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## Effects of chicken essence on recovery from mental fatigue in healthy males

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Statistical Analysis C  
Data Interpretation D  
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**Background:** Fatigue is a common symptom in modern society. There has been a recent resurgence of interest in traditional remedies for fatigue. Chicken essence, which is rich in anserine and carnosine, has been widely taken in Asian countries as a traditional remedy with various aims, including attenuation of physical and mental fatigue. However, the evidence for its efficacy specifically for mental fatigue remains unclear. We examined the effect of essence of chicken on mental fatigue in humans, using our established fatigue-inducing task and evaluation methods.




**Material/Methods:** In this placebo-controlled crossover study, 20 healthy male volunteers were randomized to receive daily oral administration of essence of chicken or placebo drink provided by Cerebos Pacific Ltd. via Suntory Holdings Ltd. for 4 weeks. The participants performed 2-back test trials as a fatigue-inducing mental task and then had a rest session. Just before and after each session, they completed cognitive task trials focusing on selective attention to evaluate the level of mental fatigue.

**Results:** After essence of chicken intake for 1 and 4 weeks, the reaction times on the cognitive task trials after the rest session were significantly shorter than those at baseline, and significant changes were not observed with placebo intake. The reaction times before and after the fatigue-inducing session were not altered by either essence of chicken or placebo intake.

**Conclusions:** We showed that daily intake of essence of chicken could be effective for the recovery from mental fatigue and is a promising candidate for use as an anti-fatigue food.

**Key words:** **essence of chicken • humans • mental fatigue • recovery • selective attention**

**Full-text PDF:** <http://www.medscimonit.com/download/index/idArt/883971>

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## Background

Fatigue is a common symptom both in sickness and in health [1–3]. Fatigue can be defined as difficulty in initiating or sustaining voluntary activities [4]; this decreases efficiency in performing daily tasks and is a risk factor of various diseases [5,6]. Thus, it is important to establish remedies for fatigue.

Recently, naturally occurring nutrients and over-the-counter supplements such as vitamins, minerals, and taurine have been widely used with expectation of attenuating fatigue. At present there is little scientific evidence for their efficacy and few established regimens for the treatment of fatigue [7,8], but there is evidence that specific nutrients such as carbohydrate contribute to energy production [9] and vitamin C contributes to antioxidation [8]. This may be because no standardized fatigue-inducing tasks with relatively short duration and no appropriate methods of evaluating fatigue have been developed.

To overcome these problems, we recently developed physical and mental fatigue-inducing tasks and appropriate methods for their evaluation [10]. We have identified the anti-fatigue effects of oral substances such coenzyme Q10 [11] and chicken essence [12] for physical fatigue using a recently developed physical fatigue-inducing task and evaluation methods. Both coenzyme Q10 and chicken essence improved physical performance and attenuated fatigue sensation due to fatigue-inducing workload trials [11,12]. However, we did not identify any anti-fatigue substances effective against mental fatigue.

There has been a recent resurgence of interest in traditional remedies for mental fatigue. Chicken essence is used as a traditional remedy with various aims [13]. Especially in Asian countries, it is widely taken for attenuation of fatigue, recovery from stress, and increasing mental efficiency [14]. Chicken essence contains large amounts of imidazole dipeptides (carnosine and anserine), which are natural antioxidants in meat extract. The antioxidant effect of imidazole peptide inhibits tissue damage and suppresses the reduction in performance level induced by mental fatigue [15–17]. Therefore, chicken essence is a promising candidate as a remedy for fatigue.

The aim of our study was to evaluate the efficacy of chicken essence, specifically on mental fatigue, by means of our established mental fatigue-inducing task and evaluation methods. Although the association between chicken essence and fatigue caused by mental workload has been indicated previously [14], that study design was totally different from ours in that it only compared chicken essence and placebo intake conditions administered for 7 days with an intra-subject design. To scientifically evaluate the anti-fatigue effect of chicken essence, we designed and conducted a placebo-controlled crossover study and evaluation sessions were performed just before

and after the fatigue-inducing and rest sessions. Evaluation sessions included cognitive task trials to assess selective attention because our previous study showed that mental fatigue specifically caused a decrease in the ability to maintain selective attention [18].

