

## ラベンダーの香りがストレス負荷時の睡眠中の自律神経活動に及ぼす影響

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**The odor of lavender maintains the pattern of autonomic nervous activities during sleep  
in humans exposed to stress**

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**Abstract**

Acute stress affects the sleep architecture and the pattern of autonomic nervous activities during sleep. The odor of lavender is semantically evaluated as a sedative, and the inhalation of lavender increases parasympathetic nervous activity and decreases the heart rate in waking humans. We examined whether the odor of lavender, with sub-threshold concentration, ameliorates the effects of stress on the sleep architecture and cardiac functions during sleep in college students exposed to first-night stress, which was brought about by sleeping in a laboratory with experimental settings. Polysomnography and the parameters of a fast Fourier's transform (FFT) analysis of heart beat intervals were compared between a lavender-inhaling group (EXP) and a control group not inhaling lavender (CONT). Heart beat intervals increased both in CONT and EXP during sleep, but those in EXP was greater especially in the latter half of sleep. FFT analysis showed that the high frequency power (HF), an indicator for cardiac parasympathetic activity, failed to increase and the ratio of low frequency power (LF) to HF (LF/HF) did not decrease during sleep in CONT. In contrast, HF increased and LF/HF decreased in EXP. Therefore, inhaling lavender maintained the normal nocturnal pattern of cardiac autonomic activities even in the sleep of participants exposed to stress. The odor of lavender caused no difference in sleep architecture between CONT and EXP. We concluded that the odor of lavender ameliorates the influence of stress on the brain mechanisms subserving the circadian rhythm of autonomic nervous activities and maintains their activity pattern during sleep.

**Key words:** Sleep, Autonomic nervous activity, Stress, Lavender, Circadian rhythm

**要 旨**

ラベンダーは、富士北麓の気候によく適合し、初夏を象徴する景観を形成するなど、この地域の観光資源のひとつになっている。ラベンダーの香りには、不安や緊張を緩和する心理効果があることがわかっている。さらに、このような心理作用に加え、副交感神経の活動を増加させることが、人やラットを用いた実験から明らかになっている。睡眠中には、副交感神経活動が増加し、心拍数が減少する。しかし、ストレスを負荷された状態での睡眠では、心拍数の減少が顕著でなく、中途覚醒や入眠潜時の延長が見られる。本研究では、睡眠中の自律神経活動と心拍数の経時変化に及ぼすストレスの影響が、ラベンダーの香りによって軽減されるか否かを検討した。男子大学生を被験者とし、人工気象室内で睡眠を取らせることで、第一夜効果としてのストレスを与えた。被験者を2群に分け、一方には睡眠中にラベンダーの香りを吸入させ（ストレス＋香り群）、他方は香り無し条件で睡眠をとらせた（ストレス群）。香りを吸入させるラベンダーの濃度は、酢酸アミルを基準とする等強度刺激法により決定した。被験者の脳波と筋電図を終夜記録し、睡眠深度を判定した。同様に終夜記録した心電図のR-R間隔を高速フーリエ解析することで、心臓の副交感神経活動を表す周波数帯パワー（HF）と交感神経活動を表す周波数帯パワー（LF及びLF/HF）を求めた。ストレス群では、入眠後4時間目までは心拍数が持続的に減少したが、その後さ

らに減少することはなかった。一方、ストレス+香り群では、4時間目以降も心拍数の減少が継続して起こり、通常の睡眠中と同じパターンを示した。心臓副交感神経活動 (HF) は、ストレス+香り群では睡眠時間中を通して持続的に上昇したのに対し、ストレス群ではHFは低値に留まり、睡眠中の上昇も見られなかった。睡眠時間中の心臓交感神経活動 (LF/HF) は、ストレス+香り群で入眠前よりも低下した状態が保たれたのに対し、ストレス群では入眠前の値から低下することはなかった。ラベンダーの香りは、心臓の副交感神経活動を亢進させ、交感神経活動を低下させることで、睡眠中の心拍数を減少させることがわかった。以上の結果から、ラベンダーの香りは、ストレスが心臓の自律神経活動に与える影響を軽減することで、睡眠中の心拍数の低下を補償することが明らかとなった。

