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The Effects of Exercise on the Psycho-cognitive Function of Brain-Derived Neurotrophic Factor (BDNF) in the Young Adults

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ABSTRACT

The benefit of exercise in inducing brain-derived neurotrophic factor (BDNF) functions in relation to cognition had been reported. Nevertheless, the ambiguity remains with regards to the types of exercise and the duration of exercise required for one to have beneficial effects. In this study, we aimed to analyse the effects of varying modes of exercises and the duration required to improve BDNF functions, specifically in the young adults. The types of exercises evaluated in the meta-analysis include (1) single bout of acute aerobic exercise, (2) repeated and frequent sessions of aerobic exercise (program exercise) over a course of several weeks, and (3) resistance training. Only a single bout of acute aerobic exercise ($z=4.92$, $p=0.00001$) is sufficient to cause an increase in BDNF following exercise intervention, while program exercise ($z=1.02$, $p=0.31$) and resistance training ($z=0.92$, $p=0.36$) demonstrated inconsistencies, some exhibited significant increase in BDNF levels while others exhibited similar results with the control groups.

Keywords: brain-derived neurotrophic factor, BDNF, meta-analysis, exercise

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1 INTRODUCTION

Physical activity or commonly known as exercise, brings about a plethora of health benefits which include (i) weight loss and prevention of obesity (Chaput et al., 2011), (ii) maintaining a normal blood sugar and insulin level (Colberg et al., 2016), (iii) reducing the risk of heart disease (Nystoriak & Bhatnagar, 2018), and (iv) reducing stress (Childs & de Wit, 2014). In addition to the above benefits, extensive studies have been conducted on the molecular mechanisms governing the effects of physical activity on human cognition. These studies have provided evidence that proteins released from muscles, fat and even liver tissues during exercise were responsible for neuronal plasticity (Yang et al., 2020) and survival (Lipsky & Marini, 2007), along with promoting brain vascularisation (Lin et al., 2014).

Amongst the various neurotrophins that have been studied, brain-derived neurotrophic factor (BDNF) has received remarkable recognition due to its involvement in developing and maintaining a physiologically normal cognitive performance (Cattaneo et al., 2016). BDNF is also accounted for cellular growth and development, regulation of mood, and mental processes of perception, specifically learning and memory (la Rosa et al., 2019; Schmolesky et al., 2013).

Exercise may affect the release of BDNF, which in turn enhances the (i) neuroplasticity in the brain (Calabrese et al., 2014), (ii) the ability of the brain to readjust to changes in surrounding and to counter injury (Cacialli et al., 2018), (iii) in acquiring newly discovered knowledge by altering autonomic networks and functions (Knaepen et al., 2010).

The effects of exercise on BDNF had been reported among neurologically impaired populations as well as the elderly (Håkansson et al., 2017; Zembron-Lacny et al., 2016; Erickson et al., 2010). However, there is no synthesis of evidence on exercise in inducing the levels of BDNF in young adults. This study aimed to review the type, intensity as well as frequency of exercise-related to BDNF levels in young adults. Consequently, this study evaluated the impact of physical activity on the levels of BDNF in young adults specifically for; (1) the difference of BDNF levels over a brief period of acute exercise in case-control and randomised control trial studies, (2) the consequence of repeated and frequent aerobic exercise versus strength exercise following a duration of time on BDNF levels.

We hope that the output of this review will shed lights on the positive effects of exercise on BDNF levels in the younger population and provide an impetus for the young to improve their learning potential, have fewer health-related problems and greater cognitive capacity. This study is important for authorities such as schools or universities to strategies programmes to aid in improving the cognitive functions of the young.

2 METHODS

The search strategy consisted of queries of multiple combinations such as (1) "brain-derived neurotrophic factor" [Medical Subject Headings (MeSH)] OR "BDNF"; (2) "exercise" (MeSH) OR "physical activity" OR "aerobic exercise" OR "resistance training"; (3) "healthy young adults"

[MeSH] OR "university students" OR "college students". Boolean operators such as AND and OR were incorporated. The web search engine used was PubMed and Google Scholar. In addition, studies that were cited in the references of the key studies were also examined. Studies that fulfilled the above criteria were retrieved. Only full-text articles written in English were included in this study.

The data were independently extracted. Data on BDNF concentrations on both control and exercise intervention groups, characteristics of the population, characteristics of exercise intervention, duration of the programme, mode of exercise, dose, along with the intensity of exercise and other additional information were also retrieved. For studies conducted on several exercise intervention groups, the one with the highest intensity was chosen to compare to the control group. Studies were then classified into categories of (i) single session of exercise, (ii) frequent and repeated session of exercise and (iii) resistance training.

Only full-text articles were included in this study for review. The other inclusion criteria were: (1) young adults, (2) intervention study design using exercise, (3) serum or plasma BDNF was measured, (4) a case-control study. Studies were excluded for (1) rodent-based studies, (2) no measurement of serum or plasma BDNF, (3) review studies, (4) subjects were elderly or patients with neurological diseases, (5) no exercise intervention, (6) duplicates, (7) no control groups.

Quality assessment was carried out by assessing the risk of bias of the included studies using a tool provided by the Cochrane Collaboration Group. Features assessed include 1. random sequence generation (selection bias), 2. allocation concealment (selection bias), 3. blinding of participants and personnel (performance bias), 4. blinding of outcome assessment (detection bias), 5. incomplete outcome data (attrition bias), 6. selective reporting (reporting bias), and 7. other bias. Each study was then assessed based on these features and was classified as low, high, or uncertain bias risk.

Data were analysed and calculated with Cochrane Review Manager (RevMan) 5.4 statistical software (Cochrane Collaboration, Oxford, England). A random-effect model was used to measure standardised mean differences, a measure of effect size, as well as 95% confidence intervals. As different assays were used to measure absolute BDNF concentrations along with different blood samples (serum and plasma), standardised mean differences were chosen for the statistical outcome (Dinoff et al., 2016). Also, standardised mean differences represent a point estimate of the effect of an intervention. If a high heterogeneity with a large variation of the outcomes between different studies is foreseen and expected, a random effect model would be favoured as opposed to a fixed-effects model. Heterogeneity is calculated using Chi-square analysis. On the other hand, inconsistencies of the results were assessed using I^2 indices. Statistical significance for the analyses was set at $p < 0.05$.

3 RESULTS

A total of 110 articles were retrieved after duplicates were removed. These articles were then screened by reading the titles and abstracts, resulting in a total of fifty-three (53) full-text articles

for further assessment of eligibility. From those 53 articles, 35 full-text articles were excluded. The articles excluded were 19 articles of non-case-control studies or randomised controlled trial studies, ten articles which had no data regarding BDNF concentrations (mean ± standard deviation) and seven articles were excluded as the studies were reported on elderly/ mental diseases/ animal studies. In the end, 17 independent studies were incorporated in this analysis which comprised 253 cases and 245 controls. The selection process of the studies incorporated is shown in Figure 1. The features of the studies included are presented in Table 1. Studies that provided information such as age in range form and did not disclose gender distribution are remarked as non-available in the table.

BDNF levels were measured using serum or plasma samples from participants in the studies. All studies collected blood from the participants at rest, prior to exercise intervention as the basal level of BDNF. After the exercise sessions, peripheral blood was collected to assess peripheral BDNF levels post-exercise.

