Der folgende Artikel stellt eine gekürzte und ergänzte Version der Arbeit dar, für die PD Dr. Christina M. Spengler (Privatdozentin für Sportphysiologie an der ETH Zürich) der Wissenschaftliche Preis 2001 der Schweizerischen Gesellschaft für Sportmedizin verliehen wurde.

Die Redaktion

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Respiratory Control, Respiratory Sensations and the Effects on Exercise Performance

Zusammenfassung

Die Atmung wird sowohl in Ruhe als auch bei körperlicher Aktivität multifaktoriell, d.h. sowohl über Feedforward- als auch über verschiedene Feedback-Mechanismen reguliert. Zudem scheint der Atmungskontroller einerseits über relativ grosse Redundanz zu verfügen und andererseits ist er sogar lernfähig bis zu einem gewissen Grad. Während körperlicher Anstrengung kann einerseits eine erhöhte Atmungsanstrengung wahrgenommen werden, andererseits kann es aber auch zum unangenehmen Gefühl der Atemnot, des «Ausser-Atem-seins» kommen. Sowohl ein überhöhter Atmungsantrieb wie auch subjektive Empfindungen wie Atemnot können eine Ausdauerleistung negativ beeinflussen. Aber nicht nur diese Faktoren, auch die Ermüdung der Atmungsmuskulatur selbst, scheinen die Ausdauer zu vermindern. Über welche Mechanismen ein spezifisches Training des Atmungssystems einerseits unangenehme Empfindungen der Atmung reduzieren, andererseits auch die Ausdauerleistung verbessern könnte, wird im vorliegenden Artikel diskutiert.

Schlüsselwörter:
Atmungsregulation, Atemnot, Atmungsmuskulatur, Ausdauer

Résumé

La respiration est réglée de façon multifactorielle par divers mécanismes de «feed-forward» ainsi que de «feed-back», et ceci au repos aussi bien que durant l'activité physique. De plus, le système de régulation semble, d'une part, disposer d'un excès d'apport relativement grand et, d'autre part, être doué d'une certaine capacité d'apprentissage. Durant l'activité physique, d'une part, un effort respiratoire accru peut être perçu, mais on peut, d'autre part, également éprouver une gêne respiratoire désagréable, comme si l'on était essoufflé. L'endurance peut être influencée négativement aussi bien par une stimulation exagérée de la ventilation que par un sentiment subjectif de manque d'air. Mais pas seulement ces deux mécanismes, également la fatigue des muscles respiratoires elle-même semble diminuer l'endurance. Le présent article discute les mécanismes par lesquelles un entraînement spécifique du système respiratoire pourrait réduire les sentiments respiratoires désagréables et améliorer l'endurance.

Mots clés:
Régulation respiratoire, manque d'air, muscles respiratoires, endurance

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Introduction

Breathing is one of the few bodily functions that requires moment to moment regulation. Normally, breathing responds quickly to changes in metabolism (as with exercise for example) to regulate arterial blood gases but breathing is also affected by prevailing behaviors (e.g., speech, posture, sleep) and the environment (e.g., temperature, light). Neural control systems in the brainstem and forebrain enable both metabolic and behavioral demands to be met by integrating afferent information (e.g., from chemoreceptors and mechanoreceptors) and influencing efferent control of the respiratory muscles (Fig. 1).

During heavy exercise, for example, mechanoreceptors of muscles and joints are increasingly activated, chemoreceptors sense the lowering of the pH due to the production and accumulation of lactic acid in the blood (from anaerobic glycolysis), the increased body temperature activates central thermoreceptors etc. All these changes can add – to different degrees – to the increase of ventilation during exercise. In addition, ventilation can increase even more at high altitude where the oxygen partial pressure (P_{O2}) is lower than at sea level (at 5500 m above sea level, P_{O2} is reduced to half). In an attempt to supply the body with a «sufficient»