キーワード：睡眠、ストレス、自律神経、概日リズム、ラベンダー

## Introduction

Inhalation of the odor of lavender is generally accepted to be a psychologically sedative for humans. Accompanying the psychological effect, the inhalation of lavender provokes changes in autonomic nervous functions, i.e. a decrease in heart rate and an increase in the activity of the parasympathetic neurons innervating the heart (Kuroda et al. 2005; Wada 2004). An increase in diastolic blood pressure during exercise is also reduced by inhaling lavender (Nagai et al. 2000). Direct recordings of the nervous activities in anaesthetized rats show that the odor of lavender decreases the activities of the sympathetic neurons innervating the adrenal gland, kidney, and adipose tissues concomitantly with an increase in the activity of the gastric branch of the vagal nerves (Shen et al. 2005; Tanida et al. 2006). These effects of inhaling lavender are neutralised by each one of the following three experimental manipulations: the blockade of histaminergic H<sub>3</sub>-receptors in the brain, the lesion of the suprachiasmatic nucleus, and ZnSO<sub>4</sub>-induced anosmia. The suprachiasmatic nucleus plays a key role as a biological clock (Aston-Jones et al. 2001; Kalsbeek and Buijs 2002) and histaminergic neurotransmission also exerts modifying effects on circadian rhythmicity and neuronal excitability (Tuomist et al. 2001). Therefore, these results obtained in the rat show the possibility that the odor of lavender affects both the sleep-wakefulness cycle and the circadian variation of autonomic nervous activities.

Indeed, the odor of lavender has been reported to improve mild insomnia based on self-evaluation of sleep quality (Lewith et al. 2005). Analysis of polysomnography (PSG) has also shown that the odor of lavender increases slow wave sleep (SWS) in healthy young adults (Goel et al. 2005). However, the effect of lavender on the autonomic nervous functions during sleep has not yet been investigated.

In general, stress reveals profound effects on sleep, which last over several days. Acute stress increases rapid eye movement (REM) sleep and waking during sleep, causes a delay of the onset of sleep, and varies the total sleep time (Palma et al. 2000; Vázquez-Palacios et al. 2004; Vein et al. 2002). In addition to the sleep architecture, acute stress influences heart rate variability during sleep by decreasing parasympathetic nervous

activities and relatively increasing sympathetic nervous activities in the heart (Hall et al. 2004).

In the present experiments, we examined whether the odor of lavender exhibits any ameliorating effect on sleep architecture and autonomic nervous functions in the heart during stressful sleep in participants governed by the first-night effect. To sleep in an unfamiliar environment usually causes intensive stress and brings about the deterioration of sleep, hence the so-called first-night effect (Agnew et al. 1996).

## Materials and Methods

### Participants

Participants were 26 healthy men aged between 19 and 33. They were paid for participation. All experimental procedures were performed in accordance with the Ethics Committee of Yamanashi Institute of Environmental Sciences, and informed consent of all the participants was obtained in written form. The participants were divided into two groups, i.e. lavender-inhaling group and non-inhaling group. Data of 3 participants were eliminated from the off-line analysis, because 2 of them reported the difficulty to sleep without alcoholic beverages and one did the history of insomnia.

### Procedures

On the day of the experiment, participants were asked to abstain from naps and alcoholic beverages and come to the laboratory 2 h before their usual bedtime. After examination of their health condition on the day and the attachment of electrodes, participants were allowed to sleep in an artificial climatic chamber in which air temperature was kept at 20°C and relative humidity at 40% with or without the odor of lavender. They were called by name to get up 8 h after the lights-out. Participants were also allowed to go to toilette *ad libitum*. After waking up, participants subjectively evaluated their sleepiness by the use of the Kwansai-Gakuin Sleepiness Scale, based on the Stanford Sleepiness Scale (Ishikawa et al. 1982).

