Title

Effects of awareness of change in load on ventilatory response during moderate exercise

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Abstract: This study was designed to determine whether awareness of change in load alters ventilatory response during moderate exercise. Subjects performed two incremental exercise protocols on a cycle ergometer. The load was increased from 1.0 to 1.5 kp in steps of 0.1 kp every 3 min. Subjects were provided true information about the load in the control protocol and untrue information that the load would remain constant in the deception protocol. Slope of ventilation against CO₂ output was significantly lower in the deception protocol than control protocol. Integrated EMG (iEMG) and ratings of perceived exertion (RPE) were similar between the two protocols, but awareness of change in load was significantly attenuated by the deception protocol. However, there was no temporal coincidence between awareness and actual change in load. These results suggest that ventilatory response during moderate exercise depends not so much on RPE but mainly on awareness or attention that is closely connected to information detection.

Key words: Control of breathing; Exercise hyperpnea; Feedforward; Feedback; Afferent signals; Emotion; Homeostasis
1. Introduction

The relationship between ventilation ($\dot{V}_E$) and carbon dioxide output ($\dot{V}_{CO_2}$) during moderate exercise is close to a straight line and can be described by a linear regression equation with a correlation coefficient in excess of 0.9 (Clark et al., 1996). It has generally been assumed from this observation that $\dot{V}_E$ follows factors proportional or related to $\dot{V}_{CO_2}$ (Haouzi, 2006) and then prevents CO$_2$/H$^+$ disturbance in arterial blood (Whipp and Ward, 1998). However, the discussion on factors allowing $\dot{V}_E$ to increase in proportion to $\dot{V}_{CO_2}$ is still controversial (Whipp and Ward, 1998; Haouzi, 2006; Mitchell and Babb, 2006; Péronnet and Aguilaniu, 2006; Poon et al., 2007; Ward, 2007).

A feedforward mechanism involving parallel activation of motor and cardiorespiratory centers (‘central command’) has been classically known as one of the factors explaining cardiorespiratory responses during exercise (Krogh and Lindhard, 1913; Goodwin et al., 1972; Eldridge et al., 1981; Williamson et al., 2006). Recently, mental imagery of exercise at rest has been reported to increase cardiorespiratory responses (Decety et al., 1991; Thornton et al., 2001; Williamson et al., 2002). Thornton et al. (2001) used imagination of exercise at rest as a cognitive tool to dissociate peripheral neural signals from central command and showed that a significant component of the cardiorespiratory response to the imaged exercise could be generated in the absence of both movement feedback and an increase in CO$_2$ production. Likewise,
Williamson et al. (2002) showed that the magnitude of a central command-mediated cardiovascular response during imagined exercise at rest can be independent of actual force production and dictated more by an individual’s sense of effort that was estimated from ratings of perceived exertion (RPE) during the image. They also localize insular and anterior cingulate cortices as brain sites related to the effort-induced cardiovascular response. Based on these findings, it has been contended that central command-mediated response does not necessarily require the parallel activation of central motor command (Williamson et al., 2002) and it has been proposed that it is the sense of effort that drives the central command-mediated response (Williamson et al., 2006).

In actual exercise, unlike in the case of imagined exercise at rest, there are always feedback inputs to the central nervous system from the working muscle. Although the sense of effort is believed to derive from a copy (efference copy/corollary discharge) of the central motor command (Sperry, 1950; Von Host, 1954), it has recently been suggested that somatosensory feedback from the working muscles during exercise modulates the central motor command (Williamson et al., 2006; Matsuura et al., 2006, 2007; Amann and Dempsey, 2008; Amann et al., 2008) and that the relationship between central motor command and sense of effort is altered by peripheral information (Carson et al., 2002; Proske, 2005). These collectively suggest that during actual exercise afferent signals from the working muscles may affect the formation of the
sense of effort. However, since change in muscle activity or workload that is responsible for the afferent signals can be perceived, there is the possibility that awareness of the change in workload will have an effect on the sense of effort and consequently on the central command-mediated response. Therefore, in the present study, we investigated whether awareness of change in load alters ventilatory response (slope of $\dot{V}_E$ against $\dot{V}_{CO_2}$ ($\dot{V}_E / \dot{V}_{CO_2}$ slope)) during moderate exercise. Since breathing can be controlled by both conscious and automatic factors (Cherniack, 2007), it is conceivable that ventilatory response to the imagined exercise at rest will involve voluntary hyperpnea. Furthermore, although one can imagine the sense of effort without actual exercise, one can never assess the awareness of change in load without performing actual exercise. Thus, in order to manipulate the subject’s awareness of change in load during exercise, we used ‘deception’ to divert the subject’s attention to the load during the exercise.

