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Review

Individual responses to aerobic exercise: The role of the autonomic nervous system

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ABSTRACT

It is well established that regular aerobic exercise training reduces all-cause mortality and improves a number of health outcomes. However, a marked heterogeneity in the training-induced changes, e.g. in terms of aerobic fitness, has been observed in healthy human subjects, even with highly standardized training programs. Mean improvements in aerobic fitness, expressed as maximal oxygen consumption, have been about 10–15% of the baseline values, but the training-induced changes have ranged from almost none to a 40% increase. The exact nature of the mechanisms responsible for this heterogeneity in response to regular aerobic exercise is not well known. In this review, we consider evidence of the association between the autonomic nervous system (ANS), aerobic fitness and aerobic training-induced changes in fitness. Results of recent studies support the hypothesis that assessment of ANS functioning includes important information concerning acute and chronic physiological processes before, during and after aerobic exercise training stimulus. Moreover, we show that daily assessment of ANS activity could serve as an indicator of appropriate physiological condition for aerobic training.

Contents

1. Introduction

Marked changes in heart rate (HR) occur during aerobic exercise and after training interventions. These changes in HR are primarily due to alterations in autonomic nervous system (ANS) activity. HR accelerates during acute exercise due to the reduced cardiac vagal modulation of HR and increased sympathetic activity. After chronic aerobic training, autonomic balance is altered toward parasympathetic predominance due to increased vagal modulation of HR and probably also due to decreased sympathetic activity. These changes in autonomic activity can be studied non-invasively using a HR variability technique (Akselrod et al., 1981,1985) or by invasively measuring sympathetic activity from the peroneal nerve with a microneurography technique (Delius et al., 1972; Hagbarth and Vallbo, 1968). In this review we focus on the association between aerobic exercise training and autonomic regulation measured with the HR variability and microneurography techniques.

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Regular physical activity and good aerobic fitness are widely accepted as factors that improve a number of health outcomes and reduce all-cause mortality (Blair et al., 1989; Ekelund et al., 1988; Haskell et al., 2007; Kesaniemi et al., 2001; Myers et al., 2002; Thompson et al., 2003). Previous studies have shown that aerobic fitness is related to cardiovascular autonomic regulation, providing evidence that aerobic training improves ANS functioning (Davy et al., 1996; De Meersman, 1993; Goldsmith et al., 1992; Tulppo et al., 1998). Aerobic training has been suggested to protect the heart against harmful cardiac events by increasing cardiac vagal modulation of HR and also by decreasing sympathetic outflow (Billman, 2002).

Interestingly, considerable heterogeneity in the responsiveness to aerobic training, assessed by the change in maximal oxygen consumption ($V_{O_{2max}}$) or peak oxygen consumption ($V_{O_{2peak}}$), has been observed even in highly standardized training programs (Bouchard and Rankinen, 2001; Hautala et al., 2003a,2006a). Mean improvements in $V_{O_{2max}}$ have been about 25%, with a range from 0% to 40% compared with the baseline (Bouchard and Rankinen, 2001).

The physiological background for the wide range of responses to aerobic training is discussed in the present review. We focus on the contribution of ANS status beyond the individual aerobic training-induced changes in $V_{O_{2max}}$ or $V_{O_{2peak}}$. Furthermore, we examine the measurement of ANS activity as a practical tool for evaluating the physiological condition for determining an appropriate aerobic training stimulus on a daily basis. Finally, we suggest future directions for research on the effects of aerobic exercise on the ANS.

2. Methods for assessing autonomic nervous system activity

Assessment of the ANS has played an important role in elucidating the centrally mediated neural mechanisms in diverse clinical and physiological settings. The most widely used methods involve measurement of an end-organ response to a physiological or pharmacological provocation. In this context, we will briefly introduce two methods; HR variability (HRV) and muscle sympathetic nerve activity (MSNA), which are both objective and reliable tools for assessing ANS functioning.