## Material and Methods

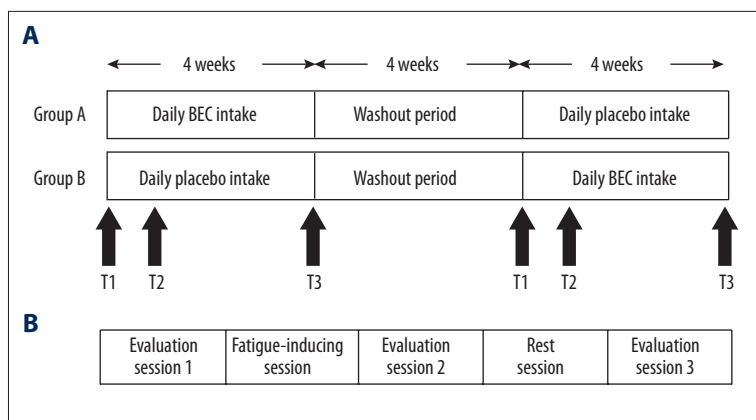
### Participants

Twenty healthy male volunteers [age,  $34.7 \pm 0.83$  years old (mean  $\pm$ SEM)] were enrolled in this study. They were recruited via an advertisement. We excluded current smokers, those with a history of medical illness, and those taking chronic, acute, and per-request medications. Good health was also ensured by physical examination by a medical doctor (M.T.). In the present study, we choose only healthy males because their physical condition is not affected by menstrual cycle.

All of the participants provided written informed consent. The study protocol was approved by the Ethics Committee of Osaka City University and was conducted in accordance with the Declaration of Helsinki.

### Experimental design

After enrolment, the participants were randomly assigned to 2 groups in a placebo-controlled crossover manner to initially receive chicken essence or placebo drink (Figure 1A). The participants receiving chicken extract were given 1 bottle of Brand's Essence of Chicken (BEC; Cerebos Pacific Ltd., Singapore) twice a day (after breakfast and dinner) for 4 weeks. BEC is produced by a process of water extraction from chicken meat for several hours under high temperature. The solid content consists mainly of proteins, amino acids, and peptides such as carnosine and anserine. A bottle of BEC (70 ml) contains 83 mg protein and peptide, 3.1 mg free amino acids, 0.8 mg hexose, 0.4 mg fat, and 3 mg caramel [19]. It also contained  $\beta$ -alanyl-L-histidine (carnosine) and  $\beta$ -alanyl-L-methyl-L-histidine (anserine) as active di-peptides [20,21]. The dose of BEC used in the present study was based on a previous human study [12]. Those receiving placebo were given 1 bottle of sample twice a day (after breakfast and dinner) for 4 weeks. A bottle of placebo (70 ml) contains 83 mg milk casein and 3 mg caramel to produce protein content, caloric content, and color similar to those of BEC. Casein is chosen as an ingredient in the placebo because it does not include peptides reported to have effects on fatigue [12] and has similar amino-acid composition as BEC. The BEC and placebo samples were provided by Cerebos Pacific Ltd. via Suntory Holdings Ltd. Experiments were conducted just before starting the sample (T1), 1 week later (T2), and 4 weeks after starting the sample (T3). The time



**Figure 1.** Experimental design (A) and procedure of experimental sessions (B). Participants were randomized to daily Brand’s Essence of Chicken (BEC) intake (Group A) or daily placebo intake (Group B) for 4 weeks. After the 4-week washout period, they received placebo (Group A) or BEC (Group B) daily for 4 weeks. Experiments were conducted just before starting the sample (T1), 1 week later (T2), and 4 weeks after starting the sample (T3) (A). On each experimental day, subjects performed fatigue-inducing and rest sessions, and evaluation sessions were performed just before and after each session (B).

interval between each intake period was set at 4 weeks as a washout period. During each intake period, the participants refrained from strenuous mental and physical activities and followed normal dietary behavior, drinking patterns, and sleeping hours. They were asked to rate their levels of fatigue on a visual analogue scale (VAS) from 0 (no fatigue) to 100 (total exhaustion) [22] every day at home.

