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Effect of menstrual cycle and gender on ventilatory and heart rate responses at the onset of exercise

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Abstract To clarify the luteal-follicular and male-female differences in ventilatory and heart rate responses at the onset of exercise, seven women and seven men performed voluntary exercise and passive movement for 20 s (brief voluntary exercise and brief passive movement) and voluntary exercise for 3 min (long voluntary exercise) in a sitting position. Voluntary exercise consisted of alternate flexion-extensions of both lower legs with a weight corresponding to about 2.5% of the subjects' body mass attached to each ankle, at a frequency of about 60 times min^{-1} . Passive movement was carried out without weights by experimenters pulling ropes attached to both of the subjects' ankles, in the same way as voluntary exercise. During these exercises and movements, minute inspiratory ventilation (V_I) and heart rate (HR) were continuously measured by breath-by-breath and beat-to-beat techniques. We calculated relative changes of V_I and HR (ΔV_I and ΔHR). Additionally, we averaged ΔV_I and ΔHR obtained during the exercise and movement for each subject, and performed a correlation analysis between the averaged ΔV_I and ΔHR . It was clarified that: (1) ΔV_I and ΔHR in the follicular phase were almost equal to those in the luteal phase; (2) there were no significant male-female differences in these parameters; (3) significant positive correlations were found in both genders only during brief voluntary exercise. We conclude that ventilatory and HR responses at the onset of voluntary exercise and passive movement are not affected by the menstrual cycle or gender.

Keywords Gender difference · Heart rate response · Menstrual cycle · Ventilatory response · Women

Introduction

In understanding physiological phenomena, gender difference is a very interesting and important topic. For example, White et al. (1983) observed lower ventilatory responses to hypoxia and hypercapnia in women than in men. Jones et al. (1999) reported that gender appeared to influence sympathetic and cardiovascular responses to various conditions (10, 12, 50%) of inspired oxygen levels. There have also been many studies about the effect of gender on minute ventilation and heart rate (HR) at the anaerobic threshold (AT) or at peak exercise in young people (Younis et al. 1990; Ogawa et al. 1992; Helgerud 1994; Rickli et al. 1997; Nindl et al. 1998). According to the results of those studies, while no gender effect seems to exist for HR at AT or peak levels of exercise, a male-female comparison of minute ventilation has been reported with various results.

It is a well-known physiological reaction that the transition from rest to light or moderate exercise is accompanied by a rapid increase in minute ventilation and HR. It has been shown that this abrupt increase in ventilation and HR usually occurs from the first breath (Eldridge and Waldrop 1991) and lasts for about 20 s, and is termed phase I (Whipp et al. 1982). This phase I response, from the first breath and lasting for about 20 s, is observed not only during voluntary exercise but also during passive movement following electrically induced muscle contractions or flexion-extensions of the lower legs with ropes (Adams et al. 1987; Miyamura et al. 1992). In past studies, it has been reported that the phase I response is influenced by various factors, e.g., posture (Weiler-Ravell et al. 1983), exercise frequency (Kelsey and Duffin 1992), exercise intensity (Miyamura et al. 1992), age (Ishida et al. 2000; Sato et al. 2000) and so on.

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To our knowledge, however, no study about the effect of gender on phase I response has been done.

Many investigators have pursued mechanisms that are responsible for the phase I response. At present, it is considered that two neural mechanisms, central command and peripheral reflex, mainly trigger the increase in ventilation and HR that appears at the onset of exercise (Mitchell 1990; Mateika and Duffin 1995). Central command arises from the activation of the cerebral cortex and hypothalamus (Goodwin et al. 1972). In contrast, peripheral reflex originates in the stimulation of group III (mechanoreceptor) and IV (metaboreceptor) muscle afferents (McCloskey and Mitchell 1972; Kaufman et al. 1983). Recently, Rabinowicz et al. (2002) have clarified the existence of gender difference in the structure of the human cerebral cortex. Hinojosa-Laborde et al. (1999), from previous reports about the sympathetic nervous system, suggest that females limit the activation or enhance the inhibition of the sympathetic nervous system more effectively than males. As it is thought that structure and function usually accompany each other, this male–female constructive difference in the cerebral cortex may have an effect on ventilatory and HR responses at the onset of exercise, and gender difference in the sympathetic nervous system may affect these responses.

However, in evaluating the phase I response in women, the menstrual cycle cannot be ignored because it is reported that female sex hormones act on the central nervous system. It has been shown in experiments with cats that progesterone exerts a respiratory effect on the hypothalamus (Bayliss et al. 1990) and that estrogen (17β -estradiol) attenuates the cardiovascular and ventilatory responses not to peripheral reflex but to central command (Hayes et al. 2002).

The purpose of the present study, therefore, was to clarify whether or not ventilatory and HR responses at the onset of voluntary exercise and passive movement differ (1) between the luteal and follicular phase and (2) between women and men.

Methods

Subjects

Seven women and seven men volunteered to participate in the present study. All women reported having a normal history of menstrual cycles. No subjects had a history of cardiorespiratory diseases, took medications that seriously affected cardiorespiratory responses and the menstrual cycle, or smoked. The subjects were informed of the experimental protocol and possible risks involved in this study before giving written consent. The ethics committee of the Research Center of Health, Physical Fitness and Sports at Nagoya University approved this study. The physical characteristics of the subjects are summarized in Table 1.

