A programme based on repeated hypoxia–hyperoxia exposure and light exercise enhances performance in athletes with overtraining syndrome: a pilot study

Davide Susta¹, Elena Dudnik² and Oleg S. Glazachev²

¹School of Health and Human Performance, Athletic Therapy and Training Programme, Dublin City University, Dublin, Ireland and ²Department of Normal Physiology, School of Medicine, I.M. Sechenov First Moscow State Medical University, Moscow, Russia

Summary

Overtraining syndrome (OTS) is a major concern among endurance athletes and is a leading cause in preventing them to perform for long periods. Intermittent exposure to hypoxia has been shown to be an effective way of improving performance without exercising. Aim of this pilot study was to evaluate intermittent hypoxia–hyperoxia training combined with light exercise as an intervention to facilitate athletes with OTS to restore their usual performance level. Thirty-four track and field athletes were recruited: 15 athletes with OTS volunteered to participate and undertook a conditioning programme consisting of repeated exposures to hypoxia (O₂ at 10%) and hyperoxia (O₂ at 30%) (6–8 cycles, total time 45 min–1 h), three times a week, delivered 1.5–2 h after a low-intensity exercise session (2 bouts of 30 min, running at 50% of VO₂max with 10 min rest between bouts) over 4 weeks. Nineteen healthy track and field athletes volunteered to participate as a control group and followed their usual training schedule. Measurements before and after the intervention included exercise capacity, analysis of heart rate variability and hematological parameters. In athletes with OTS, a 4-week light exercise combined with intermittent hypoxia–hyperoxia training improved exercise performance (191 ± 9 W versus 170 ± 44 W in exercise capacity test, \(P = 0.01\)). Heart rate variability analysis revealed an improved sympatho-parasympathetic index (low frequency/high frequency ratio, 8.01 ± 7.51 before and 1.45 ± 1.71 after, \(P = 0.007\)). Hematological parameters were unchanged. Our pilot study showed that intermittent hypoxia–hyperoxia training and low-intensity exercise can facilitate functional recovery among athletes with OTS in a relatively short time.

Introduction

Overtraining syndrome (OTS) and non-functional overreaching (NFOR) are a major concern among athletes, coaches and sport medicine doctors. The OTS is a clinical condition, usually triggered by an excessive training load coupled with inadequate recovery, affecting multiple body systems (autonomic nervous, endocrine, immune) with symptoms such as disturbances in mood state, lack of motivation to practice, lack of mental concentration, irritability, depression and sleep disturbances (insomnia, awakening unrefreshed/tired). According to a recently published European College of Sport Sciences and American College of Sport Medicine joint consensus statement, the OTS is characterized by a multifactorial aetiology resulting in underperformance and 'the key indicator of the OTS can be considered an unexplainable decrease in performance'. The same consensus statement also pointed out that the diagnosis of OTS should be made after excluding clinical conditions usually associated with a decrease in performance and ‘performance test is considered to be essential for the diagnosis of the OTS’ (Meeusen et al., 2013). The concept of decreased performance is central to the diagnosing process, so much so that some authors have suggested the OTS to be renamed ‘unexplained underperformance syndrome’ (Budgett et al., 2000). Prevalences of NFOR and OTS are relevant in runners (Morgan et al., 1987), swimmers (Morgan et al., 1988) and other endurance sports athletes (Lehmann et al., 1993). Recovery from these conditions usually lasts for weeks (NFOR) or months (OTS) as the functioning of various body systems such as the autonomic nervous system (ANS) and the...
Repeated intermittent systemic exposure to hypoxia, a treatment known as intermittent hypoxic training (IHT), has been shown to enhance exercise capacity and performance in endurance athletes (Czuba et al., 2011), by determining hematological and non-hematological adaptations (Hamlin & Hellemons, 2007), and to improve cardiopulmonary efficiency and running economy in athletes (Katayama et al., 2004; Burtscher et al., 2010). Also, exposure to hypoxia alternated with periods of exposure to normoxia (IHT) has been recently introduced and tested in a study aiming at enhancing exercise tolerance and re-balancing the ANS in patients with coronary artery disease (Glazachev et al., 2013). This new approach was designed taking into consideration that breathing a hypoxic gas mixture allows for quicker oxygen saturation after being exposed to hypoxia, potentially reducing the time of the hypoxic–hyperoxic exposure cycle. At the same time, it has been seen in animal model studies that when normoxia is replaced by hyperoxia within a cycle of hypoxia exposure, there is a stronger stimulus to enhance reactive oxygen species signalling and this form of exposure results in a better resistance of membrane structures and improved antioxidant capacity (Sazonova & Arkhipenko, 2009); this aspect could be relevant in OTS athletes in the light of a recently published research showing that in these athletes, oxidative stress and antioxidant capacity responses to exercise are attenuated (Tanskanen, 2010).