HRV refers to the amount of HR fluctuation around the mean HR (Task Force, 1996). It can easily be determined non-invasively from electrocardiogram (ECG) recordings, resulting in a time series (R-R intervals). Short-term ECG recordings (5–15 min), made under controlled conditions, e.g. a supine or standing position, can elucidate physiological or pathophysiological changes in ANS functioning. Long-term, usually 24-h recordings, can be used for ANS responses during normal daily activities. HRV is modulated by breathing (Akselrod et al., 1985; Davidson et al., 1976; Hirsch and Bishop, 1981), baroreflexes (Eckberg, 1980; Eckberg et al., 1971), genetic factors (Hautala et al., 2006b; Singh et al., 1999,2002; Uusitalo et al., 2007), and demographic and other factors, including blood pressure, blood cholesterol, cardiac dimensions, body mass index and smoking (Pikkujamsa et al., 2001). Furthermore, HRV, particularly high-frequency (HF, 0.15–0.4 Hz) oscillation in R-R variability, has been shown to relate to respiration as it quantifies the magnitude of respiratory sinus arrhythmia (Akselrod et al., 1981). The magnitude of respiratory sinus arrhythmia (Katona and Jih, 1975) and the HF power of R-R interval variability have been shown to indicate vagal outflow to the heart in several studies (Akselrod et al., 1981; Hayano et al., 1991; Pomeranz et al., 1985).

Sympathetic activity has been proposed to correspond to R-R interval fluctuation at a frequency of around 0.1 Hz (Malliani et al., 1991; Pagani et al., 1997). Therefore, the ratio between low-frequency (LF, 0.04–0.15) and HF oscillation (LF/HF ratio) has been used as an index of sympathovagal balance (Montano et al., 1994), or as an index of sympathetic activity (Pagani et al., 1986; Pagani et al., 1997). However, a paradoxical decrease in this ratio has been described during specific conditions with high sympathetic activity, e.g. during heart failure (van de Borne et al., 1997). A large body of previous studies have observed that in conditions with reciprocal changes in sympathetic and vagal outflow, the LF/HF ratio behaves as expected (Malliani et al., 1991; Montano et al., 1994; Tulppo et al., 2001,2005b). However, during increased sympathetic activity with concomitant cardiac vagal modulation of HR (Tulppo et al., 2005b), or without reduced cardiac vagal modulation, the LF/HF ratio decreases, perhaps explaining the paradoxical decrease in this ratio in some conditions, e.g. among patients with heart failure, with high sympathetic activity but without significant reduced cardiac vagal modulation of HR (van de Borne et al., 1997).

It is important to appreciate some technical requirements and limitations in using HRV measurements as indices of ANS function. The sampling frequency is an important factor for accurate detection of beat-to-beat fluctuations in R-R intervals (Tapanainen et al., 1999). A sampling frequency of 250–500 Hz has been recommended (Task Force, 1996), but most of the older studies on HRV have gathered data by using 24-h Holter ECG systems with a sampling frequency of 128 Hz. A low sampling frequency may cause jitter in the recognition of the QRS complex, creating an error in the R-R interval measurement (Merri et al., 1990). Therefore, it is preferable, especially during dynamic HRV, to collect the data with a high sampling frequency. In addition, the extent and type of editing R-R interval data have remarkably different effects on various HRV indices (Huikuri et al., 1999; Salo et al., 2001). Even though there is no universal method for editing R-R interval data, there is general consensus that artefacts, premature beats and non-sinus tachycardia episodes should be deleted before running the analyses (Task Force, 1996). Furthermore, the time delay between the last single training session and HRV recordings must be considered, since ANS function has been found to be restored to the baseline level after several hours following high-intensity aerobic exercise (Furlan et al., 1993; Hautala et al., 2001). Concerning HRV analysis in athletes, it is important to refer the possibility that HRV changes occurred in response to pre-competitive stress instead to be a pure response to training (Iellamo et al., 2003,2006). Finally, saturation of HRV, expressed as a plateau of HRV despite the lengthening of R-R interval, may mask the changes in vagal modulation at extremely low HR (Goldberger et al., 2001; Kiviniemi et al., 2004,2006).

