

Original Article

Effect of coffee and green tea on executive ability and plasma levels of inflammatory factors in soldiers with 48-hour total sleep deprivation

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Abstract: Objectives: To compare the effect of coffee and green tea on executive ability and plasma levels of inflammatory factors in soldiers with 48-hour total sleep deprivation (SD). Methods: Forty-five male soldiers were randomly divided into control group, coffee group and green tea group. All subjects underwent 48-hour total SD, and received gun disassembly and assembly test and venous blood collection before SD, 24 hours and 48 hours after SD and 24 hours after sleep recovery (SR). Plasma IL-6 and NF-kb levels were detected. Results: There was no significant difference in baseline characteristics among groups. Two-way ANOVA results indicated significant differences in the time of gun assembly and plasma levels of IL-6 and NF-kb between the coffee group or green tea group and the control group. No indicators were significantly different between the green tea group and the coffee group. Spearman correlation analysis indicated that the plasma levels of IL-6 and NF-kb were not significantly correlated with the time of gun disassembly and assembly before SD and after SR; plasma levels of IL-6 and NF-kb were significantly positively correlated with the time of gun disassembly and assembly at 48 hours after SD. Conclusions: Coffee and green tea have similar effects with regard to attenuating decreased performance and increased plasma levels of inflammatory factors caused by SD, but green tea has a better advantage in terms of maintaining the effect; Lowering plasma levels of inflammatory factors maybe the mechanism for improving executive ability of coffee and green tea during SD.

Keywords: Sleep deprivation, coffee, green tea, interleukin-6, nuclear transcription factor-kb

Introduction

Sleep deprivation (SD) is a state in which the human body is partially or completely deprived of a normal amount of sleep because of environmental factors or the body itself [1]. Long-term or complete SD, an endogenous source of stress, can cause the central nervous system and immune system to be generally suppressed [2] and result in endocrine and metabolic disorders [3]. Humans or animals with SD can have symptoms of emotional lability aggravated emotion, diminished learning and memory, decreased alertness and impaired judgment, difficulty concentrating and decreased performance, but they can also incur body weight changes, blood glucose and blood pressure fluctuations, decreased immunity, and opportunistic pathogen infections; sepsis can occur in the late stages of SD [4-6]. Quick responses and a strong body are very important in rescue

procedures during war, natural disasters and accidents, and military exercises. Under these circumstances, soldiers often inevitably face long-term or complete SD, and how to prevent it from having a significant effect on job performance in army soldiers has become the focus of current research. Previous studies about US soldiers showed that coffee can effectively improve the decreased visual alertness and attention caused by SD [7]. The best results are achieved using caffeine at a dose of 300 mg/day [8]; caffeine has the advantages of rapid action and a longer duration of action. Green tea is a common refreshing drink in China that has been reported to have antioxidant and anti-inflammatory effects. This study compared the effects of green tea and coffee with regard to attenuating SD-induced adverse effects to select a more suitable refreshing drink for Chinese army soldiers.