### Inhalation of lavender

The essential oil of lavender (*Lavendula burnatii super*, Pranarom International, Pertuis, France) was resolved with tri-

ethyl citrate (Wako Pure Chemical Industries, Osaka, Japan). Tri-ethyl citrate is an odorless compound. According to the method for comparing sensory intensities among different odorants (Tonoike 1983), the concentration of lavender oil was adjusted to 0.5%. This concentration of lavender oil possesses a sensory intensity equivalent to 1% amyl acetate. A glass bottle of 500 mL capacity containing 10 mL diluted lavender oil served as an evaporator. By means of an air pump, the headspace air was continuously conducted into the artificial climatic chamber at a rate of 6 mL/min through a nozzle placed 50 cm above the participant's head. The chamber was continuously ventilated at a rate of 30 m<sup>3</sup>/h in the direction from the head to the legs of the participants lying in the bed. The capacity of the chamber was 19.8 m<sup>3</sup>. The application of the odor of lavender was started 15 min before lights-out, and suspended when the participant woke up in the morning. Participants did not recognize the existence of the odor except for two, who clearly identified the odor of lavender. In the control group not inhaling lavender, tri-ethyl citrate was applied in the same manner.

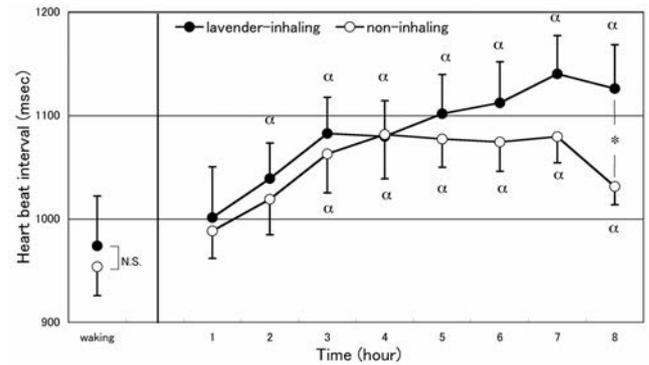
### Recordings

Sleep was monitored using a polysomnographic system (SYNAFIT EE5000, NEC, Tokyo, Japan). Electroencephalograms (EEG) were recorded from C4-A1 and C3-A2 according to the international 10-20 placement. Electrooculograms (EOG) were recorded from the right and left outer canthus, and an electromyogram (EMG) from the chin muscles. In addition, electrocardiogram (ECG) and pneumogram were recorded. The EEG and EOG were amplified with a bandwidth between 0.6 Hz and 50 Hz. The EMG was band-pass filtered between 3.2 Hz and 50 Hz. For the *post hoc* analysis (BIMUTAS II, Kissei Comtec, Matsumoto, Japan), all data were A/D converted with a sampling rate of 1000 Hz.

The sleep stages were scored at 30-sec intervals using the criteria of Rechtschaffen and Kales (1968). A spectrum analysis of heart beat intervals was computed for 252-sec epochs by the use of the fast Fourier's transform (FFT) algorithm. Spectral powers of the low frequency band (LF), 0.04-0.15 Hz, and high frequency band (HF), 0.15-0.5 Hz, were calculated by summing up the powers by frequency bins of 0.004 Hz. The ratio of LF to HF (LF/HF) was calculated. HF is generally employed as an indicator for the cardiac parasympathetic nervous activity, and LF/HF as an indicator for the cardiac sympathetic nervous activity (Kamath and Fallen 1993; Pagani et al. 1997).

### Statistical analyses

The software program used for statistical analysis was Stat View (Abacus Concepts, Berkeley, CA, USA). Differences in polysomnographic measures between the two groups, with (EXP) and without (CONT) the inhalation of lavender, were examined by Student's t-test for independent samples. Differences in heart



**Fig. 1** Changes in heart beat intervals during sleeping and waking in the lavender-inhaling group (n=13) and non-inhaling group (n=13). Means and SEMs are shown. \*: significant differences between the groups ( $p<0.05$ ),  $\alpha$ : significant differences in mean values between waking and sleeping ( $p<0.05$ ).

beat intervals and indices of FFT analysis of the intervals during waking were also examined by Student's t-test for independent samples. Cardiac measures during sleep were analyzed by two-way ANOVA for repeated measures, with groups and time courses as implementing factors. When significant differences were found, Tukey-Kramer's *post hoc* analysis was further conducted in each group. To compare the cardiac measures during sleep and waking within the group, one-way ANOVA for repeated measures was carried out. When significant differences were confirmed, differences from the values during waking were further examined by Dunnett *post hoc* analysis. The hypothesis rejection level for all tests was  $p<0.05$ .