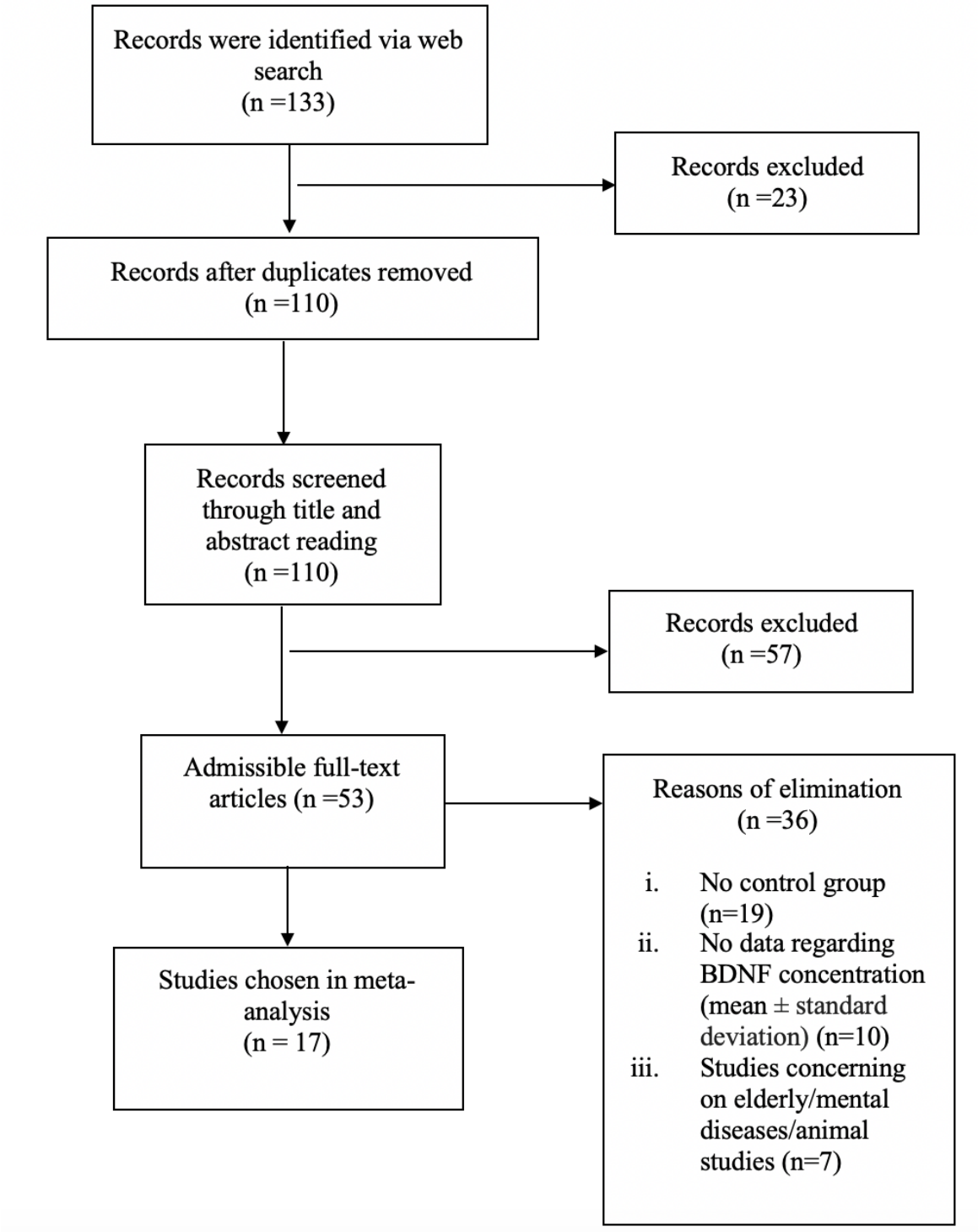


Figure 1. Flow diagram that depicts the selection process of studies incorporate

Table 1. Study features included in the meta-analysis

Description of the study	Type of sample	Age (Mean±Standard Deviation)	Gender distribution (expressed as % male)	Duration of exercise program	Exercise Mode	Exercise Intensity	Study Outcome	Reference
Low vs High Aerobic Intensity	Serum	28.8±5.6	100%	Single bout	Cycle ergometer until exhaustion or for up to 60 min	100% vVO_{2max}	Increased peripheral BDNF level in high aerobic intensity	Antunes et al., 2020
Exercise + Learning vs Learning condition	Serum	N/A	N/A	Single bout	Upper body ergometer and split-belt walking	80% VO_{2max}	Increased peripheral level of BDNF	Helm et al., 2017
High-intensity exercise vs Control group	Serum	23.6±3.1	48%	Single bout	Treadmill running for 20 min	85-90% VO_{2max} level	An elevation in BDNF level in exercise group	Hwang et al., 2016
Voluntary exercise vs Resting group	Serum	21.9±1.0	100%	Single bout	Isometric knee-extension task for 20 minutes	Moderate	An elevation in BDNF level following voluntary exercise	Kimura et al., 2019
Exercise group vs Control	Plasma	21.7±0.6	100%	Single bout		60% VO_{2max} level	Transient elevation of	

					Cycle ergometer for 30 min		plasma BDNF level following exercise intervention	Miyamoto, Kou et al., 2018
Cognitive Exercise (CE) vs Physical Exercise (PE)	Plasma	21.7±0.6	100%	Single bout	Cycle ergometer for 30 min	60% VO_{2peak} level	Physical Exercise (PE) group significantly increased plasma level of BDNF	Miyamoto, Hashimoto, et al., 2018
Low vs High Aerobic Intensity	Serum	20.8±1.1	100%	Single bout	Treadmill running until energy expenditure measured by the gas analyser reached 300 kcal	Low-intensity-50% VO_{2max} and High-intensity- 85% VO_{2max}	Serum BDNF levels significantly higher immediately after exercise following exercise of high intensity	Roh et al., 2017
Walking condition vs Relaxed condition	Serum	22.1±2.7	49%	Single bout	Treadmill walking for 20 minutes	46% VO_{2max}	Intervention group showed increased BDNF level	Schmidt-Kassow et al., 2014
Low vs High Aerobic Intensity	Serum	22.4±1.9	100%	Single bout	Treadmill walking for 30 minutes	60% VO_{2max} level	Serum BDNF levels significantly higher immediately	Tsai et al., 2016

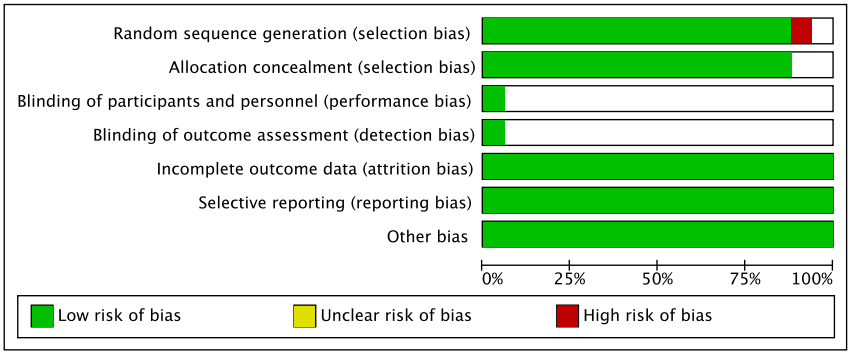
							after high intensity	
Exercise group vs Control group	Serum	N/A	N/A	8 weeks	Treadmill running to burn 200 kcal	3 days/week 40% and 60% VO_2 max	Exercise group showed significant elevation of serum BDNF levels	Jeon and Ha, 2015
Exercise group vs Control group	Serum	15.1±0.4	100%	12 weeks	Treadmill running to burn 200 kcal	4 days/week 70% VO_{2max}	Exercise group showed significant elevation of serum BDNF level	Jeon and Ha, 2017
Supervised aerobic exercise vs Control group	Serum	25.0±3.3	100%	6 weeks	Treadmill (Incremental intensity)	3 days/week until volitional exhaustion	Intervention group showed decreased BDNF level	Wagner et al., 2015
Exercise group vs Control group	Serum	24.4±2.7	100%	8 weeks	Bicycle Ergometer for 50 min	3 days/week VO_{2max} (ranging from 60% to 88%)	Intervention group showed decreased BDNF level	Wagner et al., 2017
High-Strength group (HSG) vs Control group	Serum	22.5±3.7	100%	8 weeks	Running on treadmill until	50% sVO_{2max} – 5 minutes &	Intervention group showed	Figueiredo et al., 2019

