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ORIGINAL ARTICLE

The immediate effects of lavender-based essential oil inhalation on subsequent polysomnography in people with poor sleep quality

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Abstract

Background: Although aromatherapy is considered an adjuvant therapy to promote sleep quality, few objective sleep testing instruments can confirm the effects of aromatherapy on sleep physiology. The purpose of this study was to confirm and compare the immediate effects of a single lavender essential oil (SLEO) group to a complex lavender essential oil (CLEO) group by objective polysomnography (PSG) recordings.

Methods: Participants were randomly divided into the SLEO group and CLEO group in this single-blind trial to explore the sleep effect of essential oil aroma. All the participants completed the sleep-related questionnaires and underwent two consecutive nights of PSG recordings, who had one night without aromatherapy and one night with one of the two aromas randomly assigned to them.

Results: Total of 53 participants were recruited for this study, 25 participants were in the SLEO group, and 28 were in the CLEO group. Baseline characteristics and sleep-related questionnaires were similar in both groups. Both SLEO and CLEO extended the total sleep time (TST) (Δ = 43.42 and 23.75 minutes, respectively) and sleep period time (SPT) (Δ = 38.86 and 24.07 minutes, respectively). The SLEO group further improved sleep efficiency and increased the amounts of non-rapid eye movement (NREM) and rapid eye movement (REM) sleep and decreased spontaneous arousals. However, there was no significant difference in PSG parameters between the SLEO and CLEO groups.

Conclusion: Both SLEO and CLEO extended TST and SPT, with no significant differences between these two groups. These results warrant practical applications and merit future studies (Clinical trial registration: ClinicalTrials.gov: NCT03933553).

Keywords: Chinese herbal medicine; Essential oil; Polysomnography; Randomized controlled trial; Sleep disorder; Lavender

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1. INTRODUCTION

Sleep is a vital need, and good sleep is considered an important aspect of well-being.[1] However, people have been increasingly making lifestyle choices and reporting other factors that contribute to sleep difficulties. Sleep disturbance substantially impacts human health and can lead to a variety of physical and mental health problems.[2–4] Poor sleep affects people's performance at work or school, their quality of life, and their health.[2–4] Although hypnotic drugs (primarily benzodiazepines [BZDs] and non-BZDs) are the mainstay for treating sleep disturbance, the benefits of short-term treatment are outweighed by the risks of adverse effects (AEs), including tolerance, dependency, hangover effects, and withdrawal reactions after long-term use of these medications.[2–4] Thus, there is a need for adjunctive or alternative therapies.

Aromatherapy is a complementary therapy that can help relieve stress and emotions and promote sleep quality.[5–8] One of the core materials of this present study was lavender essential

oil, which is often elected as an intervention based on its documented sedative and hypnotic properties along with its safety profile.[2–4,9] Furthermore, a meta-analysis demonstrated the clinical effects of aroma inhalation therapy on insomnia, of which lavender instead of other flavor compounds was most frequently studied and suggested to be the preferred aroma essential oil for sleep.[10,11] However, many studies on aromatherapy lack sleep detection instruments to objectively confirm the effects of aromatherapy on sleep physiology. Additionally, due to the aromatic nature of essential oils, it is very difficult to design a blinded experiment to rule out psychological factors contributing to their therapeutic effect. For this reason, blinded tests were not often used in previous studies. Moreover, most of the previous aromatherapy studies focused on changes in subjective evaluations, and the results were likely easily influenced by the perceptions and expectations of the subjects.[2–4] Therefore, the actual effect of aromatherapy on sleep under controlled laboratory conditions remains to be investigated.

Polysomnography (PSG) has been considered the gold standard for the investigation of sleep since the 1980s and is therefore considered a valid and effective method for studying the effects of aromatic interventions on human sleep and the human brain during sleep.[12] In addition, using PSG to interpret brain and other bodily functions to understand the effects of aromatherapy on sleep is more objective than observational analysis of the effects of aroma through sleep-related questionnaires or behavior change alone. Therefore, in this study, we presented a single-blind randomized controlled study to explore an inhaled single-ingredient lavender essential oil compared to a complex lavender essential oil, which contained orange, petitgrain, rose, lavender, rosewood, ho wood, and amyris. The efficacy of the two interventions was evaluated and compared through a two-night PSG study to see how aromatherapy may affect sleep physiology. Moreover, the other aim of this study was to look at the immediate effects of lavender-based essential oil inhalation on subsequent PSG for participant with poor sleep quality.

2. METHODS

2.1. Ethics statement

This study was approved by the Institutional Review Board of Kuang Tien General Hospital (IRB10744) and registered on the government website ClinicalTrials.gov (NCT03933553). All participants were given a clear explanation, and written informed consent was obtained from all subjects prior to enrollment.

