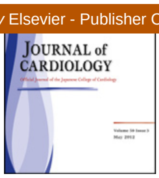
Journal of Cardiology 60 (2012) 495–502

Journal of Cardiology

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



Original article

Therapeutic effect of forest bathing on human hypertension in the elderly

Gen-Xiang Mao (MD)[a], Yong-Bao Cao (MB)[a,1], Xiao-Guang Lan (BA)[b], Zhi-Hua He (BA)[b], Zhuo-Mei Chen (PhD)[c], Ya-Zhen Wang (MM)[a], Xi-Lian Hu (PhD)[a], Yuan-Dong Lv (MB)[a], Guo-Fu Wang (PhD)[a,*], Jing Yan (MM)[a,*]

[a] *Zhejiang Provincial Key Laboratory of Geriatrics & Geriatrics Institute of Zhejiang Province, Zhejiang Hospital, Hangzhou 310013, Zhejiang Province, P.R. China*
[b] *Forestry Department of Zhejiang Province, Hangzhou 310020, Zhejiang Province, P.R. China*
[c] *Zhejiang Forestry Academy, Hangzhou 310023, Zhejiang Province, P.R. China*

ARTICLE INFO

Article history:
Received 18 April 2012
Received in revised form 6 July 2012
Accepted 9 August 2012
Available online 1 September 2012

Keywords:
Forest bathing
Hypertension
Elderly
Cardiovascular disease
Inflammation

ABSTRACT

Objective: To provide scientific evidence supporting the efficacy of forest bathing as a natural therapy for human hypertension.
Methods: Twenty-four elderly patients with essential hypertension were randomly divided into two groups of 12. One group was sent to a broad-leaved evergreen forest to experience a 7-day/7-night trip, and the other was sent to a city area in Hangzhou for control. Blood pressure indicators, cardiovascular disease-related pathological factors including endothelin-1, homocysteine, renin, angiotensinogen, angiotensin II, angiotensin II type 1 receptor, angiotensin II type 2 receptor as well as inflammatory cytokines interleukin-6 and tumor necrosis factor α were detected. Meanwhile, profile of mood states (POMS) evaluation was used to assess the change of mood state of subjects. In addition, the air quality in the two experimental sites was monitored during the 7-day duration, simultaneously.
Results: The baselines of the indicators of the subjects were not significantly different. Little alteration in the detected indicators in the city group was observed after the experiment. While subjects exposed to the forest environment showed a significant reduction in blood pressure in comparison to that of the city group. The values for the bio-indicators in subjects exposed to the forest environment were also lower than those in the urban control group and the baseline levels of themselves. POMS evaluation showed that the scores in the negative subscales were lowered after exposure to the forest environment. Besides, the air quality in the forest environment was much better than that of the urban area evidenced by the quantitative detection of negative ions and PM10 (particulate matter <10 μm in aerodynamic diameter).
Conclusion: Our results provided direct evidence that forest bathing has therapeutic effects on human hypertension and induces inhibition of the renin–angiotensin system and inflammation, and thus inspiring its preventive efficacy against cardiovascular disorders.

Introduction

It is widely understood that forest environments have favorable effects on human physiological functions, and sanatoria are often built in forest environments on mountains [1]. A number of reports have indicated that forest environments exert beneficial physiological effects on patients with allergies or respiratory diseases [2]. Factors in the forest environment that may provide beneficial physiological effects include the aroma of plants as well as such various factors as temperature, humidity, light intensity, wind, and oxygen concentrations; thus, exercise performed in such environments would appear to offer significant benefits [3].

In contrast, urban air pollution is a serious environmental problem, especially in many developing countries. Epidemiological and mechanistic animal studies from across the world have shown that both acute and chronic exposure to air pollution is associated with chronic diseases such as cardiovascular disorders [4–6], thus impacting public health. Hypertension is a major risk factor for cardiovascular diseases, and it is also closely related to the urban environment [7,8]. Along with the development of drugs to prevent cardiovascular diseases [9], non-medicinal ways have also been developed. To improve the quality of life for those living in cities, it has been suggested that society develop better methods to facilitate and promote healthy activities that can be performed in a short period, are inexpensive, and enjoyable.

Forest bathing, known as *shinrin-yoku* in Japan, has received increasing attention in recent years for its positive effects on human

---

[*] Corresponding authors at: Zhejiang Hospital, No. 12 Lingyin Road, Hangzhou 310013, P.R. China. Tel.: +86 571 87987373x5421; fax: +86 571 87985354.
E-mail addresses: zpklg@yahoo.com.cn (G.-F. Wang), zjicu@vip.163.com (J. Yan).
[1] Joint first author.

0914-5087/$ – see front matter © 2012 Japanese College of Cardiology. Published by Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.jjcc.2012.08.003

health [10,11]. Previous studies on this topic have mostly focused on the capacity of forest bathing to provide relaxation and reduce stress for people living in urban areas, mainly in terms of its physiological effects. It has also been reported that forest bathing enhances immune functions and expression of anti-cancer proteins [12,13]. However, there have as yet been no direct demonstrations as to whether forest bathing exerts any other effects on human diseases such as hypertension. In the present study, we aimed to investigate the therapeutic effect of forest bathing on hypertension in elderly subjects. We chose a forest site in Suichang County, Zhejiang Province, P.R. China, since forests occupy 90.7% of the land area of this county and there is ready access to forests. Two groups of participants with essential hypertension were sent to the forest or an urban control area for a 7-day trip, respectively, to evaluate the effect of forest bathing on blood pressure (BP). Our findings demonstrated a favorable effect of forest bathing on reducing BP and thus inspiring its preventive role against cardiovascular diseases.