2. Methods

Seven healthy male subjects provided written informed consent before participation in this study, which was approved by the Ethics Committee of Hokkaido University Graduate School of Education. The subject’s age, height and body mass (mean ± SEM) were 21.1 ± 0.6 years, 170.7 ± 1.8 cm, and 69.7 ± 2.6 kg, respectively. Each subject was instructed to refrain from taking alcohol and caffeine and from participating in strenuous exercise for a period of 24 hours prior to each test.
Each subject performed two protocols (‘control’ and ‘deception’) on a built-in computer controlled, electromagnetically braked cycle ergometer (POWERMAX-VII, Combi, Japan). The order of these tests was randomly assigned among the subjects. The interval between the two tests was 2-7 days, and trials for each subject were carried out at the same time of day. In both protocols, after a 5-min resting period sitting on the cycle ergometer, the subjects warmed up for 5 min at a resistive load of 0 kp and then started incremental exercise. Subjects were constrained to maintain pedalling rate at 80 rpm during the warming-up and incremental exercise with the aid of a metronome. This relatively rapid pedalling rate was adopted since it has been reported that fast limb movement attenuated the muscular sense (Collins et al., 1998). The electrical signals of pedalling frequency were recorded on a computer via an analog-digital converter (MacLab/8s, AD Instruments, Bella Vista, NSW, Australia) and averaged with respect to each load. The incremental exercise test started at a load of 1.0 kp. The load was imperceptibly increased from 1.0 to 1.5 kp in steps of 0.1 kp every 3 min. In the control protocol, subjects were correctly informed that the load would be progressively increased to the moderate intensity after 5 min of unloaded warming-up exercise. In the deception protocol, subjects were told that the load would be held at a low intensity after 5 min of unloaded warming-up exercise, while they were actually made to exercise in the same loading configuration as the control protocol. Duration of exercise was preinformed and elapsed time was also informed during both protocols.
In both protocols, awareness of change in load was assessed as follows: subjects were asked to press a button attached to the handlebar of the cycle ergometer when they were aware of or felt an increase in load. The electrical signals from the button were recorded on the above computer and analog-digital converter. We also asked the subjects to assess RPE using the Borg scale. Measurement of RPE was conducted only just before the end of exercise in order to prevent the subject’s attention to change in load from being the same in the two protocols.

Ventilation and gas exchange variables were measured continuously breath-by-breath using a respiratory gas analyzer (AE-280S, Minato Medical Science, Osaka, Japan) throughout 5 min of rest and exercise. Inspired and expired flows were measured using a hot-wire flow meter that is linear with respect to a flow range of 0 - 600 l · min⁻¹. A zirconium sensor and infrared absorption analyzer were used to analyze the inspired and expired fractions of O₂ and CO₂, respectively. The flow meter and gas analyzer were calibrated prior to each test with a standard 2-l syringe and precision reference gas (O₂: 15.17%, CO₂: 4.92%). Values for $\dot{V}_E$, $\dot{V}_{CO_2}$, and end-tidal CO₂ pressure ($P_{ET,CO_2}$) were calculated from 20-s averages of the breath-by-breath data. Arterial CO₂ pressure ($P_{a,CO_2}$) was predicted from the $P_{ET,CO_2}$ using the equation obtained by Jones et al. (1979).