Menstrual cycle

In the current study, the timing of the menstrual cycle was initially indicated by a menstrual cycle history questionnaire. Secondly, it

Table 1 Physical characteristics of subjects. Values are means (SE). (*n* The number of subjects)

Parameter	Follicular	Luteal	Women	Men
<i>n</i>			7	7
Age (years)	18.7 (0.2)	18.7 (0.2)	18.7 (0.2)*	19.7 (0.3)
Height (cm)	158.3 (1.8)	158.3 (1.8)	158.3 (1.8)*	173.3 (1.5)
Weight (kg)	54.0 (2.9)	54.0 (2.7)	54.0 (2.8)*	62.8 (2.0)

* $P < 0.05$ Women different from men

was confirmed by applying the methods described by Cunningham et al. (1978) and Frye and Kamon (1981), which are based on menses and ovulation. Although the aforementioned researchers estimated the dates of ovulation by a rise in basal temperature, we made our estimations not only through basal oral temperature measurements but also by the use of a Dotest LH ovulation predictor test kit (Rohto Pharmaceutical, Japan). This kit accurately detects the subject's luteinizing hormone (LH) surge by measuring their urinary LH concentration. The subjects were verbally told to test their urine right after waking up in the morning. They continued testing their urine every morning until the test indicated that they had a high concentration of LH, reflecting an LH surge, which predicted the subsequent occurrence of ovulation (Varma et al. 1983). The luteal phase and the follicular phase were defined as a period from the estimated date of ovulation to menses and from menses to the estimated date of ovulation, respectively.

Experimental procedure

The experimental procedure was designed by referring to methods of our previous studies (Miyamura et al. 1992; Ishida et al. 2000; Sato et al. 2000).

Voluntary exercise and passive movement

Subjects sat with their backs against an experimental chair with an electrogoniometer attached to the right knee joint during the experiment. During brief voluntary exercise, two weight belts, each equivalent to about 2.5% of subject's body mass, were bound around each ankle. These weights were given to equalize the relative load to muscles among the subjects. The subjects extended and relaxed both lower legs in an alternating pattern from $\sim 110^\circ$ to 20° with an anatomically flexed position defined as 0° . The start of this exercise was signaled by the experimenter's voice before the start of inspiratory periods, and the exercise was made up of sets which continued for 20 s. Each set was 1 s and consisted of an extension and relaxation of first the right limb and then the left limb. The starting point, just before the start of the inspiratory periods, was determined by the respiratory flow curve monitored on an oscilloscope. Subjects were instructed to keep the upper body as still as possible.

Brief passive movement was achieved without weights by the experimenter alternately pulling ropes that were connected to the subject's ankles at the same pace, for the same length of time, and in the same posture as in the brief voluntary exercise. All subjects were directed to relax and not to resist the motion and care was taken to immobilize the body as much as possible to avoid motion artifacts.

Protocol

Preliminary testing was carried out to familiarize the subjects with the experimental procedures. The subjects practiced the brief voluntary exercise and the brief passive movement several times so as not to respond suddenly to experimenter's voice and the movement. The actual experiment was performed at least 2 h after each

subject's last meal on a day different from the preliminary testing once for men and twice for women – once during the luteal phase and once during the follicular phase. The women participated in the experiment during the luteal and follicular phases which were also chosen in a random order. Each mode of brief voluntary exercise and passive movement was conducted after the subjects' HR and respiration were stable. Both brief voluntary exercise and passive movement were repeated seven times. To avoid a sequence effect, all the subjects performed brief voluntary exercise and passive movement in a random order. Finally, to evaluate actual exercise intensity during voluntary exercise, long voluntary exercise was conducted one time for 3 min in the same way as brief voluntary exercise, and the mean of the last 30 s (STD; 3 min steady-state value) of every cardiorespiratory parameter was analyzed. All parameters were measured in the same way as in brief voluntary exercise.

Measurements

Inspiratory minute ventilation (V_I), tidal volume (V_T), inspiratory and expiratory period, and partial pressure of end-tidal carbon dioxide ($P_{ET}CO_2$) were measured by the breath-by-breath technique. A hot-wire flowmeter (Minato Ika-gaku, RF-H, Japan) was attached to a respiratory face mask. It was calibrated prior to each experiment using a 2-l calibration pump at different flow rates. The dead space of the respiratory face mask was about 100 ml. Respiratory gases were sampled using a thin vinyl tube (inner diameter 1 mm) inserted into the face mask, with the tip being positioned as close to each subject's mouth as possible. $P_{ET}CO_2$ was calculated from end-tidal $CO_2\%$, which was obtained by analyzing gas samples being drawn continuously through the vinyl tube with the use of a gas analyzer (Minato Ika-gaku, MG-360, Japan). HR was measured beat-to-beat from the R spike using an electrocardiogram connected to a bioamplifier (Nihon Kohden, AB-621G, Japan).

All ventilatory and ECG signals were continuously displayed on the screen of an oscilloscope. They were converted from analogue to digital using an A-D converter (Canopus, ADX-98H, Japan) at a sampling frequency of 100 Hz throughout one set of voluntary exercise and passive movement. V_T was determined by digitally integrating the airflow signals. Respiratory frequency (f) was calculated from total respiratory time. V_I was obtained as the product of V_T and f . These data were stored on a hard disk unit, and analyzed afterwards on a personal computer (NEC, PC-9821Xa, Japan).