2.2. Blinding and randomization

We used a single-blinded setting with the Consolidated Standards of Reporting Trials (CONSORT) guidelines to explore the effects of essential oil aroma on sleep.[13] The type of essential oil was not provided to the participants, and this information was kept from the investigators as well. The essential oils used were a single-ingredient lavender essential oil and a complex lavender essential oil (mixed type: lavender, orange, petitgrain, rose, rosewood, ho wood, and amyris). PSG measurements were recorded for each participant on two consecutive nights of the study. For each participant, one of the two nights was chosen as the stimulus night and the other as a control night to counterbalance the randomized order. The aroma used for the stimulus night was a single lavender essential oil (SLEO) or a complex lavender essential oil (CLEO). (This means that the participants were randomly assigned one night without aromatherapy and one night with one of the two aromas; half of the participants had no aroma on the 1st night and were randomly assigned an aroma on the 2nd night, and the other half were randomly assigned an aroma on the 1st night and no aroma on the 2nd night.)

2.3. Study subjects

A total of 200 participants were approached to participate in this trial from November 2018 to November 2019 at the Neurology Clinic of Kuang Tien General Hospital. The inclusion criteria were as follows: each participant (1) was an adult between the ages of 20 and 65 with the ability to communicate and describe symptoms; (2) had a sleep disorder lasting at least 3 months and more than three nights per week; (3) had a Pittsburgh Sleep Quality Index (PSQI) score greater than 5; (4) was willing to cooperate with the study requirements, examinations, and tests, including aromatherapy, two consecutive nights of PSG, questionnaires, and blood tests; and (5) signed the informed consent form approved by the Institutional Review Board. Patients who met the following criteria were excluded from the study: (1) having abnormal olfactory function (ie, brain damage, acute and chronic sinusitis) or a history of nasal surgery; (2) taking medications that affect sleep patterns or consuming foods that cause irritation (such as coffee or refreshing drinks); (3) having asthma or an allergy to the aromas; (4) having severe cardiopulmonary disease, cancer, or other major illnesses (such on dialysis); and (5) were pregnant or breastfeeding.

All participants who decided to participate this trial had sufficient information and understanding before making decisions, and signed the informed consent. Finally, we recruited 53 participants for this study and divided them randomly into two groups: 25 in the SLEO group and 28 in the CLEO group. All the participants completed the following preparatory work before or at baseline: (1) maintaining a regular sleep schedule and daily routine during the previous week (all the participants were asked to do so beforehand); (2) avoiding napping or drinking any alcoholic/caffeinated beverages the day before the experiment (all the participants were explicitly told to follow this guideline); (3) keeping a record of the sleep schedule for the previous week; and (4) completing sleep-related questionnaires, including the Pittsburgh Sleep Quality Index (PSQI), Berlin Questionnaire for Sleep Apnea (BQ), and Hospital Anxiety and Depression Scale (HADS).

2.4. Sleep laboratory

All the experimental protocols used in the sleep laboratory followed the guidelines of the Taiwan Society of Sleep Medicine (TSSM) and were performed in accordance with applicable local laws and ordinances.[14] The hardware and software specifications of the sleep laboratory were as follows: (1) two rooms maintained at temperatures between 24 and 26 degrees Celsius were set up for experimental use; (2) one room was an experimental room for sleep, and the other was a monitoring room; (3) the experimental room was equipped with two infrared cameras and a bed with sheets and pillows; and (4) a trained technician stayed in the monitoring room to monitor the subject during the experiment.

2.5. Experimental procedure

All the participants underwent PSG for two consecutive nights (from 10:00 PM to 7:00 AM) during all PSG-identifiable sleep stages, including wake (W), sleep onset latency (SOL), non-rapid eye movement (NREM) stage 1 (N1), NREM stage 2 (N2), NREM stage 3 (N3), rapid eye movement (REM), total sleep time (TST), wake after sleep onset (WASO), and sleep efficiency (SE). The physiological changes that occurred during sleep were also recorded with PSG via electroencephalography (EEG), electrocardiography (EKG), electromyography (EMG), electrooculography (EOG), and measurements of snoring and breathing (Apnea-Hypopnea Index [AHI]) to facilitate the diagnosis of any sleep disorder. The participants arrived at the

