Physiology & Behavior 156 (2016) 94–105

Contents lists available at ScienceDirect

Physiology & Behavior

journal homepage: www.elsevier.com/locate/phb

Combined non-adaptive light and smell stimuli lowered blood pressure, reduced heart rate and reduced negative affect

Shan Dong, Tim J.C. Jacob *

School of Biosciences, Cardiff University, Cardiff CF10 3AX, UK

HIGHLIGHTS

- A non-adaptive light-smell stimulus protocol is described
- Lemon, lavender and peppermint essential oil odours were tested
- Light + smell stimulation reduced blood pressure and heart rate
- Light + lemon odour induced the greatest mood changes
- The combination of light + smell was more effective than either smell or light alone

ARTICLE INFO

Article history:
Received 10 November 2015
Received in revised form 7 January 2016
Accepted 12 January 2016
Available online 15 January 2016

Keywords:
Olfaction
Bright light therapy
Mood
Depression
Anxiety
Essential oils
Blood pressure
Heart rate

ABSTRACT

Bright light therapy has been shown to have a positive impact on seasonal affective disorder (SAD), depression and anxiety. Smell has also has been shown to have effects on mood, stress, anxiety and depression. The objective of this study was to investigate the effect of the combination of light and smell in a non-adaptive cycle. Human subjects were given smell (lemon, lavender or peppermint) and light stimuli in a triangular wave (60 s cycle) for 15 min. Blood pressure and heart rate were monitored before and after each session for 5 consecutive days and a Profile of Mood States (POMS) test was administered before and after the sensory stimulation on days 1, 3 and 5.

The light-smell stimulus lowered blood pressure, both systolic and diastolic, and reduced heart rate for all odours compared to control. Of the two sensory stimuli, the odour stimulus contributed most to this effect. The different aromas in the light-smell combinations could be distinguished by their different effects on the mood factors with lemon inducing the greatest mood changes in Dejection-Depression, Anger-Hostility, Tension-Anxiety.

In conclusion, combined light and smell stimulation was effective in lowering blood pressure, reducing heart rate and improving mood. The combination was more effective than either smell or light stimuli alone, suggesting that a light-smell combination would be a more robust and efficacious alternative treatment for depression, anxiety and stress.

1. Introduction

Light therapy is an established treatment for seasonal affective disorder (SAD) and mood disorders [10,30,32], having been successfully used for over 20 years. Bright light therapy (BLT) is the recommended first-line treatment of the majority of cases of SAD, with improvements in symptoms observed with as little as 20 min of light exposure. A Cochrane Review [45] to evaluate clinical effects of bright light therapy in comparison to an inactive placebo treatment for non-seasonal depression found a "modest though promising antidepressive efficacy" and a later systematic review of the treatment of nonseasonal depression came to the conclusion that "overall, bright light therapy is an excellent candidate for inclusion into the therapeutic inventory available for the treatment of nonseasonal depression today, as adjuvant therapy to antidepressant medication" [8]. Since then further clinical trials have been conducted on specific groups and their findings lend further support to the efficacy of BLT. For example in the treatment of Major Depressive Disorder (MDD) in the elderly, a randomised, placebo controlled trial demonstrated that BLT was comparable to antidepressant medication in effectiveness [25]. In another study both antidepressant

Abbreviations: SAD, seasonal affective disorder; POMS, Profile of Mood States; BLT, Bright light therapy; MDD, Major Depressive Disorder; GAD, Generalised Anxiety Disorder; TMD, Total Mood Disturbance; CB, Confusion-Bewilderment; AH, Anger-Hostility; DD, Dejection-Depression; TA, Tension-Anxiety; FI, Fatigue-Inertia; VA, Vigour-Activity; BP, blood pressure; HR, heart rate.

* Corresponding author at: School of Biosciences, Museum Avenue, Cardiff University, Cardiff CF10 3AX, UK.
E-mail address: jacob@cardiff.ac.uk (T.J.C. Jacob).

http://dx.doi.org/10.1016/j.physbeh.2016.01.013

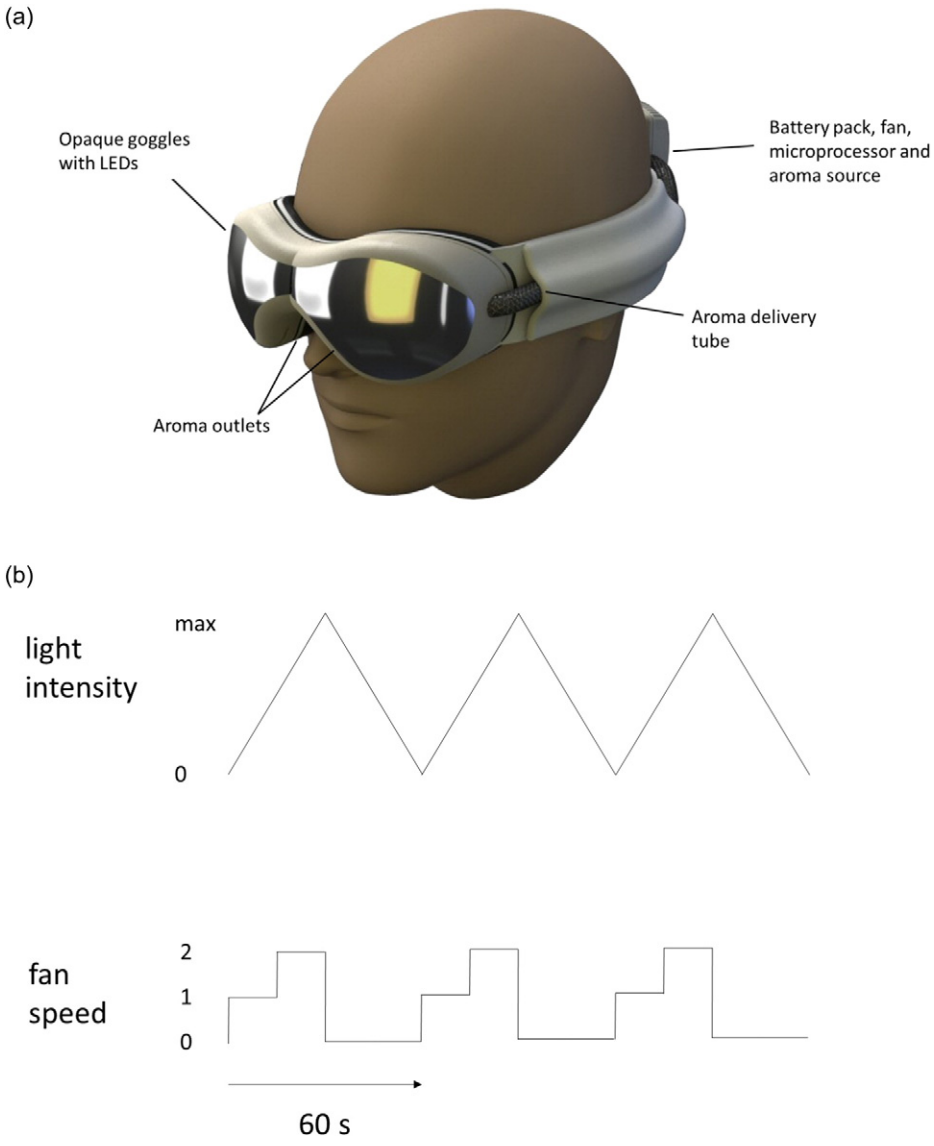

Fig. 1. (a) The stimulus delivery apparatus (see Methods for details). (b) The light and smell stimulus protocol. Diffuse full-spectrum white light (maximum 2500 lx) was presented as a triangular wave starting from zero light, rising to a maximum (2500 lx) linearly over 30 s and then declining linearly to zero over 30 s. Simultaneously an airstream containing essential oil vapour was delivered to the nostrils at two flow rates (0.17 and 0.33 l/s) to coincide with the up-ramp of the light stimulus. Three cycles are illustrated. The reason for delivering the stimuli in this manner was to overcome olfactory adaptation/habituation.

(venlafaxine) and antidepressant medication + BLT treatment strategies significantly reversed the depressive mood of patients with severe MDD; however, the latter induced significantly stronger and more rapid beneficial effects [11]. BLT has been found to be effective in treating antepartum depression in three trials [7,31,51] although in a Cochrane Database Review in 2013 only one BLT study, that of Wirz-Justice et al. (op.cit.), met its inclusion criteria and further, controlled, longer lasting studies were recommended [4]. While there is evidence to support the use of BLT to treat depression, light boxes are not regulated nor approved by the US Food and Drug Administration (FDA) nor the National Institute for Health and Care Excellence (NICE) in the UK for the treatment of depression of any sort.

Smell has been shown to have effects on mood, stress, anxiety and depression [1,6,12,15,47]. Three odours in particular, lemon, lavender and peppermint, have been demonstrated to have marked effects on mood, depression and anxiety. Work on animals showed that citrus fragrance could restore stress-induced immunosuppression [40,41] and lemon odour, as well as its main component citral, was found to be antidepressant in rats [22] and humans [23]. Lemon balm (main constituent citronellal) exhibited modulation of mood and cognitive performance [17]. Lavender (*Lavandula angustifolia*) essential oil, has been used in folk medicine for the treatment of anxiety since ancient times and mechanisms of action have recently been suggested, including the inhibitory action of linalool at sodium channels [24], a block of voltage activated calcium channels [42] and agonist activity at 5HT-1A post-synaptic receptors [2]. Peppermint odour has positive effects on mood [9,28] but there are disagreements on its effect on arousal with both an increase [3] and decrease [39] being reported. Peppermint augments cognitive performance and administrative tasks [3,28] and has been found to enhance athletic performance [27,36,37] with suggestions that both cardiovascular and central nervous system mechanisms are involved [27,46].