					the completion of 5 km + Strength exercise	+ 100% sVO_{2max} – 1 minute	increased BDNF level	
Exercise group vs Control group	Serum	20.6±1.1	100%	8 weeks	Taekwondo	85 minutes/ day, 5 days/ week at rate of perceived exertion (RPE) of 11~15	BDNF level did not differ between exercise and control groups	Kim, 2015
Strength training group vs Control group	Plasma	22.2±1.8	N/A	12 weeks	Complete body work out until exhaustion	3 days/week VO_{2max} (ranging from 70% to 80%)	Intervention group showed increased BDNF level	Schiffer et al., 2009
Training group vs Control group	Plasma	29.8±6.2	100%	6 weeks	Bicycle Ergometer for 60 min or until the target energy expenditure was reached	65-70 % VO_{2max}	Intervention group showed increased BDNF level	Seifert et al., 2010

Note. VO_{2max} = maximum rate of oxygen consumption measured. N/A=non-available

3.1 Risk of bias of included studies

The quality and risk of bias of the included studies were evaluated using the Cochrane Collaboration tool. All the included studies did not mention blinding of participants and personnel (performance bias) as well as blinding of outcome assessment (detection bias) except for Helm et al. (2017). Moreover, most of the studies portrayed the thoroughness of data and the reporting of the result. All studies had a low risk of selection bias as the word "random" grouping in their studies; only 2 studies (Figueiredo et al., 2019; Tsai et al., 2016) mentioned assigned grouping. Both studies (Figueiredo et al., 2019; Tsai et al., 2016) also had ambiguous allocation concealment; hence it was judged as unclear risk. The risk of bias diagram and summary is shown in Figure 2.



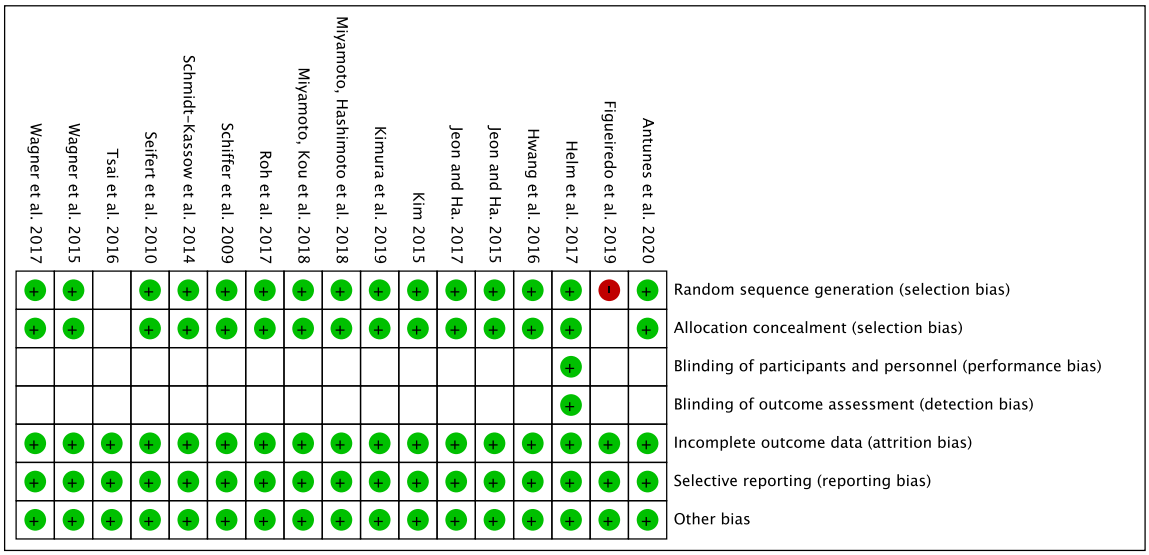


Figure 2. Risk of bias diagram and summary

3.2 Single Bouts of Acute Aerobic Exercise

Nine studies were evaluated and assessed. BDNF levels were measured before and after a short period of acute aerobic exercise in both experimental and control groups of young adults (Antunes et al., 2020; Kimura et al., 2019; Miyamoto, Hashimoto, et al., 2018; Miyamoto, Kou, et al., 2018; Helm et al., 2017; Roh et al., 2017; Hwang et al., 2016; Tsai et al., 2016; Schmidt-Kassow et al., 2014) (Table 1). The studies included were case-control studies and randomised controlled trial. From the analysis, all studies showed an elevation in peripheral BDNF level post-exercise in experimental groups. Four studies incorporated high or maximal intensity exercise until volitional exhaustion, while another four studies incorporated program with moderate-intensity exercise, and low-intensity exercise was reported in one study. Standardised Mean Differences of the BDNF levels was 0.77 (95% Confidence Interval was 0.46 to 1.07, z=4.92, p<0.00001), and a low heterogeneity was observed between the studies in which I^2=41% (Figure 3).

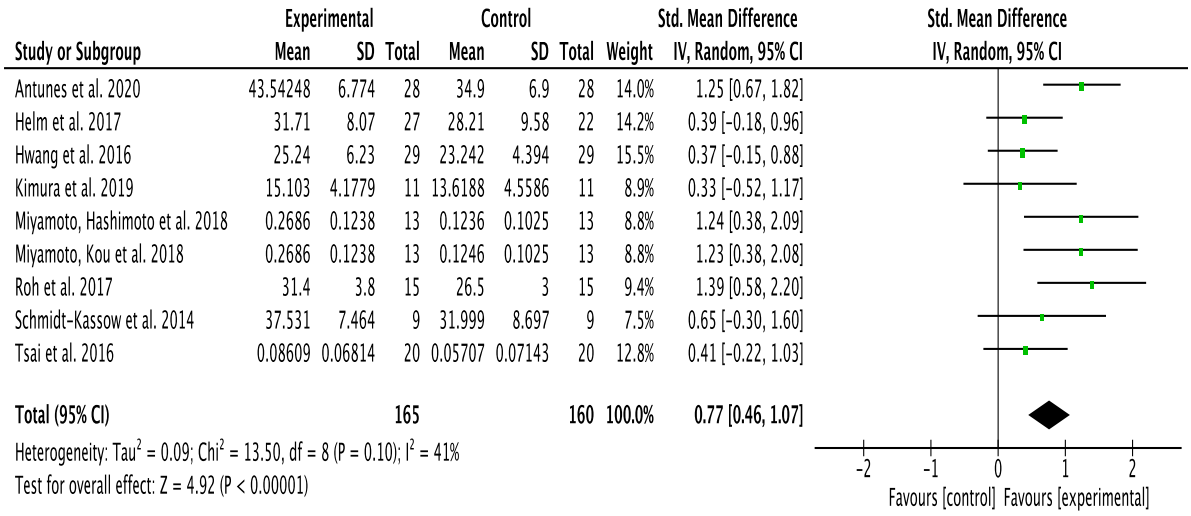


Figure 3. Forest plot shows studies investigating on a single bout of acute aerobic exercise (exercise vs control group) on BDNF levels.

