

Effects of Menopausal Hot Flashes on Mental Workload

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Abstract: This study examined the differences in psychophysiological responses during mental task performance between women with (Group S) and without (Group A) menopausal hot flashes. Twelve women who reported experiencing daily moderate or severe menopausal hot flashes (Group S) and twelve women who reported having no hot flashes (Group A) participated in a mental arithmetic (Task) and a control (Non-task) experiment that occurred twice during 30 min. Although Group S experienced frequent hot flashes during mental arithmetic task, no significant differences between the two groups emerged for the percentage of correct responses and reaction time, and cardiovascular and thermoregulatory responses. However, the STAI state anxiety score was significantly higher in Group S than in Group A during both rest and mental tasks, and stress-related cortisol secretion showed a tendency to increase in Group S compared with Group A after task. The present study indicates that there were no significant differences in physiological responses and cognitive performance between women with and without menopausal hot flashes during mental arithmetic, but women with menopausal hot flashes might perceive higher psychological stress during rest and mental arithmetic tasks than asymptomatic women.

Key words: Menopausal hot flash, Mental workload, Work performance, Psychological stress

Introduction

In Japan, middle-aged and elderly women are a precious labor source in a country where labor force has been decreasing due to the effects of the declining birthrate and the growing elderly population. However, many of middle-aged and elderly women experience various menopausal symptoms, such as hot flashes, night sweats, general fatigue, and shoulder stiffness, caused by estrogen withdrawal. The most common symptom of menopause is hot flashes: the sensation of sudden flushing and sweating, followed by chills. Previous studies have reported that isoflavone phytoestrogen derived from soybeans may decrease the

number of daily hot flashes in menopausal women¹⁻³). Although Japanese women have a relatively high intake of soybeans, the prevalence of menopausal hot flashes was still approximately 22–40%^{4, 5}).

Utian has reported that all menopausal symptoms may lead to work-related impairment, which significantly decreases the overall quality of life⁶). Previous studies associated with hot flashes have reported some evidence related to the effect of estrogen therapy on cognitive functioning^{7, 8}). These studies showed that hot flashes do not impair cognitive functioning dependent on the hippocampus and prefrontal cortex. Polo-Kantola *et al.* also reported that there was no relationship between the presence of menopausal hot flashes and decline of cognitive capacity⁹). However, these studies did not examine how cognitive performance was influenced while actual hot flashes occurred. Recently, our research

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group found that the performance of most women who experienced hot flashes during mental task was not affected by hot flashes, but work-related difficulties due to cognitive disturbance during hot flashes might arise in some women¹⁰). In addition, the studies mentioned above did not examine whether psychophysiological stress perceived by women with menopausal hot flashes during mental cognitive task, is equal to that of asymptomatic women. In reality, female workers with hot flashes may face many work-related difficulties including safety problems and low quality of life in the work place since they usually continue their work without stopping, even during a hot flash. Utian reported that physiological changes associated with menopausal symptoms often lead to increased anxiety and stress⁶). These effects indicate that menopausal symptomatic women may have higher or more sensitive responses related to psychological stress than asymptomatic women during cognitive performance. If they perceive higher psychophysiological stress in regard to work performance, it is necessary to give appropriate health care in order to increase quality of life and reduce stress caused by hot flashes for symptomatic females at work.

Therefore, the goal of this study is to examine the differences in psychophysiological responses during mental arithmetic tasks between women with and without moderate and severe menopausal hot flashes.

Methods

Subjects

Subjects were twelve women (Group S; four perimenopausal, eight postmenopausal) who reported experiencing daily moderate or severe menopausal hot flashes and twelve women who reported having no hot flashes (Group A; six perimenopausal, six postmenopausal) recruited for experiments via advertisements and fliers at community centers. Menopausal status was defined on the basis of self-reporting of menstrual bleeding. Women with menstrual bleeding in the last 12 months, but not in the last 3 months or with less regularity compared to the previous year, were classified as perimenopausal. Those who reported no menstrual bleeding in the last 12 months were classified as postmenopausal. The Kupperman Kohnenki Shogai Index (KCSI)¹¹ was used to assess climacteric complaints in the subjects. The respective mean values of Groups S and A in terms of age (52.6 ± 3.1 vs. 52.0 ± 4.1 yr), height (155.4 ± 3.5 vs. 153.9 ± 5.6 cm), body weight (55.2 ± 7.9 vs. 58.8 ± 6.7 kg) and BMI (22.8 ± 2.5 vs. 24.9 ± 3.5) were not significantly different. KCSI levels were significantly higher in Group S than in Group A (21.1 ± 8.7 vs. 12.3 ± 7.2 , respectively; $p=0.013$).

None of the subjects had been previously treated with hormone replacement therapy, nor were they taking any medication known to affect hot flashes 7 d prior to testing. All subjects were informed about the aim and scope of the study and gave written informed consent according to procedures approved by the Ethics Committee of the University of Occupational and Environmental Health. They were paid 6,000 yen for their participation in each experiment.