Materials and methods

Experimental sites

The experiment was conducted in a broad-leaved evergreen forest named White Horse Mountain National Forest Park in Suichang County (Zhejiang Province, China) from 23 to 30 July 2011. The covering area of the forest is about 84,960,000 m^2 and the predominant species are *Ormosia hosiei*, *Cinnamomum camphora*, *Magnolia officinalis* subsp. *biloba*, and *Nyssa sinensis*. For comparison, an urban area in Hangzhou was used. The two experimental sites are shown on the map in Fig. 1. Hereinafter, the two sites are referred to as the forest area and the city area, respectively.

Subjects

This study enrolled 30 patients with essential hypertension recruited from Hangzhou. Participants who met the following criteria were included: (1) patients with diagnosed essential hypertension; (2) aged from 60 to 75 years; (3) BP, with or without medical control, less than 180/110 mmHg; (4) class I–II cardiac function according to the criteria of American New York Heart Association; (5) capable of taking care of themselves in daily life. And the exclusion criteria are: (1) catching a cold and other acute diseases two weeks prior to the trial or during the trial process; (2) chronic history including cancer, serious liver, kidney, brain, heart, lung diseases, etc.; (3) acute myocardial infarction in previous three months; (4) cerebrovascular accident within six months; (5) experienced a severe trauma or a major surgery.

The study was approved by the ethics committee of Zhejiang Hospital, and the procedures were in accordance with the Helsinki Declaration of 1975 as revised in 1983. The study was fully explained to all the subjects in both spoken and written form, specifically focusing on its purpose, the precise procedures that would be used, and any possible adverse events. Signed informed consent was obtained from every subject.

Procedure

The experiment was performed from 23 to 30 July 2011. On the day before the experiment, all the subjects were fully informed about the experimental procedure; blood from each subject was sampled in the morning before breakfast in our hospital, and the samples were tested in the clinical laboratory by technicians. Two hotels offering similar conditions near each experimental site were chosen as the places of accommodation. To control for environmental conditions, the intake of all foods and physical activity were controlled, and smoking and drinking alcoholic or caffeinated beverages were prohibited. The subjects were randomly divided into two groups consisting of 12 people each and then one group was sent to the forest site, the other to the city site. The experimental schedule for this study is shown in Fig. 2. In the morning, the subjects walked along a predetermined course in each area at an unhurried pace for about 1.5 h, with a 20-min rest during the walk. In the afternoon, after taking lunch in the resting room, the subjects walked another predetermined course in each area at an unhurried pace for about 1.5 h, with a 20-min rest during the walk. The subjects were allowed to do as they wished in the hotel, though

Fig. 1. Location of the experimental sites. White Horse Mountain National Forest Park is located in Suichang County, Zhejiang Province, China. It is about 300 km far from the urban experimental site, which is situated in the downtown area of Hangzhou, a city near Shanghai.

Fig. 2. The experimental protocol for subjects exposed to the forest or urban environment.

avoiding strenuous exercise and any stimulating activities in their hours of relaxation before sleeping. The subjects were kept at each experimental site for seven days and each group was accompanied by a nurse and a doctor as a consideration for the safety of subjects. Besides, the individual administration of drugs against hypertension for each participant was carried out as usual. On the morning before breakfast on 30 July, blood of the subjects was sampled and the experiment ended.

Blood pressure measurement

The BP measurement was carried out at 7:00 a.m. to 7:30 a.m. after fasting overnight by qualified health care workers. After a 30-min rest, sitting BPs were measured via mercury sphygmomanometer according to a standard operation protocol. All subjects had an empty bladder before the measurements, and no coffee or cigarettes were allowed. Three consecutive measurements were taken with a 30-s interval between replicates. If the difference between the measurements was more than 5 mmHg, the patient was asked to rest for another 5 min, and then the measurements were repeated. The average of three consecutive BP readings was used. The heart rate (HR) was recorded, simultaneously.

Cytokine production

The serum was obtained by using a serum separator tube. Blood samples were clotted for 30 min and centrifuged for 10 min at 3000 × *g*, and then supernatant was collected as serum sample. Serum samples were analyzed using commercially available radioimmunoassay kits (Poole Albert Biotechnology Co., Ltd., Beijing, P.R. China) for interleukin-6 (IL-6), tumor necrosis factor α (TNF-α), and endothelin-1 (ET-1), according to the manufacturer's protocol.

Protocols for other assays

Enzyme-linked immunoassay for cardiovascular disease associated factors including homocysteine (Hcy), and constituents of the renin-angiotensin system (RAS) such as renin, angiotensinogen (AGT), angiotensin II (Ang II), angiotensin II type 1 receptor (AT1), angiotensin II type 2 receptor (AT2) in sera was carried out with commercial kits (CUSABIO, Wuhan, China) according to the manufacturer's protocol. Briefly, microplates pre-coated with indicated antibody were prepared, and then 10 μl testing samples and 40 μl diluents (supplied by the kits) were added to the wells. Then 100 μl horseradish peroxidase-conjugated reagents were supplemented to the wells and the plates were incubated for 1 h at 37 °C. The supernatants were removed and each well was washed with wash solution provided by the kits three times. Then the 3,3′,5,5′-tetramethylbenzidine chromogen solution was added and the plates were incubated for an additional 15 min in the dark. At last, 50 μl stop solution was added to each well and the optical density (OD) at 450 nm was recorded by using a Multiskan MS Plate Reader (MTX Lab Systems, Inc., Vienna, VA, USA). The calibration standards were assayed simultaneously and a standard curve of OD450 versus each bio-factor's concentration was performed. The level of each bio-factor in the testing samples was determined by comparing the OD450 of samples to the corresponding standard curve.