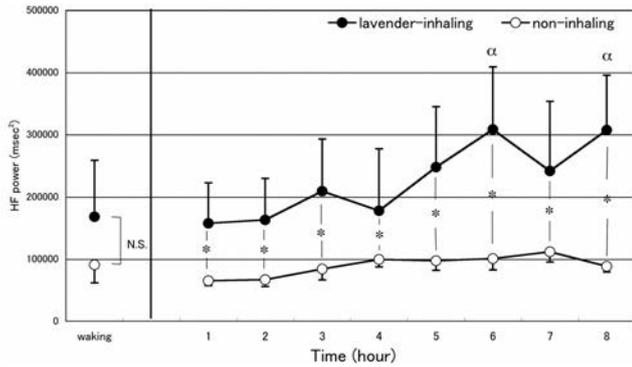
## Results

### 1. Cardiac functions

#### Heart beat intervals

Fig. 1 shows heart beat intervals during waking and sleeping in lavender-inhaling group (EXP) and not inhaling group (CONT). The average in the first 4 min after lights-out was taken as the value during waking ("waking" in the figure). Heart beat intervals from lights-out to the time of getting up, 8 h after lights-out, were averaged by the hour. There was no statistical difference in heart beat intervals during waking between EXP and CONT ( $t=0.269$ ,  $p=0.791$ ).

Two-way ANOVA for repeated measures showed that the interaction between two factors, groups and time courses, were significant (groups:  $F=0.525$ ,  $p=0.477$ ; time courses:  $F=12.622$ ,  $p<0.01$ ; interaction:  $F=2.086$ ,  $p<0.01$ ). One-way ANOVA for repeated measures showed that the effect of time course on heart beat intervals was significant in both groups (EXP:  $F=10.822$ ,  $p<0.01$ ; CONT:  $F=4.607$ ,  $p<0.01$ ). Further examination by Turkey-Kramer's *post hoc* analysis showed that the differences in heart beat intervals between the two groups were significant.



**Fig. 2** Changes in the powers of high frequency band (HF) in heart beat intervals during sleeping and waking in the lavender-inhaling group (n=13) and non-inhaling group (n=13). Means and SEMs are shown. \*: significant differences between the groups (p<0.05), α: significant differences in mean values between waking and sleeping (p<0.05).

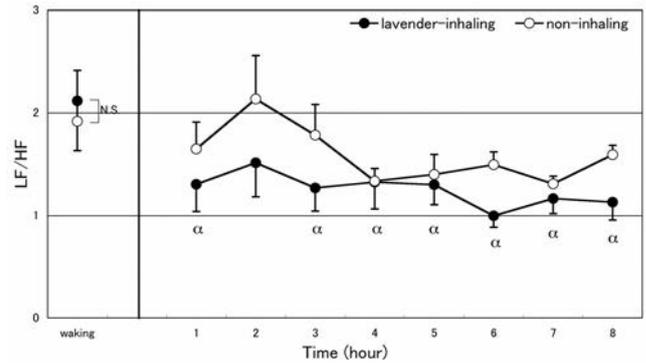
The data showed that heart beat intervals kept increasing during sleep in EXP but this increase was not apparent in CONT, especially in the latter half of sleep.

**Autonomic nervous activities in the heart**

Spectrum analysis of heart beat intervals was performed by means of the FFT method, and spectral power of the low frequency band (LF) and high frequency band (HF) were calculated.