A recent study has demonstrated the additive beneficial effects of smell (lemon) and light administered simultaneously [49] on frontal alpha asymmetry – a metric for depression, anxiety – and mood. The following study was designed to test the effect of this combination of sensory stimuli on physiological (blood pressure and heart rate) and psychological (mood state) measures for repeated trials over five

consecutive days using a non-adaptive stimulus protocol. Three odours, lemon, lavender and peppermint were tested in combination with the light stimulus. This choice was predicated on the fact that these are the odours for which there is the most extensive, objective evidence supporting physiological and psychological effects.

2. Methods

2.1. Subjects

Participants were students aged 18–28 years old from Cardiff University who had volunteered for the experiment. The study conformed to the Declaration of Helsinki (1964). Ethical approval for this study was granted by the Local Research Ethics Committee (School of Biosciences, Cardiff University, UK). Each subject was given a simple odour test – to assign a hedonic rating (±5) for a 10% solution of butyric acid and phenylethyl alcohol (PEA) – to test for olfactory dysfunction. Normosmics give a negative value for butyric acid and positive value for PEA. Subjects then completed a consent form and medical questionnaire. Personal data were anonymised after the study. Exclusion criteria included olfactory dysfunction, allergies, epilepsy, respiratory disease, pregnant women, nursing mothers, and those taking any prescription medications or exposed to chemicals (e.g. volatile organic solvents) on a regular basis in the workplace. Subjects were tested at the same time of day for each of their trials.

2.2. Biometric testing

2.2.1. Blood pressure and heart rate

Blood pressure was measured using an upper arm cuff sphygmomanometer (Omron, UK). Two recordings were made before and after each sensory treatment session and the values averaged. The same device also measured heart rate and, similarly, the values were recorded before and after the treatment session and averaged.

2.3. Pyschometric testing

Psychological state was determined with the Profile of Mood States (POMS-2) self-assessment questionnaire. The factor structure of the POMS, representing six dimensions of mood - Tension, Depression, Anger, Vigour, Fatigue, Confusion - and the associated tables of normative values were derived from psychiatric outpatients and normal college students [26]. POMS has been used extensively for the assessment of mood in many environments [35]. The POMS self-assessment questionnaire was administered before and after exposure to the sensory stimuli on days 1, 3 and 5 of the study.

2.4. Stimulus protocol

2.4.1. Combined light and odour stimulus

Light and odour stimuli were generated by specially constructed goggles (Chelker Ltd., Skipton, North Yorkshire; Fig. 1a) which delivered the two stimuli simultaneously. Light was delivered as a triangular, non-sinusoidal wave with a 60 s period and the aroma was delivered at two incremental flow rates for the rising phase and stopped during the falling phase of the light (Fig. 1b).

This protocol reduces adaptation/habituation and is referred to as a non-adaptive stimulus (see also [49]). Any prolonged, constant sensory stimulus is, after a certain period of time, ignored and therefore no longer perceived [5]. This is a central nervous system (CNS) process and is referred to as habituation. Peripheral reductions in response are also observed under these circumstances, although not always so marked, and these are referred to as adaptation (op.cit). Sensory systems are much better at detecting changes in stimulus input [20] and we therefore designed a stimulus protocol that changed with a non-sinusoidal, triangular wave pattern (Fig. 1). We chose a cycle frequency of 60 s on the basis of the timescale of olfactory adaptation/habituation observed in Jacob et al. [14].

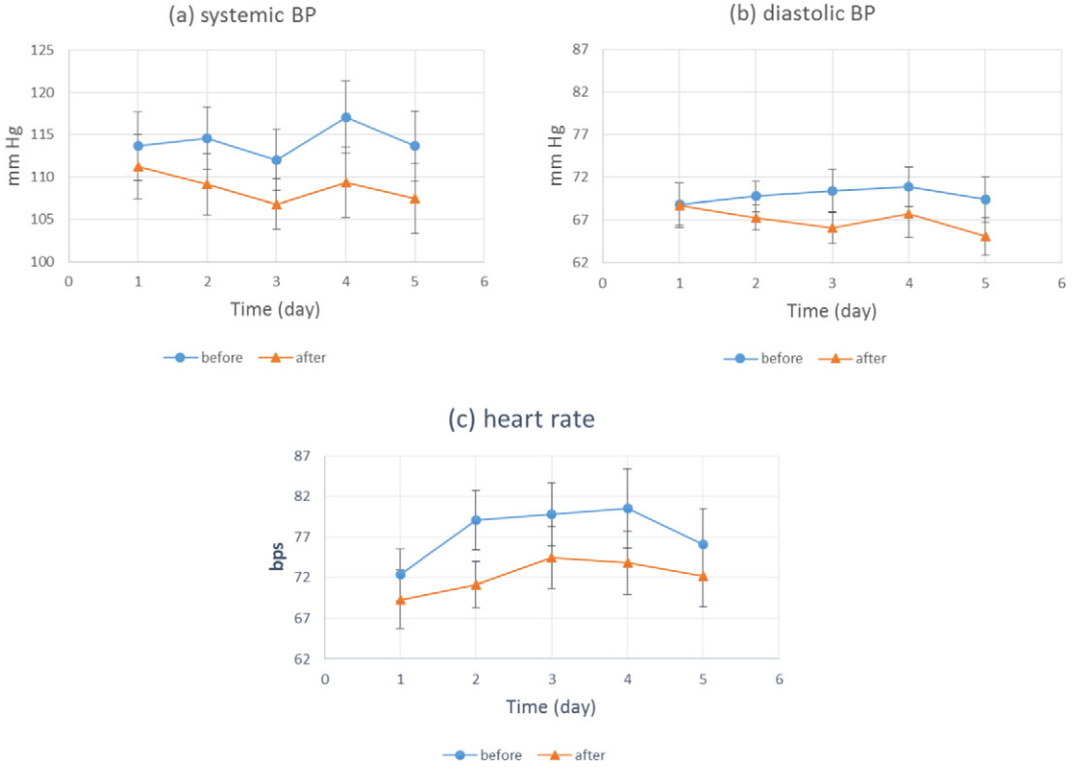

Fig. 2. Effect of light-smell (lemon) treatment on (A) systolic blood pressure, (B) diastolic blood pressure and (C) heart rate (bpm = beats per minute). Measurements were taken before (blue) and after 15 min treatment (orange) each day for 5 consecutive days. The data are presented as the mean ± standard error, $n = 14$.

Table 1
Main effects of day and treatment (light-smell (lemon)) on blood pressure and heart rate. Bold numbers in the Tables indicate significant results ($p < 0.05$).

	Day				Light-smell (lemon)				Day * light-smell			
	F(4,48)	Sig.	η^2,p	Power	F(1,12)	Sig.	η^2,p	Power	F(4,48)	Sig.	η^2,p	Power
Systemic BP	0.313	0.691	0.024	0.09	48.89	**0.0001**	0.79	1	1.323	0.274	0.092	0.38
Diastolic BP	0.365	0.833	0.027	0.13	8.634	**0.012**	0.399	0.78	2.134	0.09	0.141	0.59
Heart rate	0.89	0.476	0.064	0.26	29.47	**0.0001**	0.694	1	1.719	0.16	0.117	0.49

2-factor analysis of variance, F-statistic (degrees of freedom), Sig. = p-value, η^2,p = partial eta^2.

2.4.2. Light stimulus

The light source was an equivalent UV-free light stimulus emitting up to 2500 lx when in close proximity (2–4 cm) to the eyes. This light was delivered by white, 5700 k LEDs (Radiospares, Corby, Northants, UK), 24 in total, 12 per eye fitted into specially constructed goggles (Chelker Ltd., Skipton, North Yorkshire). Total LED power $24 \times 3.2\ V \times 10\ mA = 0.77\ W$. A triangular wave light stimulus was applied with a 60 s cycle time. The light was ramped up to a maximum of 2500 lx over 30 s and then down to a minimum over 30 s (Fig. 1b). During the up-ramp of the light, the odour (lemon, lavender or peppermint essential oil) was delivered at two flow rates (see below). The odour stimulus was switched off at the peak of the light stimulus delivery (30 s) and no odour was delivered during the down-ramp of the light. Fifteen such cycles were delivered in the course of an experiment.

2.4.3. Odour stimulus

Lemon oil (*Citrus limon* (l.) Burm. f., CAS number 8008-56-8), obtained by expression (ISO 855:2003), lavender (*Lavandula angustifolia* l. herb oil, CAS number 8000-28-0) obtained by steam distillation of the recently cut flowering tops (ISO 3515:2002) and peppermint (Mentha piperita l. herb oil, CAS number 8006-90-4) obtained by steam distillation of the aerial parts (ISO 856:2006), were used as the odour stimulus. Three to four drops of essential oil were placed on a circular (5 mm radius) absorbent cotton pad. Air was blown over the pad and odour-containing vapour was delivered by tubes to within 2–3 cm of the nostrils driven by an axial fan (5 v, 100 mA, 0.7 cu.ft./min (0.33 l/s), Farnell, Leeds, UK). The odour stimulus was synchronised to the rising phase of the light stimulus. The cycle began with the fan at half speed and after 15 s the fan switched to full speed, shutting off at 30 s. No odour was delivered during the down phase of the light ramp allowing the olfactory system to recover from adaptation to the odour [14].

2.5. Visual stimulus control

A control experiment was conducted in which the same subjects were given a visual task while wearing ear protectors - to remove auditory stimuli - and sitting comfortably in the same chair as that used for the light-smell stimulus experiments. The visual task was to observe 60 neutral images presented on a computer screen for 15 s and answer a few simple questions at the end of the 15 min session. A Profile of Mood States self-questionnaire was administered before and after the task.