Profile of mood states evaluation

The profile of mood states (POMS) assessment provides a rapid, efficient method of assessing transient, fluctuating active mood states, and it is widely used in mood and mental health assessment. In this study, we used the standard version of POMS [14], a 65-item self-administered rating scale that measures six dimensions of mood (tension-anxiety, depression-dejection, fatigue-inertia, confusion-bewilderment, vigor-activity, and anger-hostility) to assess the subjects' mood changes before and after the experiment; the POMS assessment provides detailed scores for all the scales.

Air quality assessment

The air quality in the two experimental sites was monitored during the 7-day duration, simultaneously. The level of negative oxygen ions was detected by an air ion counter (DLY-5G Type, Shanghai Zhicheng Electronics Co., Ltd., Shanghai, China). The concentration of PM10 (particulate matter considered as mass defined by size cutoff at 10 μm in aerodynamic diameter) was measured by a portable laser dust monitor (LD-3C Type, Beijing BINDA Green Technology Ltd., Beijing, China). Besides, the temperature and the relative humidity were monitored by a digital thermometer-hygrometer (1620A Type, Fluke Test Instruments Shanghai Co., Ltd., Shanghai, China). The climatic comfort index (CCI) was calculated according to the formula: $\mathrm{CCI} = (T - 21.5) + 0.04 \times (\mathrm{RH} - 55) + 0.5 \times (V - 2)$. In which T is the temperature (°C); RH is relative humidity (%); V is the wind speed (m/s). The CCI value is negative related to the body feeling of comfort. The volume of noise was recorded by a noise meter (TES-1352H Type, TES Electrical Electronic Corp. Taipei, China).

Data analysis

The results are expressed as mean ± SD. Final data analysis was performed using SPSS version 17.0 (obtained from SPSS China, Shanghai, P.R. China). Samples were initially analyzed using the Kolmogorov–Smirnov test and Levene's test for, respectively, normality and homogeneity of variances. If the samples were closed to normal distribution and had homogeneous variance, the *t* test was used for data comparison between the two groups. Otherwise, a non-parametric test (Mann–Whitney *U* test or Wilcoxon Signed Ranks test) was used for two independent or related samples. A bivariate analysis was made of the associations of changes in biological parameters and to BP. A *p*-value of less than 0.05 was considered statistically significant.

Results

Baseline characteristics of participants

A total of 30 patients with essential hypertension were enrolled. After excluding patients meeting the criteria as described above, 24 subjects with complete information participated in the final experiment. They were randomly divided into two groups consisting of 12 people each before the experiment. The age, body mass index, and baseline levels of systolic BP (SBP), diastolic BP (DBP), pulse pressure (PP), and HR were not significantly different between the two groups (Table S1). Besides, no significant differences in the baseline values of biological indicators including serum Hcy, ET-1, renin, Ang II, AT1, AT2, TNF-α, and IL-6 were observed between the two groups, either (see Table S1).

Effect of forest bathing on blood pressure

The SBP and DBP of subjects in the city group showed little change after the experiment. However, subjects who experienced a 7-day forest bathing trip showed a significant decrease in SBP and DBP compared with that of the city group (Fig. 3). In addition, a decreased PP was also observed in the forest group although the

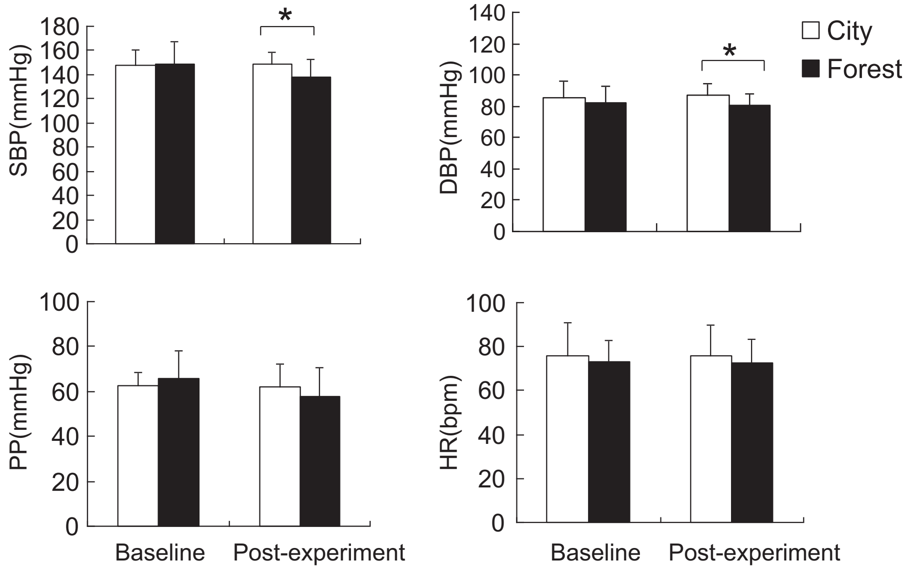


Fig. 3. Effect of forest bathing on blood pressure indicators in subjects ($n = 24$). The systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse pressure (PP) and heart rate (HR) of subjects was measured via a mercury sphygmomanometer before and after the experiment. $^{*}p < 0.05$, analyzed by Mann–Whitney U test.

change was not statistically different. On the other hand, HR did not change in either of the two groups before and after the experiment (Fig. 3). These findings suggested a favorable effect of forest bathing on reducing BP.