Aim of this pilot study is to evaluate the effects on exercise capacity of a new approach consisting of exposing athletes suffering from OTS to light exercise and repeated intermittent to hypoxia–hyperoxia.

Methods

Thirty-four young track and field athletes (14 men and 20 women, aged 18–20, body weight 71.4 ± 6.9 kg, height 176.4 ± 14.6 cm, 7–9 years sports experience) volunteered to participate in this study. The study protocol was approved by the Ethics Committee of I.M. Sechenov First Moscow State Medical University. All participants gave written informed consent to participate in the study. Athletes did not receive any reimbursement for participation and were asked to keep their usual normal diet/nutrition habits. Study protocol and informed consent were in accordance with the World Medical Association Declaration of Helsinki (http://www.wma.net/en/30publications/10policies/b3/17c.pdf). Athletes diagnosed with OTS were allocated to the OTS group (OTS, n = 15, 7 men), while healthy athletes (HA) were recruited as control group (HA, n = 19, 7 males). The diagnosis of OTS was made by physicians according to the checklist suggested by the ECSS/ACSM experts of the joint consensus group, and other clinical conditions were ruled out as explanation for decreased performance.

Participants were recruited over the course of one sport season from a homogeneous group of track and field athletes. Coaches identified athletes potentially eligible, and physicians assessed potential participants’ medical and psychological (negative moods) conditions using the checklist proposed by the ECSS/ACSM consensus experts. Clinicians assessed athletes’ moods by asking specific questions related to athletes’ perceived chronic fatigue, perceived recovery, lack of motivation to practice, difficulties in being focused, irritability, and sleep quality. Clinicians told the potentially overtrained athletes to stop training, to avoid physically demanding activities, and to ‘rest and sleep’ as much as possible. After 4 weeks of rest, athletes failing a PWC170 fitness test were allocated to OTS group. None of the participants took any medications before or during the study. Athletes in the HA kept training as usual following their season schedule.

Participants were assessed as follows. In order to tailor the IHHT on individual responses, each athlete’s individual sensitivity to hypoxia was assessed in a 10-min hypoxic test (HT), consisting of breathing a hypoxic gas mixture with low oxygen content (10% O2) through a facial mask while sitting in an armchair. Pulse rate and arterial oxygen saturation (SaO2) were monitored by pulse oximeter, and data collected were used to define the hypoxia–hyperoxia exposure protocol. Gas mixtures (10–30% O2) were generated, monitored and delivered to the participants using a prototype version of the Reoxy unit (AI Mediq S.A., Luxembourg City, Luxembourg). A second HT was repeated 3–4 days after completing IHHT to assess hypoxic tolerance dynamics.

IHHT included 5- to 7-min exposure to a hypoxic gas mixture (11% O2) followed by 2- to 3-min exposure to a hyperoxic (30% O2) gas mixture without removing the mask. Each session (40–50 min) included 6–8 hypoxia–hyperoxia cycles and was delivered three times a week. IHHT was performed 1·5–2 h after low-intensity training (2 bouts of 30 min running at 50% VO2max, with 10 min rest between bouts).

Exercise performance was tested in sessions taking place in the morning (not earlier than 2 h after breakfast), and physical working capacity was determined using a two-step progressive exercise test on a cycle ergometer (Monark 828E Test Ergometer, Vansbro, Sweden), according to PWC170 protocol (Boreham et al., 1990). Haemodynamic status, including blood pressure (BP) and heart rate (HR), was monitored non-invasively using oscillometric cuffs (Dixtal, DX 2710, Sao Paulo, Brazil) and a heart rate monitor (Polar 810s; Polar Electro, Kempele, Finland). PWC170 and parameters of cardiopulmonary efficiency (IRI, inotropic reserve index; CRI, chronotropic reserve index) were calculated.

The assessments also included an evaluation of the ANS status performed by analysing heart rate variability (HRV) accord-
A new approach to overtraining syndrome, D. Susta et al.