Measurements and data analysis

Various physiological responses were measured: heart rate (HR), blood pressure (BP), skin potential level (SPL), skin temperature, and cortisol in saliva. Perceived workload was assessed using the NASA Task Load Index (TLX). The psychological stress was examined using the Japanese form of the STAI state anxiety^{12, 13}). The STAI state anxiety scale assesses how subjects feel "right now, at this moment" with respect to each of the 20 different items. Symptom status of the subjects was monitored by video camera.

From the electrocardiography (LEG-1000, NIHON KOHDEN, Japan), data with a sampling frequency of 1 KHz, HR was derived. We continuously monitored BP using the Finapres cuff (Ohmeda, 2300 Finapres, U.S.A.) placed on the middle phalange of the left middle finger with infrared diodes positioned on the sides of the phalange and the hand supported comfortably by the subject's side, at heart level. Finapres provides non-invasive continuous beat-by-beat measurements of BP, based on the vascular unloading technique.

SPL was recorded via DC amplification (Skinos-Giken, Japan) by setting an exploring electrode on the hypothenar and the reference electrode on the upper third of the inside of the forearm, and then the changes in voltage, positive or negative, which occurred during a 1 s interval, were analyzed. SPL was used as a main parameter to predict hot flashes.

Skin temperature was recorded at 1 s intervals on a personal computer (mate NX, NEC) through an analog digital converter (Remote Scanner DE1200, NEC) using thermocouples placed on the forehead, chest, forearm, hand, thigh, leg, foot and finger. Mean skin temperature was calculated using the Hardy-DuBois formula¹⁴).

The NASA-TLX was used to assess mental workload for cognitive performance^{15, 16}). This index is a multi-dimensional rating scale (0–100) that provides an overall workload score based on six subscales: mental demand (MD), physical demand (PD), temporal demand (TD), performance (OP), effort (EF), and frustration (FR). In this study, the Adaptive Weighted Workload (AWWL) proposed by Miyake and Kumashiro was used for the overall evaluation points¹⁷).

Measurement of cortisol in saliva

The steroid hormone, cortisol, has been extensively monitored as a stress index. Previous studies have demonstrated increased cortisol levels in populations having increased distress^{18, 19}. Previous studies have also reported that salivary cortisol significantly correlates with plasma cortisol concentrations^{20, 21}. In this study, salivary cortisol was used as a physiological marker of stress in responding during mental arithmetic task^{12, 22}. In addition, cortisol concentrations typically display high levels in the morning and a decrease in the evening, indicating circadian variations typical of humans^{23, 24}. In consideration of this circadian pattern, the experiments were conducted between 13:00–18:00 h.

Saliva samples were collected by placing 2 pieces of Salivette (Sarstedt Ltd.) at the sublingual site for 3 min. After collection, saliva was extracted from the cotton by centrifugation (KUBOTA 2700) at 3.5×10^3 rpm for 15 min before storage at -30°C . Cortisol levels were determined using a Cortisol ELISA Kit (Oxford Biomedical Research, Inc. U.S.A.).

Procedures

Experiments were conducted in a climatic chamber maintained at 28°C with a relative humidity of $50 \pm 10\%$ which is a standard temperature setting in Japanese workplaces in the summer. The subjects participated in a day of mental arithmetic (Task) experiments and a day of control (Non-task) experiments. The order of Task and Non-task was randomized and counterbalanced across subjects in each group. During Non-task, subjects were asked to leisurely read a book about garden design prepared in advance.

Figure 1 shows the experimental procedure. The subjects filled out the STAI state anxiety inventory in a resting state for 17 min (Rest1), followed by Task1

or Non-task1 for 30 min. After the subjects filled out a NASA-TLX, STAI state anxiety inventory, frequency, and intensity of hot flashes after Task1 or Non-task1, they rested for 5 min (Rest2), followed by Task2 or Non-task2 for 30 min. Finally, the subjects filled out the above psychological indices and subjective assessment of hot flashes after Task2 or Non-task2, followed by rest state for 5 min (Rest3). HR, SPL, and skin temperature were continuously recorded from the onset of the experiment to its end, and saliva was sampled at the onset and the end of the experiment. BP was continuously measured at rest and during each task.

Subjective and objective hot flash measures

The subjects were required to recall frequency of hot flashes and intensity using a visual analog scale (ranked 0–10, with zero representing “no sensation” and ten representing “the most intense hot flash imaginable”) after each task or when hot flashes occurred during rest time. Freedman has reported that increased sternal skin conductance, an electrical measure of sweating, is the best objective marker of menopausal hot flashes²⁵. Skin conductance rises sharply from baseline at the onset of a hot flash, and then slowly returns to baseline. Surwillo notes that both skin conductance and skin potential are reflections of sweat gland activity²⁶. In this study, skin potential level (SPL) was used as an objective marker of hot flashes. Maximum levels of SPL vary among individuals depending on the degree of sympathetic sweating on the palm. Thus, hot flash occurrence was chiefly predicted by remarkably increased SPL, and secondly by chest skin temperature and subjective self-reported hot flashes.

