

Effects of Supplementation with Ginseng and Branched Chain Amino Acids Improved Central Fatigue and Enhanced Attention during Exercise: A Randomized, Double-blind, Placebo Controlled

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Abstract Muscle fatigue was a common problem after exercise. When fatigue occurred, body functions were affected and changed. Changbai Mountain ginseng had higher anti-fatigue substances than general commercial ginseng. And recent studies had showed that the supplementation of branched chain amino acids (BCAA), including leucine, isoleucine and valine, can increase attention and reduce fatigue. However, its effect on Changbai Mountain ginseng combined with BCAA was still unclear. Subjects were allocated to Gojinsen® drinks and placebo group (1:1 ratio) for 14 days, and then examined by maximal oxygen consumption, time to exhaustion, rating of perceived exertion (RPE), oxygen saturation (S_pO_2), blood lactate concentration, and continuous attention performance test (CPT II). The Gojinsen® group significant increased maximal oxygen consumption, time to exhaustion, and attention compared to placebo group. Moreover, the Gojinsen® group significant decreased lactate concentration and fatigue compared to placebo group. By our study, Gojinsen® drinks had anti-fatigue effect and enhanced attention, and the therapeutic potential for people suffering from exercise fatigue.

Keywords: attention, branched chain amino acids, ginseng, fatigue

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1. Introduction

Muscle fatigue was a common problem after exercise. When fatigue occurred, body functions such as muscle strength, proprioception, and muscle activation changed due to the effects of fatigue [1]. After muscle fatigue, muscle tension increased, blood circulation changed, muscle strength decreased, and soreness [2]. Common methods to reduce fatigue, relieve soreness, and improve exercise capacity, such as ice compress, hot compress, massage, lymphatic drainage, electrotherapy, cupping, diet, etc [2]. However, how to more effectively promote the elimination of fatigue and improve sports performance still needs more research to confirm.

Changbai Mountain ginseng was a wild ginseng that grows in the Changbai Mountain Range in Jilin Province, in Northeastern China. Ginseng was a perennial herb that was widely used as a tonic in traditional medicine and was

believed to have a spiritual effect [3]. Ginseng contained more than 30 kinds of ginsenosides, which were its main active ingredients [3]. The studies had showed that ginseng contains lignin as the main component of anti-stress and anti-fatigue [4]. The study showed that ginseng inhibited free radicals and enhanced immunity [5]. In addition, it also had anti-aging, anti-cancer and cardiovascular protection functions [5]. Ginseng reduced the content of serum lipid peroxide in rats and increased the activity of superoxide dismutase (SOD) [6]. Other studies had showed that after taking ginseng, it can increase the maximum oxygen consumption (VO_2 max), improve the endurance duration and reduce the accumulation of lactic acid [7]. Therefore, ginseng can effectively improve aerobic exercise and anti-fatigue ability.

In recent years, among the many supplements, branched-chain amino acids (BCAA) were often used as nutritional supplements by bodybuilders and athletes [8]. Branched chain amino acids (BCAA), including leucine, isoleucine, and valine, were the main components of

muscle tissue. Studies had showed that exercise increased the BCAA metabolism. Therefore, supplementing BCAA before exercise can slow down the decomposition of muscle protein and increase the synthesis of skeletal muscle protein [9]. Clinical studies showed that the subjects were supplemented with BCAA, and the BCAA concentration in plasma was significantly increased after exercise [10]. BCAA supplementation can delay 5-hydroxytryptamine (5-HT) accumulation, thereby reducing fatigue and improving endurance [11]. In addition, BCAA can also improve immunity. However, there were still not much clinical studies for ginseng with BCAA, and it was worth continuing to explore.

In this study, we used Gojinsen® drinks, including Changbai Mountain ginseng with BCAAs, and explore whether Gojinsen® drinks had anti-fatigue and improved attention effects.

