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 I² 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% VO$_{2max}$ | 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 | |
| Study                                                                 | Type     | Value   | Percentage | Duration     | Intervention                                                                 | Reference                        |
|-----------------------------------------------------------------------|----------|---------|-------------|--------------|-------------------------------------------------------------------------------|-----------------------------------|
| Miyamoto, Kou et al., 2018                                             | Plasma   | 21.7±0.6| 100%        | Single bout  | Cycle ergometer for 30 min                                                   | Physical Exercise (PE) group      |
| Miyamoto, Hashimoto, et al., 2018                                      | Plasma   | 21.7±0.6| 100%        | Single bout  | Cycle ergometer for 30 min                                                   | Physical Exercise (PE) group significantly increased plasma level of BDNF |
| Miyamoto, Hashimoto, et al., 2018                                      | 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} |
| Roh et al., 2017                                                       | Serum    | 22.1±2.7| 49%         | Single bout  | Treadmill walking for 20 minutes                                              | Intervention group showed increased BDNF level |
| Schmidt-Kassow et al., 2014                                            | Serum    | 22.4±1.9| 100%        | Single bout  | Treadmill walking for 30 minutes                                              | Serum BDNF levels significantly higher immediately |

Low vs High Aerobic Intensity

Walking condition vs Relaxed condition

Low vs High Aerobic 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% VO₂ 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% VO₂ max | 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 VO₂max (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 sVO₂max – 5 minutes & | 50% | Intervention group showed | Figueiredo et al., 2019 |
| 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$_{2\text{max}}$ (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$_{2\text{max}}$ | Intervention group showed increased BDNF level | Seifert et al., 2010 |

Note. VO$_{2\text{max}}$ = 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.
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](image-url)  
**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).

| Study or Subgroup       | Post-intervention | Pre-intervention | Std. Mean Difference | Std. Mean Difference |
|-------------------------|-------------------|------------------|----------------------|----------------------|
|                         | Mean   | SD    | Total | Mean   | SD    | Total | Weight | IV, Random, 95% CI | IV, Random, 95% CI |
| Artunes et al. 2020     | 43.54  | 6.77  | 28    | 26.67  | 4.89  | 28    | 12.4%   | 2.81 [2.06, 3.57]   |                      |
| Helm et al. 2017        | 31.71  | 8.07  | 27    | 24.54  | 12.23 | 27    | 13.8%   | 0.68 [0.13, 1.23]   |                      |
| Hwang et al. 2016       | 25.24  | 6.23  | 29    | 21.66  | 5.07  | 29    | 13.9%   | 0.62 [0.09, 1.15]   |                      |
| Kimura et al. 2019      | 15.10  | 4.17  | 11    | 12.84  | 4.09  | 11    | 11.7%   | 0.53 [-0.33, 1.38]  |                      |
| Miyamoto, Kondo et al. 2018 | 0.2686 | 0.1238 | 13    | 0.2505 | 0.1313 | 13    | 12.3%   | 0.14 [-0.63, 0.91]  |                      |
| Roh et al. 2017         | 31.4   | 3.8   | 15    | 24.8   | 2.7   | 15    | 11.5%   | 1.95 [1.06, 2.84]   |                      |
| Schmidt-Kassow et al. 2014 | 37.53  | 7.46  | 9     | 33.07  | 7.35  | 9     | 11.1%   | 0.57 [-0.37, 1.52]  |                      |
| Tsai et al. 2016        | 0.08609| 0.06834| 20    | 0.03978| 0.0386| 20    | 13.2%   | 0.82 [0.17, 1.47]   |                      |
| Total (95% CI)          | 152    |       | 152   | 100.0% | 1.00 [0.43, 1.58] |                      |

Heterogeneity: $ Tau^2 = 0.55; Chi^2 = 36.79, df = 7 (p < 0.00001); I^2 = 81\%$
Test for overall effect: $Z = 3.40$ (p = 0.0007)

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: -0.281; 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).
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).
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 (I²= 44%) (Figure 7).

| Study or Subgroup       | Experimental | Control | Std. Mean Difference | Std. Mean Difference |
|-------------------------|--------------|---------|----------------------|----------------------|
|                         | Mean     | SD    | Total | Mean     | SD    | Total | Weight | IV, Random, 95% CI | IV, Random, 95% CI |
| Figueiredo et al. 2019  | 92.6    | 15.9  | 11    | 67.1    | 43.9  | 10    | 29.0%  | 0.76 [-0.14, 1.65] |
| Kim 2015                | 1.58    | 0.36  | 7     | 2.22    | 1.23  | 7     | 23.4%  | -0.66 [-1.75, 0.43]|
| Schiffer et al. 2009    | 0.1172  | 0.0949| 9     | 0.0989  | 0.0786| 9     | 27.9%  | 0.20 [-0.73, 1.13] |
| Seifert et al. 2010     | 2       | 0.9   | 7     | 1.2     | 0.3   | 5     | 19.6%  | 1.02 [-0.23, 2.27] |
| Total (95% CI)          | 34      |       | 31    | 100.0%  |       |       | 0.32 [-0.36, 1.00] |

Heterogeneity: Tau² = 0.21; Chi² = 5.32, df = 3 (p = 0.15); I² = 44%
Test for overall effect: Z = 0.92 (p = 0.36)

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 I²=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),

| Study or Subgroup       | Post-intervention | Pre-intervention | Std. Mean Difference IV Random, 95% CI | Std. Mean Difference IV Random, 95% CI |
|------------------------|-------------------|------------------|----------------------------------------|----------------------------------------|
| Figueiredo et al. 2019 | 92.6              | 15.9             | 11                                     | 11                                     |
| Kim 2015               | 1.5               | 0.36             | 7                                      | 7                                      |
| Schiffer et al. 2009   | 117.2             | 94.9             | 9                                      | 9                                      |
| Seifert et al. 2010    | 2                 | 0.9              | 7                                      | 7                                      |

Total (95% CI) 34 34 100.0% 0.20 [-0.44, 0.84]
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 adaptations 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$_{2\text{max}}$ 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 have 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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