A surface electromyogram (EMG) was recorded from the left vastus lateralis (at about one third of the perpendicular distance from the superior border of the patella to
the greater trochanter) using a bipolar EMG sensor (SX230, Biometrics Ltd., Gwent, Wales, UK; interelectrode distance of 20 mm) during each exercise trial. Before attachment of the EMG sensor, the skin was shaved and cleaned with alcohol in order to reduce skin impedance. The electrodes were fixed longitudinally over the muscle belly. To facilitate further recording from the same site during the subsequent visit, electrode placement was marked on the skin surface. The ground electrode was placed over the styloid process of the right wrist. The raw EMG data were amplified using an amplifier imbedded in the EMG sensor (band width = 20-450 Hz: common mode rejection ratio, CMRR > 96 dB; input impedance > $10^{13}$ Ω; gain = 1,000) and converted into digital signals at a sampling rate of 1000 Hz using the above analog-digital converter. The data were filtered using a band-pass Finite Impulse Response filter with cut-off frequencies of 20 to 450 Hz and full-wave-rectified and then integrated (iEMG) by using analysis software (Acknowledge, BIOPAC Systems, Goleta, CA, USA). The iEMG was averaged at one-minute intervals and normalized as a percentage of the value during the 1st min of incremental exercise.

Results are presented as means ± SEM. Pearson’s product-moment correlations were determined in order to examine the relationships of $\dot{V}_E$ - $\dot{V}_{CO_2}$ and iEMG - time in the two protocols. A paired t-test was used to compare the slope and intercept of the regression line for both conditions. Differences in variables (pedal frequency, $\dot{V}_{CO_2}$, $\dot{V}_E$, $Pa_{CO_2}$, iEMG) between the two protocols with time were evaluated by two-way
ANOVA with repeated measures. RPE and frequency of subject’s awareness of change in load for both protocols were compared by a nonparametric test (Wilcoxon’s signed rank test) because normality of those data was not identified by normality tests. A value of $P < 0.05$ was regarded as statistically significant.

3. Results

Fig. 1 shows change in pedal frequencies during exercise in the two protocols. No significant exercise protocol effect was found in pedal frequencies. Pedalling frequencies averaged during control and deception protocols were $80.8 \pm 0.4$ and $81.1 \pm 0.3$ rpm, respectively.

Charts in Fig. 2 show the number of times an individual subject pressed the button when he was aware of or felt change in load during the two protocol exercises. That subject pressed the button 23 times and 3 times in the control and deception protocols, respectively. There was a significant difference between the frequencies of awareness in the two protocols ($P < 0.05$, Table 1). However, as can be seen from Fig. 2 and Table 1, the time at which subjects were aware of or felt an increase in load did not coincide with the time at which the load actually changed. On the other hand, no significant difference between the two protocols was found in RPE (Table 1).

Fig. 3 shows time courses of $\dot{V}_{\text{CO}_2}$, $\dot{V}_E$, and $\text{Pa}_\text{CO}_2$ during exercise in the two protocols. No significant exercise protocol effect was found for either $\dot{V}_{\text{CO}_2}$ or $\text{Pa}_\text{CO}_2$. 
Although no protocol difference was found in $V_E$, $V_E$ tended to be lower with an increase in load in the deception protocol than in the control protocol. Accordingly, as shown in Fig. 4, the slope of the relationship between $\dot{V}_E$ and $\dot{V}_{CO_2}$ was found to be significantly lower in the deception protocol than in the control protocol ($P < 0.01$, Table 1) and the intercept was significantly higher in the deception protocol ($2.12 \pm 0.77 \text{ l/min}$) than in the control protocol ($0.04 \pm 0.18 \text{ l/min}$) ($P < 0.05$).

Fig. 5 shows change in iEMG during exercise under the two experimental conditions. No significant exercise protocol effect was found for iEMG. The iEMG increased in an approximately linear manner with time about 3 min after the start of exercise. There was no difference in the slope of the relationship of iEMG - time between the two protocols.

4. Discussion

The present study showed that RPE during moderate exercise was not influenced by deceptive information. However, awareness of change in load was attenuated by the deceptive information and $\dot{V}_E/\dot{V}_{CO_2}$ slope during the exercise was significantly lower in the deception protocol than in the control protocol.