Data analysis and statistics

Measured values were expressed with means (SE). First, breath-by-breath and beat-to-beat data were aligned with the onset of brief voluntary exercise and passive movement and linearly interpolated between each breath and beat to yield data points at 1-s intervals. Then the mean values were calculated for each subject. Thereafter, the mean values for men, the luteal phase, and the follicular phase were computed from the average values of the individuals. The values for women were defined as the average values of the luteal and follicular phases. From the above analyses, we obtained absolute changes during brief voluntary exercise and passive movement for women and men. We also calculated the increasing rates of V_I and HR. They were obtained by dividing STD by resting values (Rest) and the values were defined as an index of exercise intensity. Rest was defined as the averages of the 30-s values before brief voluntary exercise and passive movement.

Second, we calculated relative changes of V_I and HR (ΔV_I and ΔHR) during brief voluntary exercise and passive movement for women and men. ΔV_I and ΔHR in brief voluntary exercise were expressed as a fraction (%) of absolute changes to STD. In this case STD was defined as 100%. ΔV_I and ΔHR in brief passive movement were obtained by calculating a ratio (%) of absolute changes to resting values (Rest), which was defined as 0%. ΔV_I and ΔHR

were defined as ventilatory and HR responses at the onset of voluntary exercise and passive movement in the present study. In addition, response time (RT) was calculated to investigate the kinetics of V_I and HR by referring to the methods reported by Ishida et al. (2000). They obtained RT by calculating the time to reach one-half of the gain, which was the value of the relative change at 15 s after the start of exercise and movement. In the present study, RT was defined as the time to reach one-half of the differences between ΔV_I at 15 s and ΔV_I at 0 s, and between ΔHR at 15 s and ΔHR at 0 s. To confirm whether or not absolute changes were significant when compared to Rest, one-way ANOVA with repeated measures was conducted and Dunnett's *t*-test (post hoc) was carried out for parameters in which significant differences were recognized. To evaluate differences between the luteal and follicular phase, a Wilcoxon signed rank test was used. In comparing women with men, Mann-Whitney's *U* test was used. The comparisons between the luteal and follicular phase and between women and men consisted of three analyses: (1) comparing ΔV_I and ΔHR , (2) comparing Rest, STD, and the increasing rate, and (3) RT.

Finally, to investigate whether or not gender differences were recognized in the relationship between ΔV_I and ΔHR , we calculated the averages of 20 s ΔV_I and ΔHR values ($a\Delta V_I$ and $a\Delta HR$) for brief voluntary exercise and passive movement for each subject, displayed them as a scatter plot, and performed linear regression and correlation analysis. These statistical analyses were calculated by computer software (SPSS 10.0, SPSS) and the level of significance (significant *P* level) was set at 5%.

Results

Absolute changes

Figure 1 shows absolute changes of V_I and HR during brief voluntary exercise and passive movement in the luteal and follicular phases. Both V_I and HR significantly ($P < 0.05$) increased in both phases at 1 s after the onset of brief voluntary exercise and passive movement, compared with Rest. $P_{ET}CO_2$ did not significantly change in either phase from Rest [luteal phase: 37.6 (1.0) mmHg, means (SE); follicular phase: 37.7 (1.0) mmHg] during brief voluntary exercise. Similar results were observed during brief passive movement, when Rest was 37.5 (0.67) mmHg in the luteal phase and 37.3 (1.3) mmHg in the follicular phase.

Figure 2 indicates absolute changes of V_I and HR during brief voluntary exercise and passive movement in women and men. V_I in the female group significantly rose from 6.98 (0.43) to 8.92 (0.53) $l\ min^{-1}$ at 1 s after the onset of brief voluntary exercise. Similarly, a significant increase in V_I in the male group was recognized at 1 s after the onset of brief voluntary exercise, compared with Rest [from 8.27 (0.35) to 10.1 (0.60) $l\ min^{-1}$]. $P_{ET}CO_2$ did not significantly change in either gender when compared with Rest [women: 37.7 (0.84) mmHg, men: 39.1 (1.1) mmHg]. A significant absolute change in V_I was observed at 1 s after the onset of brief passive movement for women and at 2 s for men, compared with Rest [women: from 6.49 (0.32) to 7.43 (0.46) $l\ min^{-1}$, men: from 7.50 (0.29) to 9.12 (0.48) $l\ min^{-1}$]. HR significantly increased at 1 s after the onset of brief voluntary exercise in both genders, compared with Rest [women: from 67.2 (3.6) to 76.4 (3.7) $beats\ min^{-1}$,

Fig. 1 Absolute changes in minute inspiratory ventilation (\dot{V}_I) and heart rate (HR) during brief voluntary exercise (Voluntary; *left*) and passive movement (Passive; *right*) in luteal and follicular phases (*Dashed line* luteal phase, *solid line* follicular phase). Values are expressed as means (SE)