2.6. Data analysis and statistics

The study was a treatment (×2) and time (×5) within subjects factorial design with gender as a between subjects factor for the physiological data (blood pressure and heart rate) and for the POMS data the study was a treatment (×2) and time (×3) within subjects design. Two-factor analysis of variance (repeated measures GLM) was carried out on both sets of data. Multivariate analysis of variance (Wilks' lambda) was used to compare the light + smell treatment with the control experiment (visual task), and a SPSS paired t-test was used to compare individual mood factor scores of the POMS test before and after treatment.

All statistical significant thresholds were set at $p < 0.05$.

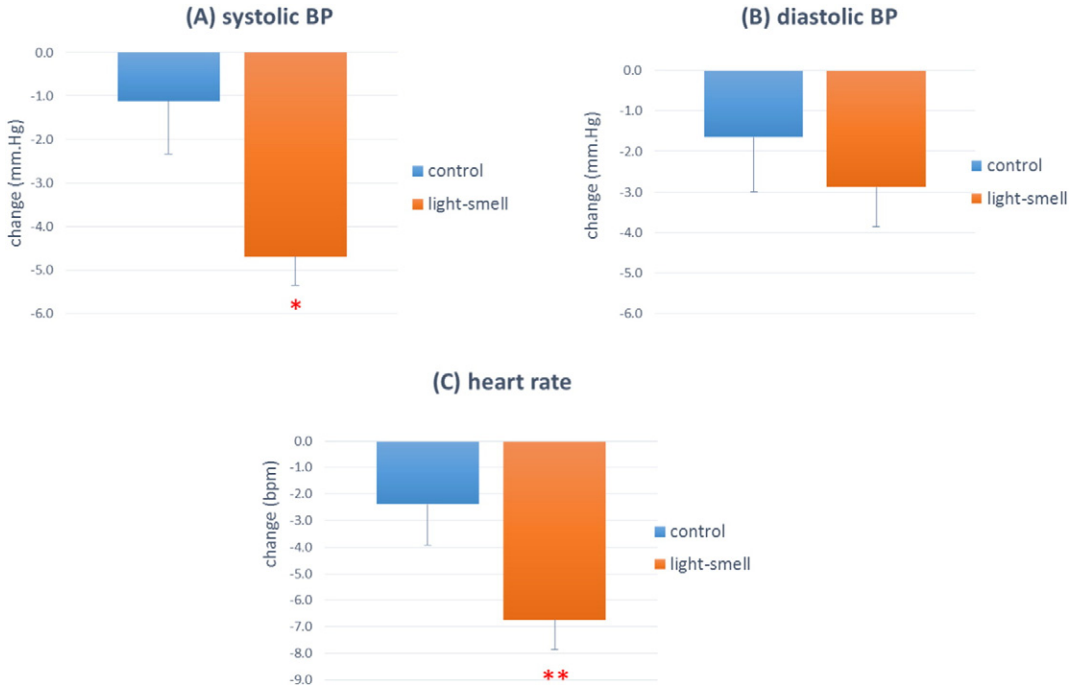

Fig. 3. Effect of light-smell (lemon) treatment on (A) systolic blood pressure, (B) diastolic blood pressure and (C) heart rate compared to a control experiment in which a visual task replaced the light-smell treatment. The data are presented as the mean change in the variables ± standard error. *$p < 0.05$, **$p < 0.01$, $n = 14$.

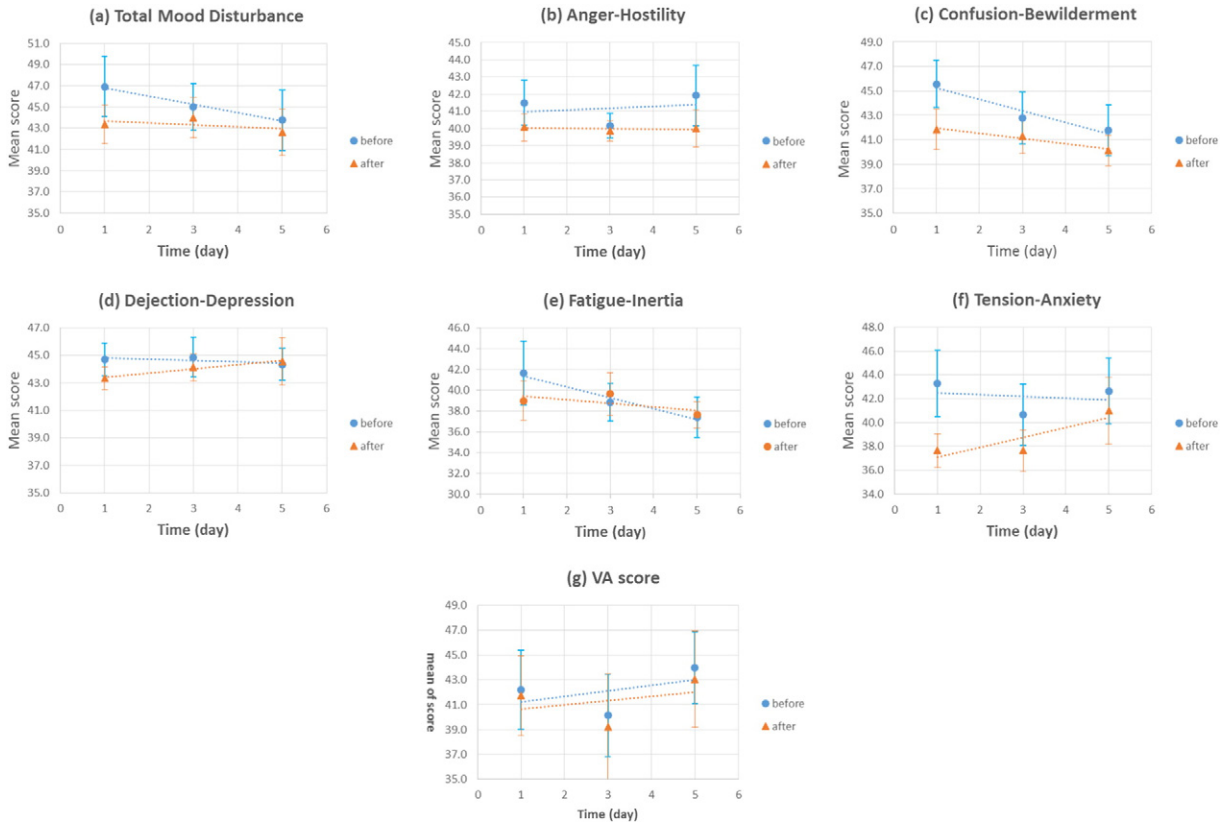

Fig. 4. Results of POMS test administered on days 1, 3 and 5 before (blue symbols) and after (red symbols) 15 min light-smell (lemon) treatment. The results are presented for each of the factors as the mean ± standard error, $n = 14$. The statistical analysis is presented in Table 2.

3. Results

Subjects were given combined light and smell stimuli in a non-adaptive cycle (see Methods). We studied three smell stimuli; lemon, lavender and peppermint essential oils, as well as light and smell stimuli alone. The combination light and smell stimulus was delivered for 15 min to 14 subjects (7F, 7M) each day at the same time for five consecutive days. Blood pressure, heart rate were taken before and after each session and a POMS test was completed before and after sessions on days 1, 3 and 5.

3.1. Light-smell (lemon) stimulus

3.1.1. Blood pressure and heart rate

As can be seen in Fig. 2, in which lemon essential oil was the odour stimulus, the light-smell treatment had an effect on blood pressure (BP) and heart rate (HR). A 2-factor analysis of variance (repeated measures GLM) showed that the light-smell treatment caused an overall significant reduction in systemic BP, diastolic BP, and HR (Table 1): these were large effects with partial eta squared (η^2_p) values of 0.79, 0.399 and 0.694 respectively. There was no significant difference between the effects over the 5 day testing period (Table 1) and the fact that there was no interaction between day and treatment (Table 1) suggests that there was no additive or cumulative effect of the treatment with repetition. Averaging the results over the 5 day test period for the 14 subjects, the systolic BP was reduced from 114.2 ± 3.0 to 108.8 ± 2.8 mmHg (−5.0%), the diastolic BP was reduced from 69.9 ± 2.0 to 67.0 ± 1.8 mmHg (−4.3%) and the HR was reduced from 77.6 ± 3.0 to 72.2 ± 2.7 bpm (−7.4%). No effect of gender was noticed when performing a between subjects analysis of variance; systemic BP ($F_{1,12} = 0.31$, ns), diastolic BP ($F_{1,12} = 1.3$, ns), and HR ($F_{1,12} = 0.01$, ns).

Table 2
POMS test: main effects of day and treatment (light-smell (lemon)).

		Day				Light-smell				Day * light-smell			
		F(2,26)	Sig.	η^2,p	Power	F(1,13)	Sig.	η^2,p	Power	F(2,26)	Sig.	η^2,p	Power
Total Mood Disturbance	TMD	0.955	0.398	0.068	0.197	2.12	0.169	0.14	0.271	0.344	0.712	0.026	0.099
Anger-Hostility	AH	0.701	0.505	0.051	0.155	6.265	**0.026**	0.325	0.639	0.984	0.387	0.07	0.181
Confusion-Bewilderment	CB	6.214	**0.006**	0.323	0.854	5.604	**0.034**	0.301	0.591	1.501	0.242	0.104	0.291
Depression-Dejection	DD	1.135	0.337	0.08	0.228	6.298	**0.006**	0.455	0.861	0.245	0.785	0.018	0.084
Fatigue-Inertia	FI	1.049	0.365	0.075	0.213	0.478	0.501	0.035	0.098	1.335	0.281	0.093	0.262
Tension-Anxiety	TA	0.242	0.635	0.018	0.084	10.44	**0.007**	0.445	0.847	2.019	0.16	0.134	0.352
Vigour-Activity	VA	2.579	0.095	0.166	0.469	0.179	0.679	0.014	0.068	0.035	0.965	0.003	0.055

2-factor analysis of variance, F-statistic (degrees of freedom), Sig. = p-value, η^2,p = partial eta^2.