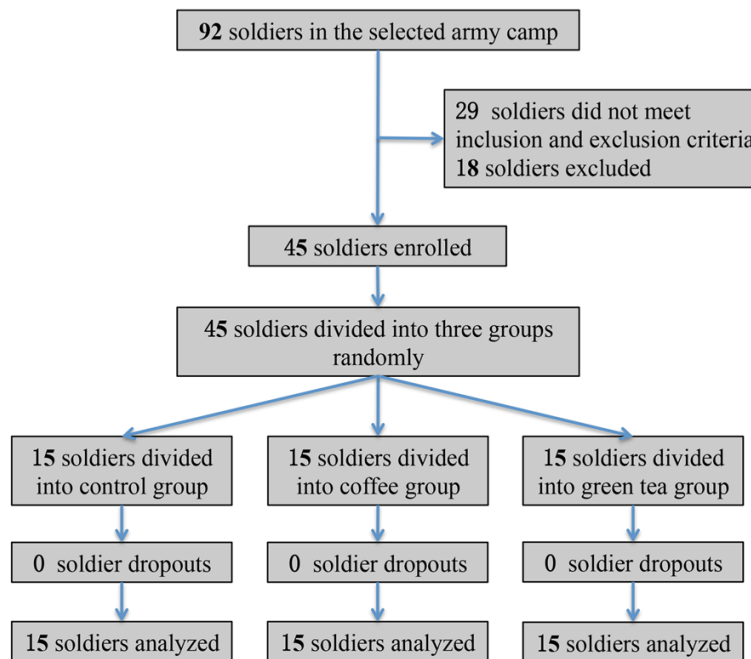


Figure 1. Flowchart of study subject selection.

Gun disassembly and assembly operations are regular training activities for Chinese soldiers, which can reflect the storage and retrieval of sets of memory in the brain and can also reflect performance and reaction time. This study used gun disassembly and assembly as the detection index for soldier executive function. Studies had found that nuclear transcription factor- κ B (NF- κ B) was likely activated in SD [9]. NF- κ B is a critical transcription factor and exists in almost all cell types because it can regulate multiple molecules in the early stages of the immune response and inflammation, similar to the function of tumor necrosis factor- α (TNF- α), IL-1 β , IL-2, IL-6, chemokines, adhesion molecules and colony-stimulating factor. Hence, NF- κ B is also thought to be an important inflammatory cytokine [10]. Previous studies have shown that complete SD can cause increased plasma concentrations of interleukin-6 (IL-6), the most common inflammatory factor. Therefore, this study will discuss the effect of 48-hour SD on Chinese soldier performance and the levels of plasma inflammatory cytokines IL-6 and NF- κ B. The effects of green tea and coffee on the executive ability and plasma levels of inflammatory factors in soldiers with 48-hour total sleep deprivation (SD) with regard to attenuating SD-induced negative effects were compared and their possible mechanisms of

performance improvement were explored, with the goal of selecting a more suitable refreshing drink for Chinese army soldiers.

Subjects and methods

Subjects

All subjects were selected from an army in Chongqing, China. The inclusion criteria were as follows: male soldiers who joined the army in the same year and underwent the same training. The exclusion criteria were as follows: (1) complaints of sleep disorders; (2) personal or family history of neuropsychiatric disease; (3) inability to successfully finish conventional military training; (4) bad habits such as heavy daily smoking (> 10/day), alcohol and gambling; (5) history of sustained central excitatory and inhibitory drug use; (6) inability to tolerate coffee or tea because of cardiac disease or other diseases; and (7) unwillingness or inability to participate the study. Ultimately, 45 soldiers were selected, and they were randomly divided into a control group, coffee group and green tea group, with 15 soldiers in each group. All subjects signed an informed consent agreement. This study was approved by the ethics committee of Daping Hospital of the Third Military Medical University (Figure 1).

Preparation before the study

One week before the study, all subjects were mobilized and informed about the steps and requirements of the trial. Fifteen soldiers in each group and 8 platoon leaders were assigned various tasks. During the 48-hour SD period, all 45 soldiers were monitored 3 different times to ensure full wakefulness. The 8 platoon leaders were recommended by the battalion commander, two of whom were responsible for organizing gun disassembly and assembly training and assessments, and 6 of whom were responsible for arranging routine military training activities and the remainder of the soldiers' schedules during SD.

One week before the study, the subjects were prohibited from drinking coffee and caffeinated beverages, tea and tea-containing beverages and alcoholic beverages, as well as other beverages with central nervous system effects. Meanwhile, each subject finished his daily sleep records on his own, including bedtimes and wake times, estimated total sleep times, sleep quality and daytime mental state. Three days prior to the study, each subject was advised to get proper rest and avoid strenuous exercise, and the subjects underwent 1 hour of daily gun disassembly and assembly training (81-1 automatic rifle) to proficiently master the disassembly and assembly procedures.

Additionally, subject data regarding age (years), body mass index, smoking and drinking history, educational background, average sleep time at 1 week before the study, and past medical history and family history were obtained.