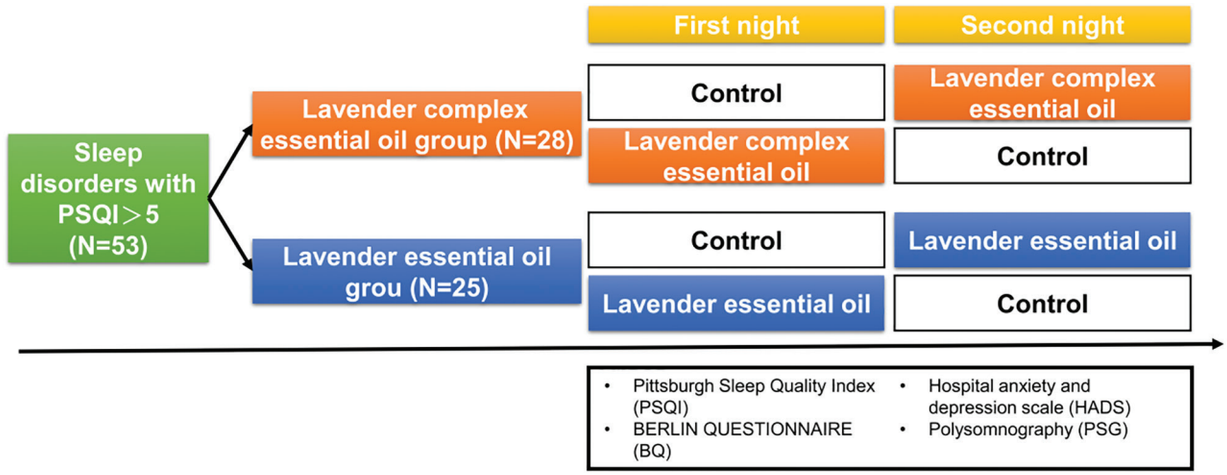

Fig. 1 Study design of essential oils. BQ = Berlin Questionnaire for Sleep Apnea; HADS = Hospital Anxiety and Depression Scale; PSG = polysomnography; PSQI = Pittsburgh Sleep Quality Index.

sleep laboratory at approximately 9:00 PM on the baseline day and did the following: (1) turned in their sleep schedule record for the previous week; (2) performed an olfactory function test; and (3) completed the questionnaires (PSQI, BQ, HADS). The participants were asked to go to bed at 10:00 PM and were woken at 7:00 AM the next day regardless of whether the first night was a stimulus night or a control night. If the first night was a control night, only water vapor was released into the laboratory; conversely, if it was a stimulus night, five drops of SLEO or CLEO diluted in 50 mL of water was gradually and continuously released in the laboratory for inhalation for 2 hours starting 10 minutes before the participants went to bed to facilitate aromatherapy. The participants who experienced side effects the day after inhalation were also documented (Fig. 1).

2.6. Measurement of outcomes

Sleep quality was evaluated by quantitative parameters of PSG, including TST, sleep period time (SPT), SE, SOL, N1, N2, N3, REM, WASO, total stage shifts, and average oxygen saturation (SpO_2).

2.7. Gas chromatography-mass spectrometry

The volatile compounds were analyzed using a SHIMADZU gas chromatography-mass spectrometry (GC-MS) system (GC-MS-QP2010, Kyoto, Japan). An Equity^{-5} capillary column (length, 30 m; inside diameter, 0.25 mm; film thickness, 0.25 μm; Supelco, Sigma-Aldrich, USA) was used. The oven temperature was programmed as follows: isothermal at 40°C, increased to 100°C at 5°C/min, and held for 5 minutes. Subsequently, the temperature was increased to 250°C at 5°C/min and held for 20 minutes. Helium (1 mL/min) was used as the carrier gas. The injection port and detector temperature were maintained at 250°C. The sample components were ionized via the electron ionization mode (70 eV). The injection volume was 1 μL of essential oil (100 ppm in ethanol 99.95%). The linear retention indices (RIs) for all the compounds were determined by coinjection of the samples with a solution containing a homologous series of C8-C22 n-alkanes.[15] The individual components were identified by comparing their RIs with those of known compounds reported in the literature and by matching their mass spectra with those of the known compounds or the GC-MS-QP2010, Kyoto, Japan spectral database.

2.8. Statistical analysis

Since all variables were not normally distributed by Shapiro-Wilk tests, we used nonparametric tests for continuous variables in this study. In Table 1, comparisons of the demographic data between the SLEO group and CLEO group were examined by a chi-square test for sex and Wilcoxon rank-sum tests for other continuous variables. In Table 2, the change in PSG measurement was defined as the value of the stimulus night minus the value of the control night, and a significant difference between both nights was evaluated using the Wilcoxon sign-rank test. The Wilcoxon rank-sum test was used to examine the differences in the SLEO and CLEO groups. To determine whether there was a first night effect, we also used the Wilcoxon rank-sum test. There were no significant first night effects in either group. Two-sided p values were adjusted for multiple testing by the Benjamini-Hochberg procedure with a false discovery rate (FDR) of 0.05. The multiple comparison correction was performed separately for different essential oil group and sex-specific subgroups (Fig. 2).