Exercise capacity of the OTS athletes was significantly improved after the intervention (IHHT and sport-specific training at low intensity). PWC170 in OTS group was improved by 20 W after 4 weeks of treatment. It is worth noting here that after treatment, OTS athletes showed a performance level (PWC170 = 191.9 ± 26.9 W) that was not different compared to HA at baseline (204.2 ± 13.8 W), but still lower than in HA group after training (278.0 ± 19.3 W, \( P = 0.023 \)). Chronotropic reserve index and IRI were significantly improved after treatment, suggesting a more efficient systemic cardiovascular performance. At the end of the 4-week treatment, IRI and CRI in OTS group were not significantly different to those recorded in HA group at baseline (Table 1).

Interestingly, haematological parameters were unchanged after the intervention: haemoglobin was 138.3 ± 2.6 g l\(^{-1}\) before and 140.7 ± 2.7 g l\(^{-1}\) after (not Significant, NS); haematocrit 40.5 ± 0.7% before and 41.6 ± 0.7% after (NS); erythrocytes 4.82 ± 0.09 \( (10^{12} \text{ l}^{-1}) \) before and 4.84 ± 0.09 \( (10^{12} \text{ l}^{-1}) \) after (NS); and reticulocyte count 0.905 ± 0.115% before and 0.979 ± 0.109% after (NS).

Enhanced exercise capacity in OTS athletes after IHHT combined with low-intensity sport-specific training was associated with significant increase of hypoxic tolerance in HT. Blood oxygen desaturation and HR during HT improved significantly after the programme. These values were similar to those recorded in HA at baseline (Table 2).

In cardiac autonomic control parameters, LF and HF power significantly decreased and increased, respectively, compared to pre-programme values. LF/HF ratio decreased, suggesting a relatively stronger parasympathetic drive and reduced sympathetic tone after the programme in OTS athletes. Table 3 shows HRV analysis parameters.

**Discussion**

Our preliminary data show for the first time that treating athletes with OTS by exposing them to repeated cycles of hypoxia–hyperoxia and light sport-specific exercise is efficacious to improve their level of performance over a relatively short period of time and to counteract some of the OTS features. After completing the programme, all OTS athletes showed significantly improved tolerance to exercise without significant hematomal changes; our findings are consistent with the results of other studies using hypoxia–normoxia exposure as an intervention to improve aerobic capacity in patients.

| Table 1  | Performance parameters. |
|----------|-------------------------|
| OTS      | HA baseline             | HA post-training     |
| PWC170(W)| 170.8 ± 44.8            | 204.2 ± 13.8*        |
| IRI (%)  | 65.8 ± 3.6              | 50.8 ± 4.1*          |
| CRI (%)  | 50.0 ± 5.3              | 37.5 ± 4.9*          |

OTS, overtraining athletes; HA, healthy athletes.

Performance parameters at baseline and after a 4-week treatment in athletes with overtraining syndrome (OTS, \( n = 15 \)) and in healthy athletes (HA, \( n = 19 \)). Values are mean ± standard deviation. P-values refer to pre- versus postintervention in OTS group. IRI was calculated as \( \text{SBP}_{\text{max}} - \text{SBP}_{\text{rest}} / \text{SBP}_{\text{rest}} \). CRI was calculated as \( \text{HR}_{\text{max}} - \text{HR}_{\text{rest}} / \text{HR}_{\text{rest}} \).

*Significantly \( (P<0.05) \) different from OTS pre values.