Direct measurement of sympathetic nerve activity from the peroneal nerve with the microneurography technique (MSNA) has been proposed as a "golden standard" for measuring the magnitude of sympathetic outflow (Tulppo et al., 2005a, b; Wallin and Charkoudian, 2007). MSNA consists of vasoconstrictor impulses, which are modulated from central nervous sites and from a large number of peripheral receptors, including arterial baroreceptors, cardiopulmonary receptors and intramuscular mechano- and metaboreceptors (Wallin and Charkoudian, 2007). MSNA occurs in the cardiac rhythm primarily during temporary reductions in blood pressure (Delius et al., 1972). Most recordings are multifiber recordings under resting conditions, i.e. the electrode picks up activity from many sympathetic fibers, and such activity is presented in mean voltage (integrated) neurograms. Finally, sympathetic outflow is expressed as burst frequency, i.e. bursts min^{-1}, as bursts 100 heart $beats^{-1}$ (Shoemaker et al., 2001; Tulppo et al., 2005a) or by calculating the area under the curve (au ms) (Hautala et al., 2007).

3. Association between the autonomic nervous system and aerobic exercise

The effect of age (Craft and Schwartz, 1995; Lakatta, 1993; Lipsitz et al., 1990), gender (Huikuri et al., 1996; Kuo et al., 1999; Ryan et al., 1994) and circadian profile (Huikuri et al., 1994; Peckova et al., 1998) on the ANS has been observed in many studies. Thus, it is clear that responses to aerobic exercise involve integration of these determinants to acute and chronic adaptations of ANS activity. Furthermore, several randomized trials have shown that aerobic training causes reductions in blood pressure in both normotensive and hypertensive individuals (Cornelissen and Fagard, 2005; Fagard, 1999, 2001; Hagberg et al., 2000; Pescatello et al., 2004). It is obvious that the effect of aerobic training on blood pressure sets an important link between cardiovascular adaptation to aerobic exercise and ANS function, mediated by the changes occurred in baroreflex sensitivity (Iellamo et al., 2000; Niemela et al., 2008; Pagani et al., 1988; Somers et al., 1991). A complete review of the effects and mechanisms of these important above-mentioned factors on ANS regulation is beyond the scope of the present paper. Therefore, the effect of aerobic fitness and aerobic training on ANS function expressed as HRV and MSNA indices only will be discussed in the present review.

3.1. Cross-sectional studies

Marked changes in HR occur at different aerobic exercise intensity levels. At the beginning of dynamic exercise, HR increases rapidly, mainly due to the reduced cardiac vagal modulation of HR. As the workload increases, HR increases due to further reduction of vagal modulation and concomitant sympathetic activation (Robinson et al., 1966; Rosenblueth and Simeone, 1934). During heavy exercise, parasympathetic activity wanes and sympathetic outflow increases in such a way that little or no vagal modulation remains (Hautala et al., 2003b; Robinson et al., 1966; Rosenblueth and Simeone, 1934; Tulppo et al., 1996,1998).

Cross-sectional studies have revealed that cardiac vagal modulation of HR, expressed as HF power, is higher in well-trained male and female subjects than in controls both in laboratory (Buchheit and Gindre, 2006; Davy et al., 1996,1998; Kenney, 1985; Rennie et al., 2003; Ueno et al., 2002) and in ambulatory conditions (Goldsmith et al., 1992,1997). In our previous study at the laboratory conditions (Tulppo et al., 1998), we observed that middle-aged healthy subjects with a better $V_{O_{2peak}}$ had significantly higher vagal modulation of HR, especially during exercise than did those with poor $V_{O_{2peak}}$ (Fig. 1). In the same random population, there were no significant differences in vagal modulation at rest between the individuals with poor and good $V_{O_{2peak}}$, despite significant differences in their basal HR. We also showed that the exercise intensity level at which vagal modulation of HR disappeared was significantly higher in subjects with good aerobic fitness than in those with poor aerobic fitness.

The central nervous system regulates cardiovascular autonomic function in a reciprocal fashion, i.e. increased vagal modulation is usually associated with decreased sympathetic activity. Since good aerobic fitness is associated with high vagal modulation, it could be assumed that good aerobic fitness may also be related to a low level of MSNA. However, cross-sectional studies have demonstrated either a positive correlation between resting MSNA and aerobic fitness (Alvarez et al., 2005; Ng et al., 1994) or no association at all (Seals, 1991; Svedenhag et al., 1984). On the contrary, in our latest study (Hautala et al., 2007), we observed that male subjects with high $V_{O_{2max}}$ had lower LF/HF ratios and lower MSNA than did subjects with low $V_{O_{2max}}$.