Table 1

Baseline characteristics of the lavender essential oil group and the lavender complex essential oil group

Parameter	SLEO group (N = 25)	CLEO group (N = 28)	p^a
Sex, n (%)			
Female	17 (68.0)	17 (60.7)	0.5809
Male	8 (32.0)	11 (39.3)	
Age, y			
Mean ± SD	50.0 ± 14.2	45.0 ± 12.2	0.1535
BMI	24.9 ± 4.5	25.3 ± 4.5	0.9148
Neck circumference, cm	34.9 ± 3.5	35.6 ± 3.5	0.4485
Sleep-related questionnaires, mean ± SD			
PSQI	12.2 ± 4.3	12.8 ± 4.0	0.6546
BQ	2.5 ± 2.1	3.0 ± 2.3	0.2785
HADS	12.0 ± 6.6	13.8 ± 5.6	0.3126

BMI = body mass index; BQ = Berlin Questionnaire for Sleep Apnea; CLEO = complex lavender essential oil; HADS = Hospital Anxiety and Depression Scale; PSQI = Pittsburgh Sleep Quality Index; SLEO = single lavender essential oil.

[a]The p was calculated with the chi-square test or Wilcoxon rank-sum test.

Table 2

Change in whole night PSG measurement for lavender essential oil and lavender complex essential oil (stimulus night–control night, mean ± SD)

	SLEO			CLEO		
Parameter	**Men, n = 8**	**Women, n = 17**	**Total, n = 25**	**Men, n = 11**	**Women, n = 17**	**Total, n = 28**
TST, min	42.38 ± 79.83	**43.91 ± 44.58**[a]	**43.42 ± 56.43**[a]	19.50 ± 29.82	26.50 ± 53.19	**23.75 ± 44.92**[a]
SPT, min	46.00 ± 127.83	**35.50 ± 64.99**[a]	**38.86 ± 87.22**[a]	**24.32 ± 17.48**[a]	**23.91 ± 24.90**[a]	**24.07 ± 21.92**[a]
Sleep efficiency (%)	10.25 ± 18.06	7.08 ± 11.54	**8.10 ± 13.64**[a]	0.15 ± 9.72	1.12 ± 12.68	0.74 ± 11.42
Sleep onset latency, min	–23.69 ± 54.96	–5.47 ± 17.85	–11.3 ± 34.18	4.09 ± 29.86	–2.62 ± 12.75	0.02 ± 20.92
NREM (SPT), %	–1.09 ± 13.31	0.60 ± 6.54	0.06 ± 8.99	–2.29 ± 9.54	0.56 ± 9.99	–0.56 ± 9.74
NREM, min	32.31 ± 81.62	**28.09 ± 33.20**[a]	**29.44 ± 51.79**[a]	11.45 ± 33.65	19.25 ± 43.6	16.19 ± 39.51
N1 min	14.38 ± 30.28	–2.05 ± 16.71	3.21 ± 22.69	15.91 ± 16.06	1.09 ± 16.68	6.91 ± 17.74
N2 min	15.94 ± 59.15	**28.93 ± 33.82**[a]	**24.77 ± 42.67**[a]	–2.45 ± 34.12	19.62 ± 46.95	10.95 ± 43.11
N3 min	2.00 ± 3.02	1.21 ± 16.28	1.46 ± 13.4	–2.00 ± 3.79	–1.45 ± 10.86	–1.67 ± 8.68
N1 (SPT), %	–6.03 ± 21.09	–2.03 ± 5.33	–3.31 ± 12.34	3.70 ± 4.89	–0.59 ± 4.31	1.09 ± 4.94
N2 (SPT), %	4.42 ± 15.43	2.51 ± 7.67	3.12 ± 10.46	–5.31 ± 11.25	1.90 ± 11.48	–0.93 ± 11.74
N3 (SPT), %	0.53 ± 0.84	0.13 ± 4.30	0.25 ± 3.55	–0.68 ± 1.02	–0.74 ± 2.95	–0.72 ± 2.35
REM (min)	10.06 ± 12.86	**12.74 ± 17.58**[a]	**11.88 ± 16.00**[a]	1.64 ± 37.04	7.68 ± 21.42	5.30 ± 28.09
REM (SPT), %	2.67 ± 3.46	2.52 ± 5.18	**2.57 ± 4.63**[a]	–0.45 ± 10.15	0.89 ± 5.18	0.37 ± 7.39
WASO (SPT), min	3.69 ± 70.8	–8.38 ± 44.8	–4.52 ± 53.23	4.82 ± 31.46	–2.59 ± 44.41	0.32 ± 39.36
WASO (SPT), %	–1.59 ± 13.72	–4.71 ± 8.56	–3.71 ± 10.3	0.95 ± 7.86	–1.30 ± 11.87	–0.42 ± 10.37
Total stage shifts	18.88 ± 42.52	9.35 ± 27.86	12.4 ± 32.64	17.18 ± 36.47	14.94 ± 40.6	15.82 ± 38.35
Average SpO_2 (%)	0.00 ± 0.76	0.18 ± 0.73	0.12 ± 0.73	–0.09 ± 0.30	–1.24 ± 3.40	–0.79 ± 2.69
TST AHI (/H)	3.28 ± 7.69	2.05 ± 4.80	2.44 ± 5.74	0.64 ± 8.48	0.68 ± 3.49	0.66 ± 5.82
REM AHI (/H)	5.43 ± 7.44	0.96 ± 10.28	2.39 ± 9.54	–6.22 ± 6.77	4.62 ± 10.05	0.36 ± 10.29
PLM index	1.83 ± 12.99	–1.03 ± 5.91	–0.12 ± 8.62	–0.64 ± 3.38	0.03 ± 4.72	–0.23 ± 4.19
Respiratory arousals	–0.05 ± 2.85	1.1 ± 1.93	0.73 ± 2.27	0.34 ± 3.03	–0.15 ± 1.82	0.04 ± 2.33
PLM arousals	–0.08 ± 0.79	–0.28 ± 1.12	–0.21 ± 1.02	0.37 ± 0.68	0.18 ± 0.47	0.25 ± 0.56
Spontaneous arousals	–3.93 ± 5.96	–2.89 ± 5.95	**–3.22 ± 5.85**[a]	0.24 ± 3.08	–0.79 ± 3.79	–0.39 ± 3.51
Total arousals	–4.08 ± 7.41	–2.06 ± 6.14	–2.71 ± 6.49	0.95 ± 3.41	–0.21 ± 4.71	0.25 ± 4.22