Mental arithmetic task

Previous study has suggested that elevated brain

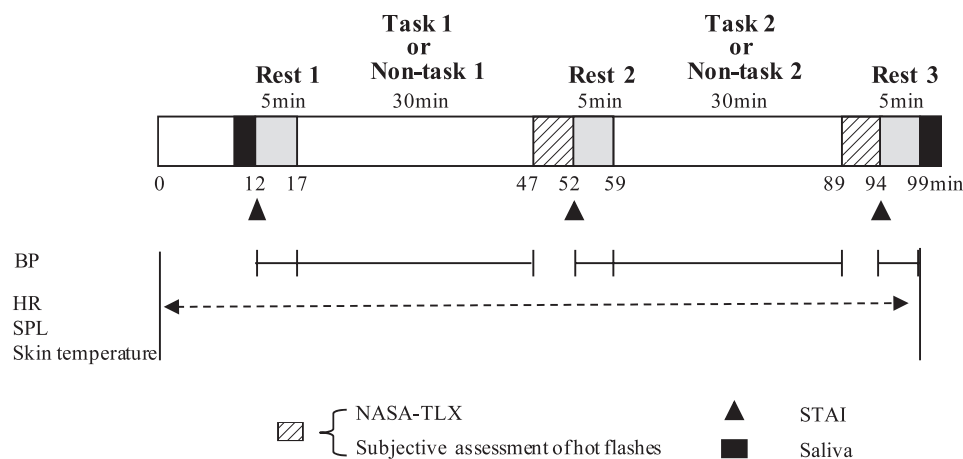


Fig. 1. Experimental procedure.

noradrenaline activity at central $\alpha 2$ -adrenoceptors is involved in the initiation of hot flashes²⁵), and mental arithmetic tasks lead to brain activation in both the prefrontal and parietal cortex²⁷⁻²⁹). Thus, mental arithmetic tasks that are commonly used to assess cognitive functioning³⁰⁻³²) may be effective in creating a task environment that triggers hot flashes in this study. In this study, the subjects performed the mental task used by Park *et al*¹⁰).

A mental arithmetic task was presented on a computer screen, and the subjects were instructed to give the last digit of the sum after adding two single-digit numbers. The task questions were shown for 0.5 s, followed by an equal sign (=) shown for 0.5 s. The answers were divided into three groups: [0·3·6], [1·4·7], [2·5·8]. Subjects were then asked to click the number group containing the last digit of the correct sum as quickly as possible within a 2 s interval. For example, the answer of “7+3=” is 10. 0 is the last digit of the sum; therefore, the subject should click the group [0·3·6] as quickly as possible. The answer numbers from each group were adjusted to appear evenly at 5 min intervals. The percentage of correct responses and the reaction time were expressed as the mean for 5 min. To minimize the effect of individual differences in math ability and boredom by repetition, the task only included single-digit addition with time pressure and step selection of answers from among three groups. The viewing distance between the subject’s eyes and the computer screen was approximately 70 cm, and the top of the display screen was at eye level so that the screen work area was slightly below the horizontal plane. Subjects were instructed to adjust the seat height so that their feet rested on the floor, adjust the backrest of their chairs to push the lower back forward slightly, and to keep their thighs parallel to the floor.

Statistical analysis

All data were expressed as the mean value \pm standard deviation (SD). Physiological parameters, NASA-TLX, STAI state anxiety, percentage of correct responses, and reaction time were analyzed using three-way repeated measures ANOVA (Huynh-Feldt correction applied) with group (Group S and Group A), subgroup (Peri- and Post-menopausal women), and time factors. Post-hoc comparisons of the mean values were performed using Bonferroni. The incidence of hot flashes between Task and Non-task in Group S was analyzed using a non-parametrical test (Wilcoxon signed rank test). $p < 0.05$ was considered significant (SPSS 11.5J, SPSS Japan Inc.).

Meanwhile, all the data, including some women in Group S who did not experience hot flashes during the experiment and two subjects in Group A who did, were included in the analysis because the aim of this study was to examine the differences in mental task performance and psychophysiological responses between women with and without daily moderate or severe menopausal hot flashes. If their data were excluded from the analysis, this study could induce a selection bias.

Results

The incidence of hot flashes in Group S was observed 26 times in ten women during Task compared with 11 times in five women during Non-task (Table 1). Four of the 26 hot flashes which were triggered in Group S occurred at the rest time immediately after each task. On the other hand, the number of hot flashes in Group A was reported 4 times in two women during Task, and one of the two women also triggered a hot flash during Non-task. The intensities of hot flashes during Task and Non-task in Group S were 4.4 ± 1.8 and 4.5 ± 1.8 , respectively, but were not significantly

Table 1. Total frequency of hot flashes during Task and Non-task in Group A and Group S

Group A

subject task	A01	A02	A03	A04	A05	A06	A07	A08	A09	A10	A11	A12	Total
Task	—	—	—	—	—	3	—	—	—	—	—	1	4
Non-task	—	—	—	—	—	1	—	—	—	—	—	—	1

Group S

subject task	S01	S02	S03	S04	S05	S06	S07	S08	S09	S10	S11	S12	Total
Task	1	—	2	2	5	—	3	1	5	1	1	5	26
Non-task	—	—	1	—	4	1	—	4	—	—	1	—	11