2. Materials and Methods

2.1. Clinical Design

This clinical study was approved by the ethics committee of the Antai Medical Care Cooperation Antai Tian-Sheng Memorial Hospital (TSMH No.13-023-A2). The study was registered in clinicaltrials.gov (No. NCT04878536). All methods were in accordance with the relevant guidelines and regulations. The subjects visited the laboratory 7 days prior to the experiment. During the first visit, subjects completed the health and exercise history questionnaire, then the height and weight was measured. The 16 subjects were divided into Ginseng group (n =8) and placebo group (n =8) in a randomized and double-blind design. 1 day before the experiment, all subjects performed VO₂ max test to examine the maximal oxygen consumption, time to exhaustion, rating of perceived exertion (RPE), oxygen saturation (S_pO₂) and blood lactate concentration. In addition, 10 minutes after the VO₂ max test, subjects performed continuous attention performance test (CPT II). 3 days later, subjects arrived to the lab every day after lunch time to ingest Gojinsen® or placebo drinks (50mL) for total 14 days. After the first day and the 14th day of ingestion, subjects performed the same test to examine acute and short-term supplement effect. Subjects were instructed to refrain from ingesting dietary ginseng and BCAAs for the period of this experiment. Inclusion criteria included: healthy male and female adults aged 20-25 years old (without heart, liver, kidney, endocrine or other major organic diseases). They each had at least 3 months experience in performing exercise (at least three days per week in the 3-month period before the study). Exclusion criteria: BMI of the study subjects must be less than 25. All subjects were required to consume the same breakfast (400 kcal) on the day before each trial. A dietary log for the preceding 24 h was collected to assess dietary intake, and reminders were given to ensure dietary compliance.

2.2. Test Sample

Supplements used in this study were Gojinsen® drinks, including 3% fresh Changbai Mountain Ginseng extract,

0.2% leucine, 0.2% valine, 0.1% isoleucine, apple juice, citric acid and water. Placebo drinks including apple juice, citric acid and water. The weight and appearance of placebo drink was similar with Gojinsen® drinks.

2.3. Endurance Exercise Performance Testing

Before 10 minutes of the endurance exercise performance testing, the subjects arrived to the laboratory and wore the oxygen uptake mask of energy metabolism analyzer (Sensor Medics, Vmax29, USA) to measure the subjects' oxygen uptake, VO₂max, an index of aerobic capacity in this study. The VO₂max was measured during the treadmill exercise by Bruce Protocol (Morehouse, 1972), a gradual increase in the speed and the slope of the treadmill every 3 minutes. The rating of perceived exertion (RPE) of subjects were also recorded every step. In this study, 72 hours prior to the experiment, subjects were prohibited to ingest the food that containing caffeine and alcohol, to avoid affecting the accuracy of the experimental data.

2.4. Analysis of S_pO₂ and Blood Lactate Concentration

Biochemical analysis item of the present study was blood lactate, the subjects' fingertip blood were collected when the subject arrived to the lab. The blood draw points were resting period prior to test, the first 12 minutes during the VO₂max test, 5 minutes and 10 minutes during recovery period. Therefore, each of the subjects in the experimental period should draw fingertip blood four times, each blood volume was 25μl. Then, fingertip capillary blood was placed in automated blood lactate analyzer (ARKRAY, YSI1500, Japan) for the analysis of blood lactate concentration. In addition, the oxygen saturation by pulse oximetry (S_pO₂) of the subjects were measured during VO₂max test and recovery period.

2.5. Continuous Attention Performance Test

In the present study, 10 minutes after maximal exercise test, the subjects performed attention tests that used Canon continuous attention software (Conners' Continuous Performance Test). The reaction time and error rate were used to assess central fatigue of the subjects. The total test time is about 10-15 minutes.

2.6. Statistical Analysis

Descriptive data were generated for all variables and expressed as mean ± standard error of the mean. A 2 (groups) × 2 (time) analysis of variance (ANOVA) with repeated measure was used to analyze the index of fatigue (time to exhaustion, maximal oxygen consumption, blood lactate concentration, RPE and continuous attention performance test). Following LSD post hoc tests were used to examine pairwise difference when significant F values were seen. Significant interactions were analyzed by simple main effects. Statistical significance in the present study was set at P ≤ 0.05.