Sleep deprivation and intervention

In this study, all subjects were deprived of sleep for 48 hours, from 6:30 am on the day that the subjects began the study to 6:30 am of the third day. During the 48-hour sleep deprivation period, all subjects underwent daily military training, avoided strenuous exercise, and participated in light physical and mental activities, such as doing housework, taking queue training, playing chess and card games, watching video news, learning regulations and ordinance, talking, and reading. All subjects participated in the same activities and the entire process was monitored to ensure that they remained awake.

The soldiers in each group received their corresponding interventions during the SD period. Fifteen soldiers in the control group were received water (tap water), which was drunk voluntarily; 15 soldiers in the coffee group were given five bags of instant coffee (daily usage was approximately 300 mg) and required to drink within 24 hours; and 15 soldiers in the green tea group were given 12 g green tea, which was made with boiling water at a temperature $> 90^{\circ}\text{C}$ within 24 hours. The amount of tea for each brewing was decided by the soldiers themselves. The duration of each tea brewing was 15 minutes, and each tea brewing was repeated at least three times. Meanwhile, the soldiers in the coffee and tea groups could also drink water.

Observation indicators

Automatic rifle gun disassembly and assembly time: The soldiers received 1-hour gun disassembly and assembly training 3 days before the study. Gun disassembly and assembly assessments were conducted at 7:00 am on the first SD day, 7:00 am on the second SD day and 7:00 am on the third SD day, and the performance quality and duration were recorded by an appointed platoon leader. Re-examination was required if the soldiers failed to reach the appropriate quality standards, and the time to reach these quality standards was used as the examination result.

Detection of serum IL-6 and NF-kb concentrations: 4 mL of venous blood was drawn before SD (6:30 am), 24 hours after SD (6:30 am on the second day), 48 hours after SD (6:30 am on the third day), and 24 hours after SD (6:30 am on the fourth day). Samples were placed at room temperature for 3-6 hours and centrifuged for 5 min at $3000 \times g/\text{min}$, and then the plasma was separated and stored at -70°C . The concentrations of serum IL-6 and NF-kb were determined by enzyme-linked immunosorbent assay (ELISA), and all procedures were performed according to kit instructions.

Statistical analysis

In univariate analysis, continuous variables were tested with the Kolmogorov-Smirnov test. Differences in demographic characteristics, plasma IL-6 levels, plasma NF-kb levels, and duration of gun disassembly and assembly between groups were assessed using one-way or two-way analysis of variance (ANOVA), Kruskal-Wallis tests, and Chi square tests, where appropriate. Spearman correlation analysis was used to examine the correlations between variables. The data are expressed as the mean \pm SD, and significance was achieved when $P < 0.05$. All statistical analyses were performed with the statistical analysis software SPSS 18.0.

Results

Baseline characteristics

Forty-five subjects were enrolled in accordance with the inclusion criteria, and they were randomly assigned to the control group, coffee

Table 1. Basic characteristics of the subjects

	Control group (n=15)	Coffee group (n=15)	Green tea group (n=15)	P value (ANOVA)
Age, years, mean \pm SD	19.47 \pm 0.83	19.67 \pm 1.05	19.33 \pm 1.05	0.648
Educational background, years, mean \pm SD	9.73 \pm 1.44	9.67 \pm 1.88	10.13 \pm 2.45	0.782
Body mass index, kg/m ² , mean \pm SD	20.12 \pm 1.35	20.28 \pm 1.81	20.34 \pm 1.62	0.932
Drinking, n (%)	6 (40%)	6 (40%)	5 (33.33%)	0.910
Current smoking, n (%)	4 (26.67%)	3 (20%)	5 (33.33%)	0.711
Average sleep duration in the past week, hours/day, mean \pm SD	7.45 \pm 0.49	7.48 \pm 0.54	7.45 \pm 0.47	0.982
Time of gun disassembly before SD, second(s), mean \pm SD	26.20 \pm 7.47	27.73 \pm 7.05	26.07 \pm 6.47	0.771
Time of gun assembly, second(s) before SD, mean \pm SD	49.13 \pm 12.06	46.87 \pm 9.13	46.60 \pm 9.39	0.761
Plasma IL-6 level before SD, pg/ml, mean \pm SD	1.63 \pm 0.35	1.60 \pm 0.40	1.69 \pm 0.32	0.791
Plasma NF-kb level, ng/ml, mean \pm SD	10.04 \pm 0.91	10.20 \pm 1.15	10.41 \pm 1.12	0.647