Effect of forest bathing on cardiovascular disease-associated factors

To further investigate the mechanism of forest bathing on hypertension, we selected several cardiovascular disease-associated factors including Hcy, ET-1, and RAS constituents such as renin, AGT, Ang II, AT1, AT2, as these factors have been reported having close linkages to essential hypertension [15–18]. A similar baseline level of these biological indicators was observed in the two groups before the experiment. At the end of the 7-day experiment, a significantly lower level of ET-1 and Hcy was observed in the forest group (Fig. 4) as well as the RAS constituents including AGT, AT1, and AT2 (Fig. 5). However, no significant alteration in these factors in the city group was observed after the experiment. Additionally, a mild reduction in renin and Ang II in the forest group was observed at the end of the experiment, although the change was not significant. Then we performed bivariate analysis for the associations between changes in biological parameters (ET-1, Hcy, renin, AGT, AT1, and AT2) and BP (SBP and DBP). As shown in Table 1, a significant association between SBP and Ang II ($p < 0.001$), ET-1 ($p < 0.01$), and Hcy ($p < 0.01$) was observed. DBP was significantly associated with Ang II ($p < 0.05$) and ET-1 ($p < 0.05$). However, in the current experiment, the BP was poorly associated with the change in renin, AT1, and AGT levels.

Table 1
The associations between changes in biological parameters and blood pressure by bivariate analysis.

	ET-1	Hcy	Renin	AGT	Ang-II	AT1	AT2
SBP							
Correlation coefficients (r)	0.421	0.506	0.184	0.188	0.580	0.269	0.051
p-Value	0.007	0.001	0.256	0.245	0.000	0.093	0.754
DBP							
Correlation coefficients (r)	0.370	0.295	0.137	0.213	0.375	0.209	0.145
p-Value	0.019	0.068	0.398	0.187	0.017	0.195	0.373

ET-1, endothelin-1; Hcy, homocysteine; AGT, angiotensinogen; Ang-II, angiotensin II; AT1, angiotensin II type 1 receptor; AT2, angiotensin II type 2 receptor; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Effect of forest bathing on serum pro-inflammatory cytokine levels

In addition to the bio-factors mentioned above, some pro-inflammatory cytokines are also involved in the development of hypertension as well as cardiovascular diseases [19,20]. So we checked the levels of IL-6 and TNF-α in this experiment. As shown in Fig. 6, the serum IL-6 level was significantly reduced in the forest-bathing group compared with its baseline level. However, the decline in IL-6 in the city group was not statistically different. On the other hand, the TNF-α level remained unaltered in both groups during the experiment.

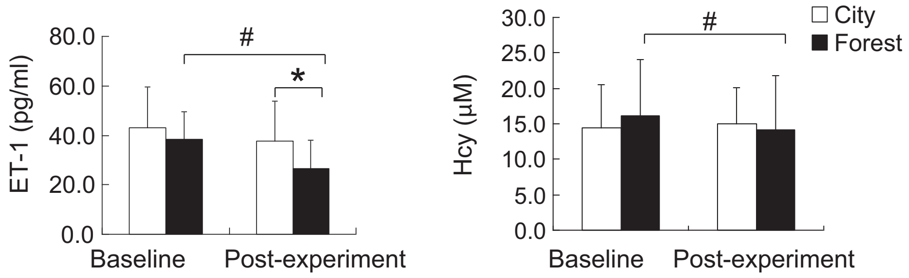


Fig. 4. Effect of forest bathing on cardiovascular disease-associated factors ($n = 24$). Serum endothelin-1 (ET-1) and homocysteine (HCY) in subjects were evaluated before and after the experiment. $^{*}p < 0.05$, analyzed by Mann–Whitney U test; $^{\#}p < 0.05$, analyzed by Wilcoxon Signed Ranks test.