It has generally been assumed that $\dot{V}_E$ follows factors proportional or related to $\dot{V}_{CO_2}$ (Haouzi, 2006). For instance, CO$_2$ flow to the central circulation has been thought to drive $\dot{V}_E$ (Wasserman et al., 1974; Wasserman and Whipp, 1983; Schneider
and Berwick, 1998). However, since $\dot{V}_{CO_2}$ at the mouth is not equal to CO$_2$ flow and changes in $\dot{V}_{CO_2}$ at the mouth in response to exercise do not reflect those in CO$_2$ flow (Sun et al., 2001), this hypothesis has been denied (Péronnet and Aguilaniu, 2006).

Alternatively, chemoreceptors and/or mechanoreceptors in the working muscles have been proposed to link the ventilatory control (McCloskey and Mitchell, 1972; Mense and Stahnke, 1983; Kaufman and Rybicki, 1987; Kaufman and Forster, 1996; Oelberg et al., 1998; Haouzi, 1999, 2006). In the present study, since the magnitude, pattern, and duration of the load imposed by the two protocols were the same, it is likely that there was no difference in mechanical and chemical stimuli to peripheral afferents (e.g. group III and IV) between the two protocols. In fact, there was no difference in pedal frequency and iEMG that reflect muscle activity between the two protocols. Furthermore, $Pa_{CO_2}$, which is involved in arterial chemoreceptors and perhaps group IV neural afferents (Oelberg et al., 1998), was not different between the two protocols. Therefore, those peripheral factors cannot explain the difference in the $\dot{V}_E/\dot{V}_{CO_2}$ slope between the two protocols, suggesting that a central factor is responsible for the observed difference in ventilatory response.

In the present study, there was no difference in RPE between the two protocols. RPE has frequently been used as an index of the sense of effort. Williamson et al. (2002) showed that when the sense of effort (RPE) was increased by mental imagery of exercise at rest, cardiovascular responses were elevated even though there was no
afferent feedback from the muscles. Based on this result, Williamson et al. (2006) proposed that it is the sense of effort that drives the central command-mediated cardiovascular response. Unlike the suggestion of Williamson et al. (2006), our results suggest that sense of effort cannot explain the observed change in the $\dot{V}_E / \dot{V}_{CO_2}$ slope.

The sense of effort is believed to arise centrally as a result of a corollary discharge of central motor command into the sensorium (Sperry, 1950; Von Host, 1954). In the present study, there was no difference in iEMG, which has been interpreted to reflect central motor command (Amann et al., 2008), between the two protocols. Furthermore, although it has been suggested that the relationship between central motor command and sense of effort is altered by peripheral information concerning the state of the contractile apparatus (Carson et al., 2002; Proske, 2005), states of the working muscle were similar in the two protocols in the present study as mentioned above. Thus, both central motor command and peripheral state must have been similar for both protocols and, as a result, there could be no difference in the sense of effort that is estimated from RPE between the two protocols.

In the present study, there was a significant difference in the awareness of change in load between the two protocols. It has been suggested that $\dot{V}_E$ strongly correlates with RPE (Robertson et al., 1986). Thus, if $\dot{V}_E$ was increased consciously by the awareness, its increase must have been reflected in RPE. However, since there was no difference in RPE between the two protocols, the awareness could have affected $\dot{V}_E$.
independently of RPE. That is, $\dot{V}_E$ would be modulated by the awareness not consciously but unconsciously. However, despite the fact that frequency of awareness was higher in the control protocol than in the deception protocol, the time at which subjects were aware of or felt an increase in load did not coincide with the time at which the load actually changed. This suggests that the subjects did not accurately perceive the afferent feedback from the working muscle and that discrimination of muscular exertion is unrelated to increase in $\dot{V}_E$.