**Significantly \( (P<0.05) \) different from OTS post values.
(Burtscher et al., 2007) and endurance athletes (Katayama et al., 2004; Hamlin & Hellemans, 2007; Burtscher et al., 2010). As well, cardiovascular response to a 10-min continuous HT was also improved and similar to the one recorded in HA. Reduced HR and systolic BP values suggest an increase in the overall cardiovascular efficiency after this novel treatment. One may have reservations about including exercise to the treatment plan was mainly based on the fact that, in our experience, athletes told to stop for a long time (e.g. 4 weeks at least) usually perceive this medical advice as a further proof of their condition severity, so potentially affecting their psychological status. Thus, after 4 weeks of total rest, adding light exercise sessions was a strategy to minimize the psychological impact of the diagnosis (OTS) on athletes mood and to keep them committed and focused. In addition, while there is evidence that intermittent hypoxia exposure improves performance in HA, cardiac patients and pulmonary patients, to the best of our knowledge, there is no evidence that low-intensity training can be useful to improve performance in athletes diagnosed with OTS. Instead, the rest is the best available treatment option for people suffering from OTS and reduced training loads might be an option only in overreaching athletes, according to the ECSS/ACSM joint consensus. As athletes with OTS have shown a reduced cardiac autonomic modulation (Hynynen et al., 2008) and rebalancing cardiovascular autonomic control by reducing its sympathetic overdriving component which has been proven to be associated with intermittent hypoxic exposure (Haider et al., 2009), we would like to suggest a recovered ANS balance as a partial explanation of our findings. Another potential contribution to explain our promising results could be linked to the role of oxidative stress/antioxidant capacity. Muscular exercise is known to increase oxidative stress, free radical production and, as part of the physiological process of adaptations to adequate training loads, athletes’ body antioxidant capacity (Finaud et al., 2006). Only recently, an altered response to oxidative stress was found to be associated with training overload, and athletes’ impaired antioxidant capacity has been suggested to play a role in the pathophysiology of NFOR/OTS (Margonis et al., 2007; Tanskanen et al., 2010). The mechanisms behind “the unexplainable decreased performance” has not been identified yet, but several studies on animal models provide a rationale

Table 2  Physiological responses to hypoxic test.

|                | OTS (n = 15) | HA (n = 19) |
|----------------|-------------|-------------|
|                | Pre         | Post        | P-value    | Baseline | Post-training |
| SaO₂ min,%     | 77.9 ± 6.8  | 84.2 ± 5.7  | 0.001      | 83.7 ± 9.0* | 85.7 ± 12.6  |
| HRmax,bpm      | 82.2 ± 14.6 | 76.6 ± 11.0 | 0.010      | 79.7 ± 13.1| 76.7 ± 9.4   |
| ΔSaO₂, %       | −19.3 ± 7.9 | −12.2 ± 5.7 | 0.002      | −14.7 ± 13.0| −12.7 ± 9.0  |
| ΔHR, bpm       | 14.6 ± 10.2 | 9.1 ± 8.2   | 0.016      | 9.7 ± 7.5*  | 10.0 ± 2.4   |

OTS, overtraining athletes; HA, healthy athletes.

Physiological responses to hypoxic test (FiO₂ = 10%, 10 min of continuous exposure) in 15 overtrained athletes (OTS) and 19 healthy athletes (HA). Values are mean ± standard deviation. SaO₂ min (minimum oxygen saturation of blood during hypoxic test exposure) and HRmax (maximum HR during HT), respectively; ΔSaO₂ and ΔHR – mean values of arterial oxygen desaturation and increment of HR in HT compared to normobaric normoxic condition. In brackets, P-values related to pre- versus postintervention results in OTS group.

*Significantly (P ≤ 0.05) different from OTS pre values.

Table 3  Heart rate variability analysis.

|                | OTS pre | OTS post | P-value | HA pre | HA post |
|----------------|---------|----------|---------|--------|---------|
| RR, ms         | 880 ± 160| 890 ± 120| NS      | 955 ± 160| 990 ± 180** |
| SD, ms         | 54.0 ± 24.7| 76.0 ± 26.8| 0.03   | 82.0 ± 24.8* | 79.0 ± 31.0 |
| HRat rest, bpm | 68.2 ± 19.6| 67.12 ± 13.7| NS     | 62.4 ± 3.8 | 60.4 ± 4.6** |
| TP, ms²        | 3118 ± 1687| 3890 ± 1246| NS     | 4503 ± 512* | 4654 ± 521 |
| VLF, ms²       | 1410 ± 754| 1298 ± 503| NS      | 1610 ± 315 | 1740 ± 404 |
| LF, ms²        | 1300 ± 661| 801 ± 673  | 0.005   | 860 ± 340 | 828 ± 420 |
| HF, ms²        | 277 ± 188| 624 ± 468  | 0.005   | 1100 ± 344*** | 1167 ± 501** |
| LF/HF          | 8.01 ± 7.51| 1.45 ± 1.71| 0.007  | 2.2 ± 1.0*  | 1.81 ± 0.95 |

OTS, overtraining athletes; HA, healthy athletes; bpm, beats per minute; RR, R-R intervals variability; SD, standard deviation of R-R intervals; HR, heart rate; TP, total power; VLF, very low frequency; LF, low frequency; HF, high frequency; LF/HF, index. P-values refer to comparing pre versus post intervention values in OTS group.