3. Results

3.1. The Ginseng with BCAA Increased Maximal Aerobic Exercise Performance, and Maximal Oxygen Consumption.

Figure 1 showed the overall flow chart of this experiment. Table 1 showed the basic information of the subjects, including age, height, weight, and BMI. It can be seen that there was no special difference between the placebo group and the Gojinsen® group. The results of time to exhaustion during maximal exercise were presented in Figure 2A. There was no significant difference in the time from acute supplementation to exhaustion ($P > .05$). However, the exhaustion time of the Gojinsen® after 14 days of supplementation was significantly higher compared to placebo group ($P < .05$). On the maximum oxygen consumption test result, we found that no significant difference was evidenced in maximal oxygen consumption after acute supplementation ($P > .05$). However, the maximal oxygen consumption of Gojinsen® group was significantly higher compare to placebo group after 14 days supplementation ($P < .05$) (Figure 2B). No significant difference was

evidenced in RPE after acute and short term supplementation ($P > .05$). Thus, these results found that ginseng with BCAA intake increased the maximal aerobic exercise performance, and maximal oxygen consumption.

3.2. The Ginseng with BCAA Decreased the Lactate and Enhanced Attention

Then, the subject had performed blood analysis to observe the blood oxygen, lactic acid concentration. No significant difference was evidenced in blood oxygen (S_pO_2) after acute and short term supplementation ($P > .05$) (Figure 3A), and the blood lactate concentration of Gojinsen® group was significantly lower compared to placebo group after 14 days supplementation ($P < .05$) (Figure 3B). Therefore, these results showed that ginseng with BCAA decreased the lactate and delay the onset of fatigue during the maximal exercise. Finally, the subjects had performed CPT II. We found that Gojinsen® can reduce error of omissions and commissions during fatigue state after acute and 14 days supplementation (Figure 4A and Figure 4B), suggesting ginseng with BCAA enhanced attention and improved central fatigue.

