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Original Article

Effect of one time coffee fragrance inhalation on working memory, mood, and salivary cortisol level in healthy young volunteers: a randomized placebo controlled trial

Thaneeya Hawiset*

School of Medicine, Mae Fah Luang University, Chiang Rai, Thailand

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ABSTRACT

Background: Olfactory system regulates the brain which controls emotional memory. Coffee is one of the most consumed beverages in the world. Drinking coffee shows beneficial effects for mood, memory, and psychomotor performance. This work aimed to determine the effects of inhaling coffee fragrance on memory, mood, and salivary cortisol level in healthy young volunteers.

Methods: Eighty young males and females, aged between 18–22 years old, were randomly assigned into two groups: a placebo group inhaling scent from carbon powder and a coffee fragrance group inhaling coffee fragrance. Subjects were assigned to inhale either placebo or coffee fragrance for five minutes. Before and after inhalation period, the clinical assessments were assigned to each subject including computerized assessment battery test for cognitive performance, and self-related visual analogue mood scales for evaluation of mood score. The salivary cortisol level was assessed with cortisol ELISA kit. In addition, the blood pressure and heart rate were also evaluated.

Results: Inhalation of coffee fragrance enhanced cognitive parameters, including continuity of attention, quality of memory, and speed of memory, and also increased the mood score of alertness. However, there were no significant changes in salivary cortisol level, blood pressure, and heart rate between pre-and post-inhalation.

Conclusion: One time of coffee fragrance inhalation may enhance working memory and stimulates alertness. However, inhaling coffee fragrance does not reduce stress or modulate autonomic response to stress.

1. Introduction

Nowadays, alternative medicine is a novel strategy for improving health and quality of life.[1] Aromatherapy is one of the integrative treatments that use essential oil to enhance mental, emotional, and physical well-being.[2] Essential oil is commonly used for inhalation and typical applications, for example, bath and skin care products for relaxing the body and reducing symptoms of stress, depression, and anxiety.[3] Aroma is a pleasant odor and is usually scented during drinking and eating.[4] Inhaling of odorant molecules activates the olfactory system by sending the nerve impulse from olfactory receptors to olfactory bulbs via olfactory nerves (CN I).[5] The nerve impulse passes through the brain regions of piriform cortex, orbitofrontal cortex, hypothalamus, and limbic system, especially amygdala and hippocampus. These regions of the brain regulate conscious discrimination, olfactory memory, and olfactory emotion.[5] Recently, essential oil studies have focused on their effects for both animals and humans. Animal studies demonstrated that lavender and rose essential oils modulate neurotransmitter system which exert anxiolytic-like effect.[6,7] Clinical studies showed that inhalation of essential oils modulates mood, cognitive performance, brain wave, salivary cortisol level, heart rate, and blood pressure.[8–11] Hence essential oil inhalation could produce pharmacological, physiological, and psychological alteration in both animals and humans.

Coffee (*Coffea Arabica L.*), a plant in Rubiaceae family, has been used worldwide for beverage. Coffee is one of the most consumed beverages in the world.[12] Coffee produces various aroma characteristics while drinking. Numerous studies showed the health benefits of drinking coffee: for example, reducing risk of cardiovascular disease, diabetes mellitus, and cancer.[12,13] Ullrich et al. reported that consumption of coffee improved mood, self-judgment, and

* Corresponding author at: School of Medicine, Mae Fah Luang University, Muang, Chiang Rai, 57100, Thailand.
E-mail address: thaneeya.haw@mfu.ac.th