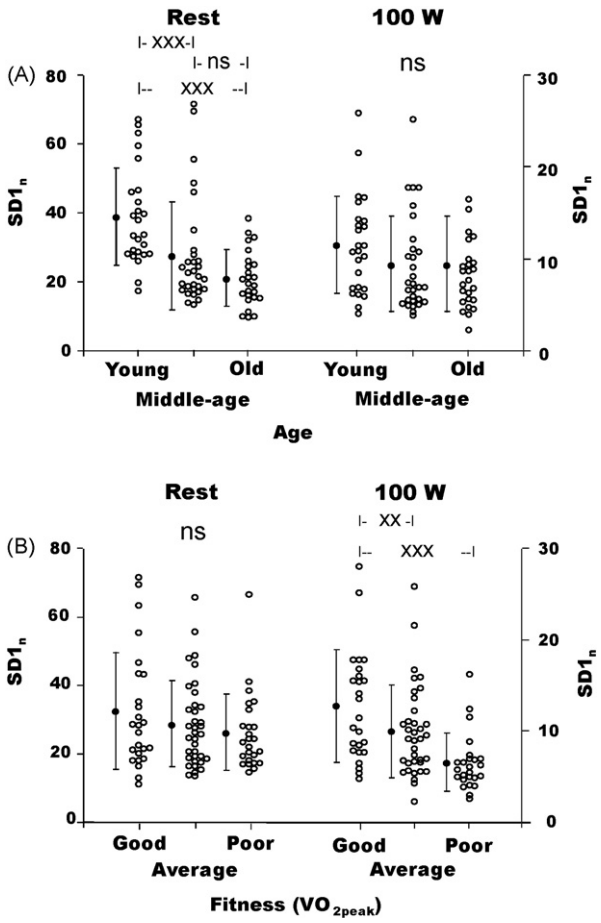

Fig. 1. Individual (○) and mean ± S.D. (●) values of cardiac vagal modulation of HR (S.D.1_n) at rest and during exercise (100 W). (A) Subjects categorized according to age and matched for peak oxygen consumption. (B) Subjects categorized according to cardiorespiratory fitness and matched for age. S.D.1_n is an index of HRV, which correlates highly to HF power (Tulppo et al., 1996). Modified from Tulppo et al. (1998).

These findings suggest that good aerobic fitness is related to high cardiac vagal modulation of HR, providing further evidence that good exercise capacity has beneficial effects on ANS regulation. Interestingly, MSNA measurements of healthy subjects under resting conditions have revealed competing results connected to aerobic fitness. The inconsistence in results between the studies remains inconclusive. It may be possible that the behavior of MSNA according to aerobic fitness is non-linear. However, this hypothesis should be confirmed with future studies.

3.2. Longitudinal studies

An obvious indicator of ANS adaptation to regular aerobic training is a lowering of HR at rest and during submaximal exercise. Maximal HR remains unchanged or may even be slightly reduced. The lowering of resting and submaximal HR is mediated by alterations in the ANS and by changes in the intrinsic properties of the heart, evidenced by changes in the intrinsic mechanism of the sinus node and the right atrial myocytes (Ekblom et al., 1973; Lewis et al., 1980).

The effects of long-term aerobic training have been shown to be associated with increased cardiac vagal modulation of HR during short-term rest recordings at laboratory conditions (al-Ani et al., 1996; Carter et al., 2003; Melanson and Freedson, 2001; Shi et al., 1995) and during long-term (24-h) dynamic ambulatory recordings (Hautala et al., 2004; Kiviniemi et al., 2006; Tulppo et al., 2003)

