal of Sports Science and Medicine*, vol. 20, no. 2, pp. 222–228, Jun. 2021, doi: 10.52082/jssm.2021.222.

[7] X.-Y. Cai, G.-P. Qian, F. Wang, M.-Y. Zhang, Y.-J. Da, and J.-H. Liang, "Association between sedentary behavior and risk of cognitive decline or mild cognitive impairment among the elderly: a systematic review and meta-analysis," F*rontiers in Neuroscience*, vol. 17, p. 1221990, 2023, doi: 10.3389/fnins.2023.1221990.

[8] P. Ponce, A. Del Arco, and P. Loprinzi, "Physical activity versus psychological stress: effects on salivary cortisol and working memory performance," *Medicina (Lithuania)*, vol. 55, no. 5, 2019, doi: 10.3390/medicina55050119.

[9] T. Iqbal, A. Elahi, W. Wijns, and A. Shahzad, "Cortisol detection methods for stress monitoring in connected health," *Health Sciences Review*, vol. 6, p. 100079, 2023, doi: 10.1016/j.hsr.2023.100079.

[10] S. Y. T. Tan *et al.*, "Expanding the use of salivary cortisol as a non-invasive outpatient test in the dynamic evaluation of suspected adrenal insufficiency," *Endocrine Connections*, vol. 12, no. 4, Apr. 2023, doi: 10.1530/EC-23-0004.

[11] H. İ. Ceylan, A. F. Silva, R. Ramirez-Campillo, and E. Murawska-Ciałowicz, "Exploring the effect of acute and regular physical exercise on circulating brain-derived neurotrophic factor levels in individuals with obesity: a comprehensive systematic review and meta-analysis," *Biology*, vol. 13, no. 5. 2024. doi: 10.3390/biology13050323.

[12] C. M. Di Liegro, G. Schiera, P. Proia, and I. Di Liegro, "Physical activity and brain health," *Genes (Basel)*, vol. 10, no. 9, Sep. 2019, doi: 10.3390/genes10090720.

[13] S. J. Fairclough *et al.*, "Cross-sectional associations between 24-hour activity behaviours and mental health indicators in children and adolescents: a compositional data analysis," *Journal of Sports Sciences*, vol. 39, no. 14, pp. 1602–1614, Jul. 2021, doi: 10.1080/02640414.2021.1890351.

[14] J. Mora-Gonzalez *et al.*, "Physical fitness, physical activity, and the executive function in children with overweight and obesity," *Journal of Pediatrics*, vol. 208, pp. 50-56.e1, May 2019, doi: 10.1016/j.jpeds.2018.12.028.

[15] J. Mora-Gonzalez *et al.*, "Fitness, physical activity, sedentary time, inhibitory control, and neuroelectric activity in children with overweight or obesity: the ActiveBrains project," *Psychophysiology*, vol. 57, no. 6, Jun. 2020, doi: 10.1111/psyp.13579.

[16] X.-Y. Cai, G.-P. Qian, F. Wang, M.-Y. Zhang, Y.-J. Da, and J.-H. Liang, "Association between sedentary behavior and risk of cognitive decline or mild cognitive impairment among the elderly: a systematic review and meta-analysis," *Frontiers in Neuroscience*, vol. 17, p. 121990, 2023, doi: 10.3389/fnins.2023.1221990.

[17] C. M. Maasakkers *et al.*, "The association of sedentary behaviour and cognitive function in people without dementia: a coordinated analysis across five cohort studies from COSMIC," *Sports Medicine*, vol. 50, no. 2, pp. 403–413, Feb. 2020, doi: 10.1007/s40279-019-01186-7.

[18] S. Li, J. Guo, K. Zheng, M. Shi, and T. Huang, "Is sedentary behavior associated with executive function in children and adolescents? a systematic review," Frontiers in Public Health, vol. 10, Feb. 2022, doi: 10.3389/fpubh.2022.832845.

[19] J. Aunger and J. Wagnild, "Objective and subjective measurement of sedentary behavior in human adults: A oolkit," *American Journal of Human Biology*, vol. 34, no. 1, p. e23546, Jan. 2022, doi: 10.1002/ajhb.23546.