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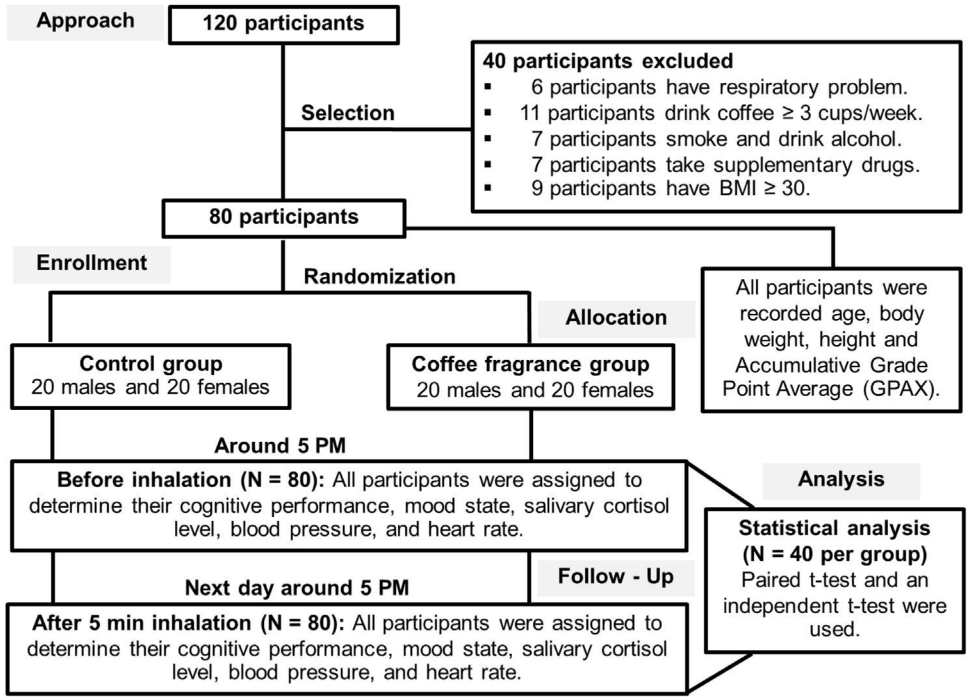

Fig. 1. The flow chart demonstrating the selection of the participants, study designs, and interventions.

cognitive performance.[14] Recently, Seo et al. reported that aroma of roasted coffee bean could reduce emotional stress in rats of which the induced stress was by sleep deprivation.[15] The roasted coffee bean aroma exerts relaxation in stressed rats by modulating mRNA and antioxidant protein expression levels of the rats' brains.[15] However, reports on the effects of inhaling of coffee fragrance on psychological, physiological, and psychomotor parameters in human are rare. Therefore, this study was performed to investigate the effects of inhaling coffee fragrance, rather than aroma, on the alterations of working memory, mood, salivary cortisol level, blood pressure, and heart rate in adolescent population.

2. Methods

2.1. Study design and participants

The experiments were randomized, double-blind and placebo-controlled. Eighty healthy young male and female volunteers, who were students from Mae Fah Luang University, aged 18–22 years old, enrolled to participate in this study. The Human Ethical Committee of Mae Fah Luang University approved this project on September 5, 2018 (No. REH-61117).

The inclusion criteria of the subjects for this study were as follows: those with (a) good health and good communication; (b) normal motor function; and (c) no menstrual period (for females) during the trial period because their estrogen hormones might influence mood and memory. The exclusion criteria of the subjects for this study were as follows: those who (a) drinkmore than 3 cups of coffee per week; (b) smoke and drink alcoholic beverages; (c) have respiratory problems such as cold, sinus, and respiratory tract infection; (d) take drugs or nutraceutical compounds which affect the nervous system; and (e) have Body Mass Index (BMI) higher than 30, which is an indication of obesity as obese people have a high risk of cognitive dysfunction and psychological disorders. All subjects were asked to sign informed consent forms; nevertheless, they could withdraw from the study anytime if they no longer wanted to participate in this study. Furthermore, the present work minimized confounding factors of stress in all participants by performing the test after examination period.

2.2. Interventions

The trials were performed in the evening around 5 PM in a quiet room, 4 m × 4 m, in two consecutive days. Their age, body weight, height and Accumulative Grade Point Average (GPAX) were recorded. For baseline (before inhalation), all participants were assigned to determine their cognitive performance, using computerized assessment battery test, and determine their mood state, using self-related visual analogue mood scales. Participants' saliva samples were collected in tubes. The blood pressure and heart rate were also monitored. Participants were appointed at about the same time and assigned to inhale either placebo or coffee fragrance for five minutes. After 5 min, their cognitive performance, mood state, salivary cortisol level, blood pressure, and heart rate were determined. Fig. 1 showed the flow chart of selection of the participants, study designs, and interventions.

2.3. Outcome measurements

2.3.1. Primary outcome

2.3.1.1. Cognitive computerized assessment battery test. The cognitive computerized assessment battery test was modified from the cognitive drug research computerized assessment battery test. This test was used to assess four domains of working memory consisting of power of attention, continuity of attention, quality of memory, and speed of memory. The program was installed into a notebook computer and the results were displayed on a high resolution monitor. The computer-based cognitive test consisted of six sets of the test. Participants chose one test with the same difficulty level to avoid the memory effect. However, the sets of testing which the participants were required to take before and after inhalations were different. The participants completed the selected cognitive test within 20 min. The cognitive tests were conducted in the following order: (1) word presentation; (2) delayed word recognition; (3)

Table 1
The description of cognitive computerized assessment battery test.