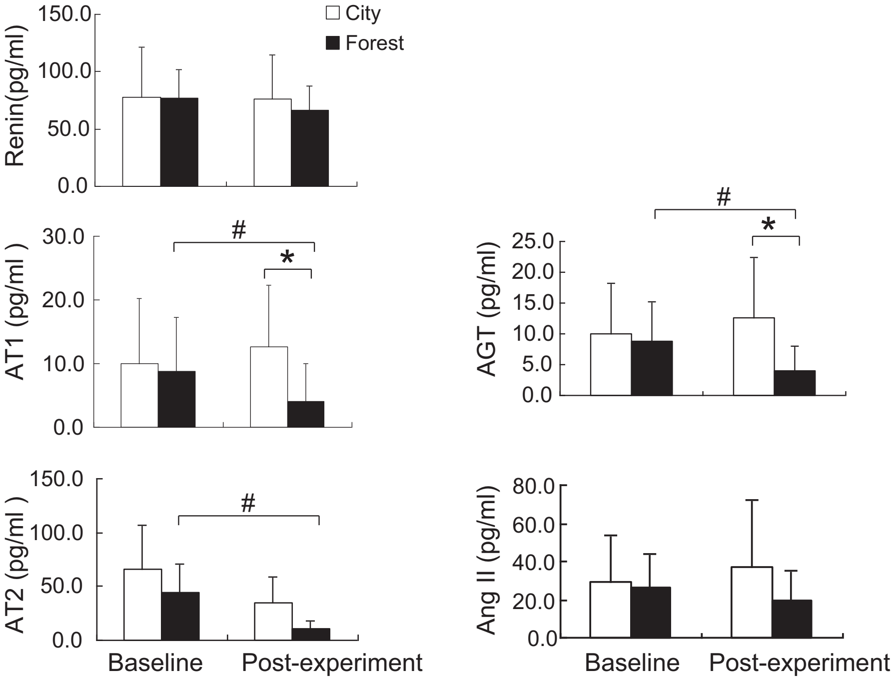


Fig. 5. Effect of forest bathing on change for the components of renin-angiotensin system (RAS) ($n = 24$). Renin, angiotensinogen (AGT), angiotensin II (Ang II), angiotensin II type 1 receptor (AT1), angiotensin II type 2 receptor (AT2) of subjects were evaluated before and after the experiment. $^{*}p < 0.05$, analyzed by Mann–Whitney *U* test; $^{\#}p < 0.05$, analyzed by Wilcoxon Signed Ranks test.

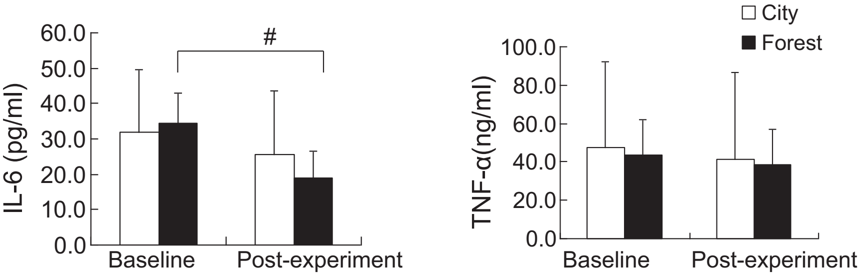


Fig. 6. Effect of forest bathing on serum pro-inflammatory cytokine levels ($n = 24$). Interleukin-6 (IL-6), tumor necrosis factor α (TNF-α) in sera from subjects were evaluated before and after the experiment. $^{\#}p < 0.05$, analyzed by Wilcoxon Signed Ranks test.

Mood state evaluation

It has been reported that there is a positive association between anxiety and hypertension [21]. In this experiment, we used the POMS standard version to assess the subjects' mood changes. As shown in Fig. 7, the scores of the participants who experienced a forest bathing trip in the negative subscales, such as depression-dejection (D); anger-hostility (A); fatigue-inertia (F); and confusion-bewilderment (C), were significantly lowered in comparison to their baseline levels. Additionally, an elevated score in the positive subscale vigor-activity (V) was also observed in the forest group, although the change was not significant. However, no obvious decline in these negative subscales was observed in the city group (Fig. 7).

Air quality assessment

The air quality was also evaluated in the current study, as it is an important environmental factor related to hypertension [4]. The air quality in both of the experimental sites was simultaneously monitored. Overall, the air quality at the forest site was much better than that of the city site. The level of negative ions in the daytime

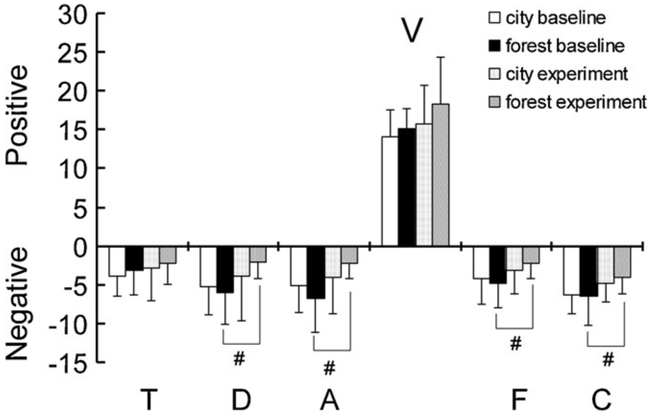


Fig. 7. Profile of mood states (POMS) evaluation of subjects exposed to forest and urban environments ($n = 24$). The standard version of POMS, including negative subscales (T: tension-anxiety; D: depression-dejection; A: anger-hostility; F: fatigue-inertia; and C: confusion-bewilderment) and a positive subscale (V: vigor-activity) was used to assess the subjects' mood changes before and after the experiment. $^{\#}p < 0.05$, analyzed by Wilcoxon Signed Ranks test.

Table 2
Quantitative detection of air quality in the two experimental sites (mean ± SD).

	City site	Forest site	*p*-Value
Negative ion (m^{-3})	231.7 ± 108.3	1159.0 ± 679.7	0.0096[a]
PM10 (mg/m^3)	0.091 ± 0.040	0.084 ± 0.027	0.6593
T (°C)	32.3 ± 4.5	25.5 ± 1.0	0.0008
RH (%)	68.3 ± 8.3	81.8 ± 2.6	0.0006
CCI	11.3 ± 4.2	5.5 ± 1.0	0.0019
Noise (dB)	76.4 ± 12.5	56.2 ± 8.1	0.0068

[a] Mann–Whitney *U* test was used; others were analyzed by using the independent-samples *t* test. PM10, particulate matter < 10 μm in aerodynamic diameter; *T*, temperature; RH, relative humidity; CCI, climatic comfort index.

at the forest site was about four-fold higher than that of the city site. And the concentration of PM10 in forest sites was lower than that of city sites, although the difference was not significant. The volume of noise at the forest site was significantly lower than that of city sites. Meanwhile, the mean CCI at the forest site for the 7-day duration was much lower that of the city site which indicated a more comfortable feeling in the forest group (Table 2).