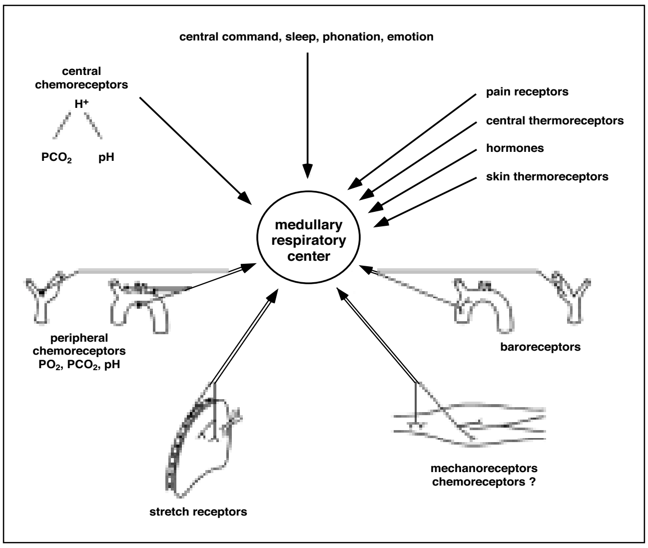

Figure 1: Central and peripheral inputs to the brainstem respiratory center.

amount of oxygen, minute ventilation is further increased automatically due to stimulation of (mostly) the peripheral chemoreceptors. This additional response may be dampened, however, due to the concomitantly occurring hyperventilation (with a decrease in CO_2-partial pressure, P_{CO_2}), such that a certain degree of oxygen-desaturation (depending on exercise intensity and altitude) remains.

As depicted in Figure 1, higher centers may interact with these receptor-mediated drives to breathe. These interactions can be of advantage, but also of disadvantage for a person. Advantageous examples are the respiratory pause during swallowing or the well-regulated airflow during talking. These most sophisticated interactions seem «normal» to us. Only during running, we are aware that it becomes more and more difficult to generate the appropriate airflow for talking and if the running speed is high enough, the ventilatory demand has increased such that airflow can not be restricted anymore to achieve the «slow» flows appropriate for speech. Eating during high intensity exercise becomes almost impossible as the high respiratory flows require mostly mouth breathing (the nasal resistance is too high) and the respiratory pause for swallowing can hardly be tolerated.

On the other hand, inputs from higher centers to the brainstem respiratory complex can also lead to inappropriate ventilation and therefore disadvantageous effects. Such disturbances may not only be of short duration, such as with hyperventilation resulting from fear or anger but hyperventilation may even become chronic, resulting in the so called «idiopathic, chronic hyperventilation syndrome» (Gardner, 1996). These patients may suffer from the symptoms described for acute hyperventilation, particularly during physical exertion which may also be accompanied by an increased sensation of breathlessness or dyspnea. Furthermore, this exaggerated ventilatory drive may compromise exercise performance.

Respiratory regulation at rest

Before taking a closer look at respiratory regulation during exercise, I would like to draw your attention to one aspect of resting respiratory regulation that might be of importance considering effects of ventilation on exercise performance. Normally, breathing is regulated breath by breath to achieve constant arterial blood gases. Voluntarily reduced tidal volumes, for example, are quantitatively compensated within the first breath subsequent to the voluntary manoeuver (Waurick et al., 1996). Mean arterial P_{CO_2} is probably the most tightly regulated respiratory variable with an average value of about 40 mmHgAlthough there are substantial differences between subjects – e.g., Shea et al. (1987a) observed end-tidal P_{CO_2} (P_{ETCO_2}) values ranging from 29 to 42 mmHg (average 37.6 mmHg) within 41 healthy adults under standardized, resting conditions – the variability within a subject between days, when measured at the same time of day, is only about 1–2 mmHg (Shea et al., 1987a). We have to be aware, however, that even subtle differences such as open vs. closed eyes, or noise vs. silence, can affect breathing (Shea et al., 1987b).