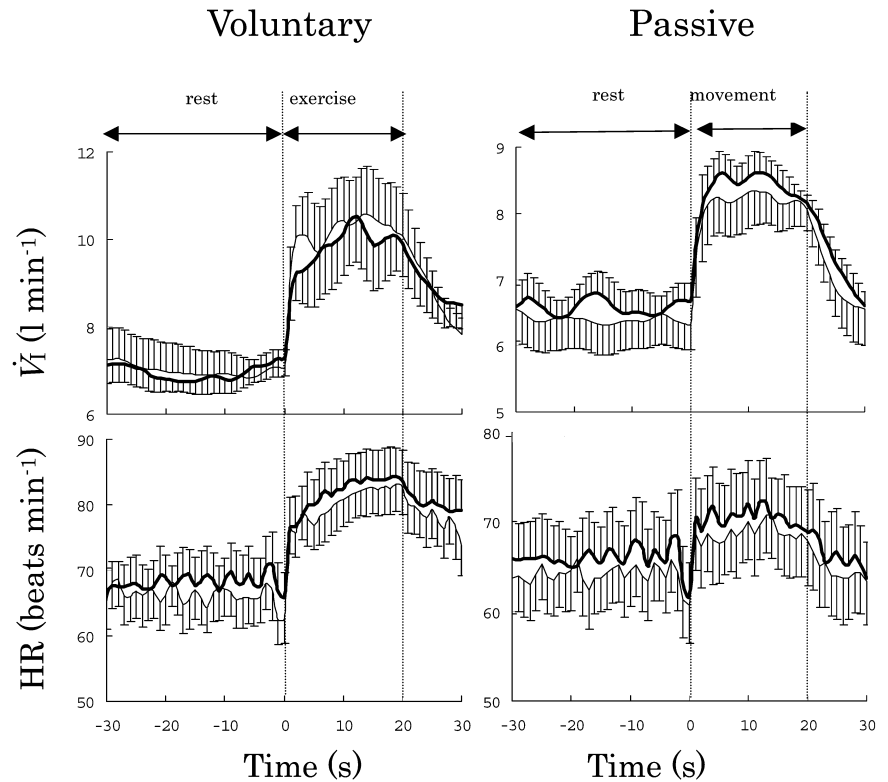
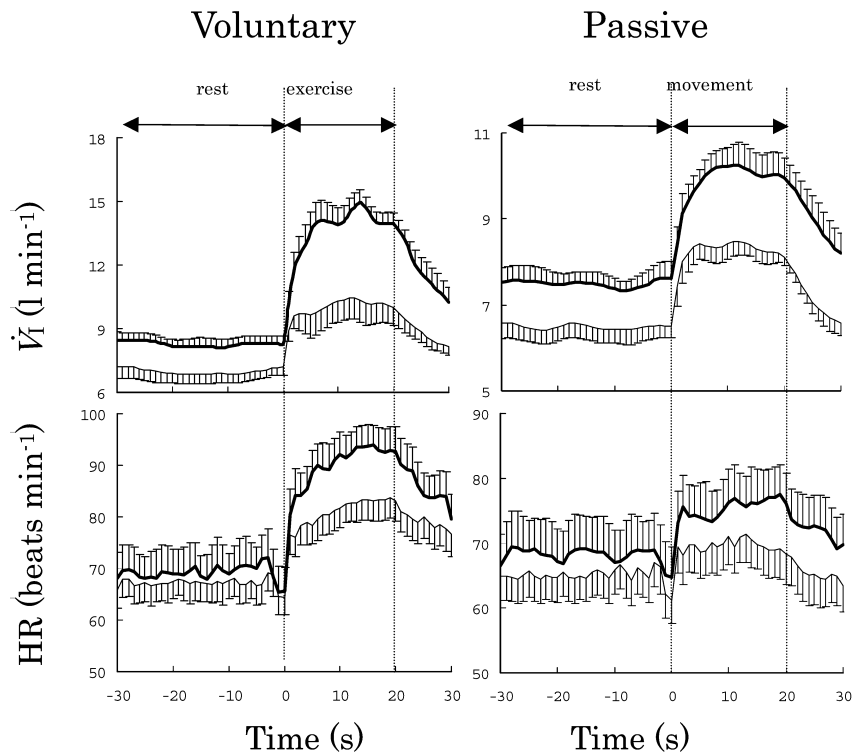


Fig. 2 Absolute changes in \dot{V}_I and HR during brief voluntary exercise and brief passive movement in women and men (*Dashed line* women, *solid line* men). Values are expressed as means (SE)



men: 69.2 (4.8) to 80.4 (4.9) beats min^{-1}]. On the other hand, during brief passive movement, a significant absolute change in HR was observed at 1 s after the onset of brief passive movement in the female group and at 2 s in the male group, compared with Rest

[women: 65.0 (3.8) to 69.5 (4.1) beats min^{-1} , men: from 68.1 (5.1) to 75.6 (4.9) beats min^{-1}]. No significant changes were detected for P_{ETCO_2} when compared with Rest [women: 37.4 (0.67) mmHg, men: 38.1 (1.2) mmHg].

Rest, STD, and the increasing rate

Table 2 describes Rest, STD, and the increasing rate of V_I and HR during voluntary exercise. There was no significant difference in Rest of V_I between the luteal and follicular phases [luteal phase: 7.00 (0.56) $l\ min^{-1}$, follicular phase: 6.96 (0.33) $l\ min^{-1}$]. Similarly, significant luteal–follicular differences were not recognized for STD or for the increasing rate of V_I . Rest of V_I in women was not significantly different from that in men. In addition, although there was a gap in the increasing rate of V_I between women and men, the gap was not significant. However, a significant male–female difference was recognized in STD of V_I [women: 13.1 (1.2) $l\ min^{-1}$, men: 19.8 (2.4) $l\ min^{-1}$, $P < 0.05$]. No luteal–follicular or male–female differences were detected in any calculation related to HR.