The cognitive computerized assessment battery tests	
Cognitive parameters	Procedures
(1) Word presentation	Fifteen words were presented in sequence on the monitor for participant to memorize these words. The stimulus duration was 1 second with an inter-stimulus interval of 1 second.
(2) Delayed word recognition	Thirty words, fifteen words demonstrated previously and fifteen distracting words, were randomly displayed one at a time on the monitor screen. Participants decided if the word was included in the fifteen-word list by pressing “yes” or “no” button within one second. The percentage of accuracy and the mean of reaction time the participants used for the test were record. The delayed word recognition test was conducted 30 minutes after the participants had seen all words.
(3) Picture presentation	Twenty pictures were presented in sequence on the monitor for participants to memorize. The stimulus duration was 3 seconds with an inter-stimulus interval of 1 second.
(4) Delayed picture recognition	Twenty pictures composing of the fourteen pictures previously presented and six new pictures were displayed one at a time on the screen in a randomized order. For each picture, the participants decided if each one was a picture in the twenty-picture list by pressing the “yes” or “no” button as quickly as possible. The percentage of accuracy and mean reaction time the participants used to response to all pictures were recorded. The delayed picture recognition test was conducted 30 minutes after the participants had been showed all pictures.
(5) Simple reaction time	The word “yes” was presented on the monitor and then the subject pressed the “yes” button as quickly as possible. The reaction time for the participants to response was recorded in milliseconds.
(6) Digit vigilance task	A single digit number was presented randomly. The number was presented simultaneously on the right and left side of the monitor screen. The participants pressed the “yes” button as quickly as possible if the digit on the left screen matched the target digit on the right screen.
(7) Choice reaction time	Either the word “yes” or the word “no” was displayed on the monitor. The participants pressed the matched button as quickly as possible when the stimulus “yes” or “no” presented on the monitor. The reaction time for the participants to response was recorded in milliseconds.
(8) Spatial working memory	A photographic representation of a house with nine windows illuminated with four yellow lights was presented on the screen. The participants were asked to memorize positions of the illuminated windows. The participants evaluated if the positions of the illuminated windows were the same positions with the previously shown, and pressed “yes” or “no” response button as quickly as possible.
(9) Numeric working memory	Five digits were displayed in sequence on the monitor for the participants to remember. Then, a series of 30 digits were displayed. The participants decided whether or not the digit was the same with the five digits previously shown. The participants pressed the “yes” or “no” response button as quickly as possible.

picture presentation; (4) delayed picture recognition; (5) simple reaction time; (6) digit vigilance task; (7) choice reaction time; (8) spatial working memory; and (9) numeric working memory. The descriptions of the cognitive tests are shown in Table 1.

The cognitive outcomes listed above were categorized into four domains as follows[16]: (1) power of attention, a determination of attention and psychomotor/information processing speed, was assessed by summing reactions times in a unit of milliseconds of three intentional tasks including simple reaction time, digit vigilance task, and choice reaction time; (2) continuity of attention, a prolonged attention determined by combining the percentage of accuracy of digit vigilance task and choice reaction time. The maximum score is 200 calculated by the sum of percent accuracy of each task, 100 percent each; (3) quality of memory, defined as ability to recall working memory determined by summing the percentage of accuracy memory scores of delayed word recognition, delayed picture recognition, spatial working memory, and numeric working memory tasks. The maximum score is 400 calculated by the sum of four tasks; and (4) speed of memory, the speed response to the stimulus in milliseconds obtained by combining the reaction time of delayed word recognition, delayed picture recognition, spatial working memory, and numeric working memory tasks.

2.3.2. Secondary outcomes

2.3.2.2. Visual analogue mood scales. Visual analogue mood scales were performed by using questionnaires. The questionnaire was based-on a subjective experience measurement of mood state. The test composed of 16 items on a 10-cm visual analogue scale. Each item was classified into three factor scores including alertness, calmness, and contentment.[17]

2.3.2.3. Salivary cortisol collection and measurement. At around 5 PM, saliva samples of participants were collected into salivette cotton tubes. Participants were asked to chew cotton roll for 2 min and then spit the cotton roll into the tube without touching the cotton roll to prevent any contamination. Participants were asked not to eat, drink, brush their teeth or exercise before collecting saliva. The samples were stored at −20 °C and analyzed within 3 months after collecting. Before cortisol determination, the salivary samples were centrifuged at 3000 rpm for 15 min, and the supernatants were used for the analysis. The saliva samples were diluted with assay buffer in 1:2 ratios. The cortisol levels were determined using cortisol EIA kit (Catalog number: EK7119, Boster Biological Technology, USA). As provided from the manufacturer, the sensitivity limit for the cortisol assays was 17.3 pg/mL.