of healthy subjects. In contrary, some controlled studies have failed to show association between aerobic training and HRV during short-term (Boutcher and Stein, 1995; Maciel et al., 1985) or long-term recordings (Loimaala et al., 2000). Several reasons may explain the controversial results of HRV studies after aerobic training. Long-term adaptation to regular aerobic training results from a complex combination of biochemical, structural, metabolic, humoral and neural factors (Furlan et al., 1993). Additional regulatory influences originate from genetic background, age and intensity of exercise and simultaneous presence of short-time after-effects from the previous activity (Pagani et al., 1995). Furthermore, some contradictory findings of aerobic training studies may be partly limited by either the small sample size (Lazoglu et al., 1996; Maciel et al., 1985) or the characteristics of the subjects, e.g. a narrow range of aerobic fitness (Byrne et al., 1996). Also, the duration of interventions (from 4 to 36 weeks), the training frequency (from 3 to 7 sessions/week) and the intensity of exercise (from ~60% to 90% of maximal HR) varies between the previous studies, and it is thus difficult to compare the results of different studies. However, long duration (12 months) of training may not necessarily lead to greater enhancement in HRV (Uusitalo et al., 2002), as prolonged (12 months) and intense training (from walking to running) may restore these changes in HRV back to the baseline level (Iwasaki et al., 2003). Finally, Sandercock et al. (2005) have recently detailed the effects of exercise training on HRV by using a meta-analysis approach. They concluded that aerobic training lasting at least 4 weeks results in significant increases in HF power, but these changes are influenced by the age of the study population. An attenuated trend of HF power response to training was exhibited in older subjects (Sandercock et al., 2005). Interestingly, as seen in Fig. 2, wide heterogeneity is evident in the baseline values of HF power, and also in the endurance training-induced changes in HF power measured at the ambulatory conditions, despite a very similar and controlled training intervention (Tulppo et al., 2003).

Taken together, large body of data shows that regular aerobic training can alter ANS balance by increasing vagal modulation of HR. Furthermore, it has also been suggested that aerobic training interventions changes ANS activity by decreasing sympathetic activity (Billman, 2002), especially among patients with cardiac disease (Roveda et al., 2003). However, aerobic training intervention studies of healthy subjects have reported increased (Sinoway et al., 1992), decreased (Grassi et al., 1994; Ray, 1999), or unchanged resting MSNA values (Sheldahl et al., 1994; Svedenhag et al., 1984). The reasons for these inconsistent results are not known.

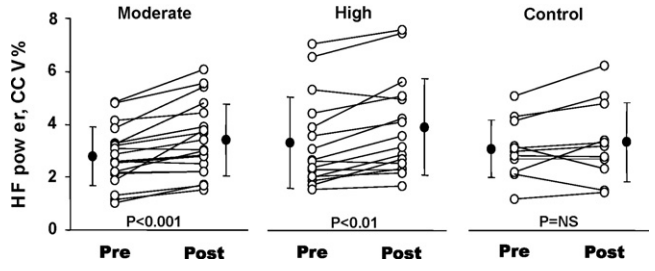

Fig. 2. Individual (○) and mean ± S.D. (●) values of cardiac vagal modulation of HR (HF power normalized by the average R-R interval [coefficient of component variance (CCV%)]), analyzed over 24 h ambulatory measurements, before (pre) and after (post) endurance exercise training for the training and control groups. The training period was 8 weeks, including six 30-min sessions a week for the moderate-volume training group (moderate) and six 60-min sessions a week for the high-volume training group (high) at an intensity of 70–80% of maximal heart rate. Modified from Tulppo et al. (2003).

4. Determinants of individual differences in response to regular aerobic exercise

Marked individual differences in the response to regular aerobic training, in terms of individual changes in $V_{O_{2max}}$ have been observed in healthy subjects after highly standardized exercise programs (Bouchard and Rankinen, 2001; Kohrt et al., 1991; Lortie et al., 1984). Mean improvements in $V_{O_{2max}}$ have been about 10–15% of the baseline values, but the training-induced changes have ranged from almost none to a 40% increase. In line with the previous studies, we have also found considerable variation in the $V_{O_{2peak}}$ training responses of healthy subjects after controlled aerobic training interventions (Hautala et al., 2003a,2006a). The individual changes in aerobic fitness have varied from a 5% decrease to a 22% increase compared with the baseline level. The HERITAGE Family Study based on 720 healthy individuals summarized the contributions of age, gender, race and baseline fitness level to the aerobic training-induced changes in $V_{O_{2max}}$. All these variables together accounted for only 11% of the variance in the response to 20 weeks of standardized training. Gender was the most powerful predictor of training response with a contribution of 5.4%, followed by age with 4% (Bouchard and Rankinen, 2001). In our own study, age as an independent predictor of training response accounted for 16% of the response. Our training intervention was relatively short (8 weeks) compared with the HERITAGE Family Study (20 weeks), which may emphasize the impact of age on short-term training response. We also had a relatively wide age range (23–52 years) compared with the training studies performed with older healthy people aged 60–71 years (Kohrt et al., 1991) or younger subjects aged 21–29 years (Lortie et al., 1984). In agreement with the previous studies, the baseline aerobic fitness level was not significantly associated with training response in our intervention.