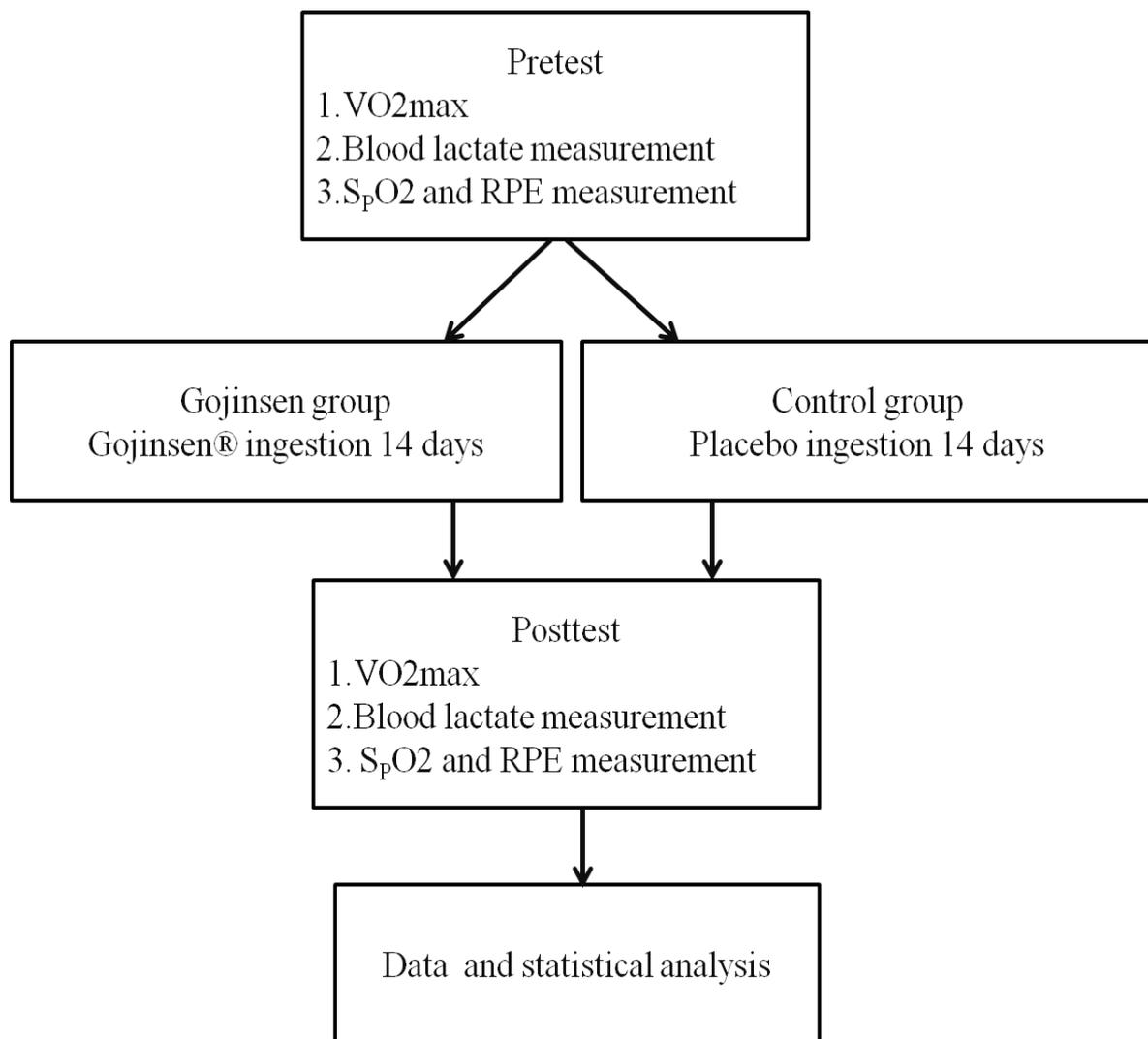
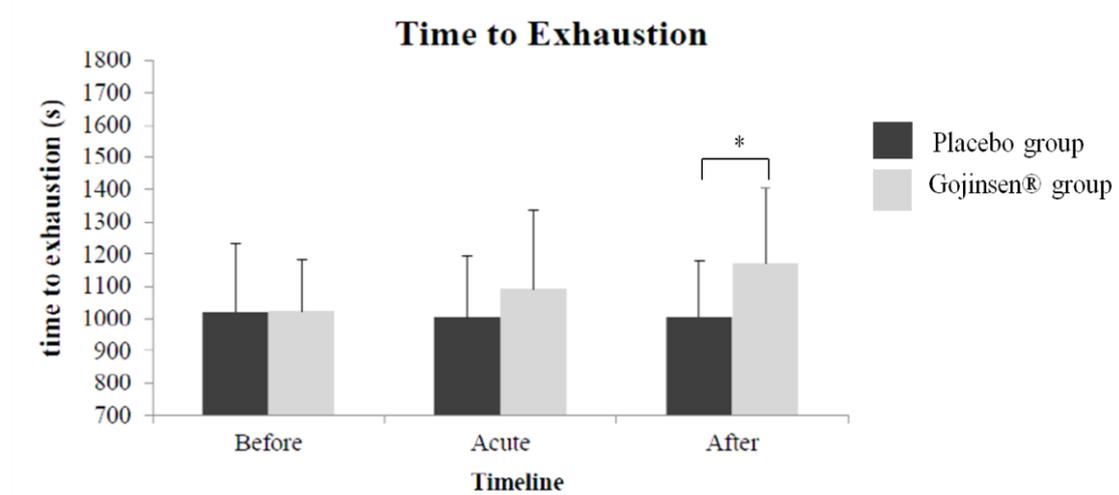


Figure 1. The flow chart of the clinical study. A total of 16 subjects were recruited, and the first test will be conducted before the trial. Then it was divided into two groups, namely the Gojinsen® and placebo groups. After taking it for 14 days, take the second test

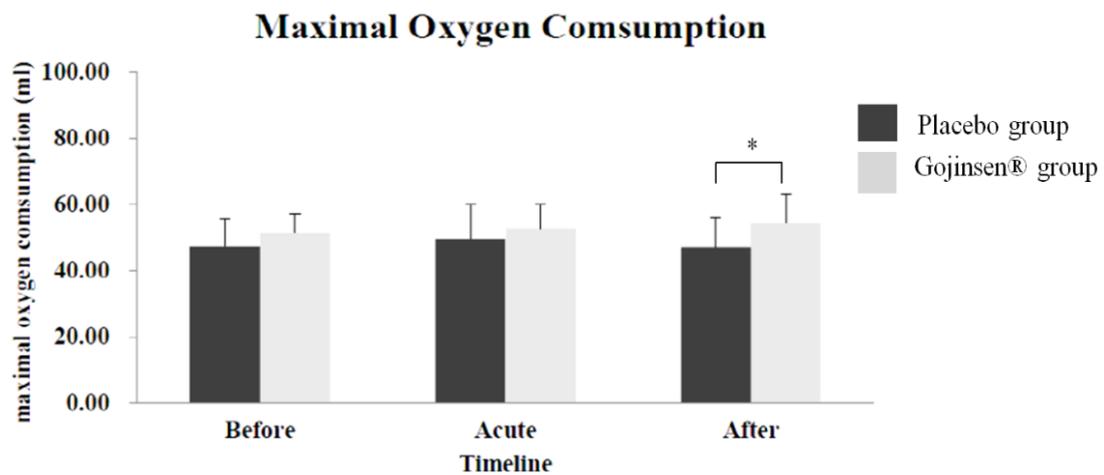
Table 1. Subject physical test results (N=16)