Discussion

The data obtained in this study suggest that forest bathing had a positive effect on therapy for essential hypertension in elders. The RAS plays an important role in the regulation of BP. Angiotensin-converting enzyme (ACE) inhibitors (ACEI) and Ang II receptor blockers (ARB) are used to inhibit the activation of RAS thus resulting in a decline in BP. Our work indicates an inhibitory role for forest bathing on RAS activation as the level of main components of RAS including AGT, Ang II, AT1, and AT2 receptor was decreased in subjects after experiencing a forest bathing trip. Ang II plays important roles in the regulation of cardiovascular functions and diseases mainly via the AT1 receptor. In contrast, Ang II-induced signaling through AT2 receptor shows vasodilation via activation of endothelial nitric oxide (NO) synthase and it also can partly antagonize the AT1 receptor mediated-signaling and thus elevated AT2 receptor level may result in a decreased BP [22]. In the current experiment, a declined SBP was observed in the forest group while the AT2 receptor level was lowered. The reasons for this finding are listed below. Firstly, although a decline in AT2 level may not be capable of inducing a decline in SBP in the forest group, it was probably due to the significant decrease in AT1 receptor level. Secondly, as the sample size was limited, the change in AT2 level in the current study may not be the same as that in a larger sample as the changes in AT1 and AT2 receptors in the current experiment were not significantly associated with the BP according to the bivariate analysis (Table 1). However, a significant association was observed between Ang II level and BP. It seems that decreased Ang II resulted in an inhibitive role on RAS and thus induced a decline in BP in subjects exposed to the forest environment.

In addition to regulating BP, Ang II is now recognized as a pleiotropic factor involved in the regulation of multiple systems both in peripheral organs and in the brain [23]. Of prime importance is the pro-inflammatory effect of Ang II in the peripheral vasculature in hypertension [24,25], because inflammation is now recognized as a major factor in the development and maintenance of this disease [26]. In hypertension, Ang II stimulates AT1 receptors resulting in enhanced production and release of multiple pro-inflammatory factors, such as IL-1, IL-6, and TNF-α [26,27]. Thus, in our present study, the IL-6 level in subjects was decreased after experiencing a forest bathing trip maybe due to the decrease in Ang II.

It has been reported that an elevated level of Hcy, known as hyperhomocysteinemia (HHcy), is associated with the increment of vascular thickness, elastin fragmentation, and arterial BP [15,28]. Consistently, a significant association between SBP and Hcy ($p < 0.01$) was observed in our study (Table 1). A mild decline in Hcy level was found in the forest group which indicated its beneficial effect on human health. On the other hand, the endothelins are a family of naturally occurring peptides that include ET-1, endothelin-2 (ET-2), and endothelin-3 (ET-3). Of the three subtypes, ET-1 is the most potent vasoconstrictor and is always involved in the progression of cardiovascular diseases [29] and our results indicated that ET-1 level was significantly associated with the SBP (Table 1). A significant decrease in ET-1 was observed in participants exposed to the forest environment which was consistent with our previous study in young adults [30]. Besides, recent evidence has accumulated indicating that ET-1 is also an important stimulus for inflammation [31]. Thus, a decline in pro-inflammatory factors in the forest bathing group may somehow be related to the ET-1 alteration.

The air quality is closely related to human health. It is believed that higher levels of negative oxygen ions are beneficial for human health. Investigations into physiological and psychological conditions showed that performance efficiency and mental state were improved by exposure to negative ions in the environment [32]. A higher number of negative ions is beneficial for down-regulating the DBP [32]. In the present study, the concentration of negative air ions was also determined, and a significantly higher level of negative air ions was recorded in the forest environment ($1159.0 \pm 679.7\ cm^{-3}$) than in the urban area ($231.7 \pm 108.3\ cm^{-3}$). Thus, our finding about the beneficial effect of forests for lower DBP may be at least partly due to the abundance of negative air ions. On the other hand, many epidemiologic studies have evaluated the association between exposure to PM and elevated BP. Several epidemiologic and controlled human studies have reported higher SBP or DBP with short- or long-term exposure to PM10 [7,33,34] and it is thought to be at least partly related to the RAS activation as PM exposure induces increased plasma levels of Ang II and produces vasoconstriction via AT1 receptor in experimental animals [35,36]. In the current experiment, although a mildly higher level of PM10 at city sites was observed, the difference between the two groups was not significant. The air quality grade was defined as “good” according to the PM10 concentration at both of the experimental sites. Thus, the PM10 in the current study may have little effect on the BP as no elevation of SBP or DBP was observed in the subjects exposed to the urban environment.

As the change in RAS was detected in current study, the medication especially the ACEI/ARB drugs for each subject was considered. The number of participants taking ACEI/ARB drugs was not significantly different between the city and forest groups (Table 3) according to a chi-square analysis ($\chi^2 = 0.178$, $p = 0.673$). However, the dosage for each subject was different. Thus, the effect of ACEI/ARB drugs on the comparison between the two groups may be complicated. However, as the individual administration of drugs for each participant was carried out as usual during the 7-day experimental period, intake of drugs maybe not affect the comparison between its pre-experimental level and post-experimental level for each group.

Modern societies are subject to high stress owing to the fast pace of life. In addition, people living in urban areas are prone to

Table 3
Number of subjects taking ACEI/ARB drugs in city and forest groups.