Table 2. Comparisons of the percentage of correct responses and reaction time between women without (Group A) and with (Group S) moderate and severe menopausal hot flashes during mental arithmetic tasks

Percentage of Correct Responses	Task 1					
	5 min	10 min	15 min	20 min	25 min	30 min
Group A	95.6 ± 3.0	96.0 ± 3.1	95.4 ± 3.9	96.0 ± 3.5	96.2 ± 3.3	96.5 ± 2.5
Group S	93.9 ± 7.0	93.8 ± 6.1	94.8 ± 5.0	90.9 ± 13.4	90.5 ± 12.1	92.1 ± 8.5

Percentage of Correct Responses	Task 2					
	5 min	10 min	15 min	20 min	25 min	30 min
Group A	97.5 ± 2.1	97.3 ± 2.1	96.6 ± 2.4	95.6 ± 3.0	96.1 ± 2.9	94.7 ± 3.4
Group S	94.6 ± 6.0	93.2 ± 8.3	95.3 ± 4.2	94.6 ± 6.4	95.6 ± 4.5	95.2 ± 5.0

Reaction Time (sec)	Task 1					
	5 min	10 min	15 min	20 min	25 min	30 min
Group A	899.6 ± 153.3	872.3 ± 160.3	870.0 ± 164.9	850.1 ± 171.2	853.9 ± 153.1	834.5 ± 157.2
Group S	944.8 ± 167.4	914.1 ± 180.1	904.0 ± 144.0	902.5 ± 168.7	881.9 ± 158.3	881.9 ± 172.0

Reaction Time (sec)	Task 2					
	5 min	10 min	15 min	20 min	25 min	30 min
Group A	826.2 ± 167.5	813.5 ± 152.1	812.1 ± 132.1	826.1 ± 134.8	830.7 ± 126.0	848.0 ± 99.4
Group S	832.7 ± 177.5	800.5 ± 171.3	814.2 ± 186.8	806.5 ± 172.4	814.4 ± 182.2	829.4 ± 167.8

The individual mean values of the percentage of correct responses and the reaction time are shown at 5 min intervals. The values show the mean ± SD.

different between the two conditions.

ANOVA analyses neither indicated significant main effects of time, group, and subgroup factors nor detected significant interactions in the percentage of correct responses. As illustrated in Table 2, a significant group × time interactions ($F(11, 220) = 2.95$; $p < 0.05$) was observed in reaction time, which was shorter at Task 2 than at Task 1 in both Group S and Group A; however, there was no significant difference between groups.

Significant main effects of time emerged for both systolic blood pressure (SBP) and HR in both Task and Non-task, but there were no significant differences between groups or subgroups. SBP was significantly higher during the mental task than at rest ($F(14, 280) = 9.59$; $p < 0.01$). HR was significantly higher during Task 1 than at rest and showed a significant decrease during Task 2 compared with Task 1 ($F(14, 280) = 11.09$; $p < 0.01$).

A significant main effect of time ($p < 0.01$) was indicated for all skin temperatures in Non-task, but there was no significant difference between Group S and Group A. In addition, the significant group × subgroup interaction ($F(1, 20) = 20.60$; $p < 0.01$) was observed in foot skin temperature, which was significantly lower in

peri-menopausal women than in post-menopausal women in Group A, but was lower in post-menopausal women than in peri-menopausal women in Group S. On the other hand, a significant main effect of time ($p < 0.01$) was indicated for forehead, chest, hand, thigh, and calf skin temperatures in Task, but there were no significant differences between Group S and Group A. Especially, the significant group × subgroup interaction ($p < 0.01$) was observed in finger ($F(1, 20) = 8.15$; $p < 0.01$) and foot skin temperatures ($F(1, 20) = 5.14$; $p < 0.05$), which was significantly lower in peri-menopausal women than in post-menopausal women in Group A. Figure 2 shows the comparisons between Group S and Group A for chest and finger skin temperatures during Task. Chest skin temperature (Fig. 2a) continued to significantly increase after the onset of the mental task in both groups, and finger skin temperature (Fig. 2b) sharply decreased after the onset of Task 1.

As illustrated in Fig. 3, for AWWL of NASA-TLX, there was no significant difference between Group S and Group A. The significant main effects of time ($F(2, 40) = 4.31$; $p < 0.05$) and group ($F(1, 20) = 7.15$; $p < 0.05$) were observed in the STAI state anxiety score, which was significantly higher in Group S than in Group A during both rest state and Task (Fig. 4). However, no