From the analysis, all studies showed an increase in peripheral BDNF level post-intervention compared to during pre-intervention. Standardised Mean Differences of the BDNF levels was 1.00 (95% Confidence Interval was 0.43 to 1.58, z=3.40, p=0.0007), and a high heterogeneity was observed between the studies in which I^2=81% (Figure 4).

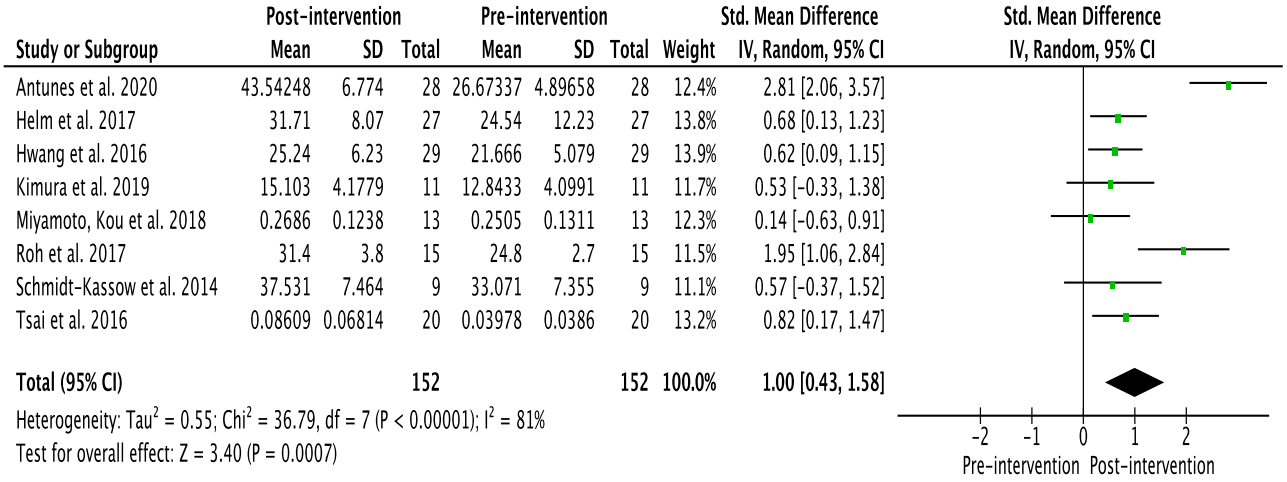


Figure 4. Forest plot shows studies investigating on a single bout of acute aerobic exercise (pre-intervention vs. post-intervention) of experimental groups on BDNF levels.

3.3 Repeated and Frequent Sessions of Aerobic Exercise (programme)

Four studies were chosen as they evaluated on the change of BDNF level following repeated and frequent sessions of aerobic exercise programme over the course of several weeks (ranging from six to twelve weeks) (Jeon & Ha, 2015, 2017; Wagner et al., 2015, 2017). Participants were assigned to either group with exercise-intervention or without exercise-intervention. The exercise programme of several weeks showed that only two studies exhibited significant elevation in peripheral levels of BDNF in experimental groups while the other two did not. In relation to intensity, all participants had undergone moderate and high or maximal intensity exercise (Standardized Mean Differences: -0.28l; 95% Confidence Interval: -0.81 to 0.26, z=1.02, p=0.31), and heterogeneity was observed between the studies in which I^2=47% (Figure 5).

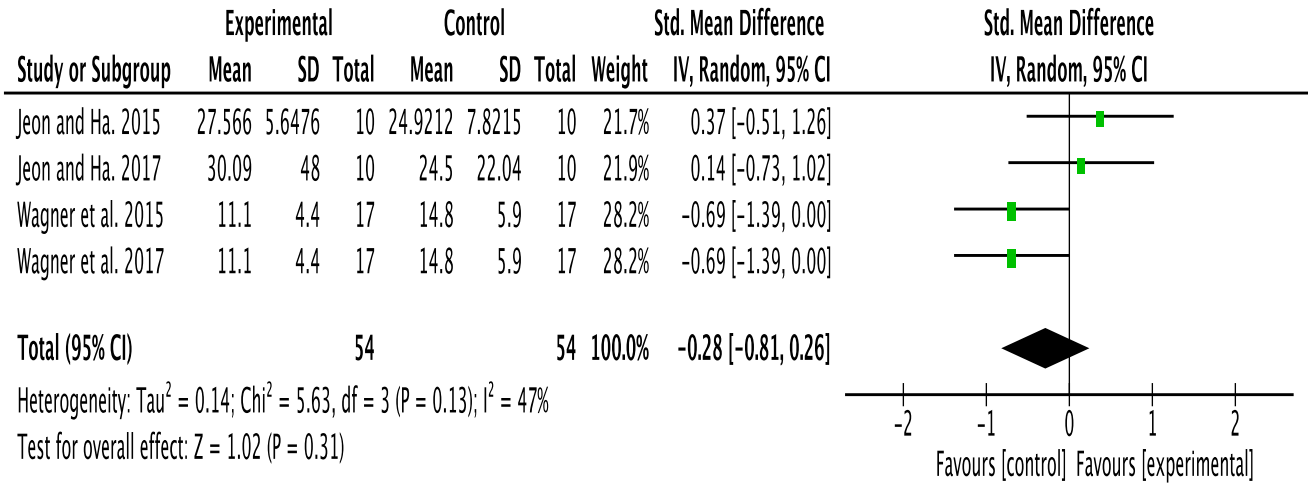


Figure 5. Forest plot shows studies investigating repeated and frequent sessions of aerobic exercise (programme) (exercise vs control group) on BDNF levels.

From the analysis, all studies showed an increase in peripheral BDNF level post-intervention compared to during pre-intervention. Standardised Mean Differences of the BDNF levels was 0.29 (95% Confidence Interval was -0.10 to 0.67, z=1.47, p=0.14), and a low heterogeneity was observed between the studies in which I^2=0% (Figure 6).