Group	Number of subjects taking ACEI/ARB drugs	
	Yes	No
City	5	7
Forest	4	8

ACEI/ARB, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers.

irritability and tiredness through being in a crowded, unpleasant environment that is characterized by noisy traffic and the unpleasant smells of automobile exhausts and it is also related to human cardiac diseases [37,38]. The scores in the negative subscales of the POMS test, such as tension, depression, anger, fatigue, and confusion, were lower in subjects staying in the forest environment than those of the urban group (Fig. 7). It may also be related to the CCI, an objective evaluation of body feeling whose value is negatively associated with a comfortable feeling. A lower CCI value in the forest site in comparison to that of the city site in the current experiment also indicated a more comfortable feeling in subjects exposed to the forest environment (see Table 2), which was consistent with the result of the POMS test. On the other hand, it was noteworthy that temperature occupied a larger proportion than that of humidity and wind in calculating CCI in the current study. Although it was hot (the mean outside air temperature was 32.3 °C, see Table 2) at the city site during the 7-day period, it was not stressful to walk outside for subjects according to several aspects. First, according to the subjects' chief complaint, no uncomfortable feeling was reported during or after walking outside. Second, the mood state of subjects in the city group was mildly improved according to the POMS evaluation as evidenced by the scores in the negative subscales which were lowered and the score for vigor was increased at the end of the experiment in comparison to its baseline level, although the change was not significant (Fig. 7). Third, little increment in BP was observed after the experiment for the city group compared with their baseline level (Fig. 3). Besides, the subjects were also willing to walk outside near the hotel in our planned time period as they often walked outside in a similar period in their daily life. Thus, despite the hot urban environment, it could be used as an appropriate control in the current study.

As the limitation of the size and age range of participants in our study, the results cannot be extrapolated to different age groups or ethnicities. To generalize the findings, further studies on a large sample are needed. Further, the factor of climate also warrants investigation. We chose July in this study as it is a hot season and the forest is suitable in summer in China. It is not clear whether similar changes would be found in other seasons or other countries.

Taken together, despite the small sample size, it is worth noting that there was a significant reduction in human hypertension after experiencing a short-term forest bathing trip. In addition, forest bathing also induces inhibition of the RAS and inflammation, and thus inspires its preventive efficacy against cardiovascular disorders.

Acknowledgments

This work was supported by a fund from the Ministry of Health of P.R. China (WKJ2011-2-014), a fund from Health Bureau of Zhejiang Province (11-CX01), and Zhejiang Provincial Key Disciplinary Fields of Geriatrics Program.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jjcc.2012.08.003.

References

[1] Yamaguchi M, Deguchi M, Miyazaki Y. The effects of exercise in forest and urban environments on sympathetic nervous activity of normal young adults. J Int Med Res 2006;34:152–9.

[2] Loureiro G, Rabaca MA, Blanco B, Andrade S, Chieira C, Pereira C. Urban versus rural environment—any differences in aeroallergens sensitization in an allergic population of Cova da Beira, Portugal? Eur Ann Allergy Clin Immunol 2005;37:187–93.

[3] Kawakami K, Kawamoto M, Nomura M, Otani H, Nabika T, Gonda T. Effects of phytoncides on blood pressure under restraint stress in SHRSP. Clin Exp Pharmacol Physiol 2004;31(Suppl. 2):S27–8.

[4] Hassing HC, Twickler TB, Kastelein JJ, Cramer MJ, Cassee FR. Air pollution as noxious environmental factor in the development of cardiovascular disease. Neth J Med 2009;67:116–21.

[5] Castro-Giner F, Kunzli N, Jacquemin B, Forsberg B, de Cid R, Sunyer J, Jarvis D, Briggs D, Vienneau D, Norback D, Gonzalez JR, Guerra S, Janson C, Anto JM, Wjst M, et al. Traffic-related air pollution, oxidative stress genes, and asthma (ECHRS). Environ Health Perspect 2009;117:1919–24.

[6] Sun Q, Hong X, Wold LE. Cardiovascular effects of ambient particulate air pollution exposure. Circulation 2010;121:2755–65.

[7] Fuks K, Moebus S, Hertel S, Viehmann A, Nonnemacher M, Dragano N, Mohlenkamp S, Jakobs H, Kessler C, Erbel R, Hoffmann B. Long-term urban particulate air pollution, traffic noise, and arterial blood pressure. Environ Health Perspect 2011;119:1706–11.

[8] Sorensen M, Hvidberg M, Hoffmann B, Andersen ZJ, Nordsborg RB, Lillelund KG, Jakobsen J, Tjonneland A, Overvad K, Raaschou-Nielsen O. Exposure to road traffic and railway noise and associations with blood pressure and self-reported hypertension: a cohort study. Environ Health 2011;10:1–11.

[9] Kishimoto I, Tokudome T, Hosoda H, Miyazato M, Kangawa K. Ghrelin and cardiovascular diseases. J Cardiol 2012;59:8–13.

[10] Tsunetsugu Y, Park BJ, Miyazaki Y. Trends in research related to "Shinrin-yoku" (taking in the forest atmosphere or forest bathing) in Japan. Environ Health Prev Med 2010;15:27–37.

[11] Lee J, Park BJ, Tsunetsugu Y, Ohira T, Kagawa T, Miyazaki Y. Effect of forest bathing on physiological and psychological responses in young Japanese male subjects. Public Health 2011;125:93–100.