Parameter	Age (yr)	Height (cm)	Weight (kg)	BMI
Gojinsen® group (n=8)	22.8±1.4	163.2±13.1	61.2±14.1	21.2±2.4
Placebo group (n=8)	22.7±1.9	166.6±11.5	63.8±15.3	23.7±2.1

A



B



C

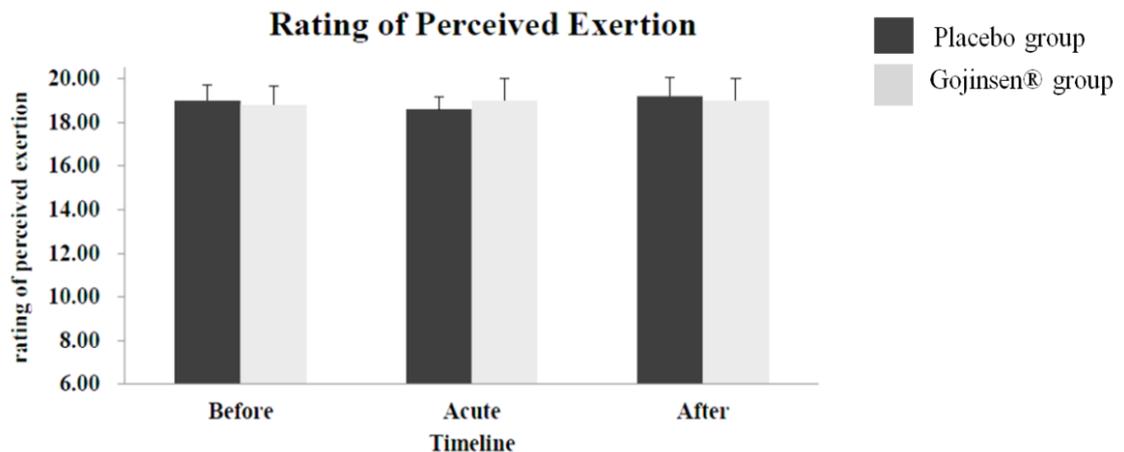


Figure 2. The ginseng with BCAA increased the maximal aerobic exercise performance, and maximal oxygen consumption. The subjects were arranged to exercise on a treadmill, and wore the oxygen uptake mask to record the (A) time to exhaustion, (B) measure the maximum oxygen uptake, and (C) the RPE by energy metabolism analyzer. Error bars represent SD. * $p < 0.05$