Rest of V_I and HR during brief passive movement were similar between the luteal and follicular phases [V_I ; luteal phase: 6.39 (0.44) $l\ min^{-1}$, follicular phase: 6.59

(0.28) $l\ min^{-1}$, HR; luteal phase: 64.0 (4.0) beats min^{-1} , follicular phase: 66.0 (4.2) beats min^{-1}]. There were no significant differences in Rest of V_I or HR during brief passive movement between women and men [V_I ; women: 6.49 (0.32) $l\ min^{-1}$, men: 7.50 (0.29) $l\ min^{-1}$, HR; women: 65.0 (3.8) beats min^{-1} , men: 68.1 (5.1) beats min^{-1}]. No luteal–follicular or male–female differences in $P_{ET}CO_2$ at rest were detected in either brief voluntary exercise or passive movement.

Relative changes

Figure 3 identifies relative changes of V_I and HR (ΔV_I and ΔHR) during brief voluntary exercise and passive movement in the luteal and follicular phases. No significant luteal–follicular differences were detected in any of the parameters.

Similarly, ΔV_I and ΔHR in the female group and in the male group are indicated in Fig. 4. Except for the

Table 2 Average of minute inspiratory ventilation (V_I) and heart rate (HR) at rest during brief voluntary exercise and at steady state during 3 min of voluntary exercise. Values are means (SE). Rest Average of the resting value for 30 s before the brief voluntary

exercise, STD average of steady state value during last 30 s of 3 min of voluntary exercise (long voluntary exercise), Increasing rate STD/Rest·100

	V_I			HR		
	Rest ($l\ min^{-1}$)	STD ($l\ min^{-1}$)	Increasing rate (%)	Rest (beats min^{-1})	STD (beats min^{-1})	Increasing rate (%)
Follicular	6.96 (0.33)	13.2 (1.5)	189.2 (17.6)	68.2 (4.0)	87.4 (6.2)	128.6 (6.5)
Luteal	7.00 (0.56)	13.0 (1.0)	188.6 (10.7)	66.2 (4.1)	85.9 (4.6)	130.7 (5.0)
Women	6.98 (0.43)	13.1 (1.2)*	188.5 (12.7)	67.2 (3.6)	86.6 (4.9)	129.5 (4.7)
Men	8.27 (0.35)	19.8 (2.4)	238.6 (26.5)	69.2 (4.8)	99.6 (6.8)	147.0 (13.2)

* $P < 0.05$ Women differ from men

Fig. 3 Luteal–follicular comparisons of relative changes in ventilation and heart rate (ΔV_I and ΔHR) during brief voluntary exercise and passive movement. ΔV_I and ΔHR , the change in V_I and HR when the steady-state value (STD), are defined as 100% for voluntary exercise and the resting value (Rest) is defined as 0% for passive movement (Dashed line luteal phase, solid line follicular phase). Values are expressed as means (SE)

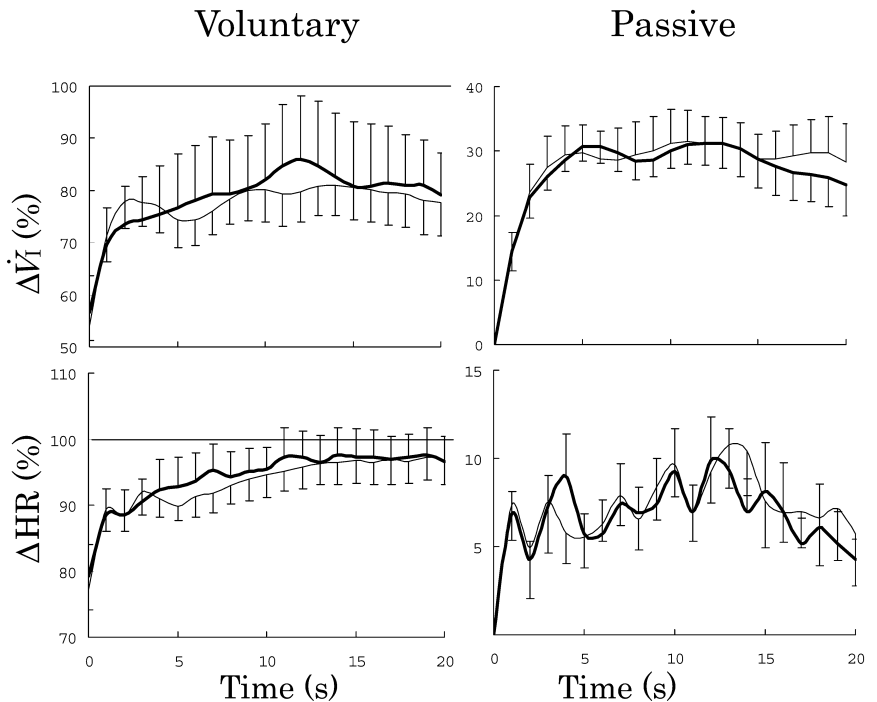
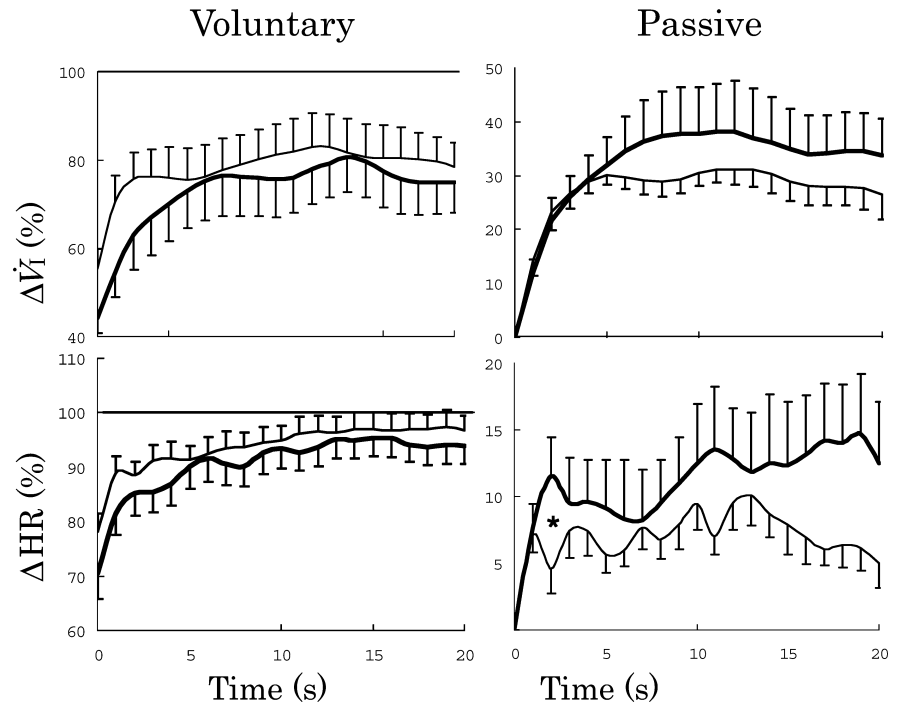