Table 3
Paired t-test for the changes between light-smell (lemon) treatment and control (POMS). Bold numbers in the Tables indicate significant results ($p < 0.05$).

		Paired differences							
					95% Confidence interval of the difference				
		Mean	Std. dev.	S.E.M.	Lower	Upper	t	df	Sig. (2-tailed)
Light-smell	Total Mood Disturbance	1.79	5.06	1.35	−1.13	4.71	1.32	13	0.209
Lemon	Anger-Hostility	1.29	1.86	0.50	0.21	2.36	2.59	13	**0.022**
	Confusion-Bewilderment(1)	3.71	4.21	1.13	1.28	6.15	3.30	13	**0.006**
	Depression-Dejection	0.57	0.76	0.20	0.14	1.01	2.83	13	**0.014**
	Fatigue-Inertia	0.57	5.27	1.41	−2.47	3.62	0.41	13	0.692
	Tension-Anxiety	3.43	3.65	0.98	1.32	5.54	3.51	13	**0.004**
	Vigour-Activity	0.79	6.99	1.87	−3.25	4.82	0.42	13	0.681
Control	Total Mood Disturbance	0.79	3.07	0.82	−0.99	2.56	0.96	13	0.355
	Anger-Hostility	0.00	0.78	0.21	−0.45	0.45	0.00	13	1.000
	Confusion-Bewilderment	1.36	2.74	0.73	−0.22	2.94	1.86	13	0.086
	Depression-Dejection	−0.36	4.18	1.12	−2.77	2.06	−0.32	13	0.754
	Fatigue-Inertia	0.86	3.82	1.02	−1.35	3.06	0.84	13	0.416
	Tension-Anxiety	0.93	4.01	1.07	−1.39	3.24	0.87	13	0.402
	Vigour-Activity	0.50	2.53	0.68	−0.96	1.96	0.74	13	0.474

The data are expressed as the difference between factors before and after treatment. The control study involved a neutral visual task (see Methods). [1] Confusion-Bewilderment was only significantly different for day 1. On days 3 and 5 there was no before–after difference, presumably as the subjects became familiar with the protocol.

3.2. Control

A control experiment was conducted in which the same subjects were given a visual task while wearing ear protectors - to remove auditory stimuli - and sitting comfortably in the same chair as that used for the light-smell stimulus experiments. There was no difference in systolic BP (paired t-test $p = 0.397$), diastolic BP ($p = 0.246$) or heart rate ($p = 0.09$) before and after the visual task. Fig. 3 compares the effect of light-smell (lemon) stimulus with the control (visual task) on the before–after differences. The data for the light-smell experiment are the averages taken over the 5 days in Fig. 2.

3.2.1. Effect of light-smell (lemon) on mood state

A Profile of Mood States (POMS) test was administered before and after 15 min light-smell (lemon) treatment on days 1, 3 and 5 (Fig. 4).

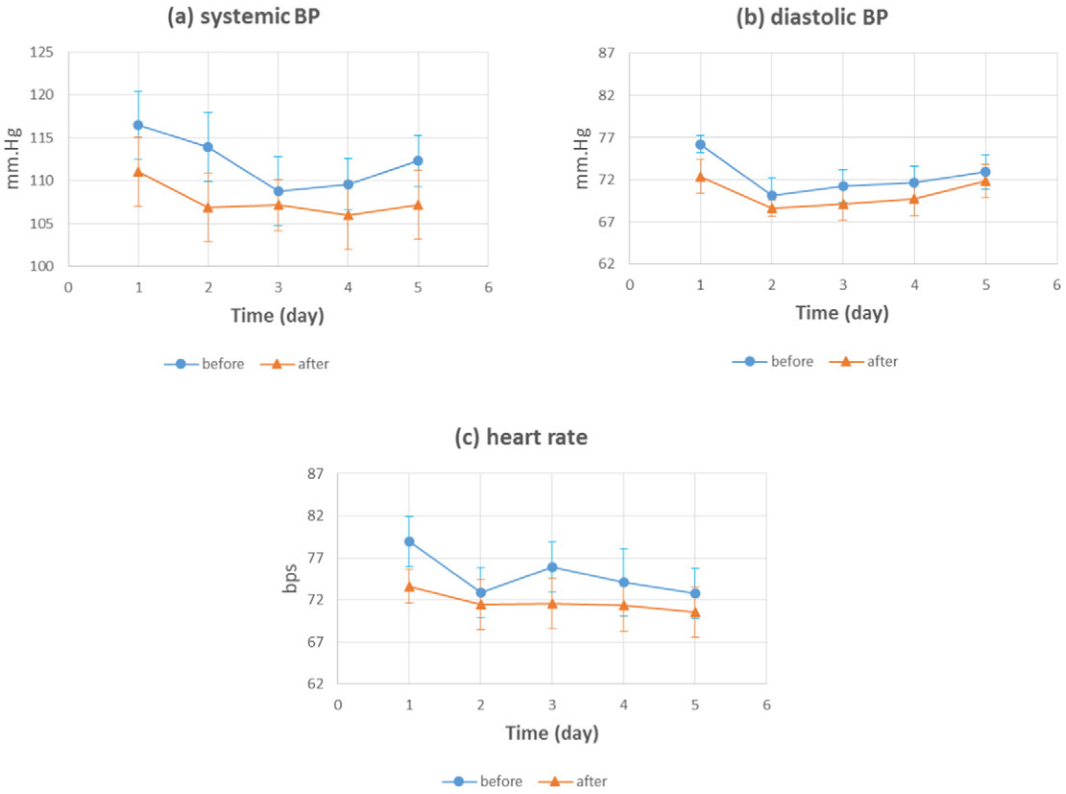

Fig. 5. Effect of light-smell (lavender oil) treatment on (A) systolic blood pressure, (B) diastolic blood pressure and (C) heart rate (bpm = beats per minute). Measurements were taken before (blue) and after 15 min treatment (orange) each day for 5 consecutive days. The data are presented as the mean ± standard error, $n = 13$.

Table 4
Main effects of day and treatment (light-smell (lavender)) on blood pressure and heart rate.

	Day				Light-smell				Day * light-smell			
	F(4,48)	Sig.	η^2,p	Power	F(1,12)	Sig.	η^2,p	Power	F(4,48)	Sig.	η^2,p	Power
Systemic BP	1.299	0.284	0.098	0.375	19	**0.001**	0.613	0.979	1.103	0.366	0.084	0.32
Diastolic BP	3.617	**0.012**	0.232	0.84	13.24	**0.003**	0.524	0.915	1.129	0.354	0.086	0.328
Heart rate	0.875	0.486	0.068	0.257	4.298	**0.06**	0.264	0.479	0.732	0.575	0.058	0.219

2-factor analysis of variance, F-statistic (degrees of freedom), Sig. = p-value, η^2,p = partial eta^2.

There was a significant main effect of the treatment on the factors Anger-Hostility (AH), Confusion-Bewilderment (CB), Dejection-Depression (DD) and Tension-Anxiety (TA) (see Table 2) but only the factor Confusion-Bewilderment was significantly affected over the 5 day period. However, there was only a significant effect for day 1 when the days were analysed separately ($p = 0.006$); days 3 and 5 exhibited no significant difference before and after the treatment ($p = 0.259$, $p = 0.18$ respectively; paired 2-tail t-test). This is probably due to the familiarisation that occurred during the course of the experimental period. Apart from Confusion-Bewilderment, there was no significant difference in the effects on the other factors with time neither was there any interaction between the two factors (Table 2), therefore, the results for days 1, 3 and 5 were averaged and Table 3 presents the effects of the light-small (lemon) treatment compared to the control experiment (visual task, see Methods).

The light-smell (lemon) treatment had a statistically significant main effect on POMS mood factors. In multivariate tests F(14,13) = 8.429, $p = 0.012$; Wilk's lambda = 0.607, partial $\eta^2 = 0.33$. However, the control treatment had no effect on any of the factors; F(14,15) = 2.406, $p > 0.05$ (n.s.), Wilks' lambda = 0.862, partial $\eta^2 = 0.138$. Significant differences (paired t-test) in individual mood factors before and after light-smell treatment where found in AH, CB, DD and TA, whereas no significant differences in any of the factors was found with the control study (visual task) (Table 3).

3.3. Light-smell (lavender) stimulus

3.3.1. Blood pressure and heart rate

When lavender essential oil was the odour stimulus, the light-smell treatment had an effect on blood pressure (BP) and heart rate (HR), which were reduced for each of the 5 days of the treatment period (Fig. 5).