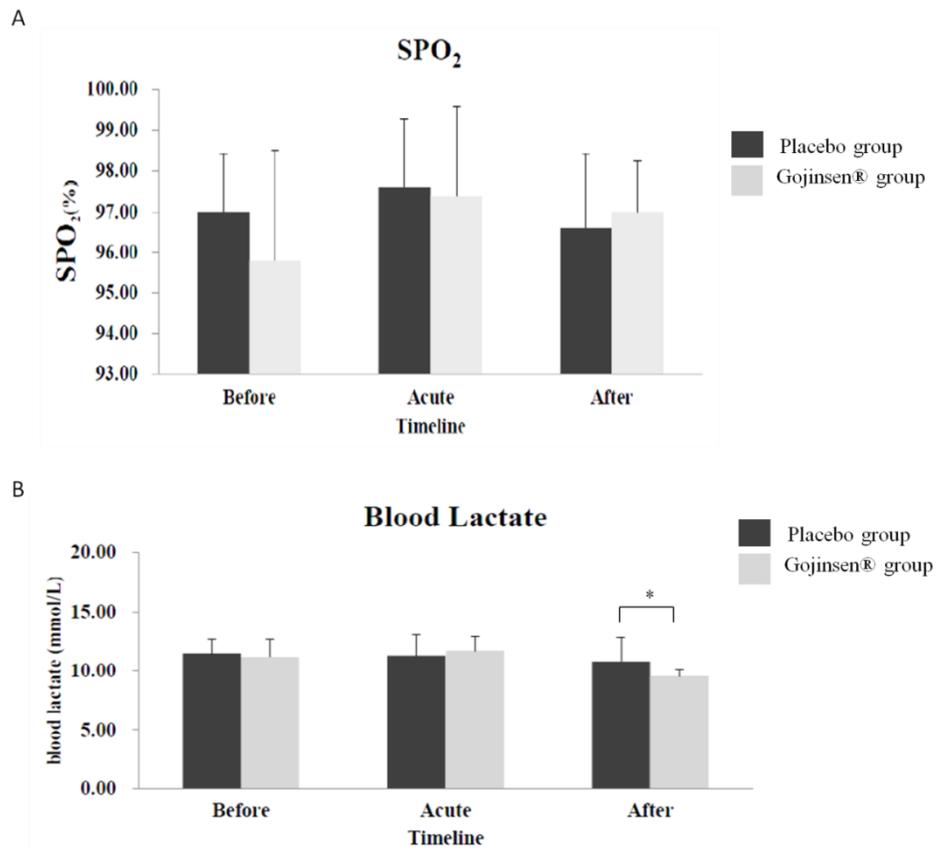


Figure 3. The ginseng with BCAA decreased lactate accumulation and not affected blood oxygen. Collect blood from the subject's fingertips, the blood was examined S_pO₂ and blood lactate concentration. The blood draw points were resting period prior to test, the first 12 minutes during the VO₂max, and 5 minutes and 10 minutes during recovery period by automated blood lactate analyzer. Error bars represent SD. *p < 0.05.