SPT was defined as the duration from sleep onset to the end of sleep.

AHI = Apnea-Hypopnea Index; CLEO = complex lavender essential oil; NREM = non-rapid eye movement; PLM = Periodic limb movement; PSG = polysomnography; REM = rapid eye movement; SLEO = single lavender essential oil; SpO_2 = oxygen saturation; SPT = sleep period time; TST = total sleep time; WASO = wake after sleep onset.

[a]Benjamini-Hochberg adjusted $p < 0.05$ indicates bold.

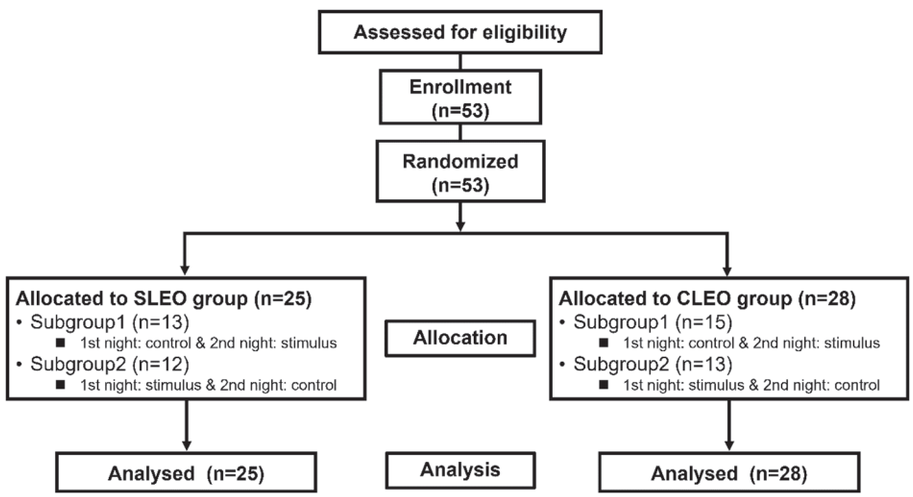

Fig. 2 CONSORT diagram of the study flow. CLEO = complex lavender essential oil; CONSORT = Consolidated Standards of Reporting Trials; SLEO = single lavender essential oil.

3. RESULTS

We collected baseline characteristics, such as sex, age, body mass index (BMI), neck circumference, and the results of the PSQI, BQ, and HADS. The mean ages were 50.0 ± 14.2 and 45.0 ± 12.2 years for the SLEO and CLEO groups, respectively (Table 1). A total of 68.0% and 60.7% of the participants were females in the SLEO group and CLEO group, respectively. The PSQI, BQ, and HADS were 12.2 ± 4.3, 2.5 ± 2.1, and 12.0 ± 6.6 in the SLEO group; while 12.8 ± 4.0, 3.0 ± 2.3, and 13.8 ± 5.6 in the CLEO group. The baseline score of PSQI, BQ, and HADS in both groups manifested poor quality of sleep, high risk of obstructive sleep apnea, and more anxious and depressive states. There were

no significant differences in any baseline characteristics between the two groups.

Table 2 shows the change in PSG measurement for the SLEO and CLEO groups (Δ = stimulus night–control night). In the SLEO group, TST (minutes; Δ = 43.42 ± 56.43; Benjamini-Hochberg adjusted $p = 0.0022$), SPT (minutes; Δ = 38.86 ± 87.22; Benjamini-Hochberg adjusted $p = 0.0128$), SE (%; Δ = 8.10 ± 13.64; Benjamini-Hochberg adjusted $p = 0.0145$), NREM (minutes; Δ = 29.44 ± 51.79; Benjamini-Hochberg adjusted $p = 0.0160$), N2 (minutes; Δ = 24.77 ± 42.67; Benjamini-Hochberg adjusted $p = 0.0237$), REM (minutes; Δ = 11.88 ± 16.00; Benjamini-Hochberg adjusted $p = 0.0052$), and REM_{SPT} (%; Δ = 2.57 ± 4.63; Benjamini-Hochberg adjusted $p = 0.0227$) were significantly increased on the stimulus night compared with the control night (adjusted $p < 0.03$); spontaneous arousals (Δ = –3.22 ± 5.85; Benjamini-Hochberg adjusted $p = 0.0184$) was significantly decreased on the stimulus night compared with the control night.