A 2-factor analysis of variance (repeated measures GLM) showed that the light-smell treatment caused an overall significant reduction in systemic BP, diastolic BP and HR (Table 4). There was no significant difference between the effects for systolic BP and heart rate over the

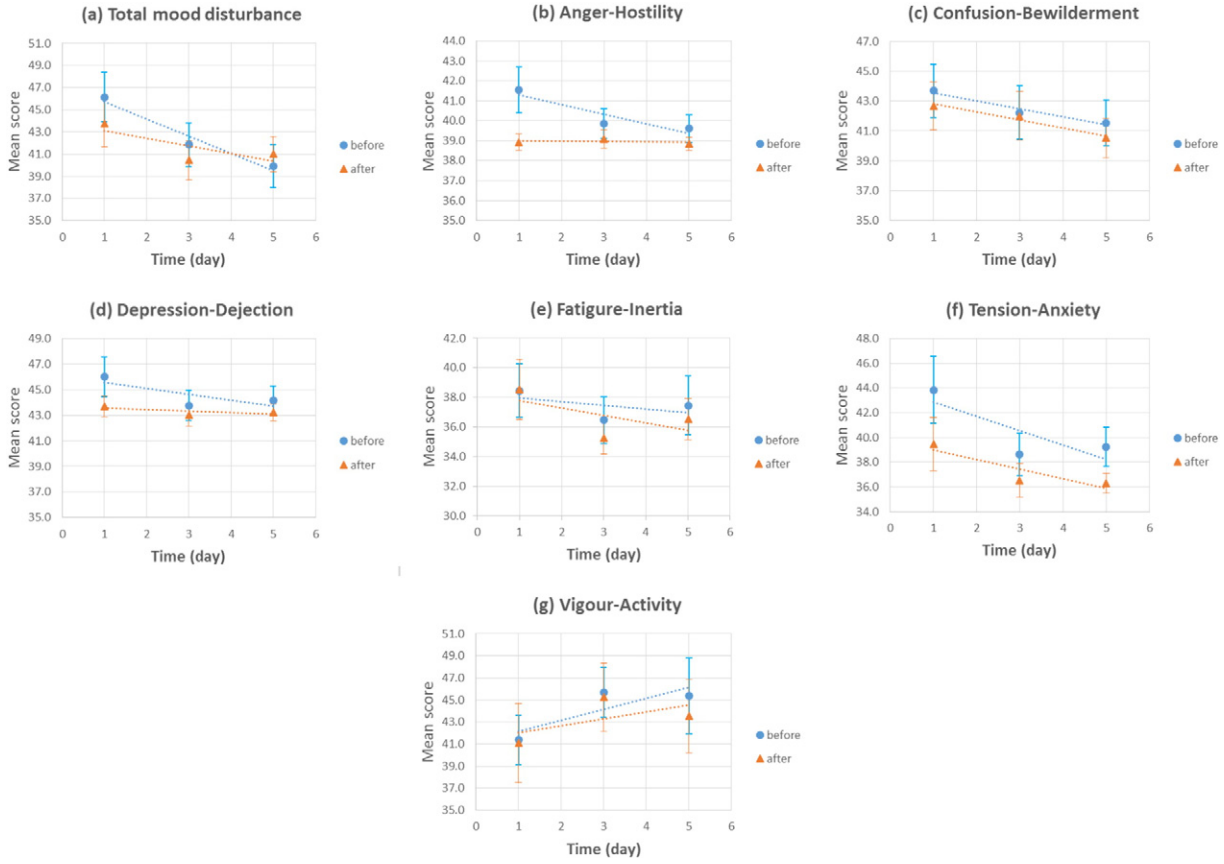

Fig. 6. Results of POMS test administered on days 1, 3 and 5 before (blue symbols) and after (red symbols) 15 min light-smell (lavender) treatment. The results are presented for each of the factors as the mean ± standard error, $n = 13$. The statistical analysis is presented in Table 5.

Table 5
POMS test: main effects of day and treatment (light-smell (lavender)).

		Day				Light-smell				Day * light-smell			
		F(2,24)	Sig.	η^2,p	Power	F(1,12)	Sig.	η^2,p	Power	F(2,24)	Sig.	η^2,p	Power
Total Mood Disturbance	TMD	3.635	**0.042**	0.232	0.614	1.978	0.186	0.141	0.254	0.521	0.601	0.042	0.126
Anger-Hostility	AH	1.245	0.297	0.094	0.203	5.682	**0.035**	0.321	0.591	4.132	**0.05**	0.256	0.674
Confusion-Bewilderment	CB	1.419	0.262	0.106	0.274	1.949	0.188	0.14	0.251	0.164	0.85	0.013	0.072
Depression-Dejection	DD	1.355	0.274	6.783	0.023	6.783	**0.023**	0.361	0.667	0.791	0.465	0.062	0.157
Fatigue-Inertia	FI	1.886	0.174	0.136	0.353	0.244	0.63	0.02	0.074	0.329	0.723	0.027	0.096
Tension-Anxiety	TA	3.767	0.065	0.239	0.482	12.48	**0.004**	0.51	0.899	1.457	0.253	0.108	0.276
Vigour-Activity	VA	2.62	0.094	0.179	0.471	0.225	0.644	0.018	0.072	0.325	0.726	0.026	0.096

2-factor analysis of variance, F-statistic (degrees of freedom), Sig. = p-value, η^2,p = partial eta^2.

5 day testing period, but there was an effect of "day" on diastolic blood pressure. However, from the data in Fig. 5(b) it can be seen that the diastolic blood pressure drops from day 1 to day 2, but thereafter increases from day 3 to day 4 to day 5. This is not therefore an additive effect with time and this is further emphasised by the lack of any interaction between day and light-smell (lavender) treatment (Table 4).

Heart rate was decreased with light-smell (lavender) treatment and the result was close to significance ($p = 0.06$). Further inspection of the data revealed that one subject gave anomalous results on day 2. Eliminating the data for this subject gave a significant difference for treatment over the 5 days ($p = 0.026$, η^2,$p = 0.375$, power = 0.65; $n = 12$).

3.3.2. Mood state

A Profile of Mood States (POMS) test was administered before and after 15 min light-smell (lavender) treatment on days 1, 3 and 5 (Fig. 6). There were significant main effects of treatment on AH, DD and TA with the largest effect on TA (η^2p = 0.51) but no effect of time (Table 5) with the exception of TMD. This is possibly because the subjects became more familiar with the experiment and therefore more comfortable as the study progressed and, being a composite of the 6 negative mood factors, it reflects the reduction in TA over the study period (Fig. 6f). There was an interaction between day and treatment for AH, the level of AH fell over the five days while the impact of the treatment lessened (Fig. 6b).

3.4. Light-smell (peppermint) stimulus

3.4.1. Blood pressure and heart rate

When peppermint essential oil was used as the odour stimulus, the light-smell treatment had an effect on blood pressure (BP) and heart rate (HR), which were reduced for each of the 5 days of the treatment period (Fig. 7). Systolic and diastolic BP and HR were all reduced for each day, but there was no evidence of an additive or cumulative effect with time (Table 6).

Analysis of variance demonstrated that the treatment of light-smell (peppermint) had a significant effect on systemic BP, diastolic BP and heart rate (HR) (Table 6). There was no effect of "day" and so no evidence of an additive effect of the treatment over time and also no interaction of the treatment with time (Table 6).

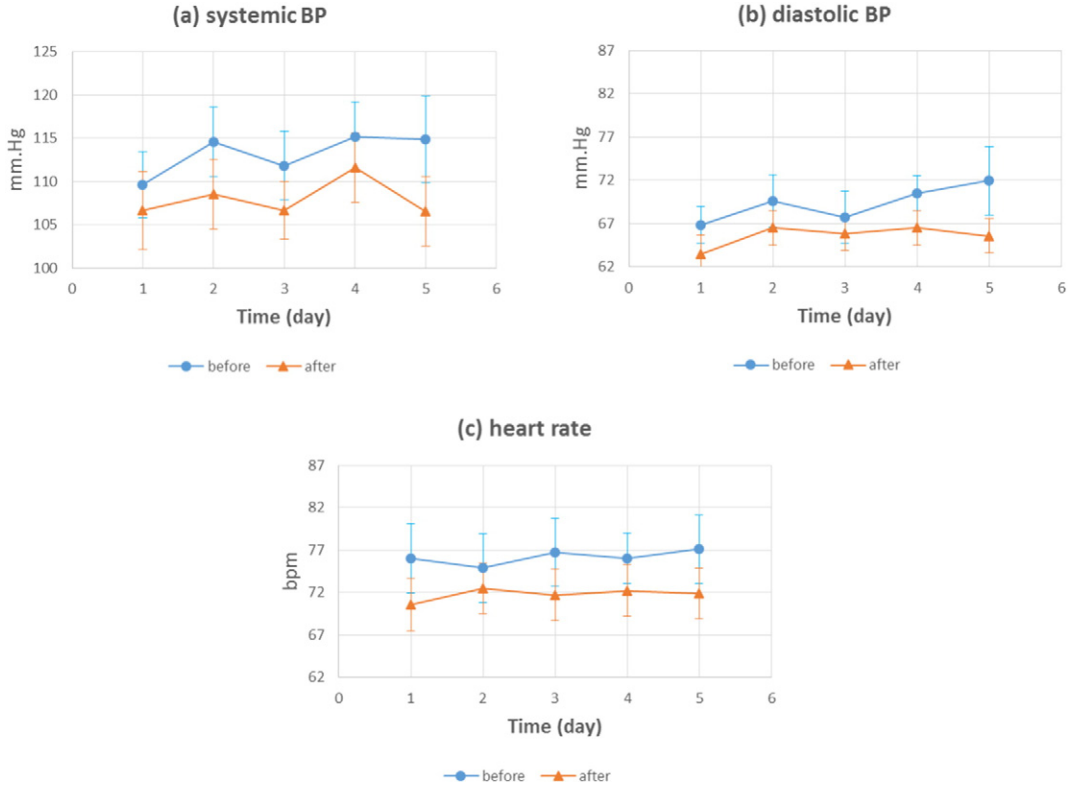

Fig. 7. Effect of light-smell (peppermint oil) treatment on (A) systolic blood pressure, (B) diastolic blood pressure and (C) heart rate (bpm = beats per minute). Measurements were taken before (blue) and after 15 min treatment (orange) each day for 5 consecutive days. The data are presented as the mean ± standard error, $n = 14$.

Table 6
Main effects of day and treatment (light-smell (peppermint)) on blood pressure and heart rate.