Fig. 2 shows the effect of inhaling lavender on HF. No significant difference was found in HF during waking between EXP and CONT (t=1.123, p=0.170). On the other hand, significant effects of groups and time courses on HF during sleep were confirmed by two-way ANOVA (groups: F=12.493, p<0.01; time courses: F=8.067, p<0.01), and interaction between these two factors, groups and time courses, were also significant (F=4.374, p<0.01). *Post hoc* analysis showed that HF was greater in EXP than HF in CONT throughout the whole night. The statistical difference between HF during waking and sleeping was examined by one-way ANOVA for repeated measures. HF was increased during sleep in EXP (F=7.342, p<0.01) but remained unchanged in CONT (F=2.054, p=0.060).

Fig. 3 shows the ratio of LF to HF (LF/HF) in EXP and CONT. No significant differences were found between the two groups either in waking (t=0.506, p=0.618) or during sleep (groups: F=3.094, p=0.094; time courses: F=1.955, p=0.065; interaction: F=0.668, p=0.699). The statistical difference in LF/HF during waking and sleeping was examined by one-way ANOVA as a repeated measure. Changes in LF/HF in EXP were significant (F=2.565, p<0.05), and *post hoc* analysis showed that LF/HF during sleep was significantly smaller than that during waking. Changes in LF/HF were not significant in CONT (F=1.153, p=0.338).



**Fig. 3** Changes in the power ratio of low frequency band (LF) to high frequency band (HF) during sleeping and waking. Means and SEMs are shown. α: significant differences in mean values between waking and sleeping (p<0.05)

**2. Sleep architecture and the sleepiness scale**

Table 1 summarized the sleep architecture composed of 13 measures of PSG in EXP and CONT. There were no significant differences among PSG measures between the two groups. The data shows that the inhalation of lavender did not affect sleep architecture. There was no statistical difference in the scores of the sleepiness scale after sleep between EXP and CONT, 3.924±0.385 vs. 3.563±0.285 (t=0.758, p=0.458).

**Table 1 Comparison of Sleep Architecture**

	Lavender-Inhaling Group (n=11)	Non-Inhaling Group (n=12)
TIM (min)	477.96 ± 1.03	479.21 ± 0.25
TST (min)	445.73 ± 7.72	429.42 ± 9.18
Sleep Onset (sec)	11.00 ± 3.22	12.33 ± 3.40
N-REM (min)	345.14 ± 7.32	333.16 ± 4.87
Stage 1 (min)	25.73 ± 5.33	26.13 ± 3.46
Stage 2 (min)	264.10 ± 7.93	259.50 ± 7.63
Stage 3 (min)	33.86 ± 3.23	27.08 ± 2.32
Stage 4 (min)	21.46 ± 4.91	20.46 ± 5.21
SWS (min)	55.31 ± 6.06	47.54 ± 6.71
REM (min)	86.05 ± 6.26	80.25 ± 5.50
Move (min)	14.55 ± 1.54	16.00 ± 1.35
Wake (min)	32.23 ± 7.12	49.79 ± 9.16
SE (%)	93.24 ± 1.51	89.61 ± 1.91

Means and SEMs are shown. TIB: total time in bed, TST: total sleep time, N-REM: total time of non-REM sleep, SWS: total time of slow wave sleep, REM: total time of REM sleep, Move: total time of body movement, Wake: total time of waking, SE: sleep efficiency (TST/TIB).

**Discussion**

Although the heart rate decreases during non-REM sleep and increases during REM sleep, the overnight trend of the heart rate shows a successive decline (Busek et al. 2005; Otzenberger et al. 1997; Snyder et al. 1964). During sleep, parasympathetic nervous activities in the heart are increased and sympathetic nervous activities are kept at a low level (Hall et al. 2004; Trinder et al. 2001). In the sleep of humans exposed to stress,