2.3.2.4. Physiological measurement. The blood pressures and heart rate of each participant were recorded by automatic blood pressure monitor (Omron HEM-7 121, New Zealand) at before and after 5 min inhalation.

2.3.3. Sample size estimations

The calculations of the sample size were done with G-power 3.1.9.2 program (University of Dusseldorf, Dusseldorf, Germany). The effect size was calculated from the values of the mean of numbers of memorization between pre-and post-inhalation groups, based on a prior study.[18] Assuming the standard deviation (SD) between groups to be 1.8, alpha error probability of 5 %, a statistical power of 95 %, and a possible attrition (drop-outs) of 20 %, a total of 80 participants (40 per group) were chosen.

2.3.4. Randomization, allocation, and blinding

Of 120 participants who agreed to test, 80 participants (40 males and 40 females) were selected. Participants were randomly allocated into 2 equal groups: placebo (carbon powder) and coffee fragrance (ground coffee) groups. The randomization was performed by a computer-generated randomization table with four random block size. Blinding of the participants and experimenters

Table 2
Demographic characteristics of participants.

Variables	Coffee (N = 40)	Placebo (N = 40)	t-test	*P*-value
Gender (M/F)	20/20	20/20		
Age (years)	20.65 ± 0.69	20.18 ± 0.86	1.23	0.1
Weight (kg)	60.38 ± 13.45	63.46 ± 11.84	1.11	0.27
Height (m)	1.67 ± 0.09	1.67 ± 0.08	−0.03	0.98
BMI (kg/m[2])	21.64 ± 3.34	22.65 ± 3.34	1.60	0.12
GPAX	3.00 ± 0.46	3.00 ± 0.53	−0.050	0.96

Note: Values are express as Mean ± SD. BMI, Body Mass Index; GPAX, Accumulative Grade Point Average; M/F, Male/Female.

was performed. The participants were asked to pick a number from a concealed box, containing pieces of paper with number 1 or 2 on them. The participants who obtained number 1 were assigned to placebo group and the participants who obtained number 2 were assigned to coffee fragrance group. Due to double blinding, neither the experimenters nor participants knew who had received which treatment.

2.3.5. *Preparations of ground coffee and placebo*

Arabica coffee bean was purchased from a local market (Doi Chang, Chiang Rai, Thailand). The coffee was processed by a wet method and roasted in a medium level (roasted 400−430 °F for about 3 min). The coffee was grounded by a blender and kept in a glass bottle. The medium roasted coffee bean was chosen because this level produced natural flavor and intense coffee scent. Moreover, the medium roasted coffee is considered to be the most popular among coffee drinkers. Odorless carbon (charcoal) powder (Sigma Aldrich, USA; CAS number: 7440-44-0) was used as a placebo. For inhalation test, three grams of either coffee or carbon powder were placed in 5-mL brown vials. The carbon powder was placed under layersof cotton balls inside the vials so that the participants would not know whether it was ground coffee or carbon powder.

2.3.6. *Analysis of volatile compounds from coffee bean*

The volatile compounds from coffee bean were analyzed using gas chromatography-mass spectrometry (GC–MS, Agilent 7890A-5975C, Agilent Technology, USA). The capillary column was DB-5HT (30 m × 250 μm × 0.1 μm). The flow rate of 1 ml/min, pressure 7.0176 psi, and average velocity 36.26 cm/s were used. The oven temperature was set at 40–250 °C. The run time was 37 min. The temperature of absorption and desorption were set at 30 °C for 30 min and 250 °C for 5 min, respectively. The mass spectrometer was set to evaluate a molecular weight of 10-750.

2.3.7. *Statistical analysis*

All data were presented as mean ± SD. An independent *t*-test (*t*-test) was performed to compare each parameter including cognitive function, mood, salivary cortisol level, and physiological function between groups. Paired *t*-test was used for the changes in those values before and after the experiments. Statistical significance was regarded at *P*-value < 0.05.