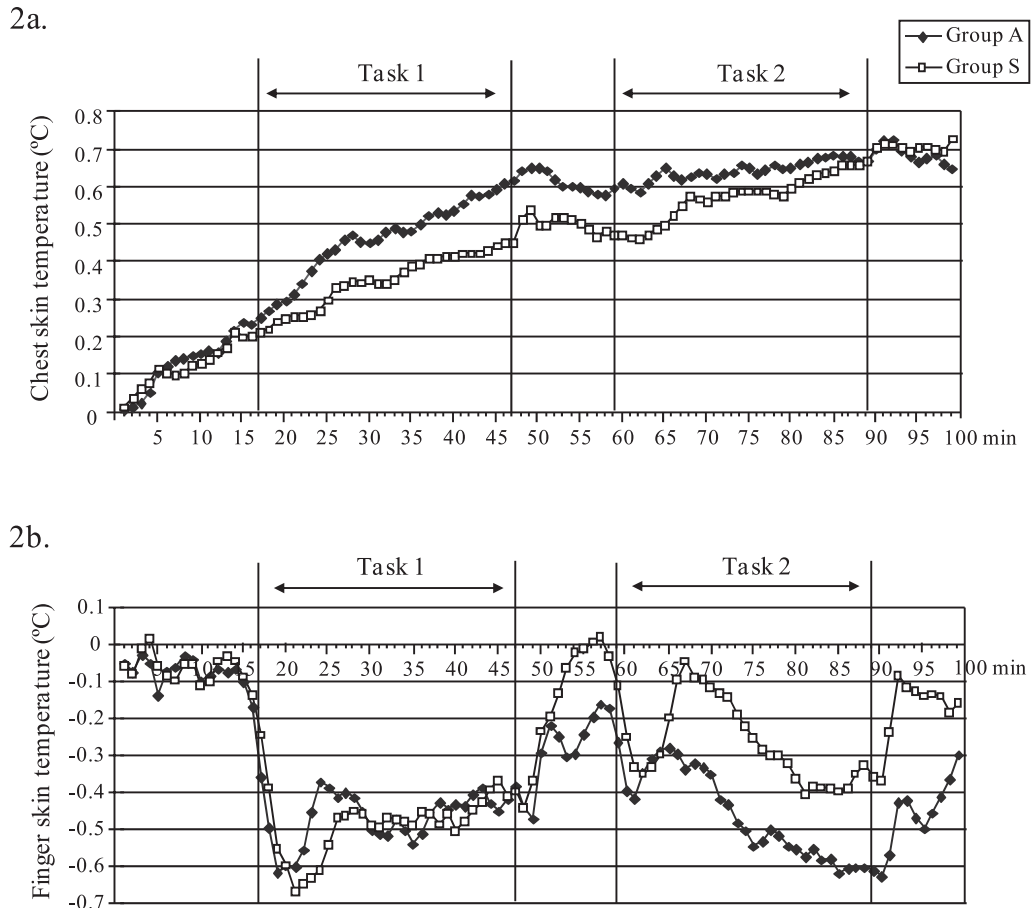


Fig. 2. Comparisons of chest (2a) and finger (2b) skin temperatures between women without (black diamond; Group A) and with (white square; Group S) moderate and severe menopausal hot flashes during mental arithmetic tasks. All subjects performed a mental arithmetic task for 30 min during both Task 1 and Task 2. The values show the mean.

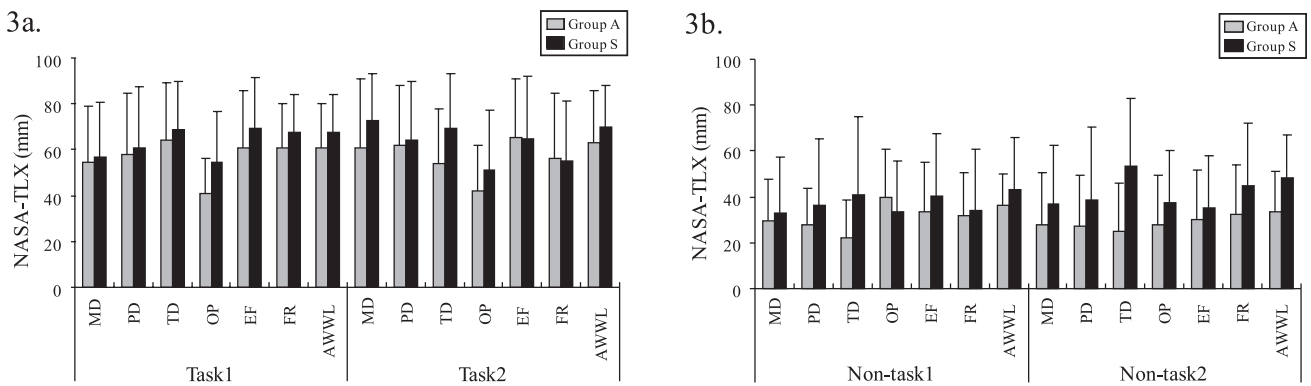


Fig. 3. Comparisons of NASA-TLX between women without (gray bar; Group A) and with (black bar; Group S) moderate and severe menopausal hot flashes during mental arithmetic tasks. The values show the mean \pm SD.

significant difference between the two groups emerged for the STAI state anxiety during Non-task.

As illustrated in Fig. 5, the cortisol level after mental task showed an increasing tendency in Group S com-

pared with Group A.