	Day				Light-smell				Day * light-smell			
	F(4,48)	Sig.	η^2,p	Power	F(1,12)	Sig.	η^2,p	Power	F(4,48)	Sig.	η^2,p	Power
Systemic BP	2.031	0.104	0.135	0.568	22.36	**0.0001**	0.632	0.992	0.983	0.425	0.07	0.217
Diastolic BP	1.501	0.216	0.103	0.433	16.81	**0.001**	0.564	0.966	0.736	0.572	0.054	0.221
Heart rate	0.107	0.98	0.008	0.07	14.6	**0.002**	0.529	0.941	0.871	0.488	0.063	0.258

2-factor analysis of variance, F-statistic (degrees of freedom), Sig. = *p*-value, η^2,p = partial eta^2.

3.4.2. Mood state

A Profile of Mood States (POMS) test was administered before and after 15 min light-smell (peppermint) treatment on days 1, 3 and 5 (Fig. 8). There were significant main effects of the treatment on TA (Fig. 8f) with a small effect (η^2,$p = 0.255$) on AH which did not quite reach significance ($p = 0.055$) (Table 7). There was no evidence of an effect of the treatment over time although several factors seemed to decrease with time during the course of the study, e.g. TMD, FI, TA, but the effect of treatment did not change (Table 7).

3.5. What happens if only one stimulus modality is used?

3.5.1. Smell only

When smell (lemon) alone was used as the stimulus there were significant reductions in systolic BP ($p = 0.002$, 2-tail paired t-test), diastolic BP ($p = 0.002$) and heart rate ($p = 0.023$) during a single 15 min session (Table 8).

3.5.2. Light only

When light was used as the only stimulus there was no change in the blood pressure, either systolic or diastolic, but there was a significant reduction in heart rate ($p = 0.040$, Table 8).

3.6. Mood state effects of light only and smell only treatments

The POMS test was administered before and after the delivery of the single stimuli treatments. The light-only treatment had no significant effect on any of the factors while the smell-only (lemon) treatment had an effect ($p = 0.054$; 2-tailed t-test) on Dejection-Depression (Table 9).

4. Discussion

In this study we demonstrate that a combination of light and smell stimulation lowers blood pressure, reduces heart rate and reduces

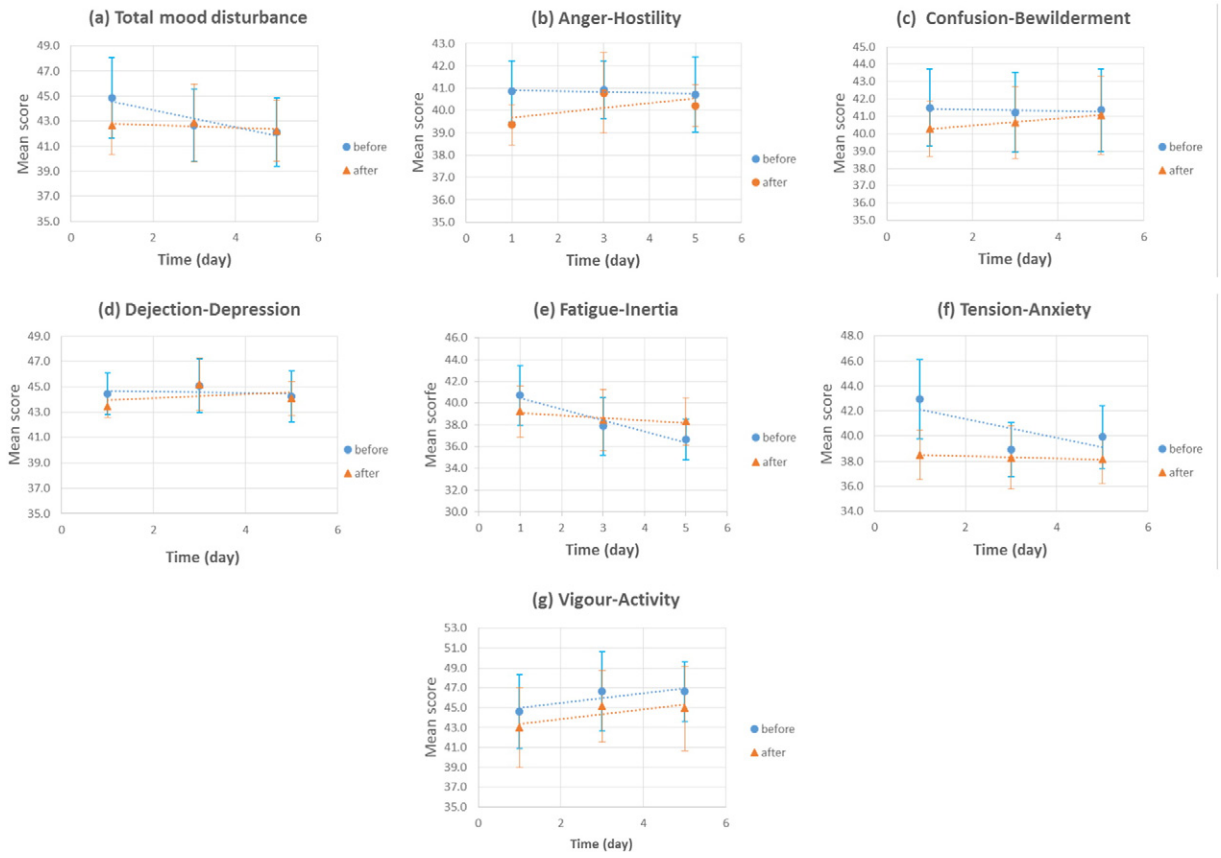

Fig. 8. Results of POMS test administered on days 1, 3 and 5 before (blue symbols) and after (red symbols) 15 min light-smell (peppermint) treatment. The results are presented for each of the factors as the mean ± standard error, $n = 14$. The statistical analysis is presented in Table 7.

Table 7
POMS test: main effects of day and treatment (light-smell (peppermint)).

		Day				Light-smell				Day * light-smell			
		F(2,24)	Sig.	η^2,p	Power	F(1,12)	sig.	η^2,p	Power	F(2,24)	Sig.	η^2,p	Power
Total Mood Disturbance	TMD	0.756	0.48	0.055	0.164	0.533	0.478	0.039	0.104	1.391	0.267	0.097	0.272
Anger-Hostility	AH	1.557	0.23	0.107	0.3	4.452	0.055	0.255	0.497	0.425	0.658	0.032	0.111
Confusion-Bewilderment	CB	0.054	0.948	0.004	0.057	1.651	0.221	0.113	0.222	0.553	0.582	0.041	0.131
Depression-Dejection	DD	1.578	0.232	0.108	0.241	0.285	0.602	0.021	0.079	0.728	0.475	0.053	0.151
Fatigue-Inertia	FI	1.086	0.332	0.077	0.18	0.1	0.757	0.008	0.06	1.756	0.207	0.119	0.251
Tension-Anxiety	TA	1.833	0.18	0.124	0.347	10.29	**0.007**	0.442	0.842	2.132	0.139	0.141	0.397
Vigour-Activity	VA	1.058	0.362	0.075	0.215	1.318	0.272	0.092	0.187	0.005	0.995	0.0001	0.051

2-factor analysis of variance, F-statistic (degrees of freedom), sig. = p-value, η^2,p = partial eta^2.

negative affect (e.g. depression, anxiety, tension). Furthermore, the dual stimulus combination of bright light and smell is more effective than either light or smell stimuli administered individually. Throughout this study a non-adaptive protocol was used to avoid adaptation/habituation to the stimuli (see Methods) which has been shown to be more effective than constant level stimuli [49]. This has the effect of providing stimulation that is continuously perceived by maintaining activity in the attentional centres of the brain.

All three odours (lemon, lavender, peppermint) when combined with light caused a reduction in both systolic and diastolic blood pressure following a 15 min exposure. There was no cumulative effect of the treatment over the 5-day trial period, the effects remained the same each day, and there was no change in the effect of treatment over the 5 days.

In terms of the effect on blood pressure and heart rate it was the smell component of the dual stimulus that had the greater effect (Table 8). The light treatment on its own had no effect on blood pressure but did significantly reduce heart rate. However, neither stimulus modality on its own had much effect on the POMS mood factors (Table 9), with the exception that Dejection-Depression was reduced by the smell only (lemon) treatment ($p = 0.026$; one-tailed t-test). A smell stimulus (lemon) and a combined smell-light stimulus were both found to have a significant effect on frontal asymmetry, a marker for depression-anxiety, while light alone did not [49]. However, a longer (1 h) exposure to bright light caused a significant but modest improvement on the POMS Dejection-Depression factor after a single session [38].

In this study citrus fragrance combined with light significantly reduced blood pressure, heart rate and reduced the factors Anger-Hostility, Confusion-Bewilderment, Dejection-Depression and Anger-Hostility. Only Confusion-Bewilderment changed with time and this is possibly explained by the subjects becoming more familiar with the experimental set-up as the trial progressed. Citrus fragrance has been given to depressive human subjects and the results indicated that the doses of antidepressants necessary for the treatment of depression could be markedly reduced. The treatment with citrus fragrance normalised neuroendocrine hormone levels and immune function and was rather more effective than antidepressants [23]. In normal human subjects lemon odour reliably enhanced positive mood [18] and negative emotions became less intense during exposure to citrus odour [48]. In work carried out in mice it was suggested that lemon oil possesses anxiolytic, antidepressant-like effects via the suppression of dopamine activity related to enhanced serotonergic neurons [21]. While there may be benefits from citrus odours, any claims have to be balanced by the fact that any effects do not universally translate into physiological changes. Subjective responses influence the effects and suggest the involvement of both pharmacological and psychological mechanisms in the response [29].

Table 8
Comparison of the effects of smell-only and light-only stimulation.