3. Results

3.1. *Demographic characteristics of participants*

Table 2 shows the demographic characteristics of participants in both groups. There were no significant differences in mean age, body weight, height, BMI, and GPAX between the groups.

Table 3
Effect of roasted coffee bean fragrance inhalation on working memory, mood, and physiological outcome measures.

Variables	Coffee (N = 40)	Placebo (N = 40)
Working memory test		
Power of attention		
Pre	1743.1 ± 165.5	1738.5 ± 240.5
Post	1703.5 ± 224.5	1716.0 ± 236.1
Continuity of attention		
Pre	184.6 ± 14.6	181.7 ± 18.9
Post	189.9 ± 9.4[a,b]	184.1 ± 14.1
Quality of memory		
Pre	325.5 ± 32.0	322.3 ± 31.2
Post	348.0 ± 28.4[c,d]	328.3 ± 22.2
Speed of memory		
Pre	4520.1 ± 629.7	4562.4 ± 829.5
Post	4012.0 ± 425.4[b,c]	4308.9 ± 699.6
Mood (VAS)		
Alertness		
Pre	6.53 ± 1.48	6.73 ± 1.59
Post	7.10 ± 1.43[a,b]	6.30 ± 1.50
Calmness		
Pre	6.00 ± 1.51	6.16 ± 1.46
Post	6.24 ± 1.54	6.21 ± 1.58
Contentment		
Pre	7.26 ± 1.46	7.29 ± 1.50
Post	7.51 ± 1.35	7.19 ± 1.79
Physiological outcomes		
Salivary cortisol (μg/dL)		
Pre	0.159 ± 0.03	0.161 ± 0.03
Post	0.157 ± 0.03	0.162 ± 0.03
SBP (mmHg)		
Pre	109.4 ± 13.2	110.9 ± 11.3
Post	107.5 ± 11.4	109.0 ± 11.3
DBP (mmHg)		
Pre	69.2 ± 9.3	71.0 ± 6.8
Post	67.1 ± 9.0	70.4 ± 7.8
Heart rate (beats/min)		
Pre	79.9 ± 12.5	81.5 ± 11.9
Post	79.3 ± 12.3	81.0 ± 11.9

Note: Values are express as Mean ± SD.
[a] *P*-value <0.05, compared between pre-and post-inhalation.
[b] *P*-value <0.05, compared between placebo and coffee fragrance groups.
[c] *P*-value <0.001, compared between pre-and post-inhalation.
[d] *P*-value <0.01, compared between placebo and coffee fragrance groups. DBP, diastolic blood pressure; SBP, systolic blood pressure; VAS, visual analogue scale.

3.2. *Effect of coffee fragrance inhalation on working memory*

Before inhalation, there was no significant difference in the working memory between the two groups of participants. The scores of before and after inhalation for working memory tasks are shown in Table 3. Participants who inhaled coffee fragrance revealed significant increase in the domain of continuity of attention (*P* = 0.036), quality of memory (*P* = 0.000), and speed of memory (*P* < 0.001) compared with baseline group. Nevertheless, a significant difference was not observed in power of attention.

Effect of coffee fragrance inhalation on mood

Scores of visual analogue mood scale are presented in Table 3. The result demonstrated no statistically significant difference at baseline between placebo and coffee fragrance groups. Participants who inhaled coffee fragrance showed a significant increase in alertness (*P* = 0.016) compared with baseline group. However, there were no significant difference in calmness and contentment.

3.3. *Effect of coffee fragrance inhalation on salivary cortisol level*

The salivary cortisol levels are presented in Table 3. The participants who inhaled coffee fragrance showed no significant changes between pre- and post-inhalation.

Effect of coffee fragrance inhalation on physiological function

The data of systolic and diastolic blood pressures and heart rate at pre-and post-inhalations are shown in Table 3. Participants with post-inhalation of coffee fragrance demonstrated no significant changes on physiological functions including systolic and diastolic blood pressure, and heart rate between groups, both pre-and post-inhalations.

3.4. Analysis of volatile compounds in coffee bean by GC–MS

A chromatogram of volatile compounds from coffee bean is shown in supplement 1. The analysis of the volatile compounds from coffee bean, the chromatogram in supplement 1, is provided in supplement 2. The major components, the compounds with more than 1 % in the sample, were 2-furanmethanol, octamethyl cyclotetrasiloxane, acetic acid, decamethyl cyclopentasiloxane, 2,5-dimethy pyrazine, butyrolactone, 2-furancarboxaldehyde, pyridine, methyl pyrazine, acetol acetate, 2,6-dimethy pyrazine, 3(2 H)-furanone, dihydro-2-methyl, and dodecamethyl cyclohexasililoxane.