Fig. 4 Male–female comparisons of relative changes in ventilation and heart rate during brief voluntary exercise and brief passive movement. * $P < 0.05$ Women differ from men (Dashed line women, solid line men). Values are expressed as means (SE)



point marking 2 s in the comparison between women and men for ΔHR in brief passive movement [women: 4.6 (1.9)%, men: 11.5 (2.9)%, $P < 0.05$], no significant male–female differences were detected in any of the parameters.

Response time

Figure 5 shows the response time (RT) of V_I and HR. RT of V_I in the luteal phase during brief voluntary exercise [1.96 (1.06) s] and brief passive movement [1.37 (0.33) s] was not significantly different from that in the follicular phase during brief voluntary exercise [1.17 (0.51) s] or brief passive movement [1.30 (0.35) s]. No luteal–follicular difference in RT of HR was detected during either brief voluntary exercise [luteal phase: 1.24 (0.30) s, follicular phase: 1.97 (0.61) s] or brief passive movement [luteal phase: 1.01 (0.38) s, follicular phase: 1.20 (0.51) s]. There were no significant differences in RT of V_I or HR during brief voluntary exercise between women and men [V_I ; women: 1.57 (0.48) s, men: 2.19 (0.59) s, HR; women: 2.10 (0.55) s, men: 2.43 (0.54) s]. In addition, when comparing them between women and men during brief passive movement, no significant differences were observed [V_I ; women: 1.31 (0.33) s, men: 1.87 (0.56) s, HR; women: 0.90 (0.35) s, men: 1.87 (1.23) s].

Relationships between ventilatory and HR responses

Figure 6 represents the results of calculating the averages of ΔV_I and ΔHR ($a\Delta V_I$ and $a\Delta HR$) during brief voluntary exercise and passive movement for each sub-

ject, displaying $a\Delta V_I$ and $a\Delta HR$ as a scatter plot, and, additionally, performing a linear regression and correlation analysis between them. In brief voluntary exercise, significant positive correlations between $a\Delta V_I$ and $a\Delta HR$ were found in both genders [women: $r = 0.92$; $P < 0.01$, men: $r = 0.82$; $P < 0.05$]. No significant male–female differences were observed between regression lines [women: $a\Delta HR = 0.39 \cdot a\Delta V_I + 63.4$, men: $a\Delta HR = 0.37 \cdot a\Delta V_I + 64.3$]. In brief passive movement, no significant correlations were recognized but a tendency for correlation was found in women ($P = 0.07$).

Discussion

In the present study, ventilatory and HR responses at the onset of voluntary exercise and passive movement were evaluated using ΔV_I and ΔHR because, in spite of there being no significant differences, there were gaps in increasing rates of V_I and HR, indices of exercise intensity, between women and men particularly in the increasing rate of V_I during voluntary exercise. Similarly, these responses were evaluated in brief passive movement with ΔV_I and ΔHR . Two major findings were identified. First, ventilatory and HR responses at the onset of voluntary exercise and passive movement were not affected by the menstrual cycle when ΔV_I and ΔHR were regarded as an index of these responses. Second, these responses did not differ between women and men when ΔV_I and ΔHR in women were compared with those in men. Additionally, there were no significant differences in the response time (RT) as an index of V_I and HR kinetics between the luteal and follicular phases or between women and men.