Interestingly, our 8-week aerobic exercise training intervention showed the marked role of baseline ANS status as a contributor to training response (Hautala et al., 2003a). Baseline HF power measured at the ambulatory conditions during the night hours (mean value of 6 h) was the most powerful determinant associated with future training response, accounting for 27% of the change as a predictor of aerobic training response, expressed as $V_{O_{2peak}}$ (Fig. 3). HF power predicted training response independently after adjustment for age, baseline fitness and body mass index. This very novel finding supports the concept that cardiac vagal modulation of HR is an important physiological determinant of training response in healthy subjects.

The mechanisms underlying the relationship between baseline vagal modulation and training response remain speculative. In accordance with the large inter-individual variation in training response to aerobic exercise, wide inter-subject variation has also been observed in ANS regulation in healthy subjects, when measured by means of HRV (Hautala et al., 2003a; Pikkujamsa et al., 2001; Tulppo et al., 2003) or MSNA indices (Hautala et al., 2007; Wallin, 2006, 2007; Wallin et al., 1993). Recent studies have shown that genetic factors may determine a large proportion (>20%) of the inter-individual variation in HRV (Singh et al., 1999,2002; Uusitalo et al., 2007), whereas demographic and other factors explain only a small proportion (~10%) of this variation in ANS regulation (Pikkujamsa et al., 1999). Similarly, it is well known that genetic background causes considerable variation in both baseline aerobic capacity and changes in aerobic fitness after training interventions (Bouchard et al., 1999; Rankinen et al., 2006). Therefore, there might be a common denominator that partly explains both adaptation to aerobic training and ANS functioning. Genetic factors are the major candidates for this denominator. It is also possible that there is a mechanistic link

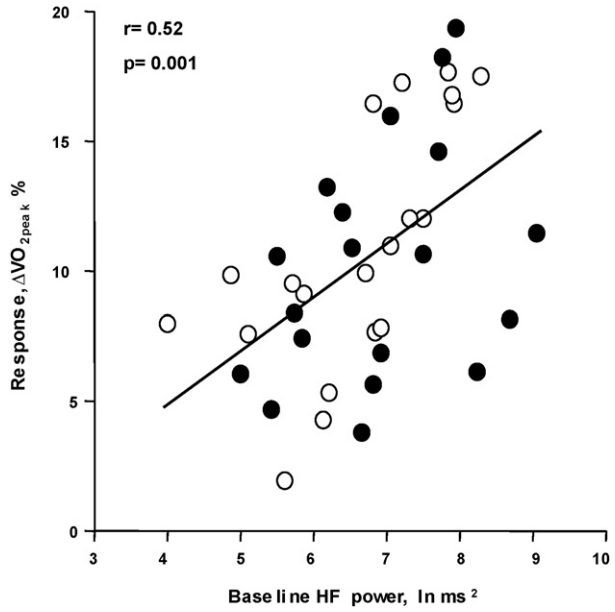

Fig. 3. Association between individual training response (changes in peak oxygen consumption; $\Delta V_{O_{2peak}}$) and cardiac vagal modulation of HR (HF power) at the baseline during nighttime (midnight to 6 AM) after adjustment for age, baseline fitness and body mass index. The average increase in peak oxygen consumption was $11 \pm 5\%$. (○) Moderate-volume training group; (●); High-volume training group (exercise training defined similarly as in Fig. 2). Modified from Hautala et al. (2003a).

between cardiac vagal functioning and training response. The cardiovascular system of subjects with good vagal functioning may have a better capacity to adapt to various external stimuli, e.g. aerobic exercise. This adaptation capacity may cause an improvement in overall cardiovascular performance after regular aerobic training, thereby also improving aerobic fitness.