After stratifying by sex, women had significantly longer TST (minutes; Δ = 43.91 ± 44.58; Benjamini-Hochberg adjusted $p = 0.0164$), SPT (minutes; Δ = 35.50 ± 64.99; Benjamini-Hochberg adjusted $p = 0.0334$), NREM (minutes; Δ = 28.09 ± 33.20; Benjamini-Hochberg adjusted $p = 0.0209$), N2 (minutes; Δ = 28.93 ± 33.82; Benjamini-Hochberg adjusted $p = 0.0277$), and REM (minutes; Δ = 12.74 ± 17.58; Benjamini-Hochberg adjusted $p = 0.0314$), on the stimulus night compared with the control night. However, there was no significant change in the men.

In the CLEO group, TST (minutes; Δ = 23.75 ± 44.92; Benjamini-Hochberg adjusted $p = 0.0431$) and SPT (minutes; Δ = 24.07 ± 21.92; Benjamini-Hochberg adjusted $p < 0.0001$) were significantly increased on the stimulus night compared with the control night. Both men and women had significantly longer SPTs (minutes; Δ = 24.32 ± 17.48; Benjamini-Hochberg adjusted $p = 0.0488$ and 23.91 ± 24.90; Benjamini-Hochberg adjusted $p = 0.0355$, respectively) after stratifying by sex.

We also compared the effectiveness, that is, the change in PSG measurement, between the SLEO and CLEO groups, but there was no significant difference, which meant that we did not have enough evidence to distinguish whether CLEO was better than SLEO or not. In addition, there were no AEs observed on either the stimulus or control nights. Supplement Tables (http://links.lww.com/JCMA/A193) provide the control night and stimuli night PSG data of two groups.

Table 3 lists the essential information regarding the SLEO and CLEO. GC-MS was performed to analyze the chemical components of the SLEO and CLEO. The GC-MS data revealed that the following four components accounted for 80.44% of the total content of SLEO: linalyl acetate was the major component (37.40%), followed by linalool (35.05%), β-caryophyllene (5.14%), and terpinen-4-ol (2.85%). A total of 26 compounds (accounting for 92.15% of the total oil content), namely, ethyl amyl ketone, β-myrcene, D-limonene, eucalyptol, trans-β-ocimene, cis-β-ocimene, trans-linalool oxide, isoterpinolene, trans-linalool oxide, linalool, phenylethyl alcohol, neo-allo-ocimene, terpinen-4-ol, α-terpineol, nerol, citronellol, linalyl acetate, lavandulyl acetate, neryl acetate, geranyl acetate, β-caryophyllene, α-humulene, β-farnesene, santalol, α-bisabolol, and n-octadecane, were observed in the CLEO. The three most abundant compounds were linalool (39.25%), D-limonene (14.09%), and linalyl acetate (12.76%).

Table 3

Composition of the single lavender essential oil and complex lavender essential oil treatments