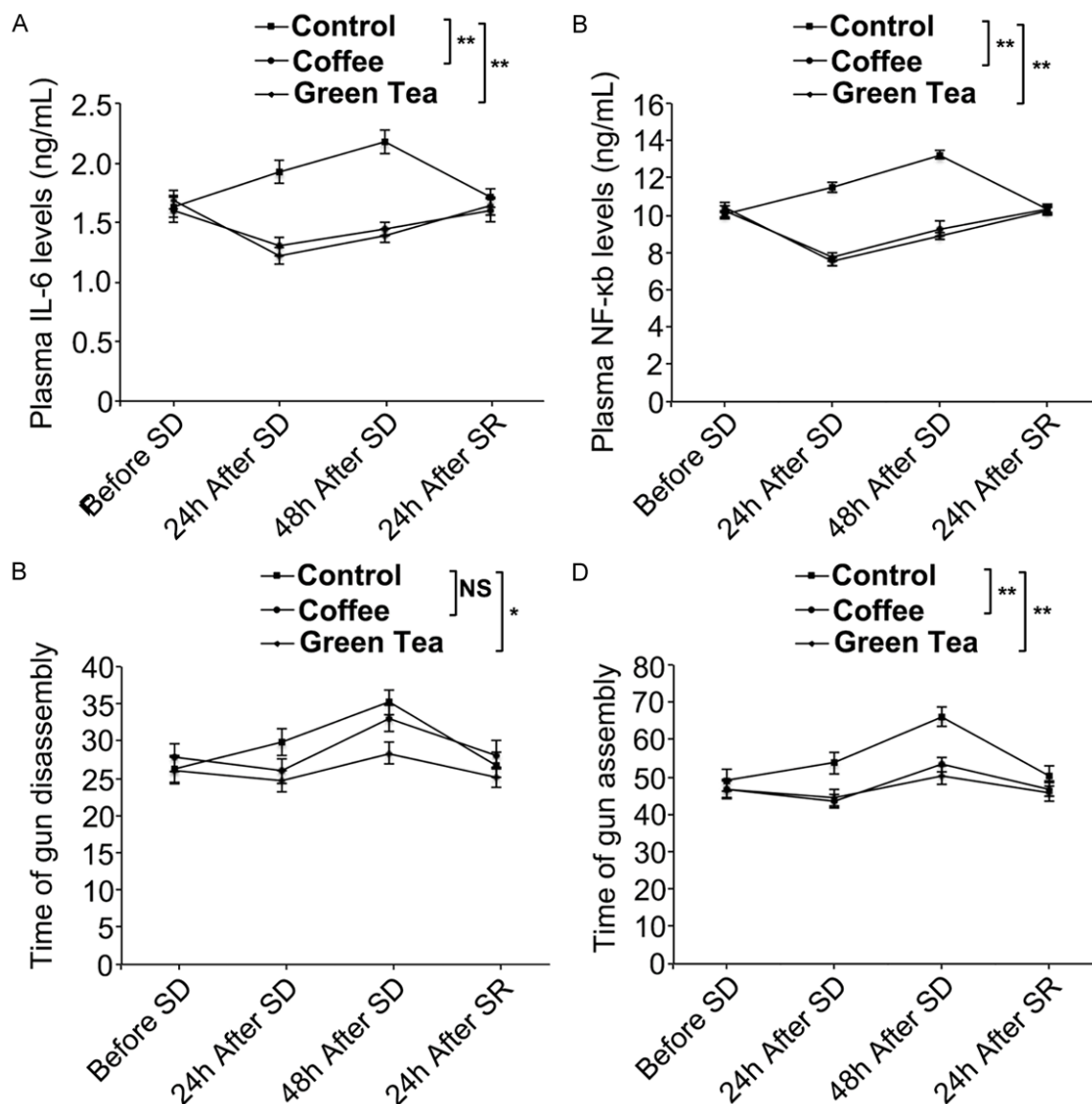


Figure 2. Plasma inflammatory factors and behavioral changes after sleep deprivation (SD) and sleep recovery (SR). Plasma IL-6 (A) and NF-kb levels (B) and time of gun disassembly (C) and assembly (D) were analyzed to investigate the changes in plasma levels of inflammatory factors and behavior after sleep deprivation and sleep recovery. **P<0.01 and *P<0.05. Two-way ANOVA analysis.

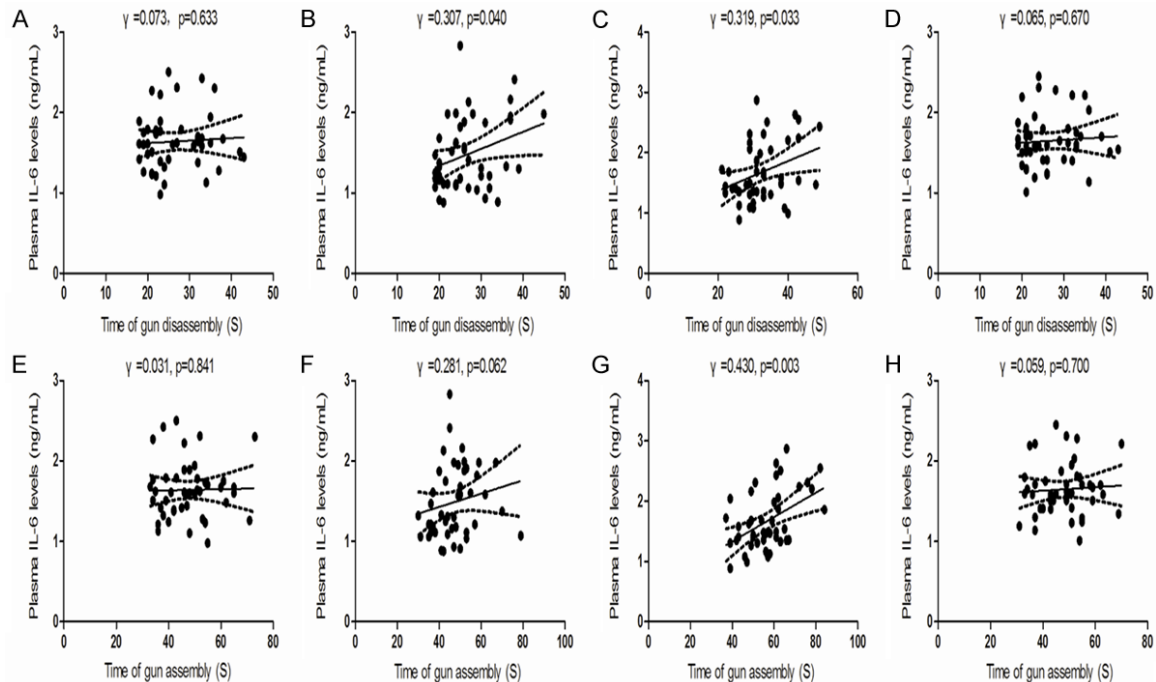


Figure 3. Correlations between time of gun disassembly or assembly and plasma IL-6 levels. Correlations between time of gun disassembly or assembly and plasma IL-6 levels at different time points were analyzed. A, E. Before SD; B, F. 24 hours after SD; C, G. 48 hours after SD; D, H. 24 hours after SR. Spearman correlation analysis.

group and green tea group according to the intervention that they received. The baseline characteristics of the three groups are shown in **Table 1**, including age, educational background, body mass index, smoking and drinking history, average daily duration of sleep during the past week, gun disassembly and assembly times, and plasma IL-6 and NF-kb levels before SD. No significant differences were observed in baseline characteristics among the three groups.