	Smell (lemon) only			Light only		
	Before	After	Sig.	Before	After	Sig.
systolic BP	112.6 ± 2.9	107.5 ± 3.1	**0.002**	107.6 ± 3.2	109.4 ± 2.8	0.379
diastolic BP	72.4 ± 1.7	68.3 ± 1.7	**0.002**	70.8 ± 2.0	69.0 ± 1.7	0.140
Heart rate	79.9 ± 3.9	72.9 ± 2.7	**0.023**	80.2 ± 3.7	72.4 ± 3.0	**0.040**

Data are presented as mean ± standard error. Sig. = p-value from 2-tailed paired t-test.

Lavender and light treatment was found to significantly lower blood pressure and reduce heart rate and reduced the negative POMS factors Anger-Hostility, Dejection-Depression and Tension-Anxiety. This treatment also produced a cumulative reduction in Anger-Hostility over time (Table 5) and Tension-Anxiety showed a downward trend although this was not significant (Fig. 6f). Lavender itself has been found to decrease the rise in blood pressure induced during hand-grip exercise [29] and an essential oil produced from *Lavandula angustifolia* is a licenced treatment for anxiety in Germany [16]. It is thought to be an agonist at 5HT-1A receptors [2] which are involved in anxiety [33]. While lavender aroma or oral supplements may have a beneficial effect, for example lavender oil has been found to have modest benefits as a treatment for agitated behaviour in severe dementia [13], methodological issues limit the extent of any conclusions that can be drawn from the published work [34].

The light-peppermint stimulus lowered blood pressure (both systolic and diastolic) and reduced heart rate on each of the five days that it was administered, although as with the other odours, there was no evidence of a cumulative effect with time. It also reduced the Tension-Anxiety factor in the POMS test and had a near-significant effect on Anger-Hostility ($p = 0.055$); although effective at changing mood peppermint had the least effect of the three odours in this study. Peppermint odour, when administered as a single stimulus, has been reported to have a variety of effects, from a decrease in the magnitude of beta waves and decrease in the finger-tip skin temperature following a mental task, implying a decrease in arousal response [39], to the opposite — an increase in exercise performance, blood pressure and respiratory rate in the young male students [27]. In accord with this latter study, peppermint has been shown to be a stimulating odour, to increase alertness, [19,43,44] and to improve performance in a mental task [3], a visual task [50] and exercise [36,37]. Under the conditions of this present study there was no influence of light-peppermint stimulus on the POMS Vigour-Activity factor possibly because the relaxing effect of the stimulus on cardiovascular parameters.

In conclusion, we have demonstrated that combined light and smell stimulation lowers blood pressure, reduces heart rate and has a positive effect on mood factors Depression-Dejection, Tension-Anxiety and Anger-Hostility following a short 15 min treatment. The odour stimulation had the most immediate physiological effect but the combination of light and smell was necessary to achieve the short-term mood changes. There were differences in the effects of the individual odours on the POMS mood factors with lemon essential oil having the most widespread effects and lavender generating a cumulative effect on the Anger-Hostility factor.

While there is qualified support in the scientific and medical communities for the use of BLT in the treatment of depression and rather less support for the use of aroma in treating anxiety, depression and stress, the combination of the two in a non-adaptive delivery protocol

Table 9
Paired t-test for the changes between light only and smell only (lemon) treatment (POMS).

		Paired differences							
					95% Confidence interval of the difference				
		Mean	Std. dev.	S.E.M.	Lower	Upper	t	df	Sig. (2-tailed)
Light only	Total Mood Disturbance	0.50	5.24	1.40	−2.53	3.53	0.36	13	0.727
	Anger-Hostility	0.86	3.11	0.83	−0.94	2.65	1.03	13	0.321
	Confusion-Bewilderment	0.64	4.75	1.27	−2.10	3.38	0.51	13	0.621
	Depression-Dejection	0.64	2.41	0.64	−0.75	2.03	1.00	13	0.336
	Fatigue-Inertia	0.29	5.53	1.48	−2.90	3.48	0.19	13	0.85
	Tension-Anxiety	2.57	5.17	1.38	−0.41	5.56	1.86	13	0.085
	Vigour-Activity	4.29	7.85	2.10	−0.25	8.82	2.04	13	0.062
Smell only lemon	Total Mood Disturbance	0.50	6.43	1.72	−3.21	4.21	0.29	13	0.776
	Anger-Hostility	1.14	3.88	1.04	−1.10	3.38	1.10	13	0.29
	Confusion-Bewilderment	1.79	5.24	1.40	−1.24	4.81	1.28	13	0.224
	Depression-Dejection	1.64	2.90	0.77	−0.03	3.32	2.12	13	0.054
	Fatigue-Inertia	−0.07	6.76	1.81	−3.98	3.83	−0.04	13	0.969
	Tension-Anxiety	1.86	4.45	1.19	−0.71	4.43	1.56	13	0.143
	Vigour-Activity	4.50	8.36	2.23	−0.32	9.32	2.02	13	0.065

The data are expressed as the difference between factors before and after treatment.

could offer a more robust and efficacious treatment alternative. The results of this study justify further investigation of the combined effect of smell and light stimulation particularly with respect to the longer term effects and the possible uses in conditions such as Generalised Anxiety Disorder (GAD) and Major Depressive Disorder (MDD).

Conflict of interest statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Acknowledgments

We would like to thank Neil Kernot (Chelker Ltd., Skipton, North Yorkshire) for his help in the design and construction of the stimulus delivery device. This work was funded from research overhead account AJ1910TJJ1, School of Biosciences, Cardiff University.

References

[1] O. Alaoui-Ismaïli, O. Robin, H. Rada, A. Dittmar, E. Vernet-Maury, Basic emotions evoked by odorants: comparison between autonomic responses and self-evaluation, Physiol. Behav. 62 (1997) 713–720.
[2] P. Baldinger, A.S. Höflich, M. Mitterhauser, A. Hahn, C. Rami-Mark, M. Spies, W. Wadsak, R. Lanzenberger, S. Kasper, Effects of Silexan on the serotonin-1A receptor and microstructure of the human brain: a randomized, placebo-controlled, double-blind, cross-over study with molecular and structural neuroimaging, Int. J. Neuropsychopharmacol. 18 (4) (2014), http://dx.doi.org/10.1093/ijnp/pyu063 (pii: pyu063).
[3] S. Barker, P. Grayhem, J. Koon, J. Perkins, A. Whalen, B. Raudenbush, Improved performance on clerical tasks associated with administration of peppermint odor, Percept. Mot. Skills 97 (2003) 1007–1010.
[4] C.L. Dennis, T. Dowswell, Interventions (other than pharmacological, psychosocial or psychological) for treating antenatal depression, Cochrane Database Syst. Rev. 7 (2013), CD006795, http://dx.doi.org/10.1002/14651858.CD006795.pub3.
[5] M. Domjan, The Principles of Learning and Behavior, seventh ed. Cengage Learning, USA: Stamford, 2015.
[6] H. Ehrlichman, L. Bastone, Olfaction and emotion, in: M.J. Serby, K.L. Chobor (Eds.), Science of olfaction, Springer-Verlag, New York 1992, pp. 410–438.
[7] C.·.N. Epperson, M. Terman, J.S. Terman, B.·.H. Hanusa, D.A. Oren, K.·.S. Peindl, K.L. Wisner, Randomized clinical trial of bright light therapy for antepartum depression: preliminary findings, J. Clin. Psychiatry 65 (2004) 421–425.
[8] C. Even, C.M. Schröder, S. Friedman, F. Rouillon, Efficacy of light therapy in nonseasonal depression: a systematic review, J. Affect. Disord. 108 (2008) 11–23.
[9] N. Goel, R.P. Lao, Sleep changes vary by odor perception in young adults, Biol. Psychol. 71 (2006) 341–349.
[10] R.N. Golden, B.·.N. Gaynes, R.D. Ekstrom, R.M. Hamer, F.M. Jacobsen, T. Suppes, K.L. Wisner, C.·.B. Nemeroff, The efficacy of light therapy in the treatment of mood disorders: a review and meta-analysis of the evidence, Am. J. Psychiatry 162 (2005) 656–662.
[11] P. Güzel Özdemir, M. Boysan, M.H. Smolensky, Y. Selvi, A. Aydin, E. Yilmaz, Comparison of venlafaxine alone versus venlafaxine plus bright light therapy combination for severe major depressive disorder, J. Clin. Psychiatry 76 (5) (2015) e645–e654, http://dx.doi.org/10.4088/JCP.14m09376.
[12] R.S. Herz, Aromatherapy facts and fictions: a scientific analysis of olfactory effects on mood, physiology and behavior, Int. J. Neurosci. 119 (2009) 263–290, http://dx.doi.org/10.1080/00207450802333953.
[13] C. Holmes, V. Hopkins, C. Hensford, V. MacLaughlin, D. Wilkinson, H. Rosenvinge, Lavender oil as a treatment for agitated behaviour in severe dementia: a placebo controlled study, Int. J. Geriatr. Psychiatry 17 (2002) 305–308.
[14] T.J.C. Jacob, C. Fraser, L. Wang, V.E. Walker, S. O'Connor, Psychophysical evaluation of responses to pleasant and mal-odour stimulation in human subjects; adaptation, dose response and gender differences, Int. J. Psychophysiol. 48 (2003) 67–80.
[15] A.J. Johnson, Cognitive facilitation following intentional odor exposure, Sensors (Basel) 11 (2011) 5469–5488, http://dx.doi.org/10.3390/s110505469.
[16] S. Kasper, M. Gastpar, W.E. Müller, H.·.P. Volz, H.J. Möller, A. Dienel, S. Schläfke, Efficacy and safety of Silexan, a new, orally administered lavender oil preparation, in subthreshold anxiety disorder—evidence from clinical trials, Wien. Med. Wochenschr. 160 (2010) 547–556.
[17] D.O. Kennedy, G. Wake, S. Savelev, N.T. Tildesley, E.K. Perry, K.A. Wesnes, A.B. Scholey, Modulation of mood and cognitive performance following acute administration of single doses of *Melissa officinalis* (Lemon balm) with human CNS nicotinic and muscarinic receptor-binding properties, Neuropsychopharmacology 28 (2003) 1871–1881.
[18] J.K. Kiecolt-Glaser, J.E. Graham, W.·.B. Malarkey, K. Porter, S. Lemeshow, R. Glaser, Olfactory influences on mood and autonomic, endocrine, and immune function, Psychoneuroendocrinology 33 (2008) 328–339.
[19] W.R. Klemm, S.D. Lutes, D.V. Hendrix, S. Warrenburg, Topographical EEG maps of human responses to odors, Chem. Senses 17 (1992) 347–361, http://dx.doi.org/10.1093/chemse/17.3.347.
[20] C. Koch, Sensation. chap. 19, in: S.·.F. Davis (Ed.), 21st Century Psychology: A Reference Handbook, eighth ed.Sage Publications Inc., Thousand Oaks, CA, USA 2008, pp. 172–177.
[21] M. Komiya, T. Takeuchi, E. Harada, Lemon oil vapor causes an anti-stress effect via modulating the 5-HT and DA activities in mice, Behav. Brain Res. 172 (2006) 240–249.
[22] T. Komori, R. Fujiwara, M. Tanida, J. Nomura, Potential antidepressant effects of lemon odor in rats, Eur. Neuropsychopharmacol. 5 (1995) 477–480.
[23] T. Komori, R.M. Fujiwara, J. Nomura, M.M. Yokoyama, Effects of citrus fragrance on immune function and depressive states, Neuroimmunomodulation 2 (1995) 174–180.
[24] J.H. Leal-Cardoso, K.·.S. da Silva-Alves, F.·.W. Ferreira-da-Silva, T. dos Santos-Nascimento, H.·.C. Joca, F.·.H. de Macedo, P.M. de Albuquerque-Neto, P.J. Magalhães, S. Lahlou, J.S. Cruz, R. Barbosa, Linalool blocks excitability in peripheral nerves and voltage-dependent Na^+ current in dissociated dorsal root ganglia neurons, Eur. J. Pharmacol. 645 (2010) 86–93, http://dx.doi.org/10.1016/j.ejphar.2010.07.014 (Epub 2010 Jul 22).
[25] R. Lieverse, E.J. Van Someren, M.M. Nielen, B.M. Uitdehaag, J.H. Smit, W.J. Hoogendijk, Bright light treatment in elderly patients with nonseasonal major depressive disorder: a randomized placebo-controlled trial, Arch. Gen. Psychiatry 68 (2011) 61–70, http://dx.doi.org/10.1001/archgenpsychiatry.2010.183.
[26] D.M. McNair, M. Lorr, L. Droppleman, Manual for the Profile of 5 Mood States, Educational and Industrial Testing Service, San Diego, CA, 1971.
[27] A. Meamarbashi, A. Rajabi, The effects of peppermint on exercise performance, J. Int. Soc. Sports Nutr. 10 (1) (2013) 15, http://dx.doi.org/10.1186/1550-2783-10-15.