[20] I. Maes, M. Ketels, D. Van Dyck, and E. Clays, "The occupational sitting and physical activity questionnaire (OSPAQ): a validation study with accelerometer-assessed measures," *BMC Public Health*, vol. 20, no. 1, p. 1072, 2020, doi: 10.1186/s12889-020-09180-9.

[21] L. Wanders *et al.*, "Association between sedentary time and cognitive function: a focus on different domains of sedentary behavior," *Preventive Medicine*, vol. 153, p. 106731, Dec. 2021, doi: 10.1016/j.ypmed.2021.106731.

[22] P. de A. Moreira *et al.*, "Association between sedentary behavior and cognitive performance in middle-aged and elderly adults: cross-sectional results from ELSA-Brasil," Int. J. Environ. Res. Public Health, vol. 19, no. 21, Oct. 2022, doi: 10.3390/ijerph192114234.

[23] R. S. Falck, J. C. Davis, and T. Liu-Ambrose, "What is the association between sedentary behaviour and cognitive function? a systematic review," *British Journal of Sports Medicine*, vol. 51, no. 10, pp. 800–811, May 2017, doi: 10.1136/bjsports-2015-095551.

[24] T. A. Salthouse, "When does age-related cognitive decline begin?," *Neurobiology of Aging*, vol. 30, no. 4, pp. 507–514, Apr. 2009, doi: 10.1016/j.neurobiolaging.2008.09.023.

[25] T. Hedden and J. D. E. Gabrieli, "Insights into the ageing mind: a view from cognitive neuroscience," *Nature Reviews Neuroscience*, vol. 5, no. 2, pp. 87–96, Feb. 2004, doi: 10.1038/nrn1323.

[26] T. Engeroff *et al.*, "Is objectively assessed sedentary behavior, physical activity and cardiorespiratory fitness linked to brain plasticity outcomes in old age?," *Neuroscience*, vol. 388, pp. 384–392, Sep. 2018, doi: 10.1016/j.neuroscience.2018.07.050.

[27] L. Wanders *et al.*, "Association between sedentary time and cognitive function: A focus on different domains of sedentary behavior," *Preventive Medicine*, vol. 153, p. 106731, 2021, doi: 10.1016/j.ypmed.2021.106731.

[28] U. G. Bronas *et al.*, "Sedentary time and white matter hyperintensity volume in older adults," *Medicine and Science in Sports and Exercise*, vol. 51, no. 8, pp. 1613–1618, Aug. 2019, doi: 10.1249/MSS.0000000000001957.

[29] M. Miranda, J. F. Morici, M. B. Zanoni, and P. Bekinschtein, "Brain-derived neurotrophic factor: a key molecule for memory in the healthy and the pathological brain," *Frontiers in Cellular Neuroscience*, vol. 13, p. 363, 2019, doi: 10.3389/fncel.2019.00363.

[30] P. Loprinzi, "The effects of sedentary behavior on memory and markers of memory function: a systematic review," *Physician and Sportsmedicine*, vol. 47, no. 4, pp. 387–394, Oct. 2019, doi: 10.1080/00913847.2019.1607603.

[31] P. D. Loprinzi, "Interrelationships between depression, exercise and subjective memory complaints," *Revue Neurologique*, vol. 175, no. 5, pp. 319–323, May 2019, doi: 10.1016/j.neurol.2018.10.006.

[32] N. Sharifian *et al.*, "Linking depressive symptoms and cognitive functioning: The mediating role of leisure activity," *Neuropsychology*, vol. 34, no. 1, pp. 107–115, Jan. 2020, doi: 10.1037/neu0000595.

[33] M. Dobielska, N. K. Bartosik, K. A. Zyzik, E. Kowalczyk, and M. S. Karbownik, "Mechanisms of cognitive impairment in depression. May probiotics help?," *Frontiers in Psychiatry*, vol. 13, Jun. 2022, doi: 10.3389/fpsyt.2022.904426.