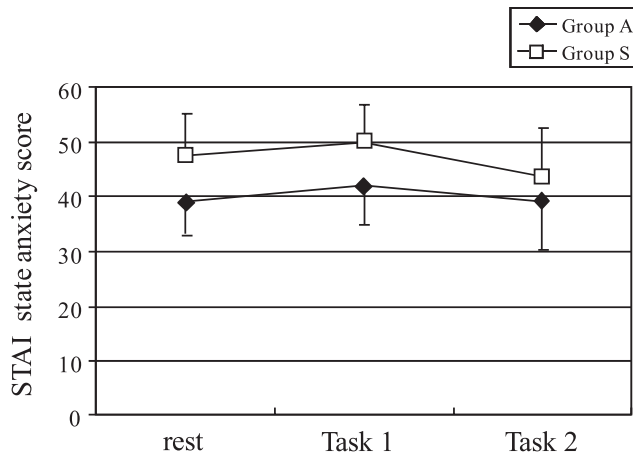


Fig. 4. Comparisons of the STAI state anxiety score between women without (black diamond; Group A) and with (white square; Group S) moderate and severe menopausal hot flashes during mental arithmetic tasks.

The values show the mean \pm SD.

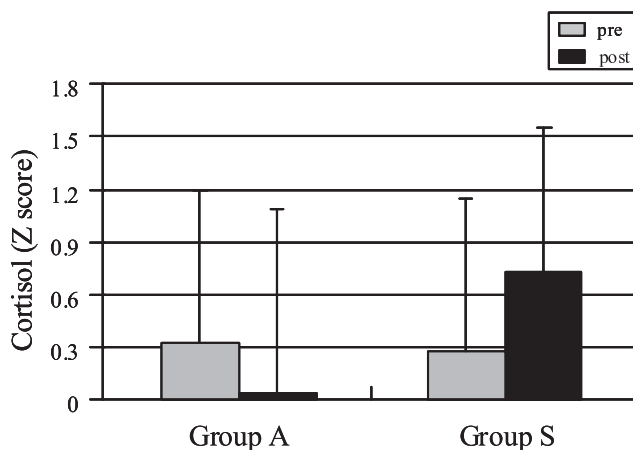


Fig. 5. Comparisons of cortisol level before (black bar; pre) and after (gray bar; post) task between women without (Group A) and with (Group S) moderate and severe menopausal hot flashes during mental arithmetic tasks.

The values show the mean \pm SD.

Discussion

There were no significant differences between women with moderate or severe menopausal hot flashes and asymptomatic women for percentage of correct responses and reaction time despite experiencing frequent hot flashes in Group S (Tables 1, 2). However, the standard deviations of percentage of correct responses during task were much larger in Group S than in Group A. For example, at 20 min to 30 min after onset of Task 1 and 10 min after onset of Task 2, the standard deviations of task scores in Group S were 3 to 4 times larger than that in Group A. A large standard deviation

indicates great variability of response. This result is consistent with our previous study that hot flashes resulted in uneven task performance in some women¹⁰. Interestingly, two women in Group A who had never had a hot flash before experienced hot flashes during mental task. This may support the result of Park *et al.* that mental workload which elevates brain noradrenaline acting can be a risk factor for hot flashes¹⁰. It is also likely that hot flashes may be triggered by a stressor such as passive electrodes attached to subjects' bodies. Deecher reported that vasomotor symptoms including hot flashes are due to either a malfunction of the thermoregulatory control mechanisms or a disruption in communication between these mechanisms³³. Thus, it is also likely that the hot flashes which occurred in the two women of Group A were triggered by a disruption in communication between the thermoregulatory control mechanisms during mental arithmetic task.

On the other hand, regardless of frequent hot flashes in Group S, this study showed similar physiological findings in women who had hot flashes and in those who did not. There were no significant differences for skin temperature responses and cardiovascular activities including HR and SBP between the two groups in both Task and Non-task. In other studies, HR and skin temperatures of the chest, forehead, finger, cheek, and upper arm increased during a hot flash^{25, 34}. However, increased heart rate and blood pressure³⁵, and reduced finger skin temperature³⁶ in this study were observed as the typical results of the vasoconstriction caused by sympathetic activation during mental arithmetic in both groups. In particular, there was no significant difference in chest skin temperature between Group S and Group A during mental task, but this index showed slight increase in Group S compared with Group A regardless of frequent hot flashes in Group S (Fig. 2). These results indicate that in menopausal symptomatic women, the vasoconstriction responses caused by stressful conditions were greater than the physiological changes due to frequent hot flashes. Furthermore, previous study has shown that hot flashes can be triggered by small elevations in core body temperature within a narrowed thermoneutral zone, which has the effect of lowering the body temperature threshold for sweating²⁵.

In this study, physiological changes related to hot flashes during mental workload were slight in Group S, but the women with hot flashes may have perceived higher stress than asymptomatic women. Previous study reported that physiological changes associated with menopausal symptoms often lead to increased anxiety and stress⁶. This means that even though the two groups had similar physiological changes during mental task, perceived mental stress most likely differed

between Group S and Group A. In fact, although there were no significant differences in mental arithmetic performance and AWWL of NASA-TLX between the two groups, the STAI state anxiety score was significantly higher in Group S than in Group A throughout the whole period including rest state and mental task ($p < 0.01$), and a mental stress-induced cortisol level showed an increasing tendency in Group S compared with Group A after task. These results suggest that Group S who experienced frequent hot flashes perceived higher stress than Group A during mental task and also had high anxiety, even during rest state, regardless of the occurrence of a hot flash. In other words, women with menopausal hot flashes may have more excessive or sensitive responses for work-related stress than asymptomatic women in the work place. Therefore, it is necessary to provide suitable health care for female workers suffering from menopause-related hot flashes in work-related stressful situations. For example, when occupational physicians and nurses who provide diverse health care services to employees make a diagnosis of menopausal hot flashes for females in the workplace, they first should examine risk factors for hot flash occurrence and then give appropriate mental health care in order to reduce high anxiety and stress caused by mood swings and unpredictable hot flashes.

