Egg white hydrolyzate reduces mental fatigue: randomized, double-blind, controlled study

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Abstract

Objectives: This study aimed to show that ingesting egg white hydrolyzate (EWH) could improve antioxidant capacity and reduce mental fatigue. Two clinical trials were conducted to examine the antioxidant capacity and the fatigue reduction function of EWH. In Study 1, 19 athlete students were received a single dose of EWH (5 g/day) or placebo. In Study 2, 74 athlete students ingested EWH (5 g/day) or placebo before training for 2 weeks.

Results: Single dose of EWH significantly increased the antioxidant ability compared with the placebo group (p < 0.05), and there was no significant difference between the groups in the oxidative stress test results on Study 1. Two-week intake of EWH significantly decreased mental fatigue compared with the placebo (p < 0.05). This study showed that ingesting EWH improved antioxidant capacity with a single dose and reduced mental fatigue after 2 weeks of ingestion.

Trial Registration Japan Medical Association Center for Clinical Trials identifier; JMA-IIA00395 (Study1) and JMA-IIA00396 (Study2), both trials were retrospectively registered on 26 October, 2018.

Keywords: Egg white peptide, Anti-fatigue, Antioxidative activity, Dietary supplement, Beverage

Introduction

Proteins, peptides, and amino acids are common sports supplements. In particular, peptides are more absorbable than amino acids of identical composition [1]. Egg white peptide (EWP) has various physiological functions, such as angiotensin-converting enzyme-inhibitory, antioxidant, and anti-inflammatory properties [2]. Among these functions of EWPs, the antioxidant property is the one that is most associated to fatigue reduction after exercise. Although the anti-fatigue effect of EWP has been reported, the subjects were not athlete and antioxidant activity in vivo has not been studied [3, 4]. Therefore, two clinical studies were conducted to investigate the antioxidant power in the blood and fatigue reduction function after exercise by ingestion of EWH. Study 1 examined the fluctuation of fatigue and antioxidant activity in vivo after a single ingestion of EWH, measured after exercise. Study 2 examined the function of reducing fatigue after exercise with EWH ingestion for 2 weeks.

Materials and methods

Ethical consideration

This study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Ethical Review Board of Nippon Sport Science University. The approval number is 017-H111 (Study 1) and 017-H112 (Study 2). This study is registered at the Japan Medical Association Center for Clinical Trials...
Nutrition facts

Isomerized sugar, granulated sugar, polysaccharide thickener, citric acid, concentrated grapefruit juice, sweetener, flavor (EWH 5 g/d)

| Ingredients                                                                 | Placebo 113 kcal | EWH 133 kcal |
|----------------------------------------------------------------------------|-----------------|--------------|
| Calories                                                                   | 113 kcal        | 133 kcal     |
| Total fat                                                                  | < 0.1 g         | < 0.1 g      |
| Sodium                                                                     | 209 mg          | 159 mg       |
| Total carbohydrate                                                        | 28 g            | 29 g         |
| Protein                                                                    | 0 g             | 4 g          |
Clinical trial design  The randomized, placebo-controlled, double-blind, parallel-group comparison study was conducted at the Tokyo Setagaya Campus, Nippon Sport Science University (Tokyo, Japan). The participants, care providers and those assessing outcomes were blinded after assignment to interventions.

The participants continuously ingested the placebo or the EWH food 1 h before exercise daily over a two-week period. The exercise performed was regular training at each club. Fatigue was evaluated by Chalder’s fatigue scale (CFS) [7] and VAS prior to ingestion, and at 1 and 2 weeks after ingestion. The VAS was the same scale used for Study 1. The CFS was a subjective evaluation of 0–3 ranks each questionnaire related to chronic fatigue, with rank 0 representing the best condition with no fatigue and rank 3 representing unbearable fatigue.

CFS was evaluated before exercise and VAS was rated before and after exercise. Subgroup analyses were performed for each club separately. The study was conducted from February 19th to March 26th, 2018.

Statistical analysis  The comparison between groups of CFS and VAS was performed by Mann–Whitney U test, and the comparison between before and after exercise was Wilcoxon signed rank sum test.

Results
Study 1
Participant background
Nineteen participants who understood the contents of this study and provided consent participated in the study. One athlete withdrew from the study due to personal reasons, with 18 participants remaining (mean age 20 ± 0.2, Additional file 2). Three unhealthy athletes were excluded because of the study aimed at assessing healthy individuals. Thus the analysis was per protocol set. Since this study design was crossover test, 30 data can be obtained from 15 participants, but eight control group and 11 EWH group blood data were also excluded because unable to be analyzed due to hemolysis or insufficient collection volume in blood tests. Finally, seven control group and 11 EWH group data were analyzed on ROMs and BAP. There were no adverse events related to EWP ingestion.

Oxidative stress and antioxidant power
There was no significant difference before and after exercise in d-ROMs, but the BAP values for both groups significantly increased after exercise compared with before exercise (p < 0.05).