**Procedures**

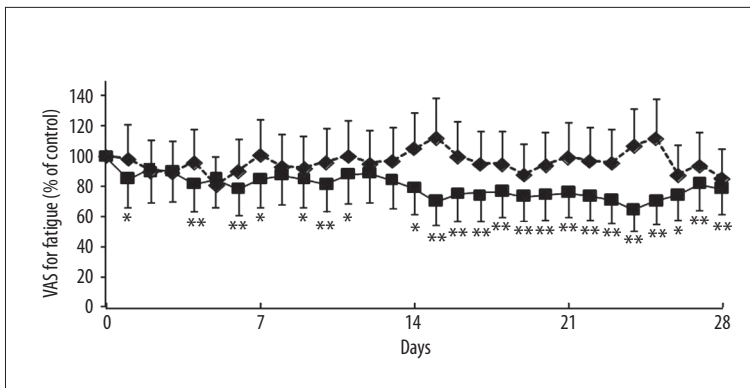
On each experimental day, they performed fatigue-inducing and rest sessions, with evaluation sessions just before and after these sessions (Figure 1B). During the fatigue-inducing session, they performed 2-back test trials for 40 minutes. These involved remembering not the last item presented to them, but the one before that. During the rest session, they could choose to read books or magazines or listen to music for 60 minutes. During the evaluation session, they performed cognitive task trials for 9 minutes and rated their subjective level of fatigue on the VAS. For 1 day before each visit, participants refrained from drinking caffeinated beverages and could ingest only water during each experimental day. This study was conducted in a quiet, temperature- and humidity-controlled environment.

**Fatigue-inducing task**

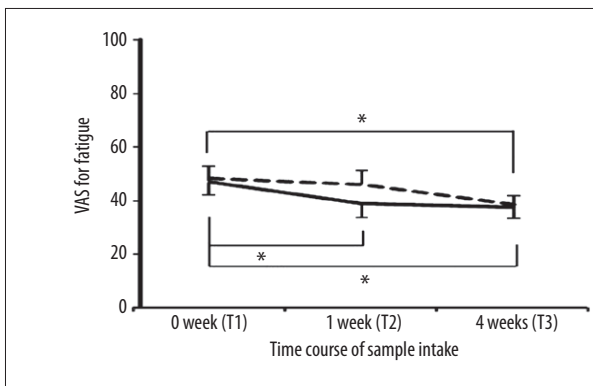
As a fatigue-inducing mental task, participants performed 2-back test trials [23] for 40 minutes [24]. One of 4 types of white letters was continually presented on a black background in the display of a laptop computer every 3 seconds. The letter size was 30×30 mm. During the trials, participants had to judge whether the target letter presented at the center of the screen was the same as the one that had appeared 2 presentations earlier. If it was, they were to press the right button with their right middle finger; if it was not, they were to press the left button. They were instructed to perform the task trials as quickly and as correctly as possible. The result of each 2-back trial, that is, a correct response or error, was continually presented on the display of the laptop computer.