In addition to this variability, a circadian (i.e., 24 hour) rhythm in respiratory control was described recently in healthy subjects (Spengler et al., 2000). This rhythm is independent of the well known diurnal rhythm in respiratory control which is thought to be induced by the behavioral rhythm of sleep and wakefulness (reviewed by Phillipson & Bowes, 1986) showing a systematic increase in the arterial P_{CO_2} and a systematic decrease in ventilation, metabolism and ventilatory chemosensitivity during sleep (e.g., Douglas et al., 1982; Berger & Phillips, 1988; Schafer, 1998). The circadian rhythm in respiratory control, however, was found to be independent of the sleep-wake cycle, assessed during a 41-hour «constant routine protocol» where subjects stayed in bed and awake under constant environmental and behavioral conditions, being exposed to tests every 2 hours. A small circadian rhythm in P_{CO_2}-«setpoint» with an amplitude of ± 0.6 mmHg (± 1.5% of the 24h-mean) was found, most likely resulting from the discrepancy of a larger rhythm in metabolism, i.e., O_2 consumption and CO_2 production (± 3.2% of the 24h-mean) than in ventilation (± 2.4%). However, a larger amplitude circadian rhythm was detected in chemosensitivity (HCVR [hypercapnic ventilatory response]: $\pm 0.4\ l \cdot min^{-1} \cdot mmHg^{-1}$; corresponding to ± 12.1% of the 24-hour mean). Stephenson et al. (2000) reported similar findings with respect to chemosensitivity, even under less controlled conditions. These rhythms were phase advanced by 6–8 hours with respect to the core body temperature (CBT) rhythm (CBT: one of the best markers of the endogenous circadian rhythm) and are therefore unlikely to be a result of the change in CBT itself (Spengler et al., 2000). This circadian rhythm in respiratory control could be caused by direct neural influences on the brainstem respiratory complex from the circadian pacemaker located in the suprachiasmatic nuclei (e.g., via the paraventricular nuclei of the hypothalamus and/or the reticular formation; reviewed in Waldrop & Porter, 1995) or indirect influences on metabolism and/or respiratory control via circadian rhythms in other variables. For example, circulating hormones have prominent endogenous circadian rhythms (e.g., Czeisler et al., 1989) and they also affect respiratory control when they are manipulated experimentally (e.g., Koepchen, 1953; Vejby-Christensen & Strange Petersen, 1973; Petersen & Vejby-Christensen, 1977; Baker et al., 1996).

What are the potential implications of a circadian rhythm in respiratory regulation? Both shift work and jet lag are more and more frequent in modern life. They both result in a shift of the endogenous circadian rhythm vs. its major «Zeitgeber», the light-dark cycle, meaning that people are sleeping at the «wrong» phase of their endogenous circadian cycle. Circadian changes in chemosensitivity would have greatest relevance in conditions when the chemoreceptive negative feedback system is known to predominate over other drives to breathe, such as during sleep, when at altitude, in many respiratory disorders, and potentially also during exercise (see later). For patients suffering from symptoms related to the chemical drive to breathe, e.g., apnea patients, their disease may worsen if they go to sleep before their usual bedtime, i.e., if they go to bed earlier than usual with respect to their endogenous circadian cycle. This assumption is based on the fact that the minimum of HCVR occurs before the usual bedtime. This kind of uncoupling of the light-dark cycle from the endogenous circadian rhythm usually occurs when traveling from west to east, e.g., from the United States to Europe.

Respiratory regulation during exercise

It is still a matter of debate to which extent the different ventilatory drives that are depicted in Figure 1,contribute to the ventilatory increase during exercise. Also, the contribution of the different drives is likely to vary depending on the intensity and duration of exercise. For steady-state exercise (exercise at a constant load) for example, Dejours (1964) proposed the following concept of action of respiratory drives (Fig. 2).

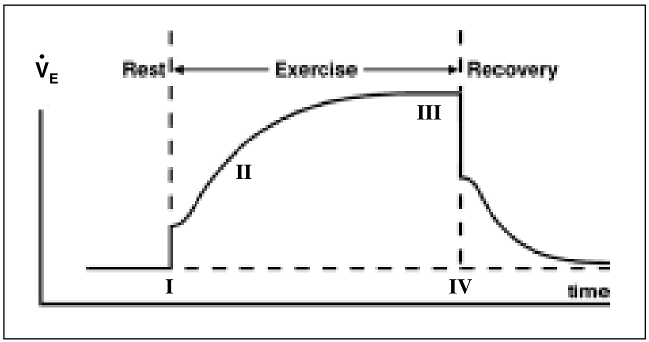

Figure 2: Minute ventilation ($\dot{V}_E$) vs. exercise duration (time) during moderate, steady-state exercise indicating the four phases (I–IV) of respiratory regulation proposed by Dejours (1964).

He proposed neurogenic stimuli being responsible for fast adaptations at the beginning and at the end of steady-state exercise and, in addition, humoral stimuli adding to drive ventilation in Phase II and III. However, during Phases II and III, the contribution of neurogenic stimuli seems to increase as the initial fast rise is smaller than the fast decrease at the end. This neurogenic drive can either result from central command (i.e., the collateral innervation of the respiratory center together with the central locomotor drive) as first proposed by Krogh & Lindhard (1913) or from mechanoreceptor-activation in muscles, tendons and joints (afferent drive). During heavy, constant-load exercise however, ventilation is rising continuously, presumably due to increases in metabolic requirements (oxygen consumption increases steadily as well) and increases in blood lactate, potassium and other blood born factors that may stimulate breathing by chemoreceptor-activation [for review see Dempsey et al. (1995) and Paterson (1997)].