Effect of SD on executive ability and inflammatory cytokine levels in the three groups

Two-way ANOVA was used to analyze the changes in gun disassembly and assembly time and plasma IL-6 and NF-kb levels before SD, 24 hours after SD, 48 hours after SD and 24 hours after sleep recovery to compare the effect of coffee and tea with regard to attenuating the negative effects caused by SD. **Figure 2** indicates significant differences between the changes in plasma IL-6 and NF-kb levels and the times of gun disassembly and assembly between the coffee group and the control group and between the green tea group and the control group ($P < 0.01$). There was a significant

difference in the time of gun disassembly and assembly between the green tea group and the control group ($P < 0.05$), but not between the coffee group and the control group. No significant difference was observed in these variables between the coffee and green tea groups. **Figure 2** shows that in the control group, the time for gun disassembly and assembly was gradually extended and that the plasma levels of IL-6 and NF-kb were gradually increased during SD and did not fully recover after sleep recovery. In the tea and coffee groups, the times for gun disassembly and assembly were slightly decreased 24 hours after SD but returned to baseline levels 48 hours after SD; the green tea group exhibited improved recovery compared with the coffee group. Additionally, plasma levels of IL-6 and NF-kb first decreased and then increased after SD in the green tea and coffee groups. This indicates that coffee and green tea have similar effects with regard to attenuating the decreased executive ability and increased levels of inflammatory factors caused by SD. However, compared with coffee, green tea can improve the time for gun disassembly to a greater extent, but the time was not significantly increased 48 hours after SD, indicating that green tea may have