[12] Li Q. Effect of forest bathing trips on human immune function. Environ Health Prev Med 2010;15:9–17.

[13] Li Q, Morimoto K, Nakadai A, Inagaki H, Katsumata M, Shimizu T, Hirata Y, Hirata K, Suzuki H, Miyazaki Y, Kagawa T, Koyama Y, Ohira T, Takayama N, Krensky AM, et al. Forest bathing enhances human natural killer activity and expression of anti-cancer proteins. Int J Immunopathol Pharmacol 2007;20:3–8.

[14] Pollock V, Cho DW, Reker D, Volavka J. Profile of Mood States: the factors and their physiological correlates. J Nerv Ment Dis 1979;167:612–4.

[15] Fan FF, Huo Y, Wang X, Xu X, Wang BY, Xu XP, Li JP. Effect of enalapril on plasma homocysteine levels in patients with essential hypertension. J Zhejiang Univ Sci B 2010;11:583–91.

[16] Remkova A, Remko M. The role of renin–angiotensin system in prothrombotic state in essential hypertension. Physiol Res 2010;59:13–23.

[17] Currie G, Freel EM, Perry CG, Dominiczak AF. Disorders of blood pressure regulation-role of catecholamine biosynthesis, release, and metabolism. Curr Hypertens Rep 2012;14:38–45.

[18] Miyauchi T, Masaki T. Pathophysiology of endothelin in the cardiovascular system. Annu Rev Physiol 1999;61:391–415.

[19] Zhang W, Wang W, Yu H, Zhang Y, Dai Y, Ning C, Tao L, Sun H, Kellems RE, Blackburn MR, Xia Y. Interleukin 6 underlies angiotensin II-induced hypertension and chronic renal damage. Hypertension 2012;59:136–44.

[20] Haraoui B, Liu PP, Papp KA. Managing cardiovascular risk in patients with chronic inflammatory diseases. Clin Rheumatol 2012;31:585–94.

[21] Player MS, Peterson LE. Anxiety disorders, hypertension, and cardiovascular risk: a review. Int J Psychiatry Med 2011;41:365–77.

[22] Yayama K, Okamoto H. Angiotensin II-induced vasodilation via type 2 receptor: role of bradykinin and nitric oxide. Int Immunopharmacol 2008;8:312–8.

[23] Benicky J, Sanchez-Lemus E, Pavel J, Saavedra JM. Anti-inflammatory effects of angiotensin receptor blockers in the brain and the periphery. Cell Mol Neurobiol 2009;29:781–92.

[24] Suzuki Y, Ruiz-Ortega M, Lorenzo O, Ruperez M, Esteban V, Egido J. Inflammation and angiotensin II. Int J Biochem Cell Biol 2003;35:881–900.

[25] Cheng ZJ, Vapaatalo H, Mervaala E. Angiotensin II and vascular inflammation. Med Sci Monit 2005;11:RA194–205.

[26] Savoia C, Schiffrin EL. Inflammation in hypertension. Curr Opin Nephrol Hypertens 2006;15:152–8.

[27] Miyoshi M, Nagata K, Imoto T, Goto O, Ishida A, Watanabe T. ANG II is involved in the LPS-induced production of proinflammatory cytokines in dehydrated rats. Am J Physiol Regul Integr Comp Physiol 2003;284:R1092–7.

[28] Steed MM, Tyagi SC. Mechanisms of cardiovascular remodeling in hyperhomocysteinemia. Antioxid Redox Signal 2011;15:1927–43.

[29] Shao D, Park JE, Wort SJ. The role of endothelin-1 in the pathogenesis of pulmonary arterial hypertension. Pharmacol Res 2011;63:504–11.

[30] Mao G, Lan X, Cao Y, Chen Z, He Z, Lv Y, Wang Y, Hu X, Wang G, Yan J. Effects of short-term forest bathing on human health in a broad-leaved evergreen forest in Zhejiang Province, China. Biomed Environ Sci 2012;25:38–45.

[31] Saleh MA, Pollock DM. Endothelin in renal inflammation and hypertension. Contrib Nephrol 2011;172:160–70.

[32] Ryushi T, Kita I, Sakurai T, Yasumatsu M, Isokawa M, Aihara Y, Hama K. The effect of exposure to negative air ions on the recovery of physiological responses after moderate endurance exercise. Int J Biometeorol 1998;41:132–6.

[33] Chuang KJ, Yan YH, Cheng TJ. Effect of air pollution on blood pressure, blood lipids, and blood sugar: a population-based approach. J Occup Environ Med 2010;52:258–62.

[34] Chen SY, Su TC, Lin YL, Chan CC. Short-term effects of air pollution on pulse pressure among nonsmoking adults. Epidemiology 2012;23:341–8.

[35] Ghelfi E, Wellenius GA, Lawrence J, Millet E, Gonzalez-Flecha B. Cardiac oxidative stress and dysfunction by fine concentrated ambient particles (CAPs) are mediated by angiotensin-II. Inhal Toxicol 2005;22:963–72.

[36] Li Z, Carter JD, Dailey LA, Huang YC. Pollutant particles produce vasoconstriction and enhance MAPK signaling via angiotensin type I receptor. Environ Health Perspect 2005;113:1009–14.

[37] Lercher P, Botteldooren D, Widmann U, Uhrner U, Kammeringer E. Cardiovascular effects of environmental noise: research in Austria. Noise Health 2011;13:234–50.

[38] Kishi T. Heart failure as an autonomic nervous system dysfunction. J Cardiol 2012;59:117–22.