**Cognitive task**

The cognitive task presentation consisted of traffic lights (a Japanese character meaning blue or red was placed on either blue or red lights) shown on the display of a personal computer screen [25,26]. Participants performed Task A for 3 minutes and Task B for 6 minutes. In Task A, they were told to press the right button with their right middle finger if the blue traffic light was presented (placed on a Japanese character meaning blue). If the red traffic light was presented (placed on a Japanese character meaning red), they were told to press the left button with their right index finger. In Task A, they had to decide to press a button depending on whether the target Japanese character presented at the center of a traffic light was blue or red. If the Japanese character meaning blue was presented, regardless of the color of the traffic light, they were to press the right button with their right middle finger; otherwise, they were to press the left button with their right index finger. In these tasks, each trial was presented 100 msec after either of the buttons was pressed. During the task period, blue or red trials were given randomly and the probability of occurrence of each color and type of sign was equal. In Task B, mismatching the color of the traffic light with the Japanese character (i.e., Stroop trials [27]), and matching the color of the traffic light with the Japanese character (i.e., non-Stroop trials) occurred an equal number of times. This task is based on the Stroop test [27], which is used as a classic experimental paradigm in research settings. In this test, the participants are asked to name the color of the letters as presented visually either in the congruent or incongruent condition. The strong interference of word reading upon color naming is called the Stroop interference effect, which occurs when the noun presented is a color name displayed visually using a different color. This paradigm demonstrates the requirement for a limited-capacity attentional system in the selection of processing centers appropriate for job execution.



**Figure 2.** Subjective levels of everyday fatigue during the time course of sample intake. Participants were asked to rate their levels of fatigue on a visual analog scale (VAS) from 0 (no fatigue) to 100 (total exhaustion) before (control) and throughout 4 weeks of the sample intake. The solid line indicates Brand's Essence of Chicken (BEC) intake and the dotted line indicates placebo intake. The values are shown as the mean and SEM. \*  $P < 0.05$ , \*\*  $P < 0.01$ , significantly different from the control (paired t-test).



**Figure 3.** Subjective levels of fatigue on the experimental days. Participants were asked to rate their levels of fatigue on a visual analog scale (VAS) from 0 (no fatigue) to 100 (total exhaustion) from 0 (baseline), 1 week later and 4 weeks after starting the sample. The solid line indicates Brand's Essence of Chicken (BEC) intake and the dotted line indicates placebo intake. Values are shown as the mean and SEM. \*  $P < 0.05$ , significant difference (one-way repeated-measures analysis of variance followed by paired t-test with Bonferroni correction).

Participants were instructed to perform the task trials as quickly and as correctly as possible. The result of each cognitive task trial (i.e., a correct response or error) was continuously presented on the display of the personal computer.

### Statistical analyses

Values are presented as the mean  $\pm$  SEM unless otherwise stated. Comparisons between the 2 groups were performed using the paired t-test. Multiple comparisons during the time course of sample intake were performed using one-way repeated-measures analysis of variance. When statistically significant or trend effects were found, intragroup differences were compared using the paired t-test with Bonferroni correction. All  $P$  values were 2-tailed and  $P$  values less than 0.05 were considered significant. Statistical analyses were performed using the SPSS 17.0 software package (SPSS, Chicago, IL).