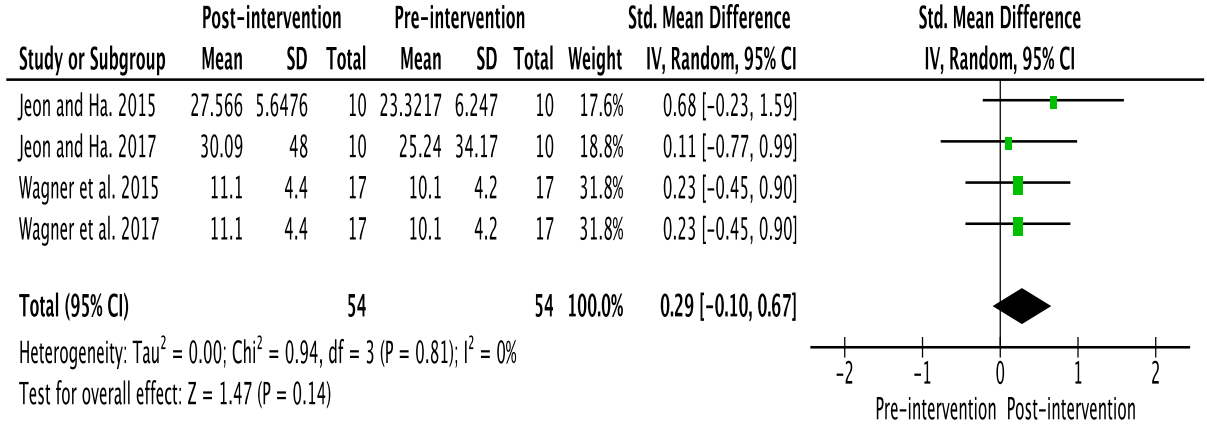


Figure 6. Forest plot shows studies investigating repeated and frequent sessions of aerobic exercise (programme) (pre-intervention vs post-intervention) of experimental groups on BDNF levels.

3.4 Resistance Training

The effects of repeated and frequent sessions of resistance exercise programme over the course of several weeks (ranging from six to twelve weeks) were evaluated (Figueiredo et al., 2019; Kim, 2015; Seifert et al., 2010; Schiffer et al., 2009) (Table 1). Participants were assigned to either group with exercise-intervention or without exercise. Out of the four studies, participants in three studies exhibited changes in resting levels of BDNF in which BDNF levels increased after several weeks of exercise intervention in experimental groups. However, one study showed a decrease in BDNF level post-intervention. In relation to intensity, participants were involved in a moderate and high or maximal intensity exercise (Standardised Mean Differences: 0.32; 95% Confidence Interval: -0.36 to 1.00, z=0.92, p=0.36), with a low observed heterogeneity between studies (I^2= 44%) (Figure 7).

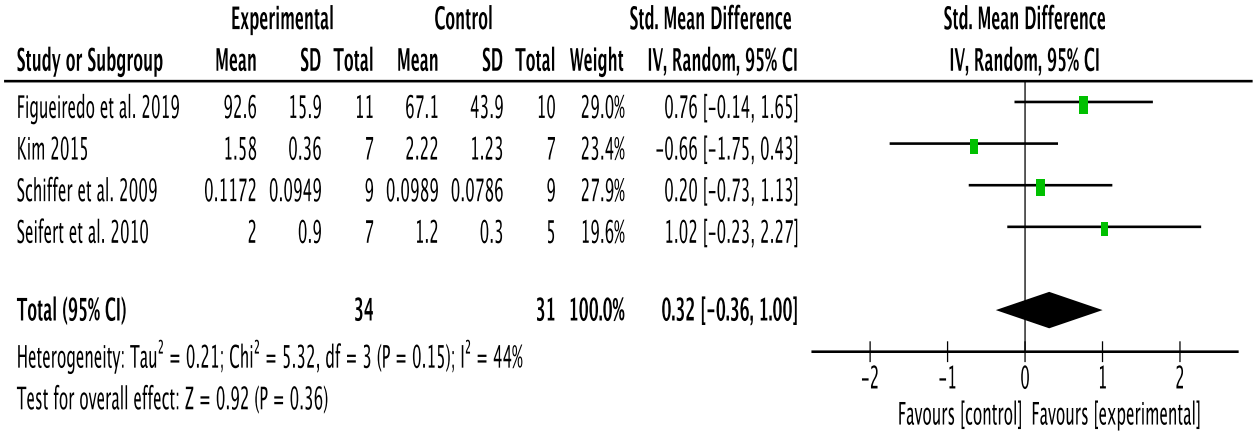


Figure 7. Forest plot shows studies investigating strength/endurance exercise (exercise vs control group) on BDNF levels.

From the analysis, two studies (Kim, 2015; Seifert et al., 2010) showed an increase in peripheral BDNF level post-intervention compared to during pre-intervention while (Figueiredo et al., 2019; Schiffer et al., 2009) showed a decrease in peripheral BDNF levels post-intervention. Standardised Mean Differences of the BDNF levels was 0.20 (95% Confidence Interval was -0.44 to 0.84, z=0.62, p=0.54), and a low heterogeneity was observed between the studies in which I^2=40% (Figure 8).

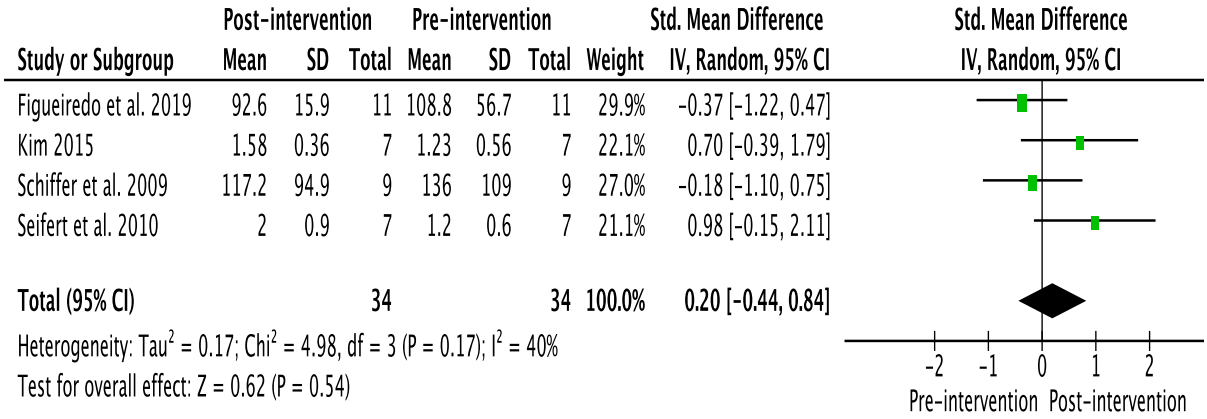


Figure 8. Forest plot shows studies investigating strength/endurance exercise (pre-intervention vs post-intervention) of experimental groups on BDNF levels.

4 DISCUSSION

An elevation of peripheral BDNF is desirable as it is associated with the brain neuroplasticity (Yang et al., 2020), memory functions and learning process (Cunha et al., 2010); in addition to the ability to delay the degenerative changes due to ageing (Oh et al., 2016). Neurotrophin is also essential to the nervous system in terms of perceiving, receiving and adapting to stimuli (Calabrese et al., 2014).

Szuhany et al.(2015) had reported the influence of exercise in relation to the resting peripheral BDNF. Nevertheless, the number of studies included in this analysis is relatively small as the population of interest is only restricted to neurologically intact healthy young adults. Therefore, this meta-analysis provides insights into the effects of different modes of exercises on BDNF levels in young, healthy adults.

From this study, a single session of acute aerobic exercise was shown to increase the peripheral BDNF level in young adults significantly. However, there were inconsistencies in the level of peripheral BDNF assessed following repeated and frequent sessions of aerobic exercise as well as resistance training intervention of several weeks as some reported a significant increase in BDNF levels (Figueiredo et al., 2019; Hötting et al., 2017; Jeon & Ha, 2017, 2015; Seifert et al., 2010; Schiffer et al., 2009) while others did not (Wagner et al., 2017, 2015; Kim, 2015). This could be due to the relatively small sample size (the total number of subjects was less than 55) despite several studies were included. This finding is similar to the one conducted by Dinoff et al. (2016),

as it emphasises the higher effectiveness of aerobic exercise compared to resistance training in elevating the levels of BDNF.