Effect of coffee and green tea

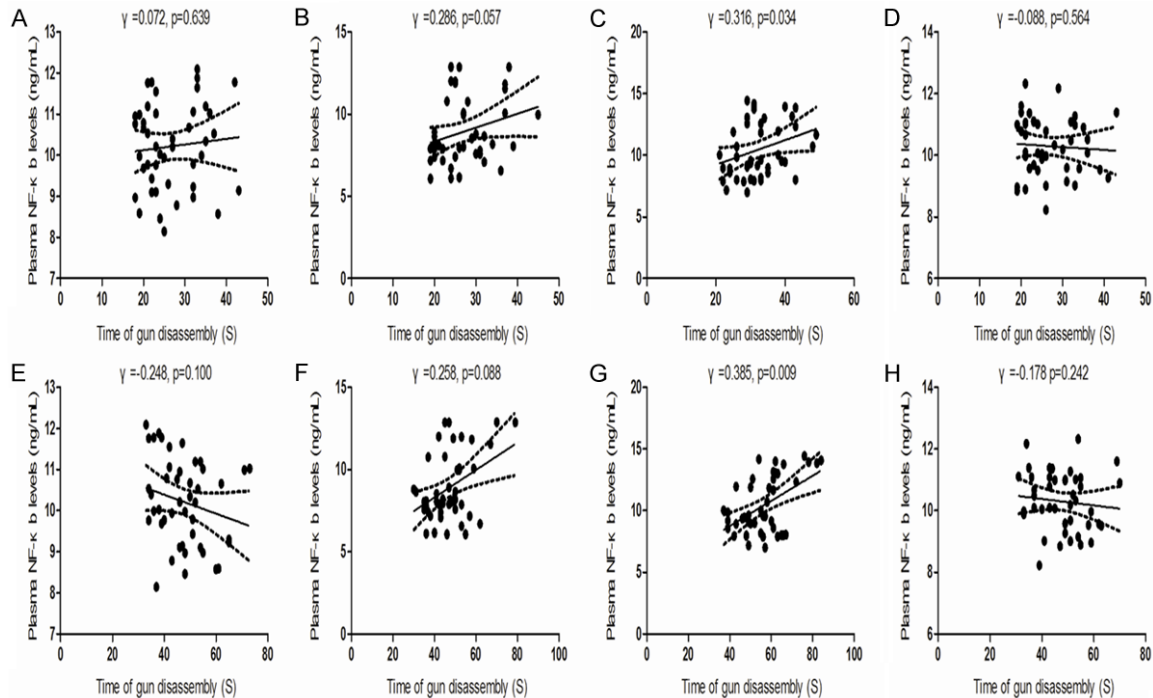


Figure 4. Correlations between time of gun disassembly or assembly and plasma NF- κ b levels. Correlations between time of gun disassembly or assembly and plasma NF- κ b levels at different time points were analyzed. A, E. Before SD; B, F. 24 hours after SD; C, G. 48 hours after SD; D, H. 24 hours after SR. Spearman correlation analysis.

better effects with regard to sustaining executive ability after SD.

Correlation analysis of executive ability and inflammatory factors

Spearman correlation analysis was used to determine the relationship between the times for gun disassembly and assembly and the levels of inflammatory cytokines IL-6 and NF- κ b and to explore the possible mechanisms underlying the improvements in executive ability facilitated by green tea and coffee. **Figures 3 and 4** indicate that there was no noticeable association between the plasma levels of IL-6 and NF- κ b and the times for gun disassembly and assembly before SD and after sleep recovery and that there was a significantly positive relationship between the plasma levels of IL-6 and NF- κ b and the times required for gun disassembly and assembly 48 hours after SD, whereas at 24 hours after SD, only plasma IL-6 levels was positively correlated with the time for gun disassembly, and NF- κ b levels were not significantly related to executive ability. Thus, coffee and green tea can improve executive ability in SD by decreasing plasma inflammatory factor levels.

Discussion

Approximately one-third of one's life is spent sleeping as the human body and brain can obtain complete rest and recovery only during sleep to maintain homeostasis, metabolism, physiological function and central nervous system related functions [11, 12]. Sleep consists of non-rapid eye movement sleep (NREM) and rapid eye movement sleep (REM), and the two phases alternately occur throughout sleep. NREM sleep (deep sleep especially) mainly promotes mental recovery, and REM sleep mainly promotes physical recovery [13]. Total SD refers to the complete deprivation of NREM and REM sleep, which can lead to physical and mental un-recovery and ultimately cause disorders of body function and decreased memory ability, cognition and learning [2]. Moreover, long-term SD can lead to death [14]. Total SD is a source of stress for the body itself [15], which can produce stress responses through pathways such as the hypothalamic-pituitary-adrenal system, increasing inflammation and promoting stress-related gene expression to maintain a steady state [16, 17]. A unique population, army soldiers inevitably undergo complete sleep deprivation during war, natural disasters, accidents,

emergency rescues, military exercises and other tasks. If we do not take measures to cope with total SD, it will inevitably decrease soldiers' abilities in implementation, alertness, visual tracking and logical reasoning, ultimately resulting in decreased ability during military operations [18, 19]. Therefore, it is particularly important to develop effective measures for military soldiers to cope with total SD.

This study used Chinese army soldiers as study subjects, applied coffee or green tea as measures to address total SD and explored the effect of coffee and green tea with regard to attenuating the negative effects caused by total SD. In this study, the authors obtained the following results: (1) without interventions, total SD can gradually decrease soldiers' implementation capacity and increase the inflammatory response; (2) drinking 300 mg coffee/day and 12 g green tea/day can greatly improve executive ability and attenuate the inflammatory response in soldiers with 48-hour total SD without having a significant effect on late sleep recovery; (3) compared with coffee, green tea can better maintain soldiers' executive ability, especially in the latter stage of SD; (4) plasma levels of inflammatory factors were not significantly correlated with executive ability in the non-SD stage but were both significantly correlated with executive ability during SD. Hence, coffee and tea can maintain soldiers' executive ability by reducing the levels of inflammatory cytokines.