*Significantly (P ≤ 0.05) different from OTS pre values.

**Significantly (P ≤ 0.05) different from OTS post values.
to support hypoxia–hyperoxia exposure as a potential way of conditioning athletes body to better cope with oxidative stress. These studies have demonstrated that exposure to hypoxia triggers adaptations enhancing total antioxidant capacity (Sazonova et al., 1987, 1994; Sazonova & Arkhipenko, 2009). Moreover, by replacing normoxic with hyperoxic gas mixtures (IHHT), it is possible to generate a stronger stimulus shown to evoke more pronounced adaptive responses than IHT (Arkhipenko et al., 1997). Cellular and tissue adaptations triggered by systemically exposing athletes to hypoxia–hyperoxia short cycles are likely to have contributed to our results. Unfortunately, our interpretations remain speculative as we could not measure the antioxidant response to exercise before and after treatment. Also, our pilot study has few other limitations: firstly, we could not randomize the participants for methodological (data on the effect of intermittent hypoxia–hyperoxia training on healthy athletes’ performance are not yet available, so it was impossible for us to calculate the sample size to support a methodologically sound and clinically meaningful RCT) and logistical reasons (both the actual treatment and a ‘sham IHHT’ were considered by coaches too time consuming and disruptive to be embedded into the very strict training schedule of HA); secondly, we could not support our findings with measures of blood biochemistry parameters and with objective measures of OTS athletes’ psychological readiness to ‘return to play’, these limitations being relevant due to the multifactorial nature of the syndrome; thirdly, we did not follow up the OTS group athletes to ascertain whether their maximal exercise capacity at the end of the season was similar to the one measured in HA; and lastly, OTS and HA groups were not gender balanced, these limitations potentially affecting data on performance.

As a positive note, it has to be pointed out that OTS athletes’ adherence to the protocol was excellent (all those recruited completed the programme) despite each scheduled session lasting between 2 and 2.5 h.

In conclusion, our study suggest that a newly developed 4-week programme including repeated hypoxic–hyperoxic exposures combined with low-intensity sport-specific exercise improves physical working capacity, ANS balance and tolerance to hypoxia in athletes with OTS, so making this new approach a viable and useful additional tool to treat a clinical condition usually perceived by athletes as a threat to their careers. Considering the usually busy schedule of top athletes, this new method is very attractive as it helps to recover in 4 weeks of time and for this reason, future research should evaluate its effectiveness in well-conducted randomized control trials. Also, future research should focus on further investigating the mechanisms behind such a promising adaptive response as well as clarifying the role of oxidative stress/antioxidant capacity in the pathophysiology of OTS and the potential role of repeated hypoxia–hyperoxia exposure in protecting athletes from developing this bewildering syndrome.

Acknowledgments

The authors acknowledge the athletes who participated in this clinical trial. Also, we thank AiMediq S.A. Company, Luxembourg, for supplying at cost an advanced prototype of a ReOxy equipment and software for intermittent hypoxic–hyperoxic training.

Conflict of interest

Dr. Davide Susta and Dr. Elena Dudnik have no financial or other interest in the product or distributor of the product. Prof. Oleg Glazachev has a consulting agreement (software design and development) with the supplier of the equipment, and he has no financial interest linked to sales or company performance. The company supplied at cost the advanced prototype used in our study.

References

Arkhipenko Yu V, Sazonova TG, Tkatchouk EN, et al. Adaptation to continuous and intermittent hypoxia: role of the active oxygen-dependent system. In: Adaptation Biology and Medicine (ed. Sharma, BK) (1997), Vol. 1 Subcellular Basis, pp. 251–259. Narosa Publishing House, New Delhi.

Boreham CA, Paliczka VJ, Nichols AK. A comparison of the PWC170 and 20-MST tests of aerobic fitness in adolescent schoolchildren. J Sports Med Phys Fitness (1990), 30: 19–23.

Budgett R, Newsholme E, Lehmann M, et al. Redefining the overtraining syndrome as the unexplained underperformance syndrome. Br J Sports Med (2000), 34: 67–68.

Burtscher M, Gatterer H, Szubski C, et al. Effects of interval hypoxia on exercise tolerance: special focus on patients with CAD or COPD. Sleep Breath (2007); 11: 209–220.