Basso and Suzuki (2017) had demonstrated in their study that acute aerobic exercises were highly associated with the improvement of cognitive functions, specifically in the prefrontal cortex region. While this may be true, Chang et al. (2017), on the other hand, reported that the outcome of a single session of exercise on cognitive function is fairly minimal. Features such as exercise mode, intensity and frequency of exercise emulate an essential role in regulating the level of BDNF. According to Kim (2015), exercise can be divided into two broad types: aerobic exercise and resistance exercise. Aerobic exercise specifically aims to augments adaptions of the heart and blood vessels that elevates the peak oxygen consumption without compromising strength, while resistance exercise augments muscle and the innervating nerves that elevate strength without compromising peak oxygen consumption (Lambert & Evans, 2005). Two studies reported that frequent and repeated sessions of aerobic exercise over the course of several weeks resulted in the augmentation of peripheral BDNF as the final outcome (Jeon & Ha, 2015, 2017). However, there were two other studies that reported otherwise (Wagner et al., 2017, 2015). The authors in the latter studies speculated that this may be due to age, type of exercise implemented along with the individuals' level of physical fitness prior to intervention and that some subjects may be non-responsive to the physical exercise following several weeks of exercise-intervention.

Previous studies conducted to evaluate the outcome of resistance exercise found that it did not bring about significant changes in the resting levels of BDNF (Goekint et al., 2010; Levinger et al., 2008). Subsequently, studies were conducted to evaluate the changes of the level of BDNF over the different duration of resistance exercises; over six weeks (Seifert et al., 2010), eight weeks (Figueiredo et al., 2019; Kim, 2015) or 12 weeks (Schiffer et al., 2009). However, there were inconsistencies in the findings of resistance exercise on peripheral BDNF level due to the variable duration (6-12 weeks duration) incorporated in the studies. A meta-analysis conducted by Knaepen et al. (2010) had proposed that the frequency of the resistance exercise adopted should be five times a week for an elevation or improvement in BDNF level, instead of three times a week. On the other hand, Kim (2015) reported that the exercise-intervention group showed a decreased in BDNF level despite a frequency of exercise of five times a week over an 8-week training duration.

It is difficult to put a specific number on the frequency, exercise period and mode of exercise needed to bring about a consequential elevation in peripheral levels of BDNF due to inconsistencies in previous findings. In short, an increased frequency of hours spent in exercise is a suggestive measure in order to observe noticeable changes in BDNF levels. Nevertheless, it is proposed that moderate to high-intensity exercises (VO_{2max} of 60-90%) with a consistent four to seven times per week instead of two to three times per week had a favourable increase in peripheral BDNF levels as a result of repeated and frequent aerobic exercise. On the other hand, low-intensity exercises are less efficacious in elevating BDNF level in healthy adults (Hötting et al., 2017). Chang et al. (2012) demonstrated a moderate level of exercise intensity is beneficial in a way that elevates the performance of working memory and the ability to switch between thinking about two different concepts, while maximal exercise intensity is accountable for the improvement in information processing speed.

Moreover, interestingly, factors such as gender could influence the concentration of BDNF post-exercise intervention. Previous studies showed that females exhibit lower concentrations of peripheral BDNF levels post-exercise compared to males (Hwang et al., 2016; Schmidt-Kassow et al., 2012, 2014). The finding in this study is consistent and similar to Szuhany et al.(2015), in which peripheral BDNF did not show a significant increase in females compared to males' post-exercise. According to Cubeddu et al. (2011), levels of BDNF differ during different menstrual cycle phases in which women with and without premenstrual syndrome (PMS) exhibit variation in patterns. Nevertheless, further studies ought to be carried out in order to assess the discrepancies observed between gender.

In this review, also we investigated the influence of genetic variation to peripheral BDNF level post-exercise. As we are all aware, genetic variation such as single nucleotide polymorphism (SNP) plays an important role in determining one's activity-induced BDNF response. For example, Val66Met is one of the most common SNP that is implicated in a reduced activity-induced BDNF response (Lemos Jr et al., 2016). Individuals with Met66Met and Val66Met genotypes has compromised BDNF emanation compared to Val66Val (Egan et al., 2003). Compromised peripheral vascular reactivity following physical activity was reported to be associated with Val66Met BDNF polymorphism (Lemos Jr et al., 2016). In the same study, participants with Val66Val had an elevation of BDNF following aerobic exercise training. In another research carried out by Helm et al. (2017), it was reported that individuals with Val66Met demonstrated to have similar peripheral serum BDNF following participation in high-intensity exercise, and no significant elevation of BDNF level was observed.

In fact, another research by Baird et al. (2018) proposed that the magnitude of the increase of levels of BDNF following exercise was not significant. Nevertheless, of the intensity of exercise, the change in BDNF is not linked to motor learning. That genotype does not differ in terms of one's BDNF response to physical activity. This finding does not disprove the theory of the influence of polymorphism on BDNF response but rather proposing that the circulating peripheral BDNF may not provide full justification and sufficient reflection to the BDNF level in the CNS, specifically the brain region.

5 CONCLUSION

Despite the small sample size, this study provides insights on the pragmatic outcome of different forms of exercise from multiple studies to BDNF levels in young adults' population as assessed by peripheral blood. For young adults, including and incorporating regular exercise as a routine may increase BDNF levels, which generally improves cognitive capacity and aids in learning and memory. We believed that exercise should be adopted as part of the activities in the education curriculum. With the current globalisation and advancement of technology, young adults must maintain a healthy and active lifestyle despite having easy access to everything and avoid idling. Nevertheless, more studies ought to be conducted specifically focusing on university or college students as studies are lacking. Incorporating exercise as part of the curriculum for student development program in the university would help improve the students' learning and memory.

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REFERENCES

Antunes, B. M., Rossi, F. E., Teixeira, A. M., & Lira, F. S. (2020). Short-time high-intensity exercise increases peripheral BDNF in a physical fitness-dependent way in healthy men. *European Journal of Sport Science*, *20*(1), 43–50. https://doi.org/10.1080/17461391.2019.1611929

Baird, J. F., Gaughan, M. E., Saffer, H. M., Sarzynski, M. A., Herter, T. M., Fritz, S. L., den Ouden, D. B., & Stewart, J. C. (2018). The effect of energy-matched exercise intensity on brain-derived neurotrophic factor and motor learning. *Neurobiology of Learning and Memory*, *156*, 33–44. https://doi.org/10.1016/j.nlm.2018.10.008

Basso, J. C., & Suzuki, W. A. (2017). The effects of acute exercise on mood, cognition, neurophysiology, and neurochemical pathways: a review. *Brain Plasticity*, *2*(2), 127–152. https://doi.org/10.3233/bpl-160040

Cacialli, P., Palladino, A., & Lucini, C. (2018). Role of brain-derived neurotrophic factor during the regenerative response after traumatic brain injury in adult zebrafish. *Neural Regeneration Research*, *13*(6), 941. https://doi.org/10.4103/1673-5374.233430

Calabrese, F., Rossetti, A. C., Racagni, G., Gass, P., Riva, M. A., & Molteni, R. (2014). Brain-derived neurotrophic factor: a bridge between inflammation and neuroplasticity. *Frontiers in Cellular Neuroscience*, *8*, 430. https://doi.org/10.3389/fncel.2014.00430