## Results

### VAS score for fatigue

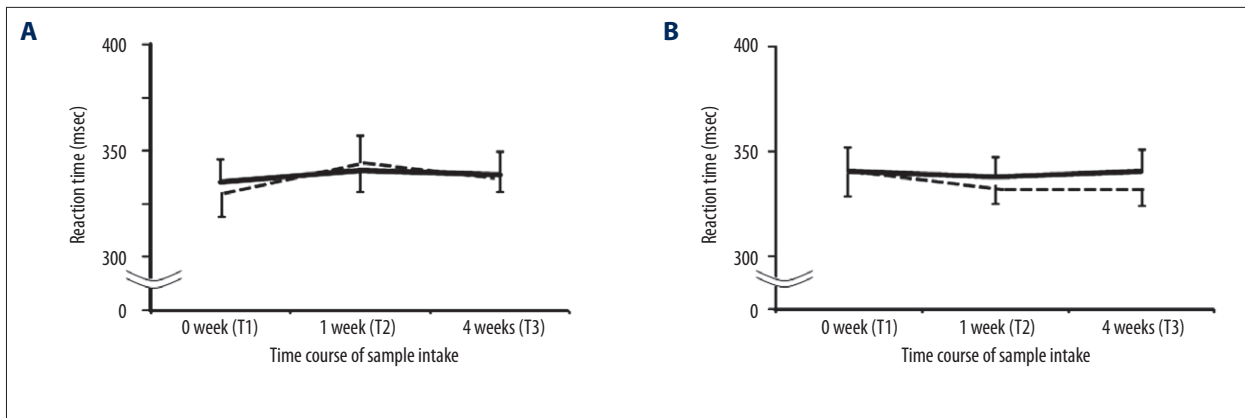
Subjective levels of fatigue are shown in Figures 2 and 3. In Figure 2, the daily VAS score for fatigue assessed at home is shown; the scores of the BEC condition were lower than those of the placebo condition throughout 4 weeks. The VAS score for fatigue after the rest session during the experiment was significantly lower in the BEC condition at T2 and T3 than at T1, and in the placebo condition the fatigue score was significantly lower only at T3 (Figure 3). The VAS score of the BEC condition was significantly lower than that of the placebo condition at 1 week after the start of sample intake.

### Cognitive task

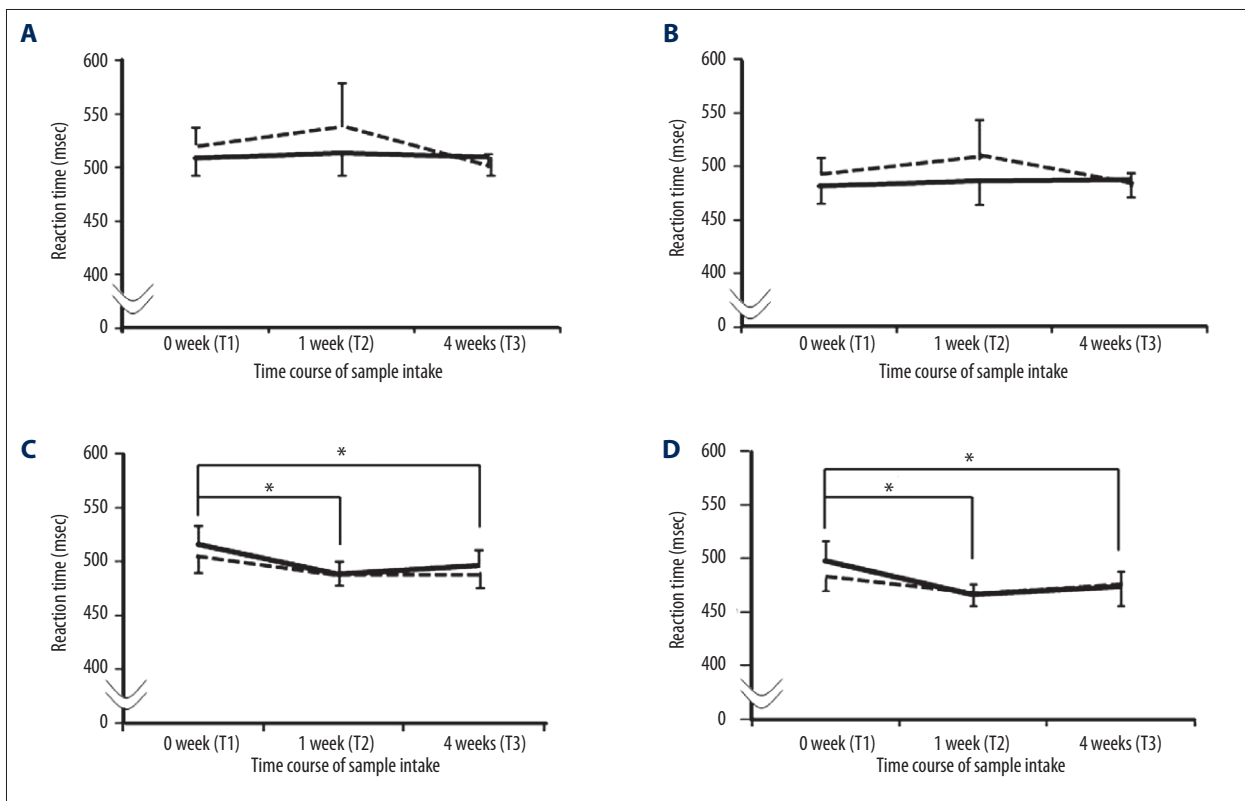
Reaction times after the fatigue-inducing and rest sessions in Tasks A and B are shown in Table 1. Reaction times in Task A after the fatigue-inducing and rest sessions exhibited no change over the time course of the experimental day in either the BEC or placebo condition (Figure 4). Reaction times in Task B of the Stroop and non-Stroop trials are shown in Figure 5. The reaction times in Stroop trials were longer than those in non-Stroop trials across the experimental day in both the BEC and placebo conditions. The reaction time in Task B of the Stroop and non-Stroop trials after the fatigue-inducing task session exhibited no change over the time course of the experimental day in either the BEC or placebo condition (Figure 5A and 5B). However, the reaction times in Task B of the Stroop and non-Stroop trials after the rest session were significantly shorter at T2 and T3 than at T1 in the BEC condition, but placebo intake did not exhibit these effects (Figure 5C and 5D).