Peak number	Rt	Compound	M.f.	SLEO Concentration (%)	CLEO Concentration (%)
1	14.628	Ethyl amyl ketone	$C_8H_{16}O$	0.81	0.48
2	14.802	β-Myrcene	$C_{10}H_{16}$	1.70	1.18
3	16.692	D-Limonene	$C_{10}H_{16}$	0.49	14.09
4	16.805	Eucalyptol	$C_{10}H_{18}O$	1.60	1.43
5	17.155	trans-β-Ocimene	$C_{10}H_{16}$	1.21	1.20
6	17.663	cis-β-Ocimene	$C_{10}H_{16}$	1.66	1.90
7	18.804	trans-Linalool oxide	$C_{10}H_{18}O_2$	0.15	0.62
8	19.491	Isoterpinolene	$C_{10}H_{16}$	<0.01%	0.10
9	19.617	trans-Linalool oxide	$C_{10}H_{18}O_2$	<0.01%	0.69
10	20.581	Linalool	$C_{10}H_{18}O$	35.05	39.25
11	20.887	Phenylethyl alcohol	$C_8H_{10}O$	<0.01%	1.15
12	21.725	Neo-allo-ocimene	$C_{10}H_{16}$	0.68	0.69
13	23.752	Endo-Borneol	$C_{10}H_{18}O$	1.03	...
14	24.182	Terpinen-4-ol	$C_{10}H_{18}O$	2.85	2.45
15	24.917	α-Terpineol	$C_{10}H_{18}O$	1.40	1.67
16	26.382	Nerol	$C_{10}H_{18}O$	<0.01%	0.85
17	26.466	Linalyl formate	$C_{12}H_{20}O_2$	0.30	...
18	26.567	Citronellol	$C_{10}H_{20}O$	<0.01%	2.58
19	27.658	Linalyl acetate	$C_{12}H_{20}O_2$	37.40	12.76
20	29.218	Lavandulyl acetate	$C_{12}H_{20}O_2$	1.30	1.62
21	32.554	Neryl acetate	$C_{12}H_{20}O_2$	0.66	0.41
22	33.424	Geranyl acetate	$C_{12}H_{20}O_2$	1.22	0.77
23	35.003	β-Caryophyllene	$C_{15}H_{24}$	5.14	1.74
24	36.812	α-Humulene	$C_{15}H_{24}$	<0.01%	0.39
25	36.964	β-Farnesene	$C_{15}H_{24}$	1.00	0.57
26	47.601	Santalol	$C_{15}H_{24}O$	<0.01%	0.28
27	48.132	α-Bisabolol	$C_{15}H_{26}O$	<0.01%	0.20
28	51.99	n-Octadecane	$C_{18}H_{38}$	<0.01%	3.08
29	<0.01%	Unknown	<0.01%	4.35	7.85

Those of the Wiley and NIST mass spectral databases and the previously published RIs. The components were identified by comparing their mass spectra and retention indices (RIs).
CLEO = complex lavender essential oil; M.f. = molecular formula; NIST = The National Institute of Standards and Technology; RIs = retention indices; Rt = retention time (min); SLEO = single lavender essential oil.

4. DISCUSSION

To the best of our knowledge, this is the first study to propose the use of PSG to detect the immediate effects of essential aroma on individuals with poor sleep quality, which provides clinicians an option of accessible, rapid, and safe intervention to promote sleep. The results showed that both the SLEO and CLEO groups extended sleep time in the participants with poor sleep quality. The SLEO group may further improve SE and influence the amounts of NREM and REM sleep. Of note, women may be more susceptible to essential oils especially in SLEO group for sleep promotion. In addition, there were no significant differences in AEs between the stimulus and control nights. These findings are crucial to understanding the plausible mechanisms of how aroma works immediately, which can be observed objectively with PSG studies.

The key strengths of this study include the application of a combination of validated and standardized measures of clinical assessment and quantitative PSG to evaluate objective sleep quality. In addition, we adopted active control to encourage the recruitment of participants into the current study, which made it less difficult and more reliable to accomplish this pilot study. Moreover, randomly selecting stimulus nights helped overcome the first night effect, which may influence nocturnal in-laboratory PSG results.

Recently, a meta-analysis that contained 34 studies demonstrated the clinical effects of aroma inhalation therapy on insomnia, of which lavender was most frequently studied and suggested to be the preferred aroma essential oil for sleep.[10] Notably, the results also revealed that aroma inhalation therapy

had more effects one to three times before bedtime than 24 hours of continuous indirect inhalation. Essential oil has been explored by various studies to improve sleep quality.[10] However, the true mode of action of fragrance aromatherapy is not fully understood. Lavender aroma is more highly recommended than other aroma oils based on its promising sleep-promoting effects and its safety profile.[10] In addition to improving sleep quality, lavender essential oil has positive effects on many clinical conditions, such as anxiety, depression, fatigue, stress, and pain, and improvements in these conditions may also improve sleep.[7,16] The greater efficacy of SLEO over CLEO in terms of SE and the amount of NREM and REM sleep may be due to its higher concentration of purer lavender essential oil, which is purported to have anxiolytic, antidepressant, analgesic, carminative (smooth-muscle relaxant), and hypnotic effects.[7,16] Whether variations in the concentration of lavender essential oil led to different effects should be further evaluated in future studies. Whether variations in the concentration of lavender essential oil lead to different effects should be further evaluated in future studies.

Essential oil could be used via inhalation, massage or oral administration and it is speculated that when using the inhalation method, inhaled lavender acts via the limbic system, particularly the amygdala and hippocampus, through the olfactory system.[17] The distinctive ambient order of lavender promotes pleasant recollections through which psychological associations initiated by positive emotions may be evoked; thus, pleasant feelings could be inherent in its hypnotic effects.[17] In the current study, we presented a single-blind approach to explore whether bedtime-inhaled essential oil aroma could have immediate effects on human sleep on subsequent PSG examinations. The rapid improvement of some parameters of the PSG study provided promising evidence and supported the notion that aroma inhalation therapy could be used before bedtime by direct inhalation accordingly.