Cattaneo, A., Cattane, N., Begni, V., Pariante, C. M., & Riva, M. A. (2016). The human BDNF gene: peripheral gene expression and protein levels as biomarkers for psychiatric disorders. *Translational Psychiatry*, *6*(11), e958--e958. https://doi.org/10.1038/tp.2016.214

Chang, Y.-K., Alderman, B. L., Chu, C.-H., Wang, C.-C., Song, T.-F., & Chen, F.-T. (2017). Acute exercise has a general facilitative effect on cognitive function: A combined ERP temporal dynamics and BDNF study. *Psychophysiology*, *54*(2), 289–300. https://doi.org/10.1111/psyp.12784

Chang, Y.-K., Labban, J. D., Gapin, J. I., & Etnier, J. L. (2012). The effects of acute exercise on cognitive performance: a meta-analysis. *Brain Research*, *1453*, 87–101. https://doi.org/10.1016/j.brainres.2012.02.068

Chaput, J.-P., Klingenberg, L., Rosenkilde, M., Gilbert, J.-A., Tremblay, A., & Sjödin, A. (2011). Physical activity plays an important role in body weight regulation. *Journal of Obesity*, *2011*. https://doi.org/10.1155/2011/360257

Childs, E., & de Wit, H. (2014). Regular exercise is associated with emotional resilience to acute stress in healthy adults. *Frontiers in Physiology*, *5*, 161. https://doi.org/10.3389/fphys.2014.00161

Colberg, S. R., Sigal, R. J., Yardley, J. E., Riddell, M. C., Dunstan, D. W., Dempsey, P. C., Horton, E. S., Castorino, K., & Tate, D. F. (2016). Physical activity/exercise and diabetes: a position statement of the American Diabetes Association. *Diabetes Care*, *39*(11), 2065–2079. https://doi.org/10.2337/dc16-1728

Cubeddu, A., Bucci, F., Giannini, A., Russo, M., Daino, D., Russo, N., Merlini, S., Pluchino, N., Valentino, V., & Casarosa, E. (2011). Brain-derived neurotrophic factor plasma variation during the different phases of the menstrual cycle in women with premenstrual syndrome. *Psychoneuroendocrinology*, *36*(4), 523–530. https://doi.org/10.1016/j.psyneuen.2010.08.006

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

Dinoff, A., Herrmann, N., Swardfager, W., Liu, C. S., Sherman, C., Chan, S., & Lanctôt, K. L. (2016). The effect of exercise training on resting concentrations of peripheral brain-derived neurotrophic factor (BDNF): a meta-analysis. *PloS One*, *11*(9), e0163037. https://doi.org/10.1016/j.biopsych.2017.02.723

Egan, M. F., Kojima, M., Callicott, J. H., Goldberg, T. E., Kolachana, B. S., Bertolino, A., Zaitsev, E., Gold, B., Goldman, D., Dean, M., & others. (2003). The BDNF val66met polymorphism affects activity-dependent secretion of BDNF and human memory and hippocampal function. *Cell*, *112*(2), 257–269. https://doi.org/10.1016/s0092-8674(03)00035-7

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

Figueiredo, C., Antunes, B. M., Giacon, T. R., Vanderlei, L. C. M., Campos, E. Z., Peres, F. P., Clark, N. W., Panissa, V. L. G., & Lira, F. S. (2019). Influence of Acute and Chronic High-Intensity Intermittent Aerobic Plus Strength Exercise on BDNF, Lipid and Autonomic Parameters. *Journal of Sports Science & Medicine*, *18*(2), 359.

Goekint, M., De Pauw, K., Roelands, B., Njemini, R., Bautmans, I., Mets, T., & Meeusen, R. (2010). Strength training does not influence serum brain-derived neurotrophic factor. *European Journal of Applied Physiology*, *110*(2), 285–293. https://doi.org/10.1007/s00421-010-1461-3

Håkansson, K., Ledreux, A., Daffner, K., Terjestam, Y., Bergman, P., Carlsson, R., Kivipelto, M., Winblad, B., Granholm, A.-C., & Mohammed, A. K. H. (2017). BDNF responses in healthy older persons to 35 minutes of physical exercise, cognitive training, and mindfulness: associations with working memory function. *Journal of Alzheimer's Disease*, *55*(2), 645–657. https://doi.org/10.3233/jad-160593

Helm, E. E., Matt, K. S., Kirschner, K. F., Pohlig, R. T., Kohl, D., & Reisman, D. S. (2017). The influence of high intensity exercise and the Val66Met polymorphism on circulating BDNF and locomotor learning. *Neurobiology of Learning and Memory*, *144*, 77–85. https://doi.org/10.1016/j.nlm.2017.06.003

Hötting, K., Schickert, N., Kaiser, J., Röder, B., & Schmidt-Kassow, M. (2017). The effects of acute physical exercise on memory, peripheral BDNF, and cortisol in young adults. *Neural Plasticity*, *2016*. https://doi.org/10.1155/2016/6860573

Hwang, J., Brothers, R. M., Castelli, D. M., Glowacki, E. M., Chen, Y. T., Salinas, M. M., Kim, J., Jung, Y., & Calvert, H. G. (2016). Acute high-intensity exercise-induced cognitive enhancement and brain-derived neurotrophic factor in young, healthy adults. *Neuroscience Letters*, *630*, 247–253. https://doi.org/10.1016/j.neulet.2016.07.033

Jeon, Y., K., & Ha, C. H. (2015). Expression of brain-derived neurotrophic factor, IGF-1 and cortisol elicited by regular aerobic exercise in adolescents. *Journal of Physical Therapy Science*, *27*(3), 737–741. https://doi.org/10.1589/jpts.27.737

Jeon, Y., K., & Ha, C. H. (2017). The effect of exercise intensity on brain-derived neurotrophic factor and memory in adolescents. *Environmental Health and Preventive Medicine*, *22*(1), 1–6. https://doi.org/10.1186/s12199-017-0643-6

Kim, Y. (2015). The effect of regular Taekwondo exercise on Brain-derived neurotrophic factor and Stroop test in an undergraduate student. *Journal of Exercise Nutrition & Biochemistry*, *19*(2), 73. https://doi.org/10.5717/jenb.2015.15060904

Kimura, T., Kaneko, F., Iwamoto, E., Saitoh, S., & Yamada, T. (2019). Neuromuscular electrical stimulation increases serum brain-derived neurotrophic factor in humans. *Experimental Brain Research*, *237*(1), 47–56. https://doi.org/10.1007/s00221-018-5396-y

Knaepen, K., Goekint, M., Heyman, E. M., & Meeusen, R. (2010). Neuroplasticity—exercise-induced response of peripheral brain-derived neurotrophic factor. *Sports Medicine*, *40*(9), 765–801. https://doi.org/10.2165/11534530-000000000-00000

la Rosa, A., Solana, E., Corpas, R., Bartrés-Faz, D., Pallàs, M., Vina, J., Sanfeliu, C., & Gomez-Cabrera, M. C. (2019). Long-term exercise training improves memory in middle-aged men and modulates peripheral levels of BDNF and Cathepsin B. *Scientific Reports*, *9*(1), 1–11. https://doi.org/10.1038/s41598-019-40040-8