Fig. 5 Luteal–follicular and male–female comparisons of response time (RT) as an index of the kinetics of \dot{V}_I and HR. It was calculated as the time taken to reach one-half of the difference between $\Delta\dot{V}_I$ and ΔHR at 15 s and that at 0 s (Grey bars Follicular phase, stippled bars luteal phase, clear bars women, black bars men). Values are expressed as means (SE)

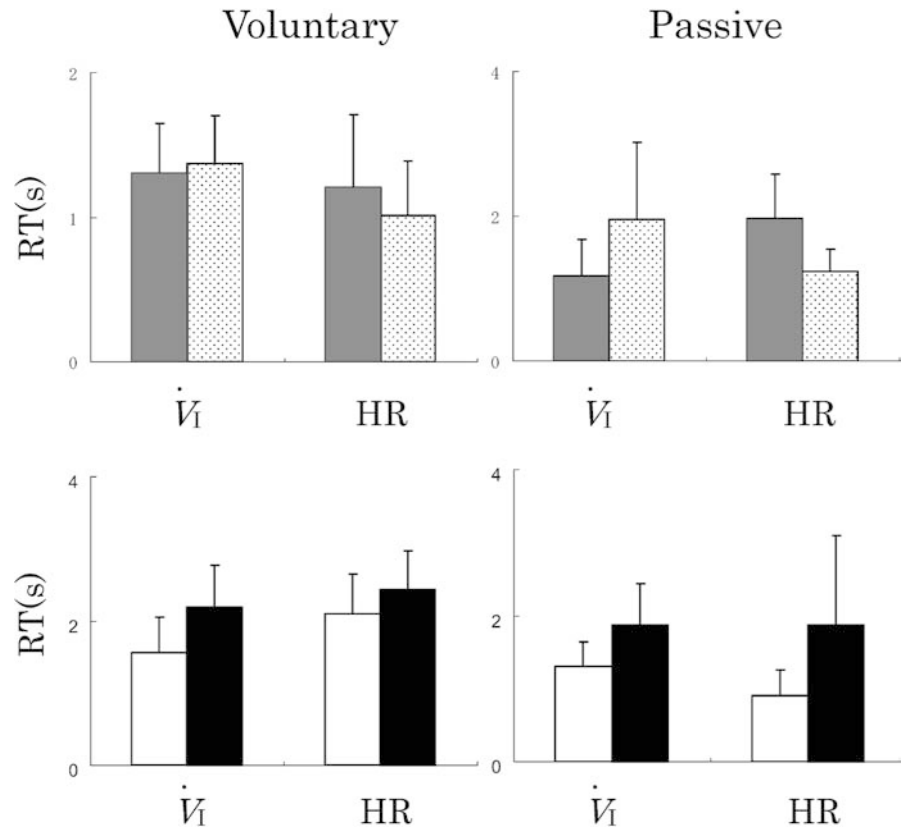
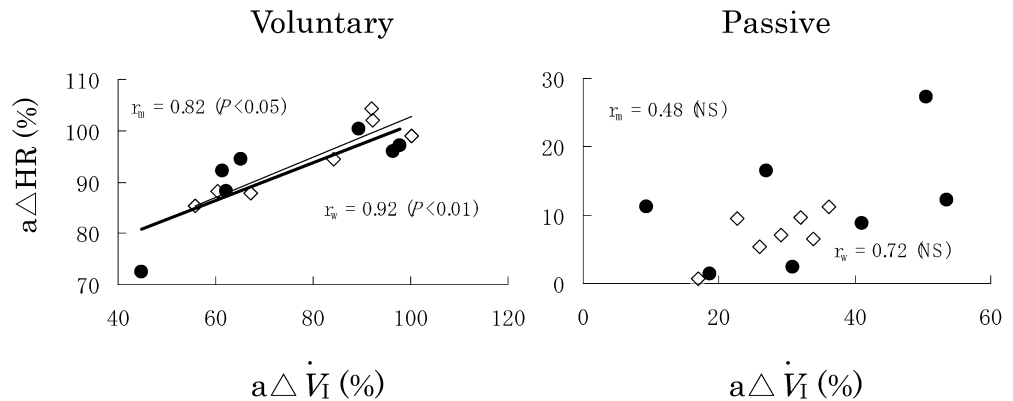


Fig. 6 Relationships between the average of individual subject's $\Delta\dot{V}_I$ ($a\Delta\dot{V}_I$) and that of individual subject's ΔHR ($a\Delta\text{HR}$) for the first 20 s of brief voluntary exercise and passive movement (Diamonds women, circles men). r_m is the coefficient of correlation in men; r_w , coefficient of correlation in women. Dashed line shows linear regression in women: $a\Delta\text{HR} = 0.39 \cdot a\Delta\dot{V}_I + 63.4$; solid line shows linear regression in men: $a\Delta\text{HR} = 0.37 \cdot a\Delta\dot{V}_I + 64.3$. (NS Not significant)