Interestingly, the meta-analysis also found that the effects of a single aroma were greater than those of a mixed aroma. The chemical composition of lavender (*Lavandula angustifolia*) is complex, and its chemical constituents composed mainly of linalyl acetate and linalool components have been proposed to be responsible for hypnotic, sedative, anxiolytic, and relaxant effects.[9,18] In addition, actual physiological changes have been found in animal studies, suggesting that linalool, a principal component of lavender, acts on gamma-aminobutyric acid (GABA) pathways and has a depressant effect on neurotransmission, such as glutamate binding; both factors may produce sedative effects.[19,20] However, there is insufficient evidence from current investigations to prove how inhaled lavender works on the human brain during sleep. Without further understanding the actions of essential oil aroma, it is difficult to evaluate its effectiveness and improve the efficiency of its application. Our study demonstrated that both TST and SPT increased in the SLEO group and further increased the percentage of SE, the most convincing parameter of sleep quality, but not in the CLEO group. In our study, the SLEO group, linalyl was 37.4% and linalool was 35.05%. In the CLEO group, linalyl was 12.76% and linalool was 39.25%. The total amount of linalyl and linalool was greater in the SLEO group than in the CLEO group, which may partially explain the different effects of the two aromas; however, dose, frequency and duration may play another important role. Besides, the relatively small sample size may not distinguish the effects of these two different aromas. Further studies are needed to evaluate the different effects between various comparisons, such as between single and mixed types of fragrances, and between different aroma types, timings of administration, frequencies, durations of exposure, and application tools.

Overnight PSG has been considered the gold standard for investigating sleep and therefore provides more objective insight into the effect of an aroma than subjective sleep questionnaires, actigraphy or temporary EEG studies. However, few studies have investigated aroma effects on sleep by means of overnight PSG. Goel et al[21] found that lavender inhalation increased slow wave sleep and reported higher vigor in the morning but did not shorten the SOL. For 35 postmenopausal women with insomnia, Dos Reis Lucena et al[22] found no significant differences between the lavender group and the control group in sleep quality. According to PSG, there was a tendency of improvement in the amount of WASO. Combined with previous studies, PSG has proven to be a useful tool for detecting the effects of essential oils.

Goel et al[21] found that lavender increased stage 2 NREM sleep and WASO latency in women, with opposite effects in men. Overall, our study was consistent with this study, which showed better improvements in females than in males, especially in the SLEO group. Sex differences in olfactory performance have been widely examined, with females generally showing superior abilities. Scent can also produce a greater physiological response in women than in men.[23] In the current study, we recruited individuals with poor sleep quality due to variable sleep disorders as a proof of concept to see how aroma may affect sleep stages and overall sleep physiology by PSG studies. The results may suggest that lavender aroma influences brain activity and may confirm the results of previous studies suggesting that the human brain can process olfactory stimuli during sleep.

This study has several limitations. First, this was a pilot study, and the sample size was relatively small. Further studies with larger sample sizes are needed to corroborate our findings. Second, our study included a mixture of sleep disorders. The aim of this study was to explore the effect of aroma oil on participants with poor sleep quality clinically defined by the PSQI. More studies with larger and more diverse samples are needed to determine the clinical potential of essential oil aroma for different sleep disorders. On the other hand, we included patients with a PSQI score >5, which is a suggested cutoff point to distinguish good and poor sleepers, with a sensitivity of 89.6% and specificity of 86.5%.[24] The PSQI itself does not have a clear cutoff value to measure the severity of sleep disorders, so participants in this trial could not be further stratified by PSQI as mild or severe, or correlated with therapeutic effects. We will include scores, such as the Insomnia Severity Index (ISI), developed by Morin, has proven to be a reliable and valid tool for detecting participants with insomnia and is therefore suitable for this purpose.[25–27] Third, we only detected the immediate effects of essential aroma on sleep, and the long-term benefit as well as the impact on PSG results when sustained over time are needed for evaluation in future studies. Fourth, we did not observe any AEs in this short study; however, the long-term safety profile of inhaled lavender essential oils should be monitored, particularly with regard to sensitization or toxicity. Fifth, we did not survey the feeling and function of the participants the day after the examination. Daytime alertness on the following morning, which can be measured by the Epworth Sleepiness Scale, is considered informative and needs to be investigated in future studies.

In conclusion, This is the first PSG study to detect the immediate effects of aromatherapy during fragrance inhalation in participants with poor sleep quality, suggesting that direct inhalation of aroma prior to sleep can be considered an adjuvant therapy to promote sleep quality. Our findings suggest that both SLEO and CLEO extend sleep time in participants with poor sleep quality. SLEO may further enhance SE and influence the amounts of NREM and REM sleep. Women may be more susceptible to essential oils for sleep promotion. Considering these findings and given the simplicity, safety and inexpensive cost of

aromatherapy, the use of lavender-based essential oils should be considered a therapeutic option for promoting sleep quality.

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APPENDIX A. SUPPLEMENTARY DATA

Supplementary data related to this article can be found at http://links.lww.com/JCMA/A193.

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