however, parasympathetic activities are not increased and sympathetic activities are not decreased (Hall et al. 2004). We have also confirmed that first-night stress acts to diminish the normal pattern of autonomic nervous activities during sleep in the same way as previously reported. In the present experiment, we have found that the inhalation of lavender retains the pattern of autonomic nervous activities even in the sleep of humans exposed to first-night stress. Direct recordings of autonomic nervous activities in anaesthetized rats have shown that the activity of parasympathetic neurons is increased by the odor of lavender (Shen et al. 2005; Tanida et al. 2006). In rats, it has also been reported that the activity of sympathetic neurons innervating the adrenal gland is decreased by the odor of lavender (Shen et al. 2005). Changes in indices for sympathetic influences on cardiac function during stress, e.g. QT-intervals and pre-ejection period, are predominantly attained by the activation of adrenal sympathetic neurons (Lechin et al. 2004). Therefore, we think that lavender decreases adrenal sympathetic nervous activity during sleep as in the case for anaesthetized rats and the decrease in circulating adrenaline as a consequence causes the prolonged intervals in the heart beat.

The first-night effect is characterized by decreases in total sleep time and sleep efficiency and increases in waking (Le Bon et al. 2001; Tamaki et al. 2005). We did not find any significant effect of inhaling lavender on the architecture of stressed sleep (Table 1). On the other hand, a previous study (Goel et al. 2005) has shown that the odor of lavender increases slow wave sleep (SWS) in healthy young adults. Here, we tentatively propose possible explanations for the lack of influence of lavender on the sleep architecture in our experiment. The first explanation is that the concentration of lavender used in our experiment is not sufficient to change sleep architecture. In a previous study (Goel et al. 2005), lavender oil was used without dilution. In our experiment, lavender oil was diluted so that almost all participants were not aware of the existence of the odor. Studies on the behavioral responses of sleeping humans to certain odorants have shown that a higher concentration of odorant is needed to cause responses (Badia et al. 1990; Carskadon and Herz 2004). In general, the afferent transmission of sensory information to the neocortex is mostly closed at the level of the thalamus during SWS (Steriade et al. 1993). Sensory gating during SWS is also confirmed in olfactory sensation whose afferent pathway passes through the thalamus (Murakami et al. 2005). The downward gating of sensory transmission during SWS is thought to reflect a consolidating process of memory traces acquired during wakefulness (Buzsáki 1989; Hasselmo 1999; Wilson and Yan 2010) or a readjusting process of strengthened and non-strengthened synapses through the sensory pathway during wakefulness (Tsuno and Mori 2009; Manabe et al. 2011). The second explanation is that brain mechanisms initiating the sleep-waking cycle and circadian rhythm of

autonomic nervous activities are not fully synchronized. Parasympathetic nervous activity reveals a circadian rhythm independent of sleep and the maximum activity appears at 4~5 AM even without a sleep episode (Burgess et al. 1997, 1999; Hilton et al. 2000). The effect of lavender on autonomic nervous activities is mediated by histaminergic neurons and the suprachiasmatic nucleus (Shen et al. 2005; Tanida et al. 2006). Histamine neurons innervating brain regions including the suprachiasmatic nucleus are originating from the tuberomammillary nucleus of the posterior hypothalamus. However, lesions of the tuberomammillary nucleus do not bring about gross effect on sleep architecture in rats (Gerashchenko et al. 2004). Even though the effect of lavender to ameliorate the influence of stress in sleeping humans is also mediated by neural networks involving the suprachiasmatic nucleus as shown in anaesthetized rats (Shen et al. 2005; Tanida et al. 2006), lavender may affect the subserving mechanism for autonomic nervous rhythmicity specifically, rather than the mechanism generating the sleep-awake cycle.

Stress is significantly related to morbidity and increased risk for mortality (Kawachi et al. 1994; Kiecolt-Glaser et al. 1995; Lantz et al. 2005). Instability of cardiac functions becomes greater during sleep (Zbrożyna and Westwood 1992). In particular, the risks of ventricular arrhythmia (Verrier et al. 1996) and angina pectoris (Nowlin et al. 1965) heighten during REM sleep. Therefore, we think that the lack of sympatho-vagal balance during stressful sleep increases the risks of adverse cardiovascular events. Our results have shown the possibility that the odor of lavender at subconscious concentration acts beneficially in preventing adverse cardiovascular events during sleep in those exposed to stress.

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