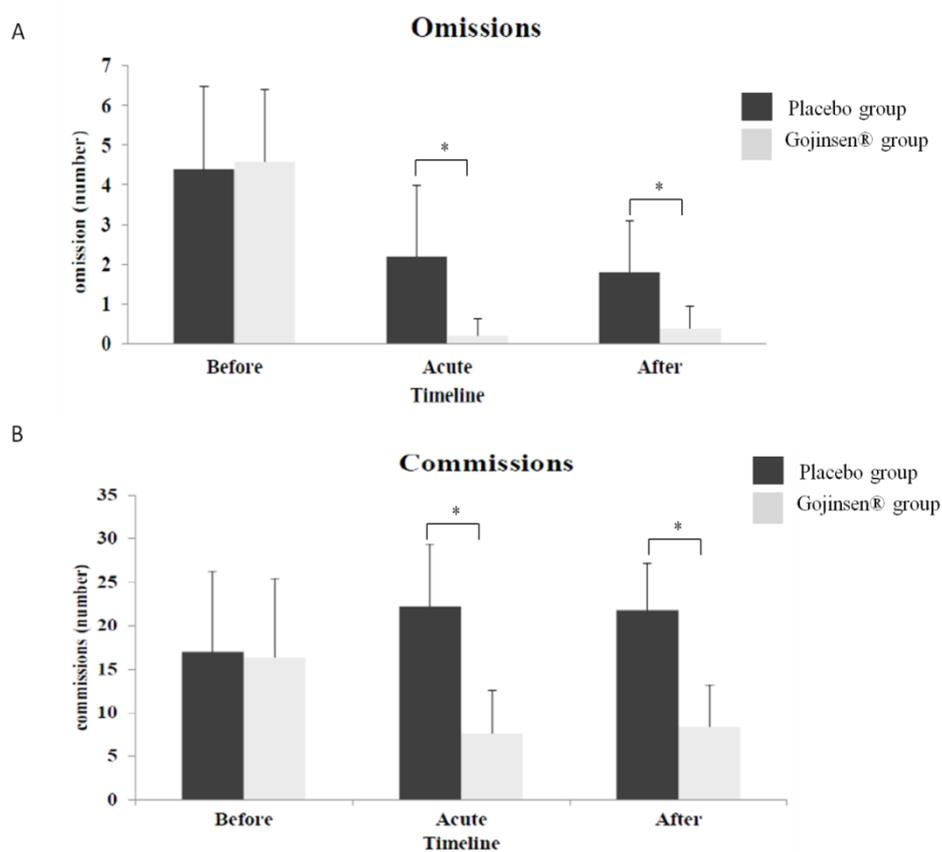


Figure 4. The ginseng with BCAA enhanced attention and reduced errors. At 10 minutes after the maximum exercise test, the subject performed a CPT II to record (A) error of omissions, and (B) error of commissions. Error bars represent SD. *p < 0.05

4. Discussion

In this study, we found that using Gojinsen® (Changbai Mountain ginseng with BCAA) supplements can increase the maximal oxygen consumption and the performance of continuous attention test during fatigue state. In addition, it can improve central fatigue and blood lactate. Therefore, Gojinsen® had the effect on anti-fatigue. The common active ingredient mixture in Changbai Mountain ginseng was ginsenoside [12]. The benefits of ginseng were attributed to biologically active compounds such as ginsenosides, volatile oils, polyphenols, flavonoids, polysaccharides and vitamins [13]. Studies had showed that ginsenoside can anti-cancer, anti-diabetics, immune regulation, and improve cardiovascular disease [14]. Long-term use of ginsenoside supplements increased muscle power and had anti-inflammatory effects [15]. Ginseng root genotypes were regulated due to regional environmental differences. Changbai Mountain ginseng may have higher biological activity than ginseng grown elsewhere. In this study, we found that the extract of Changbai Mountain ginseng had anti-fatigue and health promotion effects. Other studies had showed that supplementation of ginseng can reduce fatigue and improve cognitive ability [16]. It is currently believed that the possible mechanism is that ginseng can increase the content of dopamine, norepinephrine, serotonin and cyclic adenosine monophosphate (cAMP) in the brain and increase brain oxygen content [17]. The study also showed that under exercise test, taking ginseng for 6 weeks can increase VO₂max [7]. Supplementing ginseng extract continuously for 4 weeks can reduce the accumulation of lactic acid, ammonia and BUN, and had an anti-fatigue effect [12]. Supplementation with ginseng for 4 weeks prior to an exhaustive aerobic treadmill running reduced the leakage of creatine kinase during exercise [18].

BCAAs (leucine, isoleucine, and valine) account for one third of total muscle protein and are the only amino acids metabolized in skeletal muscle [9]. Studies had shown that oral BCAAs can reduce 5-HT activity to reduce central fatigue and increase dopamine synthesis [11]. In addition, taking BCAAs before and during prolonged exercise can relieve muscle fatigue [19]. However, the study had found that BCAAs had no effect on body function. In rats, oral BCAAs supplements reduced the serotonin and catecholamines in the brain during exercise [20]. Taking BCAAs before exercise increases fatigue time, which may be due to the role of BCAAs in maintaining long-term physical activity. Multi-choice reaction time was performed during treadmill exercise, and it was found that after subjects ingested BCAA, it can enhanced attention and shorten reaction time [21]. Moreover, ginseng with BCAAs reduced muscle breakdown, preserved muscle in athletes and decreased delayed-onset muscle soreness in volleyball players [22]. Consistent with our results, taking Gojinsen® increased the maximal aerobic exercise performance, maximal oxygen consumption, and improved fatigue and lactate. In this study, there was no significant change in blood oxygen concentration (S_pO₂) and RPE. The study showed that the blood pressure concentration changed significantly due to high altitude [23], and because the

subjects in this study were all at sea level and had exercise habits, the blood oxygen concentration was relatively stable.

5. Conclusion

Based on the above results, this study found that taking Gojinsen® for 14 days can increase oxygen consumption and attention, In addition, it can improve central fatigue and blood lactate. In order to have a healthy body, proper exercise was also necessary. Gojinsen® had anti-fatigue effect, it is believed to be more helpful to human health, and it can also make aerobic training longer. It was recommended that Gojinsen® can be used as an effective nutritional supplement.

Statement of Competing Interests

The authors have no competing interests.

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