Previous studies about US soldiers indicated that 200 mg and 300 mg of caffeine can maintain a soldier's visual reaction ability, memory, emotional state, and shooting accuracy [8], which is consistent with the results of this study. This indicates that coffee is effective at maintaining alertness and operability in military activities in SD. We chose to compare green tea and coffee to select a more suitable refreshing drink for army soldiers for the following reasons: (1) Green tea is widely produced and is inexpensive. (2) Green tea not only contains caffeine but also contains ingredients such as tea polyphenols, amino acids and vitamins, which promote human health. It has been regarded as an excellent refreshing drink nationwide in China. (3) Several studies have confirmed that green tea has anti-inflammatory, anti-cancer and lipid-lowering effects [20-22]. Combined with the results from this study,

green tea appears to be a good choice as a refreshing beverage for Chinese army soldiers to guarantee military combat capability.

It is thought that caffeine may be a common component of coffee and green tea in fighting the negative effects of SD because it can make the body remain in a state of physical fitness and central nervous system excitation in SD [23]. It has been shown that caffeine can help to maintain physical strength, mainly by regulating intracellular calcium ion concentrations to enhance skeletal muscle contractility [24], increasing neurotransmitter release to promote neuromuscular transmission [25], and promoting the maintenance and improvement of performance with its stimulatory effect on the central nervous system. The excitatory effect that caffeine has on the central nervous system is mainly mediated by adenosine receptor antagonism [26-28]. Current studies have indicated that adenosine and adenosine receptors play an important role in regulating the inflammatory response [29, 30]. Coffee and tea contain several ingredients, and both beverages have benefits other than their physiological effects on physical fitness and central nervous system excitation. Koloverou *et al* conducted a 10-year follow-up study and observed that long-term coffee drinking can significantly reduce the occurrence of the subclinical inflammatory response and significantly decrease the concentrations of plasma C-reactive protein (CRP) and amyloid A (SAA) [31]. Shen *et al* observed that diterpene kahweol, which is an important component of coffee, can exert an anti-inflammatory effect by inhibiting NF- κ B expression levels [32]. Mota *et al* reported that green tea has anti-inflammatory and analgesic effects [33]. Molina *et al* found that green tea polyphenols can significantly reduce the expression levels of plasma IL-2, IL-6, IL-1 β , and TNF- α to exert their anti-inflammatory effects [34]. Ravindranath reported that catechins in green tea can inhibit the NF- κ B-mediated inflammatory response [35]. This study suggests that drinking coffee and green tea can significantly reduce serum levels of the inflammatory cytokines IL-6 and NF- κ B, which is consistent with the abovementioned results. IL-6 and NF- κ B have been reported to be able to promote sleep [36, 37]. The elevated plasma IL-6 and NF- κ B levels resulting from SD can produce a sense of sleepiness and trigger sleep; decrease memory, learning and implementation; and increase

the body's susceptibility to inflammation. Chronic SD can even lead to septicemia and death. Our results suggest that plasma IL-6 and NF-kb levels were gradually increased and that implementation capacity was significantly reduced in soldiers who did not receive intervention during SD, which was consistent with previous findings. Although plasma IL-6 and NF-kb levels were decreased and implementation capacity was not significantly decreased in the coffee and green tea groups, we believe that the mechanism underlying the improvements facilitated by coffee and green tea with regard to the decreases in implementation ability caused by SD is mediated through suppression of the inflammatory response.

This study mainly aimed to investigate a more effective and suitable drink for Chinese military soldiers with SD; thus, the study subjects were a unique population that mainly comprised young males that experienced SD. Hence, our findings may not be applicable to the general population. Additionally, the 48-hour SD duration is not long. In a future study, we will select a healthy population to conduct a longer total SD duration and selective NREM or REM sleep deprivation and further compare the effects of green tea and coffee to more comprehensively assess the efficiency and safety of coffee and green tea in coping with SD. This study did not investigate the mechanisms of action of coffee and tea with regard to attenuating the negative effects of SD, which further study to demonstrate the roles of these beverages in anti-inflammation.

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Disclosure of conflict of interest

None.

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