It is thought that attention increases the sensitivity of information detection and that information to which attention is not directed does not surface to the conscious mind. In fact, the effect of conscious factors on exercise hyperpnea has been emphasized (Cherniack, 2007). Hence, we tried to divert the subject’s attention to change in load by using ‘deception’. Therefore, the observed decrease in awareness seemed to reflect the decrease in attention. Attention is one of the stresses that elicit emotion. Such sensory information, for instance, a feeling of fear, is conveyed to the hypothalamus via the amygdala (LeDoux et al., 1988; LeDoux, 2003). The hypothalamus is not only known to control the autonomic nervous system but has also been shown to induce a central command-mediated ventilatory response (Eldridge et al., 1981). The insular cortex and anterior cingulate cortex, which have been shown by Williamson et al (2002) to be related to the central command-mediated cardiovascular response, are also parts of the brain involved in emotional reaction as well as the
amygdala. Although we cannot verify the neuroanatomical structure, emotional change induced by awareness or attention would activate these brain sites and consequently affect the ventilatory response. Another possible factor explaining the observed difference in ventilatory response in the present study is involvement of efference copy/corollary discharge (Sperry, 1950; Von Host, 1954). Poon et al. (2007) has proposed an internal model (see Poon and Merfeld (2005) for details) paradigm in which exercise hyperpnea is controlled by interaction between the efference copies and afferent inputs. In their model, exercise stimulus is not a factor directly generating a feedforward signal but a factor inducing mental percept that emerges from optimal sensorimotor integration. Since it has been suggested that mental percept is influenced by learning, experience, imagined exercise, and anticipation of exercise (Poon et al., 2007), mental percept (internal model) may have underestimated the metabolic needs during exercise due to the effect of deceptive information in the present study.

In conclusion, deceptive information about resistive load lowered the \( \dot{V}_E / \dot{V}_CO_2 \) slope during moderate exercise. Although RPE during the exercise was not influenced by the deceptive information, awareness of change in load was attenuated by the deceptive information. However, there was no temporal coincidence between the awareness and actual change in load. These results suggest that ventilatory response during moderate exercise depends not so much on RPE but mainly on awareness or attention that is closely connected to the information detection. Additionally, this
indicates that awareness or attention is an important function for the homeostasis of CO₂/H⁺ in arterial blood during exercise.
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Figure legends

Fig. 1. Change in pedal frequency during exercise performed under the control protocol
(open circles) and the deception protocol (filled circles). Data presented are means ± SEM.

**Fig. 2.** Charts showing the frequency of awareness of change in load during exercise under the two conditions in an individual subject. Dotted lines denote the time at which the load changed. Vertical solid lines denote the time at which the subject pressed the button when he was aware of or felt an increase in load. The first solid lines are marks to locate the start of the exercise (1.0 kp).

**Fig. 3.** Changes in carbon dioxide output ($\dot{V}_{CO_2}$), ventilation ($\dot{V}_E$), and arterial carbon dioxide pressure ($Pa_{CO_2}$) during exercise performed under the control protocol (open circles) and the deception protocol (filled circles). Data presented are means ± SEM (at 3, 6, 9, 12, 15 and 18 min).

**Fig. 4.** Relationship between ventilation ($\dot{V}_E$) and carbon dioxide output ($\dot{V}_{CO_2}$) obtained during exercise performed under the control protocol (open circles) and the deception protocol (filled circles). The relationship shown was obtained from mean values for the group. Data obtained in a nonsteady state (0 - 3 min, 1.0 kp) was excluded from this figure.
Fig. 5. Change in iEMG expressed as a percentage of the 1st min value during exercise performed under the control protocol (open circles) and the deception protocol (filled circles). Data presented are means ± SEM (at 3, 6, 9, 12, 15 and 18 min).
Table 1  Slope of ventilation against CO₂ output, ratings of perceived exertion (RPE), and the number of times subjects were aware of or felt changes in resistive load (Awareness) during exercise under the two protocols.

<table>
<thead>
<tr>
<th>Subject</th>
<th>$\dot{V}<em>E/\dot{V}</em>{CO_2}$ slope</th>
<th>RPE</th>
<th>Awareness</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td>Deception</td>
<td>Control</td>
</tr>
<tr>
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</table>

* P < 0.05, ** P < 0.01. P values refer to comparisons with control values.