## Discussion

We found that oral administration of the BEC drink improved the subjective level of fatigue as well as improving cognitive



**Figure 4.** Reaction times after fatigue-inducing (A) and rest (B) sessions for Task A. Participants performed the task trials from 0 (baseline), 1 week later, and 4 weeks after starting the sample. The solid line indicates Brand's Essence of Chicken (BEC) intake and the dotted line indicates placebo intake. Values are shown as the mean and SEM.



**Figure 5.** Reaction times after fatigue-inducing (A, B) and rest (C, D) sessions for Task B of Stroop (A, C) and non-Stroop (B, D) trials. Participants performed the task trials from 0 (baseline), 1 week later, and 4 weeks after starting the sample. The solid line indicates Brand's Essence of Chicken (BEC) intake and the dotted line indicates placebo intake. Values are shown as the mean and SEM. \*  $P < 0.05$ , significant difference (one-way repeated-measures analysis of variance followed by paired t-test with Bonferroni correction).

task performances in healthy males. In particular, shorter reaction times in Task B were observed in the BEC-intake condition after 1 and 4 weeks compared to the corresponding

values at baseline, although the placebo-intake condition did not show shorter reaction times.

**Table 1.** Reaction times after the fatigue-inducing and rest sessions in Task A and B.

	Placebo	BEC
<b>Task A</b>		
<b>After fatigue – inducing session</b>		
Baseline	349.69±12.78	348.80±11.29
After 1 week	354.83±11.04	354.42±14.63
After 4 weeks	348.34±9.12	352.61±13.90
<b>After rest session</b>		
Baseline	340.34±10.41	341.06±11.61
After 1 week	332.17±8.69	338.04±9.77
After 4 weeks	329.27±8.47	340.57±10.86
<b>Task B (non-Stroop trials)</b>		
<b>After fatigue – inducing session</b>		
Baseline	508.69±15.04	492.23±18.15
After 1 week	518.39±40.21	496.88±23.26
After 4 weeks	490.71±14.67	497.33±17.26
<b>After rest session</b>		
Baseline	478.28±11.60	493.38±16.77
After 1 week	465.18±12.62	462.23±10.67*
After 4 weeks	467.60±14.17	469.64±13.59*
<b>Task B (Stroop trials)</b>		
<b>After fatigue – inducing session</b>		
Baseline	532.42±15.86	517.04±17.23
After 1 week	548.01±41.48	522.37±22.31
After 4 weeks	505.81±14.04	518.60±17.56
<b>After rest session</b>		
Baseline	503.18±12.84	514.40±17.55
After 1 week	488.95±12.63	487.80±12.25*
After 4 weeks	492.39±16.04	495.15±14.78*

Values are shown as mean ±SEM. \* P<0.05, significantly different from the reaction time of baseline (one-way repeated-measures analysis of variance followed by paired t-test with Bonferroni correction). BEC – Brand’s Essence of Chicken.