Burtscher M, Gatterer H, Faulhaber M, et al. Effects of intermittent hypoxia on running economy. Int J Sports Med (2010); 31: 644–650.

Czuba M, Waskiewicz Z, Zajac A, et al. The effects of intermittent hypoxic training on aerobic capacity and endurance performance in cyclists. J Sports Sci Med (2011); 10: 175–183.

De Vito G, Gallaway S, Nimmo M, et al. Effects of central sympathetic inhibition on heart rate variability during steady-state exercise in healthy humans. Clin Physiol Funct Imaging (2002); 22: 32–38.

Finnaud J, Lac G, Filiaire E. Oxidative stress: relationship with exercise and training. Sports Med (2006); 36: 327–358.

Glazachev OS, Pozdnyakov Y, Urinskiy A, et al. Interval normobaric hypoxic-hyperoxic training increases exercise tolerance in patients with coronary artery disease. Eur J Prev Cardiol (2013); 20(Supplement 1): S 109.

Haider T, Casucci G, Linser T, et al. Interval hypoxic training improves autonomic cardiovascular and respiratory control in patients with mild chronic obstructive pulmonary disease. J Hypertens (2009); 27: 1648–1654.

Hamlin M, Hellemans J. Effect of intermittent normobaric hypoxic exposure at rest on haematological, physiological, and performance parameters in multi-sport athletes. J Sports Sci (2007); 25: 431–441.
Hynynen E, Uusitalo A, Konttinen N, et al. Cardiac autonomic responses to standing up and cognitive task in overtrained athletes. *Int J Sports Med* (2008); **29**: 552–558.

Katayama K, Sato K, Matsuo H, et al. Effect of intermittent hypoxia on oxygen uptake during submaximal exercise in endurance athletes. *Eur J Appl Physiol* (2004); **92**: 75–83.

Lehmann M, Foster C, Keul J. Overtraining in endurance athletes: a brief review. *Med Sci Sports Exerc* (1993); **25**: 854–862.

Margonis K, Fatouros IG, Jamurtas AZ, et al. Oxidative stress biomarkers responses to physical overtraining: Implications for diagnosis. *Free Radic Biol Med* (2007); **43**: 901–910.

Meeusen R, Duclos M, Foster C, et al. Prevention, diagnosis and treatment of the overtraining syndrome: joint consensus statement of the European College of Sport Science (ECSS) and the American College of Sports Medicine (ACSM). *Eur J Sports Sci* (2013); **13**: 1–24.

Mikhailov VM. *Heart Rate Variability* (2000). 1–182. Moscow, Ivanovo, (in Russian)

Morgan W, O’Connor P, Sparling P, et al. Psychological characterization of the elite female distance runner. *Int J Sports Med* (1987); **8**: 124–131.

Morgan W, Costill D, Flynn M, et al. Mood disturbance following increased training in swimmers. *Med Sci Sports Exerc* (1988); **20**: 408–414.

Sazontova TG, Arkhipenko YUV. Intermittent hypoxia in resistance of cardiac membrane structures: role of reactive oxygen species and redox signalling. In: *Intermittent Hypoxia: From Molecular Mechanisms to Clinical Applications* (eds Xi, L, Serebrovskaya, TV) (2009), pp. 147–187. Nova Science Publishers Inc., New York, USA.

Sazontova TG, Arkhipenko YUV, Meerson FZ. Increased activity of antioxidant enzymes in rat heart during adaptation to short-term stress. (in Russian). *Bull Eksp Biol Med* (1987); **103**: 411–413.

Sazontova TG, Tkatchouk EN, Kolmykova SN, et al. Comparative analysis of peroxidation and antioxidant enzyme activities in rats adapted to different regimes of normobaric hypoxia. *Hypoxia Med J* (1994); **2**: 4–7.

Tanskanen M, Atalay M, Uusitalo A. Altered oxidative stress in overtrained athletes. *J Sports Sci* (2010); **28**: 309–317.

Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability, standards of measurement, physiological interpretation, and clinical use. *Eur Heart J* (1996); **17**: 354–381.

Urhausen A, Gabriel H, Kindermann W. Impaired pituitary hormonal response to exhaustive exercise in overtrained endurance athletes. *Med Sci Sports Exerc* (1998); **30**: 407–414.