Despite several accurate findings, this study also had several limitations. First, it was hard to clearly explain the differences in physiological responses between peri- and post menopausal women because we did not measure follicle-stimulating hormones and estradiol levels in subjects' blood. For example, the study examined group and subgroup interactions in finger and foot skin temperatures, but it was difficult to interpret whether the results were due to differences of follicle-stimulating hormones and estradiol levels or to a malfunction of the thermoregulatory control mechanisms related to hot flashes. However, this study objectively examined changes in both performance and psychophysiological responses while subjects experienced hot flashes during mental task. Thus, we obtained novel results for work-related stress associated with the occurrence of hot flashes. Next, the subjects in our experiment were instructed to perform simple mental arithmetic tasks for only an hour because the goal of this study was to examine the differences in psychophysiological responses during mental tasks between women with and without menopausal hot flashes. We succeeded in triggering some hot flashes during the task, but the task can be criticized for having insufficient contents and time compared with real work because menopausal symptomatic women face a variety of work problems such as time pressure, work difficulties, and heavy workloads in the

workplace. Therefore, practical research is required to examine psychophysiological responses associated with hot flashes during longer periods of work as well as using work contents closer to real work in the future.

Conclusion

The present study indicated that although symptomatic women experienced frequent hot flashes during mental arithmetic task, no significant differences between women with and without menopausal hot flashes emerged for mental task performance and physiological responses; however, women who have moderate or severe menopausal hot flashes perceived higher psychological stress during rest and mental tasks than asymptomatic women. This suggests that it is necessary to provide suitable health care for middle-aged and elderly female workers suffering from menopause-related hot flashes in work-related stressful situations.

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References

- 1) Brzezinski A, Adlercreutz H, Shaoul R, Rosier A, Shmueli A, Tanos V, Schenker JG (1997) Short-term effects of phytoestrogen-rich diet on postmenopausal women. *Menopause* **4**, 89–94.
- 2) Howes LG, Howes JB, Knight DC (2006) Isoflavone therapy for menopausal flushes: a systematic review and meta-analysis. *Maturitas* **55**, 203–11.
- 3) Cheng G, Wilczek B, Warner M, Gustafsson JA, Landgren BM (2007) Isoflavone treatment for acute menopausal symptoms. *Menopause* **14**, 468–73.
- 4) Ikeda T, Makita K, Ishitani K, Takamatsu K, Horiguchi F, Nozawa S (2005) Status of climacteric symptoms among middle-aged to elderly Japanese women: comparison of general healthy women with women presenting at a menopausal clinic. *J Obstet Gynaecol Res* **31**, 164–71.
- 5) Melby MK (2005) Vasomotor symptom prevalence and language of menopause in Japan. *Menopause* **12**, 250–7.
- 6) Utian WH (2005) Psychosocial and socioeconomic burden of vasomotor symptoms in menopause: a comprehensive review. *Health Qual Life Outcomes* **3**, 47.
- 7) Yaffe K, Krueger K, Sarkar S, Grady D, Barrett-Connor E, Cox DA, Nickelsen T (2001) Cognitive function in postmenopausal women treated with raloxifene. *N Engl J Med* **344**, 1207–13.
- 8) Leblanc ES, Neiss MB, Carello PE, Samuels MH, Janowsky JS (2007) Hot flashes and estrogen ther-