[34] M. H. Wang, D. M. Xiao, M. W. Liu, Y. A. Lu, and Q. Q. He, "Relationship between sedentary behaviour and anxiety symptoms among youth in 24 low- and middle-income countries," *PLoS ONE*, vol. 15, no. 10 October, p. e0241303, Oct. 2020, doi: 10.1371/journal.pone.0241303.

[35] M.-H. Wang, D.-M. Xiao, M.-W. Liu, Y.-A. Lu, and Q.-Q. He, "Relationship between sedentary behaviour and anxiety symptoms among youth in 24 low- and middle-income countries," *PLoS One*, vol. 15, no. 10, p. e0241303, 2020, doi: 10.1371/journal.pone.0241303.

[36] J. A. Hinds and E. R. Sanchez, "The Role of the Hypothalamus–Pituitary–Adrenal (HPA) Axis in Test-Induced Anxiety: Assessments, Physiological Responses, and Molecular Details," *Stresses*, vol. 2, no. 1, pp. 146–155, Mar. 2022, doi: 10.3390/stresses2010011.

[37] J. A. Hinds and E. R. Sanchez, "The role of the hypothalamus–pituitary–adrenal (HPA) axis in test-induced anxiety: assessments, physiological responses, and molecular details," *Stresses*, vol. 2, no. 1, pp. 146–155, Mar. 2022, doi: 10.3390/stresses2010011.

[38] A. Govindula, N. Ranadive, M. Nampoothiri, C. M. Rao, D. Arora, and J. Mudgal, "Emphasizing the crosstalk between inflammatory and neural signaling in post-traumatic stress disorder (PTSD)," *Journal of Neuroimmune Pharmacology*, vol. 18, no. 3, pp. 248–266, 2023, doi: 10.1007/s11481-023-10064-z.

[39] K. Kageyama, Y. Iwasaki, and M. Daimon, "Hypothalamic regulation of corticotropin-releasing factor under stress and stress resilience," *International Journal of Molecular Sciences*, vol. 22, no. 22, Nov. 2021, doi: 10.3390/ijms222212242.

[40] A. M. Alshahrani et al., "Prevalence of depressive symptoms and its correlates among male medical students at the University of Bisha, Saudi Arabia," *Healthcare*, vol. 12, no. 6. 2024. doi: 10.3390/healthcare12060640.

[41] G. Kapoor, P. Chauhan, G. Singh, N. Malhotra, and A. Chahal, "Physical activity for health and fitness: past, present and future," *Journal of Lifestyle Medicine*, vol. 12, no. 1, pp. 9–14, Jan. 2022, doi: 10.15280/jlm.2022.12.1.9.

[42] A. Mahindru, P. Patil, and V. Agrawal, "Role of Physical activity on mental health and well-being: a review," *Cureus*, vol. 15, no. 1, p. e33475, Jan. 2023, doi: 10.7759/cureus.33475.

[43] M. Teychenne, D. L. Olstad, A. I. Turner, S. A. Costigan, and K. Ball, "Sedentary behaviour and hair cortisol amongst women living in socioeconomically disadvantaged neighbourhoods: a cross-sectional study," *International Journal of Environmental Research and Public Health*, vol. 15, no. 4, Mar. 2018, doi: 10.3390/ijerph15040586.

[44] K. Roberts, "The effects of physical activity on salivary stress biomarkers in college students," in *The Proceedings of the Oklahoma Academy of Science*, 2019, pp. 99–105.

[45] B. Špiljak, M. Vilibić, A. Glavina, M. Crnković, A. Šešerko, and L. Lugović-Mihić, "A review of psychological stress among students and its assessment using salivary biomarkers," *Behavioral Sciences*, vol. 12, no. 10, p. 400, Oct. 2022, doi: 10.3390/bs12100400.

[46] A. Moreira, M. S. Aoki, A. F. S. de Arruda, D. G. da S. Machado, H. M. Elsangedy, and A. H. Okano, "Salivary BDNF and cortisol responses during high-intensity exercise and official basketball matches in sedentary individuals and elite players," *Journal of Human Kinetics*, vol. 65, pp. 139–149, Dec. 2018, doi: 10.2478/hukin-2018-0040.