Figure 1 shows the changes in d-ROMs and BAP values after exercise versus before exercise. Although there was no significant difference in d-ROMs, the BAP values in the EWH group were significantly higher after exercise than in the control group (p < 0.05).

Fatigue questionnaire
There was no significant difference between groups in Borg RPE Scale and VAS values.

Study 2
Participant background
A total of 74 participants (mean age 19.8 ± 0.1) who understood the contents of this study and provided consent participated in the study. There were no participant withdrawals during the study period. There were no adverse events related to daily EWP ingestion. The analysis was full analysis set (Additional file 3).

Fatigue questionnaire
There was no significant difference in CFS values for total fatigue and physical fatigue between the groups. Figure 2 shows the change from baseline CFS values in mental fatigue. Fatigue in the EWH group significantly decreased in total participants and in canoe club participants (p < 0.05). There was a downward trend but no significant toward fatigue in triathlon club and weightlifting club participants in the EWH group compared with those in the placebo group (p < 0.01). Regarding the VAS values, no significant differences were observed for all clubs.

Discussion
No significant differences in d-ROMs (blood oxidative stress index) were found between the EWP and placebo groups. However, BAP (blood antioxidative activity index) were significantly higher (p<0.05) in the EWP group than in the placebo group. That indicates that compared with placebo intake, EWP intake before exercise resulted in higher antioxidative activity in blood. Antioxidizing enzymes that decompose active oxygen exist in the muscle fiber cytoplasm and mitochondrial matrix. The function of these antioxidant enzymes is complemented by nonenzymatic antioxidants such as peptides [8]. The results of Study 1 show that EWH, a nonenzymatic antioxidant, rapidly enhances the in vivo antioxidant capacity in a single intake.

In Study 2, the EWH group had significantly reduced CFS values for mental fatigue compared to the control group at 1 and 2 weeks after ingestion (p < 0.05). CFS
is a fatigue index recommended by the Centers for Disease Control and Prevention as a reliable indicator [9]. Ingestion of egg white protein increases the serum amino acid levels [10], intake of egg-derived amino acids had a beneficial effect on mental functions such as emotion and cognition [11].

From these facts, it is considered that the peptide or amino acid derived from EWH is transferred to the blood and acts to reduce mental fatigue. The role of EWP in promoting nitric oxide–related signaling in vivo is considered to be one of the mechanisms of action [12]. The function of EWP is to promote signal transduction related to nitric oxide (NO) in vivo. NO and reactive oxygen (ROS) react in vivo and become active NO species (RNOS), which results in adjustments to the autonomic nervous system [12, 13]. Study 2 showed that these processes were estimated to require continuous intake of EWH for 1 to 2 weeks until a threshold is reached, resulting in recognition of a reduction in mental fatigue. The function of alleviating mental fatigue after exercise due to EWH intake confirmed by this study is a unique feature not confirmed in other food materials.

**Conclusion**

This study showed that a single intake of 5 g/day of EWH increased antioxidant power in the blood, and 2 weeks of continuous intake of EWH decreased mental fatigue.

**Limitations**

In this study, EHW’s functionality for physical fatigue was not confirmed. The turnover of human muscle proteins is about 180 days in half-life [14]. Further EWH functional studies to reduce physical fatigue need to be conducted long-term over several months based on the muscle protein metabolic cycle. Because this study targeted athlete students, whether EWH intake will have the same impact of anti-fatigue function and antioxidant capacity in the general population with no strong activity intensity is unknown. CFS is a scale for chronic fatigue, that is required the review of applicability for healthy athletes. The decrease in the number of blood analyses is a severe limitation on this study. Further research is required including the statistical planning.
Fig. 2 Changes in CFS values for mental fatigue following ingestion of placebo or EWH. **a**, all participants; **b**, canoe club; **c**, triathlon club; **d**, weightlifting club; data are presented as mean ± SE, *p < 0.05 vs placebo.

**Supplementary information**

Supplementary information accompanies this paper at https://doi.org/10.1186/s13104-020-05288-8.

**Abbreviations**

EWP: Egg white peptide; d-ROMs: Diacron-reactive oxygen metabolites; BAP: Biological antioxidant potential; Borg RPE Scale: Borg Rating of Perceived Exertion Scale; CFS: Chalder’s Fatigue Scale.

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**Authors’ contributions**

MO, HS, and HN prepared the proposal, obtained ethical approvals, applied for funding, provided data collection and wrote the manuscript. TN, MA, RS,
and MY conceived the idea and supervised the study. All authors read and approved the final manuscript.

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**Availability of data and materials**

Not applicable.

**Ethics approval and consent to participate**

Study 1 and Study 2 were both approved by the Ethical Review Board of Nippon Sport Science University (Study 1: 017-H111, Study 2: 017-H112). Oral and written consent was obtained from all participants.

**Consent for publication**

Not applicable.

**Competing interests**

This study was funded by Kewpie Corporation, Japan. MO, HS, HN, RS, and YM are employees of Kewpie Corporation. Kewpie Corporation manufactures the EWH.

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