The question arises to which extent these different mechanisms are active or even necessary in driving exercise ventilation. Considering, for example, neurogenic drives, different researchers investigated the importance of one specific drive by modifying (increasing/decreasing) it and measuring resulting ventilation. With respect to the contribution of central command to the exercise ventilatory drive, the following different approaches were taken. In experiments with presumably increased central command – exercising with weak or weakened limb muscles requiring an increased neural drive to working muscles for the same workload – the ventilatory increase with exercise was larger than normal (Ochwadt et al., 1959; Asmussen et al., 1965; Innes et al., 1992). These authors suggested an important contribution of central command to exercise ventilation. On the other hand, some studies compared the ventilatory response to voluntary, dynamic exercise (with central command) with non-voluntary (electrically induced), dynamic exercise (presumably without central command). While one study found a faster ventilatory increase during voluntary exercise (Adams et al., 1987), the others detected no difference in the ventilatory response to the two types of exercise (Asmussen et al., 1943; Adams et al., 1984; Banner et al., 1988). These studies suggest that central command is either not important in driving exercise ventilation or – if it were responsible for part of the respiratory drive under normal conditions – afferent drives can take over the part usually resulting from central drive. This latter hypothesis would favour a concept of redundancy of respiratory drives.

Redundancy of the exercise ventilatory drives

As with other vital functions, it seems intuitive to expect redundancy also for mechanisms driving ventilation and indeed, it seems to be true but to which degree? The above investigators using electrical stimulation had their subjects perform dynamic exercise, thus afferent input from chemo- and metaboreceptors as well as mechanoreceptors of muscles, tendons and joints seemed to drive ventilation sufficiently at this submaximal level. However, even when comparing the ventilatory response to electrically stimulated, isometric muscle work with the ventilatory response to voluntary, isometric contractions (Spengler et al., 1994), the ventilatory response adequately matched the metabolic needs, again supporting the concept of redundancy. On the other hand, solely passive movement of the legs can also increase ventilation to a certain degree (Concu, 1988; Waisbren et al., 1990; Ishida et al., 1993; Gozal et al., 1996; Miyamura et al., 1997). While these results show that partial afferent input is sufficient to driving ventilation, Fernandes et al. (1990) blocked afferent (but not efferent) nerve activity by epidural anesthesia and also found no difference in the ventilatory response to exercise compared to exercise without nervous block, suggesting that limb afferents «were not driving ventilation» and the efferent drive was sufficient.

While the studies discussed above indeed show that exercise respiratory drives seem to be redundant to a substantial degree, at least during submaximal exercise tasks, the concept of redundancy seems to have its limits when it comes to high intensity exercise: studies of the exercise ventilatory response of children who have no functional chemoreceptor drive to breathe (no increase in ventilation with hypoxia or hypercapnia), i.e., patients suffering from the so called «congenital central hypoventilation syndrome» (CCHS), do have a reduced ventilatory response if exercising above the anaerobic threshold, i.e., when metabolic drives acting via chemoreceptors become increasingly important (Jeyaranjan et al., 1987; Shea et al., 1993b; Spengler et al., 1998a). Nevertheless, these patients have a normal exercise ventilatory response during aerobic exercise (Paton et al., 1993; Shea et al., 1993b), suggesting that chemoreceptors either play a minor role in driving ventilation at moderate levels of exercise or – again – that their action can be taken over by other drives. The latter hypothesis is more likely for two reasons: first, in healthy subjects, peripheral chemoreceptors seem indeed to drive exercise ventilation by a certain degree (about 20–25% of total $\dot{V}_E$) at submaximal levels, as exercise ventilation is reduced when peripheral chemoreceptor activity is reduced by oxygen administration (Kobayashi et al., 1996; St. Croix et al., 1996) – and second, in CCHS patients who are «chronically» lacking a drive, limb afferent input seems to have a larger effect than in normals in stimulating breathing, i.e., these subjects' ventilation seems to be entrained to limb movements (Gozal et al., 1996) to a larger extent than the one of matched controls. This latter finding suggests that part of the ventilatory response to exercise might be a learned or conditioned response.