4. Discussions

This study aimed to determine effect of coffee fragrance inhalation on working memory, mood, salivary cortisol level, and physiological function in healthy young volunteers. The inhalation of coffee fragrance enhanced cognitive performances in the domains of continuity of attention, quality of memory, and speed of memory. Subjects who inhaled coffee fragrance were more alert. The findings of this work agree with Haskell-Ramsay et al.'s study which demonstrated that the consumption of caffeine from coffee improved digit vigilance accuracy and alertness, but reduced reaction time, tiredness, and headache.[19] However, the age, assessment time, and the method of coffee intake of this study and the previous studies are different. Present study reported that the volatile components found in roasted coffee bean were derivatives of pyrazine and pyridine, and caffeine. These compounds could be responsible for memory and mood effects shown in this study. The caffeine affects alertness, enhances concentration, and improves cognitive function.[19,20] However, the level of caffeine from the fragrance of the roasted coffee bean was low because caffeine had low vapor pressure and difficult to evaporate.[21] Caffeine is a competitive antagonist at adenosine receptor, and causes an enhanced release of norepinephrine, dopamine, and glutamate.[22] Caffeine also competitively binds to $GABA_A$ receptors, interrupts GABAergic transmission, and disrupts chloride transport.[23] From these mechanisms, caffeine is classified as a central nervous system (CNS) stimulation effect. The derivatives of pyrazine and pyridine are adenosine receptor antagonists.[24,25] The mechanisms of these derivatives could be similar to the mechanisms of caffeine on the CNS. Osaka reported that pyridine odor stimulated learning and memory.[26] Hence, the inhaling coffee fragrance seem to enhance olfactory signaling close to the brain regions which control mood and cognitive task. The volatile compounds from coffee bean bind to their receptors which rapidly generate the nerve impulses sent to the piriform cortex, orbitofrontal cortex, hypothalamus, and limbic system. The mentioned brain regions perceive smelling sense quickly within a few seconds. The strong synchronization of neuronal activity in these brain regions improves short effects on alertness and cognitive ability. Similar effects are found during inhalation. However, the mechanism of coffee fragrance inhalation on mood and memory is different from drinking coffee.

The limitations of the current study were as follows: (1) the study focused on one time coffee fragrance inhalation on working memory, mood, and salivary cortisol level. The study period was too short and the result showed short improvement of working memory and alertness. Therefore, the present work could not claim any effect of coffee fragrance inhalation on long-term enhancement of memory and emotion; (2) salivary samples contained only free cortisol. This only represents a small percentage of total cortisol when compared to plasma cortisol. (3) Because the experiment was conducted in the evening, participants might be tired from their studies. This could affect their mood and cognitive scores, as well as the salivary cortisol levels.

This study was a preliminary study of the effect of coffee fragrance inhalation on working memory, mood, and salivary cortisol in adolescents. It was postulated that inhaling coffee fragrance could help people who feel sleepy, tired, and forgetful to be refreshed, alert, and retentive. Physicians could recommend patients or people who do not drink coffee to inhale coffee fragrance to boost memory and mood. When drinking coffee, one should try to inhale coffee aroma which would stimulate alertness and cognitive ability. Further investigations are needed, particularly in elderly people who have high risk of cognitive impairment and mood disorders. Further study is also needed to clarify the active volatile compounds in roasted coffee beans, the best of roasting conditions (light, medium, and dark), the best time for assessment and inhalation, and prolong duration of assessment for the most positive effects on mood and cognitive performance.

In conclusion, one time inhaling coffee fragrance may improve short-term working memory and enhances alertness. Further investigations are needed to provide firmer conclusions of the effect of the inhalation of coffee fragrance.

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Conflicts of interest

The author declares no conflicts of interest.

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Ethical statement

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The Human Ethical Committee of Mae Fah Luang University approved this project on September 5, 2018 (Ethics No: REH-61117). Informed consent was obtained from all individual participants involved in the study.

Data availability

The data from this work will be made available upon request.

Supplementary material

Suppl. 1. A chromatogram of volatile compounds found in coffee bean analyzed by GC-MS, and Suppl. 2. The volatile compounds from coffee bean analyzed from the chromatogram can be found, in the online version, at doi:https://doi.org/10.1016/j.imr.2019.11.007.

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