Lambert, C. P., & Evans, W. J. (2005). Adaptations to aerobic and resistance exercise in the elderly. *Reviews in Endocrine and Metabolic Disorders*, *6*(2), 137–143. https://doi.org/10.1007/s11154-005-6726-5

Lemos Jr, J. R., Alves, C. R., de Souza, S. B. C., Marsiglia, J. D. C., Silva, M. S. M., Pereira, A. C., Teixeira, A. L., Vieira, E. L. M., Krieger, J. E., Negrão, C. E., & others. (2016). Peripheral vascular reactivity and serum BDNF responses to aerobic training are impaired by the BDNF Val66Met polymorphism. *Physiological Genomics*, *48*(2), 116–123. https://doi.org/10.1152/physiolgenomics.00086.2015

Levinger, I., Goodman, C., Matthews, V., Hare, D. L., Jerums, G., Garnham, A., & Selig, S. (2008). BDNF, metabolic risk factors, and resistance training in middle-aged individuals. *Medicine & Science in Sports & Exercise*, *40*(3), 535–541. https://doi.org/10.1249/mss.0b013e31815dd057

Lin, C.-Y., Hung, S.-Y., Chen, H.-T., Tsou, H.-K., Fong, Y.-C., Wang, S.-W., & Tang, C.-H. (2014). Brain-derived neurotrophic factor increases vascular endothelial growth factor expression and enhances angiogenesis in human chondrosarcoma cells. *Biochemical Pharmacology*, *91*(4), 522–533. https://doi.org/10.1016/j.bcp.2014.08.008

Lipsky, R. H., & Marini, A. M. (2007). Brain-derived neurotrophic factor in neuronal survival and behavior-related plasticity. *Annals of the New York Academy of Sciences*, *1122*(1), 130–143. https://doi.org/10.1196/annals.1403.009

Miyamoto, T., Hashimoto, S., Yanamoto, H., Ikawa, M., Nakano, Y., Sekiyama, T., Kou, K., Kashiwamura, S.-I., Takeda, C., & Fujioka, H. (2018). Response of brain-derived neurotrophic factor to combining cognitive and physical exercise. *European Journal of Sport Science*, *18*(8), 1119–1127. https://doi.org/10.1080/17461391.2018.1470676

Miyamoto, T., Kou, K., Yanamoto, H., Hashimoto, S., Ikawa, M., Sekiyama, T., Nakano, Y., Kashiwamura, S., Takeda, C., & Fujioka, H. (2018). Effect of neuromuscular electrical stimulation on brain-derived neurotrophic factor. *International Journal of Sports Medicine*, *40*(01), 5–11. https://doi.org/10.1055/s-0043-120343

Nystoriak, M. A., & Bhatnagar, A. (2018). Cardiovascular effects and benefits of exercise. *Frontiers in Cardiovascular Medicine*, *5*, 135. https://doi.org/10.3389/fcvm.2018.00135

Oh, H., Lewis, D. A., & Sibille, E. (2016). The role of BDNF in age-dependent changes of excitatory and inhibitory synaptic markers in the human prefrontal cortex. *Neuropsychopharmacology*, *41*(13), 3080–3091. https://doi.org/10.1038/npp.2016.126

Roh, H.-T., Cho, S.-Y., Yoon, H.-G., & So, W.-Y. (2017). Effect of exercise intensity on neurotrophic factors and blood-brain barrier permeability induced by oxidative--nitrosative stress in male college students. *International Journal of Sport Nutrition and Exercise Metabolism*, *27*(3), 239–246. https://doi.org/10.1123/ijsnem.2016-0009

Schiffer, T., Schulte, S., Hollmann, W., Bloch, W., & Strüder, H. K. (2009). Effects of strength and endurance training on brain-derived neurotrophic factor and insulin-like growth factor 1 in humans. *Hormone and Metabolic Research*, *41*(03), 250–254. https://doi.org/10.1055/s-0028-1093322

Schmidt-Kassow, M., Schädle, S., Otterbein, S., Thiel, C., Doehring, A., Lötsch, J., & Kaiser, J. (2012). Kinetics of serum brain-derived neurotrophic factor following low-intensity versus high-intensity exercise in men and women. *Neuroreport*, *23*(15), 889–893. https://doi.org/10.1097/wnr.0b013e32835946ca

Schmidt-Kassow, M., Zink, N., Mock, J., Thiel, C., Vogt, L., Abel, C., & Kaiser, J. (2014). Treadmill walking during vocabulary encoding improves verbal long-term memory. *Behavioral and Brain Functions*, *10*(1), 24. https://doi.org/10.1186/1744-9081-10-24

Schmolesky, M. T., Webb, D. L., & Hansen, R. A. (2013). The effects of aerobic exercise intensity and duration on levels of brain-derived neurotrophic factor in healthy men. *Journal of Sports Science & Medicine*, *12*(3), 502. https://doi.org/10.1113/ep085682

Seifert, T., Brassard, P., Wissenberg, M., Rasmussen, P., Nordby, P., Stallknecht, B., Adser, H., Jakobsen, A. H., Pilegaard, H., Nielsen, H. B., & others. (2010). Endurance training enhances BDNF release from the human brain. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*, *298*(2), R372--R377. https://doi.org/10.1152/ajpregu.00525.2009

Szuhany, K. L., Bugatti, M., & Otto, M. W. (2015). A meta-analytic review of the effects of exercise on brain-derived neurotrophic factor. *Journal of Psychiatric Research*, *60*, 56–64. https://doi.org/10.1016/j.jpsychires.2014.10.003

Tsai, C.-L., Pan, C.-Y., Chen, F.-C., Wang, C.-H., & Chou, F.-Y. (2016). Effects of acute aerobic exercise on a task-switching protocol and brain-derived neurotrophic factor concentrations in young adults with different levels of cardiorespiratory fitness. *Experimental Physiology*, *101*(7), 836–850. https://doi.org/10.1113/ep085682

Wagner, G., Herbsleb, M., Cruz, F. de la, Schumann, A., Brünner, F., Schachtzabel, C., Gussew, A., Puta, C., Smesny, S., Gabriel, H. W., & others. (2015). Hippocampal structure, metabolism,

and inflammatory response after a 6-week intense aerobic exercise in healthy young adults: a controlled trial. *Journal of Cerebral Blood Flow & Metabolism*, *35*(10), 1570–1578. https://doi.org/10.1038/jcbfm.2015.125

Wagner, G., Herbsleb, M., de la Cruz, F., Schumann, A., Köhler, S., Puta, C., Gabriel, H. W., Reichenbach, J. R., & Bär, K.-J. (2017). Changes in fMRI activation in anterior hippocampus and motor cortex during memory retrieval after an intense exercise intervention. *Biological Psychology*, *124*, 65–78. https://doi.org/10.1016/j.biopsycho.2017.01.003

Yang, T., Nie, Z., Shu, H., Kuang, Y., Chen, X., Cheng, J., Yu, S., & Liu, H. (2020). The Role of BDNF on Neural Plasticity in Depression. *Frontiers in Cellular Neuroscience*, *14*, 82. https://doi.org/10.3389/fncel.2020.00082

Zembron-Lacny, A., Dziubek, W., Rynkiewicz, M., Morawin, B., & Woźniewski, M. (2016). Peripheral brain-derived neurotrophic factor is related to cardiovascular risk factors in active and inactive elderly men. *Brazilian Journal of Medical and Biological Research*, *49*(7). https://doi.org/10.1590/1414-431x20165253