Plasticity of the exercise ventilatory response

A learning process involved in the exercise ventilatory response was, for example, suggested by Somjen (1992): «the central nervous system anticipates present and future needs on the basis of past experience». According to this theory, negative feedback is of vital importance during infancy when «by having successfully corrected errors, the central nervous system learns how to prevent them». Supported is this concept of learning or conditioning by human studies attempting to modify the respiratory response to exercise (Helbling et al., 1997; Turner & Sumners, 2002). If, for example, healthy adults are repeatedly exposed to exercise paired with an additional respiratory stimulus, such as increased P_{CO_2}, driving ventilation higher than required by the metabolic needs of the exercise, exercise alone following this conditioning period will elicit an exaggerated ventilatory response. Similarly, subjects who performed a respiratory muscle endurance training by normocapnic hyperpnea for 4 to 6 weeks, showed an increased exercise ventilatory response when tested shortly after the training period (Boutellier et al., 1992; Kohl et al., 1997). Potential mechanisms that could account for this «overshooting» ventilatory response after repeated bouts of hyperpnea could be a delayed adaptation of the respiratory center to changes in afferent nerve traffic from respiratory muscles, chest wall, pulmonary and/or upper airway receptors, to changes in neuromuscular coordination etc. Preliminary findings of hyperpnea training with patients suffering from chronic idiopathic hyperventilation could support the first hypothesis as these subjects were able to increase their severely reduced breathhold-time by a substantial amount after hyperpnea training (Jack et al., 2000), suggesting a change in perception of afferent nervous traffic from either chest wall or the lungs.

In summary, the ventilatory drives during exercise seem indeed to be redundant to a substantial degree and in addition, the exercise ventilatory response also shows a certain degree of plasticity, during development as well as in adults. This aspect is important for subjects with functional impairments affecting respiratory drives and it is promising to know that also at the adult age, modifications of the respiratory response to exercise can take place.

Mechanisms of respiratory sensations during exercise

Breathlessness in healthy subjects during exercise

Not only respiratory or cardiac patients may experience an uncomfortable respiratory sensation during physical activities, also healthy subjects, when exercising very hard, can perceive a sensation of «breathlessness». Talking about respiratory sensations in healthy subjects, we need to distinguish between the perception of an increased work of breathing or respiratory effort, i.e., «perceiving the increased ventilation», and the uncomfortable sensation of breathlessness, i.e., a «feeling of not getting nearly enough air or starving for air» despite a heavily increased ventilation. In this latter case, subjects perceive they should be breathing harder to feel comfortable but «for some reason» they can not take in more air. In other words, the human is apparently consciously aware of the appropriateness of ventilation, and discomfort is experienced with deviations in either direction (if subjects are asked to breathe less than their spontaneous drive is asking for, this results in an uncomfortable sensation as well). If healthy subjects suffer from the sensation of breathlessness during exercise, they either reduce the intensity of the exercise such that the ventilatory need becomes smaller and the subjects feel that «their ventilation is appropriate again» or – if it is not possible to decrease the workload, i.e., in a constant-load exercise test – subjects will eventually stop exercise so that they «can catch up with their breathing», as they say. Interestingly, when systematically interviewing untrained or trained healthy subjects, about half of them never experience a sensation of breathlessness when exercising (despite of being aware of the increased ventilation), while the other half knows this sensation very well, in particular when cycling or running uphill. Some of the subjects that do not experience breathlessness when exercising at sea level, may know this sensation from exercising at altitude where ventilation for a given workload is increased to compensate for the lower P_{O_2}.

Mechanisms potentially giving rise to breathlessness

Different mechanisms have been proposed to give rise to breathlessness (Adams & Guz, 1996): among these are the «respiratory corollary discharge hypothesis» (postulating that breathlessness arises from increased medullary respiratory center activity; Adams et al., 1985b; Lane et al., 1990; Lane & Adams, 1993) or the hypothesis that chemoreceptors project to the forebrain (Chronos et al., 1988; Ward & Whipp, 1989) – chemoreceptors are increasingly activated during heavy exercise when the concentration of metabolites increases and blood pH may fall due to lactic acidosis if the blood buffer capacity is «reached» and also chemoreceptors are known to give rise to breathlessness (or air hunger) when they are increasingly activated at a fixed ventilation (Banzett et al., 1996). Other proposed mechanisms giving rise to breathlessness during exercise are increased central command as well as projections of metabo- and mechanoreceptors from limbs. Whether mechanisms eliciting the sensation of breathlessness and the perception of increased respiratory effort share common pathways has yet to be determined as these two qualities of respiratory sensations were rarely assessed simultaneously during exercise. Most likely, different mechanisms add to the sensation of breathlessness during exercise similar to the different drives that increase exercise ventilation.