5. Individually tailored aerobic training prescription

Based on the fact that a standardized exercise training program results in heterogeneous responses of aerobic fitness, and that the known factors behind individual training responses, such as previously mentioned age, gender, race, and genetic factors, cannot be affected by any treatment, an individually tailored exercise training program may remain as the most practical tool for optimizing exercise training responses at the individual level. From this point of view, the main challenge is to define the training stimulus that initiates desirable metabolic and structural changes in the cardiovascular and neuromuscular systems without compromising the recovery processes, enabling repetition of productive exercise without excessive accumulation of stress (Fridén et al., 2003). In other words, a balance between exercise and recovery is warranted at the individual level to produce an optimal training stimulus and to avoid insufficient training or potential overtraining, which could hinder training responses. The frequency, intensity, length and mode of exercise are the main components of an exercise training program that should be defined when tailoring the exercise training (ACSM, 1998; Fridén et al., 2003). However, there has been a lack of tools for objectively determining these factors in exercise training programs.

As reviewed above, aerobic training results in adaptation of the ANS expressed mainly as increased cardiac vagal modulation of HR. Previous studies have shown that acute aerobic exercise and an intense training period initially decreases cardiac vagal outflow, which rebounds beyond the pre-training level during subsequent rest or a lighter training period (Garet et al., 2004; Hautala et al., 2001; Iellamo et al., 2002; Pichot et al., 2000; Tulppo et al., 1996). The rebound of HRV has been found to associate with improved performance in athletes (Garet et al., 2004). Interestingly, in addition to our previous study with sedentary healthy subjects (Hautala et al., 2003a), high cardiac vagal outflow before a training period was also associated with a good training response among athletes (Hedelin et al., 2001). Additionally, abnormal ANS regulation, measured by means of HRV or sympathoadrenal and adrenocortical activity, relates to overtraining (Hedelin et al., 2000; Hynynen et al., 2006; Lehmann et al., 1998; Mourot et al., 2004; Uusitalo et al., 1998,2000). Taken together, the status of the ANS plays an important role in aerobic training responses and the definition of training status. Therefore, HRV methods provide important physiological information on training status and serve as an indicator of an appropriate physiological condition for aerobic training.

In our recent study, the applicability of HRV in aerobic training guidance was assessed prospectively (Kiviniemi et al., 2007a). ANS activity was measured during orthostatic stress in a standing position at the ambulatory conditions. An orthostatic test is a widely used method for quantifying ANS activity in clinical practice, and its significance is well-recognized in athletic training (Hedelin et al., 2001; Hynynen et al., 2007; Uusitalo et al., 2000). Compared with supine rest, an upright position involves decreased cardiac vagal modulation of HR and a reciprocal increase in sympathetic activity, which may, therefore, provide important information on the function of both the parasympathetic and sympathetic branches of the ANS (Malliani et al., 1991; Montano et al., 1994).

In our study, the daily aerobic training prescription was based on vagally mediated HRV (HF power) measured in a standing position after wakeup every morning. Maintained or increased HRV allowed a high training load on that day. On days when decreased vagal outflow was observed, which expressed insufficient recovery from previous exercise, a lower training load or rest was prescribed for those days (Fig. 4). The main finding of this study was that $V_{O_{2peak}}$ was more effectively improved by HRV-guided training than by standard training, despite the same total training load. This manifests the benefits of HRV methods when tailoring exercise training at the individual level among healthy subjects (Kiviniemi et al., 2007a).

6. Future directions and general conclusions

The incidence and prevalence of cardiovascular diseases and diabetes have reached epidemic proportions in the western countries. A sedentary lifestyle is the most important risk factor for these diseases. However, the physiological and psychological

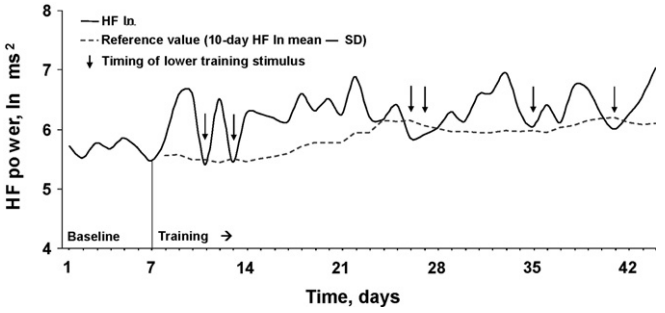

Fig. 4. Daily heart rate variability (HRV), measured in a standing position of 5 min after wakeup every morning, is expressed as high-frequency (HF ln) power. The training stimulus was lowered if HF power was less than the reference value based on 10 earlier measurements, or if HF power decreased >0.1 ln ms^2 for 2 successive days. Modified from Kiviniemi et al. (2007a).