[47] R. Fonseca-Portilla *et al.*, "Brain-derived neurotrophic factor and its associations with metabolism and physical activity in a latino sample," *Metabolic Syndrome and Related Disorders*, vol. 17, no. 2, pp. 75–80, Mar. 2019, doi: 10.1089/met.2018.0028.

[48] M. I. Zelada *et al.*, "Brain-derived neurotrophic factor (BDNF) as a predictor of treatment response in major depressive disorder (MDD): *A Systematic Review*," Int. J. Mol. Sci., vol. 24, no. 19, Sep. 2023, doi: 10.3390/ijms241914810.

[49] A. Ullrich *et al.*, "Preliminary results of the cross-sectional associations of sedentary behavior and physical activity with serum brain-derived neurotrophic factor in adults with coronary heart disease," *Scientific Reports*, vol. 12, no. 1, p. 19685, 2022, doi: 10.1038/s41598-022-23706-8.

[50] V. H. de Oliveira Segundo, K. P. M. de Azevedo, G. C. B. S. de Medeiros, Á. N. de S. Mata, and G. Piuvezam, "Association between sedentary behavior and Brain-Derived Neurotrophic Factor (BDNF) in children and adolescents: A protocol for systematic review and meta-analysis," *PLoS One*, vol. 19, no. 3, p. e0299024, 2024, doi: 10.1371/journal.pone.0299024.

BIOGRAPHIES OF AUTHORS

Yhusi Karina Riskawati serves as a dedicated lecturer who initiated the concept for this research project. Taking on a multifaceted role, she applied for grants, provided comprehensive guidance throughout the entire research process, as well as the primary advisor for students' bachelor theses related to the study. Her research focus is in physical activity, exercise and skeletal muscle physiology. She can be contacted at email: yhusi@ub.ac.id.

Faresa Aulia Rastramadhani A fourth-year medical student at the Faculty of Medicine, Universitas Brawijaya (2019-2022), she aims to improve Indonesian health and understand the link between lifestyle and mental health. This research marks her first step in this pursuit. Responsible for processing anxiety and sedentary questionnaire data, she continues to expand her knowledge and finds joy in meaningful contributions to others. She can be contacted at email: rastramadhani@gmail.com

Henny Mulyani is a medical student at the Faculty of Medicine, Universitas Brawijaya, about to start her clerkship at Saiful Anwar Hospital, Malang. New to research, she is keen on projects related to human physiology, diseases, and innovative healthcare management. In this research, she processes and analyzes data on cognitive function, physical activity, and BDNF levels. She can be contacted at email: mulyani.hennyy@gmail.com.

Ridha Saniyyah Rindradi is medical student at the Faculty of Medicine, Universitas Brawijaya, set to begin her clerkship at Saiful Anwar Hospital, Malang. With a background in social health, charity, and community outreach through AMSA and LAKESMA, her research interests include human activity physiology, mental health, and hormones. She is responsible for processing depression and cortisol levels data. She can be contacted at email: ridharindradi@gmail.com.

Muhammad Isa Mahendra is a medical student at Universitas Brawijaya, Indonesia, currently undergoing a clerkship at Saiful Anwar Hospital, Malang. Involved in scientific research organizations, he is interested in health invention and innovation, with a focus on the physiology of human activity, neuroscience, and biomolecular research. He is responsible for processing cognitive function and BDNF levels data. He can be contacted at email: isamahendra24@gmail.com.

Christyaji Indradmojo a lecturer and emergency physician with a focus on disaster preparedness, possesses versatile professional experience and a profound commitment to community health and well-being. His specific emphasis lies in empowering youth and improving the quality of life for the elderly. His involvement in the research spans from suggesting the initial research idea to active participation during experiments, and providing the final conceptualization to the manuscript. For further inquiries. He can be contacted at email: christyaji.indradmojo@kedokteran.uin-malang.ac.id.

Aswaty Nur is a lecturer and researcher in the Department of Physiology in the Faculty of Medicine, Universitas Brawijaya. Her research focus in Physiology Field including obesity, circadian rhythms and animal behaviour. Several international publications with her research group and students have been published from her previous research. She contributes in applying grant for this study and final suggestion of the manuscript. She can be contacted at email: aswatynur@ub.ac.id.