A recent study suggests that changes associated with the development of respiratory muscle fatigue during exercise might be involved in giving rise to breathlessness (Spengler et al., 1998b). While earlier studies have shown a linear relationship between breathlessness and ventilation (Stark et al., 1981; Adams et al., 1985a; Wilson & Jones, 1991), we observed a non-linear relationship, i.e., breathlessness rose exponentially with the increase in ventilation. In contrast to previous studies, we applied high-intensity, constant-load exercise while the others used submaximal or graded exercise. High intensity, constant-load exercise is known to elicit diaphragmatic fatigue (e.g., Johnson et al., 1993; Mador et al., 1993) and Gandevia et al. (1981), for example, demonstrated an increase in perceived respiratory effort with the development of respiratory muscle fatigue during maximal inspiratory contractions. Consequently one could conclude that the awareness of the increasing motor command (to achieve a given level of ventilation when respiratory muscles become fatigued) also contributes to the perception of breathlessness.

In turn, after respiratory muscle training, the perception of respiratory exertion was reported to be smaller than before the training period (Spengler et al., 1998a; Volianitis et al., 2001; Romer et al., 2002a). This change of respiratory perception could potentially result from relatively reduced motor command due to better neuromuscular coordination being sensed as requiring less effort to achieve a similar level of ventilation. Alternatively, respiratory muscle capillarisation might have improved, leading to better local O_2-transport in respiratory muscles, as well as better removal of CO_2 and metabolites. Metabolic changes activating type IV afferent fibers are suggested to being involved in the perception of «effort» or «fatigue» as well. However, I would like to suggest an additional mechanism potentially contributing to the change in perception of respiratory effort after respiratory muscle training, that is, a reduction in work of breathing due to reduced (upper) airway resistance. In our laboratory, we observed an increase in total airway resistance following prolonged normocapnic hyperpnea (unpublished observation). It is known that upper airway muscles are phasically activated during respiration and that genioglossus activity, for example, is increased with increased negative pressure (Pillar et al., 2001). Also, Scardella et al. (1993) described genioglossus fatigue developing with inspiratory loading even before thoracic inspiratory muscle fatigue can be detected. Thus, if the increase in resistance we observed were indeed a result of fatiguing upper airway dilators, hyperpnea training might be able to delay the development of this fatigue. Support for this hypothesis is given by two recent studies: on one hand, rat experiments showed that physical endurance training indeed not only activates selected upper airway muscles but also increases oxidative capacity and results in a fast-to-slow shift in the myosin heavy chain isoforms (Vincent et al., 2002); on the other hand, a study in healthy humans has shown that snorers having performed hyperpnea training, reduced the time they were snoring at night, suggesting upper airway patency could better be maintained during sleep after training (Furrer et al., 1998). During cycling, a reduction in upper airway resistance would result in a reduction in the work of breathing, thus the same level of ventilation would be perceived as requiring less effort.

In summary, we need to be aware that multiple factors, i.e., changes in central command, neuro-muscular coordination or afferent input from chemo-, metabo- or mechanoreceptors may contribute to the perception of respiratory exertion and breathlessness during exercise. Establishing the relative contribution of these different mechanisms under specific conditions and searching for ways to interact with the separate pathways through particular training modalities certainly warrants further investigations. So far, athletes that are limited in their performance by the perception of adverse respiratory sensations might wish to try and reduce these sensations through separate training of their respiratory system.

Ventilation and breathlessness affecting exercise performance

While it seems intuitive that high levels of respiratory exertion or breathlessness can impair exercise performance, make subjects reduce speed or even stop exercising, the interactions of the level of ventilation, breathlessness, the development of respiratory muscle fatigue and exercise performance is less clear. Several studies show that constant-load endurance performance is reduced when subjects are breathing more at a given workload. For example, when subjects are exercising with prefatigued respiratory muscles, respiratory drive is increased (and not decreased as one would expect), resulting in hyperventilation and a decrease in endurance performance (Mador & Acevedo, 1991). Similarly, subjects who heavily exercised their respiratory muscles (by normocapnic hyperpnea) during one month of respiratory muscle training, can present with an increased exercise ventilation (hyperventilation) and decreased endurance performance compared to before the respiratory training period when tested shortly after the last training session (Boutellier et al., 1992; Kohl et al., 1997). Why could increased ventilation result in earlier exhaustion?