Consistent with our results, it has previously been reported that essence of chicken had an effect on the recovery from mental fatigue [14]. However, that study used a simple placebo-controlled intra-subject design and simple evaluations of mental fatigue. In addition, data were collected just before and after the recovery period from mental fatigue. In contrast, we designed and conducted a placebo-controlled crossover study, and evaluation sessions were performed before and after the fatigue-inducing and rest sessions. The results of our investigation provide scientific evidence of the fatigue-recovering effect

of BEC. This evidence is significant in view of the fact that currently there are many nutrient supplements being marketed as attenuating fatigue, but which have little evidence of efficacy.

Selective attention has been reported to be impaired by mental fatigue [18,25]. Although the reaction time in Task A, a simple selective attention task, was not altered by BEC intake, BEC intake caused a shorter reaction time after the recovery period in Task B, which included Stroop trials. Because the Stroop trial involves conflict (i.e., incongruity of color and word)



and therefore needs greater levels of selective attention [27], our results suggest that BEC is effective in inducing recovery from mental fatigue specifically manifested as the impairment of conflict-controlling selective attention rather than just simple selective attention. The conflict-control of selective attention processes in Stroop trials activates the prefrontal cortex (PFC) [28,29] and the anterior cingulate cortex (ACC) [30,31]. Interestingly, the PFC and the ACC have been reported to be the brain regions that have associations with fatigue [32–34]. Thus, our results suggest that BEC intake has favorable effects in these brain regions during the recovery period from mental fatigue.

Regarding physical fatigue, muscular exercise promotes the production of radicals and other reactive oxygen species in working muscles. Growing evidence indicates that reactive oxygen species are responsible for exercise-induced protein oxidation and contribute to physical fatigue [35]. To protect against exercise-induced oxidative injury, muscle cells contain complex endogenous cellular defense mechanisms that eliminate reactive oxygen species. Furthermore, exogenous dietary antioxidants interact with endogenous antioxidants to form a cooperative network of cellular antioxidants. Accordingly, exogenous antioxidants were candidates for anti-fatigue substances, at least in terms of physical fatigue [35]. Since BEC consists of many different substances, it is difficult to identify which ones have beneficial effects on mental fatigue. However, imidazole dipeptides such as anserine and carnosine contained in BEC were reported to be powerful natural antioxidants [16,36]. In addition, Imidazole dipeptides were found to accelerate the recovery from physical fatigue via their antioxidative effects [12,36]. Taken together, one possible explanation for the acceleration of recovery from mental fatigue by BEC intake could be via its antioxidative effects in the same way as physical fatigue.

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A human study showed that administration of vitamin C, an antioxidant, improved cognitive function as well as the sense of fatigue after mental fatigue loads, and oxidation was found to contribute to mental fatigue [8]. Thus, the alternative approaches of using antioxidants may be helpful for mental fatigue.

Three limitations of the present study must be noted. First, the mechanisms by which BEC improved recovery from mental fatigue remain to be determined. Further studies are needed to identify the fatigue-recovering mechanisms of BEC. Second, the results of the present study were obtained with a small sample size. Third, the participants were only healthy males in their thirties from single country or culture. Further large-scale investigations in other populations are needed, which may help draw clearer conclusions about the mental fatigue-recovery effects of BEC.

## Conclusions

We showed that daily oral administration of BEC (essence of chicken) improved recovery from mental fatigue manifested as the impairment of cognitive function in healthy males. This is the first study to show a favorable anti-fatigue outcome using BEC. This will open new perspectives on strategies for the treatment of mental fatigue.

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