- apy do not influence cognition in early menopausal women. *Menopause* **14**, 191–202.
- 9) Polo-Kantola P, Portin R, Koskinen T, Polo O, Irjala K, Erkkola P (1997) Climacteric symptoms do not impair cognitive performances in postmenopause. *Maturitas* **27**, 13–23.
 - 10) Park MK, Satoh N, Kumashiro M (2008) Mental workload under time pressure can trigger frequent hot flashes in menopausal women. *Ind Health* **46**, 261–8.
 - 11) Abe T, Moritsuka T (Eds.) (1996) KCSI [Kupperman Kohnenki Shogai Index] (Kuppahman- Kohnenki-Shohgai-Shisuh, Abe-henpoh) Shiyoh-tebiki. Sankyoboh, Kyoto (in Japanese).
 - 12) Noto Y, Sato T, Kudo M, Kuata T, Hirota K (2005) The relationship between salivary biomarkers and state-trait anxiety inventory score under mental arithmetic stress: a pilot study. *Anesth Analg* **101**, 1873–6.
 - 13) Laidlaw TM, Naito A, Dwivedi P, Hansi NK, Henderson DC, Gruzelier JH (2006) The influence of 10 min of the Johrei healing method on laboratory stress. *Complement Ther Med* **14**, 127–32.
 - 14) Hardy JD, Dubois EF (1938) The technic of measuring radiation and convection. *J Nutr* **15**, 461–75.
 - 15) Vitense HS, Jacko JA, Emery VK (2003) Multimodal feedback: an assessment of performance and mental workload. *Ergonomics* **46**, 68–87.
 - 16) Murata A (2005) An attempt to evaluate mental workload using wavelet transform of EEG. *Hum Factors* **47**, 498–508.
 - 17) Miyake S, Kumashiro M (1993) Subjective mental workload assessment technique, an introduction to NASA-TLX and SWAT and a proposal of simple scoring methods. *Jpn J Ergon* **29**, 399–408.
 - 18) Schulz P, Kirschbaum C, Prussner J, Hellhammer D (1998) Increased free cortisol secretion after awakening in chronically stressed individuals due to work overload. *Stress Medicine* **14**, 91–7.
 - 19) Melamed S, Ugarten U, Shirom A, Kahana L, Lerman Y, Froom P (1999) Chronic burnout, somatic arousal and elevated salivary cortisol levels. *J Psychosom Res* **46**, 591–8.
 - 20) Obmiński Z, Wojtkowiak M, Stupnicki R, Golec L, Hackney AC (1997) Effect of acceleration stress on salivary cortisol and plasma cortisol and testosterone levels in cadet pilots. *J Physiol Pharmacol* **48**, 193–200.
 - 21) Putignano P, Dubini A, Toja P, Invitti C, Bonfanti S, Redaelli G, Zappulli D, Cavagnini F (2001) Salivary cortisol measurement in normal-weight, obese and anorexic women: comparison with plasma cortisol. *Eur J Endocrinol* **145**, 165–71.
 - 22) Wang J, Rao H, Wetmore GS, Furlan PM, Korczykowski M, Dinges DF, Detre JA (2005) Perfusion functional MRI reveals cerebral blood flow pattern under psychological stress. *Proc Natl Acad Sci U S A* **102**, 17804–9.
 - 23) Weitzman ED, Fukushima D, Nogeire C, Roffwarg H, Gallagher TF, Hellman L (1971) Twenty-four hour pattern of the episodic secretion of cortisol in normal subjects. *J Clin Endocrinol Metab* **33**, 14–22.
 - 24) Curtis GC (1972) Psychosomatics and chronobiology: possible implications of neuroendocrine rhythms. A review. *Psychosom Med* **34**, 235–56.
 - 25) Freedman RR (2005) Pathophysiology and treatment of menopausal hot flashes. *Semin Reprod Med* **23**, 117–25.
 - 26) Surwillo WW (1990) Psychophysiology for clinical psychologists. Ablex Publishing, Norwood.
 - 27) Burbaud P, Camus O, Guehl D, Bioulac B, Caillé J, Allard M (2000) Influence of cognitive strategies on the pattern of cortical activation during mental subtraction. A functional imaging study in human subjects. *Neurosci Lett* **287**, 76–80.
 - 28) Menon V, Rivera SM, White CD, Glover GH, Reiss A (2000) Dissociating prefrontal and parietal cortex activation during arithmetic processing. *Neuroimage* **12**, 357–65.
 - 29) Rickard TC, Romero SG, Basso G, Wharton C, Flitman S, Grafman J (2000) The calculating brain: an fMRI study. *Neuropsychologia* **38**, 325–35.
 - 30) Yasumasu T, Reyes Del Paso GA, Takahara K, Nakashima Y (2006) Reduced baroreflex cardiac sensitivity predicts increased cognitive performance. *Psychophysiology* **43**, 41–5.
 - 31) Zamarian L, Stadelmann E, Nürk HC, Gamboz N, Marksteiner J, Delazer M (2007) Effects of age and mild cognitive impairment on direct and indirect access to arithmetic knowledge. *Neuropsychologia* **45**, 1511–21.
 - 32) Ikegami K, Ogyu S, Arakomo Y, Suzuki K, Mafune K, Hino H, Nagata S (2009) Recovery of cognitive performance and fatigue after one night of sleep deprivation. *J Occup Health* **51**, 712–22.
 - 33) Deecher DC (2005) Physiology of thermoregulatory dysfunction and current approaches to the treatment of vasomotor symptoms. *Expert Opin Investig Drugs* **14**, 435–48.
 - 34) Kronenberg F (1990) Hot flashes: epidemiology and physiology. *Ann N Y Acad Sci* **592**, 52–86.
 - 35) Bacon SL, Ring C, Hee FL, Lip GY, Blann AD, Lavoie KL, Carroll D (2006) Hemodynamic, hemostatic, and endothelial reactions to psychological and physical stress in coronary artery disease patients. *Biol Psychol* **71**, 162–70.
 - 36) Young TM, Asahina M, Nicotra A, Mathias CJ (2006) Skin vasomotor reflex responses in two contrasting groups of autonomic failure: multiple system atrophy and pure autonomic failure. *J Neurol* **25**, 846–50.