A study by Harms et al. (2000) potentially offers an explanation: these authors showed reduced cycling endurance in subjects that were exercising with loaded inspiratory muscles (with added inspiratory resistance) compared to the same test without loading. On the other hand, when inspiratory muscle work was reduced by assisting inspiration with a proportional assist ventilator, cycling endurance was significantly prolonged. The authors attributed the changes in exercise endurance performance with increased/decreased respiratory muscle work to concomitant changes in leg blood flow that they had previously described under similar conditions, i.e. respiratory and locomotor muscles seem to compete for blood supply (Harms et al., 1997; Harms et al., 1998). Such changes in blood flow would have important effects on O_2-transport to and CO_2- as well as metabolite removal from the working locomotor muscles and, consequently, on the development of muscle fatigue. In addition, the authors attributed part of the changes in endurance to indirect effects of the changes in muscle fatigue as changes in the intensity of effort perception correlated with changes in exercise performance. Most likely, in the studies by Mador and Acevedo (1991), Boutellier et al. (1992) and Kohl et al. (1997), respiratory muscle work was also increased with increased minute ventilation, potentially causing a reduction in leg blood flow resulting in earlier development of leg muscle fatigue and therefore earlier exhaustion.

Considering that the level of ventilation indeed seems to affect exercise performance and presuming that central chemosensitivity is important to drive ventilation during exercise, it would be of interest to know whether the previously described circadian changes in respiratory control are more pronounced, the same or rather damped during exercise. Some investigators have reported an overall increase in CO_2-chemosensitivity (HCVR) during exercise compared to rest (e.g., Cunningham et al., 1963; Weil et al., 1972) while others found no difference (Duffin et al., 1980; Kelley et al., 1982) or even a decrease (Miyamura et al., 1976). While these differences between authors may result from different types of exercise applied or different methods used to assess HCVR, the different findings could also result from measurements during different phases of the circadian cycle. It might therefore be important for endurance athletes to be aware of their circadian cycle as ventilation would be higher for a given workload (and endurance performance would be decreased) when exercising close to the peak of the HCVR-cycle and ventilation would be lowest when exercising close to the trough of the cycle.

On the other hand, several studies have shown increases in exercise performance with reduced ventilatory drive or even without a change in minute ventilation, after subjects had exclusively trained their respiratory muscles, using normocapnic hyperpnea (Boutellier & Piwko, 1992; Boutellier et al., 1992; Spengler et al., 1999; Stuessi et al., 2001; Markov et al., 2001), using inspiratory resistive breathing (Volianitis et al., 2001; Romer et al., 2002b) or both (Sonetti et al., 2001). Also, decreases in perception of respiratory effort or breathlessness were reported (Spengler et al., 1998b; Volianitis et al., 2001; Romer et al., 2002a). How could we explain this improvement in exercise endurance performance? One possibility could be the previously described reduction in perception of respiratory effort, although no such changes were observed in the study by Sonetti et al. (2001). In addition, it is well known that exhaustive endurance exercise can cause diaphragmatic fatigue (Johnson et al., 1993; Mador et al., 1993) and inspiratory as well as expiratory muscle fatigue have been shown to induce an increase in leg muscle sympathetic nerve activity, even at rest (St.Croix et al., 2000; Derchak et al., 2002), reducing leg blood flow by vasoconstriction (Sheel et al., 2001). If – after respiratory muscle training – inspiratory, or even expiratory muscle fatigue (in case of hyperpnea training) were delayed, then – potentially – the occurrence of this sympathetic reflex that is believed to have its origin in fatigued respiratory muscles, causing vasoconstriction and a reduction in leg blood flow, would be delayed as well. As a consequence, leg muscles would fatigue later and thus, endurance exercise performance would be improved.

In summary, we have seen that the level of exercise ventilation and respiratory sensations as well as respiratory muscle fitness are all factors that can affect endurance exercise performance. While it is certainly important to keep these aspects in mind when designing exercise studies where endurance performance is one of the outcome measures, it is similarly important to be aware of these interactions when testing athletes or advising them with respect to training regimes and competitions.

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