Effect of menstrual cycle

In the present study, there were no significant differences in resting ventilation or P_{ETCO_2} between the luteal and follicular phases. This result does not agree with many reports that say resting ventilation was elevated and resting PCO_2 (P_{ETCO_2} , arterial PCO_2 , or alveolar PCO_2) was lower during the luteal phase of the menstrual cycle (Regensteiner et al. 1989; Tatsumi et al. 1995; Beidleman et al. 1999; Loeppky et al. 2001). However, several studies (White et al. 1983; Chen and Tang 1989; Edwards et al. 1996) do not report any significant luteal–follicular differences in resting ventilation. Among them, White et al. (1983) identified significantly lower resting P_{ETCO_2} in the luteal phase compared with the follicular

phase. In contrast, Edwards et al. (1996) observed no significant difference in resting P_{ETCO_2} between the luteal and follicular phases. Although, at present, we cannot explain this discrepancy based on the physiological backgrounds, the differences in experimental designs may have led to this discrepancy. In addition, the present study observed no significant luteal–follicular differences in resting HR. This result coincides with studies of Edwards et al. (1996), whereas Hessemer and Brück (1985) observed significantly higher resting HR in the luteal phase than in the follicular phase. Further investigation is needed about the effect of the menstrual cycle on resting ventilation and HR.

In the present study, two forms of exercise were performed: one was voluntary exercise and the other was

passive movement. It is considered that brief voluntary exercise mobilizes not only peripheral reflex but also central command and that brief passive movement is a form of movement in which peripheral reflex functions almost exclusively (Miyamura et al. 1992; Ishida et al. 2000). Recently, Hayes et al. (2002) administered estrogen (17β -estradiol) to decerebrate male cats and examined the cardiovascular and ventilatory responses while stimulating parts related to central command and peripheral reflex for 60 s every 15 min. They reported that estrogen attenuated these responses to central command but not to peripheral reflex. However, no significant differences in ΔV_1 and ΔHR were observed between the luteal and follicular phases for either voluntary exercise or passive movement (Fig. 3). One possible reason for the discrepancy between the Hayes et al. (2002) study and the present study is related to the differences in experimental design. Their experiment dramatically increased the concentration of estrogen over a short of time by giving it to the male cats as a bolus. This type of increase may be necessary to facilitate the attenuating effect of estrogen on the cardiovascular and ventilatory responses to central command. They also suspect from their results that the effects of estrogen on neural functions are maximized by their approach. Another possible reason for this discrepancy is that the effect of this attenuation on ventilatory and heart rate responses is small over a short period of exercise and movement. That is, even an attenuated central command might be able to cause the cardiovascular and ventilatory responses observed at the onset of exercise. Ettinger et al. (1998) investigated whether cardiovascular and muscle sympathetic nerve activity (MSNA) responses differed between the menstrual and follicular phases when women performed 2 min of static handgrip exercise at 30% maximal voluntary contraction (MVC), and observed no influence of the menstrual cycle on HR response. However, further investigations about the effects of estrogen on cardiorespiratory responses are necessary.

Gender difference

In previous studies, it has been frequently reported that gender does not affect HR at AT or during maximal exercise in young people, whereas the results of studies about the effect of gender on minute ventilation at AT and maximal exercise have been conflicting (Younis et al. 1990; Ogawa et al. 1992; Helgerud 1994; Rickli et al. 1997; Nindl et al. 1998). In the present study, it was demonstrated, for the first time, that ventilatory and HR responses at the onset of voluntary exercise and passive movement did not differ between women and men.

To our knowledge, there have been no studies about the difference in ventilatory response between women and men either at the onset of exercise or during exercise over a 2- or 3-min period. However, Ettinger et al. (1996) compared women's cardiovascular and MSNA

responses with men's when subjects performed a 2-min static handgrip exercise at 30% MVC. The result was that the HR response of women was not different from that of men throughout the exercise. The results of the present study and Ettinger et al. (1996) indicate that ventilatory and circulatory responses to a short period of exercise and movement would not be affected by gender. In other words, it is suggested that an input from central command and peripheral reflex to the cardiorespiratory center would not differ between women and men when voluntary exercise and passive movement are performed for short amounts of time.

We investigated whether or not gender difference existed in the relationship between ventilatory response and HR response. As shown in Fig. 6, significant correlations between $a\Delta V_1$ and $a\Delta HR$ during brief voluntary exercise were recognized both in women ($r=0.92$, $P<0.01$) and in men ($r=0.82$, $P<0.05$), but not during brief passive movement. Fontana et al. (1993) observed significant positive correlations between the increase in V_1 and that in HR during the final 30 s of 3 min of static handgrip exercises at 25% and 30% MVC but not at 15% MVC. Their study and the present study demonstrate that a relationship like this is observed not only during static exercise for a few minutes but also at the onset of voluntary exercise and that it is not recognized unless exercise over a certain intensity is performed. However, the linear regression equation of brief voluntary exercise for women ($a\Delta HR = 0.39 \cdot a\Delta V_1 + 63.4$) was almost equal to that for men ($a\Delta HR = 0.37 \cdot a\Delta V_1 + 64.3$) (Fig. 6). We have no information to explain this point. Nevertheless, Fontana et al. (1993) suggest that the relationship between ventilatory response and HR response is caused by a considerable degree of coordination and integration of respiratory and cardiovascular functions at a central level, despite the possibility of a differential control. If so, it would be possible that this coordination and integration of respiratory and circulatory centers occurred to the same extent in women and men.

In conclusion, the present study aimed to clarify whether or not ventilatory and HR responses at the onset of voluntary exercise and passive movement differed (1) between the luteal and follicular phase and (2) between women and men. It has been found that they are not affected by the menstrual cycle and that these responses in women are similar to those in men.

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