[28] M. Moss, S. Hewitt, L. Moss, K. Wesnes, Modulation of cognitive performance and mood by aromas of peppermint and ylang-ylang, Int. J. Neurosci. 118 (2008) 59–77.
[29] M. Nagai, M. Wada, N. Usui, A. Tanaka, Y. Hasebe, Pleasant odors attenuate the blood pressure increase during rhythmic handgrip in humans, Neurosci. Lett. 289 (3) (2000) 227–229.
[30] M.A. Oldham, D.A. Ciraulo, Bright light therapy for depression: a review of its effects on chronobiology and the autonomic nervous system, Chronobiol. Int. 31 (2014) 305–319, http://dx.doi.org/10.3109/07420528.2013.833935.
[31] D.A. Oren, K.L. Wisner, M. Spinelli, C.·.N. Epperson, K.·.S. Peindl, J.S. Terman, M. Terman, An open trial of morning light therapy for treatment of antepartum depression, Am. J. Psychiatry 159 (2002) 666–669.
[32] G. Pail, W. Huf, E. Pjrek, D. Winkler, M. Willeit, N. Praschak-Rieder, S. Kasper, Bright-light therapy in the treatment of mood disorders, Neuropsychobiology 64 (2011) 152–162.
[33] C.L. Parks, P.·.S. Robinson, E. Sibille, T. Shenk, M. Toth, Increased anxiety of mice lacking the serotonin1A receptor, Proc. Natl. Acad. Sci. U. S. A. 95 (18) (1998) 10734–10739, http://dx.doi.org/10.1073/pnas.95.18.10734.
[34] R. Perry, R. Terry, L.K. Watson, E. Ernst, Is lavender an anxiolytic drug? A systematic review of randomised clinical trials, Phytomedicine 19 (8–9) (2012) 825–835, http://dx.doi.org/10.1016/j.phymed.2012.02.013 (Epub 2012 Mar 29).
[35] V. Pollock, D.W. Cho, D. Reker, J. Volavka, Profile of mood states: the factors and their physiological correlates, J. Nerv. Ment. Dis. 167 (1979) 612–614.
[36] B. Raudenbush, N. Corley, W. Eppich, Enhancing athletic performance through the administration of peppermint odor, J. Sport Exerc. Psychol. 23 (2001) 156–160.
[37] B. Raudenbush, B. Meyer, W. Eppich, The effects of odors on objective and subjective measures of athletic performance, Int. Sport J. 6 (2002) 14–27.
[38] G.M. Reeves, G.V. Nijjar, P. Langenberg, M.A. Johnson, B. Khabazghazvini, A. Sleemi, D. Vaswani, M. Lapidus, P. Manalai, M. Tariq, M. Acharya, J. Cabassa, S. Snitker, T.T. Postolache, Improvement in depression scores after 1 hour of light therapy treatment in patients with seasonal affective disorder, J. Nerv. Ment. Dis. 200 (2012) 51–55, http://dx.doi.org/10.1097/NMD.0b013e31823e56ca.
[39] T. Satoh, Y. Sugawara, Effects on humans elicited by inhaling the fragrance of essential oils: sensory test, multi-channel thermometric study and forehead surface potential wave measurement on basil and peppermint, Anal. Sci. 19 (2003) 139–146, http://dx.doi.org/10.2116/analsci.19.139.
[40] H. Shibata, R. Fujiwara, M. Iwamoto, H. Matsuoka, M.M. Yokoyama, Recovery of PFC in mice exposed to high pressure stress by olfactory stimulation with fragrances, Int. J. Neurosci. 51 (1990) 245–247.
[41] H. Shibata, R. Fujiwara, M. Iwamoto, H. Matsuoka, M.M. Yokoyama, Immunological and behavioural effects of fragrance in mice, Int. J. Neurosci. 57 (1991) 151–159.
[42] A.M. Schuwald, M. Nöldner, T. Wilmes, N. Klugbauer, K. Leuner, W.E. Müller, Lavender oil-potent anxiolytic properties via modulating voltage dependent calcium channels, PLoS One 8 (4) (2013), e59998, http://dx.doi.org/10.1371/journal.pone.0059998. Print 2013.
[43] C. Stampi, A. Aguirre, M. Macchi, M. Moore-Ede, Peppermint aroma as a countermeasure to sleepiness during driving simulation, Sleep Res. 25 (1996) 112.
[44] S. Torii, H. Fukuda, H. Kanemoto, R. Miyanchi, Y. Hamauzu, M. Kawasaki, Contingent negative variation and the psychological effects of odour, in: S. Van Toller, G.H. Dodd (Eds.), Perfumery: The Psychology and Biology of Fragrance, Chapman Hall, New York 1988, pp. 107–120.
[45] A. Tuunainen, D.F. Kripke, T. Endo, Light therapy for non-seasonal depression, Cochrane Database Syst. Rev. 2004 (2) (2004), CD004050.
[46] T. Umezu, A. Sakata, H. Ito, Ambulation-promoting effect of peppermint oil and identification of its active constituents, Pharmacol. Biochem. Behav. 69 (2001) 339–383, http://dx.doi.org/10.1016/S0091-3057(01)00543-3.
[47] E. Vernet-Maury, O. Alaoui-Ismaïli, A. Dittmar, G. Delhomme, J. Chanel, Basic emotions induced by odorants: a new approach based on autonomic pattern results, J. Auton. Nerv. Syst. 75 (1999) 176–183.
[48] R.A. de Wijk, S.M. Zijlstra, Differential effects of exposure to ambient vanilla and citrus aromas on mood, arousal and food choice, Flavour 1 (2012) 1–24, http://dx.doi.org/10.1186/2044-7248-1-24.
[49] J. Warden-Smith, L. Paul, K. Olukogbon, E.S. Bointon, R.H. Cole, S.R. John, S. Dong, T.J.C. Jacob, A new method for integrated sensory stimulation, Int. J. Psychophysiol. (2016) (submitted for publication).
[50] J.S. Warm, W.·.N. Dember, R. Parasuraman, Effects of olfactory stimulation on performance and stress in a visual sustained task, J. Soc. Cosmet. Chem. 42 (1991) 199–210.
[51] A. Wirz-Justice, A. Bader, U. Frisch, R.D. Stieglitz, J. Alder, J. Bitzer, I. Hösli, S. Jazbec, F. Benedetti, M. Terman, K.L. Wisner, A. Riecher-Rössler, A randomized, double-blind, placebo-controlled study of light therapy for antepartum depression, J. Clin. Psychiatry 72 (2011) 986–993.