variables that may lead to a physically passive lifestyle are not known. Since voluntary physical activity and exercise training can favourably influence brain plasticity by facilitating neurogenerative, neuroadaptive and neuroprotective processes (Dishman et al., 2006), and regular aerobic training improves the cognitive capacity of the brain (Colcombe and Kramer, 2003; Colcombe et al., 2006; Hillman et al., 2008; Kramer et al., 2006), it may be reasonable to hypothesize that individually tailored aerobic training intervention based on measurable ANS functioning and neuropsychological variables has the potential to increase the level and cognitive effectiveness of physical activity among sedentary subjects throughout life.

Motivation may be the driving force for increasing the level of physical activity. In regulation of motivation, an important frontal-subcortical circuit includes the anterior cingulate cortex (ACC), the structure that is critical for the interaction between cognition and emotion (Pollatos et al., 2007). During effortful cognitive and motor behavior the ACC supports the generation of autonomic states of cardiovascular arousal (Critchley et al., 2003; Lang and Davis, 2006; Matthews et al., 2004; Tekin and Cummings, 2002). The ACC's functions during cognitive processing are closely linked to HRV, particularly to cardiac vagal modulation of HR (Matthews et al., 2004). HRV has been used as an index to predict cognitive performance in healthy adults: high HRV was associated with better performance in tasks involving executive functioning (Hansen et al., 2003,2004). Finally, the public health message encourages increased participation in physical activity, and it is widely accepted that exercise training interventions are the major method for preventing and treating lifestyle diseases. Unfortunately, very low adherence to an active lifestyle after the interventions is a problem worldwide. Therefore, individually measured cognitive-emotional resources and ANS regulation could be used to tailor individual exercise training interventions in order to increase adherence to regular physical activity and to support lifestyle changes.

From the clinical point of view, withdrawn of cardiac vagal modulation of HR, expressed as decreased HRV, indicates an increased risk of cardiovascular morbidity in various patient populations (Adamson et al., 2004; Bauer et al., 2006; Kiviniemi et al., 2007b; Kleiger et al., 1987; Liao et al., 1998) as well as among normal healthy subjects (Dietrich et al., 2006; Liao et al., 1995,1996; Tsuji et al., 1996). Interestingly, Adamson et al., observed that a decreasing trend in day-to-day HRV was associated with subsequent hospitalization or death among cardiac patients (Adamson et al., 2004). Thus, in addition to risk stratification, daily monitoring of ANS status could provide new insights for exercise training and rehabilitation among patients suffering from cardiovascular disease, as well.

In summary, the research review in this paper provides an overview of the evidence of the role of ANS activity related to acute and chronic aerobic exercise, particularly human heterogeneity in response to aerobic training interventions, in terms of $V_{O_{2max}}$ or $V_{O_{2peak}}$. We showed that good aerobic fitness and regular aerobic training are associated with increased cardiac vagal modulation of HR. In addition, we showed that ANS functioning is an important determinant of individual response to aerobic training among healthy subjects. High vagal modulation at the baseline is associated with a superimposed improvement in $V_{O_{2peak}}$ compared with less pronounced vagal modulation. Furthermore, we showed that aerobic fitness can be effectively improved during endurance training by using daily monitoring of ANS status for exercise prescription. Whenever attenuated vagal modulation of HR occurs, a lower-intensity training stimulus is beneficial in achieving a favourable response in aerobic training. The research work we reviewed might suggest that the associations between the ANS and individual responses to aerobic exercise in healthy subjects were independent of age and gender, but indeed further studies are warranted to confirm previous studies among different populations. Similarly, the studies might appear to suggest that these associations are independent of baseline aerobic fitness and the mode of exercise training, including frequency, intensity and length of a single exercise session, but again additional research that specifically addresses age, gender, aerobic fitness and training mode differences is needed to provide more comprehensive assessment of the relationship between the ANS and individual exercise training-induced changes in aerobic fitness. Finally, we suggested that ANS functioning mediated by the central nervous system together with a neuropsychological profile may provide a larger context for increasing adherence to regular physical activity and supporting lifestyle changes at the individual level.

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